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Familial and neighborhood effects on psychiatric disorders in childhood and adolescence

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Abstract

Background: More knowledge is needed on potential associations between individual-, family-, and neighborhood-level factors and psychiatric disorders in children and adolescents.

Aims: To examine associations between, individual-, family-, and neighborhood-level factors and incident internalizing (anxiety and mood) disorders and externalizing (ADHD and conduct) disorders in children and adolescents, and to estimate the relative contributions of family and neighborhood to individual variation in these disorders.

Method: We performed a three-level logistic regression on all 542,195 children born in Sweden in 1992 to 1996, nested in 427,954 families, which in turn were nested in 8,475 neighborhoods. The children were followed from 2000 to 2010 for incident internalizing and externalizing psychiatric disorders, assessed from medical records.

Results: 26,514 children (4.8%) were diagnosed with internalizing or externalizing psychiatric disorders. Approximately 29% of the total individual variance in internalizing disorders could be attributed to the family level, which includes both genetic and family environmental effects, and 5% to the neighborhood level. The corresponding figures for externalizing disorders were 43.5% and 5.5%, respectively. After adjustment for individual-level sociodemographic factors, high neighborhood deprivation was associated with increased risks of externalizing and internalizing psychiatric disorders (odds ratio [OR]=1.37, 95% credible interval [CI]=1.25-1.50 and OR=1.34, 95% CI=1.25-1.45, respectively), including conduct disorder (OR=2.01, 95% CI=1.58-2.55), anxiety disorders (OR=1.40, 95% CI=1.29-1.52), and mood disorders (OR=1.21, 95% CI, 1.09-1.35). The strongest association between neighborhood deprivation and ADHD was observed in moderately deprived neighborhoods (OR=1.31, 95% CI=1.19-1.44). **Conclusions:** These findings call for policies to promote mental health that consider potential influences from children's family and neighborhood environments.

Trial Registration: Not applicable.

Key Words: Cohort study; neighborhood SES; internalizing and externalizing psychiatric disorders

Introduction

Findings from a US national survey (NCS-A) and from NHANES show that psychological distress is common in children and adolescents (Merikangas et al., 2010a, Merikangas et al., 2010b, Kessler et al., 2012). The influence of individual-level factors such as race/ethnicity and poverty on psychological disorders is well established (Samaan, 2000a, Costello et al., 2001, Costello et al., 2003). Research into neighborhood effects dates from as early as the 1930s, when Chicago School researchers Faris and Dunham reported an ecological association between residence in disorganized neighborhoods and psychiatric disorders, particularly schizophrenia and substance abuse, in 30,000 adults treated in psychiatric hospitals. They found no visible pattern across neighborhoods in the distribution of affective disorders (Faris and Dunham, 1939). Although Faris and Dunham used aggregated data and could not take individual socioeconomic status (SES) into consideration, other studies have examined the influence of neighborhood SES on adult psychiatric disorders using multilevel modeling that separates neighborhood from individual effects (Lofors et al., 2006, Lofors and Sundquist, 2007). For example, investigators recently found that neighborhood deprivation is associated with psychiatric medication prescription in adults, independent of individual-level sociodemographic characteristics (Crump et al., 2011). The strongest associations were found for antipsychotics and anxiolytics, with adjusted odds ratios (ORs) of 1.40 and 1.24, respectively, comparing the highest to lowest quintiles of neighborhood deprivation. Other longitudinal studies from the UK of 8,000-90,000 adults found that neighborhood effects on common psychiatric disorders were explained by household and individual socioeconomic factors, rather than being a true neighborhood effect (Weich et al., 2003, Weich et al., 2005). In contrast, a literature review found spatial differences in nonaffective psychoses but an apparent absence of spatiality of affective psychoses in adults (March et al., 2008). Data from UK, the Aetiology and Ethnicity in Schizophrenia and Other Psychoses (AESOP) study

revealed that 23% of the variance in incidence of schizophrenia across wards could be attributed to neighborhood-level risk factors (Kirkbride et al., 2007). In addition, another study from the Bristol group and Chilean colleagues found a significant association between quality of the built environment of small geographical sectors and presence of common mental disorders in its adult residents (Araya et al., 2007).

While several studies have suggested a link between neighborhood characteristics and adult mental health outcomes, fewer studies have examined potential neighborhood-level effects on psychopathology in children and adolescents. Furthermore, previous studies have been limited by small sample sizes, inadequate adjustment for confounding, or modeling that did not optimally distinguish individual- and family- from neighborhood-level effects. In this study, we examined the associations of neighborhood-level deprivation and family- and individual-level factors with incidence of specific internalizing and externalizing psychiatric disorders (anxiety disorders, mood disorders, attention deficit hyperactivity disorder [ADHD], and conduct disorder) in a follow-up study of children and adolescents living in Sweden. The novel contribution of this largest cohort study in the world to date (542,195 children, nested in 427,954 families, which in turn were nested in 8,475 neighborhoods) is that it examines potential effects on internalizing as well as externalizing disorders at three levels (individuals, families, and neighborhoods) and is constructed from highly complete, nationwide register data that avoid bias from self-reporting.

Our aims were to: 1) examine associations of neighborhood-level deprivation and family- and individual-level factors with incident internalizing and externalizing psychiatric disorders in children and adolescents, as assessed based on in- and out-patient contacts; and 2) estimate the relative contributions of family and neighborhood to individual variation in internalizing and externalizing psychiatric disorders among children and adolescents.

