Title page

Title: A Systematic Review of Variables that CO2 Moderate and/or Mediate the Relationship between Child Maltreatment and Adverse Outcomes - A Study Protocol

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# ABSTRACT

**Introduction:** Child maltreatment is associated with adverse cognitive, behavioral, physical and social outcomes that often continue until adulthood. Systematic reviews on mediators and moderators of this relationship mostly investigate childhood adversities in general or only with regard to an adult population, single outcomes or single forms of maltreatment. The purpose of this review is to synthesize the evidence of variables that mediate and/or moderate the relationship between child maltreatment and diverse outcomes.

**Method:** A systematic search will be performed in Scopus, PsychInfo, Medline and Web of Science until January 2022. Eligibility criteria include children under 18 years who have been maltreated and experienced adverse outcomes until the age of 21, moderators and/or mediators that influence the relationship between maltreatment and adverse outcomes must belong to the individual level and be amenable to change. After independent screening of studies by two reviewers, data extraction and study quality of included studies will be done using adapted checklists of similar reviews, the STROBE report, the COSMIN checklist and Downs and Black Checklist. The results will be presented in narrative form and, if adequate, meta-analysis.

**Ethics and dissemination:** Ethics approval will not be required.The results of this systematic review will be submitted for publication in a peer-reviewed journal.

**Systematic review registration:** PROSPERO registration number:CRD42022297982

**Strengths and limitations of this study**

* This review aims to understand the complex interplay between more than one form of child maltreatment, various types of mediators and moderators and multiple adverse outcomes in order to identify targets for interventions.
* It will help to assess the quality of studies in this field and identify areas for improvement for future research such as study designs, statistical methods for analysis and number of outcomes, mediators and moderators.
* Only mediators and moderators on the individual level (e.g., emotion regulation, thinking styles, coping strategies etc.) that are amendable to change will be considered since these might be an accessible starting point for individual therapeutic interventions.
* Variables on other levels of Bronfenbrenner’s ecological systems theory such as mass media, neighborhood and school as well as those that are static such as ethnicity, gender, IQ will not be included.
* The varying definitions of maltreatment and types of instruments used to assess child maltreatment as well as the intended omission of limitations to specific outcomes, mediators and moderatos might make results difficult to compare.

# INTRODUCTION

The World Health Organization (WHO) defines child maltreatment (CM) as all forms of abuse (physical, sexual and emotional), neglect (physical or emotional) and child sexual exploitation that result in potential or actual harm to a child’s physical or psychological health, its development or survival (1). The global estimates of the prevalence of CM are 36.3 % for emotional abuse, 22.6 % for physical abuse, 18 % (in females) and 7.6 % (in males) for sexual abuse and 16.3 % for neglect (2, 3). However, due to an assumable big dark field and measurement issues, the estimates remain uncertain. Given the known prevalence estimates, it may be alarming that - according to recent studies and reviews - CM is significantly associated with the development of adverse emotional, cognitive, behavioral, physical and social outcomes such as psychopathology, cardiovascular disease, relationship problems, poor academic performance, deviant sexual behavior, substance abuse, delinquency and low self-esteem (4-14). These difficulties often continue until adulthood (11, 13, 15, 16). The associations between CM and its effects on future adverse outcomes are complex.

## Objectives

Although negative physical and psycho-social outcomes following CM have been established, little attention has been paid to systematically synthesizing data relating to potential mechanisms that influence this relationship at the individual level (17-22). With individual level, we refer to Bronfenbrenner's ecological systems theory (23), which distinguishes macro-level (e.g. laws, societal norms), meso-level (neighborhood, family influences) and micro-level or individual (e.g. biographical factors, genetics) variables determining health. Individual level influences acting as mediators and /or moderators of the association between CM and adverse health outcomes are e.g. psychological competencies of the exposed individuals such as emotion regulation, thinking styles and coping strategies, as opposed to family support, which according to Bronfenbrenner’s model would be attributed to the meso-level.

To our knowledge, only a few reviews on mediators and moderators of the association between CM and adverse outcomes have been published. These reviews are narrative or investigate childhood adversities in general or with regard to an adult population, specific outcomes or single forms of maltreatment (24-33). However, different forms of maltreatment and multiple adverse outcomes often co-occur (14, 34-41). To our knowledge, there is no systematic review investigating possible variables at the individual level as mediators and/or moderators of the relationship between CM and multiple adverse outcomes.

