Psychological Medicine

cambridge.org/psm

Cumulative environmental risk in early life is associated with mental disorders in childhood

Kirstie O'Hare[1], Oliver Watkeys[1], Tyson Whitten[1,2], Kimberlie Dean[1,3], Kristin R. Laurens[1,4], Felicity Harris[1], Vaughan J. Carr[1,5,6] and Melissa J. Green[1,5]

[1]Discipline of Psychiatry and Mental Health, University of New South Wales, Sydney, Australia; [2]School of Social Sciences, University of Adelaide, Adelaide, South Australia, Australia; [3]Justice Health and Forensic Mental Health Network, Sydney, New South Wales, Australia; [4]School of Psychology and Counselling, Queensland University of Technology (QUT), Brisbane, Australia; [5]Neuroscience Research Australia, Sydney, Australia and [6]Department of Psychiatry, Monash University, Melbourne, Australia

Original Article

Cite this article: O'Hare K, Watkeys O, Whitten T, Dean K, Laurens KR, Harris F, Carr VJ, Green MJ (2023). Cumulative environmental risk in early life is associated with mental disorders in childhood. *Psychological Medicine* **53**, 4762–4771. https://doi.org/10.1017/S0033291722001702

Received: 1 February 2022
Revised: 3 May 2022
Accepted: 20 May 2022
First published online: 22 July 2022

Key words:
Cumulative risk; early childhood; environmental risk score; mental illness; record linkage

Author for correspondence:
Melissa J. Green,
E-mail: melissa.green@unsw.edu.au

Abstract

Background. No single environmental factor is a necessary or sufficient cause of mental disorder; multifactorial and transdiagnostic approaches are needed to understand the impact of the environment on the development of mental disorders across the life course.

Method. Using linked multi-agency administrative data for 71 932 children from the New South Wales Child Developmental Study, using logistic regression, we examined associations between 16 environmental risk factors in early life (prenatal period to <6 years of age) and later diagnoses of mental disorder recorded in health service data (from age 6 to 13 years), both individually and summed as an environmental risk score (ERS).

Results. The ERS was associated with all types of mental disorder diagnoses in a dose–response fashion, such that 2.8% of children with no exposure to any of the environmental factors (ERS = 0), compared to 18.3% of children with an ERS of 8 or more indicating exposure to 8 or more environmental factors (ERS $\geqslant$ 8), had been diagnosed with any type of mental disorder up to age 13–14 years. Thirteen of the 16 environmental factors measured (including prenatal factors, neighbourhood characteristics and more proximal experiences of trauma or neglect) were positively associated with at least one category of mental disorder.

Conclusion. Exposure to cumulative environmental risk factors in early life is associated with an increased likelihood of presenting to health services in childhood for any kind of mental disorder. In many instances, these factors are preventable or capable of mitigation by appropriate public policy settings.

Introduction

The emergence of mental disorders in childhood is strongly associated with adverse events occurring in the prenatal period and early life (Bale et al., 2010), childhood maltreatment and trauma (Carr, Duff, & Craddock, 2018; Green et al., 2020), and adverse neighbourhood circumstances during development (Curtis et al., 2013). While most research in this area has focused on relationships between single environmental factors and single mental disorders (Guloksuz, van Os, & Rutten, 2018; Uher & Zwicker, 2017), no one risk factor is a necessary or sufficient cause of the mental disorder, and risk factors commonly co-occur (Evans, Li, & Whipple, 2013). Further, as with genetic risk factors, environmental risk factors appear to be pleiotropic, such that the same environmental factors are associated with many different types of mental disorders (Guloksuz et al., 2018). Multifactorial and transdiagnostic approaches are therefore needed to understand the impact of the environment on the development of mental disorders (Uher & Zwicker, 2017).

One approach for understanding the impact of multiple environmental risks is the use of *cumulative risk models*, which posit that developmental outcomes are better predicted by an accumulation of different risk factors, rather than a single risk factor (Evans et al., 2013). That is, the type or severity of risk experienced is less important than the absolute number of risks (Sameroff, 2006). This can be operationalised by summing binary measures of environmental exposures into a cumulative *environmental risk score* (ERS). This approach is similar to research on *adverse childhood experiences* (ACEs), where the number of childhood experiences of trauma or neglect an individual has experienced are often summed into a singular score (Hughes et al., 2017). However, proximal exposures of trauma and neglect are not the only environmental exposures to act cumulatively. There is also evidence that prenatal exposures act cumulatively to predict childhood psychopathology (Roffman et al., 2021), as do neighbourhood risk factors (Theall, Drury, & Shirtcliff, 2012). It is therefore important to understand the cumulative impacts of a range of both proximal (direct) and distal (indirect) risk factors that commonly co-occur, and which may be causally linked or reflect shared

background factors (e.g. both maternal complications and childhood victimisation are more common in individuals from socioeconomically deprived areas; Fisher et al., 2015; Kim et al., 2018). Further, the impact of both proximal and distal risk factors may be mediated through the same or similar biological pathways (e.g. dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis; Bunea, Szentágotai-Tătar, and Miu, 2017).

Recently, there has been a surge of interest in using ERSs to examine their association with psychotic disorders, both to enhance risk prediction (e.g. Cannon et al., 2016; Carrión et al., 2016; Moore et al., 2021; Padmanabhan, Shah, Tandon, & Keshavan, 2017) and to help understand the impact of the environment on the development of psychotic disorders (e.g. Guloksuz et al., 2019; Mas et al., 2020; Pries et al., 2018). However, there has been less research on other types of mental disorders. Older developmental theories assumed specific risks lead to specific outcomes, but recent evidence suggests that environmental factors are largely non-specific (Uher & Zwicker, 2017). Indeed, transdiagnostic models of psychopathology have become increasingly favoured, as they focus on processes underlying multiple disorders, which can help explain comorbidity between disorders and heterotypic continuity of mental disorders across the life course (Nolen-Hoeksema & Watkins, 2011).

Development during early childhood may be particularly susceptible to the impact of environmental factors (Appleyard, Egeland, van Dulmen, & Sroufe, 2005), given their capacity to influence vulnerability to the effects of further environmental exposures later in life (i.e. environment-environment interactions; Cicchetti, 2010; Rutten et al., 2013). For example, exposure to maltreatment in childhood appears to sensitise individuals to the effects of stressful life events in adulthood (McLaughlin, Conron, Koenen, & Gilman, 2010; Starr, Hammen, Conway, Raposa, & Brennan, 2014). With the majority of adult mental disorders preceded by childhood mental disorders (Kim-Cohen et al., 2003), early and middle childhood represent key developmental periods in which efforts to prevent adverse environmental exposures may have a greater impact by preventing a cascade of effects with potentially lifelong consequences.

The aim of the current study was to examine the relationship between environmental risk factors in early life (before 6 years of age) and health service contact for mental disorders emerging in childhood (from age 6–13 years). In a sample of 71 932 Australian children, we used record linkage data to test associations between both individual and, via calculation of an ERS, cumulative environmental risk factors and the full range of childhood mental disorder diagnoses. We hypothesised that the ERS would be associated with an increased likelihood of all categories of mental disorders measured; phobias and anxiety, depressive disorders and emotional disorders of childhood, stress reactions, hyperkinetic disorders, conduct disorders, developmental disorders (including autism spectrum disorders), and self-harm.