Methods

The Swedish nationwide population and health care registers have exceptionally high completeness and validity, with most variables being 95-100% complete (Rosen and Hakulinen, 2005). We used data from multiple Swedish nationwide registries, including healthcare data, which were linked using the unique individual Swedish 10-digit personal ID number assigned at birth or immigration to all Swedish residents. This ID number was replaced by a serial number in order to preserve confidentiality. The following sources were used to create our database: the Total Population Register, containing annual data on family, education level, and area of residence; the Multi-Generation Register, providing information on family relations; the Swedish Hospital Discharge Register, containing all hospitalizations for all Swedish inhabitants from 2000-2010; and the Outpatient Care Register, containing information from all outpatient clinics from 2001 to 2010. In the database a family consists of a maximum of two generations where people are related to each other and are registered on the same property. Each family has its own ID number. Geographic status was defined as Small Areas for Market Statistics (SAMS), which are small geographical units with boundaries defined by homogeneous types of buildings as defined by Statistics Sweden. All Swedish individuals have been geocoded to these areas. There are approximately 9,200 SAMS throughout Sweden, with an average population of 1,000. SAMS were used as proxies for neighborhoods, as in previous research (Cubbin et al., 2006, Johnell et al., 2006).

We conducted a closed cohort study: all children born in 1992 to 1996 were included at the start of the study in January 2000 (when they were aged 4 to 8 years) and were followed up for 10 years (maximum age 18 years). The follow-up period was from January 1, 2000 until the first inpatient or outpatient psychiatric diagnosis, death, emigration, or the end of the study period on December 31, 2010. Before enrollment into the study, children and

adolescents who had previously been diagnosed with any psychiatric disorder (n=2,225) were excluded in order to remove pre-existing cases. The most common diagnoses among those excluded were "Special symptoms or syndromes, not elsewhere classified" (n = 1052, 47.3%), "Specific delays in development" (n = 329, 14.8%) and "Other behavioral and emotional disorders with onset usually occurring in childhood and adolescence" (n = 127, 5.7%). Those excluded individuals constituted approximately 8% of the total number of events. In total the study included 542,195 children born in 1992 to 1996, nested in 427,954 families, which in turn were nested in 8,475 neighborhoods. We followed each individual until their first psychiatric diagnosis during the follow-up period, so that each individual could be counted only once as having an event.

Outcome variable: childhood and adolescent internalizing and externalizing psychiatric disorders

The outcome variable was a first inpatient or outpatient diagnosis of an internalizing or externalizing psychiatric disorder in childhood or adolescence. Diagnoses of psychiatric disorders were retrieved from the Hospital Discharge Register (2000-2010) and Outpatient Care Register (2001-2010). Internalizing disorders are those that children internalize, such as anxiety and mood disorders. By contrast, externalizing disorders are those that children externalize, such as ADHD and conduct disorder. Internalizing and externalizing psychiatric disorders were defined according to International Classification of Diseases (ICD)-10 codes for anxiety disorders (F40-F48 and F93), mood disorders (F30-F39), ADHD (F90), and conduct disorder (F91).

Independent variable: neighborhood-level deprivation

A summary index – the neighborhood deprivation index (NDI) – was calculated to

characterize neighborhood-level deprivation. The NDI was based on information about female and male residents aged 20 to 64 because this age group represents those who are among the most socioeconomically active in the population. It was based on four items: low education level (<10 years of formal education), low income (income from all sources, including interest and dividends, <50% of the median individual income), unemployment (excluding full-time students, those completing military service, and early retirees), and receipt of social welfare. The NDI was used to categorize neighborhood-level deprivation as low (more than one SD below the mean), moderate (within one SD of the mean), and high (more than one SD above the mean) (Winkleby et al., 2007). NDI was measured at the start of follow-up. In the middle of the observation period in 2005, 26% had moved and the most common type of move was from a neighborhood with a low NDI to another neighborhood with a low NDI (50%).

Family- and individual-level sociodemographic variables

The following covariates were measured at the start of follow-up.

Sex: male or female.

Age (4 to 8 years) was modeled as a continuous variable.

Marital status of mother: married/cohabitating vs. never married, widowed, or divorced.

Family income: calculated as annual family income divided by number of people in the family. The family income parameter took into consideration the ages of the family members using a weighted system to assess "consumption" of economic resources, whereby small children were given lower weights than adolescents and adults. The sum of all family members' incomes was multiplied by the individual's consumption weight divided by the family members' total consumption weight. The final variable was calculated as empirical quartiles from the distribution.

Maternal and paternal education levels: categorized as completion of compulsory school or less (≤9 years), practical high school or some theoretical high school (10–11 years), or completion of theoretical high school or college/university (≥12 years).

Child/adolescent, maternal, and paternal country of birth: categorized as Sweden, other Western countries (Western Europe, USA, Canada, Oceania), or other countries.

Region of residence: a large city (Stockholm, Gothenburg, or Malmö), elsewhere in southern Sweden, or northern Sweden.

Mobility: children or adolescents were classified as having "not moved" or "moved" to another neighborhood within five years before the start of the follow-up (January 1, 2000).

Statistical analysis

The age-adjusted inpatient and outpatient incidence rates for internalizing and externalizing psychiatric disorders were calculated for the total population and for each neighborhood deprivation subgroup. Person-years were calculated from the beginning of follow-up until first diagnosis of an internalizing or externalizing psychiatric disorder, death, emigration, or the closing date (December 31, 2010). To estimate the relative contribution of family and neighborhood on individual variation in internalizing and externalizing psychiatric disorders, we used three-level logistic regression with individuals nested within families, which in turn were nested within neighborhoods. This model enabled us to take into account potential influences on total individual variance from two levels. Note that the family level captures both environmental and genetic influences as children that share a family ID are full siblings in most cases, and more rarely half-siblings. Three consecutive models were fitted: an *Empty model* without any fixed effect that partitioned the variance into the three levels of analysis; *Model A*, which included all individual- and family-level variables, enabling us to investigate how much of the variance was due to individual and family sociodemographic factors; and

Model B, which also included NDI, allowing us to investigate whether NDI explained residual variation at the neighborhood level. We replicated all our models using the different subtypes of internalizing and externalizing psychiatric disorders as outcomes. Hence, we performed separate analyses for anxiety disorders (F40-F48 and F93), mood disorders (F30-F39), ADHD (F90), and conduct disorder (F91).

