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## Childhood Maltreatment and Health Impact: The Examples of Cardiovascular Disease and Type 2 Diabetes Mellitus in Adults

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### Abstract

Child maltreatment is associated with increased risk for an array of mental and physical health problems. We reviewed studies examining associations of child maltreatment, assessed either alone or in combination with other adversities, with cardiovascular disease (CVD) and Type 2 Diabetes. PubMed was searched for relevant studies until December, 2015. Forty publications met inclusion criteria. Consistent positive associations were noted across a range of childhood adversities. Child maltreatment was associated with CVD (myocardial infarction, stroke, ischemic heart disease, coronary heart disease) in 91.7% of studies, with diabetes in 88.2% of studies, and with blood pressure/hypertension in 61.5% of studies. Inclusion of mental disorders tended to attenuate associations. Sex-related differences were under-examined. Implications for future research and intervention efforts are discussed.

### Keywords

child maltreatment; early life adversity; cardiometabolic; cardiovascular; type 2 diabetes

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Childhood Maltreatment and Health Impact: The Examples of Cardiovascular Disease and Type 2 Diabetes Mellitus in Adults Exposure to adverse environments during childhood exerts a lasting influence on health and later development. In particular, child maltreatment – physical, sexual, or emotional abuse, neglect, and witnessing domestic violence – can disrupt normative developmental processes and magnify risk for health problems later in life (Shonkoff, Boyce, & McEwen, 2009). In the U.S., state and local child protective services received an estimated 3.4 million referrals of children for abuse or neglect (CDC, 2014), and population-based studies suggest even higher rates of child maltreatment and domestic violence exposure (Green et al., 2010; McLaughlin et al., 2012). Individuals experiencing

child maltreatment are at an increased risk for a range of mental disorders and physical health problems across the lifespan (Felitti et al., 1998; Green et al., 2010; McLaughlin, Conron, Koenen, & Gilman, 2010). Studies have documented associations between child maltreatment and a range of health problems including: cardiovascular disease, type 2 diabetes, respiratory diseases, gastrointestinal and musculoskeletal outcomes, chronic pain and headaches, gynecological issues and even premature mortality (Felitti & Anda, 2009; Hillis, Mercy, & Saul, 2016; Wegman & Stetler, 2009). Given this, recent policy statements from the American Academy of Pediatrics have emphasized the importance of the early environment in shaping trajectories of health and well-being (Garner et al., 2012).

Cardiometabolic diseases constitute the leading causes of morbidity and mortality for men and women in the U.S. (Danaei et al., 2009; Havranek et al., 2015), and present an escalating economic burden (Fox et al., 2016; Lloyd-Jones et al., 2010). Thus, we present a systematic review of child maltreatment and two cardiometabolic diseases, cardiovascular disease (CVD) and type 2 diabetes (hereafter referred to as diabetes), as a model for understanding associations between child maltreatment and later health problems. Traditionally, intervention efforts to prevent CVD and diabetes have focused on modifying health behaviors in adults. However, recent policy statements from the American Heart Association (AHA) note that childhood is an important period for identifying and preventing risk over the life course (Kavey et al., 2003; Lloyd-Jones et al., 2010).

Exposure to child maltreatment might contribute to risk for cardiometabolic diseases by disrupting the development of regulatory systems in the body, including the immune, metabolic, neuroendocrine, and autonomic nervous systems. Leading conceptual models of the neurobiological consequences of stress and maltreatment posit that chronic exposure to these types of adverse environments requires ongoing adaptation by regulatory systems; over time, this contributes to biological “wear and tear” that is referred to as allostatic load (McEwen, 2005, 2012; McEwen & Gianaros, 2010). The response of regulatory systems to stressors produces adaptations that are advantageous in the short-term, but detrimental in the long run (Hunter & McEwen, 2013; McEwen, 2010; Yehuda & Seckl, 2011). For example, release of glucocorticoids in response to an acute stressor produces rapid improvements in immunity but maladaptive long-term changes in brain regions with high concentrations of glucocorticoid receptors, including the hippocampus, amygdala, and prefrontal cortex (McEwen, 2012). These changes are believed to underlie a stable pro-inflammatory state that can damage arterial circulation (Havranek et al., 2015), alter glucocorticoid metabolism (Yehuda & Seckl, 2011) and insulin resistance (McEwen, 2005), and ultimately progress to cardiometabolic disease states.

