

# Online Research @ Cardiff

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository: <https://orca.cardiff.ac.uk/125973/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Selous, Camilla, Kelly-Irving, Michelle, Maughan, Barbara, Eyre, Olga, Rice, Frances and Collishaw, Stephan 2020. Adverse childhood experiences and adult mood problems: evidence from a five-decade prospective birth cohort. *Psychological Medicine* 50 (14) , pp. 2444-2451.  
10.1017/S003329171900271X file

Publishers page: <http://dx.doi.org/10.1017/S003329171900271X>  
<<http://dx.doi.org/10.1017/S003329171900271X>>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies.

See

<http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



## **Adverse childhood experiences and adult mood problems: evidence from a five-decade prospective birth cohort**

Camilla Selous<sup>a</sup>, Michelle Kelly-Irving<sup>b</sup>, Barbara Maughan<sup>c</sup>, Olga Eyre<sup>d</sup>, Frances Rice<sup>d</sup>,  
Stephan Collishaw<sup>d\*</sup>

### **Affiliations:**

<sup>a</sup>Cardiff University School of Medicine, Heath Park, Cardiff CF14 4XN, Wales, UK

<sup>c</sup>French Institute of Health and Medical Research (INSERM), Unit of Epidemiology and Public Health Analysis, UMR1027, Toulouse, France

<sup>c</sup>King's College London, MRC Social Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology and Neuroscience, 16 De Crespigny Park, Denmark Hill, London, SE5 8AF

<sup>d</sup>Cardiff University School of Medicine, Child and Adolescent Psychiatry, Division of Psychological Medicine and Clinical Neurosciences, MRC Centre for Neuropsychiatric Genetics and Genomics, Hadyn Ellis Building, Maindy Road, Cardiff CF24 4HQ, Wales, UK

**\*Corresponding author:** Professor Stephan Collishaw, Child and Adolescent Psychiatry, Division of Psychological Medicine and Clinical Neurosciences, MRC Centre for Neuropsychiatric Genetics and Genomics, Hadyn Ellis Building, Maindy Road, Cardiff CF24 4HQ, Wales, UK; collishaws@cardiff.ac.uk; 02920 688436

**Word count** 4061

## **Abstract**

**Background:** Retrospectively-recalled adverse childhood experiences (ACEs) are associated with adult mood problems, but evidence from prospective population cohorts is limited.

Aims were to test links between prospectively ascertained ACEs and adult mood problems up to age 50, to examine the role of child mental health in accounting for observed associations, and to test gender differences in associations.

**Methods:** The National Child Development Study (NCDS) is a UK population cohort of children born in 1958. ACEs were defined using parent or teacher reports of family adversity (parental separation, child taken into care, parental neglect, family mental health service use, alcoholism, and criminality) at ages 7-16. Children with no known (n=9168), single (n=2488) and multiple (n=897) ACEs were identified in childhood. Adult mood problems were assessed using the Malaise inventory at ages 23, 33, 42 and 50 years.

Associations were examined separately for males and females.

**Results:** Experiencing single or multiple ACEs was associated with increased rates of adult mood problems after adjustment for childhood psychopathology and confounders at birth (2+ vs 0 ACEs - Men: Age 23: OR = 2.36 [95% CI 1.7-3.3]; Age 33: OR = 2.40 [1.7-3.4]; Age 42: OR= 1.85 [1.4-2.4]; Age 50: OR=2.63 [2.0-3.5]); Women: Age 23: OR = 2.00 [95% CI 1.5-2.6]; Age 33: OR = 1.81 [1.3-2.5]; Age 42: OR= 1.59 [1.2-2.1]; Age 50: OR=1.32 [1.0-1.7]).

**Conclusions:** Children exposed to ACEs are at elevated risk for adult mood problems and a priority for early prevention irrespective of presence of psychopathology in childhood.

**Key words:** ACE, depression, prospective, birth cohort

## **Introduction**

Major depressive disorder (MDD) is a common and impairing mental health disorder significantly contributing to the global burden of disease as the second leading cause of years-lived-with-disability (YLDs) globally (Vos et al., 2012; Ferrari et al., 2013). Symptoms of depression that fall below the diagnostic threshold are also associated with functional impairment and with subsequent “full-blown” episodes of MDD (Johnson et al., 1992; Judd et al., 1998). The peak period of incidence of MDD occurs in early adult life and, once experienced, depression often recurs. An important public health priority is therefore the early identification of individuals at high risk in order to effectively target prevention and intervention (Stice et al., 2009). One possibility that has received considerable attention is that exposure to early life adversity is associated with long-lasting elevated risk for depression.

Epidemiological studies of adults examining retrospective accounts of adverse childhood experiences (ACEs) such as maltreatment, neglect, and maladaptive family functioning have found strong associations with assessments of adult depression (Felitti et al., 1998; Dube et al., 2001; Kilpatrick et al., 2003; Chapman et al., 2004; Collishaw et al., 2007, Hughes et al., 2017). Findings show that the greater the number of retrospectively-reported ACEs the greater the probability of a current or lifetime diagnosis of major depressive disorder. One difficulty with prior studies testing associations between contemporaneous assessments of adult depression and adult retrospectively-reported ACEs concerns potential recall bias. Adults asked to recall childhood experiences many decades after they occurred sometimes forget whether and when events occurred (Hardt & Rutter, 2004), and the likelihood of reporting adverse childhood events appears in part dependent on current mood state (Reuben et al., 2016). This could result in inflated estimates of associations between ACEs and adult depression. Evidence from two prospective studies - the Dunedin birth

cohort study and the Environmental Risk Longitudinal Twin Study (E-Risk) - shows that independent prospective accounts and retrospective reports of childhood adversity only show low-to-moderate agreement (Reuben et al., 2016; Newbury et al., 2018). Importantly, discrepancy between prospective and retrospective reports of childhood ACEs was associated with personality traits including neuroticism (Reuben et al., 2016). At present, there are relatively few long-term prospective studies examining links between ACEs and adult depression.

