## The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis



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#### Summary

Background A growing body of research identifies the harmful effects that adverse childhood experiences (ACEs; occurring during childhood or adolescence; eg, child maltreatment or exposure to domestic violence) have on health throughout life. Studies have quantified such effects for individual ACEs. However, ACEs frequently co-occur and no synthesis of findings from studies measuring the effect of multiple ACE types has been done.

Methods In this systematic review and meta-analysis, we searched five electronic databases for cross-sectional, case-control, or cohort studies published up to May 6, 2016, reporting risks of health outcomes, consisting of substance use, sexual health, mental health, weight and physical exercise, violence, and physical health status and conditions, associated with multiple ACEs. We selected articles that presented risk estimates for individuals with at least four ACEs compared with those with none for outcomes with sufficient data for meta-analysis (at least four populations). Included studies also focused on adults aged at least 18 years with a sample size of at least 100. We excluded studies based on high-risk or clinical populations. We extracted data from published reports. We calculated pooled odds ratios (ORs) using a random-effects model.

Findings Of 11621 references identified by the search, 37 included studies provided risk estimates for 23 outcomes, with a total of 253719 participants. Individuals with at least four ACEs were at increased risk of all health outcomes compared with individuals with no ACEs. Associations were weak or modest for physical inactivity, overweight or obesity, and diabetes (ORs of less than two); moderate for smoking, heavy alcohol use, poor self-rated health, cancer, heart disease, and respiratory disease (ORs of two to three), strong for sexual risk taking, mental ill health, and problematic alcohol use (ORs of more than three to six), and strongest for problematic drug use and interpersonal and self-directed violence (ORs of more than seven). We identified considerable heterogeneity (*I*<sup>2</sup> of >75%) between estimates for almost half of the outcomes.

Interpretation To have multiple ACEs is a major risk factor for many health conditions. The outcomes most strongly associated with multiple ACEs represent ACE risks for the next generation (eg, violence, mental illness, and substance use). To sustain improvements in public health requires a shift in focus to include prevention of ACEs, resilience building, and ACE-informed service provision. The Sustainable Development Goals provide a global platform to reduce ACEs and their life-course effect on health.

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#### Introduction

Studies are increasingly identifying the importance of early life experiences to people's health throughout the life course. Individuals who have adverse childhood experiences (ACEs; during childhood or adolescence) tend to have more physical and mental health problems as adults than do those who do not have ACEs and ultimately greater premature mortality.<sup>12</sup> ACEs include harms that affect children directly (eg, abuse and neglect) and indirectly through their living environments (eg, parental conflict, substance abuse, or mental illness). Physiological and biomolecular studies are increasingly establishing how childhood exposure to chronic stress leads to changes in development of nervous, endocrine, and immune systems, resulting in impaired cognitive, social, and emotional functioning

and increased allostatic load (ie, chronic physiological damage).<sup>3,4</sup> Thus, individuals who have ACEs can be more susceptible to disease development through both differences in physiological development and adoption and persistence of health-damaging behaviours.

Although studies linking childhood experiences to health go back decades,<sup>5</sup> examination of multiple ACEs enables a better assessment of the breadth of childhood adversity and its relation with adult health than does examination of single ACEs. The first major ACE study<sup>1,6</sup> examined relations between the number of ACEs reported by more than 17000 individuals in the USA and their health as adults. It found that the more ACE types that individuals reported, the greater their risks of health-harming behaviours (eg, smoking or sexual risk taking) and both infectious and non-communicable

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#### Research in context

#### Evidence before this study

Previous reviews have synthesised evidence for the long-term health effects of individual adverse childhood experience (ACE) types. However, ACEs often cluster in children's lives and a growing body of research is identifying cumulative relations between multiple ACEs and poor health. Initial evidence of this relation was published in the 1990s. Since then, an increasing number of studies have used similar methods to identify how multiple ACEs affect health-harming behaviours and development of health conditions, including non-communicable diseases.

#### Added value of this study

To our knowledge, no previous attempt has been made to synthesise evidence for the risks of poor health associated with multiple ACEs across various health-related behaviours and conditions. We found that individuals with at least four ACEs were at increased risk of all outcomes examined. Associations were weak or modest for physical inactivity, overweight or obesity, and diabetes (ORs of less than two), moderate for smoking, heavy alcohol use, poor self-rated health, cancer, heart disease, and

respiratory disease (ORs of two to three), strong for sexual risk taking, mental ill health, and problematic alcohol use (ORs of more than three to six), and strongest for problematic drug use and interpersonal and self-directed violence (ORs of more than seven)

#### Implications of all the available evidence

This systematic review and meta-analysis highlights the pervasive harms that ACEs place on health throughout the life-course and the importance of addressing the various stressors that can occur in children's lives, rather than limiting attention to any one type. Although further work is required to establish causality, the strong relations between multiple ACEs and poor health suggest that a reduction in ACEs and building of resilience to enable those affected to avoid their harmful effects could have a major effect on health. International resolutions, including the Sustainable Development Goals, provide crucial opportunities to address ACEs and our findings offer key information to advocate and inform development of more sustainable life-course approaches to health and health care than at present.

diseases (NCDs). Supported by international work to standardise measurement of ACEs and their effects on health, these findings have since been replicated in studies from low-income and middle-income<sup>7,8</sup> and high-income<sup>2,9</sup> countries. However, although previous reviews<sup>10,11</sup> have collated literature on the health effects of any ACE exposure or specific ACE types, no systematic attempt has been made to synthesise findings from studies of the effect of multiple ACEs across multiple outcomes. Consequently, no global estimates have been made of the strength of associations between multiple ACEs and adoption of health-harming behaviours, occurrence of conditions such as obesity and chronic health conditions, or risk of further exposure to violence in adult years.

In this study, we present findings from a systematic review and meta-analysis of studies measuring associations between multiple ACEs and health outcomes. The primary outcomes of interest were pooled measures of relations between multiple ACEs and health outcomes. Following precedent in the literature, we restricted analyses to exposure to at least four types of adversity during childhood, with individuals reporting no ACEs as the comparator.

#### Methods

#### Search strategy and selection criteria

The search strategy of this systematic review and metaanalysis is summarised in the panel. Searches focused on six categories of health outcomes: substance use, sexual health, mental health, weight and physical exercise, violence, and physical health status and conditions. We excluded studies based on high-risk (eg. the homeless or those in prison) or clinical populations because of often few individuals with low ACE exposure in such populations. Included studies met the following criteria: cross-sectional, case control, or cohort study, using a cumulative measure of at least four ACEs spanning both direct (eg, maltreatment) and indirect (eg, household dysfunction) types, focused predominantly on adults aged at least 18 years, a sample size of at least 100, and reported odds ratios (ORs), comparable statistics (hazard ratios or prevalence ratios), or data to enable their calculation for a health outcome. We also excluded outcomes with fewer than four studies reporting results suitable for meta-analysis. The initial literature search was done by two reviewers (KH and KAH), who then also retrieved and independently screened full-text articles. Conflicts over inclusion were resolved through discussion with MAB. Data were extracted by one reviewer (KH) and checked by two others (KAH and MAB).

#### Data analysis

Included articles were independently assessed for quality by two reviewers (KH and KAH) using criteria based on the standard principles of quality assessment.<sup>12</sup> Studies received a point for each quality criterion that they met, for a maximum score of 7. For each article, we extracted data for study type, setting, participants, ACEs, and outcomes. We extracted ORs or equivalent measures for participants with at least four ACEs versus those with none. When such data were not published, we included studies when adequate information was available to allow their calculation, including sample sizes within

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