Besides presenting the variance and the corresponding standard error (SE), we also calculated the intra-class correlation (ICC) using the latent variable method (Snijders and Bosker, 1999). This approach assumes that the propensity for the outcome is a continuous latent variable underlying our binary responses. Each individual has a propensity for the outcome, but only persons whose propensity exceeds a certain limit will have the outcome. The unobserved individual variable follows a logistic distribution with individual variance equal to 3.29 ($\pi^2/3$). The ICC is only a function of the area-level variance and does not directly depend on the prevalence of the outcome. The ICC expresses the proportion of the total variation that can be attributed to the specific level of analysis. We present two ICCs: $ICC_{neighborhood}$, calculated as $Variance_{neighborhood}$ / ($Variance_{neighborhood}$ + $Variance_{family}$ + $\pi^2/3$); and ICC_{family}, calculated as $Variance_{family}$ / ($Variance_{neighborhood}$ + $Variance_{family}$ + $\pi^2/3$). We used Markov Chain Monte Carlo (MCMC) techniques in order to estimate the parameters. We stored the results from each step in the iteration procedure (50,000 iterations after a burn-in phase of 5,000 iterations). This gave us a distribution of the parameters of interest and from this distribution we calculated the median and corresponding 95% credible interval (95% CI). The analyses were performed using MLwiN version 2.27 (Rasbash, 2013).

Ethical considerations

The design of this study was approved by the Ethics Committee at Lund University.

Results

In the total study population of 542,195 children and adolescents, 26%, 56%, and 17% lived in low-, moderate- and high-deprivation neighborhoods, respectively. During the follow-up period (January 1, 2000 through December 31, 2010), 26,514 children and adolescents (4.8%) were diagnosed with an internalizing and/or externalizing psychiatric disorder (Table 1). The incidence of internalizing and externalizing psychiatric disorders (per 10,000 person-years) was 38.0 in low-deprivation neighborhoods, 52.9 in moderate-deprivation neighborhoods, and 58.3 in high-deprivation neighborhoods. The incidence of internalizing and externalizing psychiatric disorders increased with increasing neighborhood deprivation regardless of family- or individual-level sociodemographic characteristics, except in immigrants and those with the lowest incomes and lowest parental education levels (Table 1).

Fixed neighborhood effects (aim 1)

The fixed effect of neighborhood-level deprivation was similar for incident externalizing and internalizing psychiatric disorders after adjustment for age, sex, and all other family- and individual-level sociodemographic variables (OR=1.37, 95% CI=1.25–1.50 and OR=1.34, 95% CI=1.25-1.45, respectively; Table 2). Socioeconomic factors appeared to be more strongly associated with externalizing psychiatric disorders than with internalizing psychiatric disorders. Children who had a mother with a low (<9 years) or medium education level (10-11 years) showed a clear significant gradient, with high ORs for externalizing psychiatric disorders (2.17, 95% CI=2.01-2.34 and 1.51, 95% CI=1.42-1.61, respectively), after accounting for sex, family income, country of birth for children and parents, maternal marital status, region of residence, and mobility (Table 2). Children with a single (unmarried, divorced or widowed) parent had higher odds of externalizing psychiatric disorders (OR=1.57, 95% CI=1.50-1.64) than of internalizing psychiatric disorders (OR=1.25, 95%

CI=1.20-1.30). Compared to boys, girls had higher odds of internalizing psychiatric disorders (OR=2.11, 95% CI=2.03-2.19) and lower odds of externalizing psychiatric disorders (OR=0.31, 95% CI=0.29-0.32). Lower ORs for externalizing psychiatric disorders were found in those living in Northern Sweden, and those whose parents were born in Western countries other than Sweden.

After adjustment for individual-level sociodemographic factors, high neighborhood deprivation was associated with 101% higher odds of conduct disorder (OR=2.01, 95% CI=1.58-2.55) and moderate neighborhood deprivation was associated with 50% higher odds of conduct disorder (OR=1.50, 95% CI=1.23-1.84), relative to low deprivation. The strongest association between neighborhood deprivation and ADHD was observed among those living in moderately deprived neighborhoods (OR=1.31, 95% CI=1.19-1.44) compared with those living in neighborhoods with low deprivation. There were also associations between high neighborhood deprivation and anxiety disorders (OR=1.40, 95% CI=1.29-1.52) and mood disorders (OR=1.21, 95% CI=1.09-1.35) (see lower part of Table 4).

Random neighborhood effects (aim 2)

The empty model showed that for internalizing disorders $ICC_{neighborhood}$ was 4.5% while ICC_{family} was more than 6 times higher (29.1%) (Table 3). This indicates that 4.5% of the total individual variance in internalizing disorders could be attributed to the neighborhood level, whereas 29.1% could be attributed to the family level, which includes both genetic and family environmental effects. The corresponding figures for externalizing disorders were 5.5% ($ICC_{neighborhood}$) and 43.5% (ICC_{family}); the variance at the family level was almost 8 times higher than that at the neighborhood level. For both internalizing and externalizing disorders, the variance at the neighborhood level was attenuated by approximately 20% when individual- and family-level variables were included in the model (Table 3, Model A). For

internalizing disorders, the inclusion of individual- and family-level variables actually increased the variance at the family level compared to the empty model. The inclusion of neighborhood characteristics explained only a very small part of the remaining variance at the neighborhood level (Table 3, Model B). The 95% CIs were wide in all models.