Some prospective longitudinal studies have compared psychiatric outcomes for officially substantiated cases of abuse and neglect to matched controls. Such studies benefit from certainty that recording of childhood ACEs is independent from reporting of adult mental health and these studies provide evidence of increased rates of depression in individuals who experienced maltreatment in childhood (Horwitz et al., 2001; Widom et al., 2007). However, it is unclear whether findings generalise to the general population where most adverse childhood experiences are not officially recognised (Gilbert et al., 2011). For example, in the UK around 3 children in 1000 are recorded on the child protection register. In contrast, epidemiological studies indicate that around 5-20% of children and adolescents have experienced serious forms of maltreatment (Gilbert et al., 2009; Radford et al., 2011).

Population cohorts with prospective assessments of adverse childhood experiences are relatively rare, and most of those that have been undertaken have focused on adult outcomes associated with single childhood adversities such as bullying or parental divorce (Fergusson et al., 2013; Takizawa et al., 2014). The few population cohort studies that have tested associations between prospectively-assessed cumulative indices of child adversity and depression show strong associations in adolescence (Oldehinkel et al., 2014; Newbury et al., 2018) and early-to-middle adulthood (Clark et al., 2010; Reuben et al., 2016; Copeland et al., 2018). However, a number of important issues remain to be clarified. Does the risk for mood

problems associated with prospectively-assessed ACEs extend beyond middle-adulthood? To what extent do risk associations with mood problems in later life reflect continuity of psychopathology already evident in childhood? Are risk associations particularly pronounced for chronic depression or do they diminish with time? Repeat assessment of mood problems across adulthood is required to test this. Finally, are there gender differences in risk for mood problems associated with ACEs?

The current study extends prior analyses of links between prospectively assessed ACEs and adult mood problems by addressing these questions using the UK National Child Development Study birth cohort. This cohort has previously shown evidence of associations between prospectively and retrospectively assessed ACEs and mood disorder (Clark et al., 2010) and physical health indicators ('allostatic load') (Barboza Solis et al., 2015) at age 45 years. Here, we track developmental change in associations between childhood adversity and adult mood problems using data on four occasions through adulthood up to age 50 years representing one of the longest prospective follow-ups to date. The study is able to test whether childhood adversity is associated with adult mood problems independent of associations with psychopathology already evident in childhood or adolescence. This is important to know because it is currently unclear whether screening for early mental health difficulties in childhood and adolescence is likely sufficient to prevent chronic mood problems, or whether long-term prevention of depression should also be targeted at children with experiences of ACEs but without early mental health problems. One prior study observed that risk for psychiatric disorder at age 45 years in children exposed to ACEs persists after adjusting for psychopathology in adolescence, but that study did not consider measures of psychopathology in childhood (Clark et al., 2010).

We are not aware of studies that have directly tested whether prospective risk associations and adult mood problems persist or diminish with time, nor whether they are particularly pronounced for more pernicious (recurrent) presentations of mood problems.

Finally, we are not aware of any long-term follow-ups that have directly tested gender differences in prospective associations between ACEs and depression across the life course. This is important both because there are substantial gender differences in the prevalence and developmental patterning of depression over the life course (Thapar et al., 2012; Maughan et al., 2013) and because previous research suggests both similarities and differences in the aetiological pathways linking childhood risk exposures to adult depression for males and females (Kendler & Gardner, 2014). Furthermore, it has been suggested that gender differences in depression might in part reflect increased sensitivity to psychosocial stressors amongst females (Hyde et al., 2008).

Using data collected on seven occasions starting at age 7 and following to age 50 years in the 1958 UK birth cohort (National Child Development Study, NCDS), this study aimed to test longitudinal associations between childhood adversity and adult mood problems, testing (1) whether children who experience a greater number of ACEs show increased rates of mood problems across adult life (from age 23 to age 50); (2) whether childhood ACEs are associated with increased adult mood problems after adjusting for child and adolescent mental health difficulties assessed at ages 7, 11 and 16 years; and (3) if associations between childhood ACEs and adult mood problems differ by gender.

## **Methods**

### ***Sample***

NCDS is a longitudinal study of children born in England, Scotland, and Wales in one week in March 1958 (Power & Elliot, 2005). Following the initial birth survey (n = 18,558),

representing 98% of all live births, there have been nine further survey sweeps at ages 7, 11, 16, 23, 33, 42, 46, 50 and 55 years. Surviving cohort members still resident in the UK were eligible for participation at each sweep. Of the 12553 with ACE exposure data and relevant childhood covariates, mental health data were available from 9716 (age 23), 8830 (age 33), 8790 (age 42) and 7537 (age 50) cohort members. Data were downloaded from the UK Data Archive (usage number 86906). Informed consent in NCDS was obtained from parents in childhood and from cohort members in adulthood (Shepherd, 2012).

### **Measures:**

#### *Adverse childhood experiences:*

ACEs were defined according to previous work in NCDS (Barboza Solis et al., 2015) and included six types of familial adversity assessed across childhood using parent, teacher or health visitor/interviewer reports at ages 7, 11 and/or 16 years: (1) Parental separation up to age 16 (due to death, divorce or separation) as reported by parents or health visitors; (2) Family member of child in contact with mental health services at 7 years (health visitor report) or 11 years (parent report); (3) Parental alcohol abuse age 7 (health visitor report); (4) Family member of child in prison or on probation (health visitor or parent reports at ages 7, 11, or 16); (5) Physical neglect (teacher reported child being dirty or undernourished at ages 7 or 11); (6) Child ever in public/voluntary care services or foster care (caregiver reports at ages 7, 11, or 16). For those with data available for at least four of these indicators, cohort members were divided into three groups comprising those with no ACEs (0), those with a single ACE (1) and those with multiple ACEs ( $\geq 2$ ).

