Childhood adversity and subsequent mental health status in adulthood: screening for associations using two linked surveys

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Aims. Accumulating evidence links childhood adversity to negative health outcomes in adulthood. However, most of the available evidence is retrospective and subject to recall bias. Published reports have sometimes focused on specific childhood exposures (e.g. abuse) and/or specific outcomes (e.g. major depression). Other studies have linked childhood adversity to a large and diverse number of adult risk factors and health outcomes such as cardiovascular disease. To advance this literature, we undertook a broad examination of data from two linked surveys. The goal was to avoid retrospective distortion and to provide a descriptive overview of patterns of association.

Methods. A baseline interview for the Canadian National Longitudinal Study of Children and Youth collected information about childhood adversities affecting children aged 0–11 in 1994. The sampling procedures employed in a subsequent study called the National Population Health Survey (NPHS) made it possible to link $n=1977$ of these respondents to follow-up data collected later when respondents were between the ages of 14 and 27. Outcomes included major depressive episodes (MDE), some risk factors and educational attainment. Cross-tabulations were used to examine these associations and adjusted estimates were made using the regression models. As the NPHS was a longitudinal study with multiple interviews, for most analyses generalized estimating equations (GEE) were used. As there were multiple exposures and outcomes, a statistical procedure to control the false discovery rate (Benjamini–Hochberg) was employed.

Results. Childhood adversities were consistently associated with a cluster of potentially related outcomes: MDE, psychotropic medication use and smoking. These outcomes may be related to one another since psychotropic medications are used in the treatment of major depression, and smoking is strongly associated with major depression. However, no consistent associations were observed for other outcomes examined: physical inactivity, excessive alcohol consumption, binge drinking or educational attainment.

Conclusions. The conditions found to be the most strongly associated with childhood adversities were a cluster of outcomes that potentially share pathophysiological connections. Although prior literature has suggested that a very large number of adult outcomes, including physical inactivity and alcohol-related outcomes follow childhood adversity, this analysis suggests a degree of specificity with outcomes potentially related to depression. Some of the other reported adverse outcomes (e.g. those related to alcohol use, physical inactivity or more distal outcomes such as obesity and cardiovascular disease) may emerge later in life and in some cases may be secondary to depression, psychotropic medication use and smoking.

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Background

Adverse childhood experiences are believed to increase the risk of multiple health problems later in life. However, with a few exceptions, most studies have been retrospective. For example, Afifi *et al.* (2013) reported associations between harsh physical

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discipline during childhood (retrospectively reported) and cardiovascular disease, arthritis and obesity using data from a large cross-sectional data set that contained retrospective reports of adversity. Similarly, the adverse childhood experiences (ACE) study retrospectively has linked childhood adversity to chronic medical conditions and risk factors such as smoking, obesity and physical inactivity (Felitti *et al.* 1998). McLaughlin *et al.* (2010) used data from the US National Epidemiological Survey of Alcohol and Related Conditions to document stress sensitisation, defined as a greater than additive effect of childhood adversity and later (adult-experienced) stressful events in the aetiology of major depressive episode (MDE), post-traumatic stress disorder and anxiety disorders. A similar result for MDE was reported in two analyses arising from a Canadian longitudinal survey (Colman *et al.* 2013; Patten, 2013). In the World Mental Health Surveys an association between childhood adversity and almost all (retrospectively) evaluated mental disorders was found (Kessler *et al.* 2010).