To date, no systematic review exists of the literature on child maltreatment with both CVD and diabetes. We review studies examining child maltreatment and CVD and diabetes with three aims. First, we examine evidence for associations of child maltreatment with CVD and diabetes, given the common etiological pathways implicated in the development of cardiometabolic diseases, and that diabetes is a risk factor for CVD (Kelly & Ismail, 2015). Second, accumulating evidence from adult cardiometabolic studies suggests that there are sex-related differences in the pathophysiology of cardiometabolic diseases (Dasinger & Alexander, 2016; Mehta et al., 2016). Thus, we examine sex-related differences for CVD

and diabetes in relation to child maltreatment. Finally, we examine evidence for the role of mental disorders such as depression and PTSD, common sequelae of child maltreatment that have been associated with both CVD and diabetes (Roberts et al., 2015; Suglia, Demmer, Wahi, Keyes, & Koenen, 2016; Sumner et al., 2015), in mediating the effects of child maltreatment and later health outcomes. Prior reviews have focused on violence exposure, combining interpersonal and non-personal forms of violence, stress, or specific mental disorders (e.g., PTSD) as risk factors for disease risk. We focus on associations with child maltreatment specifically, given the high prevalence of maltreatment, the central role of the family system in shaping developmental outcomes that contribute to health, and the potential for addressing modifiable risk factors through prevention and clinical intervention.

## Methods

### Inclusion criteria

In order to be included in the present review, studies had to empirically examine the association between CVD and/or diabetes in adulthood with at least one of the following child maltreatment exposures: physical, sexual, or emotional abuse or witnessing domestic violence, occurring during childhood or adolescence (< 18 years of age). Studies that included one of the aforementioned child maltreatment exposures, as part of a larger composite index of adversities that included additional indicators of neglect, family instability or dysfunction (e.g., having a parent with a history of criminality, substance use or other psychopathology, parents' divorce/separation, parental illness or loss), were also included. We report results separately for studies examining the required child maltreatment measures only and those examining child maltreatment as part of a larger adversity composite.

Additionally, we considered studies reporting the following CVD outcomes: coronary heart disease, myocardial infarction, stroke, ischemic heart disease, hypertension, and blood pressure. Studies examining either diabetes or glycated hemoglobin (HbA1C, a measure of plasma glucose concentration, with above normal levels indicating poor glycemic control) were also included. Further, analyses of associations between child maltreatment and either CVD or diabetes had to be the primary aim of the study. Finally, studies had to adjust for at least one of the following sociodemographic factors: age, sex, and/or socioeconomic status (SES).

### Exclusion Criteria

Studies assessing traumatic events that are not interpersonal by nature (e.g., natural or manmade disasters, terrorist attacks; or combat/war) or focused on exposure to media violence or community violence were excluded. Studies assessing metabolic biomarkers as outcomes (e.g., inflammatory markers, body mass index) but not disease endpoints were also excluded.

### Search Strategy and Data Extraction

Using the aforementioned definitions, a literature search was conducted in PubMed including the following parameters: 1) Medical Subject Heading and title word terms

specific to abuse, adversity, and trauma or a combination of terms for violence, assault, abuse, maltreatment, molestation, incest, and stressful, traumatic, adverse, or negative experiences, with age-related words for childhood and adolescence, 2) Medical Subject Heading and title word terms for cardiovascular disease, stroke, hypertension, ischemic heart disease, myocardial infarction, blood pressure, cardiovascular, and diabetes. The search was limited to empirical studies of humans and published in English. The search, from the database's start date through December 31, 2015, yielded 944 articles. Article titles and abstracts were screened to discard duplicates and those that met exclusion criteria. The remaining 110 articles were read in entirety to ensure that inclusion and exclusion criteria were met, and a total of 35 studies were retained. Systematic reviews, meta-analyses, and reference lists of select relevant articles were screened to identify 5 additional references that were not included through the original search, resulting in a total of 40 articles in the final Figure 1,online supplement). Two coders examined the studies. A primary coder extracted data for all studies. The second coder independently coded 20% of the studies. Coders differed on one study with respect to evidence grade; a consensus was reached after reviewing the extracted data. Information on sample characteristics, type and measurement of child maltreatment/adversity and health outcome, and results adjusted for sociodemographic factors were extracted from each study.

