

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

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4 **Mashhood Ahmed Sheikh**

5 Department of Community Medicine, University of Tromsø, 9037 Tromsø, Norway; Tel.:
6 0047-77620716; E-mail: mashhood.a.sheikh@uit.no.

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14 **Abstract**

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

37 **Keywords:** Confounder; direct effect; recall bias; differential measurement error; mental
38 health; psychological state; mood congruency; asthma; chronic bronchitis

40 ***What is already known on this subject?***

- 41 • Association of childhood adversity with asthma and chronic bronchitis is over
42 estimated due to differential recall bias, and confounding via mental health.
- 43 • Mental health mediates the association of childhood adversity with asthma and
44 chronic bronchitis.

45 ***What this study adds?***

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

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56 **Introduction**

57 Several population-based studies have shown that childhood adversity is associated with an
58 increased risk of stress-related physical health outcomes, such as asthma and chronic
59 bronchitis later in life [1-8]. The role of mental health in the association of childhood
60 adversity with onset of asthma and chronic bronchitis has been hypothesized in two ways: (1)
61 mediation, whereby childhood adversity is associated with an increased risk of mental health
62 problems, which in turn are associated with an increased risk of asthma and chronic
63 bronchitis [8] (figure 1a); and (2) confounding and differential recall bias, i.e., psychological
64 state of respondents at the time of reporting childhood adversity [7] may confound the
65 association of retrospective childhood adversity with self-reported asthma and chronic
66 bronchitis [1] (figure 1b). When considering the mediation hypothesis, childhood adversity
67 can certainly affect mental health [8, 9], while simultaneously affecting onset of asthma and
68 chronic bronchitis via psychogenic relationships [1, 3, 7, 8, 10-12]. Mental health problems
69 may also affect the *experience* of asthma and adherence to treatment and hospitalization rates
70 [13-15]. Previous evidence has suggested that almost half of all cases of psychiatric disorders
71 manifest by age 14 years and three-fourths by age 24 years [16] [see also [17]]. This could
72 imply that mental health in adulthood represents a continuation or a recurrence of childhood
73 or adolescent mental health. Accordingly, mental health may mediate the association of
74 childhood adversity with asthma and chronic bronchitis, even if it is measured in adulthood
75 [8]. The association of childhood adversity with a wide range of psychiatric disorders is well-
76 established [4, 8, 18-24]. In turn, several previous studies have shown that poor mental health
77 is associated (directly or indirectly) with an increased risk of asthma and chronic bronchitis
78 [5, 11, 25-31], and that indicators of mental health mediate the association of childhood
79 adversity with asthma and chronic bronchitis [1, 5, 8, 11, 25].

80 Regarding the second explanation (confounding and differential recall bias), several
81 researchers have raised the concern that the observed association of retrospectively-reported
82 childhood adversity with asthma and chronic bronchitis could be an artefactual correlation
83 driven by the current psychological state of the respondent via anchoring effect, affective
84 states, deficits in memory functioning, mood-congruency bias, and biased autobiographical
85 memory [7, 32-53]. Individuals with mental and physical health problems could be more
86 likely to report adverse childhood experiences [1, 7]. Indeed, even twins or siblings may
87 recall and perceive their financial and psychosocial circumstances in childhood differently
88 [54-58]. If current psychological state confounds the association of retrospectively-measured
89 childhood adversity with asthma and chronic bronchitis, the relationship of childhood
90 adversity with asthma and chronic bronchitis may flow through the mechanism of memory
91 retrieval and attribution from the adult to childhood years [7]. For instance, asthma or chronic
92 bronchitis cases may assign more significance to past events by over-reporting childhood
93 adversity in an attempt to search for explanations and to make sense of their current health [1,
94 7]. Generally, these criticisms are based on the hypothesis that self-reported childhood
95 adversity and self-reported health are not entirely distinct "things" if the correlation between
96 them is driven by subjectivity and differential measurement error, which can lead to spurious
97 correlations between them [7]. For this reason, it is necessary to know whether the
98 association of childhood adversity with asthma and chronic bronchitis is free from biases
99 related to current mental health [1, 7, 59].

