Research Article

Examining the Contribution of Childhood Maltreatment to the Gender Gap in Depression: Insights from the German National Cohort (NAKO)

Maja P. Völker[a,b], Aina L. Kresken[a], Jerome C. Foo[a,c,d], Josef Frank[a], Iris Reinhard[e], Johanna Klinger-König[f], Lea Zillich[a,g], Diana S. Ferreira de Sá[h], Rafael Mikolajczyk[i,j], Michael Leitzmann[k], Patricia Bohmann[k], Lilian Krist[l], Thomas Keil[l,m,n], Claudia Meinke-Franze[o], Steffi Riedel-Heller[p], Halina Greiser[q], Barbara Bohn[r], Hermann Brenner[s], Nadia Obi[t], Volker Harth[t], Tobias Pischon[u,v,w], Hans J. Grabe[f], Klaus Berger[x], Emanuel Schwarz[b,y,z], Jutta Mata[aa], Stephanie H Witt[a,b], Fabian Streit[b,y,z]

[a] Department of Genetic Epidemiology in Psychiatry, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany

[b] Centre for Mental Health (DZPG), Partner Site Mannheim-Heidelberg-Ulm, Mannheim, Germany

[c] Department of Psychiatry, College of Health Sciences, University of Alberta, Edmonton, AB, Canada

[d] Neuroscience and Mental Health Institute, University of Alberta, Edmonton, AB, Canada

[e] Core Facility Biostatistics, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany

[f] Department of Psychiatry and Psychotherapy, University Medicine Greifswald, Greifswald, Germany

[g] Department of Psychiatry and Psychotherapy, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany

[h] Division of Clinical Psychology and Psychotherapy, Department of Psychology, Saarland University, Germany

[i] Institute for Medical Epidemiology, Biometrics, and Informatics, Interdisciplinary Center for Health Sciences, Medical Faculty of the Martin Luther University Halle-Wittenberg, Halle (Saale), Germany

[j] German Center for Mental Health, Site Halle-Jena-Magdeburg, Halle (Saale), Germany

[k] Department of Epidemiology and Preventive Medicine, University of Regensburg, Regensburg, Germany

[l] Institute of Social Medicine, Epidemiology and Health Economics, Charité - Universitätsmeditzin Berlin, Berlin, Germany

[m] Institute of Clinical Epidemiology and Biometry, University of Würzburg, Würzburg, Germany

[n] State Institute of Health I, Bavarian Health and Food Safety Authority, Erlangen, Germany

[o] Institute for Community Medicine, University Medicine Greifswald, Greifswald, Germany

[p] Institute of Social Medicine, Occupational Health and Public Health, Medical Faculty, University of Leipzig, Leipzig, Germany

[q] German Cancer Research Center (DKFZ) Heidelberg, Division of Cancer Epidemiology, Heidelberg, Germany

[r] NAKO e.V., Heidelberg, Germany

[s] Cancer Prevention Graduate School, German Cancer Research Center (DKFZ), Heidelberg, Germany

[t] Institute for Occupational and Maritime Medicine (ZfAM), University Medical Center Hamburg-Eppendorf, Hamburg, Germany

[u] Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC), Molecular Epidemiology Research Group, Berlin, Germany

[v] Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC), Biobank Technology Platform, Berlin, Germany

[w] Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany

[x] Institute of Epidemiology and Social Medicine, University of Münster, Münster, Germany

[y] Department of Psychiatry and Psychotherapy, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany

[z] Hector Institute for Artificial Intelligence in Psychiatry, Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany

[aa] Health Psychology, School of Social Sciences, University of Mannheim, Mannheim, Germany

Short Title: Sex-Specific Associations of Maltreatment with Depression

Corresponding Author:

Fabian Streit

E-mail address: Fabian.streit@zi-mannheim.de

Keywords: Cigarette smoking, depression, childhood abuse, sex differences, epidemiology

Abstract

Background: Childhood maltreatment is a major risk factor for depression and may contribute to sex differences in depression prevalence. We examined sex-specific associations between childhood maltreatment and depression and estimated the proportion of depression cases attributable to specific maltreatment subtypes.

Methods: We analyzed baseline data from 159,045 participants (49.4% women; aged 19–72) in the German National Cohort (NAKO). Childhood maltreatment was assessed via the Childhood Trauma Screener; depression via self-reported physician's diagnosis and MINI classification (lifetime) and the PHQ-9 (current). Associations, including sex interactions, were modeled using binary logistic regressions. Mediation analyses and sex-stratified population attributable fractions (PAFs) quantified the contribution of maltreatment to depression.

Results: Maltreatment was associated with increased odds of lifetime ($OR_{physician's\ diagnosis}$=2.45 [2.38,2.53]; OR_{MINI}=2.30 [2.18,2.43]) and current depression (OR=2.90 [2.79,3.02]). Sex interactions were observed for the physician's diagnosis: physical abuse and neglect had stronger associations in women ($OR_{physical\ abuse}$=2.74 [2.59,2.90]; $OR_{physical\ neglect}$=1.36 [1.28,1.44]) than men ($_{OR physical\ abuse}$=2.36 [2.21,2.52]; $OR_{physical\ neglect}$=1.08 [1.00,1.16]), whereas sexual abuse showed stronger associations in men (OR=3.23 [2.91,3.57]) than women (OR=2.61 [2.48,2.75]). Overall, childhood maltreatment accounted for 21.2-26.2% of lifetime and 33.4% of current depression. PAFs were higher in women than men for lifetime (24.5-28.5% vs. 16.0-20.9%) and current depression (36.1% vs. 28.2%). Emotional abuse and neglect contributed the highest PAFs (up to 10.2%). Maltreatment mediated 18.9-30.0% of the association between sex and depression.

Conclusion: Maltreatment, especially emotional subtypes, account for a substantial proportion of depression in both sexes, with stronger overall associations in women. Sex-specific prevention may help reduce depression prevalence.

25 # Introduction

Childhood maltreatment is a widespread global problem with detrimental consequences for physical and mental health [1]. Commonly, five subtypes are distinguished: sexual, physical, and emotional abuse, and emotional and physical neglect [2].

A widespread consequence of maltreatment is depression [3,4]. Major depressive disorder (MDD) affects more than 330 million people worldwide and is a leading contributor to the global burden of disease [5,6]. Risk factors also include genetic predisposition, low socioeconomic status, and stressful life events [7]. There is robust evidence linking childhood maltreatment to current and lifetime depression [3,5], especially emotional abuse and neglect [8–10]. Consistent with these findings, recent studies using data from the German National Cohort (NAKO), a large population-based longitudinal health study of more than 200,000 adults in Germany [11], showed a substantial association of lifetime and current depression with sexual and physical abuse, but an even stronger association with emotional abuse and neglect [12,13].

