Child maltreatment, psychopathological symptoms, and onset of diabetes mellitus, hypothyroidism and COPD in adulthood

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Abstract

Background: The aim of this study was to assess the associations between child maltreatment (CM), psychopathological symptoms, and onset of diabetes mellitus, hypothyroidism (i.e., low metabolism), and chronic bronchitis/emphysema/COPD in adulthood.

Methods: The present analysis used data collected in 2007-2008 within the framework of the Tromsø Study, Norway (N=12,981). CM was measured with a single item, and self-reported information on psychopathological symptoms and physical health outcomes was used. The association between CM, psychopathological symptoms, and physical health outcomes was assessed with linear and Poisson regression models. Mediation was assessed with difference-in-coefficients methods.

Results: In the fully-adjusted models, CM was associated with higher levels of anxiety and depression, psychological distress, sleeping difficulty, insomnia, and use of sleeping pills or antidepressants in adulthood ($p<0.05$). Moreover, CM was associated with a more than two-folds increased risk of consultation with psychiatrist ($p<0.001$), a 26% increased risk of forgetfulness ($p<0.001$), a 15% increased risk of decline in memory ($p<0.001$), and a 96% increased risk of psychiatric problems ($p<0.001$) over the course of life. In the fully-adjusted models, CM was associated with a 27- 82% increased risk of physical health outcomes in adulthood ($p<0.05$). Indicators of psychopathological symptoms significantly ($p<0.05$) mediate the associations between CM and physical health outcomes.

Limitations: The design of this study is cross-sectional, and all measures are self-reported.

Conclusion: The associations between retrospectively-reported CM and physical health outcomes in adulthood are partially driven by psychopathological symptoms in adulthood.

Keywords: diabetes mellitus; hypothyroidism; low metabolism; chronic bronchitis; emphysema; COPD; childhood maltreatment; social epidemiology; social causation; life course; recall bias; differential error; reliability; validity

Introduction

There is a growing body of evidence that disease suffered in adulthood may originate from maltreatment in childhood (Baumeister et al., 2015; Hostinar et al., 2017; Springer et al., 2003). A recent meta-analysis showed that child maltreatment (CM) contributes to potentially pathogenic pro-inflammatory state in adulthood (Baumeister et al., 2015). The hypothalamic-pituitary-adrenocortical (HPA) axis and neuro-endocrine system helps regulate our stress response, and our immune system (Smith and Vale, 2006). Any disruption to the HPA axis and the neuro-endocrine system affects a range of psychological and physiological functions (Coates, 2010; Teicher et al., 2002). Prolonged or profound stressful experiences in life, such as CM may modify the neuro-endocrine stress response systems (Coates, 2010; Gee and Casey, 2015; Hellhammer and Wade, 1993; Teicher et al., 2002). Indeed, previous evidence suggests that chronic stress, caused by CM has a long-term influence on several physiological processes via dysregulation of the inflammatory system (Anda et al., 2006; Baumeister et al., 2015; Coates, 2010; Danese and McEwen, 2012; Heffner, 2011; Hellhammer and Wade, 1993; Hostinar et al., 2017; McEwen, 2000; Sheikh, 2018d). Other evidence suggests that child maltreatment places stress on the endocrine system, leading to impairment of important hormones that can contribute to obesity (De Bellis and Zisk, 2014; Joung et al., 2014). In turn, obesity is associated with a wide range of physical health outcomes including diabetes mellitus (Sheikh et al., 2014). Indeed, previous evidence suggests that CM is associated with stress dysregulation, immune dysfunction, and inflammation in later life (Coates, 2010; Fagundes et al., 2013; Yang et al., 2017), which may confer increased vulnerability to several physical health outcomes (Anda et al., 2006; Felitti Md et al., 1998; Hostinar et al., 2017; Sheikh, 2018a, d). Moreover, several studies suggest a bidirectional communication between the brain and the immune system (Danese and McEwen, 2012; Lorton et al., 2006; Nusslock and Miller, 2016; Procaccini et al., 2014). Other studies have shown that CM is associated

with an increased risk of diabetes mellitus, hypothyroidism (i.e., low metabolism), and chronic obstructive pulmonary disease (COPD) in adulthood (Duncan et al., 2015; Felitti Md et al., 1998; Kalmakis and Chandler, 2015; Plaza et al., 2012; Post et al., 2013; Rich-Edwards et al., 2010; Sheikh, 2018a, d; Shields et al., 2016).