Method

Study setting and record linkage

Data were drawn from Wave 2 of the New South Wales Child Developmental Study (NSW-CDS; https://nsw-cds.com.au), a longitudinal, multi-agency, population-based record linkage study (Carr et al., 2016; Green et al., 2018). The NSW-CDS Wave 2 linkage was conducted in 2016 for 91 635 children and their parents, encompassing 99.7% of children entering full-time schooling in NSW (Australia) in 2009 (at around age 5 years). Parental records were available for 72 245 children who had births registered in NSW. Record linkage was conducted by the Centre for Health Record Linkage (CHeReL; http://www.cherel.org.au/) using probabilistic record linkage methods, with an estimated false-positive linkage rate of <0.5% (Green et al., 2018). Ethical approval was obtained from the NSW Population and Health Research Ethics Committee (HREC/15/CIPHS/21).

Participants

Participants were 71 932 children (78.4% of the total cohort) who had complete data available on relevant indices drawn from administrative databases, including linked maternal records for children with births registered in NSW.

Measures

Childhood mental disorders (from age 6–13 years)

Childhood mental disorders diagnosed between 6 and 13 years were defined by the International Classification of Disease, revision 10 (ICD-10), Australian modification codes. ICD-10 codes were recorded when children accessed services within the state of NSW between 2010 and 2016 in either the NSW Ministry of Health's Mental Health Ambulatory (community-based or outpatient mental health services), the Admitted Patient Data Collection (both public and private hospital admissions), or the Emergency Department Data Collection. Indices were created for any mental disorder diagnosis and for the specific categories of phobias and anxiety (e.g. social phobia, generalised anxiety disorder), depressive disorders and emotional disorders of childhood (e.g. major depressive disorders, separation anxiety, school refusal), stress reactions (e.g. PTSD, adjustment disorders), hyperkinetic disorders (e.g. ADHD), conduct disorders, developmental disorders (e.g. autism spectrum and unspecified developmental disorders), and self-harm (see online Supplementary Materials for specific ICD-10 codes included in each category). Each disorder category was dichotomised as a binary variable, but categories were not mutually exclusive (i.e. multiple diagnoses across specific mental disorder categories were possible).

Environmental exposures (before 6 years of age)

Environmental factors were largely selected based on a review of factors included in previous ERSs, which have primarily been constructed for examination in association with psychosis, to date. Factors unavailable in the NSW-CDS, that were not relevant in the Australian context – such as season of birth, which is not consistently associated with mental disorders in Southern Hemisphere countries (McGrath & Welham, 1999) – or factors that were not relevant to the age group (e.g. substance use) were not included. Additional variables that were uniquely relevant to the Australian context (Aboriginal and/or Torres Strait Islander status) or that had not been included in previous ERSs despite links to mental disorders (e.g. parental criminal offending; Lee, Fang, and Luo, 2013) were also included in the ERS. All environmental factors selected had previous evidence of association with at least one type of mental disorder.

Child protection contact. Child protection contact was determined from data in the NSW Department of Communities and Justice Case Management System – Key Information Directory System. The case management system includes records of both

https://doi.org/10.1017/S0033291722001702 Published online by Cambridge University Press

substantiated and non-substantiated reports (i.e. reports that were judged to meet an internal threshold for risk-of-significant harm; ROSH), as well as reports that were determined not to meet this ROSH threshold, and reports that resulted in the child entering out-of-home care. In the present study, child protection contact was defined as any type of report of child protection contact recorded from 2003 to 2009.

Parental criminal offending. An indicator for any parental criminal offending between 2003 and 2009 was derived using data from the NSW Bureau of Crime Statistics and Research (BOCSAR) Reoffending dataset. The BOCSAR database includes data on all matters where there has been a determination of guilty or not guilty handled by the NSW Criminal Justice System for individuals with at least one conviction. Offending was defined as a criminal offence of any type (including violent, non-violent, and minor offences), as per the Australian and New Zealand Standard Offence Classification (Australian Bureau of Statistics, 2018) that was determined to be proven by the NSW courts.

Childhood crime victimisation. Crime victimisation was derived from data from the NSW Police Force Computerised Operational Policing System (COPS). These data include records of all criminal and non-criminal *incidents* and *events* that are reported to or detected by the NSW police. The type of contact is classified by NSW police staff as either victim, person of interest, or witness. An indicator was created for any child who experienced police contact as a victim of any type of criminal incident between 2003 and 2009.

Head injury. An indicator for any head injury that occurred between 2003 and 2009 was created using data from the NSW Ministry of Health's Admitted Patients and Emergency Department Data Collections. Head injuries were identified using ICD-10 codes S00-S09.

Socioeconomic deprivation. Deprivation was measured using the Socio-economic Indexes for Areas, Index for Relative Socio-economic Disadvantage (SEIFA-IRSD) developed by the Australian Bureau of Statistics (Pink, 2013), and based on the child's home postcode at birth, as recorded in the NSW Ministry of Health's Perinatal Data Collection. A binary indicatory of disadvantage was defined as membership in the bottom quintile of the SEIFA-IRSD.

Regionality. Regionality was determined using the Accessibility and Remoteness Index for Australia [ARIA; Department of Health and Aged Care (Australian Government), 2001], a continuous variable which can be designated into 5 quintiles. Regionality was defined by membership in quintiles 2–5 (inner regional-very remote) *v.* quintile 1 (major city), based on the child's home postcode at birth.

Neighbourhood crime. Crime rates were derived from open data from the NSW BOSCAR (NSW Bureau of Crime Statistics & Research, 2020) database. Using each child's postcode at birth, we calculated the annual number of crimes, inclusive of all offence categories, for each postcode for the year 2004 (being the modal birth year for the cohort). Neighbourhood crime rates were then calculated as the number of criminal incidents per 1000 people, relative to the population in that postcode according to the 2006 census (Australian Bureau of Statistics, 2006). A binary indicator of high neighbourhood crime was derived from membership in the top quintile of crime rate.

Aboriginal and/or Torres Strait Islander status. An indicator for Aboriginal and/or Torres Strait Islander status was determined on the basis of either the child or their parent(s) being designated as of Aboriginal and/or Torres Strait Islander descent in any record in the NSW-CDS collection. We note that Aboriginal and/or Torres Strait status is not *inherently* a risk factor but, rather, was included here as a covariate to provide a proxy measure of exposure to adversities caused by systemic racism and disadvantage (Paradies, 2018).

Perinatal factors. Indicators for six perinatal factors were determined from data recorded in the NSW Ministry of Health's Perinatal Data Collection. The factors were: obstetric and pregnancy complications (any history of maternal diabetes, gestational diabetes, hypertension, or pre-eclampsia); any maternal smoking during pregnancy; 3 or more previous pregnancies; pre-term birth (<37 weeks gestation), low birth weight for gestational age (defined as <10th percentile; Dobbins, Sullivan, Roberts, and Simpson, 2012) and no (or late; >16 weeks) antenatal visits.