For the different subtypes of internalizing and externalizing psychiatric disorders (Table 4), $ICC_{neighborhood}$ in the empty models was highest for conduct disorder (8.9%) and lowest for anxiety disorders (3.6%). ICC_{family} was highest for ADHD and lowest for anxiety disorders. However, precision of the variance parameters for the family level was low.

In an extended analysis we investigated whether the relationship between family income and internalizing and externalizing disorders changed as a function of neighborhood deprivation. To estimate cross-level interaction effects (Aguinis et al., 2013), we first fitted a random slope model with separate slopes for each income group. Then we included the neighborhood deprivation variable and an interaction between individual income and neighborhood deprivation in order to investigate if this interaction actually explained the random slopes included in the model. For both internalizing and externalizing disorders (Table 5, Model A) there was a small random slope parameter for each income group. This means that the effect of income seems to vary to a small extent between different neighborhoods. For internalizing disorders, the random slope terms decrease in Model B compared to Model A (Table 5). The included interaction terms explain a significant part of the small random slopes included in the model. This pattern was not the same for externalizing disorders, where the included interaction terms explained the random slope terms to a small degree only. Furthermore, for both internalizing and externalizing disorders, the interaction term between low income and high neighborhood deprivation seemed to be of considerable effect size and conclusive: the effect of low income was less important in high-deprivation neighborhoods (OR=0.82 and OR=0.69) than in low-deprivation neighborhoods.

Discussion

This national cohort study is the largest study to date to examine potential effects of neighborhood and family on incidence of internalizing and externalizing psychiatric disorders in children and adolescents. After adjustment for individual-level sociodemographic factors, high neighborhood deprivation was associated with an approximately one-third higher risk of internalizing or externalizing psychiatric disorders relative to low neighborhood deprivation. Specifically, high neighborhood deprivation was associated with a 2-fold higher odds of conduct disorder, a 40% higher odds of anxiety disorders, and a 21% higher odds of mood disorders. For ADHD, the strongest association with neighborhood deprivation was observed among children living in moderately (31% higher odds) rather than highly deprived neighborhoods. Although we cannot reliably explain why those children living in moderately deprived neighborhoods had the highest odds of obtaining an ADHD diagnosis, some explanations are plausible, albeit not conclusive. In Sweden, a diagnosis of ADHD in school children allows for additional school resources to that child and it is possible that our results reflect a higher level of empowerment in middle-class parents with better possibilities to argue for a referral and specialist examination of a child with ADHD symptoms.

We also found that familial factors seemed to have a much greater influence on these disorders than neighborhood-level factors, at least at the population level. Familial effects (which include both genetic and family environmental effects) accounted for nearly 6 times as much of the total variation in internalizing disorders, and nearly 8 times as much of the total variation in externalizing disorders, compared with neighborhood-level effects. The strongest individual-level risk factors included having unmarried parents, low parental education levels, and low family income. Compared with boys, girls had 2-fold higher odds of internalizing disorders but less than half the odds of externalizing disorders.

Although previous smaller studies have examined neighborhood and familial effects on psychiatric disorders in children and adolescents, none to our knowledge has examined their relative contributions in a large population-based cohort. Studies of neighborhood effects have varied widely in methodology and adjustment for confounding, but most have suggested significant associations between neighborhood contextual characteristics and psychiatric disorders in children and adolescents. The largest of these was a Swedish national survey of 64,706 school-aged children; that survey reported that residence in neighborhoods with poor physical characteristics or low social capital was associated with increased odds of "depression/anxiety" or "ADHD/disruptive behavior" (Butler et al., 2012). Survey data from the National Comorbidity Survey Replication Adolescent Supplement (NCS-A) study of 10,123 U.S. adolescents also found that neighborhood disadvantage (based on census tracts) was associated with increased risk of emotional disorders, but only in urban settings (Rudolph et al., 2013). The Great Smoky Mountains Study (which included 933 White and 323 Native American children) reported that poverty and family deviance were associated with child psychiatric disorders, but only in White children (Costello et al., 1997). Other cross-sectional studies with small sample sizes have reported evidence for a link between neighborhood deprivation and depression or other psychosocial problems (Reijneveld et al., 2005, Mair et al., 2008). The underlying mechanisms are not well delineated but likely involve multiple contextual factors, including poor social networks, crime, and lack of social capital, which contribute to psychopathology in susceptible individuals (Costello et al., 2003). Several studies have reported that high levels of social capital and cohesion, such as self-reported social trust or participation in neighborhood organizations, may mitigate the effects of neighborhood deprivation on mental health (Costello et al., 1997, Samaan, 2000b, Merikangas et al., 2010a).

We found that familial random effects (including both genetic and family environmental

factors) accounted for 6 to 8 times as much of the total variation in psychiatric disorders, compared with neighborhood random effects. The relative contributions of familial and neighborhood effects have seldom been examined in children and adolescents. However, our estimates were similar to those from a UK study of younger children (2-year-old twins), which suggested that family environment accounted for 20% and neighborhood deprivation 5% of the variation in children's behavior problems (Caspi et al., 2000). A systematic review of 23 studies that examined family relationships in childhood found strong evidence that abusive relationships were associated with depression, anxiety, and post-traumatic stress disorder, and that other forms of parent-child relationship dysfunction such as emotional unresponsiveness were associated with suicide attempts in adolescence (Weich et al., 2009). The potential pathways linking family dysfunction with psychiatric outcomes in childhood and adolescence are complex and likely involve the interplay of genetic factors, educational and socioeconomic factors, and parental psychopathology or substance use. Additional large prospective cohort studies with detailed family relationship data are needed to further delineate these mechanisms and to identify effective interventions at different levels.

