

Association between exposure to the natural environment, rurality, and attention-deficit hyperactivity disorder in children in New Zealand: a linkage study

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Summary

Background Several small experimental studies and cross-sectional observational studies have shown that exposure to the natural environment might protect against attention-deficit hyperactivity disorder (ADHD) or moderate the symptoms of ADHD in children. We aimed to assess whether exposure to the natural environment protects against ADHD and whether this hypothesised protective effect varies across a child's life course.

Methods We did a longitudinal study with data collected from all children born in New Zealand in 1998, excluding those without an address history, those who were not singleton births, and those who died or emigrated before 18 years of age. We used Statistics New Zealand's Integrated Data Infrastructure to identify children with ADHD and to define covariates. ADHD was defined according to hospital diagnosis or pharmacy records (two or more prescriptions for ADHD drugs). Exposure to green space for each year of a child's life (from gestation to 18 years of age) was estimated at the meshblock level (the smallest geographical unit for which the New Zealand Census reports data) using normalised difference vegetation index (NDVI), and land-use data from Landcare Research New Zealand. We used logit models to assess the associations between ADHD prevalence and minimum, maximum, and mean lifetime NDVI, as well as rural living, controlling for sex, ethnicity, mother's educational level, mother's smoking status, mother's age at parturition, birth order, antibiotic use, and low birthweight.

Findings Of the 57 450 children born in New Zealand in 1998, 49 923 were eligible and had available data, and were included in the analysis. Children who had always lived in a rural area after 2 years of age were less likely to develop ADHD (odds ratio [OR] 0·670 [95% CI 0·461–0·974], as were those with increased minimum NDVI exposure after age 2 years (standardised OR for exposure vs first quartile: second quartile 0·841 [0·707–0·999]; third quartile 0·809 [0·680–0·963]; fourth quartile 0·664 [0·548–0·805]). In early life (prenatal to age 2 years), neither rural living nor NDVI were protective against ADHD. Neither mean nor maximum greenness was significantly protective against ADHD.

Interpretation Rurality and increased minimum greenness were strongly and independently associated with a reduced risk of ADHD. Increasing a child's minimum lifetime greenness exposure, as opposed to maximum or mean exposure, might provide the greatest increment of protection against the disorder.

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Introduction

Globally, around 7·2% of children have attention-deficit hyperactivity disorder (ADHD),^{1,2} which can lead to a range of adverse outcomes, including poor academic performance,³ difficulty interacting socially with peers,⁴ reduced lifetime earnings,⁵ and increased suicide risk.⁶ Although ADHD has a genetic component,⁷ several environmental risk factors have also been identified, including maternal alcohol use and smoking during pregnancy,⁸ underweight or premature birth,⁹ lead and pesticide exposure,¹⁰ poor nutrition,¹¹ and infections.¹² In addition, several studies have shown that exposure to the natural environment might be protective against ADHD¹³ or moderate its symptoms in children.^{14–16}

Several experimental studies have investigated the effect of exposure to the natural environment on the symptoms

of ADHD in children. van den Berg and van den Berg¹⁶ studied two groups of six children (aged 9–17 years) who stayed at a residential care facility for ADHD in the Netherlands. Groups were randomly assigned to visit either a natural setting (woods) or an urban setting (town) for half a day. Both groups concentrated better upon visiting the natural setting than the urban setting. Similarly, Faber Taylor and Kuo¹⁷ studied the effect of a 20-min guided walk on concentration (measured using a digit span backwards test) in 17 children with ADHD. Each child was exposed to three settings: a city park and two well kept urban settings, with a 1-week separation between each walk. The greatest improvements in concentration were seen after the walk in the park setting.

A number of population-level observational studies have also examined the relationships between exposure

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Research in context

Evidence before this study

We searched Scopus and Google Scholar on Nov 15, 2018, with the search terms “ADHD” (or “attention-deficit hyperactivity disorder”), “greenness”, “natural environment”, “mental health”, “behavior”, and “NDVI”, in various combinations, with no particular date or other restrictions. A small number of cross-sectional studies suggest that children with greater exposure to the natural environment are less likely to be diagnosed with ADHD. In addition, some small experimental studies have shown that exposure to the natural environment might moderate symptoms in children already diagnosed with ADHD. However, few longitudinal studies have examined the association between ADHD and exposure to the natural environment.