CM may affect psychopathological symptoms (Sheikh, 2018a, f; Teicher and Samson, 2013), which in turn may affect (directly, or indirectly via medication) physical health outcomes (Danese and McEwen, 2012; Mock and Arai, 2011; Pan et al., 2010; Rubin et al., 2008; Scott et al., 2011; Sheikh, 2018d; Yoon et al., 2013). Indeed, elevated levels of inflammatory markers have been reported in individuals with psychopathological symptoms (Baumeister et al., 2014; Coccaro et al., 2014), and among those with a history of CM (Coelho et al., 2013). Accordingly, mental health may also mediate the association between CM and physical health. The mediation model (i.e., CM→mental health→physical health) has convincing support from previous longitudinal studies and could be most plausible for physical health outcomes that are "stress-related" such as COPD. Indeed, previous evidence suggests that poor mental health is associated (directly or indirectly via medication) with an increased risk of a wide range of physical health outcomes (Blanchette et al., 2008; Cohen et al., 2000; Correll et al., 2015; Correll et al., 2017; Coupland et al., 2011; Hippisley-Cox et al., 2001; Huang et al., 2017; Mock and Arai, 2011; Pan et al., 2010; Rubin et al., 2008; Scott et al., 2011; Tata et al., 2005; Vancampfort et al., 2015; Yoon et al., 2013). For instance, use of tricyclic tranquilizers can cause metabolic syndrome (Van Reedt Dortland et al., 2010). Similarly, depression (Pan et al., 2010), and use of antidepressants (Pan et al., 2010; Rubin et al., 2008; Yoon et al., 2013) are independently associated with an increased risk of diabetes mellitus. Other evidence demonstrated that antipsychotic medication is associated with a higher risk for cardio-metabolic diseases (Correll et al., 2015; Correll et al., 2017; Vancampfort et al., 2015). Accordingly, several studies using a variety of mental and physical

health indicators, including biological indices has shown that mental health mediates the CM-physical health association (Mock and Arai, 2011; Scott et al., 2011).

The aim of this study was to assess (1) the association between CM and psychopathological symptoms in adulthood; (2) the association between CM and three physical health outcomes (diabetes mellitus, hypothyroidism, and COPD in adulthood, and; (3) the mediating role of psychopathological symptoms in these associations.

Methods

Study population

The Tromsø Study is a longitudinal prospective cohort study and its participants are considered representative of the adult population residing in the municipality of Tromsø (Jacobsen et al., 2012). The present analysis includes cross-sectional data collected for Tromsø VI in 2007-2008; 19,762 subjects were invited and 12,981 (65.7%) returned the questionnaire (Sheikh, 2018d). To preserve temporality between CM and physical health outcomes in adulthood, we excluded respondents that may have been diagnosed with these physical outcomes in childhood (Sheikh, 2018d). Accordingly, respondents that reported a diagnosis of diabetes mellitus (n=53), hypothyroidism (n=88), and COPD (n=325) before the age 18 years were excluded. The remaining study samples used in the analysis were: n=12,928 for CM→diabetes mellitus association; n=12,893 for CM→hypothyroidism association, and; n=12,656 for CM→COPD association.

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 maltreatment)

Information on childhood maltreatment (Sheikh, 2018c) were obtained through the question: "Have you over a long period experienced the following as a child?: being beaten, kicked, or

the victim of other types of violence". Those responding positively to the question were considered as maltreated in childhood.

Outcome (physical health outcomes)

The questions on self-reported diagnosis of three physical health outcomes: diabetes mellitus, hypothyroidism, and chronic bronchitis/emphysema/COPD were included in the questionnaire. Participants completed a separate question for each health outcome, as follows: "Do you have, or have you had [physical health outcome]?". Other physical outcomes, such as cancer were not measured in Tromsø Study.

Confounding variables

The potential confounding variables age, sex, parental history of psychiatric disorders, diabetes mellitus, dementia, and asthma were chosen based on *a priori* knowledge of the correlates of CM and physical health outcomes in adulthood (Sheikh, 2018a, c, d). Valid information on age and sex was obtained from Statistics Norway by using the unique personal identification number of each participant.