Paternal and maternal Age. Data from the NSW Registry of Births, Deaths and Marriages were used to determine paternal and maternal age at the time of their child's birth. Two indicators were calculated of (1) Advanced paternal age (⩾40 years at the day of their child's birth), and (2) Young maternal age (⩽21 years at the day of their child's birth).

Data analysis and ERS calculation

Unadjusted associations between each risk exposure and each childhood mental disorder (relative to children without any mental disorder) were calculated using binary logistic regression. The majority of environmental factors were not associated with child sex (online Supplementary Table S2) so sex was not included as a covariate in analyses. Environmental risk factors were selected to be included in the ERS based on significant, positive associations with at least one mental disorder (or 'any mental disorder'), excluding variables that had *both* positive and negative associations with different mental disorders. An ERS was calculated for each child, representing the total number of environmental risk exposures the child experienced. The association between the ERS and each mental disorder was then calculated via binary logistic regression. Figures were generated using the ggplot2 package (Wickham, 2016).

Statistical analyses were performed in RStudio version 1.3.1093 using R version 4.0.3.

Results

Descriptive data for the cohort are summarised in Table 1. The mean age of the child cohort was 13.2 years (S.D. = 0.4 years),

https://doi.org/10.1017/S0033291722001702 Published online by Cambridge University Press

Table 1. Prevalence of mental disorders, environmental risk factors, and environmental risk score

Characteristic	Number of children
Total number of children	71 932
Sex (Male)	37 206 (51.2%)
Mental disorders	
Any mental disorder	2843 (4.0%)
Phobias and anxiety	699 (1.0%)
Depressive and emotional disorders	218 (0.3%)
Stress reactions	158 (0.2%)
Hyperkinetic disorders	177 (0.3%)
Conduct disorders	229 (0.3%)
Developmental disorders	383 (0.5%)
Self-harm	98 (0.2%)
Environmental risk factors	**Number of children exposed**
Child protection contact	12 359 (17.2%)
Parental criminal offending	11 982 (16.7%)
Childhood crime victimisation	2050 (2.8%)
Head injury	3155 (4.4%)
Socioeconomic deprivation	13 578 (18.9%)
Regionality	15 623 (21.7%)
Neighbourhood crime exposure	13 695 (19.0%)
Aboriginal and/or Torres Strait Islander Status	5103 (7.1%)
Advanced paternal age (>40 years)	9793 (13.6%)
Young maternal age (<21 years)	3883 (5.4%)
3 or more prior pregnancies	6018 (8.4%)
Premature birth	4526 (6.3%)
Small for gestational age	7877 (11.0%)
No/late (>16 weeks) antenatal visit	16 779 (23.3%)
Maternal prenatal complications	7838 (10.9%)
Maternal smoking during pregnancy	9714 (13.5%)
Environmental risk score	**Number of children**
0	23 150 (32.2%)
1	21 967 (30.5%)
2	13 151 (18.3%)
3	6790 (9.4%)
4	3617 (5.0%)
5	1827 (2.5%)
6	937 (1.3%)
7	400 (0.6%)
8–10	153 (0.2%)

and the mean age of children (who had a diagnosis of any mental disorder) at their first mental health system contact was 6.7 years (S.D. = 3.7 years).

Associations between environmental exposures and childhood mental disorders

All environmental factors showed significant positive associations with at least one mental disorder, except for advanced paternal age which was not associated with any type of mental disorder (Table 2). Two factors – regionality and no/late antenatal visits – had both positive and negative associations with different mental disorders and were therefore not included in the ERS calculation. Regionality was positively associated with any mental disorder, phobias and anxiety, stress reactions, and self-harm but negatively associated with hyperkinetic disorders (i.e. children living in urban environments were at greater likelihood of health service contact for hyperkinetic disorders compared to children living in rural/remote environments). No/late antenatal visits were positively associated with conduct disorders but negatively associated with phobias and anxiety and emotional disorders (i.e. children whose mothers had had no [or late] antenatal visits were *less* likely to be diagnosed with a phobia/anxiety or emotional disorder).

Associations between ERS and childhood mental disorders

Of the 16 environmental risk factors examined, 13 were summed into an ERS (excluding advanced paternal age, regionality, and no/late antenatal visits). The median ERS score was 1 (IQR = 2; range 0–10). The ERS was associated with all types of mental disorders (see Table 3), and the pattern of associations reflected a dose–response relationship between the number of environmental exposures (higher ERS) and a greater likelihood of mental disorder diagnoses (Fig. 1). Among children with an ERS of zero, only 2.8% had a diagnosis of a mental disorder, while 18.3% of children with an ERS of eight or more had a mental disorder diagnosis. Of the specific mental disorders, the ERS had the strongest association with stress reactions (OR 1.50, 95% CI 1.35–1.54) and self-harm (OR 1.47, 95% CI 1.37–1.58), and the weakest association with phobias and anxiety (OR 1.19, 95% CI 1.15–1.24). The patterns of association between the ERS and specific mental disorder diagnoses were also dose–response in form (Fig. 2), though the proportion of children with phobias and anxiety, and emotional disorders, was slightly lower for children with an ERS of 6+ than children with an ERS of 5.

Discussion

In this study of 71 932 Australian children, a cumulative ERS comprised of traumatic life events, prenatal adversities, and adverse neighbourhood features experienced before age 6 years, was associated with all types of childhood mental disorder diagnoses between the ages of 6 to 13 years. Effect sizes for the associations with the ERS were similar in magnitude across all of the 7 mental disorder categories measured, ranging from children having a 1.19 increase in odds of phobias and anxiety disorders per 1 point increase in ERS, to a 1.50 increase in odds of stress reactions per 1 point increase in ERS. Risk of the mental disorder increased in a dose–response fashion with increases in ERS, such that 18.3% of children with an ERS of ⩾8 had a diagnosed mental disorder compared to 2.8% of children with an ERS of zero.

All environmental risk factors tested were associated with at least one type of mental disorder, excepting advanced paternal age. The latter was unexpected given that past research has found a link between advanced paternal age and psychiatric

https://doi.org/10.1017/S0033291722001702 Published online by Cambridge University Press

Table 2. Unadjusted ORs (95% CIs) for the association between childhood mental disorders and each environmental risk exposure