Sex differences also play a key role in depression: Women are twice as likely to be diagnosed with depression [10,14–16] and report depressive symptoms more frequently [17,18]. There is growing evidence that childhood maltreatment may contribute to this disparity both through differences in the impact of maltreatment experiences and differences in their prevalence across sexes. First, women are reported to experience childhood maltreatment differently than men, and show varying vulnerabilities to its subtypes [3,19–23], with higher susceptibility to psychopathology following early maltreatment exposure [5,15,22]. Second, women report childhood maltreatment more frequently [24,25] and appear to be victims of more severe and non-visible forms of maltreatment such as sexual and emotional abuse [26–29]. In the NAKO, 28.7% of women reported a history of childhood maltreatment, compared to 23.5% of men [13]. Specifically, women reported higher rates of sexual (9.7% vs. 2.6%) and emotional (10% vs. 6.2%) abuse, and emotional neglect (8.5% vs. 6.6%) than men, while men reported slightly higher frequencies of physical abuse than women (8.4% vs. 7.8%) [13].

Although the overall link between childhood maltreatment and depression is well-established, the evidence on how specific subtypes affect depression risk in men and women remains inconsistent and sometimes contradictory [18,24,25]. Clarifying these subtype-specific associations is essential for understanding the mechanisms through which maltreatment contributes to depression risk across sexes.

One way to quantify the contribution of childhood maltreatment to depression is Population Attributable Fractions (PAFs; Levin, 1953). PAFs range from 0% to 100% and estimate the share of disease cases in a population that can be attributed to exposure to a specific risk factor [30],

corresponding to the potential reduction in the disease proportion if exposure to this risk factor was eliminated [30,31]. PAFs are determined by both the strength of the association between risk factor and outcome, and the prevalence of the risk factor, and can be stratified by sex to investigate sex-specific contributions. Originally developed to assess the impact of a single, independent risk factor on disease burden, PAFs have been expanded to account for multiple, potentially correlated risk factors, thereby better reflecting real-world exposure patterns [32].

Recently, this approach was applied to quantify the contribution of childhood maltreatment and its subtypes to depression: Li et al. [30] estimated that half of MDD cases worldwide could be attributed to childhood maltreatment when the subtypes are considered collectively. However, PAF varied substantially across maltreatment subtypes, with emotional abuse and neglect often showing the largest contributions [30,33]. While these studies did not examine sex-specific differences, other research suggests that these contributions vary between men and women [31,34]. One study in Australia found that a greater proportion of lifetime depression in women (22.8%) than men (15.7%) could be attributed to sexual and physical abuse [35]. Moreover, Xiao et al. [34] investigated all five maltreatment subtypes and sex differences among students in China, but limited their study to current depressive symptoms. Nevertheless, the results showed comparable patterns to those for lifetime depression by Li et al. [30] and Moore et al. [35], with individual contributions of each subtype to depression (6.1%–29.4%) being consistently higher for women.

The overall aims of the present study was to assess whether: a) the subtypes of childhood maltreatment differ in their association with lifetime and current depression in men and women and b) sex differences in both the strength of these associations and the prevalence of the childhood maltreatment subtypes result in sex differences in the share of depression that can be attributed to childhood maltreatment.

Methods

The present analysis used data from the baseline assessment of the NAKO, a prospective, population-based, long-term cohort study [11] that investigates the causes, risk factors, and mechanisms of common diseases.

Sample

Between 2014 and 2019, a total of 205,415 individuals were recruited from 18 research centers across Germany, randomly selected from population registries based on age and sex [11,36]. The recruited sample comprises women and men aged 19 to 72 years, with a higher representation of individuals in the age groups ≥40 years. All participants provided written informed consent before

participating in the study. Participants were excluded if they were unable to provide explicit consent, answer questions due to insufficient knowledge of German, or did not complete a minimum set of questionnaires and assessments, resulting in a final sample of 205,053 individuals [11]. All participants underwent a Level-1 (L1) program including interviews and touchscreen questionnaires, physical and medical examinations, and the collection of biomaterial [11]. A subset of ~28% participants underwent a more in-depth Level-2 (L2) assessment. The study was approved by the local ethics committees of all involved study centers and conducted in accordance with the Declaration of Helsinki.

Measures

Physician's Diagnosis of Depression

For lifetime depression, in a standardized face-to-face interview, participants were asked whether they had ever received a diagnosis of depression from a physician or psychotherapist [17].

MINI Depression Classification

Additionally, for lifetime depression, the Major Depression Module of the Mini-International Neuropsychiatric Interview (MINI, German v5.0.0) was used [37]. All participants received a filter question on the occurrence of lifetime depression. If affirmed, they were asked about the two cardinal symptoms of depression (i.e., depressed mood, loss of interest or pleasure). If any cardinal symptom was affirmed, only L2 participants received the remaining MINI questions about symptomatology and impairment. For present MINI analyses, only L2 participants with a complete MINI classification were used and dichotomized (positive/negative MINI classification).

Patient Health Questionnaire

The depression module of the Patient Health Questionnaire 9 (PHQ-9) [38], comprising nine questions, was used to measure self-reported depressive symptoms over the past two weeks. A sum score ranging from 0 to 27 was calculated, reflecting the severity of current depressive symptoms [17]. The widely used PHQ-9 cut-off score of ≥ 10 (i.e., moderate to severe depressive episode) was used for all analyses [39].

Childhood Trauma Screener

The German version of the Childhood Trauma Screener (CTS) [40], an ultra-short version of the Childhood Trauma Questionnaire (CTQ) [2], was used to determine the presence of the five

122 childhood maltreatment subtypes using a single item per subtype [40]. Responses to the questions
123 were provided on a five-point Likert scale [41]. For the present analysis, any maltreatment and all
124 subtypes were analyzed as binary variables ('no/low trauma' or 'moderate/severe trauma') based on
125 established thresholds [42] (see Supplementary Table S1). If subjects reported any subtype of
126 childhood maltreatment, it was scored as any maltreatment.

127 ***Education***

128 Participants' education levels were categorized according to the International Standard
129 Classification of Education 97 (ISCED97) [43]. Subjects were grouped into 3 categories: low (level
130 1/2), intermediate (level 3/4), and high (level 5/6) education [44]. An additional category, 'in
131 progress' (level 0), was included for participants, primarily under 30 years of age, who were still
132 engaged in education or training at the time of the study.

133 ***Relative Income Position***

134 The relative income position assesses the income position of the individual relative to the overall
135 median in Germany. It was derived from the monthly net income and financial need of the
136 household.

137 **Statistical Analyses**

138 Statistical analyses were conducted using R software (v4.4.0). All analyses were adjusted for the
139 following sociodemographic variables: age in years, age^2 (to account for both linear and non-linear
140 age effects), and education level [12], with sex used solely as a stratification/interaction variable (see
141 below). Sensitivity analyses were conducted with relative income position as additional covariate to
142 further account for socioeconomic status. Only subjects with complete information on age (n =
143 204,725), sex (n = 204,725), education level (n = 190,290), physician's diagnosis of depression (n =
144 203,152), MINI (n = 57,803), PHQ-9 (n = 189,340), and CTS (n = 172,038) were included in the
145 analyses (see Figure 1).

146 To assess the sex differences of all included variables and the respective effect sizes,
147 regression models were used to estimate odds ratios (ORs) for categorical variables, Cohen's *d [45]*
148 for continuous variables, and Cramer's *V* [46] for ordinal variables (see Table 2).