These various outcomes may reflect chains of causal events that unfold in multiple stages over the lifetime. For example, mood disorders, obesity, diabetes and cardiovascular disease may represent long-term effects of increased allostatic load (McEwen, 2003). This, in turn, may be related to adverse events during childhood and resulting stress-sensitisation. Early life adversity may reduce (for example, through epigenetic methylation) expression of a glucocorticoid receptor gene promoter in the hippocampus, producing a long-standing diminishment of glucocorticoid-mediated negative feedback inhibition of stress responses (Weaver *et al.* 2004; Meaney *et al.* 2007; Szyf *et al.* 2008). Consistent with this idea, adults having a history of childhood adversity show increased reactivity in stressful circumstances, see reviews by Taylor *et al.* (2004; Taylor, 2010). Based on this literature it is likely that children exposed to childhood adversities are specifically at higher risk of conditions characterised by heightened stress reactivity, such as major depression. They may also engage in behaviours motivated by attempts to regulate heightened stress reactivity such as smoking, alcohol consumption and use of psychotropic medications. Some of these behaviours may secondarily increase the risk of other adverse health outcomes such as obesity secondary to psychotropic medication use or cardiovascular disease secondary to smoking. A similar situation may unfold in association with other disorders, such as anxiety disorders. However, major depression was the only mental disorder recorded in the data sources used in the present study. In the present study, we examined a large number of such associations to broadly assess patterns of association, focusing on a young adult population.

We hypothesised the associations between childhood adversity and adult outcomes would be seen for major depression, and for behaviours that may occur in association with psychological distress such as smoking and excessive alcohol consumption.

Methods

The study was approved by the University of Calgary Conjoint Ethics Review Board.

Data sources

To prospectively evaluate a set of associations we linked respondents common to two longitudinal Canadian surveys. One of these studies was the National Longitudinal Study Survey of Children and Youth (NLSCY) (Statistics Canada, 2012). Data collection for the NLSCY began initially in 1994 with interviews of a representative community sample of children aged 0–11 years ($n = 22\,831$). The study used a probability-based sampling procedure that included multiple stages and unequal selection probabilities. These design features mean that weighted frequency estimates are more accurate than unweighted ones. For example, in most of the sampling frame, one child was selected from each selected household. This would result in a drastic influence of household size on the probability of selection, a design feature that must be offset using sampling weights, which are provided by Statistics Canada for this purpose. Such weighting was used for frequency estimates but was not possible, and was not considered important, for the odds ratio (OR) estimates. Measures of association are unlikely to be biased as a result of unequal selection probabilities. A portion of the NLSCY sample was subsequently reassessed in a series of interviews starting at the age of 12 because they also participated in a longitudinal general health study called the National Population Health Survey, or NPHS (Statistics Canada, 2012), $n = 17\,276$. For the present study, Statistics Canada created a database that included variables from both studies linked at the individual level. The sample, which include $n = 1977$ was only interviewed once in the NLSCY (in 1994) and was then interviewed several times in the NPHS, depending on the year in which respondents became 12 years old and were considered eligible for the adult interview used in that study. The NPHS then subsequently collected follow-up data using biannual interviews until 2010. For example, an 11-year-old NLSCY respondent sampled in 1994 would have been followed to age 27 in the NPHS and would have been interviewed eight times in the NPHS (i.e. in 1996, 1998, 2000, 2002,

2004, 2006, 2008 and 2010). An infant born in 1994 would have participated in the three final NPHS cycles at the ages of 12, 14 and 16 (in 2006, 2008 and 2010)

Assessment of childhood adversities from the NLSCY data

The NLSCY included a series of questions directed towards the person most knowledgeable (PMK) about the child. In the first cycle of the NLSCY, the PMK was the mother 91.3% of the time (89.9% biological mother and 1.4% the step, adoptive or foster mother) and 9.2% was the father (in 0.5% of children the PMK was not a parent). Some of these questions were only asked when the child was in a specific age range (e.g. adversities in school when the child was attending school). When the child was aged 0–3 years the PMK was asked about perinatal events and complications. None of these perinatal variables were associated with the health outcomes assessed in the study, and so are not discussed further. The PMKs of children 4 years or older were asked about school adversities affecting the child and whether the child had needed to change schools two or more times. We coded affirmative responses to the following items as representing school adversities: (not) feeling safe at school, (not) feeling safe going to and from school, children saying ‘nasty and unpleasant things’ (to the child) at school and being bullied at school. When it was meaningful to do so, and where the available sample size would support it, the adversities were classified at multiple levels. For example, neighbourhood adversities were coded at four levels (see below).