### Evidence Grade Criteria

Using criteria similar to prior reviews (Slopen, Goodman, Koenen, & Kubzansky, 2013; Suglia, Sapra, & Koenen, 2015), each study was given an evidence grade, ranging from one to four with a higher score indicating a higher quality study. One point each was assigned for the following four criteria: sample size >500 subjects, prospective designs including repeated measures on the same individual with a time lag between the exposure and outcome, use of validated exposure measures (e.g., Childhood Trauma Questionnaire, Conflicts Tactics Scale), and a validated outcome measure (e.g., medical chart review) or an objectively measured outcome (e.g., BP taken by study staff).

### Results

Of the 40 publications included in this review, 14 studies examined the association of child maltreatment with CVD and diabetes in the same study (Table 2, for Tables 2-4, see online supplementary materials)). Twenty-three studies examined CVD only (Supplementary Table 3), and three studies assessed diabetes only (Supplementary Table 4). Summary of methodological details for all studies are presented first, followed by disease-specific associations based on type and/or severity of child maltreatment. Sex-stratified findings, and associations with mental disorders, are summarized when available.

The majority of the studies were conducted in high-income countries (as defined by current World Bank gross national income criteria for 2013); US ( $n = 32$ ), non-US high-income countries ( $n = 4$ ), and one study drew samples from US and Canada. Two multi-country studies were part of the World Mental Health assessments (Scott et al., 2011; Stein et al., 2010) and one study was conducted in Brazil (Parrish et al., 2013). A majority of studies included both females and males ( $n = 34$ ), while one twin study included only male

participants (Rooks et al., 2015). Most studies used a cross-sectional design ( $n = 25$ ). Retrospective report of maltreatment was common, with only three studies utilizing combined retrospective and prospective assessments of maltreatment (Duncan et al., 2015; Thomas, Hypponen, & Power, 2008; Widom, Czaja, Bentley, & Johnson, 2012). In terms of maltreatment assessments, more than half the studies ( $n = 26$ ) utilized at least one of the following three standardized assessments: Childhood Trauma Questionnaire, Conflict Tactics Scale, or the ACES module. Thirteen studies utilized another standardized measure or multi-method assessment (e.g., county records) to ascertain maltreatment history. Eleven studies used other non-validated questionnaires or item-level data to designate maltreatment. Six studies (15%) received the highest possible evidence grade, and nine studies (22.5%) received a 3-point evidence grade. Seven studies focused on physical and/or sexual abuse. Thirty-three studies assessed multiple types of maltreatment, including 13 studies that also included other adversities such as family instability or dysfunction. Summary statistics for each health outcome are presented in Table 1 stratified by whether studies assessed maltreatment exposure (abuse, neglect, and witnessing violence) or if they reported only on a composite including maltreatment with other adversities.

With respect to health outcomes, participant self-report based on a health professional's diagnosis, hospital admission, symptoms, or medication use was the most common mode of assessment ( $n = 23$ ). The remaining 17 studies used assessments typically conducted by research staff (e.g., blood draw, or BP taken during research evaluation) or confirmation via another method (e.g., medical records, doctor report).

Evaluation of whether CVD/diabetes associations with child maltreatment varied based on age of exposure was not possible because most studies defined child maltreatment as occurring before age 18 years, although some studies used other thresholds (Suglia, Clark, Boynton-Jarrett, Kressin, & Koenen, 2014; Widom et al., 2012).