#### *Adult mood problems*

The 15-item psychological subscale of the Malaise Inventory was used to index mood problems at ages 23, 33, and 42 (Rutter et al., 1970). We excluded additional somatic items

because many of these become more common as people age (Rodgers et al., 1999). The 15 psychological items (e.g. ‘Do you often suddenly become scared for no good reason?’; ‘Do you often feel miserable or depressed?’) were each coded 0 ‘no’ or 1 ‘yes’ and then summed to create a total score at each age. The 15-item subscale showed acceptable internal consistency ( $\alpha = 0.75 - 0.87$ ) and has good external validity with respect to interview-assessed major depressive disorder and mental health service use using a threshold of 5+ to indicate significant mood problems (Rodgers et al., 1999). At age 50, a shortened 9-item version of the Malaise Inventory ( $\alpha = 0.79$ ) was administered in NCDS. We used an adjusted threshold of 3+ to indicate presence of mood problems at age 50 (Takizawa et al., 2014). Recurrent mood problems were defined as above-threshold symptom scores on 2 or more occasions. Additional analyses used eight psychological Malaise items common across all four occasions to test variation in associations between ACEs and mood symptoms (range 0-8) across ages 23, 33, 42, and 50 years.

### *Childhood Covariates*

Abbreviated 9-item versions of the Rutter A and Rutter B scales (Rutter et al., 1970) were used to obtain parent (ages 7, 11 and 16) and teacher (age 16) reports of child mental health problems including symptoms of hyperactivity, conduct problems and emotional problems. Individual items were coded as 0 ‘never’, 1 ‘sometimes’ or 2 ‘frequently’ and summed to derive total symptom scores for each informant at each age (range 0-18). The top decile on each measure was used to identify significant problems. Information on potential social and perinatal confounders was collected at birth: low birth weight (<2500 g); maternal smoking after 4 months of pregnancy; young maternal age (<18 years at birth of study child); paternal low social class (semiskilled or unskilled occupation); no maternal education past minimum school-leaving age (15/16 years).

## **Analysis**

Inverse probability weights were constructed using multiple logistic regression to calculate predicted probabilities of a cohort member being present in each adult data collection ‘sweep’ on the basis of measured childhood predictors. In NCDS, adult respondents tended to under-represent men, those with a greater number of ACEs or with child mental health problems, participants from semi- or unskilled childhood social class backgrounds, those whose mothers had left education at the minimum school leaving age, and individuals who had lower reading and maths test scores at age 7 years. Weights were effective in accounting for measured predictors of attrition [Supplementary Table 1] and these were included in all analyses that follow.

Main analyses were stratified by gender and examined links between ACEs (0, 1, 2+) and presence of mood problems using logistic regression analyses. Odds ratios with 95% confidence intervals were calculated comparing rates of above-threshold mood problems at each adult assessment for individuals with no ACE (reference), one ACE and multiple ACEs. Analyses further tested ACE-by-gender interactions to examine differences in associations for men and women. Multiple regression analyses adjusted for childhood mental health (above threshold difficulties at 7, 11 or 16 years) and other potential confounders (low birth weight, maternal smoking during pregnancy, maternal age (<18 years at birth of study child), paternal social class (unskilled vs other), maternal education).

Further analyses tested whether associations between ACEs and adult mood problems varied across adulthood. To ensure comparability of measurement across time, analyses focused on cohort members’ mean mental health symptom score using the eight psychological Malaise items common across all four occasions. Multivariate multilevel linear regression models

tested the interaction between ACEs (0 reference, 1, or 2+) and age (23 reference, 33, 42, 50 years) with mean Malaise score as the outcome (range: 0-8). Analyses were undertaken in Stata with measurement occasion (age) nested within individuals and ID specified as a random effect. Two models were run, one for men and one for women, and each model included childhood covariates (any above threshold mental health problem at ages 7, 11 or 16 years, low birth weight, maternal smoking during pregnancy, maternal age, paternal social class, maternal education). Unstandardized coefficients (b) and 95% confidence intervals are reported reflecting predicted differences in mean Malaise symptom score.

## **Results**

### *Prevalence of ACEs and mood problems in the 1958 birth cohort*

Of the 12553 cohort members with childhood ACEs and covariate data, 9168 (73.0%) were not reported to have any measured ACEs, 2488 (19.8%) experienced a single ACE, and 897 (7.1%) multiple ACEs. The prevalence of reported childhood adversities ranged from 1.0% (parental alcoholism) to 13.4% (parental separation). The prevalence of mood problems in the cohort as a whole differed by age and gender, with rates increasing from 7.2% at age 23 years to 17.5% at age 50 years in men, and from 18.2% at age 23 years to 26.7% at age 50 in women. See Supplementary Tables 2 and 3 for details.

### **ACEs and child mental health**

Each specific type of adversity showed statistically significant associations with presence of child mental health problems (supplementary table 4). As shown in Table 1, boys with one ACE (ORs = 1.57-2.20,  $ps < 0.001$ ) or multiple ACEs (ORs=2.34-4.74,  $ps < 0.001$ ) and girls with one (ORs = 1.49-2.13,  $ps < 0.001$ ) or multiple ACEs (ORs = 2.42-4.98,  $ps < 0.001$ ) had

increased odds of child mental health problems (>90% decile Rutter scores) at ages 7, 11 and 16 years. There were no significant interactions by gender (all  $p > 0.1$ ).

### **ACEs and adult mood problems**

Parental separation (ORs = 1.40-1.43, all  $p < 0.01$ ), having been in care (ORs = 1.89-2.51, all  $p < 0.001$ ), physical neglect (ORs = 1.55-2.02, all  $p < 0.001$ ), family member mental illness (ORs = 1.42-2.13, all  $p < 0.01$ ), and family criminality (ORs = 1.49-2.28, all  $p < 0.001$ ) were each associated with increased odds of adult mood problems at every adult assessment (ages 23, 33, 42 and 50). Parental alcoholism was associated with mood problems at most but not all follow-ups. See supplementary Table 4 for details.

