Adverse childhood experiences and adult health: the need for stronger study designs to evaluate impact

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INTRODUCTION
Early life is regarded as a crucial period of neurobiological, emotional, social and physical development in all animal species and may have long-term implications for health across the life course. The first studies examining the preadult origins of chronic disease were probably published more than 50 years ago and based on rodent models.1 By briefly administering a suboptimal diet to newborn mice, Dubos and others1 demonstrated a marked impact on subsequent growth and resistance to infection. In the 1970s, Forsdahl,2 using infant mortality rates as a proxy for living conditions at birth, arguedably provided the first evidence in humans for an association with heart disease in later life. In the last two decades, findings from longitudinal studies with extended mortality and morbidity surveillance have implicated a host of preadult characteristics as potential risk factors for several chronic disease outcomes, including perinatal and postnatal growth,3 coordination,4 intelligence,5 mental health,6 overweight,7 physical stature,8 raised blood pressure,9 10 cigarette smoking,11 12 physical strength13 and diet14 among many others.15

An array of prospective studies has also demonstrated associations of childhood socioeconomic disadvantage—indexed by paternal social class or education, the presence of household amenities and domestic overcrowding—with somatic health outcomes in adulthood, chiefly premature mortality and cardiovascular disease.16 17 Parallel work has been undertaken by psychologists and psychiatrists exploring the consequences of childhood maltreatment for later psychopathologies—perhaps the most well examined health endpoint in this context.18 19 Collectively, these early life circumstances have been more widely defined to comprise the separate themes of material deprivation (eg, economic hardship and long-term unemployment); stressful family dynamics (eg, physical and emotional abuse, psychiatric illness or substance abuse by a family member); loss or threat of loss (eg, death or serious illness of a parent or a sibling, parental separation and public care)—among many other characteristics—and a continuum of severity can be constructed (table 1).20 21 Broadly referred to as adverse childhood experiences (widely known as ‘ACE’), survey data suggest that as many as 6 in 10 adults in the general population report at least one childhood adversity,22 though this prevalence is based on recall in adult populations, which may lead to a distortion in its estimation (see later). Adverse childhood experiences, rather like poor health behaviours,24 tend to cluster, and this has led to a growing body of work examining the impact of accumulated early adversity rather than a single characteristic.25 26

Given the considerable current research interest in adverse childhood experiences—according to PubMed, in 2019, there were more than 1000 publications on the topic, representing a doubling over the prior 2-year period (figure 1)—in the present overview, we describe the potential mechanisms that may underlie the link between this early life characteristic and adult health, the current evidence for such an association, the validity of adversity data, and public health implications with future directions for the field.

POTENTIAL MECHANISMS OF EFFECT
Adverse childhood experiences may have an influence on subsequent health outcomes via biological, psychological, and social processes, and their effects may be direct or indirect. Of the direct mechanisms, a widely held view is that people who experience a high and/or varied load of adversities in early life may become more susceptible to disease occurrence and potentially have a worse illness prognosis, via differences in physiological development. These mechanisms of biological embodiment will be outcome specific: those relevant to stroke, a disease, may have little in common with those for suicide, a behaviour, for instance. Over the life course, however, adverse childhood experiences are likely to be linked with an interrelated, extant, and serial set of behavioural, psychological and physical disorders—as described in synergistic theory27—such that networks of disease and adverse behaviours cascade in people experiencing major socioeconomic adversity disadvantage.28

Although not a universal observation,29 30 early adversity appears to lead to chronically elevated levels of both cortisol31—the most common human glucocorticoid and a biomarker of psychosocial stress—and systemic inflammation,32 33 which themselves have been linked to major causes of adult disease, such as cardiovascular disease34 and mental health.35 Related, there is some support for epigenetic modification of certain characteristics, most notably NRC31—the receptor to which cortisol and other glucocorticoids bind—in participants exposed to preadult disadvantage.36 NRC31 codes for the glucocorticoid receptor and altered glucocorticoid levels have, in turn, been linked to adult mental

Table 1  Selected indicators of early adverse experience linked to adult health based on existing reviews

| Indirect | Direct |
|----------|--------|
| Family financial problems | Neighbourhood safety |
| Parental separation or divorce | Emotional, psychological or verbal abuse |
| Family conflict or discord | Neglect |
| Death of parent or close relative or friend | Bullying |
| Parental incarceration/criminality | Separation from family (eg, public care) |
| Witnessing violence or violence victimisation | Serious childhood illness or injury |
| Household drug/substance abuse | Homelessness |
| Household mental illness | Dating violence |
|                         | Physical abuse |
|                         | Sexual abuse |

Adversities are categorised according to their mode of action (indirect or direct), though other groupings have been advanced.28 Adversities are arranged in ascending order of severity within each group, though this is most certain ‘adversities’ may actually be positive when the carer is abusive, such as paternal separation, death, and incarceration, or when the child moves into public care. Adversities may have featured in studies of adult health outcomes either individually or comprising a summary score.
health problems. Complementary evidence suggests that, relative to their unaffected counterparts, maltreated children have a lower volume of prefrontal cortex and experience greater activation of the hypothalamic–pituitary–adrenal axis, which is central to the human stress response.

Traumatic experiences in childhood have been repeatedly shown to have lasting impacts on psychopathology, such as major depression, substance abuse, and post-traumatic stress disorder, and these mental health problems may link adverse childhood experiences to physical illnesses. Additionally, as well as representing a key public health concern in their own right, psychiatric experiences to physical illnesses. Addition-

operationalisations of which can make synthesis of findings challenging. For inclusion in a recent systematic review, the authors required studies to report on risk estimates for four or more adversities and for there to be a minimum of three published papers featuring the same health endpoint; this resulted in 22 outcomes across 37 studies.

