1 Use of Green Spaces and Blood Glucose in Children; a Population- 2 based CASPIAN-V Study

3
4 Payam Dadvand^{1,2,3}, Parinaz Poursafa⁴, Ramin Heshmat⁵, Mohammad Esmaeil
5 Motlagh⁶, Mostafa Qorbani⁷, Xavier Basagaña^{1,2,3}, Roya Kelishadi⁸

6
7 ¹ ISGlobal, Barcelona, Spain

8 ² Universitat Pompeu Fabra (UPF), Barcelona, Spain.

9 ³ CIBER Epidemiología y Salud Pública (CIBERESP), Spain

10 ⁴ Environment Research Center, Research Institute for Primordial Prevention of Non-
11 communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran.

12 ⁵ Chronic Diseases Research Center, Endocrinology and Metabolism Population Sciences
13 Institute, Tehran University of Medical Sciences, Tehran, Iran.

14 ⁶ Department of Pediatrics, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

15 ⁷ Non-communicable Diseases Research Center, Alborz University of Medical Sciences, Karaj,
16 Iran.

17 ⁸ Child Growth and Development Research Center, Research Institute for Primordial Prevention
18 of Non-communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran.

19 20 Corresponding Authors:

21 Payam Dadvand, ISGlobal, Doctor Aiguader 88, 08003 Barcelona, Catalonia, Spain; email:
22 payam.dadvand@isglobal.org; Tel. [+34 93 214 73 29](tel:+34932147329); Fax. [+34 93 316 05 75](tel:+34933160575)

23
24 Roya Kelishadi, Child Growth and Development Research Center, Research Institute for
25 Primordial Prevention of Non-communicable Disease, Isfahan University of Medical Sciences,
26 Hezarjerib Ave, Isfahan, Iran. Tel: +98 311 7923060; Fax: +98 311 6687898

27 Email: kroya@aap.net Tel: +98 311 7923060; Fax: +98 311 6687898

ABSTRACT

A limited but emerging body of evidence is suggestive for a beneficial association between contact with green spaces and glucose homeostasis in adults; however, such an evidence for children is non-existent. We evaluated the association between time spent in green spaces and fasting blood glucose (FBG) levels and impaired fasting glucose (IFG, $\text{FBG} \geq 110 \text{ mg/dL}$) in a population-based multicentric sample of 3,844 Iranian schoolchildren aged 7-18 years (2015). Participants were instructed to report the average hours per week spent in green spaces separately during each season and in each type of green space (parks, woods/other natural green spaces, and private gardens/agricultural field) for a 12-month period preceding the interview. We developed linear and logistic mixed effects models with centre as random effect to evaluate the association of time spent in green spaces (separately for each type as well as all types together) with FBG and IFG, respectively, controlled for a wide range of covariates including household indicators of socioeconomic status. We observed inverse associations between time spent in green spaces, especially in natural green spaces, and FBG levels. Specifically, 1.83 hours increase in the total time spent in green spaces was associated with -0.5 mg/dl (95% confidence intervals: $-0.9, -0.1$) change in FBG levels. We also observed reduced risk of IFG associated with time spent in green spaces; however, the association was statistically significant only for the time spent in natural green spaces. There were suggestions for stronger associations for those residing in urban areas and those from lower socioeconomic status groups; however, the interaction terms for socioeconomic status and urbanity were not statistically significant. Further longitudinal studies are required to replicate our findings in other settings with different climates and population susceptibilities.

54 **Keywords**

55 Natural environment, ecosystem services, diabetes, metabolic syndrome, built
56 environment, park, middle east

57 **Capsule:** Time spent in green spaces, especially in natural green spaces, was associated
58 with lower fasting blood glucose levels and the risk of impaired fasting glucose in
59 adolescents.

1. Introduction

During the past few decades, there has been a notable increase in the global prevalence of non-communicable diseases (NCDs), representing an alarming epidemic worldwide (Abajobir et al., 2017a; Abajobir et al., 2017b). As a result, NCDs such as cardiovascular conditions and diabetes have become the leading cause of morbidity and mortality globally (Abajobir et al., 2017a; Abajobir et al., 2017b). The origins of cardiovascular conditions and diabetes could be traced back in childhood (Camhi and Katzmarzyk, 2010; Kelishadi and Poursafa, 2014). Accordingly, childhood could be considered as a window of opportunity for environmental and behavioural interventions aimed at preventing these diseases occurring later in life through tackling their risk factors. In this context, metabolic impairments including hyperglycemia are among the leading risk factors for these diseases that could be tackled during this period.

The increase in the global prevalence of NCDs has coincided with the rapid and ongoing increase in the population residing in urban areas where residents often have limited access to natural environment (UN Department of Economic and Social Affairs, 2015). Contact with natural environments including green space has been associated with improved physical and mental health and wellbeing (Nieuwenhuijsen et al., 2017). A limited but growing body of evidence has suggested a protective association between exposure to green space and type 2 diabetes mellitus in adults (Astell-Burt et al., 2014a; Bodicoat et al., 2014; Dalton et al., 2016; Maas et al., 2009). Increase in physical activity (Huus et al., 2016; Marson et al., 2016), reduction of psychological stress (Faresjo, 2015), enrichment of immunoregulation-inducing microbial input from the environment (Paun et al., 2017), and mitigation of exposure to air pollution (Butalia et

al., 2016; Rao et al., 2015) and noise (Dzhambov, 2015) could possibly underlie such a protective association. Although through these pathways, contact with green spaces could potentially exert a beneficial impact on glucose homeostasis and reduce risk of hyperglycemia in children, the available evidence on such influences in children is very scarce. Moreover, the vast majority of studies evaluating health effects of green spaces, so far, have been conducted in high-income countries. As ethnicity and lifestyle habits might influence such effects, the generalizability of studies in these countries to the rest of the world could be limited.