100 The association of retrospectively-measured childhood adversity with asthma and
101 chronic bronchitis is unique in the sense that it is impossible to separate the mediating and
102 confounding mechanisms of mental health. The statistical approach [difference-in-
103 coefficients method [60]] to estimate the effect of childhood adversity on asthma and chronic
104 bronchitis, independent of respondent's mental health is exactly the same whether

105 respondent's mental health is hypothesized as a mediator or as a confounder [7, 60-62].
106 Estimation of "direct effect" is not appropriate in this setting, because the term implies the
107 effect of an exposure on an outcome that is not mediated via specific mediator(s) [60], and it
108 does not take into account the potential confounding and recall bias by some *hypothesized*
109 mediating variables, such as indicators of mood state. Similarly, the estimation of "indirect
110 effect" [difference between total and direct effect [60]] is not meaningful in this setting,
111 because the estimate of childhood adversity may be attenuated by controlling for indicators of
112 mental health not only due to mediation, but also because of potential confounding by
113 respondent's mental health. Therefore, the "independence hypothesis" [7] may be more
114 meaningful, as it tests whether childhood adversity is associated with asthma and chronic
115 bronchitis, *independent* of potential confounders and respondent's mental health. In addition,
116 the independence hypothesis ignores the distinction between a mediator and a confounder [7];
117 instead, it focuses on the influence of childhood adversity on asthma and chronic bronchitis
118 that is neither mediated nor confounded by respondent's mental health.

119 In this study, we used a wide range of indicators of mental health, without assuming
120 the direction of the associations between them. We assumed that some indicators of mental
121 health may confound the childhood adversity→asthma and chronic bronchitis associations,
122 while others may mediate the childhood adversity→asthma and chronic bronchitis
123 associations. However, our focus was not to separate the mediating and confounding
124 mechanisms of mental health, but rather to focus on the estimation of the *independent* effect
125 [7] of childhood adversity on asthma and chronic bronchitis, and to assess if childhood
126 adversity is associated with asthma and chronic bronchitis even after accounting for a wide
127 range of indicators of mental health.

128 The aim of this study was to estimate the effect of childhood adversity on asthma and
129 chronic bronchitis, independent of potential confounding and mediating variables (including
130 respondent's mental health).

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132 **Methods**

133 *Study population*

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

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139 *Ethical approval*

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

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145 *Study variables*

146 Exposure (childhood adversity)

147 Childhood adversity is defined as a conglomerate of factors that have been used in a similar
148 manner in previous studies [64, 65]. The present analysis used four indicators of
149 retrospectively-reported childhood adversity. Childhood financial conditions was used as an
150 indicator of economic background, and was obtained through the question: "How was your
151 family's financial situation when you were a child?" Participants replied using a 4-point scale
152 ranging from *very difficult* (1) to *very good* (4) [7]. Those who answered difficult or very
153 difficult were considered to have this childhood adversity [7]. The test-retest reliability of
154 childhood financial conditions was good in the Tromsø Study [7, 23]. Information on adverse
155 childhood experiences were obtained through the question: "Have you over a long period
156 experienced any of the following as a child?: (i) being tormented or threatened with violence;

157 (ii) being beaten, kicked, or the victim of other types of violence; and (iii) someone in your
158 close family using alcohol or drugs in such a way that caused you worry [7]. Each of these
159 adverse childhood experiences were considered a childhood adversity [64, 65]. The internal
160 reliability of these adverse childhood experiences was good in the Tromsø Study [1]. A
161 composite variable was then constructed as the sum of all four childhood adversities, thus
162 scores ranged from 0 to 4 (mean: 0.51, standard deviation [SD]: 0.78). Cronbach's alpha for
163 the four indicators of childhood adversity was 0.49 (mean inter-item covariance: 0.19).

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165 Outcomes (asthma and chronic bronchitis)

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

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170 Confounding variables

171 The potential confounding and mediating variables, age, sex, parental history of psychiatric
172 problems/asthma/dementia, education, smoking, social support, and respondent's mental
173 health, were chosen based on *a priori* knowledge of the correlates of childhood adversity and
174 asthma and chronic bronchitis [1, 5, 7, 8, 11, 23-25, 66-68]. With reference to the literature
175 on mediation analysis, if there are any *measured* variables that may confound the mental
176 health→asthma/chronic bronchitis association (e.g., education,
177 smoking, and social support) and are affected by childhood adversity, then they should be
178 included in the multivariable regression model as confounding variables. Note that
179 controlling for both intermediate confounders and potential mediators (indicators of mental
180 health) implies that one is also considering potential intermediate confounders as mediators
181 [60]. This is similar to the setting in which both the intermediate confounder and mediator are

182 considered jointly as a single mediator [69], not as separate variables [60]. This implies that
183 any unmeasured variables that affect both the intermediate confounder and onset of asthma or
184 chronic bronchitis, and are affected by childhood adversity, may still induce some
185 intermediate confounding.