Added value of this study

This large linkage study strengthens the evidence that exposure to the natural environment protects against ADHD. We showed

that increasing a child’s minimum lifetime greenness exposure (from age >2 years to 18 years) provides the greatest protection against ADHD. Greenness exposure in early life (prenatal to age 2 years) was not protective against ADHD, suggesting that exposure to the natural environment might moderate the symptoms of ADHD rather than preventing its development. Living in a rural area and greenness exposure (measured by normalised difference vegetation index [NDVI]) were independently and significantly protective against ADHD in a multivariate model, suggesting that NDVI is not merely a proxy for rural living.

Implications of all the available evidence

Exposing children to the natural environment might moderate the symptoms of ADHD. Increasing a child’s minimum greenness exposure throughout life, as opposed to their maximum or mean exposure, might provide the greatest increment of protection.

to the natural environment and the prevalence of symptoms of ADHD. In a sample of 452 US families who had a child diagnosed with ADHD, Kuo and Faber Taylor¹⁵ noted that children who engaged in more outdoor activities in green settings had reduced ADHD symptoms. Amoly and colleagues¹³ showed, using geocoded home addresses and questionnaires from teachers, that increased time in green space or at beaches was associated with less severe mental health issues including ADHD (defined using teacher questionnaires) among a sample of 2111 children aged 7–10 years from 35 schools in Barcelona. Knopf and colleagues¹⁸ examined the prevalence of ADHD in a nationally representative sample of 17450 children in Germany and found that children living in rural areas were significantly less likely to be prescribed ADHD medication than were urban children. Another German study¹⁹ that followed a cohort of 66823 children from birth (in 2000–04) until 2014 showed that air pollution was a risk factor for ADHD, and that residential greenness (measured using normalised difference vegetation index [NDVI]) was protective against ADHD. In Spain, Dadvand and colleagues²⁰ found that higher lifelong exposure to greenness (measured by NDVI) was associated with improved attention, as measured by computer-based tests, in two birth cohorts. Finally, in a study by Berry and colleagues,²¹ 204 undergraduates were shown images of a natural scene, a built scene, or geometric patterns, then tested for their willingness to delay receiving a monetary reward. Students who had viewed natural images were less impulsive than students who had viewed built scenes or geometric patterns.

The underlying mechanisms linking the natural environment to a reduction in ADHD symptoms are unclear, but could be related to reduced stress,²² which can exacerbate symptoms in patients with ADHD.²³ Concentration difficulties associated with ADHD might

also be partly mitigated by exposure to green space, as suggested by attention-restoration theory.²⁴ This theory posits that the natural environment can be psychologically restorative because humans interact with the natural environment through so-called soft fascination, which is effortless, in contrast to their interaction with many non-natural environments, which require directed attention and might erode capacity to focus. Exposure to the natural environment might also reduce impulsivity,²¹ which is, along with problems focusing, a diagnostic criterion for ADHD.²⁵ Finally, exposure to the natural environment can affect commensal microbiome diversity,²⁶ which has been linked to ADHD. Specifically, using a case-control design (14 cases and 17 controls), Prehn-Kristensen and colleagues²⁷ found that children with ADHD had lower gut microbial diversity, and Aerts and colleagues²⁸ found that the gut biome of children with ADHD was less diverse. Furthermore, using functional MRI, they found that this lower microbial diversity was associated with decreased neural reward anticipation, which is a well established indicator of ADHD.

Most studies to date have been cross-sectional or focused on the short-term effects of the natural environment on small samples of children already diagnosed with ADHD. Therefore, we did a longitudinal study of the relationship between exposure to the natural environment and risk of ADHD in a large linkage study of children in New Zealand.

Methods

Study sample and data sources

Our sample consisted of all children born in New Zealand in 1998. We excluded children without an address history, those who were not singleton births, and those who died or emigrated before 18 years of age. Beyond birth records, we had little to no data for many of the excluded children.

We identified our sample, obtained data on outcomes and covariates, and did our analysis within Statistics New Zealand's Integrated Data Infrastructure (IDI), which was established in 1999 and contains routinely collected individual-level data on 95% of residents of New Zealand.²⁹ The IDI consists of a central spine to which data on health, education, benefits, criminal justice, population (births, deaths, and immigration), income and work, and housing are linked. The IDI provides residential history for individuals based on residential meshblocks, which are the smallest geographical units for which Statistics New Zealand reports data (geocodes and precise addresses for individuals are not provided). Residential history is derived from multiple sources and algorithms are used to resolve conflicts on the basis of the reliability of data sources. On average, 95 people live in a meshblock, and there were 46 637 meshblocks nationally in 2013. In urban areas, the mean meshblock size was 20.4 hectares, and the mean area for a rural meshblock was 2498 hectares. For comparison, many previous studies of the relationship between the natural environment and health outcomes have defined exposure metrics in buffers around participants' residential addresses ranging in radius from 50 m (0.8 hectares)³⁰ to 1000 m (314 hectares).³¹ Our sample included children who lived in 24 486 of the 46 637 meshblocks in New Zealand.