A series of additional items were asked of the PMK of all children in the sample (age 0–11). These included questions about neighbourhood problems, which were assessed in two ways. First, PMKs were asked whether there were problems with: garbage, alcohol, drugs, ‘groups of young people causing trouble’ or burglary in the neighbourhood. These neighbourhood problems were examined in the current analyses at three levels, each represented using an indicator variable: one, two or 3+ neighbourhood problems. A second set of items assessed neighbourhood cohesion. Neighbourhood cohesiveness was assessed using an *ad hoc* scale developed specifically for the NLSCY. This scale included five items, each with four response options (strongly disagree to strongly agree). An example of an item from this scale is: ‘If there is a problem around here, the neighbours get together to deal with it.’ We used the lower quartile of scale scores as an indicator of poor neighbourhood cohesiveness.

The PMKs were also asked whether the child experienced any of the following events that ‘caused a great amount of worry or unhappiness’ such as hospital

stays, deaths in the family and other events. Although the previously listed adversities (e.g. health adversities, neighbourhood problems) can all be regarded as stressful events, we refer to these specific circumstances as ‘major stressful events’ in this report. The PMK was also asked to report whether the child had any long-term conditions that had been diagnosed by a health professional. An additional item asked whether the child was physically less active than ‘other children of the same age’. The age of the biological mother at the time of the child’s birth was recorded and, based on number of available observations, was categorised in our analysis as 14–19 *v.* 20+ years. The age of the biological father at the child’s birth was also recorded and, based on the availability of observations, was categorised as 16–24 *v.* 25+. Another variable used in the current analysis was whether the child was living with a lone biological mother and the number of changes to the usual place of residence. The latter variable was included as a count in the data analysis.

The interview also assessed depression in the PMK using an abbreviated 12-item version of the CES-D rating scale for depressive symptoms (Radloff, 1977). Here, a score of 21+ was regarded as evidence of depression in the PMK (Poulin *et al.* 2005). Excessive alcohol consumption by the PMK was also recorded, specifically whether the PMK consumed five or more drinks or more at least once per month in the 12 months preceding the interview. The PMK was also asked to report indicators of adversity at school and the number of schools attended when the child was over the age of 4 at the time of the interview.

In the NLSCY, certain questions were asked directly to the children themselves when age-appropriate. Children aged 10 and 11 were directly asked about negative aspects of their parenting (e.g. my parents (do not) smile at me, (do not) know where I am and what I am doing, (do not) praise me). Children in this age group were also asked directly about harassment and bullying (in addition to questions about bullying that were directed towards the PMK, as noted above).

In summary, there were a large number of childhood adversities and events assessed in these surveys and the linkage between them offered an opportunity to screen for associations between these exposures and proximal health effects during young adulthood. A summary of adversities recorded in various age groups is presented in Table 1.

Assessment of adult health outcomes using data collected in the NPHS

The NPHS consistently included the Composite International Diagnostic Interview Short Form

Table 1. Summary of childhood adversities assessed in the 1994 NLSCY interview, by age group