149 To assess whether sex moderates the association between any childhood maltreatment or its
150 subtypes and depression, binary logistic regressions were conducted with childhood maltreatment
151 (*any maltreatment* and all subtypes) as predictors and binary depression measures (physician's
152 diagnosis, MINI classification, PHQ-9) as outcomes with sex-by-maltreatment interaction terms

(resulting in 18 regression models: 6 maltreatment variables × 3 depression outcomes). Additionally, 36 sex-stratified models (6 maltreatment variables × 3 outcomes × 2 sexes) were calculated separately to examine the simple main effects of each maltreatment variable on depression within each sex.

PAFs [47] were computed to estimate the proportion of depression cases in the cohort that could be attributable to childhood maltreatment. Levin's formula (1953), $PAF = P_e(RR_e - 1) / (1 + P_e[RR_e - 1])$, was applied, where P_e is the prevalence of the risk factor in the population and RR_e is the risk ratio of exposure to the risk factor [48]. As a sensitivity analysis, PAFs were also calculated with Miettinen's formula, $PAF = P_C(RR -1) / RR$, where P_c is the proportion of cases exposed to the risk factor in the population. To calculate the PAFs, 15 independent logistic regression models were calculated—one for each combination of the five maltreatment subtypes and the three depression outcomes (physician's diagnosis, MINI Classification, PHQ-9). Each model was adjusted for age, age², and education, and was run separately for the complete sample and stratified by sex. Sensitivity analyses were performed with additional adjustment for relative income position as a proxy for socioeconomic status. Estimated marginal probabilities were obtained from those regression analyses using the R package emmeans [49]. Based on these estimated marginal probabilities, risk ratios (RRs) were calculated. The adjusted RRs were used to compute the PAFs [50]. Subsequently, individual PAFs were calculated for each subtype, for the total sample, and stratified by sex. To account for the intercorrelation of maltreatment subtypes, individual PAFs were weighted to avoid overestimating their contribution to the overall PAF [48]. The weighting component was determined based on the communalities of the subtypes, i.e., the shared proportion of variance among subtypes. These were derived by computing tetrachoric correlations between the binary maltreatment variables, followed by a principal component analysis. Only the first component had an eigenvalue greater than 1, indicating a reasonable explanatory power; therefore, only its loadings were used to calculate the weights. Then the sum of squares of all factor loadings was calculated to extract the communalities. The weighting factor was determined according to its communality (weight (w) = 1 – communality). Afterwards, the individual PAFs were multiplied by their respective weights and aggregated into a comprehensive overall PAF (overall PAF = 1 – [(1 – w*PAF1) (1 – w*PAF2) (1 – w*PAF3)...]). Finally, individual weighted PAFs $overall\ PAF$

were recalculated by multiplying them by the overall PAF [48]. All applied statistical analyses are listed in Table 1. To evaluate the significance of sex differences in the sex-stratified PAF estimates (18 comparisons: overall PAF, and five subtype PAFs, for lifetime and current depression), the difference between men and women was calculated for each pair of bootstrap resamples (i.e., PAF_{men} –

186 PAF_{women}). Then, *p*-values were calculated based on the distribution of this difference. The number of
187 instances where the resampled differences were in the opposite direction compared to the original
188 difference was divided by the number of bootstraps (i.e., 5,000). To account for two-sided testing,
189 this value was multiplied by two. In cases where no bootstrap estimates in the opposite direction to
190 the original observations were obtained, p-values corresponded to $p < 0.0004$ (i.e., fewer than
191 2/5,000). Frequencies, means, ORs, PAFs, and RRs are reported with unadjusted 95% confidence
192 intervals (CI). For the PAFs, 95% CIs were obtained using bootstrapping with 5,000 resamples
193 separately for each sex (2.5% and 97.5% quantiles) [51]. Bonferroni correction was applied to adjust
194 p-values for 18 independent tests, using the number of tested sex interactions and sex differences in
195 PAFs, respectively [52]. Bootstrapped *p*-values for the PAF comparisons, < 0.0004, are reported as
196 the corresponding adjusted *p*-value: $p_{adj} < 0.0072$. Simple main effects in the sex-stratified regression
197 analyses were corrected for 36 independent tests using the Bonferroni method, and adjusted p-
198 values (p_{adj}) were reported. Graphics were created with the R package *ggplot2 [53]*.

199 To assess to what degree sex differences in maltreatment prevalence or effect sizes account for
200 women's higher depression prevalence, separate mediation models were estimated for each
201 depression outcome. Analyses were performed using the counterfactual-based causal mediation
202 framework implemented in the *cmest* function from the R package *CMAverse [54].* The five
203 maltreatment subtypes were included as parallel binary mediators, allowing for correlations among
204 the subtypes, and analyses were adjusted for age, age² and education. Models were estimated
205 allowing for exposure–mediator interaction, enabling the decomposition of the total effect into
206 components attributable to differential exposure and interaction. Specifically, mediation effects were
207 quantified using excess relative risk measures. These include the excess relative risk due to the pure
208 natural indirect effect (ERpnie), which reflect differential exposure to maltreatment, and the excess
209 relative risk due to mediated interaction (ERintmed), which reflect sex-specific differences in
210 susceptibility. The proportions of the total effect explained by these components were reported.
211 Statistical inference was based on nonparametric bootstrap resampling with 5,000 replications.

212 ***Table 1:*** *Overview of Statistical Analyses for Each Hypothesis with Predictor, Outcome, and sex-specific analysis*

Aim	Statistical Analysis	Independent Variable	Dependent Variable	Assessment of sex differences

1	Binary logistic regression with interaction term	Childhood maltreatment and the five subtypes [categorical: 'yes', 'no']	Physician's diagnosis of depression [categorical: 'physician's diagnosis', 'no physician's diagnosis']	Interaction variable sex [categorical: 'men', 'women']
			MINI classification [categorical: 'positive MINI classification', 'negative MINI classification']	
			Current depressive symptoms (PHQ-9 cut-off ≥ 10 [categorical: 'current depressive symptoms', 'no current depressive symptoms'])	
2	Population attributable fractions	Childhood maltreatment and the five subtypes [categorical: 'yes','no']	Physician's diagnosis of depression [categorical: 'physician's diagnosis', 'no physician's diagnosis']	Stratification by sex [categorical: 'men', 'women']
			MINI classification [categorical: 'positive MINI classification', 'negative MINI classification']	
			Current depressive symptoms (PHQ-9 cut-off ≥ 10 [categorical: 'current depressive symptoms', 'no current depressive symptoms'])	
3	Mediation analysis	Independent variable: sex [categorical: 'men', 'women'] Mediators: five maltreatment subtypes [categorical: 'yes','no']	Physician's diagnosis of depression [categorical: 'physician's diagnosis', 'no physician's diagnosis']	Assessed via mediation model (differential exposure and mediated interaction) [categorical: 'men', 'women']
			MINI classification [categorical: 'positive MINI classification', 'negative MINI classification']	
			Current depressive symptoms (PHQ-9 cut-off ≥ 10 [categorical: 'current depressive symptoms', 'no current depressive symptoms'])	

Note. PHQ-9 = Patient Health Questionnaire 9. MINI = Mini-International Neuropsychiatric Interview. Round brackets indicate the coding of a variable. Square brackets specify the measurement scale and levels of the

variable. Regressions were calculated with interactions for the whole sample and sex-stratified without the interaction term. The five mediators were tested in parallel. Analyses were adjusted for age, age² and education.