### Cardiovascular Disease

CVD, myocardial infarction (MI), stroke, coronary heart disease (CHD), blood pressure (BP), and hypertension were the most commonly examined outcomes. Many studies grouped various indicators of CVD together in their analyses. Due to the large number of CVD studies, results are grouped into: 1) studies examining a CVD end point (i.e., MI, stroke, ischemic heart disease, CHD) and 2) studies assessing BP or hypertension only (See Table 1).

**CVD end points**—Across 24 studies incorporating various types of CVD endpoints, 22 (91.7%) observed a significant association between child maltreatment and CVD risk. The two studies reporting null associations were based on data from the Midlife Development in the United States project, which reported no associations between childhood adversities and self-reported stroke, heart disease or hypertension (Schafer & Ferraro, 2012), and a community-based study in New Zealand, which examined self-reported heart problems and high BP (Romans, Belaise, Martin, Morris, & Raffi, 2002).

Of the studies showing increased risk for CVD end points, 40% of studies assessing maltreatment only and 58.33% studies assessing maltreatment in an adversity composite

reported evidence of variations in findings as a function of the type or severity of maltreatment. Studies varied considerably in their associations across type of abuse, neglect, and family dysfunction (Fuller-Thomson, Brennenstuhl, & Frank, 2010; Rich-Edwards et al., 2012; Scott et al., 2011; Wilson et al., 2012). For instance, Wilson and colleagues (2012) reported that emotional neglect and any child maltreatment were associated with increased odds of chronic cerebral infarction but not with other types of adversity including parental violence. Multiple studies reported a linear dose-response relationship between increasing number of adversities and CVD end points (Dong et al., 2004; Felitti et al., 1998; Gilbert et al., 2015; Roy, Janal, & Roy, 2010; Scott et al., 2011).

**Variation by Sex**—With respect to sex-related findings reported by five studies, one study found no sex-related differences in CVD end points (Afifi, Mota, MacMillan, & Sareen, 2013), and two studies reported increased odds of a CVD end point for women only (Hosang et al., 2013), including a U.S population-representative study, which reported a 9-fold increase for risk of CVD for women with a history of child maltreatment (Batten, Aslan, Maciejewski, & Mazure, 2004). A separate U.S population-representative study found an association of childhood physical abuse with stroke for men, but an association of childhood neglect and sexual abuse with CVD for women (Goodwin & Stein, 2004). Increased risk of MI for men, but not women, who were sexually abused was reported in one study (Fuller-Thomson, Bejan, Hunter, Grundland, & Brennenstuhl, 2012).

**The Role of Mental Health**—More than half the studies assessing a CVD end point ( $n=13$ ) included an assessment of mental health disorders. Nine studies assessed for depression, and some assessed anxiety disorders ( $n=5$ ) and PTSD ( $n=4$ ). Some studies included multiple mental disorders in their assessments (Afifi et al., 2013; Goodwin & Stein, 2004; Rooks et al., 2015; Scott et al., 2011). The lack of uniformity in how mental disorders were incorporated into statistical models, especially in combination with other types of covariates (sociodemographic or health behaviors), makes systematic analysis of the role of mental disorders in the association of child maltreatment with CVD challenging. However, nearly all studies reported attenuation of the associations of child maltreatment with a CVD end point after accounting for co-occurring mental disorders. Whether or not maltreatment remained a significant predictor varied based on type of maltreatment (e.g., physical abuse or sexual abuse) and the specific CVD end point (Afifi et al., 2013; Dong et al., 2004; Fuller-Thomson et al., 2012; Fuller-Thomson et al., 2010; Goodwin & Stein, 2004; Monnat & Chandler, 2015; Morton, Mustillo, & Ferraro, 2014; Parrish et al., 2013; Rich-Edwards et al., 2012; Rooks et al., 2015).

