Retrospectively reported childhood adversity is associated with asthma and chronic bronchitis, independent of mental health

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Citation:
Abstract

Several researchers have raised the concern that the cross-sectional association of retrospectively reported childhood adversity with self-reported onset of asthma and chronic bronchitis in adulthood may be confounded, as well as mediated by an individual's mental health. The aim of this study was to assess the effect of retrospectively reported childhood adversity on self-reported onset of asthma and chronic bronchitis in adulthood, independent of potential confounding and mediating variables (including respondent's mental health). We used data collected in 2007–2008 within the framework of the Tromsø Study (N = 12,981), a representative study of adult men and women in Norway. The associations of childhood adversity with asthma and chronic bronchitis were assessed with Poisson regression models. Relative risks (RR) and 95% confidence intervals (CI) were estimated with bias-corrected bootstrapping. Childhood adversity was associated with a 9% increased risk of asthma (RR = 1.09, 95% CI: 1.02, 1.16) and a 14% increased risk chronic bronchitis (RR = 1.14, 95% CI: 1.03, 1.26) in adulthood, independent of age, sex, parental history of psychiatric problems/asthma/dementia, education, smoking, social support, and respondent's mental health. Controlling for indicators of respondent's mental health reduced the strength of associations of childhood adversity with asthma and chronic bronchitis; however, the associations were still present in the same direction (p < .05). These findings suggest that the association of retrospectively reported childhood adversity with asthma and chronic bronchitis is independent of respondent's mental health. We recommend controlling for indicators of the respondent's mental health to assess an unbiased association of retrospectively measured childhood adversity with self-reported asthma and chronic bronchitis.

Keywords: Confounder; direct effect; recall bias; differential measurement error; mental health; psychological state; mood congruency; asthma; chronic bronchitis
What is already known on this subject?

- Association of childhood adversity with asthma and chronic bronchitis is overestimated due to differential recall bias, and confounding via mental health.
- Mental health mediates the association of childhood adversity with asthma and chronic bronchitis.

What this study adds?

- Childhood adversity is independently associated with an increased risk of asthma and chronic bronchitis.
- The association of retrospectively reported childhood adversity with asthma and chronic bronchitis is not driven entirely by respondent's mental health.
Introduction

Several population-based studies have shown that childhood adversity is associated with an increased risk of stress-related physical health outcomes, such as asthma and chronic bronchitis later in life [1-8]. The role of mental health in the association of childhood adversity with onset of asthma and chronic bronchitis has been hypothesized in two ways: (1) mediation, whereby childhood adversity is associated with an increased risk of mental health problems, which in turn are associated with an increased risk of asthma and chronic bronchitis [8] (figure 1a); and (2) confounding and differential recall bias, i.e., psychological state of respondents at the time of reporting childhood adversity [7] may confound the association of retrospective childhood adversity with self-reported asthma and chronic bronchitis [1] (figure 1b). When considering the mediation hypothesis, childhood adversity can certainly affect mental health [8, 9], while simultaneously affecting onset of asthma and chronic bronchitis via psychogenic relationships [1, 3, 7, 8, 10-12]. Mental health problems may also affect the experience of asthma and adherence to treatment and hospitalization rates [13-15]. Previous evidence has suggested that almost half of all cases of psychiatric disorders manifest by age 14 years and three-fourths by age 24 years [16] [see also [17]]. This could imply that mental health in adulthood represents a continuation or a recurrence of childhood or adolescent mental health. Accordingly, mental health may mediate the association of childhood adversity with asthma and chronic bronchitis, even if it is measured in adulthood [8]. The association of childhood adversity with a wide range of psychiatric disorders is well-established [4, 8, 18-24]. In turn, several previous studies have shown that poor mental health is associated (directly or indirectly) with an increased risk of asthma and chronic bronchitis [5, 11, 25-31], and that indicators of mental health mediate the association of childhood adversity with asthma and chronic bronchitis [1, 5, 8, 11, 25].
Regarding the second explanation (confounding and differential recall bias), several researchers have raised the concern that the observed association of retrospectively-reported childhood adversity with asthma and chronic bronchitis could be an artefactual correlation driven by the current psychological state of the respondent via anchoring effect, affective states, deficits in memory functioning, mood-congruency bias, and biased autobiographical memory [7, 32-53]. Individuals with mental and physical health problems could be more likely to report adverse childhood experiences [1, 7]. Indeed, even twins or siblings may recall and perceive their financial and psychosocial circumstances in childhood differently [54-58]. If current psychological state confounds the association of retrospectively-measured childhood adversity with asthma and chronic bronchitis, the relationship of childhood adversity with asthma and chronic bronchitis may flow through the mechanism of memory retrieval and attribution from the adult to childhood years [7]. For instance, asthma or chronic bronchitis cases may assign more significance to past events by over-reporting childhood adversity in an attempt to search for explanations and to make sense of their current health [1, 7]. Generally, these criticisms are based on the hypothesis that self-reported childhood adversity and self-reported health are not entirely distinct "things" if the correlation between them is driven by subjectivity and differential measurement error, which can lead to spurious correlations between them [7]. For this reason, it is necessary to know whether the association of childhood adversity with asthma and chronic bronchitis is free from biases related to current mental health [1, 7, 59].