Indicators of current psychopathological symptoms

Current psychopathological symptoms 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 (Sheikh, 2018d). 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). 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). Psychological distress during the last week was measured using the Hopkins Symptom Checklist (HSCL-10) (Sheikh, 2018b, e; Sheikh et al., 2018). The HSCL-10 consists of 10 items on a four-point scale, ranging from *not at all* (1) to *extremely* (4). The HSCL-10 had an acceptable degree of internal consistency in this sample (Cronbach's alpha: 0.87, mean inter-item correlation: 0.42, McDonald's omega coefficient for composite reliability: 0.87) (Sheikh, 2018e). An HSCL-10 score between 10 and 40 was calculated by summing the 10 indicators, where 40 represented the highest and 10 represented the lowest score for psychological distress (mean: 12.78, SD: 3.60). 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). 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). Consultation with a psychiatrist was measured by the question: "Have you during the past year visited a psychiatrist?" (0=no, 1=yes). 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). 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). Memory examination was measured by the question: "Have you been examined for memory problems?" (0=no, 1=yes). Prevalence of psychiatric problems was measured by the question: "Do you have, or have you had psychiatric problems?" (0=no, 1=yes) (Sheikh, 2018f).

Statistical Analysis

All statistical analyses were conducted using Stata version 15. Missing values were generated with multiple imputation (with chained equations) to avoid any bias in the association of interest introduced by excluding individuals with missing data (Sheikh, 2018d). A comparison between the complete-case (excluding missing) and the imputed datasets is presented with proportions (%), and mean (standard error, SE) (Sheikh, 2018d). We estimated Pearson product-moment correlations between physical health outcomes (see Table 1). No statistically significant multiplicative interactions between CM and confounding variables or indicators of current psychopathological symptoms were observed. The association between CM and current psychopathological symptoms was assessed with ordinary least square (OLS) regression models (for continuous or ordinal outcomes) and Poisson regression models (for binary outcomes) (see Table 2). The association between psychopathological symptoms and physical health outcomes (see Table 3), and between CM and physical health outcomes (see Table 4 and Table 5) were assessed with Poisson regression models (Sheikh, 2018d, f). Relative risks (RRs) and corresponding 95% CIs were estimated.

Assessing mediation via current psychopathological symptoms

Potential mediation via psychopathological symptoms was assessed with the difference-in-coefficients method (Sheikh, 2018b, d, f). Indicators of current psychopathological symptoms were included in the models to assess the indirect effects (Sheikh, 2018d). In order to assess whether a specific set of psychopathological symptoms play a stronger role in the association between CM and physical health, we divided psychopathological symptoms in three categories: affective symptoms (anxiety and depression, depression, sleeping difficulty, insomnia, use of sleeping pills, and use of antidepressants); general mental health (consultation with psychiatrist, use of tranquilizers, and prevalence of psychiatric problems); and deficits in memory (forgetfulness, decline in memory, and memory examination). SEs

were derived with bias-corrected bootstrapping (Sheikh, 2018b, d, f) for hypothesis testing, and 95% CIs are presented.

Results

Over 2.8% of the respondents reported having a consultation with a psychiatrist during the past year, and 10.6% reported prevalence of psychiatric problems (Table S1). In this sample, 800 (6.2%) participants reported childhood maltreatment (Table S1). The prevalence of physical health outcomes were: 4.7% for diabetes mellitus, 8.5% for hypothyroidism, and 2.8% for COPD (Table S1). Indicators of physical health outcomes were significantly ($p<0.001$) associated with each other in the predicted direction (Table 1).

In the fully-adjusted models, accounting for age, sex, and parental history of chronic conditions, CM was associated with higher levels of anxiety and depression ($\beta=0.12$, 95% CI: 0.09, 0.16; $p<0.001$), depression ($\beta=0.26$, 95% CI: 0.21, 0.31; $p<0.001$), psychological distress during the past week ($\beta=1.70$, 95% CI: 1.37, 2.02; $p<0.001$), difficulty in sleeping during the past couple of weeks ($\beta=0.20$, 95% CI: 0.15, 0.25; $p<0.001$), insomnia ($\beta=0.33$, 95% CI: 0.25, 0.41; $p<0.001$), use of sleeping pills ($\beta=0.08$, 95% CI: 0.03, 0.13; $p<0.001$), and use of antidepressants ($\beta=0.05$, 95% CI: 0.01, 0.10; $p<0.05$) during the last four weeks (Table 2). Similarly, CM was associated with a more than two-fold increased risk of consultation with psychiatrist during the past year (RR=2.15, 95% CI: 1.60, 2.87; $p<0.001$), a 26% increased risk of forgetfulness (RR=1.26, 95% CI: 1.13, 1.40; $p<0.001$), a 15% increased risk of memory examination (RR=1.15, 95% CI: 1.07, 1.23; $p<0.001$), and a 96% increased risk of self-reported psychiatric problems over the course of life (RR=1.96, 95% CI: 1.69, 2.26; $p<0.001$) (Table 2). Table 3 shows that indicators of psychopathological symptoms are associated with diabetes mellitus, hypothyroidism, and COPD in adulthood (cross-sectional association).