The current study has several important strengths. It is the largest population-based cohort study to date of neighborhood and familial effects on incident psychiatric disorders in childhood and adolescence. The use of nationwide outpatient and inpatient diagnoses allowed more complete ascertainment of psychiatric disorders than in previous studies, giving more robust and generalizable results. The availability of data for all Swedish children and adolescents prevented bias that may potentially result from self-reporting, a common concern in survey-based studies. The diagnoses were linked to sociodemographic data that are highly complete for this national population, thus enabling appropriate adjustment for potential confounders. Neighborhoods were defined on the basis of small geographic units with 1000-2000 people, which is generally consistent with how residents define their communities

(Bond Huie, 2001). Neighborhood deprivation was determined using a well-specified principal component analysis based on Swedish national census data, and multilevel modeling was used to distinguish individual-, family-, and neighborhood-level effects.

Limitations include the possibility of residual confounding. Although we adjusted for sociodemographic factors at the individual level, it is possible that unmeasured confounders may account for remaining neighborhood-level associations that we observed. Also, we were unable to examine psychiatric disorders that did not present for treatment. We did not have access to data on health care utilization or specialist care. However, differential access to mental health services according to neighborhood or socioeconomic status is less of a problem in Sweden than in other countries such as the USA because of the Swedish universal health care system. In addition, we were unable to assess "reverse causation", i.e., the possibility that families with psychiatric disorders are more likely to migrate to high-deprivation neighborhoods, so that living in such neighborhoods may be a consequence rather than a cause of psychiatric disorders. Other longitudinal or quasi-experimental studies with longer follow-up and multilevel modeling are needed to evaluate more directly reverse causation. Finally, compared with the USA, lower disparities across Swedish neighborhoods may reduce neighborhood effect sizes and statistical power for detecting significant differences. If it were possible to replicate the current study in the USA, larger neighborhood-level effect sizes are possible given the larger socioeconomic and neighborhood disparities relative to Sweden.

In summary, this large national cohort study found that neighborhood deprivation was independently associated with specific internalizing and externalizing psychiatric disorders in Swedish children and adolescents during 10 years of follow-up. Familial factors (both genetic and environmental) explained a larger part of the individual variance in internalizing and externalizing disorders than neighborhood factors. Although individuals who live in highly

deprived neighborhoods may be strongly affected by their neighborhood environments, these findings may imply that familial factors are more important than neighborhood factors at the population level. Additional prospective studies are needed to elucidate the mechanisms by which neighborhood deprivation and family environment affect mental health in early life and to identify better targets for intervention at multiple levels.

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The funding agencies had no role in the design and conduct of the study; the collection, analysis, and interpretation of the data; or the preparation, review, or approval of the manuscript.

References

Aguinis H, Gottredson RK, Culpepper SA Best-Practice Recommendations for Estimating Cross-Level Interaction Effects Using Multilevel Modeling. Journal of Management 2013; 39:1490-1528.

Araya R, Montgomery A, Rojas G, Fritsch R, Solis J, Signorelli A, et al. Common mental disorders and the built environment in Santiago, Chile. Br J Psychiatry 2007; 190:394-401.

Bond Huie S The concept of neighborhood in health and mortality research. . Sociological Spectrum 2001; 21:341-358.

Butler AM, Kowalkowski M, Jones HA, Raphael JL The relationship of reported neighborhood conditions with child mental health. Acad Pediatr 2012; 12:523-531.

Caspi A, Taylor A, Moffitt TE, Plomin R Neighborhood deprivation affects children's mental health: environmental risks identified in a genetic design. Psychological science 2000; 11:338-342.

Costello EJ, Compton SN, Keeler G, Angold A Relationships between poverty and psychopathology: a natural experiment. Jama 2003; 290:2023-2029.

Costello EJ, Farmer EM, Angold A, Burns BJ, Erkanli A Psychiatric disorders among American Indian and white youth in Appalachia: the Great Smoky Mountains Study. American journal of public health 1997; 87:827-832.

Costello EJ, Keeler GP, Angold A Poverty, race/ethnicity, and psychiatric disorder: a study of rural children. Am J Public Health 2001; 91:1494-1498.

Crump C, Sundquist K, Sundquist J, Winkleby MA Neighborhood deprivation and psychiatric medication prescription: a Swedish national multilevel study. Ann Epidemiol 2011; 21:231-237.

Cubbin C, Sundquist K, Ahlen H, Johansson SE, Winkleby MA, Sundquist J Neighborhood deprivation and cardiovascular disease risk factors: protective and harmful effects. Scand J Public Health 2006; 34:228-237.

Faris RE, Dunham HW Mental disorders in urban areas. An ecological study of schizophrenia and other psychoses 1939; Chicago/London: The Univesity of Chicago Press.

Johnell K, Lindstrom M, Melander A, Sundquist J, Eriksson C, Merlo J Anxiolytic-hypnotic drug use associated with trust, social participation, and the miniaturization of community: a multilevel analysis. Soc Sci Med 2006; 62:1205-1214.

Kessler RC, Avenevoli S, Costello EJ, Georgiades K, Green JG, Gruber MJ, et al. Prevalence, persistence, and sociodemographic correlates of DSM-IV disorders in the National Comorbidity Survey Replication Adolescent Supplement. Arch Gen Psychiatry 2012; 69:372-380.

Kirkbride JB, Morgan C, Fearon P, Dazzan P, Murray RM, Jones PB Neighbourhood-level effects on psychoses: re-examining the role of context. Psychological medicine 2007; 37:1413-1425.