Because the Inland Revenue Department is one of the major sources of address history within the IDI, children's residential history is sparser than that of adults. Therefore, we used maternal data to supplement a child's residential history if their residential history suggested cohabitation. We assumed a mother and child lived together if, for years when residential history was available for both mother and child, their residential meshblock matched more than half the time. We also used the mother's residential history to determine the child's prenatal meshblock.

As this study involved anonymised, linked, routinely collected data, and did not involve participant recruitment, it was classified as low risk by the Massey University Ethics Committee (#4000017243) and was approved by Statistics New Zealand (#MAA2017-11). Our research adhered to the principles of the Declaration of Helsinki.

Outcomes

We defined a child as having ADHD if one of two conditions occurred before 18 years of age: a child was diagnosed with ADHD in hospital (code F90.9 in the International Classification of Diseases 10th revision); or a child received two or more prescriptions for methylphenidate hydrochloride, atomoxetine, or dexamfetamine sulfate. These three drugs are the main ADHD drugs funded by PHARMAC (the New Zealand agency that provides access to publicly funded pharmaceuticals) and are, in New Zealand, used almost exclusively for the

treatment of ADHD. Although the drugs can be used to treat narcolepsy, narcolepsy is extremely rare in children. We chose a two-prescription threshold because more than one prescription suggests that ADHD is ongoing. In addition, 2% (n=986) of our sample received two or more prescriptions, which is the lower bound of the published 2–5% prevalence of ADHD in New Zealand,^{2,32} but lower than the global prevalence of 7.2%.¹ Because prescription data from before 2005 were not available in the IDI, we did not capture data on children who were prescribed ADHD medication before 7 years of age, unless prescribing continued until 2005 or the child was diagnosed while in hospital (at any age).

To ensure that results were not an artifact of our definition of ADHD, we did a sensitivity analysis using three alternative ADHD definitions based on having either a hospital diagnosis or one of the following: one or more (2.1% of sample [n=1057]), five or more (1.8% of sample [n=894]), or ten or more (1.6% of sample [n=798]) prescriptions for ADHD drugs.

Exposures

We used three metrics to describe exposure to the natural environment at the meshblock level. We computed NDVI, a greenness index derived from satellite imagery, using Landsat 7 data up to 2013 and Landsat 8 data thereafter. To evaluate the effects of the Landsat 7 scan line corrector failure, we computed NDVI for both platforms for the year 2013, which showed a mean NDVI discrepancy between the two platforms across all terrestrial meshblocks of less than 0.015 (SD 0.018). The observed level of scan line corrector-induced variability was lower than the uncertainty introduced by atmospheric effects and was, therefore, considered negligible for the purposes of this study. Large water bodies were represented as individual polygons, delineated precisely using high-resolution airborne imagery, and were excluded from the calculation of NDVI. Small waterbodies (eg, streams and ponds) were included in NDVI calculations, but occupied only a small area relative to the size of a Landsat pixel (30 m) and the area of a meshblock.

The mean annual NDVI value for a meshblock was the mean of the maximum value in each 30-m pixel within that meshblock. Combining these data with residential history, we calculated maximum NDVI for each year of a child's prenatal period and life. Little to no information was available on the dose–response relationship between the natural environment and ADHD, including possible minimum or maximum dosage thresholds. Therefore, to explore dose and threshold effects, we calculated the minimum, maximum, and mean of these annual NDVI values across a child's lifetime (eg, minimum NDVI across a child's lifetime was the smallest value among that child's annual maximum NDVI values). To explore possible differential effects across a child's life course, we calculated mean, minimum, and maximum NDVI for two periods: early life (prenatal to age 2 years) and later