To date, studies of the health effects of green spaces have mainly used proximity to green spaces as a proxy for access to these spaces, and hence the use of these spaces by the study participants. However, in real life, proximity to green spaces would not necessarily translate into use of these spaces. Such a disagreement between residential proximity to green spaces and use of these spaces can have important implications for studying the association between green spaces and health, particularly for those associations for which physical activity is a key mediator. Therefore, studies of health effects of green spaces could benefit from information on the use of green spaces by study participants.

The aim of this study was to evaluate the association between use of green spaces and fasting blood glucose (FBG) levels and impaired fasting glucose (IFG) in Iranian children. Towards this aim, it also disentangled the associations for different types of green spaces and evaluated the variation of these associations by socioeconomic status (SES), level of urbanity, and sex.

2. Methods

2.1. Study setting and population

The study was conducted in the context of the fifth survey of the Childhood and Adolescence Surveillance and Prevention of Adult Noncommunicable disease study (CASPIAN-V). CASPIAN surveys started in 2003 and have been repeated periodically. The CASPIAN-V survey was conducted in 2015 in urban and rural areas of 30 provinces (out of 31 provinces) of Iran. It applied a multistage stratified cluster sampling method to recruit a population-based sample of 14,400 schoolchildren aged 7-18 years across the country. Detailed description of CASPIAN-V sampling and data collection methods have been published elsewhere (Motlagh et al., 2017). Briefly, from each province, 480 students were recruited. A cluster sampling method was used to enrol a population-based sample of schoolchildren. In each province, sampling was conducted through 48 clusters each encompassing 10 schoolchildren. All schoolchildren in each cluster were selected from the same school. For each province we compiled eight lists of schools based on the combinations of sex (Iran has single-sex education, so there are separate schools for girls and boys), place of residence (urban/rural) and education level (primary school/secondary school): (1) urban and primary school, (2) urban and secondary school, (3) rural and primary school, and (4) rural and secondary school, separately for girls and boys. Iranian Ministry of Education provided us with the number of students and the name of schools in each combination, based of which, we proportionally chose the number of participants (and hence clusters) for each combination. Given the fact that we had equal proportion of boys and girls in all provinces, we assigned half of the clusters to girls and the other half to girls in each

province. Then we assigned clusters to the aforementioned combinations proportionally to the number of students studying in primary and secondary schools of the urban and rural areas of that province. Consequently, in each province the ratio of participants in urban and rural areas and in each grade was proportional to the number of schoolchildren studying in urban and rural areas and in each grade of that province.

In each province, 14 clusters out of 48 clusters were randomly selected for blood sampling resulting in a total of 4200 students (Figure 1). The current study was based on this subset of CASPIAN-V participants with available blood sample.

Study protocols were reviewed and approved by the Research and Ethics Council of Isfahan University of Medical Sciences (Project Number: 194049). After complete explanation of the study objectives and protocols, written informed consent was obtained from the parents or legal guardians of schoolchildren and verbal consent was obtained from the schoolchildren.

2.2. Questionnaire data

Two sets of questionnaires were developed for schoolchildren and their parents. Data on use of green spaces were obtained through the schoolchildren's questionnaire, while data on covariates were obtained from parents. Face-to-face interviews by trained interviewers were conducted to obtain these data. The description of questionnaires applied in CASPIAN-V and conditions under which the interviews were conducted have been detailed elsewhere (Motlagh et al., 2017).

2.2.1. Green space use

Schoolchildren were instructed to report the average hours per week spent in green spaces during working and non-working days separately during each season (spring, summer, autumn, and winter) and in each type of green space (parks, woods/other natural green spaces, and private gardens/agricultural field) for a 12-month period preceding the interview (see Green Spaces Questionnaire in Supplementary Materials, page 2). For each green space type, the weekly average of time spent in that space was calculated by first adding up the reported hours for working and non-working days for each season and then averaging the resulting seasonal values. Those categories for which no time was reported were assumed to be zero (Amoly et al., 2014). The total weekly hours spent in green spaces was estimated by averaging the values for all the three green space time.

2.2.2. Covariate data

Data on socio-demographic characteristics (e.g. maternal and paternal educational attainment, employment, marital status, home ownership, and school type), family medical history (e.g. history of diabetes mellitus in schoolchild's mother, father, aunts, uncles, or grandparents), schoolchild history of low birth weight and dietary pattern (please see 2.2.3) were obtained from parents through questionnaires. Weight and height of the parents were measured following the protocols described elsewhere (Angoorani et al., 2017). Accordingly for each parent body mass index was calculated as weight/height^2 and obesity was defined as $\text{BMI} \geq 30$.