Lofors J, Ramirez-Leon V, Sundquist K Neighbourhood income and anxiety: a study based on random samples of the Swedish population. Eur J Public Health 2006; 16:633-639.

Lofors J, Sundquist K Low-linking social capital as a predictor of mental disorders: a cohort study of 4.5 million Swedes. Soc Sci Med 2007; 64:21-34.

Mair C, Diez Roux AV, Galea S Are neighbourhood characteristics associated with depressive symptoms? A review of evidence. J Epidemiol Community Health 2008; 62:940-946, 948 p following 946.

March D, Hatch SL, Morgan C, Kirkbride JB, Bresnahan M, Fearon P, et al. Psychosis and place. Epidemiologic reviews 2008; 30:84-100.

Merikangas KR, He JP, Brody D, Fisher PW, Bourdon K, Koretz DS Prevalence and treatment of mental disorders among US children in the 2001-2004 NHANES. Pediatrics 2010a; 125:75-81.

Merikangas KR, He JP, Burstein M, Swanson SA, Avenevoli S, Cui L, et al. Lifetime prevalence of mental disorders in U.S. adolescents: results from the National Comorbidity Survey Replication--Adolescent Supplement (NCS-A). J Am Acad Child Adolesc Psychiatry 2010b; 49:980-989.

Rasbash J, Browne, W. J., Healy, M., Cameron, B., Charlton, C. M. J. A User's Guide to MLwiN, v2.27 2013: University of Bristol.

Reijneveld SA, Brugman E, Verhulst FC, Verloove-Vanhorick SP Area deprivation and child psychosocial problems--a national cross-sectional study among school-aged children. Soc Psychiatry Psychiatr Epidemiol 2005; 40:18-23.

Rosen M, Hakulinen T Use of disease registers. In: Handbook of epidemiology, 2005; (Ahrens, W. and Pigeot, I., eds), pp 232-251 Berlin: Springer-Verlag.

Rudolph KE, Stuart EA, Glass TA, Merikangas KR Neighborhood disadvantage in context: the influence of urbanicity on the association between neighborhood disadvantage and adolescent emotional disorders. Soc Psychiatry Psychiatr Epidemiol 2013.

Samaan RA The influences of race, ethnicity, and poverty on the mental health of children. Journal of health care for the poor and underserved 2000a; 11:100-110.

Samaan RA The influences of race, ethnicity, and poverty on the mental health of children. J Health Care Poor Underserved 2000b; 11:100-110.

Snijders T, Bosker R Multilevel analysis. An introduction to basic and advanced multilevel modeling.1999; London: Sage Publications.

Weich S, Holt G, Twigg L, Jones K, Lewis G Geographic variation in the prevalence of common mental disorders in Britain: a multilevel investigation. Am J Epidemiol 2003; 157:730-737.

Weich S, Patterson J, Shaw R, Stewart-Brown S Family relationships in childhood and common psychiatric disorders in later life: systematic review of prospective studies. Br J Psychiatry 2009; 194:392-398.

Weich S, Twigg L, Lewis G, Jones K Geographical variation in rates of common mental disorders in Britain: prospective cohort study. Br J Psychiatry 2005; 187:29-34.

Winkleby M, Sundquist K, Cubbin C Inequities in CHD incidence and case fatality by neighborhood deprivation. Am J Prev Med 2007; 32:97-106.

Table 1. Distribution of population, number of childhood and adolescent internalizing and externalizing psychiatric disorders, and age-standardized incidence (per 10000 person years) by neighborhood-level deprivation

	Population		Events		Neighborhood deprivation		
	No.	%	No.	%	Low	Moderate	High
Total population (%)	542195				145933 (26%)	304758 (56%)	91504 (17%)
Total events			26514		38.0	52.9	58.3
Anxiety disorders (F40-F48, F93)			9192	34.7	13.2	18.5	19.6
Mood disorders (F30-F39)			5754	21.7	8.6	11.9	10.6
Attention deficit hyperactivity disorder (F90)			10625	40.1	15.1	11.9	25.4
Conduct disorder (F91)			943	3.6	1.0	4.4	2.8
Sex							
Male	277543	51.2	13801	52.1	38.6	53.2	62.4
Female	264652	48.8	12713	47.9	37.3	52.6	54.0
Age at diagnosis (years)							
4-6			222	0.8	32.4	49.1	65.4
7-9			2081	7.8	20.6	29.1	33.5
10-12			4781	18.0	24.0	31.7	39.1
13-15			10773	40.6	49.3	73.0	79.4
16-18			8657	32.7	50.2	66.3	69.9
Family income							
Low	135912	25.1	7027	26.5	46.3	58.0	48.3
Middle-low	135695	25.0	7850	29.6	48.5	58.1	72.0
Middle-high	135179	24.9	6662	25.1	40.1	51.2	65.7
High	135409	25.0	4975	18.8	30.7	41.8	59.9
Marital status of mother							
Married/cohabiting	312868	57.7	12512	47.2	33.4	44.6	42.2
Never married, widowed, or divorced	229327	42.3	14002	52.8	46.5	63.0	78.3
Region of residence							
Large cities	271880	50.1	12192	46.0	33.3	52.3	52.6
Southern Sweden	180787	33.3	9976	37.6	47.8	55.5	68.6
Northern Sweden	89528	16.5	4346	16.4	42.7	48.9	58.3
Paternal education level							
≤9 years	97272	17.9	6342	23.9	59.0	70.2	65.3
10–11 years	288809	53.3	14866	56.1	42.3	53.5	60.2
≥12 years	156114	28.8	5306	20.0	29.3	38.3	41.0
Maternal education level							
≤9 years	75374	13.9	5072	19.1	63.8	78.2	59.9