It is important to understand the complex interplay between different forms of CM exposure, various types of mediators and moderators and diverse outcomes in order to identify targets for interventions or the right target groups. The main objective of the present systematic review is to provide an overview of different factors that influence this relationship and might improve children’s resilience to adverse outcomes after maltreatment. This review will focus on individual variables that are amenable to change and can help health care providers improve the well-being of children, adolescents and young adults by strengthening relevant protective factors or early detection of low prognosis. Furthermore, this review will support the development of novel instruments for the diagnosis of resources and may hence help inform intervention strategies. The review questions will be the following:

1. Which variables mediate the relationship between CM and adverse outcomes until the age of 21 years and to what extent?
2. Which variables moderate the relationship between CM and adverse outcomes until the age of 21 years and to what extent?
3. What kind of study designs and data analysis methods are used for moderation and mediation analyses?

# METHODS AND DESIGN

The systematic review will be conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (42). The review protocol has been written according to the PRISMA-P (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols) guideline (43). The checklist can be found in appendix A. The protocol has been registered at the International Prospective Register of Systematic Reviews in January 2022 (PROSPERO, registration number: CRD42022297982).

## Search Strategy

The following databases were searched with no limit on the earliest publication until January 19th, 2022: Scopus, Web of Science, PsycInfo (via Ovid) and MEDLINE (via Ovid). Journal articles, in press articles and conference papers were searched in English, German, French and Spanish. The search will be updated prior to analyses. We selected keywords based on the population (e.g., children, adolescents), exposure (e.g., maltreatment, abuse, neglect) and moderation/mediation (e.g., mediate, moderate, mechanism). Reviews and meta-analyses on similar topics regarding CM and mediators/moderators were used to develop the search terms (24, 25, 44). The initial search strategy was tested on Scopus and adapted for use in other databases after it had been finalized. The search strategy for each database can be found in appendix B. Reference lists of included papers and reviews on related topics will also be searched to identify any additional relevant papers.

## Eligibility criteria

### Population

Children and adolescents who have been maltreated before the age of 18 and have experienced adverse outcomes until the age of 21. The study population can be a general or clinical population.

### Exposure

One or multiple of the following: Physical, emotional or sexual abuse or physical or emotional neglect before the age of 18. Other adverse childhood experiences such as dating violence/intimate partner violence experienced by the child in intimate relationships, violence during adulthood, loss of a parent, poverty, poor parent-child relationship, parental potential to maltreat children, neighborhood/community violence, violence or bullying by peers, parents’ attachment disorders, parenting stress and difficulties with the upbringing other than maltreatment as well as studies on determining risk factors for child maltreatment will be excluded. Types of maltreatment will be defined according to the WHO and International Society for Prevention of Child Abuse and Neglect (45). Physical abuse is defined as the use of intentional force against a child resulting in harm to the child’s health, development or survival such as hitting, shaking, strangling, biting and burning. Sexual abuse involves a child in sexual activity that she or he does not fully comprehend, is unable to give informed consent to, for which she or he is developmentally not prepared or that violates laws or social taboos of society. Emotional abuse involves isolated incidents or failure over time to provide a supportive and developmentally appropriate environment such as threatening, discriminating, ridiculing, restriction of movement and rejection or hostile treatment. Neglect is defined as the failure to provide for the development and well-being of the child in one or more of the following areas: health, education, emotional development, nutrition, shelter and safe living conditions. The measurement of maltreatment may be through self-report, report through a caregiver, questionnaires, interviews or medical, police and social work records. The abuse must have been committed by an adult.

### Outcome

There will be no restrictions on possible outcomes due to the wide range of adverse outcomes after maltreatment. The different outcomes often co-occur and it is important to describe the complex interplay between more than one form of child maltreatment and multiple adverse outcomes (40, 41). Psychopathological outcomes following CM include disorders specified in the Diagnostic and Statistical Manual of Mental Disorders V (DSM-V) or the International Statistical Classification of Diseases and Related Health Problems (ICD-11) (or previous versions) such as depression, anxiety and chronic diseases. Outcomes such as problems with relationships, deviant sexual behavior, memory function, problems in school and internalizing and externalizing behavior are also included among others. The outcome has to be measured during childhood or early adulthood until the age of 21 years. It has to be recorded after maltreatment has taken place. We are not aware of any framework that categorizes the diversity of possible outcomes. Since existing literature (39) makes biopsychosocial categorizations, we pursued this idea further. Due to the overlapping multitude of outcomes, we plan to form the categories: psychological, biological-psychological, psychological-social, biological, biological-social, social, and biopsychosocial. This will enable us to assign outcomes more precisely. For example, self-harming behavior would be assigned to the category biological-psychological since both psychological aspects (pathological behavior) and biological aspects (physical injury) are fulfilled.