The association of retrospectively-measured childhood adversity with asthma and chronic bronchitis is unique in the sense that it is impossible to separate the mediating and confounding mechanisms of mental health. The statistical approach [difference-in-coefficients method [60]] to estimate the effect of childhood adversity on asthma and chronic bronchitis, independent of respondent’s mental health is exactly the same whether
respondent’s mental health is hypothesized as a mediator or as a confounder [7, 60-62].

Estimation of “direct effect” is not appropriate in this setting, because the term implies the
effect of an exposure on an outcome that is not mediated via specific mediator(s) [60], and it
does not take into account the potential confounding and recall bias by some hypothesized
mediating variables, such as indicators of mood state. Similarly, the estimation of “indirect
effect” [difference between total and direct effect [60]] is not meaningful in this setting,
because the estimate of childhood adversity may be attenuated by controlling for indicators of
mental health not only due to mediation, but also because of potential confounding by
respondent’s mental health. Therefore, the “independence hypothesis” [7] may be more
meaningful, as it tests whether childhood adversity is associated with asthma and chronic
bronchitis, independent of potential confounders and respondent’s mental health. In addition,
the independence hypothesis ignores the distinction between a mediator and a confounder [7];
instead, it focuses on the influence of childhood adversity on asthma and chronic bronchitis
that is neither mediated nor confounded by respondent’s mental health.

In this study, we used a wide range of indicators of mental health, without assuming
the direction of the associations between them. We assumed that some indicators of mental
health may confound the childhood adversity → asthma and chronic bronchitis associations,
while others may mediate the childhood adversity → asthma and chronic bronchitis
associations. However, our focus was not to separate the mediating and confounding
mechanisms of mental health, but rather to focus on the estimation of the independent effect
[7] of childhood adversity on asthma and chronic bronchitis, and to assess if childhood
adversity is associated with asthma and chronic bronchitis even after accounting for a wide
range of indicators of mental health.
The aim of this study was to estimate the effect of childhood adversity on asthma and chronic bronchitis, independent of potential confounding and mediating variables (including respondent's mental health).
Methods

Study population

The Tromsø Study is a cohort study, representative of the adult population residing in the municipality of Tromsø [7, 63]. The present analysis includes cross-sectional data collected for the Tromsø VI survey in 2007-2008; 19,762 subjects were invited to the Tromso VI survey, and 12,981 (65.7%) returned the Tromso VI questionnaire [7].

Ethical approval

This investigation was carried out in accordance with the latest version of the Declaration of Helsinki. The Tromsø Study has been approved by the Regional Committee for Medical and Health Research Ethics, the Data Inspectorate, and the Norwegian Directorate of Health. Written informed consent was obtained from all participants included in the study.