Age group covered (n) ^a	Respondent	Adversities covered	Measure employed	Format used in analysis
Age 0–11 (n = 1977)	PMK	Neighbourhood problems with...		0, 1, 2 or >2 problems
		Garbage	Yes/no item	
		Alcohol	Yes/no item	
		Drugs	Yes/no item	
		'Groups of young people causing trouble'	Yes/no item	
		Burglary	Yes/no item	
		Neighbourhood cohesion	5-item scale	Lower quartile
		Major stressful events ^b		One or more events
		Death of parent	Yes/no item	
		Death of family member	Yes/no item	
		Parents being separated	Yes/no item	
		Move	Yes/no item	
		A stay in foster care	Yes/no item	
		Other separation from parents	Yes/no item	
		Illness or injury of family member	Yes/no item	
		Abuse or fear of abuse	Yes/no item	
		Change in household member	Yes/no item	
		Alcohol/mental health issues in house	Yes/no item	
		Hospital stay	Yes/no item	
		Illness or injury of child	Yes/no item	
		Conflict between parents	Yes/no item	
		Other trauma	Yes/no item	
		Long-term medical conditions	Yes/no item	One or more
		(Low) physical activity	Yes/no item	Yes responses
		Young age of biological mother	Age recorded	14–19 years
		Young age of biological father	Age recorded	16–24 years
		Raised by lone biological mother	Yes/no item	Yes responses
		Number of changes in usual place of residence	Number recorded	Included as count
		Depression of PMK	CES-D scale	Score ≥21
		Alcohol (5+) PMK	Number recorded	>1 time in past year
Age 4–11 (n = 1330)	PMK	Needed to change schools	Number recorded	2+ times
		Adversity at school		One or more
		(not) feeling safe at school	Yes/no item	
		(not) feeling safe going to and from school	Yes/no item	
		Children say 'nasty and unpleasant things'	Yes/no item	

Continued

Table 1. Continued

Age group covered (n) ^a	Respondent	Adversities covered	Measure employed	Format used in analysis
Age 10 and 11 (n = 350)	Child	Being bullied at school	Yes/no item	One or more
		Bullied on my way to and from school	Yes/no item	
		Feel like an outsider or left out of things at school	Yes/no item	
		Negative parenting		
		My parents (do not) smile at me	Yes/no item	
		(do not) know where I am	Yes/no item	
		(do not) know what I am doing	Yes/no item	
		(do not) praise me	Yes/no item	
		(do not) appreciate me	Yes/no item	
		Threaten to punish me	Yes/no item	
		(do not) speak of the good things I do	Yes/no item	
		Hit me or threaten to do so	Yes/no item	
		(do not) seem proud of the things I do	Yes/no item	
		Adversity at school (see list above)		
Health outcomes		Major depressive episode	CIDI-SFMD	One or more
		Physical inactivity	Activity questions	5 of 9 criteria
		Educational attainment	Education level	<1.5 kcal/kg/day
		Alcohol consumption	7 day diary	<High school
		Binge drinking	5+ drinks/occasion	>Guidelines
		Antidepressant use	Self-report	>1 in past year
		'Sleeping pill' use	Self-report	Yes response
		Smoking	Self-report	Yes response
				Daily or occasional

^aTotal *n* for the linked dataset was 1977.^bEvents that caused a great amount of worry or unhappiness, see text for examples of possible events.

(CIDI-SF) (Kessler *et al.* 1998) for major depression, which assesses probable past year MDE, during each of its biannual interviews. Each cycle of the NPHS also included items assessing participation in 21 recreational activities, which were combined with metabolic indicator (MET) values (Statistics Canada, 2012) and time spent in the activities to calculate energy expenditures. The metabolic indicators represented a ratio of estimated energy expenditure during participation in an activity compared with the estimated energy expenditures in a resting state. A total of estimated energy expenditure from 1.5 kcal/kg/day to participation in recreational physical activity was used to categorise respondents into physically active or inactive categories. This level of activity corresponds to approximately 30 min of walking exercise per day (Statistics Canada, 2012).

The NPHS included a seven day alcohol consumption diary allowing classification of excessive consumption based on Canadian 'low risk' drinking guidelines (14 per week for men and 9 per week in women) (Centre for Addiction and Mental Health, 2010). It was also possible to identify respondents consuming five or more drinks on one occasion at least once a month (a common definition of binge drinking). Alcohol dependence was also measured in the 1996 NPHS cycle using the CIDI Short Form (Kessler *et al.* 1998) for that disorder. The NPHS documented a variety of other adult health outcomes that have been associated with childhood adversities. These included the use of antidepressant medications (Anda *et al.* 2007), sleep medication use (Chapman *et al.* 2011) and smoking (Chapman *et al.* 2011). In summary, the NPHS provided an opportunity to screen for associations between the large number of adversities listed above and several types of negative health outcome.