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

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203 Indicators of respondent’s mental health

204 Respondent’s mental health was assessed by several questions on anxiety; depression;
205 insomnia; psychological distress; use of sleeping pills, antidepressants, and tranquilizers;
206 memory problems; and prevalence of psychiatric problems [7]. Anxiety and depression was

207 measured by a question with three response alternatives (1=I am not anxious or depressed,
208 2=I am somewhat anxious or depressed, 3=I am very anxious or depressed) [7]. Depression
209 was also measured by the question: “Have you been feeling unhappy and depressed during
210 the past two weeks?”, with four possible responses (1=not at all, 2=no more than usual,
211 3=rather more than usual, 4=much more than usual) [7]. Psychological distress [64, 65, 67,
212 68] was measured using the 10-item Hopkins Symptom Checklist (HSCL-10), which has
213 been shown to have an acceptable degree of internal consistency in this sample (Cronbach's
214 alpha: 0.90, mean inter-item correlation: 0.43, McDonald's omega coefficient for composite
215 reliability: 0.91)[7, 23, 68]. The 10 items in the HSCL-10 are rated by the respondent on a
216 four-point scale, ranging from not at all (1) to extremely (4). A HSCL-10 score was
217 calculated by summing the score of all 10 items, thus possible scores ranged from 10 to 40,
218 with 40 representing the highest and 10 representing the lowest psychological distress (mean:
219 12.78, SD: 3.60) [7]. Sleeping difficulty was measured by the question: “Have you had
220 difficulty sleeping during the past couple of weeks?” (1=not at all, 2=no more than usual,
221 3=rather more than usual, 4=much more than usual) [7]. Insomnia was measured by the
222 question: “How often do you suffer from sleeplessness?” (1=never, or just a few times a year,
223 2=1-3 times a month, 3=approximately once a week, 4=more than once a month) [7, 68].
224 Consultation with a psychiatrist was measured by the question: “Have you during the past
225 year visited a psychiatrist?” (0=no, 1=yes) [7]. Use of sleeping pills, antidepressants, and
226 tranquilizers was measured by three separate questions: “How often have you used sleeping
227 pills/antidepressants/tranquilizers during the last 4 weeks?” (1=not used, 2=less frequently
228 than every week, 3=every week, but not daily, 4=daily) [7]. Forgetfulness was measured by
229 the question: “Do you often forget where you have placed your things?” (0=no, 1=yes), and
230 decline in memory was measured by the question: “Has your memory declined?” (0=no,
231 1=yes) [7]. Memory examination was measured by the question: “Have you been examined

232 for memory problems?" (0=no, 1=yes) [7]. Prevalence of psychiatric problems [24, 68] was
233 measured by the question: "Do you have, or have you had psychiatric problems for which
234 you sought help?" (0=no, 1=yes) [7]. Prevalence of psychiatric disorders was measured by
235 the question: "Do you have, or have you had psychiatric disorder (s)?" (0=no, 1=yes) [8].

236

237 *Statistical Analysis*

238 All statistical analyses were conducted using Stata version 15. Fifty datasets were
239 imputed for generating missing values with multiple imputation with chained equations. A
240 comparison between the complete-case (excluding missing) and the imputed datasets is
241 presented with proportions (%), and mean (standard error, SE) (Table 1). No statistically
242 significant multiplicative interactions between childhood adversity and confounding
243 variables, or between childhood adversity and indicators of mental health were observed. The
244 associations of childhood adversity with asthma, and chronic bronchitis (Table 2) were
245 assessed with Poisson regression models. Relative risks (RRs) were estimated and both the
246 unadjusted (crude) and adjusted estimates (from multivariable regression models) are
247 presented. Error variance were derived with first-order Taylor-series linearization method
248 [70, 71] in Stata, and 95% confidence intervals (CIs) are presented. We estimated RRs
249 instead of odds ratios, because odds ratios can over-estimate risk, particularly when the
250 outcome is not rare [60]. Previous literature has repeatedly argued that neither confounding
251 nor mediation should not be assessed using odds ratios [60, 72-76], because an odds ratio is
252 not a collapsible measure [77] and attenuations in odds ratios do not necessarily correspond
253 to confounding or mediation [78, 79]. In practice, estimates of exposure in logistic regression
254 analyses may attenuate after entering an additional covariate in the model due to unobserved
255 heterogeneity, even if the additional covariate neither confounds nor mediates the exposure-
256 outcome association [79, 80]. Since the aim of this study was to estimate the effect of

257 childhood adversity on asthma and chronic bronchitis, independent of respondent's mental
258 health, presenting adjusted estimates on an odd ratio scale could be misleading.

