RESEARCH PAPER

Adverse childhood experiences and the development of multimorbidity across adulthood—a national 70-year cohort study

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Abstract

Aim: To examine impact of adverse childhood experiences (ACE) on rates and development of multimorbidity across three decades in adulthood.

Methods: Sample: Participants from the 1946 National Survey of Health and Development, who attended the age 36 assessment in 1982 and follow-up assessments (ages 43, 53, 63, 69; $N = 3{,}264$, 51% males). Prospectively collected data on nine ACEs was grouped into (i) psychosocial, (ii) parental health and (iii) childhood health. For each group, we calculated cumulative ACE scores, categorised into 0, 1 and ≥ 2 ACEs. Multimorbidity was estimated as the total score of 18 health disorders. Serial cross-sectional linear regression was used to estimate associations between grouped ACEs and multimorbidity during follow-up. Longitudinal analysis of ACE-associated changes in multimorbidity trajectories across follow-up was estimated using linear mixed-effects modelling for ACE groups (adjusted for sex and childhood socioeconomic circumstances).

Findings: Accumulation of psychosocial and childhood health ACEs were associated with progressively higher multimorbidity scores throughout follow-up. For example, those with ≥ 2 psychosocial ACEs experienced 0.20(95% CI 0.07, 0.34) more disorders at age 36 than those with none, rising to 0.61(0.18, 1.04) disorders at age 69. All three grouped ACEs were associated with greater rates of accumulation and higher multimorbidity trajectories across adulthood. For example, individuals with ≥ 2 psychosocial ACEs developed 0.13(−0.09, 0.34) more disorders between ages 36 and 43, 0.29(0.06, 0.52) disorders between ages 53 and 63, and 0.30(0.09, 0.52) disorders between ages 63 and 69 compared with no psychosocial ACEs.

Interpretations: ACEs are associated with widening inequalities in multimorbidity development in adulthood and early old age. Public health policies should aim to reduce these disparities through individual and population-level interventions.

Keywords: older people, lifecourse, socioeconomic, trajectory, multimorbidity, adverse childhood experiences

Key Points

- Childhood adversity was associated with a progressively increasing burden of multimorbidity across adulthood into early old age.
- Combination of serial-cross sectional + longitudinal analysis adds to existing knowledge of cross-sectional associations.
- Interventions to ameliorate inequalities in healthy ageing warrant further investigation and implementation.
- Public health policies should consider the effect of ACEs and early-life socioeconomic circumstances.

Introduction

The prevalence of multimorbidity, defined as ≥2 health disorders in an individual, has increased substantially in recent decades and emerges earlier in the lifecourse [1]. A quarter of British adults, and a half of individuals >65 years have multimorbidity [2]. These proportions are expected to increase [3]. The growing burden of premature chronic disease, alongside medical advances, and increased life expectancy despite ongoing health problems, are the main drivers of increasing multimorbidity [4]. People with multimorbidity are likely to experience poorer quality of life, impaired functional ability, more severe health outcomes and require greater inpatient and ambulatory care [5, 6]. However, current fragmented and siloed care provision is ill-suited to address the holistic challenge of multimorbidity [2, 7].

Adverse childhood experiences (ACEs) affect more than half of individuals worldwide and are associated with health disorders in adulthood (e.g. cardiovascular, respiratory and mental health disorders) and health-risk behaviours (e.g. smoking, drug misuse) [8]. ACEs encompass physical, sexual and emotional maltreatment and markers of household dysfunction (e.g. parental mental health problems, parental divorce) [9, 10]. Limited studies have demonstrated associations between ACEs and increased risk for multimorbidity in adulthood [11–17]. However, this evidence is predominantly from cross-sectional analyses using retrospective recall of ACEs, which may be subject to participants' recall bias and inaccurate childhood accounts [18–21]. Furthermore, childhood socioeconomic disadvantage is associated with both increased risk of ACEs and multimorbidity in adulthood; hence, it is important to account for this when studying the impact of ACEs on later life health [22, 23]. However, the extent of the impact of ACEs on long-term development of multimorbidity across adulthood, and whether it may be explained by childhood socioeconomic circumstances, remains unexplored.