Analysis

As noted above, some of the measures of adversity were only asked to specific subsets of the study sample. In these cases, the analysis was restricted to that subset. To maximise the use of the follow-up data (which included repeated interviews, every 2 years, in the NPHS), we selected a method of analysis that could incorporate repeated observations from each respondent: Generalized Estimating Equations (GEE). As the outcome variables were binary, logistic regression was used. For this reason, the associations were quantified using OR. GEE analysis allows non-independent observations, such as repeated observations in an individual respondent, to be included in the model, and to allow the pattern of dependency between non-independent observations to be specified. We employed an unstructured correlation matrix (in

which each observation's association with others can have its own correlation), after determining the produced better goodness of fit statistics than independent (meaning that the repeated observations are uncorrelated) and exchangeable patterns (meaning that a single correlation coefficient can explain the correlation between repeated observations). Robust standard errors were used in all analyses. Extensive risk factor adjustments could not be made due to sample size limitations, however, when associations were observed in unadjusted estimates, logistic regression models adjusting for additional covariates were fit to the data. It may be surprising that the sample size limited risk factor modelling since the sample size was nearly 2000. However this did occur since: a minority of respondents experienced the adversities and outcomes, a different set of adversities were measured depending on age in 1994 and the adversities were often associated with one another. As a result, the extent of multivariable modelling was limited. However, where possible multivariable models adjusted for multiple adversities were made. Initial models made *a priori* planned adjustments for specific covariates judged to be probable confounding variables. Next, forward stepwise regression was employed. This was accomplished by first examining the bivariate associations and then adding additional variables to an evolving model, retaining or removing those variables depending on statistical significance.

As the analysis screened for a large number of associations it produced multiple estimates and a procedure was used to address multiplicity. The most common option, a Bonferroni adjustment was felt to be excessively conservative given the aims of the study. A Bonferroni correction would control the chance of any Type I error at 5%, whereas it was considered sufficient to control the false detection rate for each test at 5%. For this purpose, the Benjamini–Hochberg procedure was used. This was implemented using spreadsheet-based method described by Thiessen *et al.* (2002). Unlike the Bonferroni adjustment, which produces an adjusted *p*-value, the Benjamini–Hochberg procedure results in a series of *p*-values that are then applied to a sequential series of tests. With control of the overall false detection rate at 5%, the significant tests are expected to be false positives 5% of the time. For the PMK-reported adversities applicable to the entire sample, there were 14 associations examined and 14 Benjamini–Hochberg adjusted critical values which were therefore used to assess the significance of each of the 14 resulting *p*-values. For the age 4+ child-reported adversities and the age 10 and 11 child-reported adversities there were two adversities assessed in each case, see Table 1. Application of the Benjamini–Hochberg

procedure when there are only two tests results leads to critical values of $p = 0.025$ for the smallest p -value and 0.0125 for the larger one.

To further explore the observed associations, two epidemiological parameters that assess the impact of risk factors on disease frequency were calculated for adversities and outcomes that displayed consistent associations: the attributable fraction (AF) among the exposed and the population attributable fraction (PAF). The AF estimates the proportion of cases among those exposed to a risk factor (in this case, those with a childhood adversity) that could be prevented if that exposure could be removed or its effects ameliorated. The PAF estimates the proportion of cases in the total population that could be prevented by removing the exposure, or ameliorating its effects. The AF among the exposed was calculated as the risk difference between those exposed and not exposed to each adversity divided by the risk in the exposed population. PAF was calculated as the difference between the risk of outcome in the total population and the risk in the non-exposed divided by the risk in the total population. Both of these sets of estimates should be interpreted with caution since the subjects had not necessarily experienced the full risk interval. Nevertheless, they are reported here since their relative values provide a sense of the potential relative impact of the various adversities on population health. All analyses used Stata, version 12.1 (Stata Corp, 2012).