Study variables

Exposure (childhood adversity)

Childhood adversity is defined as a conglomerate of factors that have been used in a similar manner in previous studies [64, 65]. The present analysis used four indicators of retrospectively-reported childhood adversity. Childhood financial conditions was used as an indicator of economic background, and was obtained through the question: “How was your family’s financial situation when you were a child?” Participants replied using a 4-point scale ranging from very difficult (1) to very good (4) [7]. Those who answered difficult or very difficult were considered to have this childhood adversity [7]. The test-retest reliability of childhood financial conditions was good in the Tromsø Study [7, 23]. Information on adverse childhood experiences were obtained through the question: “Have you over a long period experienced any of the following as a child?: (i) being tormented or threatened with violence;
(ii) being beaten, kicked, or the victim of other types of violence; and (iii) someone in your close family using alcohol or drugs in such a way that caused you worry [7]. Each of these adverse childhood experiences were considered a childhood adversity [64, 65]. The internal reliability of these adverse childhood experiences was good in the Tromso Study [1]. A composite variable was then constructed as the sum of all four childhood adversities, thus scores ranged from 0 to 4 (mean: 0.51, standard deviation [SD]: 0.78). Cronbach’s alpha for the four indicators of childhood adversity was 0.49 (mean inter-item covariance: 0.19).

Outcomes (asthma and chronic bronchitis)

Participants completed separate questions in the questionnaire on self-reported diagnosis of asthma and chronic bronchitis, as follows: “Do you have, or have you had asthma?” (no=0, yes=1), and “Do you have, or have you had bronchitis/emphysema/COPD?” (no=0, yes=1)

Confounding variables

The potential confounding and mediating variables, age, sex, parental history of psychiatric problems/asthma/dementia, education, smoking, social support, and respondent’s mental health, were chosen based on a priori knowledge of the correlates of childhood adversity and asthma and chronic bronchitis [1, 5, 7, 8, 11, 23-25, 66-68]. With reference to the literature on mediation analysis, if there are any measured variables that may confound the mental health → asthma/chronic bronchitis association (e.g., education, smoking, and social support) and are affected by childhood adversity, then they should be included in the multivariable regression model as confounding variables. Note that controlling for both intermediate confounders and potential mediators (indicators of mental health) implies that one is also considering potential intermediate confounders as mediators [60]. This is similar to the setting in which both the intermediate confounder and mediator are
considered jointly as a single mediator [69], not as separate variables [60]. This implies that any unmeasured variables that affect both the intermediate confounder and onset of asthma or chronic bronchitis, and are affected by childhood adversity, may still induce some intermediate confounding.

Valid information on age and sex was obtained from Statistics Norway, using the unique personal identification number of each respondent [8]. Participants completed a separate question for parental history of chronic conditions (psychiatric problems, asthma, and dementia) as: “Does your mother/father have/has your mother/father ever had [health outcome]?” (yes, no). Education level was measured on a 5-point scale as: 1) college or university (4 years or more); 2) college or university (less than 4 years); 3) high school diploma; 4) vocational school or technical school; and 5) primary and secondary school or similar (i.e., 7–10 years of schooling). The test-retest reliability of education level was very good (Kappa: 0.91, 95% CI: 0.91, 0.92) in the Tromsø Study [67]. Daily smoking was measured by the question, “Do you or did you smoke cigarettes daily?” (never/yes, previously/yes, now). Social support was measured with two questions on instrumental support and emotional support. Instrumental support was measured as: “Do you have enough friends who can give you help and support when you need it?” (yes = 0, no = 1). Emotional support was measured as: “Do you have enough friends you can talk confidentially with?” (yes = 0, no = 1). Cronbach alpha for the two indicators on social support was 0.77 (inter-item covariance: 0.63; 95% CI: 0.62, 0.64).