We hypothesized that greater accumulation of ACEs would be associated with a greater burden of multimorbidity across adulthood. Therefore, using a national birth cohort (The 1946 MRC National Survey of Health and Development) with almost 70 years of follow-up, we examined associations between different forms of ACEs, recorded at the time of event, and multimorbidity development across adulthood and into later life. We also investigated whether experiencing a greater number of ACEs was associated with an earlier onset and more rapid accumulation of multimorbidity between ages 36 and 69 years.

Methods

Study participants and setting

The study sample was drawn from the 1946 MRC National Survey of Health and Development (NSHD), a primarily White British birth cohort which originated from a maternity survey of 13,687 births in England, Wales and Scotland during one week in March 1946. From this, a nationally representative and socially stratified group of 5,362 individuals born to married parents was selected for follow-up [24]. The final study sample included 3,264 individuals (Figure S1, Supplemental methods are available in *Age and Ageing* online). Data collection in childhood was conducted by health care and educational professionals at regular intervals. There were five assessments from mid-adulthood to early old age (ages 36-, 43-, 53-, 63- and 69-years), which included self-completed questionnaires and home visits by trained research nurses [24].

The NSHD study obtained ethical approval from Greater Manchester Local Research Ethics Committee and the Scotland Research Ethics committee. More information is available from the study's website: https://www.nshd.mrc.ac.uk/.

Adverse childhood experiences

Nine adverse childhood experiences (ACEs) were chosen based on the literature and previous use in studies using the NSHD (Table 1, operationalisation/reporting details in Table S1, Supplemental methods are available in *Age and Ageing* online) [25, 26], Childhood was defined as birth until age 15 years. We separated these nine ACEs into three groups to represent 'psychosocial', 'parental health' and 'childhood health' ACEs. This was an *a priori* conceptual decision to examine the independent effects of each group, given their likely differing pathways of effect on multimorbidity (see Supplemental methods are available in *Age and Ageing* online).

Each ACE was coded as a binary variable ('0' indicating absence and '1' its presence). The values of these binary variables were summed to create continuous cumulative scores for each of the three groups to model repeated exposure to ACEs, which is an established technique [9]. The continuous psychosocial and parental health ACE scores were categorised as 0, 1 and ≥2 whereas the childhood health ACE score was categorised as 0 and ≥1 (as very few participants experienced two childhood health ACEs).

Multimorbidity

Multimorbidity was based on 18 health disorders previously classified by Khanolkar *et al.* (Table S4, Supplemental methods are available in *Age and Ageing* online) [23]. A binary variable was created for each disorder with '1' indicating presence and '0' indicating absence at each of the five adulthood assessments. These values were summed to create continuous, unweighted 'multimorbidity scores' at each adulthood assessment [27]. The multimorbidity score was defined as the unweighted sum of disorders accumulated by an individual at each assessment and was the main outcome.

Covariates

Covariates included sex (assigned at birth), paternal occupational social class (POSC) and childhood socioeconomic adversity (CSA).

Table 1. Description of study participants from the 1946 National Survey of Health and Development (NSHD)

Covariates		Participants (N = 3,264)	Percentage (%)
Sex	Male	1,643	50.3
	Female	1,621	49.7
Participants with ACE	Parental death	207	6.3
	Parental divorce/separation	192	5.9
	Regular/Permanent separation from mother	191	5.5
	Residential instability	579	17.7
	Parental physical illness	806	24.7
	Parental psychiatric illness	76	2.3
	Severe/chronic parental illness	466	14.3
	Childhood physical illness	530	16.2
	Childhood psychiatric illness	32	1.0
Psychosocial ACE score	0	2,308	70.7
	1	768	23.5
	≥2	188	5.8
Parental health ACE score	0	2,396	73.4
	1	399	12.2
	≥2	469	14.4
Childhood health ACE score	0	2,705	82.9
	≥1	559	17.1
Paternal occupational social class	Manual	1,908	58.4
	Non-manual	1,356	41.6
Childhood socioeconomic adversity score	0	2,654	81.3
	1	408	12.5
	2	128	3.9
	≥3	74	2.3

POSC was recorded at age 11, catalogued by the 'Classification of Occupations' (1970). Categories included, 'Professional/Intermediate', 'Skilled non-manual', 'Skilled manual' and 'Partly skilled/unskilled manual'. These categories were collapsed into a binary variable indicating manual vs. non-manual occupation, following previous practice in the NSHD [26, 28].