Results

There were $n = 1977$ respondents in the linked sample. After weighting for design effects, the sample had an approximately equal proportion of boys and girls at the time of the 1994 interview: 51.7% boys and 48.3% girls. The sample had 15.7% rural and 84.3% urban residence. In the NLSCY data, 16.3% were identified as being raised by a lone mother.

The annual prevalence of MDE in the linked sample ranged from 1.5 to 6.2% during follow-up. As expected, MDE was associated with the several of the childhood adversities. The adversities included major stressful events (OR = 1.9, 95% CI: 1.5–2.5), number of changes in residence (OR = 1.1, 95% CI: 1.0–1.2), neighbourhood cohesion (lower quartile) (OR = 1.5, 95% CI: 1.2–2.1), having a biological mother between the ages of 14 and 19 when child was born (OR = 1.9, 95% CI: 1.2–3.2), reporting three or more neighbourhood problems (OR = 1.6, 95% CI: 1.1–2.2) and school adversity (OR = 1.7, 95% CI: 1.2–2.3). The number of changes of residence was treated as a count so that the OR of 1.1 indicates a 10% increase in the odds of depression associated with each move.

A similar pattern was seen for psychotropic medication use, although the number of significant associations was smaller. The proportion of the sample that reported using antidepressants, for example, in the 30 days preceding any one or more NPHS interviews was 5.9% (95% CI 4.6–7.2). Elevated antidepressant medication use was observed in association with an increasing number of changes in residence (OR = 1.2, 95% CI: 1.1–1.3) and two (OR = 2.8, 95% CI: 1.5–5.2) or more (OR = 2.1, 95% CI: 1.2–3.9) neighbourhood problems. A similar pattern of association was observed for sleeping pill use, where both changes in residence (OR = 1.1, 95% CI: 1.0–1.2) and being raised by a lone mother (OR = 1.7, 95% CI: 1.1–2.7) were significant. The OR was 1.5, with an associated p -value of 0.097 (the Benjamini–Hochberg procedures required a p -value of 0.021 or less for significance of the third smallest p -value in this family of tests).

The prevalence of daily or occasional smoking on at least one wave of the NPHS was: 30.2% (95% CI: 27.6–32.8). A large number of adversities were associated with smoking. These included major stressful events (OR = 1.5, 95% CI: 1.2–1.8), being raised by a lone mother (OR = 1.5, 95% CI: 1.2–2.0), chronic conditions as a child (OR = 1.4, 95% CI: 1.1–1.7), adversity at school (OR = 1.8, CI: 1.4–2.2), depression in the PMK (OR = 2.2, 95% CI: 1.3–3.9) and changes in residences (OR = 1.1, 95% CI: 1.0–1.1). Alcohol-use outcomes were generally not associated with adversity. There was, however, a single exception: negative parenting (as directly reported by the 10- and 11-year-old children) was associated with the child subsequently exceeding the alcohol consumption guidelines (OR = 2.4, 95% CI: 1.3–4.3).

Neither physical activity nor educational attainment was associated with childhood adversities. Physical inactivity during childhood was, however, associated with physical inactivity in adulthood (OR = 2.3, 95% CI: 1.8–3.0). In the analysis of educational attainment, we estimated the proportion of respondents over the age of 17 at the last cycle of data collection that had not graduated from high school. The proportion of respondents falling into this category was 8.0% (95% CI 5.1–10.1). The only childhood adversities associated with this outcome were the number of changes in residence (OR = 1.2, 95% CI: 1.1–1.3) and adversity at school (OR = 2.0, 95% CI: 1.1–3.5).