Risk exposure	Any mental disorder	Phobias and anxiety	Emotional disorders	Stress reactions	Hyperkinetic disorders	Conduct disorders	Developmental disorders	Self-harm
Child protection contact	**3.46 (3.20–3.74)**	**2.41 (2.04–2.82)**	**3.81 (2.91–4.98)**	**5.94 (4.34–8.15)**	**4.58 (3.41–6.16)**	**5.74 (4.43–7.46)**	**2.99 (2.43–3.68)**	**6.19 (4.16–9.27)**
Parental criminal offending	**1.77 (1.62–1.92)**	**1.43 (1.19–1.71)**	**1.69 (1.23–2.28)**	**2.39 (1.70–3.32)**	**1.92 (1.37–2.65)**	**2.26 (1.69–2.97)**	1.12 (0.86–1.44)	**1.62 (1.00–2.53)**
Childhood crime victimisation	**3.71 (3.23–4.24)**	**2.73 (2.02–3.60)**	**3.08 (1.84–4.86)**	**5.27 (3.23–8.17)**	**3.64 (2.13–5.84)**	**5.40 (3.62–7.79)**	**2.82 (1.88–4.05)**	**5.71 (3.10–9.74)**
Head injury	**1.47 (1.26–1.72)**	1.32 (0.95–1.80)	0.83 (0.38–1.57)	1.32 (0.62–2.44)	**2.63 (1.58–4.13)**	**1.98 (1.19–3.08)**	**1.79 (1.20–2.57)**	**3.34 (1.78–5.78)**
Socioeconomic deprivation	0.98 (0.89–1.08)	0.91 (0.74–1.10)	0.79 (0.54–1.13)	**1.56 (1.08–2.20)**	1.18 (0.81–1.66)	1.23 (0.89–1.67)	**1.48 (1.17–1.86)**	1.55 (0.97–2.40)
Regionality	**1.22 (1.12–1.33)**	**1.36 (1.15–1.60)**	1.10 (0.80–1.50)	**1.72 (1.22–2.39)**	*0.65 (0.42–0.96)*	0.93 (0.67–1.27)	0.97 (0.75–1.23)	**1.67 (1.08–2.53)**
Neighbourhood crime exposure	**1.10 (1.00–1.21)**	0.98 (0.81–1.18)	1.05 (0.74–1.44)	1.21 (0.82–1.74)	1.41 (0.99–1.96)	1.25 (0.91–1.69)	1.18 (0.92–1.49)	1.38 (0.85–2.15)
Aboriginal and/or Torres Strait Islander Status	**2.11 (1.88–2.36)**	**1.37 (1.05–1.75)**	**2.10 (1.40–3.03)**	**2.59 (1.66–3.87)**	**2.16 (1.38–3.24)**	**2.06 (1.38–2.96)**	**1.57 (1.12–2.15)**	**3.37 (2.00–5.39)**
Advanced paternal age (>40 years)	1.09 (0.98–1.21)	1.23 (0.99–1.49)	1.13 (0.77–1.62)	0.82 (0.48–1.30)	1.04 (0.67–1.56)	1.15 (0.79–1.62)	1.16 (0.87–1.51)	1.06 (0.58–1.80)
Young maternal age (<21 years)	**2.05 (1.80–2.32)**	**1.47 (1.10–1.93)**	1.58 (0.94–2.49)	**2.70 (1.65–4.17)**	**2.37 (1.46–3.65)**	**2.65 (1.77–3.84)**	**1.60 (1.09–2.27)**	**4.51 (2.69–7.23)**
3 or more prior pregnancies	**1.23 (1.08–1.39)**	1.01 (0.76–1.31)	0.99 (0.59–1.55)	1.50 (0.90–2.36)	1.24 (0.74–1.96)	1.34 (0.86–2.00)	1.24 (0.88–1.71)	0.59 (0.21–1.30)
Premature birth	**1.28 (1.11–1.46)**	1.15 (0.85–1.52)	1.10 (0.62–1.80)	0.69 (0.29–1.36)	0.99 (0.50–1.73)	1.59 (0.99–2.41)	**1.89 (1.36–2.57)**	1.32 (0.59–2.56)
Small for gestational age	**1.46 (1.31–1.62)**	1.25 (0.99–1.55)	1.05 (0.68–1.57)	1.53 (0.98–2.30)	**2.23 (1.54–3.16)**	1.18 (0.78–1.71)	**2.06 (1.59–2.63)**	1.47 (0.82–2.47)
No/late (>16 weeks) antenatal visit	1.02 (0.93–1.11)	*0.81 (0.67–0.97)*	*0.61 (0.41–0.86)*	1.08 (0.74–1.53)	1.22 (0.87–1.69)	**1.39 (1.04–1.84)**	1.19 (0.95–1.49)	1.19 (0.74–1.83)
Maternal prenatal complications	1.06 (0.94–1.19)	1.24 (0.99–1.54)	1.06 (0.68–1.58)	1.25 (0.77–1.94)	0.93 (0.55–1.47)	1.05 (0.68–1.55)	**1.58 (1.20–2.06)**	1.72 (0.98–2.82)
Maternal smoking during pregnancy	**1.93 (1.77–2.12)**	**1.32 (1.08–1.60)**	**1.72 (1.23–2.36)**	**2.25 (1.56–3.18)**	**2.53 (1.81–3.49)**	**2.72 (2.03–3.59)**	**1.83 (1.43–2.32)**	**3.26 (2.12–4.92)**

Note: ORs, Odds ratio; 95% CIs, 95% confidence interval. Bold indicates significant values (i.e. 95% CI not inclusive of 1). Italics indicates significant effect in the protective direction.

Table 3. Unadjusted ORs (95% CIs) for the association of environmental risk score with childhood mental disorders

Mental disorder	Association with ERS	R^2
Any mental disorder	**1.30 (1.27–1.32)**	0.027
Phobias and anxiety	**1.19 (1.15–1.24)**	0.008
Emotional disorders	**1.25 (1.17–1.33)**	0.012
Stress reactions	**1.50 (1.35–1.54)**	0.045
Hyperkinetic disorders	**1.36 (1.26–1.46)**	0.023
Conduct disorders	**1.39 (1.31–1.48)**	0.028
Developmental disorders	**1.30 (1.24–1.37)**	0.018
Self-harm	**1.47 (1.37–1.58)**	0.039

Note: ORs, Odds ratio; 95% CIs, 95% confidence interval. R^2, Nagelkerke Pseudo R^2; Bold indicates significant values (i.e. 95% CI not inclusive of 1).

disorders in offspring (de Kluiver, Buizer-Voskamp, Dolan, & Boomsma, 2017). The mechanism for this relationship is not well understood and may reflect genetic (e.g. *de novo* mutations, epigenetic changes) and/or environmental or social factors that are associated with delayed parenthood (de Kluiver et al., 2017). There may be factors specific to the current study, including the early offspring developmental period being considered or other factors unable to be measured (e.g. parenting style differences), that mitigate or mask the effects of advanced paternal age. Of the 16 environmental risk factors examined, four were associated with all types of mental disorders: child protection contact, childhood crime victimisation, Aboriginal and/or Torres Strait Islander status, and maternal smoking. Two risk factors [no (or late) antenatal visits, and regionality] had both negative and positive relationships with specific disorders. Interestingly, regionality had a protective association with hyperkinetic disorders (i.e. children born in urban environments were more likely to have been diagnosed with a hyperkinetic disorder), consistent with previous evidence of children in urban environments having increased rates of diagnoses of ADHD (Madsen, Ersbøll, Olsen, Parner, & Obel, 2015); however, this may reflect easier access to services to receive a diagnosis rather than the increased prevalence of the disorder among urban children. Further, children whose mothers attended no (or late) antenatal visits were *less* likely to be diagnosed with a phobia or anxiety disorder, or an emotional disorder. This could reflect levels of parental engagement with the health system, with those parents who were less likely to attend antenatal visits also being less engaged with child health services. This effect was more pronounced for internalising disorders which typically