In addition to POSC, we included less commonly used indicators of socioeconomic position (SEP) such as indicators of socioeconomic adversity (e.g. household overcrowding) as these are associated with ACEs [29]. Furthermore, they are also indicators of childhood SEP given the historical context of the NSHD [30]. The values of seven such binary variables were summed to derive CSA (Table S2 is available in *Age and Ageing* online). This was further categorised as 0, 1, 2 or ≥3 childhood socioeconomic adversities as per previous studies incorporating CSA scores in the NSHD [25, 31].

Statistical analysis

Multiple linear regression was used to investigate associations between all nine individual ACEs and multimorbidity scores at each of the five adulthood assessments. We were guided by a Directed Acyclic Graph (DAG) using *a priori* covariate selection to identify confounders and distinguish them from colliders or mediators (Figure S3, Supplementary methods are available in *Age and Ageing* online) [32]. We ran unadjusted models assessing associations between individual ACEs and multimorbidity. Models were subsequently adjusted for sex and childhood socioeconomic indicators

(POSC and CSA). Associations between each of the three ACE groups and multimorbidity at each age, were modelled with adjustment as above. All models were repeated and stratified by sex.

Longitudinal associations between ACEs and changes in multimorbidity trajectories throughout adulthood was examined using linear mixed-effects modelling for each of the three ACE groups. This accounts for clustering of observations in the same individual over time and the deviations of individual-level trajectories from an overall population-average trajectory. Non-linearity in multimorbidity trajectories was assessed using four splines between ages 36–43, 43–53, 53–63 and 63–69 years. This resulted in four separate slopes (one slope for each spline), with the slope of each indicating the rate of accumulation of disorders per year within that spline period. We included interactions between ACE scores and all four spline variables to account for the possible differences in rate of accumulation of disorders between the different splines. This 'full model' was mutually adjusted for all covariates (sex, POSC, CSA).

The analysis sample (N = 3,264) for this study consisted of cohort members who attended the assessment at age 36 and any of the age 43-, 53-, 63- or 69-years assessments and had data on all covariates of interest. Missing data on the 18 health disorders used to estimate multimorbidity were addressed by multiple imputation (with 25 imputations) assuming missing at random (MAR). The imputation model included childhood and adulthood social class, and educational level (available for >94% of study participants). The wealth of available data supports the assumption made by the
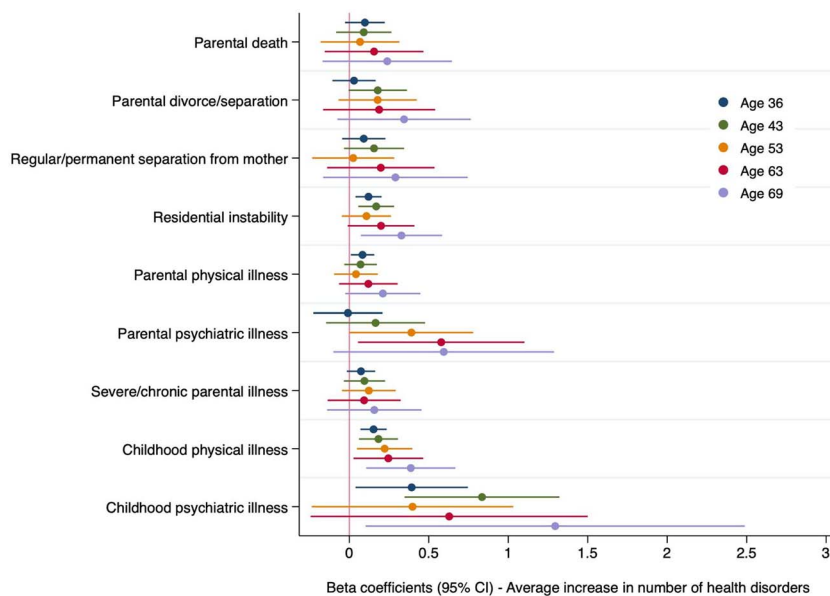
Figure 1. Associations between individual ACEs and multimorbidity in 3,264 participants from the 1946 National Survey of Health and Development (estimates are from linear regression models adjusted for sex, paternal occupational social class and childhood socioeconomic adversity).