Indicators of respondent’s mental health

Respondent’s mental health was assessed by several questions on anxiety; depression; insomnia; psychological distress; use of sleeping pills, antidepressants, and tranquilizers; memory problems; and prevalence of psychiatric problems [7]. Anxiety and depression was
measured by a question with three response alternatives (1=I am not anxious or depressed, 2=I am somewhat anxious or depressed, 3=I am very anxious or depressed) [7]. Depression was also measured by the question: “Have you been feeling unhappy and depressed during the past two weeks?” with four possible responses (1=not at all, 2=no more than usual, 3=rather more than usual, 4=much more than usual) [7]. Psychological distress [64, 65, 67, 68] was measured using the 10-item Hopkins Symptom Checklist (HSCL-10), which has been shown to have an acceptable degree of internal consistency in this sample (Cronbach's alpha: 0.90, mean inter-item correlation: 0.43, McDonald's omega coefficient for composite reliability: 0.91)[7, 23, 68]. The 10 items in the HSCL-10 are rated by the respondent on a four-point scale, ranging from not at all (1) to extremely (4). A HSCL-10 score was calculated by summing the score of all 10 items, thus possible scores ranged from 10 to 40, with 40 representing the highest and 10 representing the lowest psychological distress (mean: 12.78, SD: 3.60) [7]. Sleeping difficulty was measured by the question: “Have you had difficulty sleeping during the past couple of weeks?” (1=not at all, 2=no more than usual, 3=rather more than usual, 4=much more than usual) [7]. Insomnia was measured by the question: “How often do you suffer from sleeplessness?” (1=never, or just a few times a year, 2=1-3 times a month, 3=approximately once a week, 4=more than once a month) [7, 68]. Consultation with a psychiatrist was measured by the question: “Have you during the past year visited a psychiatrist?” (0=no, 1=yes) [7]. Use of sleeping pills, antidepressants, and tranquilizers was measured by three separate questions: “How often have you used sleeping pills/antidepressants/tranquilizers during the last 4 weeks?” (1=not used, 2=less frequently than every week, 3=every week, but not daily, 4=daily) [7]. Forgetfulness was measured by the question: “Do you often forget where you have placed your things?” (0=no, 1=yes), and decline in memory was measured by the question: “Has your memory declined?” (0=no, 1=yes) [7]. Memory examination was measured by the question: “Have you been examined
for memory problems?” (0=no, 1=yes) [7]. Prevalence of psychiatric problems [24, 68] was measured by the question: “Do you have, or have you had psychiatric problems for which you sought help?” (0=no, 1=yes) [7]. Prevalence of psychiatric disorders was measured by the question: “Do you have, or have you had psychiatric disorder(s)?” (0=no, 1=yes) [8].

**Statistical Analysis**

All statistical analyses were conducted using Stata version 15. Fifty datasets were imputed for generating missing values with multiple imputation with chained equations. A comparison between the complete-case (excluding missing) and the imputed datasets is presented with proportions (%), and mean (standard error, SE) (Table 1). No statistically significant multiplicative interactions between childhood adversity and confounding variables, or between childhood adversity and indicators of mental health were observed. The associations of childhood adversity with asthma, and chronic bronchitis (Table 2) were assessed with Poisson regression models. Relative risks (RRs) were estimated and both the unadjusted (crude) and adjusted estimates (from multivariable regression models) are presented. Error variance were derived with first-order Taylor-series linearization method [70, 71] in Stata, and 95% confidence intervals (CIs) are presented. We estimated RRs instead of odds ratios, because odds ratios can over-estimate risk, particularly when the outcome is not rare [60]. Previous literature has repeatedly argued that neither confounding nor mediation should not be assessed using odds ratios [60, 72-76], because an odds ratio is not a collapsible measure [77] and attenuations in odds ratios do not necessarily correspond to confounding or mediation [78, 79]. In practice, estimates of exposure in logistic regression analyses may attenuate after entering an additional covariate in the model due to unobserved heterogeneity, even if the additional covariate neither confounds nor mediates the exposure-outcome association [79, 80]. Since the aim of this study was to estimate the effect of
childhood adversity on asthma and chronic bronchitis, independent of respondent's mental health, presenting adjusted estimates on an odd ratio scale could be misleading.
Results

The distributions of variables were similar in the complete-case dataset (excluding those with missing values) and the imputed datasets (Table 1). In this sample, 62.8% of respondents reported no childhood adversity, 27.9% reported any one childhood adversity, 6.4% reported any two childhood adversities, 2.3% reported any three childhood adversities, and 0.6% reported all four childhood adversities. The prevalence of asthma and chronic bronchitis in adulthood were 10.1% and 4.8%, respectively (Table 1). A minor proportion of the respondents had missing values on childhood adversity (7.4%), asthma (2.5%), and chronic bronchitis (2.7%). Missing values on childhood adversity was associated with a higher age (p=0.031), a lower education level (p<0.001), lack of instrumental support (p=0.015), a higher psychological distress (p=0.009), and prevalence of psychiatric disorders (p<0.001). Missing values on asthma were associated with a higher age (p<0.001), a lower education level (p=0.042), prevalence of psychiatric problems (p=0.001), prevalence of psychiatric disorders (p<0.001), a higher psychological distress (p=0.001), and memory examination (p=0.008). Missing values on chronic bronchitis were associated with a higher age (p<0.001), a higher psychological distress (p=0.001), a decline in memory (p=0.010), memory examination (p=0.003), psychiatric problems (p<0.001), and psychiatric disorders (p<0.001).