### Moderators and Mediators

Variables that moderate or mediate the relationship between CM and adverse outcomes can be protective factors or risk factors. A low level of the risk factor (such as low rumination or low perceived strain) will be seen as a protective factor as well. Moderators and mediators have to amenable to change (for example through therapy), belong to the individual level and be either affective, cognitive, social and/or behavioral. We will only consider mediators and moderators on the individual level that are amenable to change (e.g. reflective function, internalizing problems, substance use) since these are a good starting point for individual therapeutic interventions. Protective and risk factors that are static such as high intelligence, gender at birth or genetic predispositions and are not accessible to change will be excluded. Mediators have to be measured before the outcome to establish a clear timeline. Those measured after the outcome will be excluded since possible causality might be reversed.

### Study design

There are no restrictions on the design for the first step of the screening process of included studies although the search strategy includes different terms on the design in order to obtain a manageable number of results. To ensure that studies which do not include the study design in their title or abstract are also included, a second search will be conducted for titles only without the terms for the study design. Studies might therefore include randomized-controlled trials, case-control studies, cross-sectional or cohort studies that had assessed the association between CM and adverse outcomes and the effect of one or more mediating and moderating variables on this relationship. Depending on the number of included studies, we plan on conducting reviews on different study designs. We suspect that our search results will encompass two major study types that might have to be analyzed separately: longitudinal studies and cross-sectional studies. While our primary aim remains the exploration of potential variables acting as mediators and/or moderators at the individual level, depending on the number of studies per study type, their quality and their comparability, we might summarize the evidence in a quantitative way for some study types, and for others, just narratively present the scope of evidence.

### Including criteria

Studies will be included if they are original empirical studies published or in press or conference proceedings, the exposure is CM prior to the age of 18 years and at least one other factor was investigated as a mediating or moderating effect.

### Language of publication

Studies conducted in any country and reported in English, German, French or Spanish are included based on the language capabilities of the review team. To ensure a uniform procedure, information in German, French and Spanish language studies were extracted in the original language and then translated using an artificial intelligence translation tool (DeepL).

### Exclusion Criteria

Studies on individuals older than 21 years, single case studies, case series, studies on the prevention of CM or on risk factors for maltreatment are excluded. Book chapters, letters, commentaries, reviews, meta-analyses, editorials, discussion papers, dissertations, animal studies and qualitative studies will be excluded. Studies that focus on maltreatment by individuals younger than 18 years old, intimate partner violence in adolescent’s relationships, violence or bullying by peers, determining risk factors for CM, parental potential to maltreat children, community violence, loss of a parent, parents’ attachment disorders and difficulties with the upbringing other than maltreatment will not be included. Studies that do not differentiate between maltreatment experienced in childhood and adulthood will be excluded. Static factors as mediators or moderatos such as gender, genetic factors and intelligence will be excluded.

## Data management

Studies will be exported from the respective databases to Endnote X9 in order to import them to Covidence (46). Covidence is used to remove duplicates, screen titles and abstracts, execute quality assessment and data extraction and to calculate inter-rater agreement between reviewers for the screening process.

## Data collection and analysis

### Selection process

Two reviewers will independently screen titles and abstracts based on the inclusion and exclusion criteria. Studies will be rated as maybe when title or abstract do not provide enough information to determine inclusion or exclusion. The full text will then be screened. Articles which clearly do not meet the inclusion criteria based on title and abstract or the full text will be excluded. Inconsistencies between the two reviewers will be resolved through discussion or in consultation with a third independent reviewer (BG or LK). After piloting the selection criteria, the inter-rater agreement will be calculated for the first 15 % of the articles. If the agreement is high enough (i.e. Cohen’s Kappa > 0.6), the remaining articles will be screened by either DC or JS. If the agreement is not high enough, the reviewers will go through their conflicts and discuss the selection criteria before continuing to screen. More articles will be screened by both reviewers until the inter-rater-agreement is satisfactory. Reference lists of included papers and reviews on similar topics will be searched by DC, BG and LR to identify any additional relevant papers. In a second stage, reviewers (DC and JS) will independently screen full texts to determine if studies can be included or excluded for quality assessment and data extraction based on the defined criteria. The inter-rater-agreement will be calculated again. The reasons for excluded studies will be documented.