MAR mechanism regarding observable data explaining the systematic differences between it and missing data, although the MAR mechanism is largely untestable [33, 34] (discussed in Supplemental methods are available in *Age and Ageing* online).

All analyses were conducted using Stata version 16 (StataCorp LP, College Station, Texas).

Results

Table 1 displays descriptive characteristics of the study sample (*N* = 3,264). About, 29.3% of participants reported ≥1 psychosocial ACE, while 26.6 and 17.1% reported ≥1 parental health ACE and childhood health ACE, respectively. The most common ACE was 'Parental physical illness' (24.7%). Multimorbidity increased progressively from 16% at age 36 to 80% at age 69 (Figure S2 is available in *Age and Ageing* online).
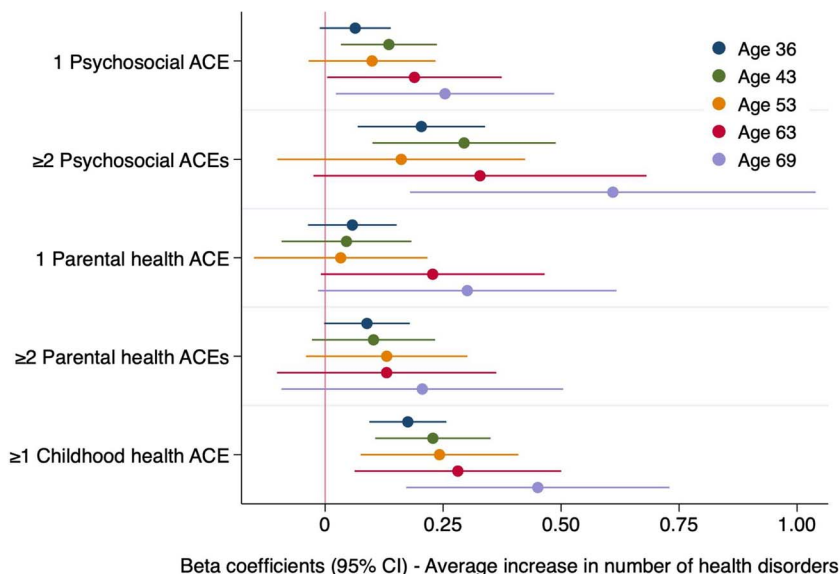
Cross-sectional associations between ACEs and multimorbidity across follow-up

Residential instability and parental psychiatric illness were associated with higher multimorbidity scores in adulthood with estimates increasing in size with age (Figure 1, Table S8 is available in *Age and Ageing* online). For example, residential instability was associated with 0.12 (95% CI 0.04–0.20) more disorders at age 36 that increased to 0.33 (0.07–0.58) more disorders at age 69 after adjustment for covariates. Parental psychiatric illness was not associated with multimorbidity at ages 36 and 43. However, it was associated with higher multimorbidity scores at older ages (0.39 at age 53, 0.58 at age 63 and 0.59 at age 69).

The most consistent associations were found between childhood health ACEs and multimorbidity, with estimates increasing in size progressively across adulthood. Childhood physical illness was associated with 0.15 (0.07–0.24) higher multimorbidity scores at age 36 which increased to 0.39 (0.11–0.67) higher scores at age 69, after adjustment. Corresponding estimates for childhood psychiatric illness were 0.39 (0.04–0.75) at age 36 and 1.30 (0.10–2.49) at age 69. In general, adjustment for POSC/CSA only marginally attenuated the above estimates (Tables S7/S8 and Figure S4 are available in *Age and Ageing* online).