In summary, the analysis indicated a large set of associations between childhood adversities and major depression, smoking and psychotropic medication use. However the use of psychotropic medications would often be an appropriate treatment of common mood and anxiety disorders, so the remainder of the analysis focused on major depression and smoking. AF and PAF estimates for these outcomes are reported

Table 2. Estimates of attributable fraction (among exposed) and population attributable fraction for risk factors associated with major depression and smoking*

	Major depression		Smoking	
	Attributable fraction, exposed (AF)	Attributable fraction, population (PAF)	Attributable fraction, exposed (AF)	Attributable fraction, population (PAF)
Neighbourhood cohesion	0.25	0.08		
Adversity at school	0.36	0.15	0.24	0.09
Major stressful events	0.51	0.21	0.23	0.07
Underage biological mother	0.36	0.03		
Raised by lone mother			0.12	0.02
Depression of PMK			0.22	0.01
Negative parenting	0.29	0.15		

*Because neighbourhood problems and number of changes in residence were categorised at several levels, AF and PAF were not calculated for these variables.

in Table 2 for each of the binary variables found to be significantly associated with those outcomes. Major stressful events during childhood were the exposures associated with the highest AF and PAF for both outcomes. This is due to the combination of the strong associations seen for these variables and the high frequency of exposure. The PARs suggest that 21% of major depression in the population and 7% of smoking is attributable to major stressful events during childhood.

To explore the resilience of these associations to adjustment for potential confounding variables,

logistic regression models were used to adjust for variables judged, *a priori*, to be potential confounders. In the MDE analysis, each of the significant associations was adjusted for sex, maternal depression and smoking status. In the smoking analysis, these models included adjustments for sex, maternal depression and maternal smoking status. Unadjusted and adjusted ORs are presented in Table 3. Table 4 presents models arising from forward variable selection. In the depression models, childhood adversity, sex, neighbourhood cohesion and smoking were consistently associated with MDE. In the smoking models,

Table 3. Unadjusted and adjusted ORs for risk factors associated with major depression and smoking

	Major depression		Smoking	
	Unadjusted OR	Adjusted OR*	Unadjusted OR	Adjusted OR†
Neighbourhood cohesion	1.5 (1.2–2.1)	1.5 (1.1–2.0)		
3+ neighbourhood problems	1.6 (1.1–2.2)	1.5 (1.0–2.2)		
Adversity at school	1.7 (1.2–2.3)	1.6 (1.2–2.2)	1.8 (1.4–2.2)	1.6 (1.3–2.0)
Major stressful events	1.9 (1.5–2.5)	1.8 (1.4–2.4)	1.5 (1.2–1.8)	1.4 (1.1–1.7)
Underage biological mother‡	1.9 (1.2–3.2)	1.6 (0.9–2.7)		
Raised by lone mother			1.5 (1.2–2.0)	1.3 (1.0–1.6)§
Chronic condition in child			1.4 (1.1–1.7)	1.3 (1.1–1.6)
Depression in PMK			2.2 (1.3–3.8)	1.9 (1.1–3.4)
Number of residence changes	1.1 (1.0–1.2)	1.1 (1.0–1.2)††	1.1 (1.0–1.1)	1.0 (1.0–1.1)§

*Adjusted for sex, depression in the PMK (almost always biological mother) and smoking status. Note that negative parenting is not included in the table, as this variable was not associated with either of these outcomes.

†Adjusted for sex, smoking in the PMK and major depression at any cycle.

‡Age 14–19 at the time of birth of the child.

§ $p=0.003$ for number of residence changes in the depression analysis, $p=0.07$ in the smoking and lone mother analysis and $p=0.10$ in the smoking and number of changes in residence analysis.

Table 4. Two logistic regression models (model 1 predicting major depression, model 2 predicting smoking) with multiple covariate adjustments

Model 1		Model 2	
Major depression		Smoking	
	Odds ratio (95% CI)		Odds ratio (95% CI)
Female sex	2.4 (1.8–3.1)	Female sex	0.9 (0.6–1.2)
Smoking	2.4 (1.9–3.2)	Major depressive episode	1.8 (1.2–2.6)
Neighbourhood cohesion	1.4 (1.1–1.9)	Smoking of the PMK*	1.4 (1.0–2.0)
Major stressful events	1.7 (1.3–2.2)	Negative parenting	1.5 (1.0–2.1)
		Depression in the PMK*	5.6 (2.1–14.9)

*Person most knowledgeable, usually the biological mother.

depression, negative parenting and both maternal smoking and depression in the PMK were consistently associated with smoking in young adulthood. Generally, there was little evidence of confounding in any of these analyses. On a few occasions the lower bounds of confidence intervals (CI) fell below the value of 1.0 for the OR adjusted analyses (p -values are reported each time that this occurred, see Table 3), but this occurred in the absence of substantial change in the estimates themselves, suggesting that the associations reported are not artefacts of confounding by these variables. One exception is that the association of smoking with childhood adversities tended to weaken with adjustment for MDE, see Table 3.