This analysis was preregistered on the Open Science Framework (OSF; https://osf.io/ezjyv) [55]. Bootstrapped analyses estimating confidence intervals of the PAFs, *p*-values for PAF differences, and the additional calculation of PAFs with Miettinen's formula, sensitivity and mediation analyses were added to the analysis plan after preregistration. The number of comparisons used for Bonferroni correction of the sex-stratified main effects was revised from the preregistered 18 tests to 36 tests to better capture the actual number of tests.

Results

Descriptive Statistics

Descriptive statistics are presented in Table 2. The final sample included 159,045 participants (mean age = 48.6 years, SD = 12.8; 49.4% female). Overall, 13.9% (17.7% of women, 10.1% of men) of the sample reported lifetime depression and 7.5% (9.0% of women, 5.9% of men) reported current depressive symptoms. Childhood maltreatment was more common among women (28.3%) than men (23.2%). The prevalence of specific subcategories of maltreatment across both sexes ranged from 6.0% to 9.7%. Women reported considerably higher frequencies of sexual abuse, emotional abuse, and emotional neglect. Conversely, men were more often exposed to physical abuse than women. Physical neglect did not differ significantly between men and women (see Table 2).

In the complete sample, any maltreatment showed a significant association with lifetime depression ($OR_{physcian's\ diagnosis}$ = 2.45, 95% CI [2.38, 2.53]; ORMINI = 2.30, 95% CI [2.18, 2.43], all $p_{adj} < 0.001$) and current depressive symptoms (OR = 2.90, 95% CI [2.79, 3.02], $p_{adj} < 0.001$). A significant sex interaction was observed for physician's diagnosis ($\beta = 0.13$, SE = 0.03, z = 4.23, $p_{adj} < 0.001$) indicating a stronger association between any maltreatment and physician's diagnosis in women (OR = 2.53, 95% CI [2.43, 2.62]), compared to men (OR= 2.19, 95% CI [2.09, 2.30]), but no sex x any maltreatment interaction was found for MINI classification ($\beta = 0.10$, SE = 0.06, z = 1.79, $p_{adj} = 0.07$; OR_{women} = 2.36, 95% CI [2.19, 2.54]; OR_{men} = 2.13, 95% CI [1.95, 2.31]), and current depressive symptoms ($\beta = 0.04$, SE = 0.04, z = 0.90, $p_{adj} = 1.000$; OR_{women} = 2.88, 95% CI [2.73, 3.03]; OR_{men} = 2.80, 95% CI [2.63, 2.97]; Figure 2, Tables S2-S5). Sensitivity analyses are consistent with these results (Tables S6-S9).

Associations of Childhood Maltreatment Subtypes with Depression and Potential Sex Interactions

Each maltreatment subtype was significantly, but with varying association strengths, associated with an increased frequency of lifetime and current depression across sexes (all $p_{adj} < 0.001$) except for the association between physical neglect and lifetime depression in men (physician's diagnosis: p_{adj} = 0.881, MINI: $p_{adj} = 0.66$).

Significant sex interactions in physician's diagnosis were observed for sexual abuse ($\beta = -.22$, SE = 0.06, z = –3.78, $p_{adj} = 0.002$) with stronger associations in men (OR = 3.23, 95% CI [2.91, 3.57]) than in women (OR = 2.61, 95% CI [2.48, 2.75]), and for physical abuse ($\beta = 0.14$, SE = 0.04, z = 3.21, p_{adj} = 0.016), and physical neglect ($\beta = 0.21$, SE = 0.05, z = 4.41, $p_{adj} < 0.001$) with stronger associations in women ($OR_{physical\ abuse}$ = 2.74, 95% CI [2.59, 2.90], $OR_{physical\ neglect}$ = 1.36, 95% CI [1.28, 1.44]) than men ($OR_{physical\ abuse}$ = 2.36, 95% CI [2.21, 2.52], $OR_{physical\ neglect}$ = 1.08, 95% CI [1.00, 1.16]). All interactions for

MINI classification, and current depression were consistent in direction with those for physician's diagnosis; however, they did not reach significance (all $p_{adj} > 0.05$; see Figure 2, Tables S2-S5). Sensitivity analyses are consistent with these results (Tables S6-S9).

Table 2: *Descriptive Statistics and Association Estimate of All Used Variables for the Total Sample and Separated by Sex*

	Total (N = 159,045)	Men (n = 80,519)	Women (n = 78,526)	Association estimate for sex difference	p-Value
Age (mean ±)	48.6 (12.8)	48.9 (12.9)	48.3 (12.8)	$d = 0.05$[a]	< 0.001**
Sex (men)	50.6%	-	-	-	-
Education	-	-	-	$V = 0.10$[b]	< 0.001**
Education high	56.6%	61.6%	51.6%	-	-
Education medium	39.2%	34.7%	43.8%	-	-
Education low	1.7%	1.3%	2.1%	-	-
Education in progress	2.5%	2.5%	2.6%	-	-
Physician's diagnosis of depression	13.9%	10.1%	17.7%	OR = 1.91 [1.85, 1.96]	< 0.001**
MINI classification$_1$	14.6%	11.9%	17.6%	OR = 1.58 [1.50,1.67]	< 0.001**
PHQ-9 ≥ 10	7.5%	5.9%	9.0%	OR = 1.58 [1.52,1.64]	< 0.001**
CTS Any Maltreatment	25.7%	23.2%	28.3%	OR = 1.31 [1.28,1.34]	< 0.001**
CTS Sexual Abuse	6.0%	2.5%	9.5%	OR = 4.08 [3.88,4.29]	< 0.001**

CTS Physical Abuse	8.0%	8.3%	7.7%	*OR* = 0.93 [0.89,0.96]	< 0.001**
CTS Emotional Abuse	8.0%	6.2%	10.0%	*OR* = 1.68 [1.62,1.74]	< 0.001**
CTS Emotional Neglect	7.4%	6.4%	8.3%	*OR* = 1.32 [1.27,1.37]	< 0.001**
CTS Physical Neglect	9.7%	9.8%	9.7%	*OR* = 0.99 [0.96,1.03]	0.69

Note. MINI = Mini-International Neuropsychiatric Interview. PHQ-9 = Patient Health Questionnaire. CTS = Childhood Trauma Screener. OR = Odds Ratio. N, total number of participants in the sample; n, number of participants in sex-stratified groups. Descriptive results are given as mean values (standard deviation) for continuous variables. For categorical variables (physician's diagnosis, MINI, binary PHQ-9, and binary CTS), the values display frequencies (% yes). T-tests (continuous) and χ^2-tests (categorical) for independent samples were performed to compare means and frequencies between the sexes. ORs with 95% confidence intervals for categorical variables, Cohen's *d* for continuous variables, and Cramér's *V* for ordinal variables are reported as effect sizes. ** $p < .001$.

[1]Data for MINI classification was available for 45,847 participants.

[a]very small effect. [b]small effect.