10–11 years	294416	54.3	15292	57.7	41.4	54.4	62.4
≥12 years	172405	31.8	6150	23.2	31.6	38.8	43.6
Country of birth: child							
Sweden	531871	98.1	26142	98.6	38.0	53.0	59.7
Other Western countries	4573	0.8	164	0.6	35.0	40.8	35.6
Other countries	5751	1.1	208	0.8	20.5	43.4	35.3
Country of birth: father							
Sweden	455911	84.1	22733	85.7	37.5	53.1	73.7
Other Western countries	36273	6.7	1796	6.8	44.9	55.6	44.6
Other countries	50011	9.2	1985	7.5	40.5	47.7	36.2
Country of birth: mother							
Sweden	457206	84.3	23139	87.3	38.0	53.8	75.1
Other Western countries	33846	6.2	1542	5.8	38.7	51.2	42.7
Other countries	51143	9.4	1833	6.9	35.7	40.7	33.6
Mobility							
Not moved within the last 5 years	361247	66.6	15789	59.5	34.7	46.2	53.3
Moved within the last 5 years	180948	33.4	10725	40.5	44.1	67.7	66.5

Table 2. Results (fixed effects) from the multilevel logistic models for 542,195 children born in 1992 to 1996 measuring the effects of neighborhood deprivation and individual socioeconomic factors on childhood and adolescent internalizing and externalizing psychiatric disorders		
	Internalizing disorders (Anxiety and mood disorders)	**Externalizing disorders (ADHD and conduct disorder)**
Neighborhood-level deprivation (ref. Low)		
Moderate	1.26 (1.20; 1.34)	1.10 (1.02; 1.17)
High	1.34 (1.25; 1.45)	1.37 (1.25; 1.50)
Age at baseline	1.35 (1.33; 1.37)	0.99 (0.97; 1.00)
Sex: Female (ref. Male)	2.11 (2.03; 2.19)	0.31 (0.29; 0.32)
Family income (ref. High)		
Middle-high	1.18 (1.12; 1.25)	1.21 (1.12; 1.30)
Middle-low	1.27 (1.20; 1.34)	1.39 (1.30; 1.49)
Low	1.15 (1.09; 1.22)	1.19 (1.11; 1.28)
Maternal education level (ref. ≥12 years)		
≤9 years	1.31 (1.23; 1.40)	2.17 (2.01; 2.34)
10–11 years	1.06 (1.01; 1.11)	1.51 (1.42; 1.61)
Paternal education level (ref. ≥12 years)		
≤9 years	1.25 (1.18; 1.33)	2.18 (2.02; 2.35)
10–11 years	1.06 (1.01; 1.10)	1.63 (1.52; 1.74)
Marital status (ref. Married/cohabiting)		
Never married, widowed, or divorced	1.25 (1.20; 1.30)	1.57 (1.50; 1.64)
Country of birth: child (ref. Sweden)		
Other Western countries	0.63 (0.37; 0.78)	0.60 (0.44; 0.81)
Other countries	0.87 (0.71; 1.07)	0.70 (0.53; 0.91)
Country of birth: Mother (ref. Sweden)		
Other Western countries	0.98 (0.90; 1.06)	0.68 (0.60; 0.75)
Other countries	0.76 (0.69; 0.84)	0.50 (0.44; 0.56)
Country of birth: Father (ref. Sweden)		
Other Western countries	1.05 (0.97; 1.14)	0.85 (0.77; 0.94)
Other countries	0.85 (0.77; 0.94)	0.96 (0.85; 1.07)
Region of residence (ref. Large cities)		
Southern Sweden	1.19 (1.14; 1.25)	1.08 (1.02; 1.15)
Northern Sweden	1.00 (0.94; 1.06)	0.87 (0.81; 0.94)
Mobility (ref. Not moved)		
Moved	1.33 (1.28; 1.38)	1.59 (1.52; 1.67)

Numbers are odds ratios (ORs) and 95% credible intervals (CIs)

Table 3. Results (Random effects) from the multilevel logistic models for 542,195 children born in 1992 to 1996 measuring the effects of neighborhood deprivation and individual socioeconomic factors on childhood and adolescent internalizing and externalizing psychiatric disorders

	Internalizing disorders (Anxiety and mood disorders)	Externalizing disorders (ADHD and conduct disorder)
Empty Model		
$Variance_{neighborhood}$	0.221 (0.195; 0.249)	0.357 (0.316; 0.401)
$Variance_{family}$	1.441 (1.254; 1.661)	2.803 (2.500; 3.100)
$ICC_{neighborhood}$	4.5%	5.5%
ICC_{family}	29.1%	43.5%
Model A		
$Variance_{neighborhood}$	0.182 (0.158; 0.209)	0.279 (0.241; 0.319)
$Variance_{family}$	1.511 (1.278; 1.720)	2.654 (2.392; 2.894)
$ICC_{neighborhood}$	3.7%	4.5%
ICC_{family}	30.3%	42.8%
Explained $variance_{neighborhood}$ (vs. Empty Model)	17.6%	21.8%
Explained $variance_{family}$ (vs. Empty Model)	-	5.3%
Model B		
$Variance_{neighborhood}$	0.173 (0.148; 0.209)	0.273 (0.236; 0.312)
$Variance_{family}$	1.527 (1.288; 1.765)	2.716 (2.453; 3.000)
$ICC_{neighborhood}$	3.5%	4.3%
ICC_{family}	30.6%	43.8%
Explained $variance_{neighborhood}$ (vs. Model A)	4.9%	2%
Explained $variance_{family}$ (vs. Model A)	-	-

ICC = Intra-class correlation

Model A: adjusted for age, sex, family income, parental education level, country of birth of children, mother marital status, parental country of birth, region of residence, and mobility.