Controlling for age, sex, and parental history of chronic conditions, CM was associated with a 47% increased risk of diabetes mellitus (RR=1.47, 95% CI: 1.10, 1.91), a

42% increased risk of hypothyroidism (RR=1.42, 95% CI: 1.13, 1.78), and a more than two-fold increased risk of COPD (RR=2.19, 95% CI: 1.49, 3.04) (Table 4).

Indicators of current psychopathological symptoms significantly mediate the association between CM and physical health outcomes; however, the direct effects remained statistically significant ($p<0.05$) in the same direction (Table 4). In the fully-adjusted models, CM was associated (direct effects) with an increased risk of diabetes mellitus (RR=1.38, 95% CI: 1.04, 1.79), hypothyroidism (RR=1.27, 95% CI: 1.03, 1.56), and COPD (RR=1.82, 95% CI: 1.28, 2.56) (Table 4).

Table 5 presents the indirect effects separately for affective symptoms, general mental health, and deficits in memory. 'Affective symptoms' was a more significant mediator than 'general mental health' and 'deficits in memory' (Table 5). Moreover, 'general mental health' was a more significant mediator than 'deficits in memory' (Table 5).

Discussion

We sought to evaluate the associations between CM, psychopathological symptoms, and physical health outcomes in a large cross-sectional sample of the general Norwegian population. CM was associated with an increased risk of psychopathological symptoms and onset of diabetes mellitus, hypothyroidism, and COPD in adulthood. The results showed that inclusion of indicators of psychopathological symptoms attenuated the relationship between CM and physical health outcomes in adulthood; however, the direct effects remained statistically significant in the same direction. Although, only three items measured 'deficits in memory', the weak indirect effects may suggest that a major limitation of the association between retrospectively-reported CM and physical health is not inaccuracy of memory. However, the psychopathological symptoms measured in this study do not consider patients such as those who develop dementia or Alzheimer's disease later in life. It must be noted that psychopathological symptoms itself may in fact be a somatic illness with the inflammatory processes occurring in the brain rather than in another anatomical region. Given the established links between the brain and the immune system (Danese and McEwen, 2012; Lorton et al., 2006; Nusslock and Miller, 2016; Slavich et al., 2010; Vogelzangs et al., 2013), it is plausible to assume that the direct effects presented here may reflect the impact of CM on physical health outcomes, independent of inflammatory processes in the brain.

Although ours is not the first study to examine the mediating role (Mock and Arai, 2011; Scott et al., 2011) of psychopathological symptoms in the association between CM and physical health outcomes in adulthood (Sheikh, 2018d), the present study offered three advantages. First, we used a priori selection of variables for confounding. Second, we assessed the associations in a large representative sample of adult men and women. Third, we included a wide range of indicators to assess the current psychopathological symptoms. Although, this study did not explore the specific mechanisms via dysregulation of neuro-

endocrine system, immune system, inflammation and cortisol levels, these findings are consistent with previous evidence on the long-term effects of CM on mental and physical health outcomes in adulthood.

CM and physical health outcomes were measured retrospectively. The design of this study is cross-sectional; therefore, the temporal associations cannot be ascertained with certainty. Self-reported physical health outcomes could have differed from medical diagnoses made by physicians. Since the present study had a cross-sectional design, there was a potential for upward bias in estimates due to shared-method variance that cannot be ignored (Sheikh, 2018b, c, d, e). Although Tromsø Study is a prospective cohort study, we used data from a cross-sectional wave (Tromsø VI) because CM was not measured in other waves. The measurement of CM relies on a single item; therefore, it is limited in scope and utility. Other indicators of childhood adversity, such as sexual abuse, separation of parents, witnessing domestic violence in the home, living with someone with psychiatric disorders, living with someone who has been incarcerated, etc., were not measured in the Tromsø Study (Sheikh, 2018f). Moreover, the measurement of CM does not provide an account of perpetrator, or the extent or duration of maltreatment. Accordingly, it is likely that there is a considerable non-differential measurement error in CM, which might result in an under-estimation (biased downwards) of its association with physical health outcomes (Fosgate, 2006). The measurement error in CM is not limited due to its retrospectively recall but may reflect differences is what is understood "as victim of other types of violence" (Sheikh, 2018d). Indeed, even if one accounts for the current psychopathological symptoms, we cannot exclude the possibility that there is measurement error in the CM variable (Cerdá et al., 2012; Weis, 1989). Consequently, it is likely that a reliable measure of CM would lead to stronger associations with physical health outcomes. A reliable instrument for measuring CM could also strengthen the argument that mental health mediates the association between CM and