Number of ACEs was associated with increased rates of adult mood problems at all ages [Table 2]. Individuals with a single ACE (men: ORs = 1.46-2.08; women: ORs = 1.33-1.78; all  $p < 0.001$ ) and those with multiple ACEs (men: ORs = 2.25-3.15; women: ORs = 1.49-2.58; all  $p < 0.01$ ) had increased odds of mood problems compared to those with no ACEs. ACEs were also associated with recurrent mood problems, i.e. above-threshold symptom scores on two or more occasions in adulthood, (men: single ACE OR = 1.87 [1.5-2.3],  $p < .001$ ; multiple ACEs OR = 2.84 [2.1-3.8],  $p < .001$ ; women: single ACE OR = 1.50 [1.3-1.8],  $p < .001$ ; multiple ACEs OR = 1.89 [1.5-2.5],  $p < .001$ ).

### **Adjustment for childhood covariates**

Table 3 summarises multivariable models of associations between ACEs and adult mood problems separately for males and females. As shown, there was little attenuation in associations between single or multiple ACE exposure and risk of adult mood problems when controlling for child psychopathology (any above-threshold Rutter score) and for socio-

demographic confounders. Final multivariable models showed that men who had experienced multiple ACEs had substantially increased rates of mood problems throughout adult life, including high rates of recurrent problems (OR = 2.36 [1.7-3.2],  $p < 0.001$ ). For women, risk associations were evident on most occasions, but appeared to reduce over time (age 23: OR = 2.00 [1.5-2.6],  $p < .001$ ; age 50: OR = 1.32 [1.0-1.7],  $p = 0.053$ ). Tests of interactions by gender indicated significantly different associations between ACEs and mood problems at age 50 (OR = 0.75 [0.6-0.9],  $p = 0.001$ ) and risk of recurrent mood problems (OR = 0.83 [0.7-1.0],  $p = 0.03$ ), in both instances reflecting stronger associations between ACEs and mood problems for men. Gender interactions were not significant at 23 years (OR = 0.89 [0.7-1.1],  $p = 0.22$ ), 33 years (OR = 0.87 [0.7-1.1],  $p = 0.20$ ) and 42 years (OR = 0.93 [0.8-1.1],  $p = 0.35$ ).

### **Testing for change in association between ACEs and mood symptoms by age**

Secondary analyses tested for change in association between ACEs and mean mood symptoms (using eight common psychological Malaise items, range 0-8). Controlling for childhood covariates (family demographics and child mental health), the model for women found main effects of age (33 vs 23: unstandardized coefficient  $b = -.31 [-.36, -.25]$ ,  $p < .001$ ; 42 vs 23:  $b = .23 [.17, .30]$ ,  $p < .001$ ; 50 vs 23:  $b = .18 [.11, .25]$ ,  $p < .001$ ), and ACEs (1 vs 0:  $b = .41 [.29, .53]$ ,  $p < .001$ ; 2+ vs 0:  $b = .85 [.63, 1.07]$ ,  $p < .001$ ). Tests of interactions between ACEs and age showed that when compared to age 23, there were reduced associations between ACEs and mood symptoms at ages 33 years (1 vs 0 ACE:  $b = -.03 [-.16, .10]$ ,  $p = .65$ ; 2+ vs 0:  $b = -.28 [-.54, -.01]$ ,  $p = .04$ ), 42 years (1 vs 0:  $b = -.23 [-.38, -.09]$ ,  $p = .001$ ; 2+ vs 0:  $b = -.43 [-.70, -.16]$ ,  $p = .002$ ), and 50 years (1 vs 0:  $b = -.10 [-.27, .08]$ ,  $p = .29$ ; 2+ vs 0:  $b = -.38 [-.70, -.05]$ ,  $p = .02$ ). The model for men found main effects of age (33 vs 23:  $b = -.10$  [95% CI =  $-.14, -.06$ ],  $p < .001$ ; 42 vs 23:  $b = .42 [.37, .47]$ ,  $p < .001$ ; 50 vs 23:  $b = .35 [.29, .40]$ ,  $p < .001$ ), and ACEs (1 vs 0:  $b = .29 [.20, .39]$ ,  $p < .001$ ; 2+ vs 0:  $b = .75 [.57, .93]$ ,  $p < .001$ ).

.001), but no significant variation in risk associations between ACEs and mood problems by age (ACE x age interaction: all  $ps > .05$ ).

### ***Discussion***

This five-decade UK population study tested associations between prospectively assessed adverse childhood experiences and mood problems in adult life. Multiple ACEs were associated with increased rates of self-reported adult mood problems, including recurrent depressed mood. These associations cannot be ascribed to differences in reporting of ACEs between adults with and without mood problems due to the prospective longitudinal nature of the study. Individuals with multiple ACEs had higher rates of adult mood problems even accounting for mental health problems already evident in childhood. When examining the pattern of associations over time, findings showed strong persistence of risk associations to age 50 but also some evidence of attenuation across time for women.

The findings support the conclusions from previous retrospective studies that individuals who experience ACEs are a high risk group for adult depression, and extends findings from some prior longitudinal research (Clark et al., 2010; Reuben et al, 2016; Copeland et al., 2018) by using repeated and extended assessments of mood problems up to age 50 years. In general, (and in this study particularly for females) there was a dropping off in the magnitude of associations with increasing age. This is to be expected given the important role of proximal stressors in precipitating episodes of depression (Kendler & Gardner, 2010). Nonetheless, there were robust associations between adverse childhood events and mood problems assessed up to four decades later.