	Total sample (n=49 956)*
Sex	
Female	24 250 (48.5%)
Male	25 705 (51.5%)
Ethnicity†	
European	27 876 (56.3%)
Māori	14 149 (28.7%)
Pacific	4208 (8.5%)
Middle Eastern, Latin American, or African‡	191 (0.4%)
Asian	2652 (5.4%)
Other	281 (0.6%)
Maternal smoking§	
Never	19 832 (50.6%)
Ever	19 324 (49.4%)
Maternal education§	
No high-school qualifications	8770 (22.4%)
Some high-school or higher qualifications	30 386 (77.6%)
Birthweight	
Low	6061 (12.1%)
Normal or higher	43 894 (87.9%)
Always lived in rural meshblock	3419 (6.8%)
Maternal age at parturition, years¶	29 (5.7)
Birth order	1.49 (0.92)
Number of antibiotic prescriptions in 2005–16	6.17 (7.04)
Mean lifetime NDVI	0.549 (0.091)
Data are n (%) or mean (SD). NDVI=normalised difference vegetation index. *In accordance with Integrated Data Infrastructure protocols, all sample sizes have been rounded to the nearest multiple of three. †Missing n=598. ‡Aggregate ethnicity category used in New Zealand. §Missing n=10 799. ¶Missing n=10 914. Missing n=30.	
Table 1: Characteristics of children born in New Zealand in 1998	

life (age >2–18 years; which might include years after a child receives their first prescription or hospital diagnosis). We split these variables into quartiles to better elucidate the dose–response relationship between the natural environment and ADHD. We chose to define exposures in this way because ADHD is typically a chronic, ongoing condition.

We also described a child's exposure to the natural environment using the 2012 Land-Cover Database, produced by Landcare Research New Zealand, which categorises all land cover in New Zealand into one of 35 classes. We calculated the proportion of each meshblock covered by each of the land-cover classes. As with NDVI, we calculated mean lifetime exposure, early-life exposure, and later-life exposure.

Finally, we designated meshblocks as urban or rural using definitions from the 2013 New Zealand Census, which defines urban areas as cities, towns, and other conurbations (an aggregation of urban settlements) of 1000 people or more.

Covariates

We used IDI data to control for individual-level variables associated with risk of ADHD in previous research, including sex and ethnicity; underweight or premature birth; birth order; parental smoking; parental education and occupation; infections and antibiotic use; and parental age at childbirth.

Past research has also found a positive association between traffic-related air pollution and ADHD;³³ therefore, we calculated the density of major roads in each meshblock using data from Land Information New Zealand and mean annual nitrogen dioxide (NO₂) concentrations at the meshblock level. These NO₂ estimates were developed by the National Institute of Water and Atmospheric Research and are based on the sum of two semi-empirical models: an urban background estimate and a local increment from nearby roads.

Finally, we used the New Zealand Deprivation Index (NZDep), a well validated index calculated from nine census variables,³⁴ to account for the overall socio-economic conditions in each meshblock, with higher values indicating higher social deprivation.

Statistical analysis

Four key covariates—mother's smoking status (n=10799), mother's educational level (n=10799), antibiotic use (n=6912), and mother's age at parturition (n=10914)—had a large number of missing values, and key covariates (eg, ethnicity) were significantly different in the subsample that had missing values compared with the rest of the sample. To estimate values for these missing observations, we used chained multiple imputation that was able to accommodate four imputed variables with a pattern of missing values that were not perfectly nested within each other (not every observation that had a missing value for antibiotic use also had a missing value for mother's smoking status). We used ten repetitions (results using 100 replications were identical to three decimal places) and seeded the imputation process to ensure that results could be replicated. The final analytical sample was slightly smaller than the eligible sample because of missing values in other covariates that we did not impute. The distributions from which the imputed values were drawn were estimated with regression models (linear for continuous variables and logit for binary variables) that included all the independent variables from the final regression model plus ADHD occurrence.

We did the analysis in four stages. First, we imputed missing values. Second, we estimated a logit model of ADHD incidence with variables describing a child's exposure to the natural environment and rurality. Third, we tested whether results were sensitive to our definition of ADHD. Fourth, we estimated stratified models on subsamples of our data based on key covariates.

We used a backwards stepwise selection process to estimate logit models of ADHD incidence, with variables dropped from the model using progressively lower p value

thresholds (final threshold $p < 0.05$). For groups of related variables (eg, those describing a mother's socioeconomic status), we retained the variable with the lowest p value when individually regressed against ADHD. Additionally, to avoid including highly collinear combinations of variables in models, we estimated simple linear models of the number of ADHD prescriptions (results not shown). This estimation allowed us to calculate variance-inflation factors for all independent variables. If the variance-inflation factor for any variable exceeded 2.0 in these linear models, we did not include it in our logit models. Variables not significantly associated with health outcomes of interest can still be confounders,³⁵ so we systematically reintroduced dropped variables and retained them if they induced a 10% or greater change in exposure variables of interest. We took care to reintroduce variables that past research showed to be associated with ADHD risk.