Analysis of grouped ACEs revealed that combined psychosocial ACEs were associated with higher multimorbidity across most of adulthood (Figure 2, Table S10 is available in *Age and Ageing* online). Furthermore, these estimates increased in size with age and were related to the burden of ACEs; namely having ≥2 psychosocial ACEs was associated with higher multimorbidity scores compared to 1 ACE. Compared to individuals with no psychosocial ACEs, those with 1 and ≥ 2 ACEs had 0.14 (0.03–0.24) and 0.29 (0.10–0.49) higher multimorbidity scores at age 43, increasing to 0.25 (0.02–0.49) and 0.61 (0.18–1.04) at age 69, respectively. Combined parental health ACEs were associated with higher multimorbidity scores at older ages, but these were slightly attenuated after adjustment for socioeconomic covariates (Tables S9/S10 are available in *Age and Ageing* online). Combined childhood health ACEs were associated with higher and progressively increasing multimorbidity scores across adulthood (from 0.18 at age 36 to 0.45 at age 69).

Sex-stratified analysis results were largely similar to full-sample analysis, though estimates were less precise due to the

Figure 2. Associations between ACE scores and multimorbidity in 3,264 participants from the 1946 National Survey of Health and Development (estimates are from linear regression models adjusted for sex, paternal occupational social class and childhood socioeconomic adversity).

reduced sample size (Tables S14/S15 are available in *Age and Ageing* online). Estimates for childhood physical illness were larger and more consistently associated with multimorbidity in males compared to females (e.g. at age 63, males: 0.36 [0.06, 0.66] and females: 0.11 [−0.21, 0.42]).

Impact of ACEs on multimorbidity developmental trajectories across adulthood

Individuals with ACEs had a greater rate of accumulation and steeper multimorbidity trajectories across adulthood compared to those without ACEs. These findings were consistent for all three grouped ACEs.

Psychosocial ACE accumulation was associated with steeper multimorbidity trajectories throughout follow-up (Figure 3A, Table S11 is available in *Age and Ageing* online). For example, compared to individuals with no psychosocial ACEs, those with ≥2ACEs experienced 0.13 (−0.09, 0.34) more disorders between ages 36 and 43 years, 0.29 (0.06, 0.52) more disorders between ages 53 and 63 years and 0.30 (0.09, 0.52) more disorders between ages 63 and 69 years. Our results revealed a pattern of both earlier onset and faster rate of development of multimorbidity in these individuals.

Similarly, individuals with 1 or ≥ 2 parental health ACEs experienced steeper multimorbidity trajectories across follow-up compared to those with none (Figure 3B, Table S12 is available in *Age and Ageing* online). For example, individuals with 1 parental health ACE developed 0.21 (0.05, 0.37) more disorders between ages 53 and 63 than those with none. However, there were no differences in the rate of accumulation of multimorbidity between those with 1 and ≥2 ACEs (i.e. the trajectories were similar and ran concurrently).

Finally, compared to having no childhood health ACEs, those with ≥1 childhood health ACEs displayed a steeper trajectory throughout follow-up and developed 0.05 (−0.09, 0.18) more disorders between ages 36 and 43 and 0.19 (0.06, 0.32) more disorders between ages 63 and 69. (Figure 3C, Table S13 is available in *Age and Ageing* online).

Discussion

Summary of findings and comparison with existing literature

Psychosocial, parental health and childhood health ACEs were associated with a greater burden of multimorbidity across adulthood and into early old age, with associations becoming stronger with age. Experiencing a higher total number of psychosocial and childhood health ACEs was associated with a progressively increasing burden of multimorbidity and an earlier onset and greater rate of accumulation of multimorbidity. These associations were minimally modified by adjustment for childhood socioeconomic factors. Individually, experiences of residential instability and childhood physical/psychiatric illness displayed the strongest and most consistent associations with greater multimorbidity across follow-up independent of childhood socioeconomic circumstances.

Existing evidence linking ACEs to increased risk of multimorbidity is mainly from cross sectional studies, with limited evidence for increasing risk over time [11–17].