In this cohort, associations between childhood adversity and adult mood problems were not accounted for by psychopathology assessed in childhood and adolescence. Associations

between ACEs and adult mood problems may therefore reflect mechanisms other than persistence of psychopathology across the life course. It was beyond the scope of this study to test alternative mechanisms, but associations between ACEs and adult mood problems may reflect continuity of social adversity and increased exposure to stressful life events in adulthood (Harper et al., 2003; Bird, 2007; Kendler & Gardner, 2010). Individuals are not passive recipients of their environments and people interact with and to some extent shape their environmental experiences (Kendler et al., 2003; Kendler & Baker, 2007). It is also important to consider the biological underpinnings of links between early life adversity and later depression (Hertzman, 1999; Danese et al., 2009; Shonkoff et al., 2012; Barboza Solis et al., 2015). Stress is associated not only with short-term adaptive biological responses but also with longer-lasting signs of ‘physiological wear-and-tear’ affecting the hypothalamic-pituitary-adrenal (HPA) axis, cardio-vascular, metabolic and immune systems (Danese et al., 2009; Barboza Solis et al., 2015). What is unclear is the extent to which early adversity shows shared or specific associations with physiological indices and depression in adulthood. Further, given evidence of bidirectional relationships between depression and chronic ill health (Brunner et al., 2014), it is important to consider whether and how physiological changes associated with ACEs are related to change in risk for mood problems across development. A third possibility is that associations between ACEs and adult mood problems are mediated by maladaptive behavioural or cognitive coping responses. For example, ACEs are also strongly associated with substance abuse and dependence (Kendler et al., 2000), which in turn are well-established risk factors for depression (Boden & Fergusson, 2011). These and other potential mechanisms through which early adversity may affect risk of later depression merit further investigation in future studies.

Finally, the study considered gender differences in patterns of associations between ACEs and mood problems and how these changed across adulthood. It has previously been suggested that females may be more sensitive to certain inter-personal forms of adversity and that this may partly account for the female preponderance of depression (Hyde et al., 2008). As expected, we found that mood problems were more prevalent amongst women than men at all ages, though gender differences did narrow over time. However, this study found no evidence that ACE associations with adult mood problems were more pronounced for women. If anything, the evidence here pointed to the opposite, with persistence of risk associations across adulthood for males and a fading of risk associations for women. Due caution is required as other childhood adversities not captured by the measures used here may show a different pattern of effects. For example, the study did not include measures of sexual abuse, bullying, harassment, or discordant peer relationships.

Nevertheless, this is an interesting finding and accords with other prospective high risk studies that have shown that adverse childhood experiences are associated with deleterious adult mental health outcomes at least as strongly in men as in women (e.g. Schilling et al., 2007; Choi et al., 2017). The finding of apparent greater persistence of risk associations across the life course for men compared to women requires replication, and if found to be robust then potential explanations will need to be tested. Different possibilities might include gender differences in biopsychosocial risk mechanisms (e.g. physiological response to stress, development of substance use problems, availability of social support; Choi et al., 2017; Kuehner, 2017), methodological artefact (e.g. differences in reporting of mood problems across adult life among women and men), and change in the relative importance of other more proximal predictors of mood problems in adulthood for men and women.

## **Strengths and limitations**

This study is one of the longest prospective cohorts to consider associations between ACEs and adult mood problems. Prospective studies such as this are important because of the potential for recall bias to inflate associations between measures of adult mental health and concurrent retrospective reports of childhood adversity (Reuben et al., 2016). The availability of directly comparable measures of mood problems on four occasions in adulthood is a further strength as it permitted us to test whether risk associations persisted or diminished across time.

There are also limitations. We were limited by the availability of measures included within this historical cohort study. It is likely that the ACEs measure used in this study represents a significant underestimate of the overall burden of childhood adversity. Relatively common experiences such as physical and sexual abuse, domestic violence, were not prospectively recorded, and it also possible that parents and teachers under-reported those adversities that were included (e.g. parental alcoholism). We chose to focus on familial adversities, and so did not include reports of peer bullying. Maltreatment and bullying are known to have strong and enduring negative effects on adult mental health (Gilbert et al., 2009; Takizawa et al., 2014), and it is likely that the estimated risk associated with childhood ACEs in this study would have been greater had it been possible to include maltreatment in this study.

Additionally, it was beyond the scope of the study to test in detail the role of specific childhood adversities in predicting life-course mood problems. However, findings showed a broadly consistent pattern across all six adversity variables used to operationalise the 'ACEs' measure. That is, findings did not appear to be driven by a single type of childhood adversity. In terms of outcome measures, adult mood problems were assessed using a symptom screen and it was not possible here to consider clinical diagnoses. However as noted, the Malaise

inventory has good validity when compared to interview-assessed major depressive disorder and mental health service use (Rodgers et al., 1999), and prior evidence from this study has shown links with interview-based diagnosis of depression (Clark et al., 2010).

As with nearly all cohort studies, it is important to consider evidence of selective attrition. Participants from more disadvantaged family background, those with a greater number of ACEs, and those with child mental health problems were less likely to remain in the study to age 50. Analyses included inverse probability weights which appeared to work well in accounting for measured childhood predictors of non-response at each age. Nevertheless, it is still possible that unmeasured factors associated with non-participation might have biased findings. Given the social stratification of adversity (Aber, 1997) and the selective loss of those at highest risk, results may present conservative estimates of the prevalence and risk of mood problems associated with childhood adversity.

It is important to see the study findings within their historical context. It is not certain that findings are generalizable to more recent generations. Certain ACEs (e.g. parental separation) have shown marked changes in prevalence (Amato, 2010). Furthermore, whilst it would be hoped that there is better recognition and intervention for children at risk of mental health problems today than in the past, evidence from cross-cohort comparisons suggests that the reverse may also be true (Gore Langton et al., 2011; Sellers et al in press).

It was beyond the scope of this paper to test hypotheses about risk mechanisms. ACEs likely index a broad spectrum of risk, including familial/inherited liability. It is not possible to infer causality regarding associations between ACEs and adult mood problems because of the possibility of residual confounding, including both genetic and social factors unmeasured in

this study that may be associated both with ACEs and with adult mood problems. In addition to testing explanatory mechanisms, it will also be important for future research to consider protective factors that act as risk buffers for children exposed to adversity (Collishaw et al., 2007; Collishaw et al., 2016).