### Data Extraction

A template based on the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology: Explanation and Elaboration) report (47), the COSMIN Risk of Bias Checklist (COnsensus‐based Standards for the selection of health Measurement INstruments) (48) and similar reviews (24-29, 49) will be modified for the purpose of this review and used to extract relevant data from included studies. The template will be piloted using 10 eligible articles. Based on the pilot adjustments to the template will be made when deemed necessary. The pilot will be done independently by three reviewers (DC, JS and LR). After pilot testing and relevant adjustments, reviewers will independently extract data of eligible articles and the other will check the accuracy of the extracted data. Discrepancies will be discussed. If no consensus can be reached another reviewer will decide. The preliminary data extraction template covers the following topics: title, authors, publication year/year of study, country, aim of study, study design, follow-up period if applicable, sample source, method of recruitment, sample size, patient characteristics such as age, gender, socioeconomic status and ethnicity, study setting, type of maltreatment, age of exposure to and duration of maltreatment, measurement of maltreatment, type of mediator/moderator, measurement of moderators/mediators, type of outcome, measurements of adverse outcomes, confounders, measurement of confounders, method of data analysis, statistical outcomes. If any new categories are identified during the review, they will be added, and the extraction database will be modified as needed. Studies with insufficient data will be excluded if contacting the corresponding authors by email will not contribute to clarification.

### Quality Assessment

The data extraction form for quality assessment is based on relevant items from the STROBE report (47), the COSMIN checklist (48) and Downs and Black (50) Checklist for measuring study quality. The items will be adapted for this review and will include the following: clear aim/hypothesis; clear description of outcomes, maltreatment, mediators/moderators, results, control variables, population, and procedure; recruitment bias; statistical methods used; missing data; study design; follow-up period; comparability of different groups; blinding and randomization if applicable. Items which assess the validity of measures were added for the outcome measure, the measure of CM and the mediators and moderators. Incongruent ratings will be solved through discussion and, if necessary, a third author. We plan to email corresponding authors in case of missing information. Quality criteria will be applied to the moderation/mediation analysis methods (sample size, quality of moderation/mediation analysis). A narrative summary of the quality for each study will be provided. The quality assessment will be done by DC and LR.

### Data analysis and synthesis

A narrative summary of study characteristics will be performed. All included studies will be presented in tables providing information on authors, country, sample size, gender, age, form of maltreatment, measurement of maltreatment, moderator/mediator, measurement of moderator/mediator, adverse outcome(s), measurement of adverse outcome(s). By our systematic search, we allow for different study designs, however we expect to differentiate primarily between cross-sectional and longitudinal studies, with the latter having a higher quality for results on mediating or moderating effects by design. Thus, all analyses will very likely be subdivided by study design category. Other tables will present information on the quality of the included studies, such as clear aim, measurement of variables, and report of results. More tables will provide information on the moderators and mediators, data analysis, if moderation/mediation was supported and the quality rating. We will present a narrative synthesis of moderators and mediators separately for different adverse outcomes.

A meta-analysis will be performed if there are enough similar studies with comparable information on CM as well as outcomes and mediators/moderators, and depending on the heterogeneity among the comparable studies and their quality. Studies are expected to represent differences in method (i.e. types of maltreatment, study design, statistical methods used) and it remains open whether they reflect a single underlying effect size. Therefore, besides narrative synthesis and meta-analysis, we might use scoping or evidence-gap map methodology, to assess and count the outcomes used within the studies found. This might enable us to present the overall scope of all the evidence existing on the association of CM with health outcomes and its mediators/moderators.

For meta-analysis, Cohen's d will be used to describe longitudinal associations between the child maltreatment exposure, the outcome and the respective moderator/mediator variable. If corresponding measures of estimation uncertainty (standard error, 95% confidence interval) are not given, we will try to contact authors and request the necessary information. For those studies whose authors will not provide us with response or cannot not provide the requested information, we will use standard conversion formulas as implemented in Stata (51), or the Cochrane effect size calculator (52) if a respective Stata command is not available.

If the findings allow for meta-analysis, we will use random-effects inverse variance models with the Sidik-Jonkman robust variance estimator based on a restricted maximum likelihood (REML) estimate of between-study heterogeneity (2) (53Klicken oder tippen Sie hier, um Text einzugeben.). Following the Cochrane recommendations for meta-analysis, groups of studies should comprise at least two studies or five outcome estimators (54).