**Blood pressure and hypertension**—Among the 13 studies assessing BP and/or hypertension only, a positive association between child maltreatment and hypertension (Riley, Wright, Jun, Hibert, & Rich-Edwards, 2010; Suglia et al., 2014) or higher BP (Crowell et al., 2015; Lehman, Taylor, Kiefe, & Seeman, 2009; McIntyre et al., 2012; Norman, Hawkley, Ball, Berntson, & Cacioppo, 2013; Stein et al., 2010) was noted in eight studies (61.5%). One study reported an association between child maltreatment and BP among individuals with four or more adversities and who were older than 30 years (Su et al., 2015). Of the remaining studies, one study reported low systolic BP associated with

emotional neglect, but not other types of maltreatment (van Reedt Dortland, Giltay, van Veen, Zitman, & Penninx, 2012). Four studies found no association between child maltreatment and BP (Gooding et al., 2014; Nomura & Chemtob, 2007; Rapoza et al., 2014), including a prospective study in which BP was assessed by nurses, and child maltreatment was ascertained via court records (Widom et al., 2012); although high levels of adversity in the control group of this study likely contributed to this pattern. The association between BP or hypertension varied based on the type or severity of maltreatment (Parrish et al., 2013; Suglia et al., 2014), and a dose-response association was observed in studies measuring multiple adversities (Riley et al., 2010; Stein et al., 2010).

**Variation by Sex**—Only one study focusing on hypertension reported sex-related differences. In a prospective nationally representative school-based sample, Suglia and colleagues (, 2014) found that a history of childhood sexual abuse was associated with increased risk for hypertension for women only.

**The Role of Mental Health**—Six studies assessing BP/hypertension, included assessments of mental health conditions. As with CVD end points, studies commonly assessed for depression ( $n=6$ ), anxiety disorders ( $n=2$ ) and PTSD ( $n=2$ ). Among studies reporting significant associations between child maltreatment and BP/hypertension, three studies reported attenuated effects after adjusting for mental disorders in their models, although maltreatment continued to remain a significant predictor in all cases (Gooding et al., 2014; Parrish et al., 2013; Stein et al., 2010), and one study reported that the effects of maltreatment were no longer significant, though other health behaviors were also included in the model (Suglia et al., 2014).

## Type 2 Diabetes Mellitus

Of the 17 studies examining diabetes as an outcome, 15 (88.2%) reported significant associations between child maltreatment and diabetes (Romans et al., 2002; Springer, Sheridan, Kuo, & Carnes, 2007; see Table 1))Several studies found an increased risk for diabetes in relation to more severe types of abuse such as physical or sexual abuse, relative to other adversities, or in relation to increasing number of adversities (Afifi et al., 2013; Bellis et al., 2015; Campbell, Walker, & Egede, 2015; Duncan et al., 2015; Felitti et al., 1998; Freedman et al., 2015; Gilbert et al., 2015; McIntyre et al., 2012; Morton et al., 2014; Rich-Edwards et al., 2010; Schafer & Ferraro, 2012). Two studies noted associations specific to neglect. Widom and colleagues (2012) found that neglect (with or without abuse), but not physical and/or sexual abuse without neglect, were associated with elevated HbA1C levels. Goodwin and colleagues (2004) also reported a significant association between neglect and diabetes in women. Finally, Thomas and colleagues (2008) observed prospective associations between aspects of emotional neglect by the mother, but not other child maltreatment variables, in relation to diabetes, although these associations disappeared after adjustment for childhood SES. Using retrospective report in adulthood, components of household dysfunction were associated with greater odds of diabetes, while other forms of maltreatment were not.

**Variation by Sex**—With respect to sex differences, two studies found associations between child maltreatment and diabetes or HbA1C levels for women, but not men (Goodwin & Stein, 2004; Widom et al., 2012). One study found significant associations with diabetes only for men who experienced three or more lifetime incidents of sexual abuse (Duncan et al., 2015).

**The Role of Mental Health**—About one-third of the studies ( $n=6$ ), included assessments of mental health conditions, including depression ( $n=3$ ), anxiety disorders ( $n=3$ ) and PTSD ( $n=4$ ). In three studies, mental disorders attenuated the association with diabetes, but child maltreatment remained significantly associated with diabetes (Goodwin & Stein, 2004; Scott et al., 2011; Widom et al., 2012).