### **Implications**

Childhood family adversities are highly prevalent and often unrecognised by official bodies (Gilbert et al., 2009). Most children exposed to even extreme adversity remain unrecognized by official authorities, and care provision is far from optimal (Cawson et al., 2000; Gilbert et al., 2009). Findings of this study demonstrate that individuals with adverse childhood experiences are a high risk group with long-term risk for adult mood problems, even when there is no evidence of mental health problems in childhood and adolescence. The findings are important for prevention (regardless of the causal nature of the ACEs-mood problems relationship) because they identify a group of children who are at increased risk of later mood problems who might benefit from early preventative intervention. Next steps for future research are to better understand the mechanisms by which childhood adversity confers risk for adult mood difficulties, and to determine whether existing early prevention programmes for depression can improve long-term outcomes in those at risk.

### **Acknowledgements**

The authors express their gratitude to the National Child Development Study participants, and to the UK data archive for providing access to the anonymised data.

### **Financial support**

This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

### **Conflict of interests**

None.

### **Ethical standards**

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

### **References**

- Aber JL, Bennett NG, Conley DC, Li J** (1997). The effects of poverty on child health and development. *Annual Review of Public Health*, **18**, 463-483.
- Amato PR** (2010). Research on divorce: Continuing trends and new developments. *Journal of Marriage and Family*, **72**, 650–666.
- Anda RF, Felitti VJ, Bremner JD, Walker JD, Whitfield CH, Perry BD, Dube SR, Giles WH** (2006). The enduring effects of abuse and related adverse experiences in childhood. *European Archives of Psychiatry and Clinical Neuroscience*, **256**, 174-186.
- Barboza Solís C, Kelly-Irving M, Fantin R, Darnaudéry M, Torrisani J, Lang T, Delpierre C** (2015). Adverse childhood experiences and physiological wear-and-tear in midlife: Findings from the 1958 British birth cohort. *Proceedings of the National Academy of Sciences*, **112**, E738-E746.
- Bird K** (2007). The intergenerational transmission of poverty: An overview (Working Paper 99) Manchester, IDPM/Chronic Poverty Research Centre (CPRC).
- Boden JM, Fergusson DM** (2011). Alcohol and depression. *Addiction*, **106**, 906-914.
- Brunner WM, Schreiner PJ, Sood A, Jacobs DR** (2014). Depression and risk of incident asthma in adults. The CARDIA Study. *American Journal of Respiratory and Critical Care Medicine*, **189**, 1044–1051.

**Cawson P, Wattam C, Brooker S, Kelly G** (2000). Child maltreatment in the United Kingdom: A study of the prevalence of abuse and neglect. NSPCC: London.

**Chapman DP, Whitfield CL, Felitti VJ, Dube SR, Edwards VJ, Anda RF** (2004). Adverse childhood experiences and the risk of depressive disorders in adulthood. *Journal of Affective Disorders*, **82**, 217–225.

**Choi NG, DiNitto DM, Marti N, Choi BY** (2017). Association of adverse childhood experiences with lifetime mental and substance use disorders among men and women aged 50+ years. *International Psychogeriatrics*, **29**, 359-372.

**Clark C, Caldwell T, Power C, Stansfeld S** (2010). Does the influence of childhood adversity on psychopathology persist across the lifecourse? A 45-year prospective epidemiologic study, *Annals of Epidemiology*, **20**, 385-394.

**Collishaw S, Hammerton G, Mahedy L, Sellers R, Owen MJ, Craddock N, Thapar AK, Harold GT, Rice F, Thapar A** (2016). Mental health resilience in the adolescent offspring of parents with depression: a prospective longitudinal study. *The Lancet Psychiatry*, **3**, 49-57.

**Collishaw S, Pickles A, Messer J, Rutter M, Shearer C, Maughan B** (2007). Resilience to adult psychopathology following childhood maltreatment: Evidence from a community sample. *Child Abuse and Neglect*, **31**, 211–229.

**Copeland WE, Shanahan L, Hinesley J, Chan RF, Aberg KA, Fairbank JA, van den Oord EJCG, Costello EJ** (2018). Association of childhood trauma exposure with adult psychiatric disorders and functional outcomes. *JAMA Network Open*, **1**, e184493.

**Danese A, Moffitt TE, Harrington H, Milne BJ, Polanczyk G, Pariante CM, Poulton R, Caspi A** (2009). Adverse childhood experiences and adult risk factors for age-related disease: depression, inflammation, and clustering of metabolic risk markers. *Archives of Pediatrics and Adolescent Medicine*, **163**, 1135-1143.

**Dube SR, Anda RF, Felitti VJ, Chapman DP, Williamson DF, Giles WH** (2001).

Childhood abuse, household dysfunction, and the risk of attempted suicide throughout the life span. *JAMA*, **286**, 3089-3096.

**Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, Koss MP, Marks JS** (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. *American Journal of Preventative Medicine*, **14**, 245-258.

**Fergusson DM, McLeod GF, Horwood JL** (2014). Parental separation/divorce in childhood and partnership outcomes at age 30. *Journal of Child Psychology and Psychiatry*, **55**, 352-360.

**Ferrari AJ, Charlson FJ, Norman RE, Patten SB, Freedman G, Murray CJL, Vos T, Whiteford HA** (2013). Burden of depressive disorders by country, sex, age, and year: Findings from the Global Burden of Disease Study 2010. *PLoS Medicine*, **10**, e1001547.

**Gilbert R, Kemp A, Thoburn J, Sidebotham P, Radford L, Glaser D, MacMillan HL** (2009) Recognising and responding to child maltreatment. *Lancet*, **373**, 167–180.

**Gore Langton E, Collishaw S, Goodman R, Pickles A, Maughan B** (2011). An emerging income differential for adolescent emotional problems. *Journal of Child Psychology and Psychiatry*, **52**, 1081–1088.

**Hardt J, Rutter M** (2004). Validity of adult retrospective reports of adverse childhood experiences: Review of the evidence. *Journal of Child Psychology and Psychiatry*, **45**, 260–273.