2.2.3. Diet

Parents were asked to report the consumption frequency of cookies/sweets/cakes, cheese puffs/junk snacks, carbonated beverages, fresh/dry fruits, fresh/package juice, fresh/cooked vegetables, milk, yogurt, cheese, fast foods (e.g. sausages, hamburgers, etc.), tea, sugar with tea, and coffee. The frequency of consumption could be reported as daily, weekly, rarely, and never. Further details on methodology and validation of this questionnaire has been published elsewhere (Kelishadi et al., 2012). Given the large number of dietary variables for each participant (14 items), we applied factor analysis with polychoric correlation matrix to identify dietary patterns and reduce the dimension of dietary data. We applied those factors with Eigenvalue of more than one (Kaiser, 1960) to control our analyses (please see 2.4-2.6) for dietary pattern. This strategy resulted in selection of three factors that altogether could explain 93% of variation in our 14 dietary items.

2.3. Blood sample

Parents of eligible schoolchildren were instructed to take them to the assigned laboratory in each province for blood sampling. There, 6 mL venous blood sample was collected after 12 hours of overnight fasting. All collection tubes were centrifuged at 2500–3000×g for 10 min. Immediately after centrifugation, serum samples were aliquoted into 200 µL tubes and stored at –70°C. All samples were then transferred by cold chain to Isfahan Mahdiah Laboratory, Isfahan, Iran. FBG was measured enzymatically by a Hitachi 917 automated biochemistry analyser (Roche Diagnostics, Indianapolis, IN).

2.4. Main analyses

208

209 2.4.1. Fasting blood glucose

210 Because of the multilevel nature of the data, we used linear mixed effects models with
211 FBG as the outcome variable, time spent in green spaces as fixed effect predictor, and
212 recruitment centre as the random effect. The analyses were adjusted for a number of
213 covariates identified *a priori*: child's age, sex, low birth weight, diet (three factors as
214 described in 2.2.4), parental history of diabetes mellitus (at least one parent was
215 diagnosed by diabetes mellitus: yes/no), family history of diabetes mellitus (at least one
216 uncle or aunt was diagnosed by diabetes mellitus: yes/no), parental obesity (at least one
217 parent being obese: yes/no), urbanity (urban/rural), and indicators of SES including
218 parental educational attainment (highest degree attained by either parents: no or primary
219 school/secondary school/university), home ownership (owning the home: yes/no), and
220 marital status (single parent: yes/no).

221

222 2.4.2. Impaired Fasting Glucose

223 We defined IFG as $\text{FBG} \geq 110 \text{ mg/dl}$ based on the World Health Organization (WHO)
224 recommendation (WHO, 2006). We developed logistic mixed effects models using IFG
225 (yes/no) as outcome together with identical set of random effect and fixed effect
226 exposure and covariates to the aforementioned analyses for FBG.

227

228 2.5. Sensitivity analyses

229

230 The main analyses were conducted using recruitment centre as the random effect. To
231 evaluate the potential influence of sampling clusters on our analyses, we added cluster
232 as another random effect to the models (i.e. two random effects: recruitment centre and

cluster). We also further adjusted our analyses for parental employment (highest level of employment by either parents: unemployed/employee/self-employed), school type (private/public), breastfeeding (at least six of exclusive breastfeeding: yes/no), history of diabetes in grandparents, and exposure to environmental tobacco smoke (yes/no).

2.6. Further analyses

2.6.1. Green space type-specific analyses

We repeated the main analyses, using time spent at (i) parks, (ii) woods/other natural green spaces, and (iii) private gardens/agricultural field as the exposure (one at a time) to disentangle the association of different types of green spaces with FBG.

2.6.2. Variation of associations by urbanity, socioeconomic status, and sex

To explore potential variations in the association between use of green spaces and FBG across strata of urbanity, SES, and sex, we stratified the aforementioned main analyses by urbanity (urban and rural), parental education (primary, secondary, and university), and sex (girls and boys). Among indicators of SES included in our analyses, we chose parental education because it could be considered as a better indicator of the SES in the Iranian society and also this choice was consistent with our previous studies of the health effects of green spaces in children (Dadvand et al., 2015a; Dadvand et al., 2014a). We also checked the statistical significance of the multiplicative interaction term of time spent in green spaces and urbanity, SES, and sex by comparing models with and without interaction term using likelihood ratio test.

3. Results

3.1. Sample characteristics

Of 4,200 children selected for the blood sampling, 3,844 (91.5%) participated and provided blood samples (Figure 1). The sociodemographic characteristics of these participants are presented in Table 1. The medians (IQR) of the total time spent in green spaces and FBG were 1.25 (1.83) hours per week and 92 (13) mg/dl, respectively.

3.2. Association with FBG

As presented in Table 2, longer time spent in green spaces (in total) was associated with lower FBG level. Adding cluster as another random effect to the models or further adjustment of our analyses for parental employment status, school type, breastfeeding, history of diabetes in grandparents, and exposure to environmental tobacco smoke did not change our findings notably (Data not shown). With regards to different types of green spaces, time spent in all green space types were inversely associated with FBG level, however, the associations were statistically significant only for natural green spaces and marginally significant for private gardens/agricultural field (p-value=0.05) (Table 2).

After stratifying the analysis of the association between time spent in green spaces (in total) and FBG based on urbanity, while we observed a statistically significant inverse association for those residing in urban areas, the association for those living in rural areas was relatively weaker and not statistically significant (Table 3). We also observed suggestions for a trend across strata of parental education with stronger associations for

those who had parents with lower educational attainments and a statistically significant association for only those with parents with no or primary school education (Table 3). Our stratified analyses based on sex did not show a notable difference between girls and boys (Table 3). The interaction terms for urbanity, parental education, and sex were not statistically significant (Table 3).