## Discussion

The vast majority of studies reviewed observed a significant association between child maltreatment and both CVD and diabetes in adulthood. Certain forms of maltreatment, such as physical and sexual abuse, were more consistently associated with risk for cardiometabolic diseases than other forms of adversity (Duncan et al., 2015; Rich-Edwards et al., 2012; Rich-Edwards et al., 2010; Scott et al., 2011; Suglia et al., 2014; Thomas et al., 2008). Many studies examining maltreatment as part of a composite measure of adversity, reported a dose-response relationship between number of childhood adversities and heightened risk for cardiometabolic diseases (Campbell et al., 2015; Felitti et al., 1998; Friedman, Montez, Sheehan, Guenewald, & Seeman, 2015; Gilbert et al., 2015; Scott et al., 2011; Stein et al., 2010; Wilson et al., 2012). This type of dose-response relationship suggests that reducing the number of co-occurring adversities among maltreated children could help to prevent the downstream cardiometabolic consequences of maltreatment.

### Sex-related Findings

Few studies examined sex differences in the association of child maltreatment with cardiometabolic diseases, and among those that did, we found no consistent pattern of sex-related variations. This is consistent with a recent meta-analysis noting similar insufficient data to draw conclusions about sex-related differences based on adverse childhood events exposure and diabetes (Huang et al., 2015). In contrast, research on the developmental programming of the cardiovascular system which suggests a strong basis for sex-related differences that magnify with age (Dasinger & Alexander, 2016), and a recent statement by the AHA noting sex-related differences in the pathophysiology and presentation of acute MI (Mehta et al., 2016). Recent studies have also found sex differences in diabetes in relation to depression and anxiety (Demmer et al., 2015; Suglia et al., 2016). Thus, more rigorous examination of childhood adversity and sex-related cardiometabolic outcomes is warranted.

### Role of Mental Disorders

Most studies in our review showed that adjusting for mental disorders attenuated the relationship between child maltreatment and cardiometabolic disease (e.g., Afifi et al., 2013; Goodwin & Stein, 2004; Scott et al., 2011; Stein et al., 2010; Suglia et al., 2014; Widom et al., 2012), although whether child maltreatment remained significantly associated with



disease outcomes varied across studies. However, findings related to mental disorders must be interpreted with some caution because studies varied greatly in terms of how they modeled the statistical effects of mental disorders (e.g., time-varying or lifetime, in combination with other disorders, or combined with health behaviors, when entered in the statistical models). The available evidence indicates that mental disorders are a partial mediator of the association of child maltreatment with cardiometabolic disease, explaining some of the shared variance in this association.

### Future Directions

Five additional points are highlighted by our study, in relation to future directions for research. First, only six studies obtained the highest evidence grade (i.e., sample size >500, prospective designs, validated measures for assessing child maltreatment and health outcome in adulthood). Four areas for methodological improvements are suggested: 1) While prospective studies that assess maltreatment during childhood and cardiometabolic disease in adulthood would be ideal, these studies will be costly and take decades to accomplish. A reasonable alternative involves identifying adults with documented reports of child maltreatment based on child protective services; several influential studies have used this method (Scott, McLaughlin, Smith, & Ellis, 2012; Widom et al., 2012). 2) Using documented cases of child maltreatment can also help address bias (e.g., mood-dependent recall) inherent in retrospective self-reports of maltreatment. A key issue with this approach, however, is that documented cases of maltreatment may represent the severe end of the maltreatment continuum or reflect factors associated with increased likelihood of child protective services involvement (e.g., low SES, non-White race/ethnicity). 3) Assessing health outcomes using objective methods or medically verified cases would improve upon the use of self-reports of health problems. 4) Prospective follow up on documented cases of child maltreatment to assess incident cardiometabolic disease in initially disease-free individuals is another area for methodological improvement. Thus, a variety of designs can be used to estimate associations between child maltreatment and cardiometabolic disease to build on the existing literature.

Second, this review identified significantly more studies examining child maltreatment and CVD than diabetes, even though these cardiometabolic diseases share many risk factors. Further research is needed to understand etiological mechanisms that may be unique or overlapping for these cardiometabolic diseases, particularly stemming from child maltreatment and related adversities.