278

279 **Population Attributable Fractions for Depression Overall and Stratified by Sex**

280 The overall PAF for the share of lifetime depression attributable to the five maltreatment
281 subtypes across the whole sample was 26.2% for physician's diagnosis (95% CI [25.40, 27.08]) and
282 21.2% for MINI classification (95% CI [19.76, 22.71]). The contributions of individual subtypes,
283 weighted by their communalities, ranged from 1.5% to 7.5% for physician's diagnosis and from 0.8%
284 to 6.4% for MINI classification, with the highest PAFs for emotional abuse (physician's diagnosis:
285 7.5%; MINI: 10.3%) and neglect (physician's diagnosis: 6.5%, MINI: 7.9%; Supplementary Tables S10).
286 Sex-stratified analyses (Supplementary Tables S11-S13) revealed significantly higher overall PAFs in
287 women than men (all $p_{adj} < 0.007$): Among women, 28.5% (95% CI [27.3%, 29.7%]) for physician's
288 diagnosis and 24.5% (95% CI [22.4%, 26.6%]) for MINI classification were attributable to childhood
289 maltreatment. For men, 20.9% (95% CI [19.6%, 22.3%]) of physician's diagnosis and 16.0% of MINI
290 classification (95% CI [14.1%, 18.0%]) were linked to childhood maltreatment. In women, individual
291 PAFs for subtypes ranged from 2.0% to 7.9% for physician's diagnosis and 1.2% to 6.8% for MINI
292 classification, and in men, from 0.6% to 6.2% for physician's diagnosis and 0.2% to 5.4% for MINI
293 classification. For both sexes, emotional abuse and neglect, and for women also sexual abuse, were
294 found to have the largest contribution to depression cases. Emotional (PAF_{women} = 7.9%; PAF_{men} =
295 6.2%) and sexual (PAF_{women} = 6.7%; PAF_{men} = 2.9%) abuse, and physical (PAF_{women} = 2.0%; PAF_{men} =
296 0.6%) and emotional neglect (PAF_{women} = 6.8%; PAF_{men} = 6.0%) accounted for a significantly greater
297 proportion of physician's diagnosis in women than in men (all $p_{adj} < 0.005$). Physical abuse was the
298 only subtype to not show a significant difference in the contribution to physician's diagnosis between
299 men and women (PAF_{women} = 5.1%; PAF_{men} = 5.2%, p_{adj} = 1.000).

300 For MINI classification, a significantly greater proportion was explained by sexual abuse (PAF_{women} =
301 6.3%; PAF_{men} = 2.1%) and emotional neglect (PAF_{women} = 5.8%; PAF_{men} = 4.2%) in women than men (all
302 $p_{adj} < 0.007$).

303 For current depressive symptoms, the overall PAF attributable to the five maltreatment subtypes was
304 33.4% (95% CI [32.2%, 34.6%]), with individual subtype contributions ranging from 2.6% to 9.6%. The
305 highest PAFs were observed for emotional abuse (PAF = 9.6%) and neglect (PAF = 8.4%, Figure 3).

306 The overall PAF for current depressive symptoms was significantly greater for women than men (p_{adj}
307 < 0.005): In women 36.1% (95% CI [34.5%, 37.7%]) of current depression were estimated to be
308 attributable to the five subtypes of maltreatment, while in men only 28.4% (95% CI [26.7%, 30.2%])
309 cases were attributable to childhood maltreatment.

For current depression, higher PAFs in women than in men were observed for emotional (PAF_{women} = 10.2%; PAF_{men} = 8.2%, $p_{adj} < 0.005$) and sexual (PAF_{women} = 8.0%; PAF_{men} = 3.3%, $p_{adj} < 0.005$) abuse, whereas for emotional neglect and physical subtypes, no significant sex difference was found (all $p_{adj} > 0.05$). Comparisons between the sex-stratified PAFs are presented in Supplementary Table S13. The sensitivity analysis showed that the PAFs calculated with Miettinen's formula were identical to those calculated with Levin's formula (see also [56]).

Mediation of Sex Effects on Depression by Childhood Maltreatment

Mediation analyses showed that childhood maltreatment partially mediated the association between sex and physician's diagnosis, accounting for 18.9% of the total effect ($p < 0.001$). For MINI classification, 24.6% of the total effect of sex was mediated by childhood maltreatment subtypes ($p < 0.001$). For current depressive symptoms (PHQ-9), 30.0% of the total effect was mediated ($p < 0.001$). Across all outcomes, the explained proportion of the sex difference in depression was primarily driven by differential exposure to childhood maltreatment, while contributions from mediated interaction effects, reflecting sex-specific susceptibility to maltreatment, were substantially smaller (ERpnie vs. ERintmed: physician's diagnosis: 15% vs. 4%; MINI: 21% vs. 4%; PHQ-9: 26% vs. 4%). Mediated interaction effects were statistically significant only for the physician's diagnosis ($p < .001$), but not for MINI classification or current depressive symptoms (both $p > .1$; see Supplementary Table S18).

Discussion

This study investigated sex-specific associations between childhood maltreatment and both lifetime and current depression in a large population-based cohort (NAKO). While depression was substantially more prevalent in women, sex differences in childhood maltreatment varied by subtype. Childhood maltreatment was associated with increased depression risk in both sexes, with subtype-specific associations varying by sex and a greater overall contribution to depression rates observed in women.

Across both sexes, any maltreatment and the single maltreatment subtypes showed ORs of >2 for both depression measures, with emotional subtypes - and for men, also sexual abuse - showing the strongest associations (OR > 3). Physical neglect showed substantially lower associations with depression (all OR < 1.5; and non-significant for physician's diagnosis in men, and for MINI overall and in men), consistent with previous analyses of the NAKO dataset [12,13].

Any maltreatment showed a significant interaction with sex for physician's diagnosis only, with a stronger association in women, which is in line with previous studies, showing that women are more

342 prone to develop lifetime depression than men after childhood maltreatment [22,23]. Similarly, sex
343 interactions of maltreatment subtypes were only observed for physician's diagnosis, with stronger
344 associations for physical subtypes in women and for sexual abuse in men. These findings have been
345 reported in a recent article based on the NAKO dataset, examining lifetime MDD [13].

346 A possible explanation is that men might be less likely to report sexual abuse due to stigma, shame,
347 and gender stereotypes, which might intensify its psychological impact [57]. In contrast, the weaker
348 association between physical abuse and neglect and lifetime depression in men may reflect their
349 lower tendency to perceive such events as traumatic [4]. Men are often socialized to be tough,
350 resilient, and independent, and tend to perceive life events as more controllable [4,58]. Sex-specific
351 social norms may promote more adaptive, problem-focused coping in men, but also externalizing
352 behaviours (e.g., aggression or substance abuse). In contrast, women may be more prone to
353 emotion-focused coping or internalizing responses [3,4,58].

354 As the results from this study and the existing evidence from other studies on the sex-specific impact
355 of the subdimensions remain inconsistent, conclusions should be drawn with caution. Given that the
356 NAKO comprises the largest sample among these studies, the significant sex-specific associations
357 observed for three of five subcategories on lifetime depression indicate that sex plays a role in the
358 associations.