3.3. Association with impaired fasting glucose

Of 3,844 participants with available data on FBG, 161 (4.2%) had IFG. An IQR increase in the total time spent in green spaces was associated with reduced risk of IFG; however, the association was nearly statistically significant (p-value=0.08) (Table 2). This finding was robust to the aforementioned sensitivity analyses for the FBG. In terms of the green space types, we observed statistically significant reduction in the risk of IFG association with the time spent in natural green spaces (Table 2). We also observed inverse associations between time spent in private gardens/agricultural field and parks and the risk of IFG, but none attained statistical significance (Table 2). While for those living in urban areas, there was a statistically significant reduction in the risk of IFG, the association for those living in rural areas was null (Table 3). Across strata of parental education, there were indications for stronger associations for the participants whose parents had lower educational attainments with statistically significant associations only for those whose parents had no or primary school education (Table 3). After stratifying the analyses based on sex, we observed some suggestions for a stronger association for girls compared to boys (Table 3). However, none of the interaction terms for urbanity, parental education, and sex were statistically significant (Table 3).

4. Discussion

To our knowledge, this study, based on a representative sample of Iranian schoolchildren, is the first to evaluate the association between contact with green spaces and glucose homeostasis in children and also the first to investigate the association between this contact and FBG levels in general. Moreover, it adds to the very limited available evidence on the health effects of green spaces in low and middle-income countries and also on disentangling the health effects of different types of green spaces. We observed inverse associations between time spent in green spaces, especially in natural green spaces, and FBG levels and the risk of IFG. There were suggestions for stronger associations for those residing in urban areas and those from lower SES groups; however, the interaction terms for these factors were not statistically significant.

4.1. Interpretation of results in the context of available evidence

We are not aware of any previous epidemiological studies on our investigated association of contact with green spaces with IFG in children nor with FBG in general; therefore, it is not possible to compare our findings with those of others. However, our findings are consistent with a number of previous observations. A recent study of 837 German adolescents reported lower insulin resistance (HOMA-IR) associated with more residential surrounding greenness, characterized as NDVI average across a 1000m buffer around the residential address (Thiering et al., 2016). A large cross-sectional study of more than 300 thousand participants including around 71 thousand children aged less than 18 in the Netherlands showed lower risk of medically diagnosed diabetes

mellitus associated with higher neighbourhood greenness; however, the study did not report estimates separately for children (Maas et al., 2009). Similarly, a cross-sectional study in Australia including 276,072 middle-aged and elderly participants also reported lower risk of medically diagnosed type 2 diabetes associated with higher greenness in the neighbourhood (Astell-Burt et al., 2014a). Another large cross-sectional study of more than ten thousands adults in UK reported that higher neighbourhood greenness was associated with lower risk of screen-detected type 2 diabetes mellitus (Bodicoat et al., 2014). The only available longitudinal study of the association between residential surrounding greenspace and incidence of diabetes mellitus showed a protective association in a sample of about 24 thousand adults in UK (Dalton et al., 2016). However, it should be noted that in adults, type 2 diabetes is more prevalent while in children type 1 diabetes is more prevalent and these two types of diabetes seem to have different pathogenesis (Kliegman et al., 2016).

The available evidence comparing the health benefits of different types of green spaces, especially in children, is still very limited. Among different types of greenspace evaluated in our study, we observed the most consistent evidence for the natural green spaces (e.g. woods) and to a lesser extent for private gardens/agricultural fields. Our findings for urban parks were not conclusive. These observations were in line with the findings of our previous study including more than three thousands Spanish schoolchildren showing that while residential proximity to natural green spaces was associated with lower risk of sedentary lifestyle and obesity, residential proximity to urban parks was not associated with these outcomes (Dadvand et al., 2014a). Similarly, a recent study of 2,909 Scottish children reported that while access to private garden was associated with better behavioural development, area of parks surrounding the

participant's residential address did not show such an association (Richardson et al., 2017).

We found indications for stronger associations for participants from lower SES groups. This observation is consistent with a number of previous studies suggesting that individuals from lower SES are more likely to benefit from green spaces (Dadvand et al., 2012a; Dadvand et al., 2012b; Dadvand et al., 2014b; De Vries et al., 2003; Maas et al., 2009; McEachan et al., 2016; van den Berg et al., 2016). One explanation could be that individuals from lower SES groups generally have worse health status and at the same time are more likely to reside in neighbourhoods with more environmental problems, making them more prone to benefit from health promotion interventions such as green spaces compared to higher SES groups (Bolte et al., 2010; De Vries et al., 2003; Su et al., 2011). Furthermore, people from lower SES groups are generally less mobile and tend to spend more time in vicinity of their homes (Maas, 2008; Schwanen et al., 2002). Thus, the availability of green spaces near their homes has the potential to increase the probability of them using these spaces (Maas, 2008; Schwanen et al., 2002). The larger health benefits of green spaces for lower SES groups is in line with suggested potential of these spaces in reducing SES inequalities in health (Mitchell and Popham, 2008).