physical health in adulthood. Another limitation of this study is that measurement of physical health outcomes also relied in self-reports (Cigolle et al., 2016). Matching the survey data from the Tromsø Study with administrative/population register data on individual health outcomes could strengthen the argument that CM is associated with these physical health outcomes. Specific type of diabetes mellitus was not measured in the questionnaire; therefore, the associations presented here applies to cases of both type 1 and type 2 diabetes mellitus.

It must be noted that the possibility of unmeasured or unaccounted-for intermediate confounding cannot be ruled out. For instance, mental health in childhood and adolescence may affect both mental and physical health in adulthood, and could itself be affected by CM. Unless the intermediate confounding is tackled, the support for mediation hypothesis as a causal mechanism will remain questionable (Kaufman, 2009; Kaufman et al., 2004; Naimi et al., 2014). On the other hand, even though causal inference about the mediating hypothesis remains questionable, the potential biological pathways cannot be ignored.

In summary, the results of this study showed that CM is associated with an increased risk of psychopathological symptoms and onset of diabetes mellitus, hypothyroidism, and chronic bronchitis/emphysema/COPD in adulthood. Moreover, indicators of psychopathological symptoms significantly attenuated the associations between CM and physical health outcomes. These findings suggest that CM affects physical health, both directly (i.e., independent of psychopathological symptoms) and indirectly (via psychopathological symptoms).

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Table 1. Bivariate Pearson product-moment correlations between physical health outcomes (n=12,981)

	1	3	5
	r	r	r
1. Diabetes mellitus	1.00		
3. Hypothyroidism	0.05 [a]	1.00	
5. COPD	0.07 [a]	0.08 [a]	1.00

[a] $p<0.001$

Table 2. Influence of childhood maltreatment on current psychopathological symptoms (N=12,981).

	Anxiety and depression	
	Unadjusted	Adjusted [a]
	β (95% CI)	β (95% CI)
Childhood maltreatment	0.12 (0.09, 0.15) [b]	0.12 (0.09, 0.16) [b]
	Depression	
	0.26 (0.21, 0.31) [b]	0.26 (0.21, 0.31) [b]
	Psychological distress (HSCL-10)	
	1.64 (1.30, 1.97) [b]	1.70 (1.37, 2.02) [b]
	Sleeping difficulty	
	0.17 (0.12, 0.22) [b]	0.20 (0.15, 0.25) [b]
	Insomnia	
	0.26 (0.18, 0.34) [b]	0.33 (0.25, 0.41) [b]
	Consultation with psychiatrist	
	RR (95% CI)	RR (95% CI)
	2.42 (1.80, 3.24) [b]	2.15 (1.60, 2.87) [b]
	Use of sleeping pills	
	β (95% CI)	β (95% CI)
	0.03 (-0.01, 0.08)	0.08 (0.03, 0.13) [b]
	Use of antidepressants	
	0.05 (0.01, 0.09) [d]	0.05 (0.01, 0.10) [d]
	Use of tranquilizers	
	0.01 (-0.02, 0.04)	0.02 (-0.01, 0.04)
	Forgetfulness	
	RR (95% CI)	RR (95% CI)
	1.18 (1.06, 1.31) [c]	1.26 (1.13, 1.40) [b]
	Decline in memory	
	1.07 (1.00, 1.14) [e]	1.15 (1.07, 1.23) [b]
	Memory examination	
	1.08 (0.59, 2.00)	1.18 (0.63, 2.20)
	Prevalence of psychiatric problems	
	2.11 (1.82, 2.44) [b]	1.96 (1.69, 2.26) [b]

[a] Adjusted for age, sex, parental history of health outcomes (psychiatric disorders, diabetes mellitus, and asthma).
[b] $p < 0.001$
[c] $p < 0.01$
[d] $p < 0.05$
[e] $p < 0.1$
RR: relative risk; CI: confidence interval.

Table 3. Association between psychopathological symptoms and physical health outcomes (N=12,981).