Finally, to aid interpretation of coefficients, we standardised—by subtracting the mean and dividing by the SD—all NDVI variables and the number of antibiotic prescriptions.

All data analysis was done using Stata software (version 15).

Role of the funding source

This study did not receive any external funding. The corresponding author had full access to all the data in the study and was responsible for the decision to submit for publication.

Results

Of the 57450 children born in New Zealand in 1998, 7494 (13.0%) were excluded, and the remaining 49956 (87.0%) eligible children were included in the sample. Descriptive statistics for the sample are shown in table 1. 22079 (44.2%) children were non-European, including 14149 (28.3%) who were Māori. 3419 (6.8%) children had always lived in a rural area, 6061 (12.1%) had low birthweight, and 8770 (22.4%), of 39157 with available data, were born to mothers who did not complete high school or the equivalent.

After excluding 33 children with missing data on covariates that were not imputed, the final analytical sample consisted of 49923 children. Having always lived in a rural meshblock (age >2–18 years) was protective against ADHD (odds ratio [OR] 0.670, 95% CI 0.461–0.974), as was increasing minimum NDVI (age >2–18 years; 0.834, 0.773–0.901; figure 1, appendix). Table 2 shows estimates of the associations of ADHD with NDVI and rural living among children born in New Zealand in 1998, adjusted for ethnicity, sex, birth order, antibiotic use, mother's smoking status, mother's education, low birthweight, and mother's age at parturition (household income was not significantly associated with ADHD; appendix). Splitting minimum NDVI into quartiles revealed a possible dose-response relationship between minimum greenness and ADHD

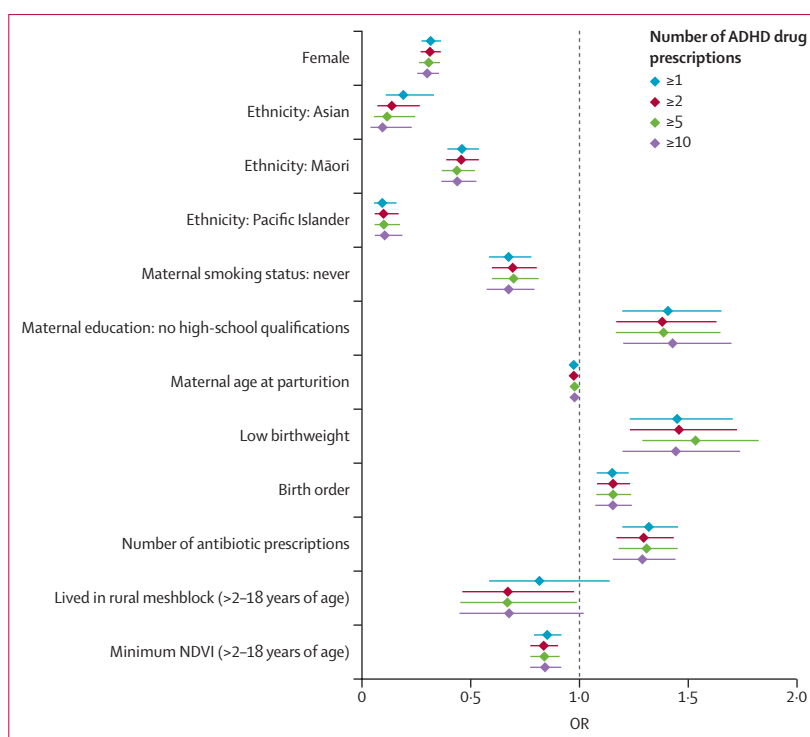


Figure 1: ADHD prevalence among children born in New Zealand in 1998 (n=49 923)* by definition of ADHD
Data are OR (95% CI). Numerical data are provided in the appendix. ADHD definitions consisted of hospital diagnosis or one of the following: at least one ADHD drug prescription; at least two ADHD drug prescriptions; at least five ADHD drug prescriptions; or at least ten ADHD drug prescriptions. ADHD=attention-deficit hyperactivity disorder. NDVI=normalised difference vegetation index. OR=odds ratio. *In accordance with Integrated Data Infrastructure protocols, all sample sizes have been rounded to the nearest multiple of three.

(table 2). We tested several metrics describing whether a child moved between an urban and a rural area, or between more and less green neighbourhoods, and none were significant (appendix).

In contrast to later-life exposure, minimum NDVI in early life (prenatal to age 2 years) was not significantly associated with ADHD (results not shown), nor were any of our measures of mean NDVI (table 2). Maximum NDVI (age >2–18 years) was a risk factor for ADHD, but this relationship was only significant in the third quartile (table 2). Further subdividing later-life exposure was not possible because of multicollinearity.