Our findings were also suggestive for stronger protective associations between contact with green spaces and FBG levels and IFG risk for those residing in urban areas compared to those living in rural areas. The available evidence on variation of the health effects of green spaces between urban and rural areas is limited and not consistent (De Vries et al., 2003; Maas et al., 2009; Maas et al., 2006; Markevych et al., 2014; Mitchell

and Popham, 2007; Triguero-Mas et al., 2015). We need to highlight that given that the interaction terms for urbanity and parental education were not statistically significant, our observed variation of associations across strata of urbanity and parental education should be interpreted with caution.

Our analyses did not suggest a considerable difference in the strength of associations between boys and girls. Similar to urbanity, the body of evidence on differences between sexes with regards to the health benefits of green spaces is inconsistent. While some are not supportive for such a variation (Barton and Pretty, 2010; Dadvand et al., 2014a), those that show such variation differ on whether the associations are stronger for females or males (Astell-Burt et al., 2014b; Barton and Pretty, 2010; Currie et al., 2016; Markevych et al., 2014; Richardson and Mitchell, 2010; Richardson et al., 2017; Tamosiunas et al., 2014).

4.3. Potential mechanisms

Previous studies have suggested that children are more likely to engage in moderate-to-vigorous physical activity when they are in green spaces (McCrorie et al., 2014) and physical activity has been shown to improve glucose homeostasis (Huus et al., 2016; Marson et al., 2016). Contact with green space has also been associated with improved mental health including reduction of stress in children (McCormick, 2017) while psychological stress has been associated with increased risk of diabetes type 1 in this age group (Faresjo, 2015). An emerging body of evidence is also suggestive that an impairment of the immunoregulatory pathways due to a reduced exposure to macro- and microorganisms and microbiota in our urbanized societies might play a role in the

development of type 1 diabetes (Paun et al., 2017; Rook, 2013) with childhood as an important window of vulnerability (Rook et al., 2014). Therefore, the ability of green spaces to enhance immunoregulation-inducing microbial input from the environment (Rook, 2013) could have been another potential mechanism underlying our observed associations (Paun et al., 2017). Moreover, the ability of green spaces to reduce exposure to air pollution (Dadvand et al., 2012; Dadvand et al., 2015b) and noise (Dzhambov and Dimitrova, 2014) could lead to a beneficial impact of green spaces on glucose homeostasis, since exposure to these two environmental hazards has been reported to be associated with higher risk of diabetes (Butalia et al., 2016; Dzhambov, 2015).

4.5. Limitations

Our study, given its cross-sectional design, had a limited capability for establishing a causal relationship. Moreover, we relied on self-reported time spent in green spaces which could have resulted in exposure misclassification. A solution to minimize such a misclassification is to use Global Positioning System (GPS) devices or smartphones to collect objective data on the time children spend in different microenvironments including green spaces. This approach can be applied by future studies on this association. Furthermore, we did not have data on other objective measures of exposure to green space such as residential surrounding greenness or proximity to green spaces, enabling us to compare the association of these different aspects of exposure to green spaces with glucose homeostasis. Ideally, the studies of the health effects of green spaces should be controlled for indicators of SES at both household and neighbourhood levels to minimize the likelihood of residual SES confounding. We did not have access

to indicators of neighbourhood SES; however, our findings were robust to adjustment for a wide range of household SES indicators such as parental education, parental employment status, house ownership, marital status, and school type. Additionally, our data on covariates were mainly obtained through questionnaires which could have been subjected to inaccuracy. Moreover, we did not have data on puberty to evaluate its influence on our investigated associations.

5. Conclusions

In a population-based sample of schoolchildren, we observed that longer time spent in green spaces, particularly in natural green spaces, was associated with lower FBG levels. We also observed reduced risk of IFG associated with longer time spent in green spaces; however, the associations were statistically significant for only time spent in natural green spaces. There were also suggestions for stronger associations for participants residing in urban areas compared to those living in rural areas and also for those from lower SES groups. These findings, if established by future studies, could offer policymakers an effective and practical mitigating measure to slow down and ideally reverse the current ongoing rise in the global prevalence of diabetes and ultimately reduce the burden associated with NCDs. Further studies are required to replicate our findings in other settings with different climates and population susceptibilities.

Acknowledgements: The study was conducted on the data obtained in a national surveillance program in Iran. Payam Dadvand is funded by a Ramón y Cajal fellowship (RYC-2012-10995) awarded by the Spanish Ministry of Economy and Finance.

References

Abajobir, A.A., Abate, K.H., Abbafati, C., Abbas, K.M., Abd-Allah, F., Abdulkader, R.S., et al., 2017a. Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 390, 1260-1344.

Abajobir, A.A., Abbafati, C., Abbas, K.M., Abd-Allah, F., Abera, S.F., Aboyans, V., et al., 2017b. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 390, 1151-1210.

Amoly, E., Dadvand, P., Forns, J., López-Vicente, M., Basagaña, X., Julvez, J., et al., 2014. Green and Blue Spaces and Behavioral Development in Barcelona Schoolchildren: The BREATHE Project. *Environ Health Perspect* 122, 1351-1358.

Angoorani, P., Heshmat, R., Ejtahed, H.-S., Motlagh, M.E., Ziaodini, H., Taheri, M., et al., 2017. The association of parental obesity with physical activity and sedentary behaviors of their children: the CASPIAN-V study. *J Pediatr (Rio J)* <https://doi.org/10.1016/j.jpmed.2017.06.024>.