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262 **Results**

263 The distributions of variables were similar in the complete-case dataset (excluding those with
264 missing values) and the imputed datasets (Table 1). In this sample, 62.8% of respondents
265 reported no childhood adversity, 27.9% reported any one childhood adversity, 6.4% reported
266 any two childhood adversities, 2.3% reported any three childhood adversities, and 0.6%
267 reported all four childhood adversities. The prevalence of asthma and chronic bronchitis in
268 adulthood were 10.1% and 4.8%, respectively (Table 1). A minor proportion of the
269 respondents had missing values on childhood adversity (7.4%), asthma (2.5%), and chronic
270 bronchitis (2.7%). Missing values on childhood adversity was associated with a higher age
271 ($p=0.031$), a lower education level ($p<0.001$), lack of instrumental support ($p=0.015$), a
272 higher psychological distress ($p=0.009$), and prevalence of psychiatric disorders ($p<0.001$).
273 Missing values on asthma were associated with a higher age ($p<0.001$), a lower education
274 level ($p=0.042$), prevalence of psychiatric problems ($p=0.001$), prevalence of psychiatric
275 disorders ($p<0.001$), a higher psychological distress ($p=0.001$), and memory examination
276 ($p=0.008$). Missing values on chronic bronchitis were associated with a higher age ($p<0.001$),
277 a higher psychological distress ($p=0.001$), a decline in memory ($p=0.010$), memory
278 examination ($p=0.003$), psychiatric problems ($p<0.001$), and psychiatric disorders ($p<0.001$).
279 Indicators of childhood adversity were correlated with each other ($r=0.08-0.51$; $p<0.001$) in
280 the predicted direction (data not shown).

281 No statistically significant ($p>0.05$) childhood adversity*age multiplicative interaction
282 was observed. Two estimates are presented in Table 2: model 1 presents crude (unadjusted)
283 associations; model 2 presents estimates from the multivariable regression model, adjusted
284 for confounding variables and indicators of mental health. The bivariate (unadjusted)
285 association of childhood adversity with asthma, and chronic bronchitis indicated that
286 childhood adversity is associated with increased risk of both asthma (RR=1.16, 95% CI: 1.09,

287 1.23) and chronic bronchitis (RR=1.30, 95% CI: 1.20, 1.42) (Table 2). The relative risks
288 should be interpreted in terms of the extent to which a one-point increase in the childhood
289 adversity measure is associated with an increased risk of asthma or chronic bronchitis. After
290 controlling for confounding and mediating variables, childhood adversity was associated with
291 a 9% increased risk of asthma (RR=1.09, 95% CI: 1.02, 1.16), and a 14% increased risk of
292 chronic bronchitis (RR=1.14, 95% CI: 1.03, 1.26) (Table 2). In the complete-case analysis,
293 all associations remained in the same direction (data not shown)

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312 **Discussion**

313 This study sought to estimate the independent effect of childhood adversity on asthma and
314 chronic bronchitis in a large and representative cross-sectional sample of the general
315 Norwegian population. After adjusting for a wide range of indicators of respondent's mental
316 health, we found that childhood adversity was independently associated with asthma and
317 chronic bronchitis. Accordingly, this study supports the view that the association of
318 childhood adversity with asthma and chronic bronchitis is not driven entirely by respondent's
319 mental health, as this association remained in the same direction after controlling for a wide
320 range of indicators of mental health. The results of the present study correspond with other
321 evidence [1, 7, 8, 81-88], in that the association of childhood adversity with health was
322 primarily independent of selected confounding and mediating variables (including
323 respondent's mental health). However, it must be noted that estimation of *independent effect*
324 is a conservative approach, as the magnitude of the casual association of childhood adversity
325 with asthma or chronic bronchitis could be underestimated proportioned to how much of its
326 indirect effects are mediated through controlled variables. Moreover, it is important to
327 highlight the implications for assessing independent effect vs direct/indirect effects: the
328 independent hypothesis suggests that one should rather focus on establishing childhood
329 adversity as a risk factor whereas the mediation hypothesis focuses on understanding the
330 mechanism by which childhood adversity affects physical health.