Discussion

This study determined that a group of related adult health outcomes (depression, smoking and psychotropic medication use) are consistently associated with a variety of childhood adversities. Several other variables were not as consistently associated (excessive alcohol consumption, low educational attainment and physical inactivity). One possible interpretation is that depression may be a primary or more proximal outcome of childhood adversity and that at least some subsequent smoking and psychotropic medication use is secondary to this primary outcome. Both smoking (Chaiton *et al.* 2009) and medication use (Beck *et al.* 2005) are known to be strongly associated with MDE. Consistent with this idea, the associations between various adversities and smoking tended to weaken with adjustment for MDE, see Table 3.

An influential study linking adverse childhood events to adult health status was the ACE study (Felitti *et al.* 1998) and the current investigation was to some extent an effort to replicate these findings using

a prospective approach. However, it should be pointed out that the two studies differ in several important respects beyond the prospective *v.* retrospective distinction. The ACE study was conducted on an adult sample across the age range whereas the prospective follow-up of our linked sample meant that all of the subjects were under the age of 30 when the data collection ended, and most were younger than this. Many of the conditions found to be associated with childhood adversities in the ACE study (including chronic lung disease, cancers and ischaemic heart disease) would not yet have emerged during the age-range employed in our study. However, the association of childhood adversities with smoking implies that associations with lung disease, cancers and ischaemic heart disease may have emerged with longer follow-up, suggesting a chain of causal events potentially linking childhood adversity to a plurality of adverse outcomes, as reported by ACE, across the lifespan. Some of the negative associations found in the current investigation may have been due to the modest sample size and relatively brief follow-up interval.

One of the most striking findings was the consistent way in which the number of changes in residence during childhood emerged as being associated with several of the adult outcomes examined. Although the OR were small, it should be remembered that this variable was included as a count, so these OR imply large effects from a large number of changes in residence. This variable is likely to represent a proxy for other more meaningful exposures, such as psychosocial or material challenges correlated with frequent moves. Disruption of social networks may also be a mechanism. Unfortunately, the dataset did not allow a more detailed exploration of these issues.

The main strength of this study is that it was able to examine a number of associations without relying on retrospective reporting of childhood adversities.

However, as the linkage was only possible for a subset of NLSCY participants the sample sizes were too low to support extensive multivariable analyses. In particular, where multiple adversities were associated with some of the outcomes examined, the individual effects of specific adversities could not be teased out in multivariate analyses due to sample size constraints. Confounding may have occurred as it was not possible to make simultaneous adjustments for large numbers of potential confounding variables. All subjects entered the NPHS at the age of 12 even though their participation in the NLSCY occurred between the ages of 0 and 11, so adjustment for age was not necessary. Effect modification by sex is also a possibility, although no sex by exposure interactions achieved statistical significance in this analysis. As these were population studies, brief measures were often employed (e.g. questionnaires and single items). Such measures are subject to inaccuracy. For example, a PMK that had abused a child might not have reported this abuse, lowering the sensitivity of the relevant items.

Childhood adversity is believed to be connected to adult health at least partially through mechanisms linking those adversities to long-term changes in stress responsiveness. As such, associations with conditions characterised by HPA activation such as major depression are biologically plausible. Our analysis supports this, as the two other outcomes that were consistently associated with childhood adversity are closely connected to depression: smoking and psychotropic medication use.

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Conflict of Interest

None.

Ethical Standard

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

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