Astell-Burt, T., Feng, X., Kolt, G.S., 2014a. Is Neighborhood Green Space Associated With a Lower Risk of Type 2 Diabetes? Evidence From 267,072 Australians. *Diabetes Care* 37, 197-201.

Astell-Burt, T., Mitchell, R., Hartig, T., 2014b. The association between green space and mental health varies across the lifecourse. A longitudinal study. *J Epidemiol Community Health* 68, 578-583.

Barton, J., Pretty, J., 2010. What is the Best Dose of Nature and Green Exercise for Improving Mental Health? A Multi-Study Analysis. *Environ Sci Technol* 44, 3947-3955.

Bodicoat, D.H., O'Donovan, G., Dalton, A.M., Gray, L.J., Yates, T., Edwardson, C., et al., 2014. The association between neighbourhood greenspace and type 2 diabetes in a large cross-sectional study. *BMJ Open* 4.

Bolte, G., Tamburlini, G., Kohlhuber, M., 2010. Environmental inequalities among children in Europe--evaluation of scientific evidence and policy implications. *Eur J Public Health* 20, 14-20.

Butalia, S., Kaplan, G.G., Khokhar, B., Rabi, D.M., 2016. Environmental Risk Factors and Type 1 Diabetes: Past, Present, and Future. *Can J Diabetes* 40, 586-593.

Camhi, S.M., Katzmarzyk, P.T., 2010. Tracking of cardiometabolic risk factor clustering from childhood to adulthood. *Int J Pediatr Obes* 5, 122-129.

Currie, M.J.B., Lackova, P., Dinnie, E., 2016. Greenspace matters: exploring links between greenspace, gender and well-being with conservation volunteers. *Landscape Research* 41, 641-651.

Dadvand, P., de Nazelle, A., Figueras, F., Basagaña, X., Sue, J., Amoly, E., et al., 2012a. Green space, health inequality and pregnancy. *Environ Int* 40, 110-115.

Dadvand , P., de Nazelle, A., Triguero-Mas, M., Schembari, A., Cirach, M., Amoly, E., et al., 2012. Surrounding Greenness and Exposure to Air Pollution During Pregnancy: An Analysis of Personal Monitoring Data *Environ Health Perspect* 120, 1286-1290.

Dadvand, P., Nieuwenhuijsen, M.J., Esnaola, M., Forn, J., Basagaña, X., Alvarez-Pedrerol, M., et al., 2015a. Green spaces and cognitive development in primary schoolchildren. *Proc Natl Acad Sci U S A* 112, 7937-7942.

Dadvand, P., Rivas, I., Basagaña, X., Alvarez-Pedrerol, M., Su, J., De Castro Pascual, M., et al., 2015b. The Association between Greenness and Traffic-related Air Pollution at Schools. *Sci Total Environ* 523, 59-63.

Dadvand, P., Sunyer, J., Basagaña, X., Ballester, F., Lertxundi, A., Fernández-Somoano, A., et al., 2012b. Surrounding Greenness and Pregnancy Outcomes in Four Spanish Birth Cohorts. *Environ Health Perspect* 120, 1481-1487.

Dadvand, P., Villanueva, C.M., Font-Ribera, L., Martinez, D., Basagaña, X., Belmonte, J., et al., 2014a. Risks and benefits of green spaces for children: A cross-sectional study of associations with sedentary behavior, obesity, asthma, and allergy. *Environ Health Perspect* 122, 1329-1325.

Dadvand, P., Wright, J., Martinez, D., Basagaña, X., McEachan, R.R.C., Cirach, M., et al., 2014b. Inequality, green spaces, and pregnant women: Roles of ethnicity and individual and neighbourhood socioeconomic status. *Environ Int* 71, 101-108.

Dalton, A.M., Jones, A.P., Sharp, S.J., Cooper, A.J.M., Griffin, S., Wareham, N.J., 2016. Residential neighbourhood greenspace is associated with reduced risk of incident diabetes in older people: a prospective cohort study. *BMC Public Health* 16, 1171.

De Vries, S., Verheij, R.A., Groenewegen, P.P., Spreeuwenberg, P., 2003. Natural environments-healthy environments? An exploratory analysis of the relationship between greenspace and health. *Environ Plan A* 35, 1717-1732.

Dzhambov, A.M., 2015. Long-term noise exposure and the risk for type 2 diabetes: A meta-analysis. *Noise Health* 17, 23-33.

Dzhambov, A.M., Dimitrova, D.D., 2014. Urban green spaces' effectiveness as a psychological buffer for the negative health impact of noise pollution: A systematic review. *Noise Health* 16, 157-165.

Faresjo, M., 2015. The Link between Psychological Stress and Autoimmune Response in Children. *Crit Rev Immunol* 35, 117-134.

Huus, K., Å...kerman, L., Raustorp, A., Ludvigsson, J., 2016. Physical Activity, Blood Glucose and C-Peptide in Healthy School-Children, a Longitudinal Study. *PLoS ONE* 11, e0156401.

Kaiser, H.F., 1960. The Application of Electronic Computers to Factor Analysis. *Educ Psychol Meas* 20, 141-151.

Kelishadi, R., Majdzadeh, R., Motlagh, M.-E., Heshmat, R., Aminaee, T., Ardalan, G., et al., 2012. Development and Evaluation of a Questionnaire for Assessment of Determinants of Weight Disorders among Children and Adolescents: The Caspian-IV Study. *Int J Prev Med* 3, 699-705.