Experience of 'moving country or linguistic region' is associated with increased odds of multimorbidity, but only as part of a cumulative 'stressful life event' exposure tool in cross-sectional analysis [15]. To our knowledge, our study is the first to report associations between childhood residential
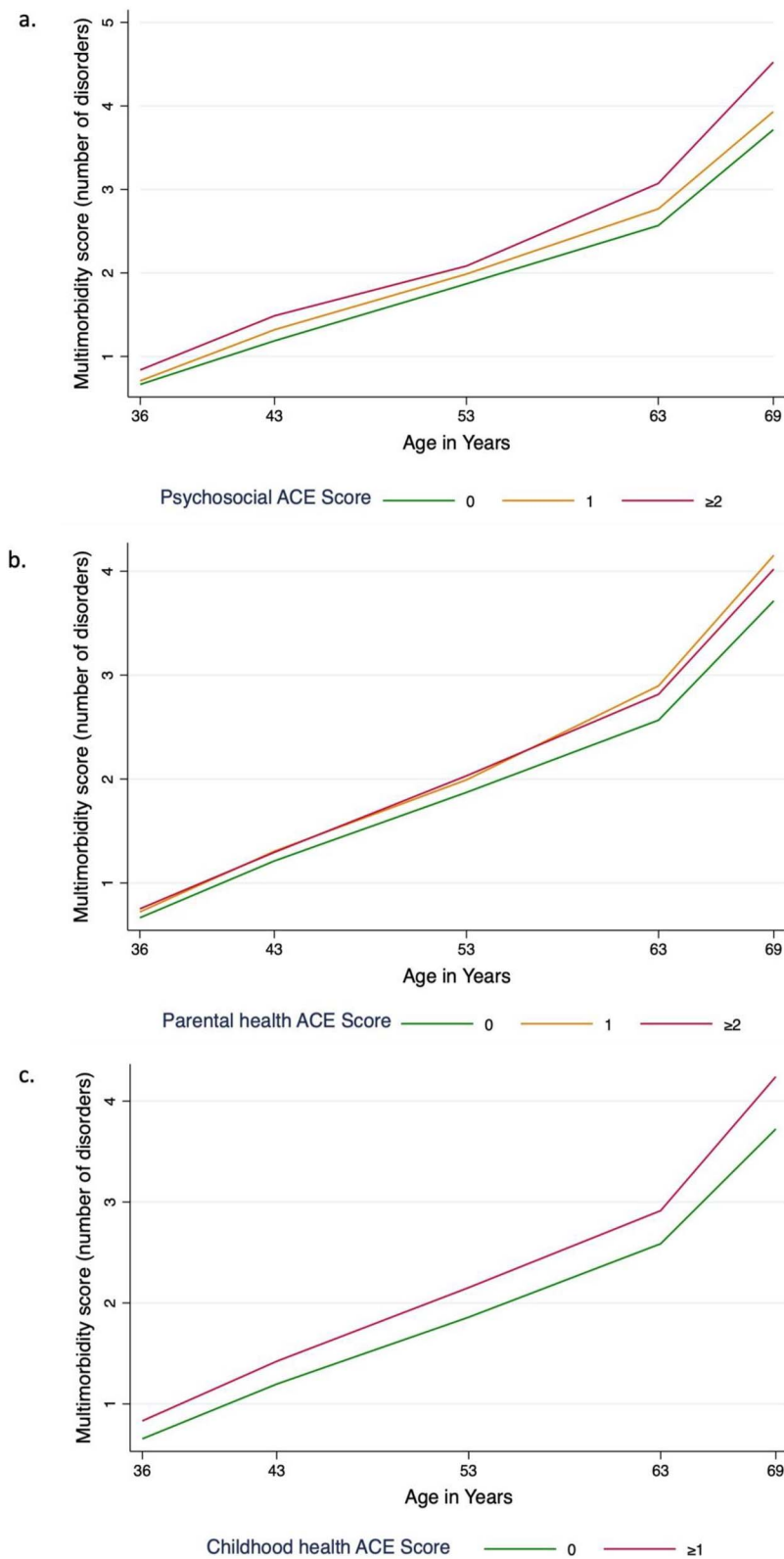
Figure 3. Psychosocial ACE (a), Parental health ACE (b) and Childhood health ACE (c)-associated inequalities in multimorbidity trajectories across adulthood and early old-age in 3,264 participants from the 1946 National Survey of Health and Development (estimates from linear spline mixed-effects modelling adjusted for sex, paternal occupational social class and childhood socioeconomic adversity). Significant ($P < 0.05$) interaction terms include: (1) [53–63 # ≥2 psychosocial ACEs, 0.29 (95% CI 0.06, 0.52)], (2) [63–69 # ≥2 psychosocial ACEs, 0.30 (0.09, 0.52)], (3) [53–63 # 1 parentalhealth ACE, 0.21 (0.05, 0.37)], (4) [63–69 # ≥1 childhoodhealth ACE, 0.19 (0.06, 0.32)].