Endpoints with the strongest relationship with adversity were behaviours (ORs 5.2–37.5)–violence victimisation or perpetration, drug use and suicide—rather than those characterised by disease processes that occur over years and possibly decades such as liver or digestive disease, respiratory disease (OR ~3), vascular disease, or injury (unintentional and intentional), as well as hampering help-seeking behaviour, diagnosis and treatment. Further indirect mediating effects include the impact of preadult adversity on later socioeconomic status and health behaviours, such as smoking, heavy alcohol intake, low exercise levels and poor diet, all of which have well established links with chronic disease in later life.

CURRENT EVIDENCE FOR AN ASSOCIATION OF EARLY ADVERSITY WITH ADULT HEALTH

The existing literature features an array of health outcomes in adulthood that have been correlated with adverse childhood experiences, the different experiences that was made in childhood followed by prospective ascertainment of health outcome in adulthood—are rare and largely limited to a few birth cohort studies either conducted in the field or generated from the linkage of routinely gathered data. Field-based studies with the required extended follow-up period have typically been carried out in the era preceding the current research interest in childhood adversities; thus, construction of the exposure variable is often post hoc and often found wanting relative to contemporary, theory-driven definitions of this exposure. Meanwhile, electronic record-based studies, while typically offering higher statistical power and precision, miss undiagnosed morbidity and perhaps capture only those cases of adversity that come to the attention of social services; also often absent is a breadth of data, most obviously on potentially important confounding factors.

Genuine prospective studies—that with an assessment of adverse experiences that was made in childhood followed by prospective ascertainment of health outcome in adulthood—are rare and largely limited to a few birth cohort studies either conducted in the field or generated from the linkage of routinely gathered data. Field-based studies with the required extended follow-up period have typically been carried out in the era preceding the current research interest in childhood adversities; thus, construction of the exposure variable is often post hoc and often found wanting relative to contemporary, theory-driven definitions of this exposure. Meanwhile, electronic record-based studies, while typically offering higher statistical power and precision, miss undiagnosed morbidity and perhaps capture only those cases of adversity that come to the attention of social services; also often absent is a breadth of data, most obviously on potentially important confounding factors.

VALIDITY OF EARLY ADVERSITY DATA AND OTHER METHODOLOGICAL CONSIDERATIONS

The genuine prospective studies apart, a core issue in the synthesis of evidence on the health sequelae of adversity is the validity of the distantly recalled exposure data. There are obvious reasons to expect several biases to exert an impact on the quality of the data elicited many years following adverse events, including simply forgetting—potentially as a protective mechanism—and the influence of intervening life events such that it is unlikely that an individual with contemporary experience of somatic illness and, particularly, mental health problems, will provide the same unbiased account of early life misery as a person free of such conditions. Perhaps unsurprisingly then, agreement between retrospective and prospective assessments of childhood maltreatment is poor, with a recent aggregation of kappa statistics across 16 studies that had both prospective and retrospective measurement being as low as 0.2, an observation that accords with narrative reviews. Expressed differently, this indicates that prospective and retrospective measurements of early disadvantage tend to capture almost mutually exclusive groups of people. What makes this finding more striking is that, in 15 of the 20 studies identified, ‘distant’ recall was made early in the adult life course (<30 years of age), and in several, participants were in adolescence. Even midlife recollection
of early life socioeconomic status based on occupational social class—essentially an enquiry about the type of job held by the study member’s father—showed only moderate levels of agreement with reports from the earlier era.41

The implications of these unfavourable psychometric properties for the examination of associations with adult health outcomes may be acute. For studies exploring mental health outcomes, effects seem to be stronger when based on the retrospectively captured adversity data.42

For somatic outcomes, in analyses of data from a birth cohort study, overcrowding at age 11 years based on prospectively gathered parental reports when the study member was aged 11 years was unrelated to standard queries about asthma or wheezy bronchitis at age 50 years, whereas retrospectively gathered data on this marker of preadult adversity appeared to confer protection against the same respiratory outcome.43

In a rare study with objective health outcomes, retrospectively captured data on early life poverty showed no relation with death or vascular disease events, whereas prospectively gathered records on hygiene and living conditions revealed the expected gradients.44 Despite these concerns of distant recall of early adversity, however, a cross-sectional study regarded by some observers as the progenitor study in the field of early adversity and adult health was in fact based on the simultaneous assessment of exposures and outcomes made via self-report in middle-aged and older aged people. Published two decades ago,45 it has, according to Scopus, been cited a striking 6500 times and has recently been reprinted.46

Lastly, a concern that may impact on all field-based studies is health-related selection into and out of the study population, such that children exposed to the greatest degree of adversity are perhaps least likely to participate. This issue is perhaps less problematic when cohort studies are based on electronic linkage to health, social, and welfare registries, although, as described, it is likely that only treated illnesses47 and the most severe cases of adversity are captured.

PUBLIC HEALTH IMPLICATIONS AND FUTURE RESEARCH PRIORITIES

While cross-sectional studies suggest there may be emerging links between adverse childhood experiences and a wide range of health outcomes, not all of which have clear explanatory mechanisms, this evidence base is not yet of sufficient quality to make definitive conclusions regarding public health impact. Findings in social epidemiology should be subject to the same level of scrutiny and doubt deployed in other spheres of science. In cardiovascular medicine, for instance, following very encouraging signals from an abundance of well-designed prospective cohort studies,68–70 pharmacological control of blood pressure,71 serum cholesterol72 and diabetes3 in randomised controlled trials has been shown to cause reductions in cardiovascular disease event rates. Genuine prospective cohort studies, natural experiments, and trials—the latter also very rare in our search of the databases45—are now needed in the field of adverse childhood experiences to quantify health consequences, specify the most harmful exposures, and then to confidently steer policy.

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