Land cover within a child's residential meshblock, neighbourhood deprivation (NZDep), NO₂ concentration, and proximity to roads were not significantly associated with ADHD. When we re-estimated the reported models as simple linear models by replacing the binary dependent variable with the number of ADHD prescriptions, none of the independent variables had a variance inflation factor greater than 2.0 (results not shown). Findings for the associations between covariates and ADHD were consistent with previous research. Female sex, non-European ethnicity, and no maternal smoking were associated with a reduced risk of ADHD. Low birthweight and increasing birth order were associated with an increased risk of ADHD (table 2).

See Online for appendix

	Minimum NDVI model		Mean NDVI model		Maximum NDVI model	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Covariates						
Female (vs male)	0.312 (0.269–0.362)	<0.001	0.314 (0.270–0.364)	<0.001	0.313 (0.270–0.364)	<0.001
Ethnicity (vs European)						
Asian	0.139 (0.072–0.270)	<0.001	0.143 (0.074–0.278)	<0.001	0.151 (0.078–0.294)	<0.001
Māori	0.458 (0.388–0.539)	<0.001	0.451 (0.383–0.532)	<0.001	0.450 (0.382–0.531)	<0.001
Middle Eastern, Latin American, or African†	0.622 (0.197–1.964)	0.42	0.638 (0.202–2.017)	0.44	0.679 (0.215–2.146)	0.51
Other	0.549 (0.203–1.484)	0.24	0.558 (0.207–1.508)	0.25	0.556 (0.206–1.503)	0.29
Pacific	0.100 (0.059–0.170)	<0.001	0.098 (0.058–0.167)	<0.001	0.103 (0.06X–0.175)	<0.001
Mother's smoking status: never (vs ever)	0.690 (0.595–0.800)	<0.001	0.686 (0.592–0.795)	<0.001	0.689 (0.594–0.799)	<0.001
Mother's education: no high-school (vs high-school or higher)	1.382 (1.170–1.632)	<0.001	1.390 (1.177–1.642)	<0.001	1.395 (1.181–1.648)	<0.001
Mother's age at parturition	0.972 (0.960–0.986)	<0.001	0.971 (0.958–0.984)	<0.001	0.971 (0.958–0.984)	<0.001
Low birthweight (vs normal or higher birthweight)	1.459 (1.033–1.725)	<0.001	1.454 (1.229–1.720)	<0.001	1.455 (1.230–1.722)	<0.001
Birth order	1.155 (1.081–1.233)	<0.001	1.156 (1.082–1.235)	<0.001	1.153 (1.079–1.231)	<0.001
Number of antibiotic prescriptions (standardised)	1.295 (1.170–1.433)	<0.001	1.286 (1.162–1.424)	<0.001	1.289 (1.165–1.427)	<0.001
Exposures at >2-18 years of age						
Always lived in rural meshblock (vs lived ≥1 year in urban meshblock)	0.563 (0.392–0.806)	0.002	0.487 (0.342–0.693)	<0.001	0.439 (0.310–0.621)	<0.001
Minimum NDVI standardised‡ (vs quartile 1)						
Quartile 2	0.841 (0.707–0.999)	0.049	..	..	..	..
Quartile 3	0.809 (0.680–0.963)	0.017	..	..	..	..
Quartile 4	0.664 (0.548–0.805)	<0.001	..	..	..	..
Mean NDVI standardised‡ (vs quartile 1)						
Quartile 2	..	..	1.045 (0.870–1.256)	0.64	..	..
Quartile 3	..	..	1.016 (0.847–1.219)	0.86	..	..
Quartile 4	..	..	0.924 (0.766–1.116)	0.41	..	..
Maximum NDVI standardised‡ (vs quartile 1)						
Quartile 2	..	..	..	..	1.065 (0.874–1.296)	0.53
Quartile 3	..	..	..	..	1.224 (1.016–1.475)	0.034
Quartile 4	..	..	..	..	1.150 (0.953–1.389)	0.15

Models were adjusted for ethnicity, sex, birth order, antibiotic use, mother's smoking status, mother's educational level, low birthweight, and mother's age at parturition. Missing data were accounted for by multiple imputation (ten imputations total). NDVI=normalised difference vegetation index. OR=odds ratio. *In accordance with Integrated Data Infrastructure protocols, all sample sizes have been rounded to the nearest multiple of three. †Aggregate ethnicity category used in New Zealand. ‡All NDVI variables were standardised by subtracting the sample mean and dividing by the SD.