instability and not only with an increased risk of multi-morbidity, but also with a gradient effect across adulthood. Negative residential instability in childhood is often the result of parental separation/bereavement, socioeconomic shocks and other life events; and evidence highlights that 'good' house moves (e.g. better area or house quality) are not associated with adverse outcomes [35]. Experience of 'childhood serious illness/accident' has previously been associated with increased odds of multimorbidity in cross-sectional studies [15]. Our findings were not unexpected as illness in childhood is expected to be associated with greater illness in adulthood.

We also found parental divorce/separation and parental physical illness were associated with progressively greater subsequent multimorbidity, although estimates in early old age (ages 63 and 69) were substantially attenuated by adjustment for childhood socioeconomic factors. Prior studies have linked both parental divorce and parental physical illness with an increased risk of multimorbidity but not as single exposures; rather as a component of a composite ACE score [11, 13, 15, 17].

Gonzalez *et al*. previously found parental mental illness in childhood to be associated with increased risk of specifically developing depression alongside either migraines or back pain in later life [14]. Our study builds on this by demonstrating a greater burden of multimorbidity at ages 53 and 63 in those with experience of parental psychiatric illness.

To our knowledge, only one previous study with a longitudinal design (limited to 4 years follow up in a sample aged 45–101) demonstrated accelerated accumulation of disorders in those who had experienced 'early parental physical abuse' and 'poor early parental mental health' (both retrospectively collected) [36]. Our study extends this by demonstrating earlier onset and more rapid accumulation of multimorbidity across adulthood with 33 years of follow-up, associated with a greater number of psychosocial and childhood health ACEs using prospectively collected ACE data.

Potential mechanisms and pathways

ACE-related stress and an implied lack of psychological support/nurturance in childhood may promote emotional dysregulation and adoption of health-risk behaviours, such as smoking, substance abuse, sexual risk-taking, overeating, and physical inactivity [8]. ACE-induced stress may also lead to chronic disruption in the (neuro)endocrine, metabolic, immune and autonomic nervous systems, and compromise somatic growth [37]. Long-term aberrations, termed 'allostatic (over)load', are considered to result in detrimental biological ageing and accelerated deterioration of function [38]. Integration of health-risk behaviours and physiological disruption pathways in a model of biological embedding is linked to enhanced inflammation and hypothalamic–pituitary–adrenal (HPA) overactivation, entwined with hormonal dysregulation and health-risk

behaviours [39, 40]. Epigenetic changes have been identified following ACEs [41]. As expected, in addition to stress imposed by all three groups of ACEs, childhood physical and psychiatric illnesses may continue or cause other disorders in adulthood (e.g. Type 1 diabetes, leading to renal/cardiovascular disease). Certain parental physical and psychiatric illnesses also have a genetic component, again potentially contributing to later life multimorbidity.

The minimal modification of observed associations by childhood socioeconomic circumstances suggests that while advantaged childhood SEP is protective for later life health, childhood SEP does not fully explain associations between ACEs and multimorbidity. However, estimates for associations of parental divorce and parental physical illness with multimorbidity in early old age were modestly attenuated suggesting that childhood socioeconomic factors may play a role in specific ACEs. For instance, childhood socioeconomic disadvantage, known to be associated with later life multimorbidity, may arise from familial income loss (due to parental death/divorce/illness) [23]. This association may have been more pronounced in this cohort given that dual-parental income was less common [42]. Indeed, socioeconomically disadvantaged individuals are more likely to divorce and to experience more severe financial consequences [43].