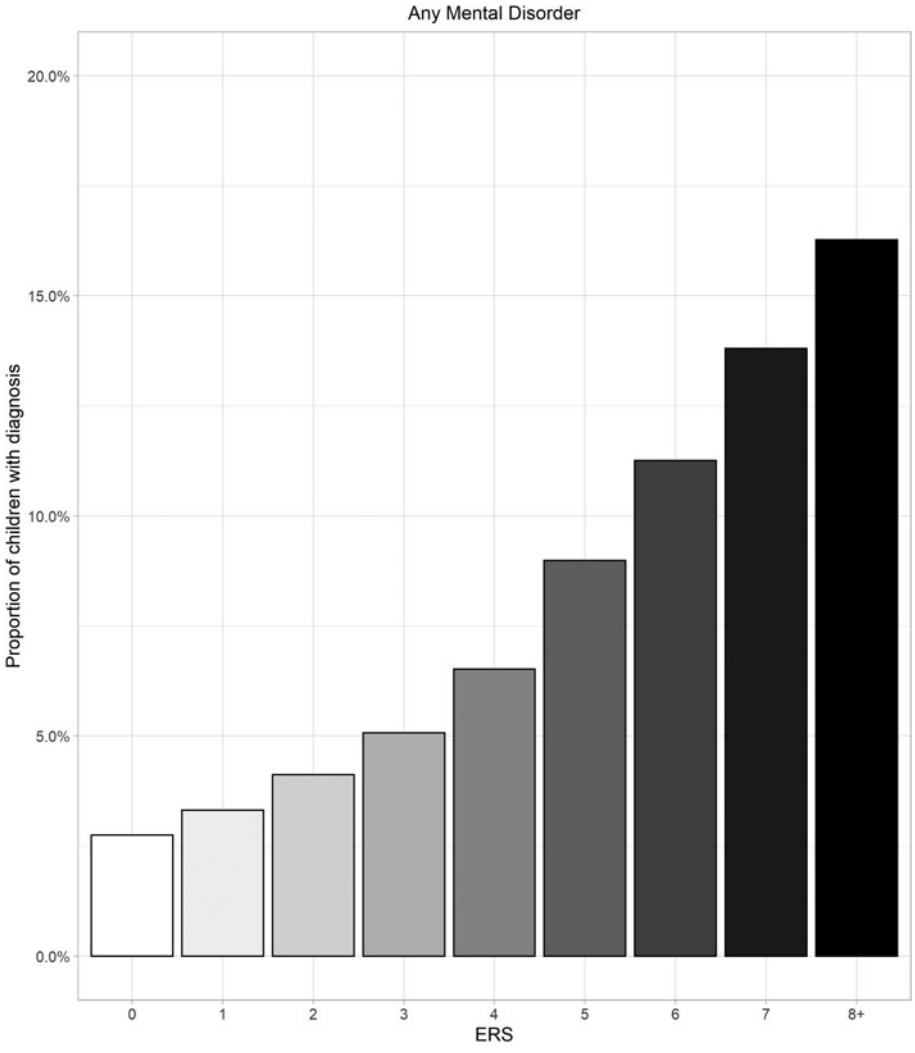

Fig. 1. Proportion of children with any diagnosis of mental disorder by environmental risk score (ERS).

https://doi.org/10.1017/S0033291722001702 Published online by Cambridge University Press

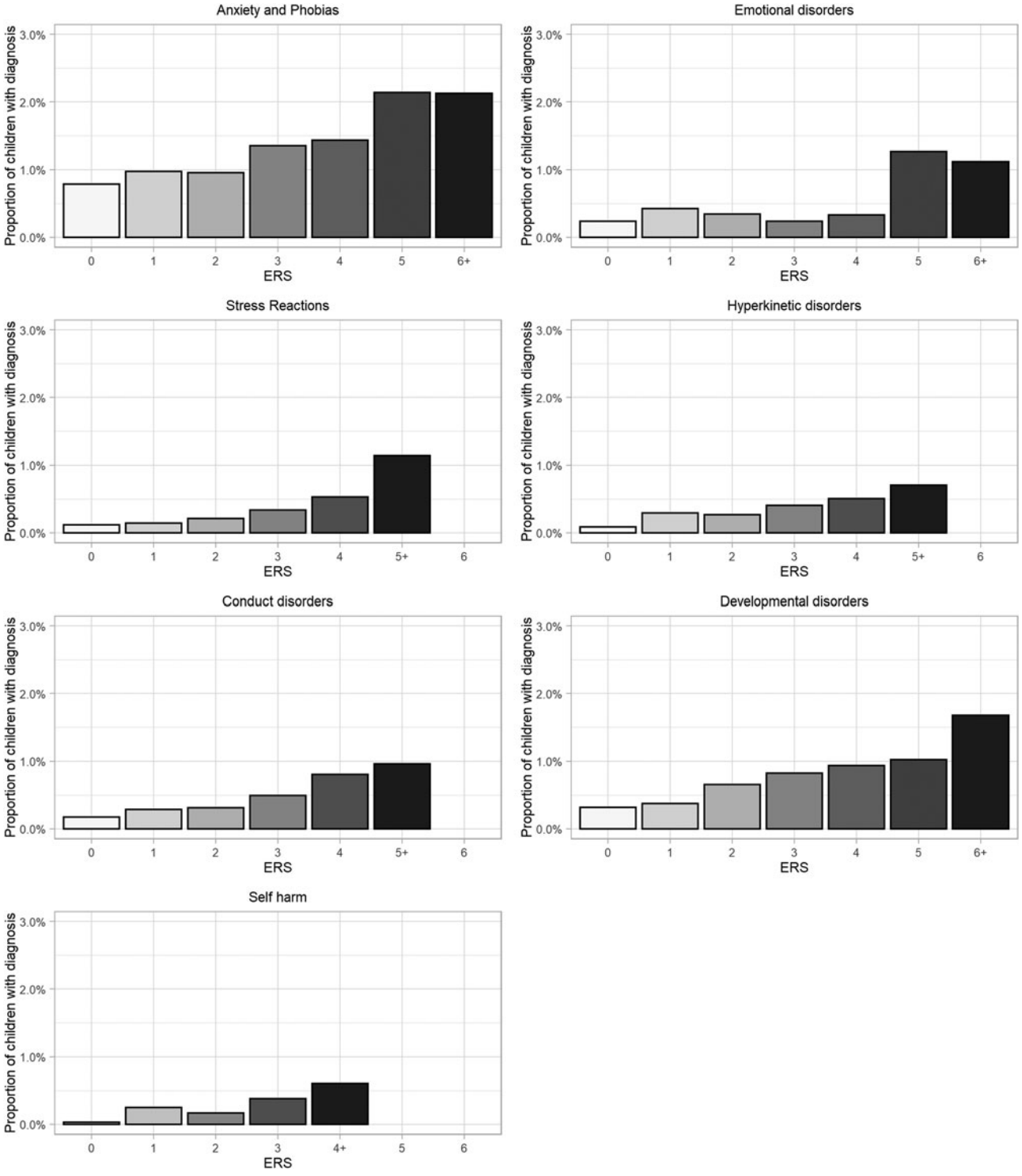

Fig. 2. Proportion of children with specific diagnoses by environmental risk score (ERS). ERSs are categorised as to avoid display of small cell sizes (i.e. <15).

have less overt symptoms and may be more likely to remain underdiagnosed.