Table 2: Associations of attention-deficit hyperactivity disorder with sociodemographic and minimum, mean, and maximum greenness (NDVI) among children born in New Zealand in 1998 (n=49 923)*

The protective effect of NDVI was not sensitive to different definitions of ADHD. By contrast, when we used a less restrictive definition (one or more ADHD drug prescriptions), living in a rural meshblock was not significantly associated with ADHD (figure 1 and appendix).

In the stratified analysis (figure 2), minimum NDVI and rural living had wider CIs than those in the full model, which was expected because of the smaller sample size within each stratum. The protective effect of NDVI was significant for boys but not for girls, and for children of European ethnicity but not for those of Māori ethnicity. The loss of a significant protective effect of

NDVI in the female-only model might have, in part, occurred because ADHD is less common in girls than in boys. Rural living did not show any significant protective effects in the subgroup analyses. The OR point estimate was slightly lower for children of European ethnicity than for those of Māori ethnicity but, in contrast to NDVI, was slightly higher (indicating a slightly reduced protective effect) for boys than for girls.

We did a post-hoc comparison of the minimum NDVI model presented in table 2 (in which imputation was used to estimate missing values) to an equivalent model that dropped observations with missing values (case-wise deletion; appendix). The models were consistent,

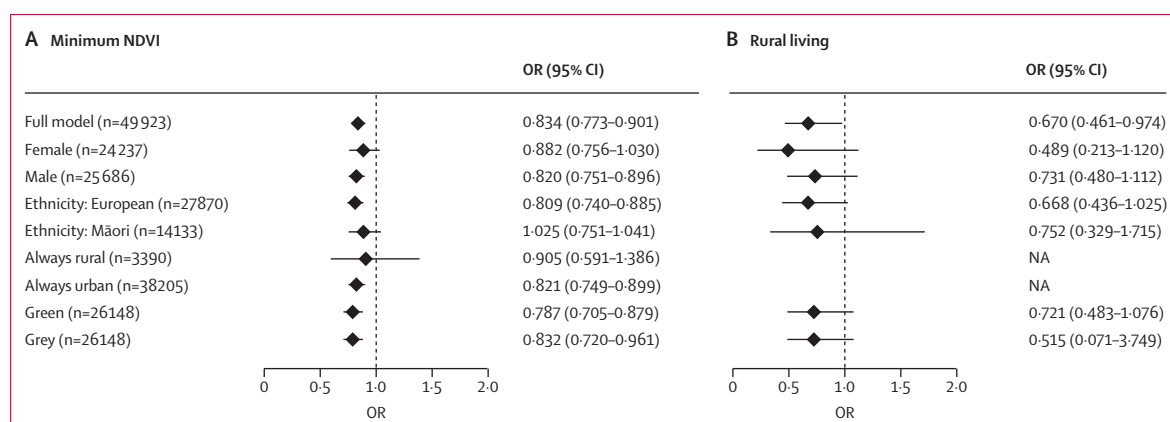


Figure 2: Association of ADHD with minimum NDVI (age >2–18 years) and rural residence for different strata of the full sample (n=49 923)*

Data are OR (95% CI). "Green" denotes children whose minimum NDVI exposure (age >2–18 years) was above the median NDVI value, and "grey" denotes those with NDVI values below the median. ADHD=attention-deficit hyperactivity disorder. NDVI=normalised difference vegetation index. OR=odds ratio. *In accordance with Integrated Data Infrastructure protocols, all sample sizes have been rounded to the nearest multiple of three.

although the SEs in the case-wise deletion model were higher, leading to some loss of significance. In particular, the second NDVI quartile was not significantly associated with ADHD prevalence in the case-wise deletion model.

Research in other countries has consistently found that greenness is positively associated with socioeconomic status, which can raise environmental justice concerns. To determine whether this is the case in New Zealand, we calculated the mean value for minimum NDVI (age >2–18 years) for different strata of socioeconomic status in the sample (appendix). Consistently with other countries, greenness was inversely correlated with socioeconomic status, except in the fourth quartile of neighbourhood deprivation. The higher greenness in the fourth quartile is probably because rural areas in New Zealand are, on average, greener and more socially deprived than are urban areas.

Discussion

In a cohort of children born in 1998 in New Zealand, increased minimum NDVI exposure and living in a rural area in later life (>2–18 years of age) were protective against ADHD. The effects of other covariates were consistent with previous research. Maximum NDVI in later life was associated with an increased risk of ADHD, although only in the third quartile. Nonetheless, it is possible that above some maximum threshold, greenness might be a risk factor for ADHD.