	Diabetes mellitus	**Hypothyroidism**	**COPD**
	RR (95% CI) [a]	RR (95% CI) [a]	RR (95% CI) [a]
Anxiety and depression	1.58 (1.33, 1.88) [b]	1.34 (1.19, 1.51) [b]	1.95 (1.67, 2.27) [b]
Depression	1.30 (1.16, 1.46) [b]	1.20 (1.11, 1.30) [b]	1.52 (1.37, 1.68) [b]
Psychological distress (HSCL-10)	1.05 (1.04, 1.07) [b]	1.04 (1.03, 1.05) [b]	1.10 (1.09, 1.11) [b]
Sleeping difficulty	1.10 (0.98, 1.23)	1.18 (1.09, 1.27) [b]	1.40 (1.26, 1.55) [b]
Insomnia	1.07 (1.00, 1.15) [e]	1.10 (1.04, 1.15) [b]	1.36 (1.27, 1.45) [b]
Consultation with psychiatrist	1.54 (0.97, 2.45) [e]	1.34 (0.99, 1.83) [e]	1.68 (1.02, 2.77) [d]
Use of sleeping pills	1.05 (0.93, 1.17)	1.14 (1.06, 1.23) [b]	1.38 (1.27, 1.51) [b]
Use of antidepressants	1.14 (1.00, 1.29) [e]	1.14 (1.04, 1.24) [c]	1.31 (1.16, 1.47) [b]
Use of tranquilizers	1.25 (1.08, 1.43) [c]	1.11 (1.01, 1.24) [d]	1.45 (1.29, 1.63) [b]
Forgetfulness	1.04 (0.88, 1.23)	1.14 (1.01, 1.29) [d]	1.36 (1.13, 1.64) [b]
Decline in memory	1.04 (0.89, 1.23)	1.16 (1.02, 1.31) [d]	1.28 (1.07, 1.53) [c]
Memory examination	1.58 (1.00, 2.50) [d]	1.82 (1.32, 2.51) [b]	1.59 (0.91, 2.76) [e]
Prevalence of psychiatric problems	1.66 (1.33, 2.08) [b]	1.60 (1.37, 1.87) [b]	2.05 (1.64, 2.56) [b]

[a] Adjusted for age, sex, child maltreatment, and parental history of health outcomes (psychiatric disorders, diabetes mellitus, and asthma)
[b] $p < 0.001$
[c] $p < 0.01$
[d] $p < 0.05$
[e] $p < 0.1$
RR: relative risk; CI: confidence interval.

Table 4. Influence of current psychopathological symptoms on the association between childhood maltreatment and physical health outcomes.

	Diabetes mellitus		
	Total effect [a]	Direct effect [b]	Indirect effect
	RR (95% CI)	RR (95% CI)	RR (95% CI)
Childhood maltreatment	1.47 (1.10, 1.91)	1.38 (1.04, 1.79)	1.07 (1.02, 1.12)
	Hypothyroidism		
	1.42 (1.13, 1.78)	1.27 (1.03, 1.56)	1.12 (1.07, 1.17)
	COPD		
	2.19 (1.49, 3.04)	1.82 (1.28, 2.56)	1.21 (1.12, 1.36)

[a] Adjusted for age, sex, parental history of health outcomes (psychiatric disorders, diabetes mellitus, and asthma)

[b] Adjusted for age, sex, parental history of health outcomes (psychiatric disorders, diabetes mellitus, and asthma)+ current psychopathological symptoms (anxiety, 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, and memory examination).

RR: relative risk; CI: confidence interval.

Table 5. The indirect effect of childhood maltreatment on physical health outcomes via affective symptoms, general mental health, and deficits in memory.

	Indirect effect
	RR (95% CI) [a]
	Diabetes mellitus
Via affective symptoms	1.09 (1.05, 1.16)
Via general mental health	1.02 (1.01, 1.05)
Via deficits in memory	1.00 (1.00, 1.01)
	Hypothyroidism
Via affective symptoms	1.08 (1.05, 1.10)
Via general mental health	1.05 (1.04, 1.07)
Via deficits in memory	1.02 (1.00, 1.02)
	COPD
Via affective symptoms	1.19 (1.09, 1.37)
Via general mental health	1.01 (0.94, 1.03)
Via deficits in memory	1.03 (1.01, 1.05)

[a] Adjusted for age, sex, parental history of health outcomes (psychiatric disorders, diabetes mellitus, and asthma)
RR: relative risk; CI: confidence interval.