331 Several mechanisms may explain the association of childhood adversity with asthma
332 and chronic bronchitis. Evidence from stress biology shows that childhood adversity can
333 have lasting effects on brain development, brain stress regulatory flow systems, and
334 psychophysiological responses, including enhanced activity and dysregulation of the
335 hypothalamic–pituitary–adrenal axis, neuroendocrine immune circuitry and autonomic
336 nervous system function [8, 89-94]. These alterations can result in impairment of the body's

337 immune function and cardiorespiratory system [6, 95, 96], which in turn may increase the
338 risk of respiratory infections, and eventually asthma and chronic bronchitis [8, 89, 97-99].
339 Other evidence suggests that hormones and inflammation related to stress can lead to
340 contractions of smooth muscle and excess of mucus production, which in turn may increase
341 the risk for incident asthma [100]. Another perspective on the association of childhood
342 adversity with asthma and chronic bronchitis is stress-sensitization model [101, 102], which
343 suggests that exposure to childhood adversity may elevate sensitivity [23, 24, 64], immune
344 biomarkers [103], and pro-inflammatory responses via the process of biological embedding
345 of stress [104], allostatic load theory [105], or body programming [106].

346 Some limitations should be considered for the interpretation of these findings. All
347 variables (except age and sex) are self-reported. Childhood adversity was measured with four
348 single-item indicators; therefore, it is likely that there is considerable non-differential
349 measurement error (i.e., unreliability) in childhood adversity [7, 82, 88, 107, 108], which
350 would lead to an under-estimation of its association with asthma and chronic bronchitis.
351 Some potential confounding variables are missing in this study; for instance, a stressful social
352 milieu could contribute to adverse childhood experiences and onset of asthma [109]. Potential
353 confounding by a stressful social milieu is difficult to capture in survey research, particularly
354 with reference to problems related to retrospective reports. The strengths of this study include
355 a large and representative sample, and adjustment for respondent's mental health via a wide
356 range of indicators. Finally, it must be noted that the independence hypothesis may only be
357 relevant when childhood adversity is retrospectively reported [7]. For prospective studies, or
358 studies where information on childhood adversity is collected via objective sources, the
359 independence hypothesis may not be meaningful, as the role of mental health as a mediator
360 could be assessed without worrying about the potential bias (via mental health) in recalling
361 and reporting childhood adversity.

362 It is plausible that onset of asthma or chronic bronchitis acts as a mediator in the
363 association of childhood adversity with mental health (i.e., reverse causality between
364 asthma/chronic bronchitis and mental health). Indeed, respondent's mental health could be a
365 consequence of asthma or chronic bronchitis, rather than a cause or confounder [110]. In such
366 case, including indicators of respondent's mental health in the multivariable regression model
367 for asthma or chronic bronchitis may induce a spurious (non-causal) association between
368 childhood adversity and asthma/chronic bronchitis due to collider-stratification bias.
369 However, the crude association of childhood adversity with asthma and chronic bronchitis
370 was in the same direction, without controlling for indicators of mental health.

371 Often the disagreement between prospective and retrospective measures of childhood
372 adversity (such as childhood abuse) are used to highlight the bias in self-reports. While
373 objective measures of childhood abuse (e.g., via school records, child protection services,
374 medical records, court ruling, etc.) are helpful in ignoring differential or non-differential
375 recall bias and confounding via mental health, the disadvantage is that only a minor
376 proportion of childhood abuse cases are identified via official records. A concordance
377 between one *potentially* under-estimated measure (official records) and another *potentially*
378 biased measure (retrospectively-reported childhood abuse) will always be low because the
379 underlying mechanisms of measurement error are substantially different in both cases.
380 Retrospective measurement of childhood adversities such as childhood abuse is not just
381 "convenient", it may also be the only way to measure unreported, unidentified events and
382 experiences that no one other than the victim knows about [111]. If both prospective and
383 retrospective measurements of childhood abuse are available, then it is more meaningful to
384 classify the unexposed group (reference group) as that which did not report childhood abuse
385 and shows no evidence of childhood abuse via objective indices. Classifying unexposed
386 individuals by combining information from both official records and self-reports would be

387 more meaningful in the establishment of a causal association between childhood abuse and
388 health, rather than focusing on the discrepancy between estimates of prospective vs
389 retrospective measures of childhood abuse and health. However, it must be noted that
390 retrospective assessments can still be assessed at multiple time points prospectively, which
391 would be stronger than the current cross-sectional approach.