When early life environmental factors were summed into an ERS, significant associations were evident with both a global index of 'any type' of mental disorder diagnosis, as well as all specific types of diagnoses examined. Effect sizes were largely consistent across the different types of disorders – the smallest association between the ERS and a specific type of mental disorder was with phobias and anxiety disorders (OR 1.19, 95% CI 1.15–1.24), and the largest with stress reactions (OR 1.50, 95% CI 1.35–1.54). These findings extend previous evidence of an ERS associated with psychotic disorders (e.g. Pries et al., 2019; Stilo et al., 2017), showing that cumulative exposure to environmental risk also predicts other mental disorders that emerge in childhood. While the strength of the association varied slightly between disorder types, these findings support the idea

https://doi.org/10.1017/S0033291722001702 Published online by Cambridge University Press

that cumulative environmental risk represents a transdiagnostic indicator of risk for the full spectrum of mental disorders. The proportion of children with a mental disorder diagnosis increased in a dose–response fashion with the ERS (Fig. 1), where only 2.8% of children with an ERS of zero had a mental disorder, increasing incrementally through to 18.3% of children with an ERS of ⩾8 being diagnosed with a mental disorder by age 13 years. The same dose–response pattern was observed for most of the disorder subcategories, though there was little difference in the proportion of children with an ERS of 5 or 6+ who were diagnosed with anxiety and phobias, and emotional disorders (Fig. 2).

The current findings extend previous research showing that children who have been exposed to prenatal risk factors (Roffman et al., 2021), trauma or neglect (Hughes et al., 2017) and neighbourhood adversity (Curtis et al., 2013) are more likely to develop mental disorders; here, we demonstrate that an accumulation of these risk factors across the early life-course increases the likelihood of developing later mental disorders in a dose-dependent fashion. Furthermore, we extend previous findings which have shown that cumulative social risk factors (Saunders et al., 2021) and cumulative perinatal risk factors (Chittleborough, Searle, Smithers, Brinkman, & Lynch, 2016) predict early childhood (age 5 years) developmental vulnerability, by demonstrating that these associations extend to diagnoses of mental disorders in middle childhood (age 6–11 years).

The finding that early childhood environmental exposures (before age 6 years) are associated with childhood mental disorders calls for policies that prioritise reducing exposure to adverse environmental risks in early life. In NSW, there is a 'first 2000 days' framework which recognises the importance of the first 5 years of a child's life, and prioritises working with families during these years, including targeted specialist support for children most at risk of adverse outcomes (Mendoza Diaz et al., 2020). The current findings suggest that the *number* of different risk factors a child experiences is an important consideration when determining which children are most in need of targeted support. Further, the findings support inter-agency interaction to identify children most at risk, since children may encounter environmental adversities in a range of contexts.

The current study findings should be interpreted with consideration of several limitations. First, mental disorder diagnoses were derived from a routinely collected emergency department, inpatient hospital, and outpatient mental health service records, such that children with mental disorders diagnosed by general practitioners and private specialists would not be captured by these records; other children who did not have access to these services, or who did not receive care despite being mentally unwell, would have been missed. The prevalence of mental disorders in our sample was therefore likely underestimated; this misclassification of children's mental disorder status would have only weakened (rather than exaggerated) the strength of any associations. Second, neighbourhood risk factors were defined on the basis of geographical boundaries determined by the Australian Bureau of Statistics and may not necessarily reflect the day-to-day neighbourhood/s with which the child engages. Third, in some cases, creating binary indicators to reflect exposure to environmental risk factors may have led to the loss of valuable information as to the type, timing, and severity of risk, important for understanding associations. Fourth, the additive model of environmental risk used cannot account for interactions between environmental factors, which may be important in the aetiology of mental disorders (Uher & Zwicker, 2017). However, there is no conclusive evidence favouring an interactive model over an additive model (Stepniak et al., 2014; Vassos et al., 2020) and correlations between environmental factors were small in our cohort (online Supplementary Table S3). Last, the choice of environmental risk factors to be included in the ERS was limited by what data had been collected by each agency and do not represent all possible environmental adversities. Strengths of the study include the longitudinal nature, the large sample size, and the representativeness of the sample to the source population (Carr et al., 2016; Green et al., 2018). Further, the use of multiagency record linkage data avoids recall or interviewer biases, minimises attrition, and allowed examination of a range of different types of risk factors.

In conclusion, we show here that cumulative exposure to risk in early childhood, as determined from routinely collected administrative data, is associated with the full range of mental disorders in middle childhood. This extends previous research showing that prenatal factors (Roffman et al., 2021), neighbourhood factors (Theall et al., 2012), and experiences of trauma or neglect (Hughes et al., 2017) are associated with mental disorders by demonstrating their cumulative effects on risk for mental disorders. Further, the relationship between cumulative environmental risk and mental disorder appears to be a transdiagnostic risk factor associated with all categories of childhood mental disorders. In general, the cumulative ERS used in this study had the same pattern of association across different types of disorders, but self-harm and stress reactions had the strongest association with the ERS, and phobias and anxiety disorders the weakest. Taken together, these findings support the need for public policies that focus on preventing the accumulation of environmental adversities or mitigating their effects in the first five years of life, and demonstrate that, while proximal experiences of trauma and neglect are important risk factors for childhood mental disorders, the child's wider context, including neighbourhood and prenatal risk exposures, is an important consideration.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291722001702.

Acknowledgements. This research used population data owned by the NSW Department of Communities and Justice; NSW Ministry of Health; NSW Registry of Births, Deaths and Marriages; the Australian Coordinating Registry (on behalf of Australian Registries of Births, Deaths and Marriages, Australian Coroners and the National Coronial Information System); the Australian Bureau of Statistics; the NSW Bureau of Crime Statistics and Research, and the NSW Police Force. This paper uses data from the Australian Early Development Census (AEDC). The AEDC is funded by the Australian Government Department of Education, Skills and Employment. The findings and views reported are those of the author and should not be attributed to these Departments or the NSW and Australian Government. The record linkage was conducted by the Centre for Health and Record Linkage.

Financial support. This research was conducted by the University of New South Wales with financial support from the Australian Research Council (ARC) Linkage Project (LP110100150, with the NSW Ministry of Health, NSW Department of Education, and the NSW Department of Communities and Justice representing the Linkage Project Partners), Discovery Project (DP170101403) and ARC Future Fellowship (FT170100294 awarded to KRL), as well as the National Health and Medical Research Council (NHMRC) Project Grants (APP1058652 and APP1148055), NHMRC Partnership Project (APP1133833), and NHMRC Investigator Grant (APP1175408 awarded to KD).

Conflict of interest. None.

References

Appleyard, K., Egeland, B., van Dulmen, M. H. M., & Sroufe, L. A. (2005). When more is not better: The role of cumulative risk in child behavior outcomes. *Journal of Child Psychology and Psychiatry*, *46*, 235–245. https://doi.org/10.1111/j.1469-7610.2004.00351.x.

Australian Bureau of Statistics. (2006). *Census of population and housing: Nature and content*. Australia: Australian Bureau of Statistics. Retrieved from https://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/2008.02006.

Australian Bureau of Statistics. (2018). *Australian and New Zealand offence classification* (*ANZSOC*). Canberra: Australian Bureau of Statistics: Commonwealth of Australia. Retrieved from https://www.ausstats.abs.gov.au/Ausstats/subscriber.nsf/0/181552DD634CCCCCCA2574970016EE08/$File/12340_2008%20%28second%20edition%29.pdf.