**Harper C, Marcus R, Moore K** (2003). Enduring poverty and the conditions of childhood: Lifecourse and intergenerational poverty transmissions. *World Development*, **31**, 535–554.

**Hertzman C** (1999) The biological embedding of early experience. *Annals of the New York Academy of Sciences*, **896**, 85–95.

**Horwitz AV, Widom CS, McLaughlin J, Raskin H** (2001). The impact of childhood abuse and neglect on adult mental health: A prospective study. *Journal of Health and Social Behavior*, **42**, 184–201.

**Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, Jones L, Dunne MP** (2017). The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. *The Lancet Public Health*, **2**, e356-e366.

**Hyde J, Mezulis A, Abramson L** (2008). The ABCs of depression: Integrating affective, biological, and cognitive models to explain the emergence of the gender difference in depression. *Psychological Review*, **115**, 291-313.

**Johnson J, Weissman MM, Klerman GL** (1992). Service utilization and social morbidity associated with depressive symptoms in the community. *JAMA*, **267**, 1478-1483.

**Judd LL, Akiskal HS, Maser JD, Zeller PJ, Endicott J, Coryell W, Paulus MP, Kunovac JL, Leon AC, Mueller TI, Rice JA** (1998). A prospective 12-year study of subsyndromal and syndromal depressive symptoms in unipolar major depressive disorders. *Archives of General Psychiatry*, **55**, 694-700.

**Kendler KS, Baker JH** (2007). Genetic influences on measures of the environment: a systematic review. *Psychological Medicine*, **37**, 615-626.

**Kendler KS, Bulik CM, Silberg J, Hetttema JM, Myers J, Prescott CA** (2000). Childhood sexual abuse and adult psychiatric and substance use disorders in women: An epidemiological and cotwin control analysis. *Archives of General Psychiatry*, **57**, 953-959.

**Kendler KS, Gardner CO** (2010) Dependent stressful life events and prior depressive episodes in the prediction of major depression: The problem of causal inference in psychiatric epidemiology. *Archives of General Psychiatry*, **67**, 1120-1127.

**Kendler KS, Gardner CO** (2014). Sex differences in the pathways to major depression: a study of opposite-sex twin pairs. *American Journal of Psychiatry*, **171**, 426-35.

- Kendler KS, Gardner CO, Prescott CA** (2003). Personality and the experience of environmental adversity. *Psychological Medicine*, **33**, 1193-1202.
- Kilpatrick DG, Saunders BE, Smith DW** (2003). *Youth victimization: Prevalence and implications. Research in brief*. Washington, DC: US Department of Justice, Office of Justice Programs.
- Kuehner C** (2017). Why is depression more common among women than among men? *Lancet Psychiatry*, **4**, 146-158.
- Maughan B, Collishaw S, Stringaris A** (2013). Depression in childhood and adolescence. *Journal of the Canadian Academy of Child and Adolescent Psychiatry*, **22**, 35-40.
- Newbury JB, Arseneault L, Moffitt TE, Caspi A, Danese A, Baldwin JR, Fisher HL** (2018). Measuring childhood maltreatment to predict early-adult psychopathology: comparison of prospective informant-reports and retrospective self-reports. *Journal of Psychiatric Research*, **96**, 57-64.
- Oldehinkel AJ, Ormel J, Verhulst FC, Nederhof E** (2014). Childhood adversities and adolescent depression: A matter of both risk and resilience. *Development and Psychopathology*, **26**, 1067-1075.
- Power C, Elliott J** (2005). Cohort profile: 1958 British birth cohort (National Child Development Study). *International Journal of Epidemiology*, **35**, 34-41.
- Radford L, Corral S, Bradley C, Fisher H, Bassett C, Howat N, Collishaw S** (2011). *Child Abuse and Neglect in the UK Today*. London: NSPCC.
- Reuben A, Moffitt TE, Caspi A, Belsky DW, Harrington H, Schroeder F, Hogan S, Ramrakha S, Poulton R, Danese A** (2016). Lest we forget: comparing retrospective and prospective assessments of adverse childhood experiences in the prediction of adult health. *Journal of Child Psychology and Psychiatry*, **57**, 1103–1112.

**Rodgers B, Pickles A, Power C, Collishaw S, Maughan B** (1999). Validity of the Malaise Inventory in general population samples. *Social Psychiatry and Psychiatric Epidemiology*, **34**, 333-341.

**Rutter M, Tizard J, Whitmore K** (1970). *Education, Health and Behaviour*. Longman: London.

**Schilling EA, Aseltine RH, Gore S** (2007). Adverse childhood experiences and mental health in young adults: a longitudinal survey. *BMC Public Health*, **7**, 30.

**Shepherd P** (2012). 1958 National Child Development Study ethical review and consent. *International Journal of Epidemiology*, **35**, 836-843.

**Shonkoff JP, Gardner AS, Siegel BS, Dobbins MI, Earls MF, McGuinn L, Pascoe J, Wood DL** (2012). The lifelong effects of early childhood adversity and toxic stress. *Pediatrics*, **129**, e232-e246.

**Stice E, Shaw H, Bohon C, Marti CN, Rohde P** (2009). A meta-analytic review of depression prevention programs for children and adolescents: factors that predict magnitude of intervention effects. *Journal of Consulting and Clinical Psychology*, **77**, 486-503.

**Takizawa R, Maughan B, Arseneault L** (2014). Adult health outcomes of childhood bullying victimization: Evidence from a five-decade longitudinal British birth cohort. *American Journal of Psychiatry*, **171**, 777-784.

**Thapar A, Collishaw S, Pine D, Thapar A** (2012). Depression in adolescence. *Lancet*, **379**, 1056-1067.

**Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, Aboyans V, Abraham J** (2012). Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*, **380**, 2163-2196.

**Wells J, Horwood L** (2004). How accurate is recall of key symptoms of depression? A comparison of recall and longitudinal reports. *Psychological Medicine*, **34**, 1001-1011.