Kelishadi, R., Poursafa, P., 2014. A review on the genetic, environmental, and lifestyle aspects of the early-life origins of cardiovascular disease. *Curr Probl Pediatr Adolesc Health Care* 44, 54-72.

Kliegman, R.M., Stanton, B.M.D., St.Geme, J.W., Schor, N.F., 2016. Nelson Textbook of Pediatrics, 20th Edition. Elsevier, Inc., Canada.

Maas, J., 2008. Vitamin G: Green environments-Healthy environments. Nivel, Utrecht.

Maas, J., Verheij, R.A., de Vries, S., Spreeuwenberg, P., Schellevis, F.G., Groenewegen, P.P., 2009. Morbidity is related to a green living environment. J Epidemiol Community Health 63, 967-973.

Maas, J., Verheij, R.A., Groenewegen, P.P., De Vries, S., Spreeuwenberg, P., 2006. Green space, urbanity, and health: how strong is the relation? J Epidemiol Community Health 60, 587-592.

Markevych, I., Tiesler, C.M.T., Fuertes, E., Romanos, M., Dadvand, P., Nieuwenhuijsen, M.J., et al., 2014. Access to urban green spaces and behavioural problems in children: Results from the GINIplus and LISApplus studies. Environ Int 71, 29-35.

Marson, E.C.a., Delevatti, R.S., Prado, A.K.G., Netto, N., Krueh, L.F.M., 2016. Effects of aerobic, resistance, and combined exercise training on insulin resistance markers in overweight or obese children and adolescents: A systematic review and meta-analysis. Prev Med 93, 211-218.

McCormick, R., 2017. Does Access to Green Space Impact the Mental Well-being of Children: A Systematic Review. J Pediatr Nurs 37, 3-7.

McCrorie, P.R.W., Fenton, C., Ellaway, A., 2014. Combining GPS, GIS, and accelerometry to explore the physical activity and environment relationship in children and young people - a review. Int J Behav Nutr Phys Act 11, 93.

McEachan, R.R.C., Prady, S.L., Smith, G., Fairley, L., Cabieses, B., Gidlow, C., et al., 2016. The association between green space and depressive symptoms in pregnant women: moderating roles of socioeconomic status and physical activity. *J Epidemiol Community Health* 70, 253-259.

Mitchell, R., Popham, F., 2007. Greenspace, urbanity and health: relationships in England. *J Epidemiol Community Health* 61, 681-683.

Mitchell, R., Popham, F., 2008. Effect of exposure to natural environment on health inequalities: an observational population study. *Lancet* 372, 1655-1660.

Motlagh, M.E., Ziaodini, H., Qorbani, M., Taheri, M., Aminaei, T., Goodarzi, A., et al., 2017. Methodology and Early Findings of the Fifth Survey of Childhood and Adolescence Surveillance and Prevention of Adult Noncommunicable Disease: The CASPIAN-V Study. *Int J Prev Med* 8, 4.

Nieuwenhuijsen, M.J., Khreis, H., Triguero-Mas, M., Gascon, M., Dadvand, P., 2017. Fifty Shades of Green: Pathway to Healthy Urban Living. *Epidemiology* 28, 63-71.

Paun, A., Yau, C., Danska, J.S., 2017. The Influence of the Microbiome on Type 1 Diabetes. *J Immunol* 198, 590-595.

Rao, X., Patel, P., Puett, R., Rajagopalan, S., 2015. Air Pollution as a Risk Factor for Type 2 Diabetes. *Toxicol Sci* 143, 231-241.

Richardson, E.A., Mitchell, R., 2010. Gender differences in relationships between urban green space and health in the United Kingdom. *Soc Sci Med* 71, 568-575.

Richardson, E.A., Pearce, J., Shortt, N.K., Mitchell, R., 2017. The role of public and private natural space in children's social, emotional and behavioural development in Scotland: A longitudinal study. *Environ Res* 158, 729-736.

Rook, G.A.W., 2013. Regulation of the immune system by biodiversity from the natural environment: An ecosystem service essential to health. *Proc Natl Acad Sci U S A* 110, 18360-18367.

Rook, G.A.W., Lowry, C.A., Raison, C.L., 2014. Hygiene and other early childhood influences on the subsequent function of the immune system. *Brain Res* doi:10.1016/j.brainres.2014.04.004.

Schwanen, T., Dijst, M., Dieleman, F.M., 2002. A microlevel analysis of residential context and travel time. *Environ Plan A* 34, 1487-1508.

Su, J.G., Jerrett, M., de Nazelle, A., Wolch, J., 2011. Does exposure to air pollution in urban parks have socioeconomic, racial or ethnic gradients? *Environ Res* 111, 319-328.

Tamosiunas, A., Grazuleviciene, R., Luksiene, D., Dedele, A., Reklaitiene, R., Baceviciene, M., et al., 2014. Accessibility and use of urban green spaces, and cardiovascular health: findings from a Kaunas cohort study. *Environ Health* 13, 20.

Thiering, E., Markevych, I., Brüske, I., Fuertes, E., Kratzsch, J., Sugiri, D., et al., 2016. Associations of Residential Long-Term Air Pollution Exposures and Satellite-Derived Greenness with Insulin Resistance in German Adolescents. *Environ Health Perspect* 124, 1291-1298.