Bale, T. L., Baram, T. Z., Brown, A. S., Goldstein, J. M., Insel, T. R., McCarthy, M. M., … Nestler, E. J. (2010). Early life programming and neurodevelopmental disorders. *Biological Psychiatry*, *68*, 314–319. https://doi.org/10.1016/j.biopsych.2010.05.028.

Bunea, I. M., Szentágotai-Tătar, A., & Miu, A. C. (2017). Early-life adversity and cortisol response to social stress: A meta-analysis. *Translational Psychiatry*, *7*, 1274. https://doi.org/10.1038/s41398-017-0032-3.

Cannon, T. D., Yu, C., Addington, J., Bearden, C. E., Cadenhead, K. S., Cornblatt, B. A., … Kattan, M. W. (2016). An individualized risk calculator for research in prodromal psychosis. *American Journal of Psychiatry*, *173*, 980–988. https://doi.org/10.1176/appi.ajp.2016.15070890.

Carr, A., Duff, H., & Craddock, F. (2018). A systematic review of reviews of the outcome of noninstitutional child maltreatment. *Trauma, Violence, & Abuse*, *21*, 828–843. https://doi.org10.1177/1524838018801334.

Carr, V. J., Harris, F., Raudino, A., Luo, L., Kariuki, M., Liu, E., … Green, M. J. (2016). New south wales child development study (NSW-CDS): An Australian multiagency, multigenerational, longitudinal record linkage study. *BMJ Open*, *6*, e009023. https://doi.org/10.1136/bmjopen-2015-009023.

Carrión, R. E., Cornblatt, B. A., Burton, C. Z., Tso, I. F., Auther, A. M., Adelsheim, S., … McFarlane, W. R. (2016). Personalized prediction of psychosis: External validation of the NAPLS-2 psychosis risk calculator with the EDIPPP project. *American Journal of Psychiatry*, *173*, 989–996. https://doi.org/10.1176/appi.ajp.2016.15121565.

Chittleborough, C. R., Searle, A. K., Smithers, L. G., Brinkman, S., & Lynch, J. W. (2016). How well can poor child development be predicted from early life characteristics?: A whole-of-population data linkage study. *Early Childhood Research Quarterly*, *35*, 19–30. https://doi.org/10.1016/j.ecresq.2015.10.006.

Cicchetti, D. (2010). Resilience under conditions of extreme stress: A multilevel perspective. *World Psychiatry*, *9*, 145–154. https://doi.org/10.1002/j.2051-5545.2010.tb00297.x.

Curtis, S., Pain, R., Fuller, S., Khatib, Y., Rothon, C., Stansfeld, S. A., & Daya, S. (2013). Neighbourhood risk factors for Common Mental Disorders among young people aged 10–20 years: A structured review of quantitative research. *Health & Place*, *20*, 81–90. https://doi.org/10.1016/j.healthplace.2012.10.010.

de Kluiver, H., Buizer-Voskamp, J. E., Dolan, C. V., & Boomsma, D. I. (2017). Paternal age and psychiatric disorders: A review. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, *174*, 202–213. https://doi.org/10.1002/ajmg.b.32508.

Department of Health and Aged Care [Australian Government]. (2001). *Measuring remoteness: Accessibility/remoteness index of Australia* (*ARIA*). Canberra, Australia: Department of Health.

Dobbins, T. A., Sullivan, E. A., Roberts, C. L., & Simpson, J. M. (2012). Australian national birthweight percentiles by sex and gestational age, 1998–2007. *Medical Journal of Australia*, *197*, 291–294. https://doi.org/10.5694/mja11.11331.

Evans, G. W., Li, D., & Whipple, S. S. (2013). Cumulative risk and child development. *Psychological Bulletin*, *139*, 1342. https://doi.org/10.1037/a0031808.

Fisher, H. L., Caspi, A., Moffitt, T. E., Wertz, J., Gray, R., Newbury, J., … Arseneault, L. (2015). Measuring adolescents' exposure to victimization: The Environmental Risk (E-Risk) Longitudinal Twin Study. *Development and Psychopathology*, *27*, 1399–1416. https://doi.org/10.1017/S0954579415000838.

Green, M. J., Harris, F., Laurens, K. R., Kariuki, M., Tzoumakis, S., Dean, K., … Carr, V. J. (2018). Cohort profile: The New South Wales child development study (NSW-CDS) – Wave 2 (child age 13 years). *International Journal of Epidemiology*, *47*, 1396–1397k. https://doi.org/10.1093/ije/dyy115.

Green, M. J., Hindmarsh, G., Kariuki, M., Laurens, K. R., Neil, A. L., Katz, I., … Carr, V. J. (2020). Mental disorders in children known to child protection services during early childhood. *Medical Journal of Australia*, *212*, 22–28. https://doi.org/10.5694/mja2.50392.

Guloksuz, S., Pries, L.-K., Delespaul, P., Kenis, G., Luykx, J. J., Lin, B. D., … van Os, J. (2019). Examining the independent and joint effects of molecular genetic liability and environmental exposures in schizophrenia: Results from the EUGEI study. *World Psychiatry*, *18*, 173–182. https://doi.org/10.1002/wps.20629.

Guloksuz, S., van Os, J., & Rutten, B. P. F. (2018). The exposome paradigm and the complexities of environmental research in psychiatry. *JAMA Psychiatry*, *75*, 985–986. https://doi.org/10.1001/jamapsychiatry.2018.1211.

Hughes, K., Bellis, M. A., Hardcastle, K. A., Sethi, D., Butchart, A., Mikton, C., … Dunne, M. P. (2017). The effect of multiple adverse childhood experiences on health: A systematic review and meta-analysis. *The Lancet Public Health*, *2*, e356–e366. https://doi.org/10.1016/S2468-2667(17)30118-4.

Kim, M. K., Lee, S. M., Bae, S.-H., Kim, H. J., Lim, N. G., Yoon, S.-J., … Jo, M.-W. (2018). Socioeconomic status can affect pregnancy outcomes and complications, even with a universal healthcare system. *International Journal for Equity in Health*, *17*, 2. https://doi.org/10.1186/s12939-017-0715-7.

Kim-Cohen, J., Caspi, A., Moffitt, T. E., Harrington, H., Milne, B. J., & Poulton, R. (2003). Prior juvenile diagnoses in adults with mental disorder: Developmental follow-back of a prospective-longitudinal cohort. *Archives of General Psychiatry*, *60*, 709–717. https://doi.org/10.1001/archpsyc.60.7.709.

Lee, R. D., Fang, X., & Luo, F. (2013). The impact of parental incarceration on the physical and mental health of young adults. *Pediatrics*, *131*, e1188–e1195. https://doi.org/10.1542/peds.2012-0627.

Madsen, K. B., Ersbøll, A. K., Olsen, J., Parner, E., & Obel, C. (2015). Geographic analysis of the variation in the incidence of ADHD in a country with free access to healthcare: A Danish cohort study. *International Journal of Health Geographics*, *14*, 24. https://doi.org/10.1186/s12942-015-0018-4.