Results will be analyzed using a forest plot. We plan to analyze data separately for different outcomes and mediators/moderators. Heterogeneity will be calculated using I2 (53). We will take into account the content complexity of study characteristics (e.g. the diversity of maltreatment studied or of the outcome measures used). Publication bias will be assessed using funnel-plots (55) and Egger’s regression test for funnel plot asymmetry (56Klicken oder tippen Sie hier, um Text einzugeben.).

## ETHICS AND DISSEMINATION

Ethical and safety considerations

Because of ethical considerations regarding the possibility of retraumatization, we did not involve children and adolescents exposed to maltreatment directly into our research project and the necessary decision-making. Instead, we involved professional stakeholders with ample experience in child protection in a participatory approach. Please refer for more details to the patient and public involvement section.

Dissemination plan

The results of the project will be published in international peer-reviewed article(s). Extracted data and analysis syntax will be available from the corresponding author upon request.

## Patient and public involvement

Our research team involved a diverse group of professionals experienced in child abuse and neglect and advised with them to develop the research questions and review procedures. This included members of the local child protection group, forensic physicians, medical doctors and management of the children's hospital, and the head of the local interdisciplinary care and legal clarification institution for cases of child abuse (Child advocacy center / Childhood House Düsseldorf). Children and adolescents exposed to maltreatment were not involved directly because of the possibility of retraumatization.

# DISCUSSION

Prior studies, reviews and meta-analyses have highlighted the negative impact of CM on several adverse outcomes such as psychopathology, cardiovascular disease, relationship problems, deviant sexual behavior, substance abuse, delinquency and low self-esteem (4-6, 9-11, 13). However, to our knowledge only few studies have investigated the impact of moderating and/or mediating variables on the relationship between CM and multiple adverse outcomes. A better understanding of these relationships and mechanisms has important implications for children’s resilience after maltreatment. The results could help identifying the long-term consequences of CM in combination with risk and protective factors. This can help inform prevention and intervention strategies to target resources and help health care providers to mitigate the consequences of CM and improve well-being among children, adolescents and young adults by strengthening relevant protective factors. Furthermore, this review can aid in the development of novel instruments for the diagnosis of resources that foster resilience. The review might be a good basis to identify gaps in current evidence and to make recommendations for future research in this area aiming to understand mechanisms of the relationship between maltreatment and adverse outcomes. It will help to assess the quality of studies in this field and identify areas for improvement such as study designs and statistical methods for analysis.

## Limitations

It must be acknowledged that this review has some limitations. Only mediators and moderators at the individual level that are amenable to change will be considered since these might be an accessible starting point for individual therapeutic interventions. Variables on other levels of Bronfenbrenner’s ecological systems theory such as mass media, neighborhood and school as well as those that are static such as ethnicity, gender, IQ will not be included. Inferences of causation will not be possible for the cross-sectional studies in the review. The varying definitions of maltreatment and types of instruments used to assess CM might make results difficult to compare and influence the results of the search strategy. In addition, this review is not limited to specific outcomes, mediators and moderatos, which further influences the sensitivity of the search strategy and comparison of results. We therefore might only be able to conduct meta-analysis for a limited amount of certain specific and comparable outcomes. This review aims to give a diverse and broad overview on the topic of how different variables influence adverse outcomes after CM.

# DECLARATIONS

## Author’s Contributions

JS, BG and EM conceived the idea; JS planned and designed the study protocol, FDB revised it and gave advice on methods and extraction plans;JS will perform the screening; EM, BG and LK will search eligible papers for additional articles; LR will conduct the quality assessment; JS and LR will conduct the data extraction; Sobir performed the initial writing up; all authors contributed to the manuscript and agreed on methods for the study selection, extraction, synthesis and the final written manuscript of the protocol; all authors have read and approved the final manuscript, FDB will be the guarantor of the review.

**Conflict of interest** Not applicable.

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## Abbreviations

CM: child maltreatment; COSMIN: COnsensus‐based Standards for the selection of health Measurement Instruments; DSM: The Diagnostic and Statistical Manual of Mental Disorders; ICD: International Classification of Diseases; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PRISMA-P: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols; STROBE: Strengthening the Reporting of Observational Studies in Epidemiology; WHO: World Health Organization.

## Acknowledgements

Not applicable.

## Ethics approval and consent to participate

Ethics approval and patient consent for publication as well as consent to participate are not required for this study.

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