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

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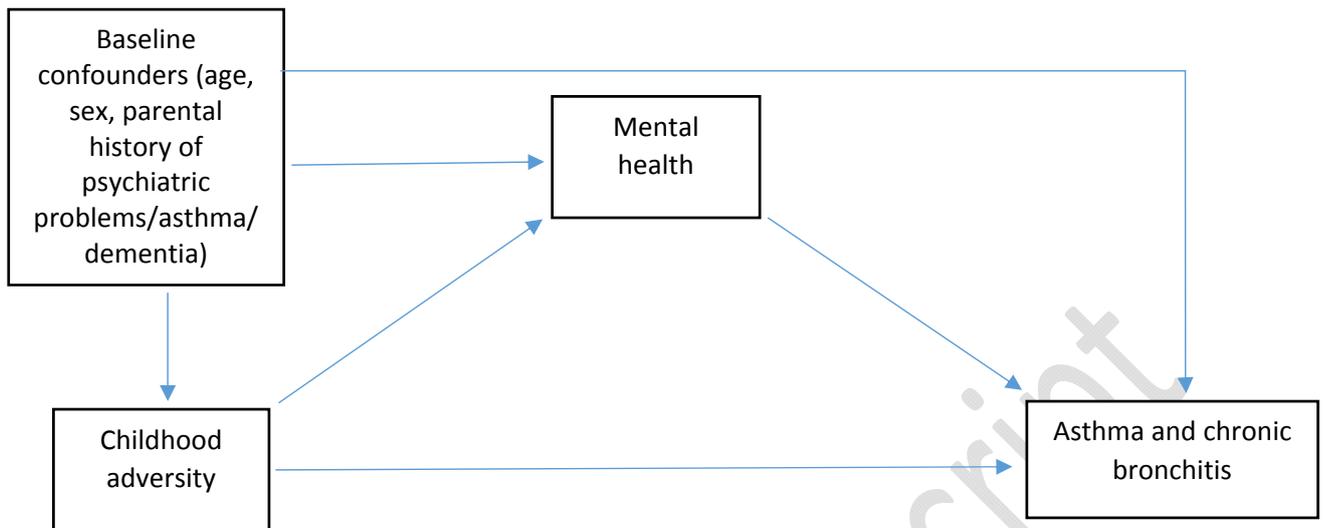
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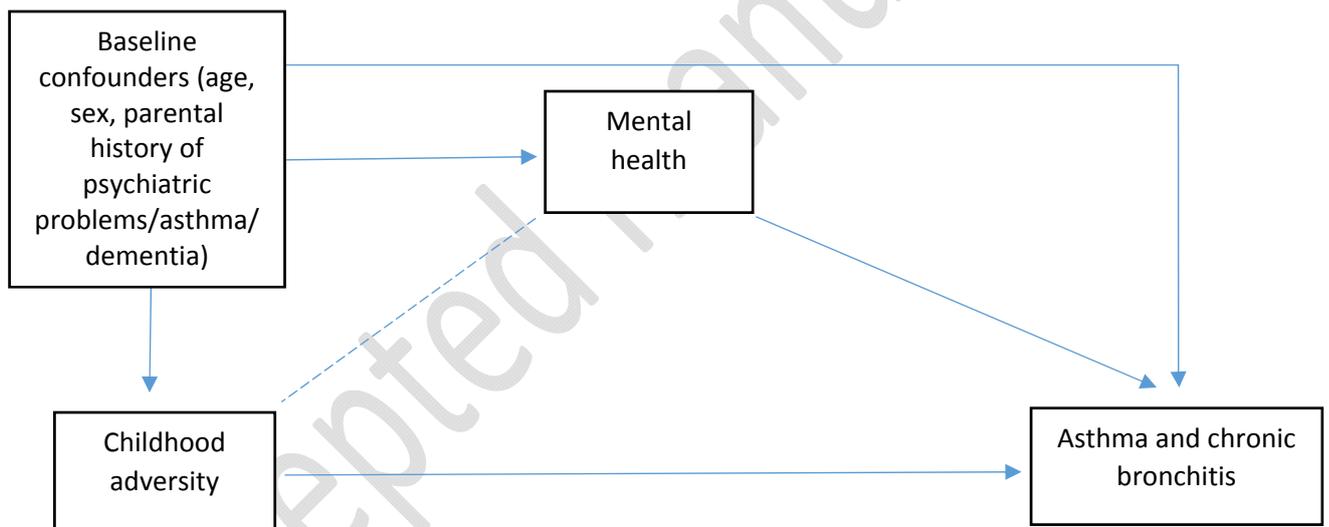
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702 Figure 1a. Role of mental health as a mediator in the association of childhood adversity with asthma
703 and chronic bronchitis