**Widom CS, DuMont K, Czaja SJ** (2007). A prospective investigation of major depressive disorder and comorbidity in abused and neglected children grown up. *Archives of General Psychiatry*, **64**, 49-56.

**Table 1** Unadjusted associations between ACEs and mental health problems at ages 7, 11 and 16 in childhood by gender.

		7 years		11 years		16 years (parent report)		16 years (teacher report)		
		%	OR [95 %CI]	%	OR [95 % CI]	%	OR [95 % CI]	%	OR [95 % CI]	
ACE	Male	0	8.5	-	8.7	-	5.8	-	8.3	-
		1	14.4	1.81 [1.5-2.2] ***	13.1	1.57 [1.3-1.9] ***	11.4	2.07 [1.6-2.6] ***	16.6	2.20 [1.8-2.7] ***
		≥ 2	17.8	2.63 [1.8-3.0] ***	19.9	2.60 [2.0-3.4] ***	22.7	4.74 [3.6-6.3] ***	29.8	4.69 [3.6-6.0] ***
	Female	0	6.9	-	5.5	-	7.3	-	5.9	-
		1	9.9	1.49 [1.2-1.9] ***	8.2	1.53 [1.2-2.0] **	14.3	2.13 [1.7-2.7] ***	11.8	2.13 [1.7-2.7] ***
		≥ 2	15.2	2.42 [1.8-3.2] ***	14.6	2.93 [2.1-4.0] ***	20.3	3.25 [2.4-4.4] ***	23.8	4.98 [2.7-6.7] ***

ACE = Adverse childhood experiences; OR [95% CI] = Odds ratio [95% confidence interval] with 0 ACEs as reference group; \* p<0.05; \*\* p<0.01; \*\*\* p <0.001. N<sub>boys</sub> (7 years: 6453; 11 years: 5787; 16 years parent reports: 4814; 16 years teacher reports: 5027). N<sub>girls</sub> (7 years: 6110; 11 years: 5504; 16 years parent reports: 4609; 16 years teacher reports: 4853)

**Table 2** Unadjusted associations between ACEs and adult mood problems at ages 23, 33, 42 and 50 years by gender

	ACES	23 years		33 years		42 years		50 years	
		%	OR [95 % CI]						
<b>Males</b>	0	5.4	-	5.1	-	14.1	-	14.6	-
	1	10.7	2.08 [1.6-2.7] ***	9.9	2.02 [1.5-2.6] ***	19.3	1.46 [1.2-1.8] ***	22.7	1.72 [1.4-2.1] ***
	2+	15.2	3.12 [2.3-4.3] ***	14.5	3.15 [2.2-4.4] ***	26.8	2.25 [1.7-2.9] ***	33.7	2.96 [2.3-3.9] ***
<b>Female</b>	0	15.7	-	11.3	-	21.7	-	24.7	-
	1	22.6	1.56 [1.3-1.9] ***	18.5	1.78 [1.5-2.2] ***	26.9	1.33 [1.1-1.6] **	31.9	1.43 [1.2-1.7] ***
	2+	32.5	2.58 [2.0-3.3] ***	22.8	2.30 [1.7-3.1] ***	34.1	1.89 [1.5-2.4] ***	32.8	1.49 [1.1-2.0] **

ACE = Adverse childhood experiences; OR [95% CI] = Odds ratio [95% confidence interval] with 0 ACEs as reference group; \*p<0.05; \*\*p<0.001; \*\*\*p<0.001. Nmen (23 years: 4832; 33 years: 4335; 42 years: 4290; 50 years: 3689). Nswomen (23 years: 4884; 33 years: 4495; 42 years: 4300; 50 years 3848).

**Table 3** ACEs and risk for adult mood problems: comparison of unadjusted and adjusted models.

	23 years	33 years	42years	50 years
	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]
Male	N = 4832	N = 4335	N = 4290	N = 3689
Unadjusted model				
0 ACEs	-	-	-	-
1 ACE	2.09 [1.6-2.7] ***	2.02 [1.5-2.6] ***	1.46 [1.2-1.8] ***	1.72 [1.4-2.1] ***
2+ ACEs	3.13 [2.3-4.3] ***	3.15 [2.2-4.4] ***	2.25 [1.7-2.9] ***	2.96 [2.3-3.9] ***
Adjusted model				
0 ACE	-	-	-	-
1 ACE	1.85 [1.4-2.4] ***	1.81 [1.4-2.4] ***	1.36 [1.1-1.7] **	1.64 [1.3-2.0] ***
2+ ACEs	2.36 [1.7-3.3] ***	2.40 [1.7-3.4] ***	1.85 [1.4-2.4] ***	2.63 [2.0-3.5] ***
Female	N = 4884	N = 4495	N = 4500	N = 3848
Unadjusted model				
0 ACE	-	-	-	-
1 ACE	1.56 [1.3-1.9] ***	1.78 [1.5-2.2] ***	1.33 [1.1-1.6] **	1.43 [1.2-1.7] ***
2+ ACEs	2.58[2.0-3.3]***	2.30 [1.7-3.1] ***	1.89 [1.5-2.4] ***	1.49 [1.1-2.0] **
Adjusted model				

0 ACE	-	-	-	-
1 ACE	1.39 [1.2-1.7] ***	1.56 [1.3-1.9] ***	1.23 [1.0-1.5] *	1.35 [1.1-1.6] **
2+ ACEs	2.00 [1.5-2.6] ***	1.81 [1.3-2.5] ***	1.59 [1.2-2.1] **	1.32 [1.0-1.7]

ACEs = Adverse childhood experiences; OR [95% CI] = Odds ratio [95% Confidence Interval] with 0 ACEs as reference group; \*p<0.05; \*\*p<0.01; \*\*\*p<0.001. Adjusted model controlling for low birth weight, marital status at birth, paternal social class, maternal education, maternal age and child psychopathology (any above threshold Rutter score ages 7-16).