Indicators of childhood adversity were correlated with each other (r=0.08-0.51; p<0.001) in the predicted direction (data not shown).

No statistically significant (p>0.05) childhood adversity*age multiplicative interaction was observed. Two estimates are presented in Table 2: model 1 presents crude (unadjusted) associations; model 2 presents estimates from the multivariable regression model, adjusted for confounding variables and indicators of mental health. The bivariate (unadjusted) association of childhood adversity with asthma, and chronic bronchitis indicated that childhood adversity is associated with increased risk of both asthma (RR=1.16, 95% CI: 1.09,
1.23) and chronic bronchitis (RR=1.30, 95% CI: 1.20, 1.42) (Table 2). The relative risks should be interpreted in terms of the extent to which a one-point increase in the childhood adversity measure is associated with an increased risk of asthma or chronic bronchitis. After controlling for confounding and mediating variables, childhood adversity was associated with a 9% increased risk of asthma (RR=1.09, 95% CI: 1.02, 1.16), and a 14% increased risk of chronic bronchitis (RR=1.14, 95% CI: 1.03, 1.26) (Table 2). In the complete-case analysis, all associations remained in the same direction (data not shown).
This study sought to estimate the independent effect of childhood adversity on asthma and chronic bronchitis in a large and representative cross-sectional sample of the general Norwegian population. After adjusting for a wide range of indicators of respondent’s mental health, we found that childhood adversity was independently associated with asthma and chronic bronchitis. Accordingly, this study supports the view that the association of childhood adversity with asthma and chronic bronchitis is not driven entirely by respondent’s mental health, as this association remained in the same direction after controlling for a wide range of indicators of mental health. The results of the present study correspond with other evidence [1, 7, 8, 81-88], in that the association of childhood adversity with health was primarily independent of selected confounding and mediating variables (including respondent’s mental health). However, it must be noted that estimation of independent effect is a conservative approach, as the magnitude of the casual association of childhood adversity with asthma or chronic bronchitis could be underestimated proportioned to how much of its indirect effects are mediated through controlled variables. Moreover, it is important to highlight the implications for assessing independent effect vs direct/indirect effects: the independent hypothesis suggests that one should rather focus on establishing childhood adversity as a risk factor whereas the mediation hypothesis focuses on understanding the mechanism by which childhood adversity affects physical health.

Several mechanisms may explain the association of childhood adversity with asthma and chronic bronchitis. Evidence from stress biology shows that childhood adversity can have lasting effects on brain development, brain stress regulatory flow systems, and psychophysiological responses, including enhanced activity and dysregulation of the hypothalamic–pituitary–adrenal axis, neuroendocrine immune circuitry and autonomic nervous system function [8, 89-94]. These alterations can result in impairment of the body’s
immune function and cardiorespiratory system [6, 95, 96], which in turn may increase the
risk of respiratory infections, and eventually asthma and chronic bronchitis [8, 89, 97-99].
Other evidence suggests that hormones and inflammation related to stress can lead to
contractions of smooth muscle and excess of mucus production, which in turn may increase
the risk for incident asthma [100]. Another perspective on the association of childhood
adversity with asthma and chronic bronchitis is stress-sensitization model [101, 102], which
suggests that exposure to childhood adversity may elevate sensitivity [23, 24, 64], immune
biomarkers [103], and pro-inflammatory responses via the process of biological embedding
of stress [104], allostatic load theory [105], or body programming [106].