Model B: Full model, adjusted for the neighborhood-level variable and age, sex, family income, parental education level, country of birth for children, parental marital status, parental country of birth, region of residence, and mobility.

Table 4. Results from the multilevel logistic models for 542,195 children born in 1992 to 1996 measuring the effects of neighborhood-social deprivation and individual socioeconomic factors on childhood and adolescent anxiety disorders, mood disorders, attention deficit hyperactivity disorder, and conduct disorder

	Anxiety disorders (F40-F48, F93)	Mood disorders (F30-F39)	Attention deficit hyperactivity disorder (F90)	Conduct disorder (F91)
Empty Model				
$Variance_{neighborhood}$	0.171 (0.140; 0.204)	0.360 (0.306; 0.420)	0.387 (0.343; 0.437)	0.553 (0.333; 0.790)
$Variance_{family}$	1.273 (0.927; 1.516)	1.728 (1.378; 2.148)	3.043 (2.714; 3.387)	2.348 (0.992; 3.468)
$ICC_{neighborhood}$	3.6%	6.7%	5.8%	8.9%
ICC_{family}	26.9%	32.1%	45.3%	37.9%
Model A				
$Variance_{neighborhood}$	0.139 (0.108; 0.170)	0.285 (0.230; 0.342)	0.320 (0.279; 0.363)	0.412 (0.221; 0.619)
$Variance_{family}$	1.339 (1.100; 1.672)	1.884 (1.486; 2.327)	2.867 (2.552; 3.149)	2.975 (2.376; 3.716)
$ICC_{neighborhood}$	2.9%	5.2%	4.9%	6.2%
ICC_{family}	28.1%	34.5%	44.3%	44.6%
Explained variance (N1)	19%	21%	17%	25%
Explained variance (F1)	-	-	6%	-
Model B				
$Variance_{neighborhood}$	0.126 (0.098; 0.157)	0.282 (0.230; 0.337)	0.309 (0.267; 0.354)	0.382 (0.171; 0.590)
$Variance_{family}$	1.186 (0.998; 1.413)	1.985 (1.687; 2.197)	2.764 (2.545; 3.074)	2.851 (2.127; 3.353)
$ICC_{neighborhood}$	2.7%	5.1%	4.9%	5.9%
ICC_{family}	25.8%	35.7%	43.4%	43.7%
Explained variance (N2)	9%	1%	3%	7%
Explained variance (F2)	11%	-	4%	4%
Neighborhood Deprivation				
High	1.40 (1.29; 1.52)	1.21 (1.09; 1.35)	1.06 (0.99; 1.15)	2.01 (1.58; 2.55)
Moderate	1.29 (1.21; 1.37)	1.21 (1.11; 1.31)	1.31 (1.19; 1.44)	1.50 (1.23; 1.84)
Low	Ref	Ref	Ref	Ref

ICC = Intra-class correlation

Model A: adjusted for age, sex, family income, parental education level, country of birth of children, parental marital status, parental country of birth, region of residence, and mobility.

Model B: Full model, adjusted for the neighborhood-level variable and age, sex, family income, parental education level, country of birth of children, parental marital status, parental country of birth, region of residence, and mobility.

Explained variance (N1): Explained variance at the neighborhood level (Empty model vs. Model A)

Explained variance (F1): Explained variance at the family level (Empty model vs. Model A)

Explained variance (N2): Explained variance at the neighborhood level (Model A vs. Model B)

Explained variance (F2): Explained variance at the family level (Model A vs. Model B)

Table 5. Results (fixed and random effects) from multilevel logistic models including random slope term for individual income and interaction effects between neighborhood deprivation and family income

	Internalizing disorders (Anxiety and mood disorders)	Externalizing disorders (ADHD and conduct disorder)
Model A		
$Variance_{neighborhood}$	0.287 (0.219; 0.368)	0.225 (0.180; 0.291)
Random slope (Low income)	0.052 (0.007; 0.125)	0.022 (0.008; 0.059)
Random slope (Middle-low income)	0.045 (0.045; 0.120)	0.046 (0.020; 0.080)
Random slope (Middle-high income)	0.045 (0.020; 0.011)	0.032 (0.180; 0.050)
Model B		
$Variance_{neighborhood}$	0.229 (0.192; 0.273)	0.253 (0.197; 0.303)
Random slope (Low income)	0.022 (0.009; 0.045)	0.029 (0.014; 0.050)
Random slope (Middle-low income)	0.029 (0.016; 0.076)	0.024 (0.010; 0.083)
Random slope (Middle-high income)	0.001 (0.000; 0.002)	0.027 (0.006; 0.078)
Interaction Terms (odds ratio and 95% CI)		
Low income*Moderate neighborhood deprivation	0.89 (0.87; 1.17)	1.00 (0.84; 1.19)
Middle-low income*Moderate neighborhood deprivation	0.63 (0.52; 0.77)	0.96 (0.82; 1.13)
Middle-high income*Moderate neighborhood deprivation	0.95 (0.84; 1.08)	1.00 (0.85; 1.16)
Low income*High neighborhood deprivation	0.82 (0.68; 0.99)	0.69 (0.54; 0.87)
Middle-low income*High neighborhood deprivation	1.02 (0.90; 1.15)	0.91 (0.72; 1.16)
Middle-high income*High neighborhood deprivation	0.84 (0.68; 1.03)	1.04 (0.82; 1.32)

Model A: adjusted for age, sex, family income, parental education level, country of birth of children, parental marital status, parental country of birth, region of residence, and mobility.
Model B: adjusted for the neighborhood-level variable and age, sex, family income, parental education level, country of birth of children, parental marital status, parental country of birth, region of residence, mobility, and the interaction terms between Income and neighborhood deprivation.