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



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

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719 Table 1. General characteristics of the study sample (N=12,981).

720

		Complete- case data	Imputed data
		n (%)	%
Age	mean [standard error (SE)]	57.5 (0.1)	_ ^b
Sex	Male	6053 (46.6)	_ ^b
	Female	6928 (53.4)	_ ^b
Parental history of psychiatric problems	Yes	1037 (8.0)	_ ^b
Parental history of asthma	Yes	1517 (11.7)	_ ^b
Parental history of dementia	Yes	1387 (10.7)	_ ^b
Education	Mean (SE)	2.7 (0.01)	2.7 (0.01)
Daily smoking ^a	Never	4767 (37.3)	37.3
	Yes, previously	5407 (42.3)	42.3
	Yes, now	2610 (20.4)	20.4
Instrumental support	Yes	11014 (88.9)	88.8
Emotional support	Yes	10821 (87.2)	87.1
Anxiety and depression	Mean (SE)	1.2 (0.01)	1.2 (0.01)
Depression	Mean (SE)	1.5 (0.01)	1.5 (0.01)
Psychological distress (HSCL-10)	Mean (SE)	12.8 (0.04)	13.0 (0.04)
Sleeping difficulty	Mean (SE)	1.6 (0.01)	1.6 (0.01)
Insomnia	Mean (SE)	1.7 (0.01)	1.7 (0.01)
Consultation with psychiatrist ^a	Yes	336 (2.7)	2.8
Use of sleeping pills	Mean (SE)	1.2 (0.01)	1.2 (0.01)
Use of antidepressants	Mean (SE)	1.1 (0.01)	1.1 (0.01)
Use of tranquilizers	Mean (SE)	1.1 (0.01)	1.1 (0.01)
Forgetfulness ^a	Yes	3203 (27.2)	27.6
Decline in memory ^a	Yes	5955 (50.0)	50.3
Memory examination ^a	Yes	146 (1.2)	1.3
Prevalence of psychiatric problems ^a	Yes	1308 (10.4)	10.6
Prevalence of psychiatric disorders ^a	Yes	14 (0.1)	_ ^b
Childhood adversity ^{a, c}	Mean (SE)	0.5 (0.01)	0.5 (0.01)
	None	7483 (62.2)	62.8
	1	3351 (27.9)	27.9
	2	827 (6.9)	6.4
	3	290 (2.4)	2.3
	4	76 (0.6)	0.6
Asthma ^a	Yes	1253 (9.9)	10.1
Chronic bronchitis/emphysema/COPD ^a	Yes	569 (4.5)	4.8

721 ^a The numbers for some variables do not add up to 12,981 due to missing values.722 ^b There were no missing values, so no imputations were made for these variables.723 ^c The four childhood adversities considered were: difficult or very difficult subjective childhood

724 financial conditions, psychological abuse, physical abuse, and substance abuse distress in childhood.

725 SE: standard error; HSCL-10: Hopkins Symptom Check List-10.

726

727 Table 2. Association of childhood adversity with asthma and chronic bronchitis
 728 (n=12,981).

	Model 1	Model 2 ^a
	Crude (unadjusted)	Independent effect
	RR (95% CI)	RR (95% CI)
Asthma		
Childhood adversity	1.16 (1.09, 1.23) ^b	1.09 (1.02, 1.16) ^c
Chronic bronchitis/emphysema/COPD		
Childhood adversity	1.30 (1.20, 1.42) ^d	1.14 (1.03, 1.26) ^e

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^a 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).

^b $p < 0.001$

^c $p = 0.015$

^d $p < 0.001$

^e $p = 0.011$

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