Mas, S., Boloc, D., Rodríguez, N., Mezquida, G., Amoretti, S., Cuesta, M. J., … PEPs Group. (2020). Examining gene–environment interactions using aggregate scores in a first-episode psychosis cohort. *Schizophrenia Bulletin*, *46*, 1019–1025. https://doi.org/10.1093/schbul/sbaa012.

McGrath, J. J., & Welham, J. L. (1999). Season of birth and schizophrenia: A systematic review and meta-analysis of data from the Southern Hemisphere (Details of this paper were presented at the Winter Workshop on Schizophrenia Research, Davos, Switzerland, February 1998.). *Schizophrenia Research*, *35*, 237–242. https://doi.org/10.1016/S0920-9964(98)00139-X.

McLaughlin, K. A., Conron, K. J., Koenen, K. C., & Gilman, S. E. (2010). Childhood adversity, adult stressful life events, and risk of past-year psychiatric disorder: A test of the stress sensitization hypothesis in a population-based sample of adults. *Psychological Medicine*, *40*, 1647–1658. https://doi.org/10.1017/S0033291709992121.

Mendoza Diaz, A., Burman, C., Finlay Jones, A., Short, K., Woolfenden, S., Downs, J., & Eapen, V. (2020). *First* 2000 *days overview*. Australia: NSW Health. Retrieved from https://www.health.nsw.gov.au/kidsfamilies/programs/Factsheets/brighter-beginnings.pdf.

Moore, T. M., Calkins, M. E., Rosen, A. F. G., Butler, E. R., Ruparel, K., Fusar-Poli, P., … Gur, R. E. (2021). Development of a probability calculator for psychosis risk in children, adolescents, and young adults. *Psychological Medicine*, 1–9. https://doi.org/10.1017/S0033291720005231.

Nolen-Hoeksema, S., & Watkins, E. R. (2011). A heuristic for developing transdiagnostic models of psychopathology: Explaining multifinality and divergent trajectories. *Perspectives on Psychological Science*, *6*, 589–609. https://doi.org/10.1177/1745691611419672.

NSW Bureau of Crime Statistics and Research. (2020). *Offence open data: Recorded criminal incident by month – by postcode*. NSW Bureau of Crime Statistics and Research. Retrieved from https://www.bocsar.nsw.gov.au/Pages/bocsar_datasets/Offence.aspx.

https://doi.org/10.1017/S0033291722001702 Published online by Cambridge University Press

Padmanabhan, J. L., Shah, J. L., Tandon, N., & Keshavan, M. S. (2017). The 'polyenviromic risk score': Aggregating environmental risk factors predicts conversion to psychosis in familial high-risk subjects. *Schizophrenia Research*, *181*, 17–22. https://doi.org/10.1016/j.schres.2016.10.014.

Paradies, Y. (2018). Racism and indigenous health. In *Oxford research encyclopedia of global public health*. Retrieved from https://doi.org/10.1093/acrefore/9780190632366.013.86.

Pink, B. (2013). *Socio-economic indexes for areas* (*SEIFA*) *2011*. Canberra: Australian Bureau of Statistics.

Pries, L.-K., Guloksuz, S., ten Have, M., de Graaf, R., van Dorsselaer, S., Gunther, N., … van Os, J. (2018). Evidence that environmental and familial risks for psychosis additively impact a multidimensional subthreshold psychosis syndrome. *Schizophrenia Bulletin*, *44*, 710–719. https://doi.org/10.1093/schbul/sby051.

Pries, L.-K., Lage-Castellanos, A., Delespaul, P., Kenis, G., Luykx, J. J., Lin, B. D., … Guloksuz, S. (2019). Estimating exposome score for schizophrenia using predictive modeling approach in two independent samples: The results from the EUGEI study. *Schizophrenia Bulletin*, *45*, 960–965. https://doi.org/10.1093/schbul/sbz054.

Roffman, J. L., Sipahi, E. D., Dowling, K. F., Hughes, D. E., Hopkinson, C. E., Lee, H., … Dunn, E. C. (2021). Association of adverse prenatal exposure burden with child psychopathology in the adolescent brain cognitive development (ABCD) study. *PLoS One*, *16*, e0250235. https://doi.org/10.1371/journal.pone.0250235.

Rutten, B. P. F., Hammels, C., Geschwind, N., Menne-Lothmann, C., Pishva, E., Schruers, K., … Wichers, M. (2013). Resilience in mental health: Linking psychological and neurobiological perspectives. *Acta Psychiatrica Scandinavica*, *128*, 3–20. https://doi.org/10.1111/acps.12095.

Sameroff, A. (2006). Identifying risk and protective factors for healthy child development. In A. Clarke-Stewart & J. Dunn (Eds.), *Families count: Effects on child and adolescent development* (pp. 53–76). Cambridge: Cambridge University Press.

Saunders, N. R., Janus, M., Porter, J., Lu, H., Gaskin, A., Kalappa, G., & Guttmann, A. (2021). Use of administrative record linkage to measure medical and social risk factors for early developmental vulnerability in Ontario, Canada. *International Journal of Population Data Science*, *6*, 1407–1407. https://doi.org/10.23889/ijpds.v6i1.1407.

Starr, L. R., Hammen, C., Conway, C. C., Raposa, E., & Brennan, P. A. (2014). Sensitizing effect of early adversity on depressive reactions to later proximal stress: Moderation by polymorphisms in serotonin transporter and corticotropin-releasing hormone receptor genes in a 20-year longitudinal study. *Developmental Psychopathology*, *26*, 1241–1254. https://doi.org/10.1017/s0954579414000996.

Stepniak, B., Papiol, S., Hammer, C., Ramin, A., Everts, S., Hennig, L., … Ehrenreich, H. (2014). Accumulated environmental risk determining age at schizophrenia onset: A deep phenotyping-based study. *The Lancet Psychiatry*, *1*, 444–453. https://doi.org/10.1016/S2215-0366(14)70379-7.

Stilo, S. A., Gayer-Anderson, C., Beards, S., Hubbard, K., Onyejiaka, A., Keraite, A., … Morgan, C. (2017). Further evidence of a cumulative effect of social disadvantage on risk of psychosis. *Psychological Medicine*, *47*, 913–924. https://doi.org/10.1017/S0033291716002993.

Theall, K. P., Drury, S. S., & Shirtcliff, E. A. (2012). Cumulative neighborhood risk of psychosocial stress and allostatic load in adolescents. *American Journal of Epidemiology*, *176*, S164–S174. https://doi.org/10.1093/aje/kws185.

Uher, R., & Zwicker, A. (2017). Etiology in psychiatry: Embracing the reality of poly-gene-environmental causation of mental illness. *World Psychiatry*, *16*, 121–129. https://doi.org/10.1002/wps.20436.

Vassos, E., Sham, P., Kempton, M., Trotta, A., Stilo, S. A., Gayer-Anderson, C., … Morgan, C. (2020). The Maudsley environmental risk score for psychosis. *Psychological Medicine*, *50*, 2213–2220. https://doi.org/10.1017/S0033291719002319.

Wickham, H. (2016). *Ggplot2: Elegant graphics for data analysis*. Springer International Publishing.

https://doi.org/10.1017/S0033291722001702 Published online by Cambridge University Press