359 The PAFs indicated that a notable share of depression occurrences in the NAKO sample might be
360 attributable to childhood trauma, with the emotional subtypes accounting for the largest proportion.
361 Sex-stratified PAFs revealed that, consistent with previous articles, a significantly higher proportion
362 of depression cases in women were attributable to childhood maltreatment than in men [31,34,35],
363 with nearly all subtypes contributing more strongly to depression in women, particularly the
364 emotional subtypes and sexual abuse. The findings highlight that, in addition to the strength of the
365 observed associations, the prevalence of the subtypes substantially contributes to the PAFs. For
366 instance, although sexual abuse had a stronger association with physician's diagnosis in men (ORmen
367 ≈ 3.20, ORwomen ≈ 2.65), it was about 3.5 times more prevalent among women, therefore
368 explaining proportionally more of women's depression cases. This offers a potential explanation of
369 the stronger association of sexual abuse and depression in men, as they appear to have less male
370 counterparts with comparable experiences and may experience stronger stigmatisation. Additionally,
371 men were found to disclose sexual abuse less often, suggesting a high number of undetected cases.
372 Given the 2:1 female-to-male ratio in overall depression prevalence, close to an estimated five out of
373 six depression cases attributable to sexual abuse were observed in women. The mediation analyses
374 indicate that sex differences in maltreatment prevalence and effects contribute to a meaningful but

375 moderate proportion of the higher depression prevalence in females for the investigated depression
376 outcomes. Nevertheless, the majority of the sex differences in depression remained independent of
377 childhood maltreatment, highlighting that additional biological, social, or gender-related mechanisms
378 likely contribute to women's higher depression risk. Importantly, the explained proportion was
379 largely driven by sex differences in the prevalence of childhood maltreatment subtypes rather than
380 by sex-specific differences in their associations with depression.

381 Despite the observed sex differences in the present study, the results demonstrate that childhood
382 trauma significantly influences and contributes to depression in both sexes. Most maltreatment
383 subtypes show substantial associations with depression in both sexes (OR > 2, except physical neglect
384 potentially due to low item sensitivity [42]), and the PAF models indicate that childhood
385 maltreatment accounted for between 20.9% to 36.1% of NAKO depression cases, corresponding to a
386 large share of NAKO depression occurrences in both sexes. Together, these findings suggest that
387 childhood maltreatment represents an important shared pathway to depression in both sexes,
388 contributing proportionally—and even more so in absolute numbers—to the population burden of
389 depression among women than among men.

390 The present study has substantial strengths. It was carried out using data from the largest available
391 dataset with CTS data from Germany to our knowledge. This allowed analyses with high statistical
392 power [59], and the comprehensive investigations of sex-specific associations, and the investigation
393 of childhood maltreatment subtypes and different depression definitions. Calculating PAFs not only
394 takes into account both the association between childhood maltreatment and depression and the
395 prevalence of the risk factors, but also the interrelatedness of the maltreatment subtypes [27],
396 offering a broader understanding of the potential reduction in depression cases if exposure to
397 childhood maltreatment were eliminated.

398 This study has several limitations. First, the retrospective self-report measures (i.e., CTS, physician's
399 diagnosis, MINI) [60] are susceptible to biases, particularly for sensitive information such as
400 childhood maltreatment which some individuals might be unwilling to disclose [41]. Moreover,
401 individuals with (current) depression may recall childhood experiences more negatively [60].
402 Additionally, the CTS measures each subtype with a single item, which may limit the depth and
403 specificity compared to the full CTQ or impact effect estimates [61]. Furthermore, information on the
404 timing and severity of childhood maltreatment was not recorded [12,62]. Nonetheless, the five-item
405 CTS is an economical approach, suitable for large-scale cohorts like the NAKO. Furthermore,
406 participants over 40 years of age were oversampled, which limited the sample's representativeness.
407 Although the response (~ 15.6%) is relatively high for a large-scale cohort study [36,63], selection bias

remains relevant, as participants with low SES, who are more often affected by maltreatment [41] and depression [17], and individuals with severe depression are likely underrepresented in the sample. Moreover, only biological sex has been assessed in the NAKO, potentially masking effects specific to transgender or non-binary individuals.

Given the cross-sectional design of the present analysis, future longitudinal NAKO data [11] will provide more valuable insights into the maltreatment-depression relationship and its public health implications. Further research should also integrate biological factors, social networks and socio-behavioral measures that may influence subtype-specific and sex-specific associations [5,7,58,67].

Conclusion

The findings highlight the significant impact of childhood maltreatment and its subtypes on both lifetime and current depression, with sex-specific associations observed only for physician's diagnosis. To our knowledge, this is the only study differentiating subtype-specific childhood maltreatment associations with both lifetime and current depression. A substantial share of depression cases, especially among women, is attributable to maltreatment. Sex-specific prevention and coping strategies could help reduce overall depression prevalence [68].

Statements

Acknowledgement

We thank all participants, the complete staff at the NAKO study centers, the data management and integration center, and the NAKO head office who enabled the conduction of the study and made the collection of all data possible.

Statement of Ethics

The present study was initially approved by the ethical committee of the Bavarian State Medical Association (Nr. 13023). Subsequently, all local ethical committees approved the study.

Written consent was obtained from all participants before participation.

Conflict of Interest Statement

HJG has received travel grants and speakers' honoraria from Neuraxpharm, Servier, Indorsia, and Janssen Cilag.

Funding Sources

This project was conducted with data (Application No. NAKO-679) from the German National Cohort (NAKO) (www.nako.de). The NAKO is funded by the Federal Ministry of Education and Research [project funding reference numbers: 01ER1301A/B/C, 01ER1511D, 01ER1801A/B/C/D, and 01ER2301A/B/C], the federal states, and the Helmholtz Association, with additional financial support from the participating universities and the participating institutes of the Leibniz Association and the Helmholtz Association. This research was supported by the Hector Foundation II and was endorsed by the German Center for Mental Health (DZPG).

Author Contributions

MPV, ALK, JF, JKK, LZ, ES, KB, JM, SHW, FS contributed to the conception and design of the study. JF and IR advised statistical analyses. MPV and ALK performed statistical analyses. MPV, ALK, JCF, DFS, FS wrote the manuscript. FS supervised this work. RM, ML, PB, LK, TK, CMF, SRH, HG, BB, HB, NO, VH, TP, KB were involved in the data collection. All authors critically evaluated the manuscript.

Data Availability Statement

The datasets analyzed in the current study are not publicly available due to privacy restrictions but can be requested through the NAKO transfer hub (https://transfer.nako.de/). Data access for this study was granted under application number NAKO-679.

References

Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, et al. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. Lancet Public Health. 2017 Aug;2(8):e356–66.

2 Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, et al. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. Child Abuse Negl. 2003 Feb;27(2):169–90.

3 Wang X, Lu J, Liu Q, Yu Q, Fan J, Gao F, et al. Childhood experiences of threat and deprivation predict distinct depressive symptoms: A parallel latent growth curve model. J Affect Disord. 2022 Dec;319:244–51.

4 Dong C, Wang Z, Jia F, Tian H, Zhang Y, Liu H, et al. Gender differences in the association between childhood maltreatment and the onset of major depressive disorder. J Affect Disord. 2024 Apr;351:111–9.

5 Gallo EAG, Munhoz TN, Loret de Mola C, Murray J. Gender differences in the effects of childhood maltreatment on adult depression and anxiety: A systematic review and meta-analysis. Child Abuse Negl. 2018 May;79:107–14.