Third, the association of child maltreatment with BP and/or hypertension was less consistent than for CVD endpoints or diabetes. One possible interpretation of this finding is that the pathways linking maltreatment with CVD involve mechanisms other than hypertension and poor BP regulation. Allostatic load models argue that the cumulative damage to multiple regulatory systems ultimately confer risk for CVD and other health outcomes in the context of chronic adversity. Thus, other mechanisms such as maladaptive hormonal and metabolic remodeling of brain regions may be involved in the development of cardiometabolic diseases (McEwen, 2010). It is notable that even across studies with higher evidence grades, and when BP was not based on self-report, findings were variable. Thus, further investigation of

mechanisms that may or may not involve BP regulation in influencing cardiometabolic diseases is necessary.

Fourth, future studies should focus on elucidating mechanisms through which child maltreatment contributes to the development of such long-term health outcomes. For instance, there is evidence that child maltreatment is associated with increased violence exposure in adulthood (McMahon et al., 2015). It is possible that child maltreatment creates a diathesis that serves to enhance sensitivity to stressors at later developmental stages. There is evidence of such sensitization in predicting psychopathology (McLaughlin et al., 2010), and a similar mechanism may also place individuals at an increased risk for physical health problems due to sensitization of regulatory systems to the effects of stressors. Indeed, Kiecolt-Glaser and colleagues (2011) reported this type of sensitization whereby individuals exposed to child maltreatment had amplified inflammatory responses to stressors in adulthood. An alternate possibility is that mental disorders such as depression or PTSD mediate the association between maltreatment and cardiometabolic diseases. Pathways stemming from mental disorders, such as posttraumatic reactions (i.e., physiological reactivity to trauma-related reminders, and changes in attention, memory, executive functioning, inhibition of impulses and fear, and the capacity to interpret and regulate responses) can create recurring stressors leading to repeated arousal of stress response systems (D'Andrea, Sharma, Zelechoski, & Spinazzola, 2011).

Finally, it is notable that the majority of samples came from the U.S. and/or high-income countries. There may be differences in associations between child maltreatment and subclinical measures of cardiometabolic biomarkers between high and low-/ middle-income countries (Slopen et al., 2013). Systematic variations in diet and other lifestyle factors, and genetic differences could be contributing factors. Our review included a study from Brazil (Parrish et al., 2013), and two multi-country studies that did not report significant inter-country differences in the associations of child maltreatment with CVD or diabetes (Scott et al., 2011; Stein et al., 2010), hence there was limited data to address this issue. More information is necessary to determine whether or not patterns of associations between child maltreatment and cardiometabolic diseases vary across sociocultural contexts.

### Public Health Implications

To help translate available evidence into effective public health policies, and intervention efforts, we highlight three key points in this regard. First, given the evidence for long-term health problems following a history of child maltreatment, taking a life course approach to prevention and treatment is critical (Szilagyi & Halfon, 2015). Second, sensitive periods of development, which are marked by greater developmental plasticity and responsiveness to environmental inputs, present an opportunity for intervention efforts. Some evidence suggests that intervention during these periods are likely to yield more long term benefits, and may be more cost effective (Knudsen, Heckman, Cameron, & Shonkoff, 2006). Third, given the wide range of deleterious outcomes stemming from early life adversity, medical specialties beyond those traditionally tasked with mental health care, need to consider the role of an individual's psychosocial history in treatment (Bethell, Newacheck, Hawes, & Halfon, 2014).

Towards this end, interventions such as recognizing child maltreatment as a public health issue (Schickedanz, Dreyer, & Halfon, 2015) and integrating primary and mental health care are increasingly being considered a national mandate (Kolko & Perrin, 2014). Universal mental health screening in primary care settings (Wissow et al., 2013) and feasibility of referrals for specialized treatment (Berger-Jenkins, McCord, Gallagher, & Olfson, 2012), beginning in early childhood (Simpson et al., 2016), are some of the early steps in this direction.

### **Clinical Implications**

Preventive interventions, such as the Nurse Family Partnership, Minding the Baby, and Child Parent Psychotherapy (Lieberman, Van Horn, & Ippen, 2005; Olds et al., 2007; Sadler et al., 2013), which focus on known risk factors for child maltreatment (e.g., poverty, parental psychopathology) and improving the parent-child relationship, provide an opportunity to prevent early adversity in the first place. Greater investment in such programs is critical.