Triguero-Mas, M., Dadvand, P., Cirach, M., Martínez, D., Medina, A., Mompert, A., et al., 2015. Natural outdoor environments and mental and physical health: Relationships and mechanisms. *Environ Int* 77, 35-41.

UN Department of Economic and Social Affairs, 2015. *World Urbanization Prospects; The 2014 Revision* United Nations, New York.

van den Berg, M., van Poppel, M., van Kamp, I., Andrusaityte, S., Balseviciene, B., Cirach, M., et al., 2016. Visiting green space is associated with mental health and vitality: A cross-sectional study in four european cities. *Health Place* 38, 8-15.

WHO, 2006. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: Report of a WHO/IDF consultation. World Health Organization, Geneva.

Table 1. Description^a of sociodemographic characteristics of study participants.

Characteristics	Description ^a
Age (years)	12 (5)
Sex	
Female	1,831 (47.6%)
Male	2,013 (52.4%)
Single parent	
No	3,594 (93.5%)
Yes	250 (6.5%)
Parental education^b	
No or primary school	1,069 (28.1%)
Secondary school	2,048 (53.9%)
University	686 (18.0%)
Parental employment status^c	
Unemployed	302 (7.9%)
Employee	2,194 (57.6%)
Self-employed	1,313 (34.5%)
School type	
Public	3,494 (91.3%)
Private	332 (8.7%)
Home ownership	
Owing home	3,136 (82.4%)
Not owning home	672 (17.7%)
Urbanity	
Urban	2,776 (72.2%)
Rural	1,068 (27.8%)
Exposure to environmental tobacco smoke	
No	2,249 (58.5%)
Yes	1,595 (41.5%)
History of low birth weight	
No	3,472 (90.3%)
Yes	372 (9.7%)
Breastfeeding history	
Six months or more	3,291 (85.6%)
Less than six months	553 (14.4%)
Parental obesity^d	
No	2,641 (69.2%)
Yes	1,178 (30.8%)
Parental history of diabetes mellitus^e	
No	3,321 (87.1%)
Yes	492 (12.9%)
Family history of diabetes mellitus^f	
No	3,090 (81.1%)
Yes	719 (18.9%)

^a Results are presented as count (%) for categorical variables and as median (interquartile range) for continuous variables.

^b Highest educational attainment by either parents.

^c Highest employment level by either parents.

^d At least one parent being obese.

^e At least one parent was diagnosed by diabetes mellitus.

^f At least one uncle or aunt was diagnosed by diabetes mellitus.

Table 2. Adjusted^a associations between one interquartile range (IQR) increase in time spent in green spaces (in total and in each green space type) and fasting blood glucose levels (mg/dl) and impaired fasting glucose.

Time spent in green spaces	IQR ^b	Fasting blood glucose		Impaired fasting glucose	
		Regression coefficient (95% CIs)	p-value	Odds ratio (95% CIs)	p-value
Total	1.83	-0.5 (-0.9, -0.1)	0.03	0.81 (0.65, 1.02)	0.08
Urban parks	2.25	-0.2 (-0.6, 0.3)	0.51	0.88 (0.70, 1.09)	0.23
Woods/other natural green spaces	1.50	-0.3 (-0.6, -0.1)	0.02	0.84 (0.70, 1.00)	0.05
Private gardens	3.25	-0.5 (-0.9, 0.0)	0.05	0.89 (0.71, 1.12)	0.32

^a Adjusted for age, sex, low birth weight, diet, parental and family history of diabetes mellitus, parental obesity, urbanity, parental educational attainment, home ownership, and marital status.

^b Hours per week.

Table 3. Adjusted^a regression coefficients (95% confidence intervals) indicating change in fasting blood glucose (mg/dl) and odds ratios indicating risk of impaired fasting glucose associated with one interquartile range (IQR) increase in time spent in green spaces stratified by urbanity, parental education, and sex.

	Fasting blood glucose			Impaired fasting glucose		
	Regression coefficient (95% CIs)	p-value	p-value for interaction	Odds ratio (95% CIs)	p-value	p-value for interaction
Urbanity			0.64			0.39
Urban	-0.6 (-1.1, -0.1)	0.02		0.74 (0.55, 0.99)	0.04	
Rural	-0.3 (-1.1, 0.6)	0.53		1.00 (0.67, 1.51)	0.99	
Parental education^b			0.40			0.19
No or primary school	-0.8 (-1.5, -0.1)	0.02		0.46 (0.23, 0.93)	0.03	
Secondary school	-0.5 (-1.1, 0.2)	0.16		0.84 (0.63, 1.12)	0.24	
University	-0.1 (-0.8, 0.7)	0.88		0.96 (0.62, 1.48)	0.85	
Sex			0.96			0.27
Female	-0.5 (-1.0, 0.1)	0.09		0.68 (0.45, 1.04)	0.07	
Male	-0.5 (-1.1, 0.1)	0.14		0.89 (0.69, 1.14)	0.35	

^a Adjusted for age, sex, low birth weight, diet, parental and family history of diabetes mellitus, parental obesity, urbanity, parental educational attainment, home ownership, and marital status.

^b Highest educational attainment by either parents.

Figure legends

Figure 1. Sampling procedure in CASPIAN-V study.