The protective effect of increased minimum greenness and the non-significance of mean greenness suggest that interventions to increase exposure to greenness that focused on the least green areas would be the most protective against ADHD. The results suggest that there might be a minimum threshold of greenness below which children suffer adverse health consequences, including an increased risk of developing ADHD. However, it is not clear whether this threshold is absolute or relative. In addition, as this was a linkage study that

did not collect biological samples, our results provide no insights into the mechanisms linking greenness and ADHD. Notably, without access to longitudinal data on a child's lifetime greenness exposure, we would have been unable to identify the protective effect of minimum greenness. This underlines the values of longitudinal databases such as Statistics New Zealand's IDI.

Before age 2 years, neither exposure to greenness nor rural living were protective against ADHD. This might be because most children are diagnosed with ADHD when they are older than 2 years, or because exposure to the natural environment simply moderates current symptoms of ADHD rather than protecting against the development of ADHD.

Living in a rural area and NDVI were independently, and significantly, protective against ADHD in a multivariate model, suggesting that NDVI is not merely a proxy for rural living. When we restricted our analysis to children who had always lived in an urban area, NDVI was still protective. Both rural living and greenness exposure might partly exert their protective effect through increased microbial exposure, as suggested for asthma.³⁶ The positive association between number of antibiotic prescriptions and ADHD risk supports this mechanism. However, higher birth order (having older siblings) was also a risk factor for ADHD, and, if microbial exposure were the primary mechanism linking greenness and ADHD, we would expect having older siblings to be protective.

The protective effect of living in a rural area should be interpreted with care. Children living in rural areas might not have the same access to health care as do urban children, so they might be less likely to be prescribed drugs to treat ADHD or admitted to hospital for ADHD treatment.¹⁸ In addition, rural areas are significantly greener than urban areas, and, because rural meshblocks are larger, meshblock-level exposure is subject to greater exposure misclassification. Future

research could valuably focus on ascertaining whether the observed protective effect of rural living is an artifact of health-care access. If not, it would be useful to identify the elements of rural living that are most protective against ADHD.

Our study had several limitations. First, as a single observational study, we were unable to establish a causal link between greenness and ADHD. Second, because we used coarse overall greenness metrics, we could not conclude which elements of the natural environment are most protective. For example, NDVI cannot distinguish between the effects of highly maintained parks and natural green areas. Improvements in remote-sensing technology (notably, Lidar) will allow future studies to use more sophisticated exposure metrics that will help design, and target, effective green public health interventions. Third, we did not have access to data on ADHD diagnoses by primary care doctors, although we did have detailed hospitalisation and prescription data, and the results were not sensitive to different definitions of ADHD. However, the 2% prevalence of ADHD in our study was at the lower bound of the reported 2–5% prevalence in New Zealand, and was below the global prevalence of 7–2%. Therefore, we probably underestimated the true prevalence of ADHD in New Zealand. Children who were diagnosed with ADHD but not treated using drugs or diagnosed while in hospital were not included in our sample. This undercounting might be an issue especially in rural areas, where getting medical care and filling prescriptions can be more difficult. In addition, our definition of ADHD involved multiple prescriptions or a hospital diagnosis, which occurred at several points in time. Therefore, in some cases, our exposure measures include time periods after diagnosis. This is another potential source of classification error. Finally, exposure metrics were based on residential meshblock rather than residential address, which introduces measurement error, especially in sparsely populated rural areas with large meshblocks. Restricting the analyses to more populated urban areas (thus reducing measurement error) strengthened rather than weakened the association (figure 2), suggesting that measurement error was unlikely to explain the significant inverse association between increased minimum greenness and ADHD. In addition, we had no information on how long children spent outside, the activities they engaged in, or the amount of screen time they were exposed to, which might result in measurement error.

In conclusion, in this longitudinal study of the relationship between natural environment exposure and ADHD, rurality and increased minimum greenness were strongly and independently associated with a reduced risk of ADHD. Exposing children to the natural environment might moderate the symptoms of ADHD, and increasing a child's minimum greenness exposure might provide the greatest increment of protection.

Contributors

GHD developed the research question, did the analysis, and wrote the majority of the paper. YLM contributed to the analysis and writing of the paper. DG developed the exposure metrics and edited several drafts of the paper. A'tM contributed to the analysis. JD helped develop the research question and contributed to the writing and editing of the paper.

Declaration of interests

We declare no competing interests.

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