Physicians, particularly pediatricians, maybe well placed to conduct mental health screenings and referrals (Garner et al., 2012). In addition to training physicians (Kerker et al., 2015), providing mental health consultation services (Hobbs Knutson, Masek, Bostic, Straus, & Stein, 2014), and implementing co-located primary and mental health care (Briggs et al., 2012; Guevara, Greenbaum, Shera, Bauer, & Schwarz, 2009; Williams, Shore, & Foy, 2006) are other models of care that are being evaluated and implemented, and align well with the life course multidisciplinary approach to health care.

Tertiary care through treatments that help parents provide a more supportive emotional context for their children, in contrast to typical patterns of parenting seen in the context of maltreatment, familial trauma or psychopathology (Schechter & Willheim, 2009), can help buffer the effects of child maltreatment. Whether evidence-based psychotherapies for children, families, and adults also improve markers of physical health requires further investigation. Preliminary evidence of changes in immune or related biomarkers (Black & Slavich, 2016; Bower & Irwin, 2016; Morgan, Irwin, Chung, & Wang, 2014) and molecular mechanisms (Conklin et al., 2015; Niles, Mehta, Corrigan, Bhasin, & Denninger, 2014) in response to psychological treatments, provides some support for the idea that treatments used to address maltreatment-related mental health sequelae may also be effective in treating health problems.

### **Limitations**

Factors such as health behaviors (e.g., smoking, exercise), nutrition, and other mental disorders (e.g., eating disorders, substance use) that have been associated with child maltreatment and cardiometabolic problems independently and that may differ by sex are important to consider, but are not discussed here. Additionally, while cardiometabolic diseases serve as a useful paradigm for understanding associations between early life experiences and later health outcomes, mechanisms underlying associations between child maltreatment and other diseases may only partially overlap with cardiometabolic diseases, have unique associations with certain types of child maltreatment (e.g., sexual abuse and reproductive problems), and have other public health and clinical implications.

## Conclusions

Child maltreatment is associated with cardiometabolic diseases in adulthood. Future directions for methodological improvements include the use of prospective study designs, documented cases of child maltreatment, and objective assessments or medically verified cases for health outcomes, particularly to predict incident cardiometabolic disease in initially disease-free individuals. Also, more rigorous assessments of mechanisms underlying associations between maltreatment history and later health (e.g., mental disorders) are needed. Sex-dependent differences in CVD and diabetes, in the context of maltreatment history, are under-examined and require more investigation. Finally, a majority of studies have been conducted in high-income countries. Research from diverse sociocultural contexts is necessary to understand whether patterns of associations between child maltreatment and cardiometabolic health may differ from high-income countries. Clinically, early identification of at-risk children and families, and a life course approach to treating health problems, are central to prevention and intervention efforts.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table 1**

**Summary Statistics of Studies**

Outcome	No. of studies assessing the outcome N	Increased risk of outcome with any adversity % (N)	Variations in increased risk, based on adversity type / severity % (N)	Studies reporting sex-stratified findings % (N)	Studies accounting for mental disorders % (N)
Studies Assessing Child Maltreatment					
CVD EP	11	90.91 (10)	40.00 (4)	44.44 (4)	72.73 (8)
BP/HTN	7	28.57 (2)	50.00 (1)	16.67 (1)	57.14 (4)
T2DM	7	71.43 (5)	60.00(3)	40.00 (2)	57.14 (4)
Studies Assessing Child Maltreatment and Other Adversities					
CVD EP	13	92.31 (12)	58.33 (7)	8.33 (1)	38.46 (5)
BP/HTN	6	100.00 (6)	33.33 (2)	0.00 (0)	33.33 (2)
T2DM	10	100.00 (10)	70.00 (7)	20.00 (2)	20.00 (2)

CVD EP = Cardiovascular Disease End Points (myocardial infarction, stroke, CVD, coronary heart disease), BP = Blood Pressure, HTN = Hypertension, T2DM = Type 2 Diabetes Mellitus