6 Chen X-D, Li F, Zuo H, Zhu F. Trends in prevalent cases and disability-adjusted life-years of depressive disorders worldwide: Findings from the Global Burden of Disease Study from 1990 to 2021. Depress Anxiety. 2025 Jan;2025(1). DOI: 10.1155/da/5553491

7 Fava M, Kendler KS. Major depressive disorder. Neuron. 2000 Nov;28(2):335–41.

8 Gerke J, Koenig AM, Conrad D, Doyen-Waldecker C, Pauly M, Gündel H, et al. Childhood maltreatment as risk factor for lifetime depression: The role of different types of experiences and sensitive periods. Ment Health Prev. 2018 Jun;10:56–65.

9 Schilling C, Weidner K, Brähler E, Glaesmer H, Häuser W, Pöhlmann K. Patterns of childhood abuse and neglect in a representative German population sample. PLoS One. 2016 Jul;11(7):e0159510.

10 Radell ML, Abo Hamza EG, Daghustani WH, Perveen A, Moustafa AA. The impact of different types of abuse on depression. Depress Res Treat. 2021 Apr;2021:6654503.

11 Peters A, German National Cohort (NAKO) Consortium, Peters A, Greiser KH, Göttlicher S, Ahrens W, et al. Framework and baseline examination of the German National Cohort (NAKO). Eur J Epidemiol. 2022 Oct DOI: 10.1007/s10654-022-00890-5

12 Streit F, Völker MP, Klinger-König J, Zillich L, Frank J, Reinhard I, et al. The interplay of family history of depression and early trauma: associations with lifetime and current depression in the German national cohort (NAKO). Front Epidemiol. 2023 May;3:1099235.

13 Klinger-König J, Erhardt A, Streit F, Völker MP, Schulze MB, Keil T, et al. Childhood trauma and somatic and mental illness in adulthood. Dtsch Arztebl Int. 2024 Jan;121(1):1–8.

14 Kessler RC, Bromet EJ. The epidemiology of depression across cultures. Annu Rev Public Health. 2013;34:119–38.

15 Zhou J, Feng L, Hu C, Pao C, Zou Z, Wang G. Gender-specific associations between types of childhood maltreatment and major depressive disorder: A matched case-control study. Asia Pac Psychiatry. 2023 Jun;15(2-3):e12538.

16 Weiss EL, Longhurst JG, Mazure CM. Childhood sexual abuse as a risk factor for depression in women: psychosocial and neurobiological correlates. Am J Psychiatry. 1999 Jun;156(6):816–28.

17 Streit F, Zillich L, Frank J, Kleineidam L, Wagner M, Baune BT, et al. Lifetime and current depression in the German National Cohort (NAKO). World J Biol Psychiatry. 2023 Dec;24(10):865–80.

18 Sunley AK, Lok A, White MJ, Snijder MB, van Zuiden M, Zantvoord JB, et al. Ethnic and sex differences in the association of child maltreatment and depressed mood. The HELIUS study. Child Abuse Negl. 2020 Jan;99(104239):104239.

19 Chen X, Zhang S, Huang G, Xu Y, Li Q, Shi J, et al. Associations between child maltreatment and depressive symptoms among Chinese college students: An analysis of sex differences. Front Psychiatry. 2021 Jul;12:656646.

20 Chen T-T, Chen C-Y, Liu C-Y, Lee J, Ganna A, Feng Y-CA, et al. Genetic architectures of childhood maltreatment and causal influence of childhood maltreatment on health outcomes in adulthood. Mol Psychiatry. 2025 Aug;30(8):3404–12.

21 Cohen JR, McNeil SL, Shorey RC, Temple JR. Maltreatment subtypes, depressed mood, and anhedonia: A longitudinal study with adolescents. Psychol Trauma. 2019 Oct;11(7):704–12.

22 Prachason T, Mutlu I, Fusar-Poli L, Menne-Lothmann C, Decoster J, van Winkel R, et al. Gender differences in the associations between childhood adversity and psychopathology in the general population. Soc Psychiatry Psychiatr Epidemiol. 2024 May;59(5):847–58.

23 Carr A, Duff H, Craddock F. A systematic review of reviews of the outcome of noninstitutional child maltreatment. Trauma Violence Abuse. 2020 Oct;21(4):828–43.

24 Arnow BA, Blasey CM, Hunkeler EM, Lee J, Hayward C. Does gender moderate the relationship between childhood maltreatment and adult depression? Child Maltreat. 2011 Aug;16(3):175–83.

25 Gershon A, Minor K, Hayward C. Gender, victimization, and psychiatric outcomes. Psychol Med. 2008 Oct;38(10):1377–91.

26 MacMillan HL, Fleming JE, Streiner DL, Lin E, Boyle MH, Jamieson E, et al. Childhood abuse and lifetime psychopathology in a community sample. Am J Psychiatry. 2001 Nov;158(11):1878–83.

27 Mo X, Gai RT, Tachibana Y, Bolt T, Takahashi Y, Nakayama T. The burden of disease and the cost of illness attributable to child maltreatment in Japan: long-term health consequences largely matter. BMC Public Health. 2020 Aug;20(1):1296.

28 Moody G, Cannings-John R, Hood K, Kemp A, Robling M. Establishing the international prevalence of self-reported child maltreatment: a systematic review by maltreatment type and gender. BMC Public Health. 2018 Dec;18(1). DOI: 10.1186/s12889-018-6044-y

29 Dreßing H, Hoell A, Scharmann L, Simon AM, Haag A-C, Dölling D, et al. Sexual violence against children and adolescents: A German nationwide representative survey on its prevalence, situational context, and consequences. Dtsch Arztebl Int. 2025 May;122(11):285–91.

30 Li M, D'Arcy C, Meng X. Maltreatment in childhood substantially increases the risk of adult depression and anxiety in prospective cohort studies: systematic review, meta-analysis, and proportional attributable fractions. Psychol Med. 2016 Mar;46(4):717–30.

31 Afifi TO, Enns MW, Cox BJ, Asmundson GJG, Stein MB, Sareen J. Population attributable fractions of psychiatric disorders and suicide ideation and attempts associated with adverse childhood experiences. Am J Public Health. 2008 May;98(5):946–52.

32 Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable fractions. Am J Public Health. 1998 Jan;88(1):15–9.

33 Dragioti E, Radua J, Solmi M, Arango C, Oliver D, Cortese S, et al. Global population attributable fraction of potentially modifiable risk factors for mental disorders: a meta-umbrella systematic review. Mol Psychiatry. 2022 Aug;27(8):3510–9.

34 Xiao W, Li S, Xu H, Zhang Y, Wei R, Tao F, et al. Population attributable fractions of adverse childhood experiences for emotional problems and self-harming behaviors among middle school students in China. Asian J Psychiatr. 2023 Jul;85(103621):103621.

35 Moore SE, Scott JG, Ferrari AJ, Mills R, Dunne MP, Erskine HE, et al. Burden attributable to child maltreatment in Australia. Child Abuse Negl. 2015 Oct;48:208–20.

36 Rach S, Sand M, Reineke A, Becher H, Greiser KH, Wolf K, et al. The baseline examinations of the German National Cohort (NAKO): recruitment protocol, response, and weighting. Eur J Epidemiol. 2025 Apr DOI: 10.1007/s10654-025-01219-8

37 Lecrubier V, Weiller E, Herugeta T, Amorim P, Borora LI, Lépine JP. Mini international neuropsychiatric interview German version 5.0. 0. München: Psychiatrischen; 1997.