Strengths and limitations

A major strength is the long-term follow up of the same individuals from birth to age 69 with data on health disorders across adulthood (from age 36) allowing for both serial cross-sectional and longitudinal analyses with a longer follow-up compared to previous studies. The NSHD is also socially stratified and geographically distributed and despite attrition, it remains representative with respect to socioeconomic and mortality patterns of people born in the UK at that time [44]. A significant strength is prospectively collected ACE data. Retrospective ACE data may be compromised by recall bias, whereby those with poor adulthood mental/self-rated health report more childhood issues than they otherwise would [18, 20, 21]. Conversely, underreporting may occur, possibly caused by shame, aversion to re-experiencing trauma, or good self-rated functioning [18]. Prospective data avoid the delayed reporting of ACEs, making it less prone to recall issues, although binarized ascertainment of ACEs is inherently problematic.

Despite its advantages, the NSHD may not be generalisable to subsequent generations who have experienced a greater burden of multimorbidity [1]. The cohort lacks ethnic diversity and findings are generalisable to White, British-born individuals. More generally, the socioeconomic context of the NSHD needs to be considered. For example, the post-war housing shortage likely affected 'residential instability' while less modern healthcare and sustained austerity (food-rationing until the mid-50s) likely affected parental and childhood health. Society also underwent considerable shifts in the latter part of the 20th century such as reduced

social stigma towards divorce, expansion of the welfare state, and the rise of dual-income households; the latter reducing the financial consequences of parental divorce, death and illness.

Only 18 disorders were used to estimate multimorbidity although this is comparable to most studies investigating associations between ACEs and multimorbidity [11, 13–17, 36]. Furthermore, multimorbidity data were based on self-reporting of physician-diagnosed diseases although this method has proven reliability, including in the NSHD [45]. We used a simple disease count; more complex, weighted multimorbidity measurement tools exist but their utility depends on analysis-specific conceptualised relationships with other variables [46, 47]. Commonly used indicators of multimorbidity (e.g. Charlson Comorbidity Index) may exclude mental health, respiratory, and renal disorders, which we have included. The advantage of simple disease counts is that they permit external comparison of our results with existing literature on ACE-associations [12, 13, 36, 46].

Measuring adversity with a simple ACE count assumes equal weighting for all events [18]. However, although other methods have been explored (e.g. explanatory factor analysis with integration of severity and chronicity), the use of a simple count aids comparison with the existing literature [9, 31]. Unfortunately, data on some psychosocial ACEs (e.g. witnessing domestic violence, living in an unsafe neighbourhood, being bullied, sibling death, and physical/emotional/sexual abuse) were not collected. While retrospective data existed on parental maltreatment and overprotection/affection, we chose to not use this due to the highly subjective nature of the former and high missingness of the latter [19].

Conclusions and implications for public health

ACEs including parental divorce/separation, residential instability, parental psychiatric illness, parental physical illness, childhood physical illness and childhood psychiatric illness were associated with a progressively increased burden of multimorbidity through adulthood into early old age. This largely held true after controlling for early life socioeconomic factors. Experiencing a higher total number of psychosocial and parental health ACEs was associated with increased and earlier and more rapid development of multimorbidity. While ACE-multimorbidity estimates are small in size on average at the individual level, they should be considered significant at the population level and considered in future public health policies.

The independent, long-lasting effects of ACEs on the accumulation of multimorbidity in later life emphasise the need for interventions starting in childhood to ameliorate inequalities in healthy ageing. Indeed, psychosocial interventions have shown promise in mitigating HPA aberrations, although this needs confirmation with long-term follow-up [48]. Multimorbidity places an ever-increasing burden on healthcare provision [5]. Interventions aimed at reducing ACEs and early-life socioeconomic disadvantage might be expected to reduce the future burden of multimorbidity, in addition to wider social benefits.

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