Some limitations should be considered for the interpretation of these findings. All
variables (except age and sex) are self-reported. Childhood adversity was measured with four
single-item indicators; therefore, it is likely that there is considerable non-differential
measurement error (i.e., unreliability) in childhood adversity [7, 82, 88, 107, 108], which
would lead to an under-estimation of its association with asthma and chronic bronchitis.
Some potential confounding variables are missing in this study; for instance, a stressful social
milieu could contribute to adverse childhood experiences and onset of asthma [109]. Potential
confounding by a stressful social milieu is difficult to capture in survey research, particularly
with reference to problems related to retrospective reports. The strengths of this study include
a large and representative sample, and adjustment for respondent’s mental health via a wide
range of indicators. Finally, it must be noted that the independence hypothesis may only be
relevant when childhood adversity is retrospectively reported [7]. For prospective studies, or
studies where information on childhood adversity is collected via objective sources, the
independence hypothesis may not be meaningful, as the role of mental health as a mediator
could be assessed without worrying about the potential bias (via mental health) in recalling
and reporting childhood adversity.
It is plausible that onset of asthma or chronic bronchitis acts as a mediator in the association of childhood adversity with mental health (i.e., reverse causality between asthma/chronic bronchitis and mental health). Indeed, respondent’s mental health could be a consequence of asthma or chronic bronchitis, rather than a cause or confounder [110]. In such case, including indicators of respondent’s mental health in the multivariable regression model for asthma or chronic bronchitis may induce a spurious (non-causal) association between childhood adversity and asthma/chronic bronchitis due to collider-stratification bias. However, the crude association of childhood adversity with asthma and chronic bronchitis was in the same direction, without controlling for indicators of mental health.

Often the disagreement between prospective and retrospective measures of childhood adversity (such as childhood abuse) are used to highlight the bias in self-reports. While objective measures of childhood abuse (e.g., via school records, child protection services, medical records, court ruling, etc.) are helpful in ignoring differential or non-differential recall bias and confounding via mental health, the disadvantage is that only a minor proportion of childhood abuse cases are identified via official records. A concordance between one potentially under-estimated measure (official records) and another potentially biased measure (retrospectively-reported childhood abuse) will always be low because the underlying mechanisms of measurement error are substantially different in both cases. Retrospective measurement of childhood adversities such as childhood abuse is not just “convenient”, it may also be the only way to measure unreported, unidentified events and experiences that no one other than the victim knows about [111]. If both prospective and retrospective measurements of childhood abuse are available, then it is more meaningful to classify the unexposed group (reference group) as that which did not report childhood abuse and shows no evidence of childhood abuse via objective indices. Classifying unexposed individuals by combining information from both official records and self-reports would be
more meaningful in the establishment of a causal association between childhood abuse and health, rather than focusing on the discrepancy between estimates of prospective vs retrospective measures of childhood abuse and health. However, it must be noted that retrospective assessments can still be assessed at multiple time points prospectively, which would be stronger than the current cross-sectional approach.

These findings do not support the conclusion that the association of childhood adversity with asthma and chronic bronchitis is an artefact of respondent’s mental health. In summary, the results of this study showed that the association of childhood adversity with asthma and chronic bronchitis is independent of respondent’s mental health in a large cross-sectional sample of adults in Norway.
References


[99] F.D. Martinez, Role of respiratory infection in onset of asthma and chronic obstructive pulmonary disease, Clinical & Experimental Allergy 29 (1999) 53-58.


Figure 1a. Role of mental health as a mediator in the association of childhood adversity with asthma and chronic bronchitis

Baseline confounders (age, sex, parental history of psychiatric problems/asthma/dementia)

Childrenhood adversity

Mental health

Asthma and chronic bronchitis

Figure 1b. Role of mental health as a confounder in the association of childhood adversity with asthma and chronic bronchitis

Baseline confounders (age, sex, parental history of psychiatric problems/asthma/dementia)