38 Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med. 2001 Sep;16(9):606–13.

39 Löwe B, Spitzer RL, Gräfe K, Kroenke K, Quenter A, Zipfel S, et al. Comparative validity of three screening questionnaires for DSM-IV depressive disorders and physicians' diagnoses. J Affect Disord. 2004 Feb;78(2):131–40.

40 Grabe HJ, Schulz A, Schmidt CO, Appel K, Driessen M, Wingenfeld K, et al. Ein Screeninginstrument für Missbrauch und Vernachlässigung in der Kindheit: der Childhood Trauma Screener (CTS). Psychiatr Prax. 2012 Apr;39(3):109–15.

41 Klinger-König J, Streit F, Erhardt A, Kleineidam L, Schmiedek F, Schmidt B, et al. The assessment of childhood maltreatment and its associations with affective symptoms in adulthood: Results of the German National Cohort (NAKO). World J Biol Psychiatry. 2023 Dec;24(10):897–908.

42 Glaesmer H, Schulz A, Häuser W, Freyberger H, Brähler E, Grabe H-J. Der Childhood Trauma Screener (CTS) - Entwicklung und Validierung von Schwellenwerten zur Klassifikation. Psychiatr Prax. 2013 Apr;40(04):220–6.

43 Organization UUNESAC, UNESCO United Nations Educational, Scientific and Cultural Organization. International Standard Classification of Education, ISCED 1997. Advances in Cross-National Comparison. 2003;195–220.

44 Dragano N, Reuter M, Greiser KH, Becher H, Zeeb H, Mikolajczyk R, et al. Socio-demographic and employment-related factors in the German National Cohort (GNC; NAKO Gesundheitsstudie). Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2020 Mar;63(3):267–78.

45 Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. London, England: Routledge; 2013.

46 Cramer H. Mathematical methods of statistics (PMS-9), volume 9. Princeton, NJ: Princeton University Press; 1999.

47 Levin ML. The occurrence of lung cancer in man. Acta Unio Int Contra Cancrum. 1953;9(3):531–41.

48 Mukadam N, Sommerlad A, Huntley J, Livingston G. Population attributable fractions for risk factors for dementia in low-income and middle-income countries: an analysis using cross-sectional survey data. Lancet Glob Health. 2019 May;7(5):e596–603.

49 Lenth R, Singmann H, Love J, Buerkner P, Herve M. Emmeans: Estimated marginal means, aka least-squares means. R package version

50 Bruzzi P, Green SB, Byar DP, Brinton LA, Schairer C. Estimating the population attributable risk for multiple risk factors using case-control data. Am J Epidemiol. 1985 Nov;122(5):904–14.

51 Wehrens R, Putter H, Buydens LMC. The bootstrap: a tutorial. Chemometr Intell Lab Syst. 2000 Dec;54(1):35–52.

52 Armstrong RA. When to use the Bonferroni correction. Ophthalmic Physiol Opt. 2014 Sep;34(5):502–8.

53 Wickham H. Ggplot2: Elegant graphics for data analysis. New York, NY: Springer; 2009.

54 Shi B, Choirat C, Coull BA, VanderWeele TJ, Valeri L. CMAverse: A suite of functions for reproducible causal mediation analyses. Epidemiology. 2021 Sep;32(5):e20–2.

55 Reinhard I, Streit F, Frank J, Völker M, Kresken AL. Childhood maltreatment and depression in NAKO. 2024 Sep DOI: 10.17605/OSF.IO/EZJYV

56 Lin C-K, Chen S-T. Estimation and application of population attributable fraction in ecological studies. Environ Health. 2019 Jun;18(1):52.

57 Stoltenborgh M, van Ijzendoorn MH, Euser EM, Bakermans-Kranenburg MJ. A global perspective on child sexual abuse: meta-analysis of prevalence around the world. Child Maltreat. 2011 May;16(2):79–101.

58 Matud MP. Gender differences in stress and coping styles. Pers Individ Dif. 2004 Nov;37(7):1401–15.

59 Berger K, Rietschel M, Rujescu D. The value of “mega cohorts” for psychiatric research. World J Biol Psychiatry. 2022 Mar;1–5.

60 Baldwin JR, Coleman O, Francis ER, Danese A. Prospective and retrospective measures of child maltreatment and their association with psychopathology: A systematic review and meta-analysis. JAMA Psychiatry. 2024 Aug;81(8):769–81.

61 Glaesmer H. Assessing childhood maltreatment on the population level in Germany: findings and methodological challenges. Child Adolesc Psychiatry Ment Health. 2016 Jun;10(1):15.

62 Klinger-König J, Krause E, Wittfeld K, Friedrich N, Völzke H, Grabe HJ. The age of onset and duration of childhood abuse: An extension of the childhood trauma screener. Child Abuse Negl. 2025 May;163(107354):107354.

63 Batty GD, Gale CR, Kivimäki M, Deary IJ, Bell S. Comparison of risk factor associations in UK Biobank against representative, general population based studies with conventional response rates: prospective cohort study and individual participant meta-analysis. BMJ. 2020 Feb;368:m131.

64 Hapke U, Cohrdes C, Nübel J. Depressive symptoms in a European comparison - Results from the European Health Interview Survey (EHIS) 2. J Health Monit. 2019 Dec;4(4):57–65.

65 Witt A, Brown RC, Plener PL, Brähler E, Fegert JM. Child maltreatment in Germany: prevalence rates in the general population. Child Adolesc Psychiatry Ment Health. 2017 Sep;11(1):47.

66 Steffen A, Thom J, Jacobi F, Holstiege J, Bätzing J. Trends in prevalence of depression in Germany between 2009 and 2017 based on nationwide ambulatory claims data. J Affect Disord. 2020 Jun;271:239–47.

67 Kessler RC. Epidemiology of women and depression. J Affect Disord. 2003 Mar;74(1):5–13.

68 Ferrara P, Corsello G, Basile MC, Nigri L, Campanozzi A, Ehrich J, et al. The economic burden of child maltreatment in high income countries. J Pediatr. 2015 Dec;167(6):1457–9.

Figure Legends

Figure 1: *Flow Chart of Sample Selection Displaying Exclusion Criteria*

Note. The figure illustrates the number of excluded subjects and the resulting sample sizes due to missing values. NAKO = German National Cohort. MINI = Mini-International Neuropsychiatric Interview.

Figure 2: *Odds Ratios of Childhood Maltreatment and its Subtypes with Lifetime Depression and Current Depressive Symptoms, Stratified by Sex*

Note. Odds ratios are presented with 95% confidence intervals. ** $p_{adj} < 0.001$. * $p_{adj} < 0.05$ for the interaction effect.

Figure 3: *Population Attributable Fractions of Childhood Maltreatment and its Subtypes for Lifetime Depression and Current Depressive Symptoms Among Men and Women*

Note. PAF = Population Attributable Fractions. $N_{men} = 80{,}519$. $N_{women} = 78{,}526$. Sums of individual PAF estimates may differ slightly from overall PAF estimates due to rounding.