Childrenhood adversity

Mental health

Asthma and chronic bronchitis

Figure 1. Role of mental health as a mediator (a) and confounder (b) in the association of childhood adversity with asthma and chronic bronchitis.
Table 1. General characteristics of the study sample (N=12,981).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Complete-case data</th>
<th>Imputed data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (%)</strong></td>
<td><strong>%</strong></td>
<td><strong>%</strong></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>mean [standard error (SE)]</td>
<td>57.5 (0.1)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6053 (46.6)</td>
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</tr>
<tr>
<td>Female</td>
<td>6928 (53.4)</td>
<td></td>
</tr>
<tr>
<td><strong>Parental history of psychiatric problems</strong></td>
<td>Yes</td>
<td>1037 (8.0)</td>
</tr>
<tr>
<td><strong>Parental history of asthma</strong></td>
<td>Yes</td>
<td>1517 (11.7)</td>
</tr>
<tr>
<td><strong>Parental history of dementia</strong></td>
<td>Yes</td>
<td>1387 (10.7)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td>Mean (SE)</td>
<td>2.7 (0.01)</td>
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<td><strong>Daily smoking</strong></td>
<td>Never</td>
<td>4767 (37.3)</td>
</tr>
<tr>
<td></td>
<td>Yes, previously</td>
<td>5407 (42.3)</td>
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<td></td>
<td>Yes, now</td>
<td>2610 (20.4)</td>
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<td><strong>Instrumental support</strong></td>
<td>Yes</td>
<td>11014 (88.9)</td>
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<td><strong>Emotional support</strong></td>
<td>Yes</td>
<td>10821 (87.2)</td>
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<td><strong>Anxiety and depression</strong></td>
<td>Mean (SE)</td>
<td>1.2 (0.01)</td>
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<td><strong>Depression</strong></td>
<td>Mean (SE)</td>
<td>1.5 (0.01)</td>
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<td><strong>Psychological distress (HSCL-10)</strong></td>
<td>Mean (SE)</td>
<td>12.8 (0.04)</td>
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<tr>
<td><strong>Sleeping difficulty</strong></td>
<td>Mean (SE)</td>
<td>1.6 (0.01)</td>
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<td><strong>Insomnia</strong></td>
<td>Mean (SE)</td>
<td>1.7 (0.01)</td>
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<td><strong>Consultation with psychiatrist</strong></td>
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<td>336 (2.7)</td>
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<td><strong>Use of sleeping pills</strong></td>
<td>Mean (SE)</td>
<td>1.2 (0.01)</td>
</tr>
<tr>
<td><strong>Use of antidepressants</strong></td>
<td>Mean (SE)</td>
<td>1.1 (0.01)</td>
</tr>
<tr>
<td><strong>Use of tranquilizers</strong></td>
<td>Mean (SE)</td>
<td>1.1 (0.01)</td>
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<td><strong>Forgetfulness</strong></td>
<td>Yes</td>
<td>3203 (27.2)</td>
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<td><strong>Decline in memory</strong></td>
<td>Yes</td>
<td>5955 (50.0)</td>
</tr>
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<td><strong>Memory examination</strong></td>
<td>Yes</td>
<td>146 (1.2)</td>
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<td><strong>Prevalence of psychiatric problems</strong></td>
<td>Yes</td>
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<td><strong>Prevalence of psychiatric disorders</strong></td>
<td>Yes</td>
<td>14 (0.1)</td>
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<td><strong>Childhood adversity</strong></td>
<td>Mean (SE)</td>
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<td><strong>Asthma</strong></td>
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<td>1253 (9.9)</td>
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<tr>
<td><strong>Chronic bronchitis/emphysema/COPD</strong></td>
<td>Yes</td>
<td>569 (4.5)</td>
</tr>
</tbody>
</table>

a The numbers for some variables do not add up to 12,981 due to missing values.
b There were no missing values, so no imputations were made for these variables.
c The four childhood adversities considered were: difficult or very difficult subjective childhood financial conditions, psychological abuse, physical abuse, and substance abuse distress in childhood.
SE: standard error; HSCL-10: Hopkins Symptom Check List-10.
Table 2. Association of childhood adversity with asthma and chronic bronchitis (n=12,981).

<table>
<thead>
<tr>
<th></th>
<th>Model 1</th>
<th>Model 2&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR (95% CI)</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td><strong>Crude (unadjusted)</strong></td>
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<tr>
<td><strong>Asthma</strong></td>
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<tr>
<td>Childhood adversity</td>
<td>1.16 (1.09, 1.23)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.09 (1.02, 1.16)&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td><strong>Chronic bronchitis/emphysema/COPD</strong></td>
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<tr>
<td>Childhood adversity</td>
<td>1.30 (1.20, 1.42)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1.14 (1.03, 1.26)&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Adjusted for age, sex, parental history of psychiatric problems, parental history of asthma, parental history of dementia, education, smoking, social support + respondent’s current mental health (anxiety and depression, depression, psychological distress (HSCL-10), sleeping difficulty, insomnia, consultation with psychiatrist, use of sleeping pills, use of antidepressants, use of tranquilizers, forgetfulness, decline in memory, memory examination, psychiatric problems, psychiatric disorders).

<sup>b</sup> p<0.001
<sup>c</sup> p=0.015
<sup>d</sup> p<0.001
<sup>e</sup> p=0.011

RR: relative risk; CI: confidence interval; COPD: chronic obstructive pulmonary disease.