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State care in childhood and adult mortality: a systematic review and meta-analysis of prospective cohort studies

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Summary

Background Removal from family of origin to state care can be a highly challenging childhood experience and is itself linked to an array of unfavourable outcomes in adult life. We aim to synthesise evidence on the risk of adult mortality in people with a history of state care in early life, and assess the association according to different contexts.

Methods In this systematic review and meta-analysis, we focused on four health outcomes hypothesised to be associated with exposure to early state care: total mortality, cardiovascular disease, cancer, and suicide. We searched the electronic databases PubMed and Embase from inception to Jan 21, 2022, for studies fulfilling the following criteria: it was a prospective study in which the assessment of care was made up to 18 years of age; it included an unexposed comparator group; the focus of the study was temporary out-of-home care and not adoption; mortality surveillance was extended into adulthood; standard estimates of association (eg, relative risk, odds ratios, or hazard ratios) and variance (eg, CIs and SE) were provided; the study appeared in a peer-reviewed journal; and the study was published in English. An adapted Cochrane Risk of Bias Tool was used to assess study quality. We extracted estimates of association and variance from qualifying studies and augmented these findings with analyses of unpublished data from individual participants in two UK birth cohorts—ie, the 1958 and 1970 studies (total n=21 936). We computed hazard ratios with accompanying 95% CIs for care and each health outcome separately for each study, and then pooled the results using a random-effects meta-analysis. This review is registered at PROSPERO, CRD42021254665.

Findings We identified 210 potentially eligible published articles, of which 14 met our inclusion criteria (two studies were unpublished). Of 3 223 580 individuals drawn from 13 studies, those who were exposed to care in childhood had twice the risk of total mortality in adulthood relative to those without a history of care in childhood (summary risk ratio 2.21 [95% CI 1.62–3.02]), with study-specific estimates varying between 1.04 and 5.77 ($I^2=98%$). Despite some attenuation, this association remained following adjustment for other measures of early-life adversity; extended into middle and older age; was stronger in higher-quality studies; and was of equal magnitude according to sex, geographical region, and birth year. There was some suggestion of sensitive periods of exposure to care, whereby individuals who entered state care for the first time in adolescence (2.47 [0.98–6.52]) had greater rates of mortality than those doing so early in the life course (1.75 [1.25–2.45]). In four studies including 534 890 people, children in care had more than three times the risk of completed suicide in adulthood relative to their unexposed peers (3.35 [2.41–4.68]), with study-specific estimates ranging between 2.42 and 5.85 ($I^2=72%$). The magnitude of this association was weaker after adjustment for multiple covariates; in men than in women; and in lower-quality studies.

Interpretation Our results for adult mortality suggest child protection systems, social policy, and health services following care graduation are insufficient to mitigate the adverse experiences that might have preceded placement into care and those that might accompany it.

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Introduction

Early life is regarded as a key period of neurobiological, psychological, social, and physical development.^{1,2} There is growing evidence that pre-adult adverse experiences might have long-term implications for health.³ Adversity in this context does not only comprise material deprivation⁴ but also stressful family dynamics (eg, family illness, including alcoholism), loss or the threat thereof (eg, parental separation, including incarceration), and maltreatment (eg, sexual and psychological abuse). Of these factors, removal from family of origin to placement

in the care of the state might be a particularly influential early-life experience.⁵

Children in state care—also known as out-of-home care, public care, being looked after, or substitute care—have been temporarily transferred to alternative accommodation owing to problematic circumstances at home, the inability of the parents to provide a safe environment, or their own anti-social behaviour, among other reasons.⁶ In recent years, there has been a rise in the prevalence of looked-after children in several countries, such as the USA and the UK;^{7–9} although estimates vary

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Research in context

Evidence before this study

Exposure to state care during childhood has emerging links with an array of unfavourable social, psychological, and behavioural characteristics. Although this implicates care as a risk indicator for adult mortality, a search of electronic databases from inception to Jan 21, 2022, did not yield a published synthesis of the evidence base. In particular, there remains little clarity regarding the role of confounding factors; the influence of the timing of care entry on mortality; whether the impact of care extended into middle age and beyond; and, as has been hypothesised, whether women with experience of family disruption, such as being placed in care, have a greater vulnerability to its deleterious health impacts than men.

Added value of this study

Drawing on 12 published and two unpublished prospective cohort studies, this systematic review and meta-analysis found that exposure to state care in childhood was associated with a doubling in the risk of total mortality. This association, although attenuated, remained following statistical adjustment for other risk factors in early life, including other adversities; extended into later adulthood such that it did not exclusively occur immediately following graduation from care; was stronger in higher-quality studies; and was of equal magnitude in men and women. There was also a suggestion of

sensitive periods of exposure to care, whereby individuals who entered state care for the first time in adolescence had greater rates of total mortality in adulthood than those doing so in childhood. The magnitude of the association between childhood care and adult risk of death by suicide was somewhat higher than that for total mortality. Again, this association was not completely explained by other risk factors in early life, and the magnitude was somewhat stronger in higher-quality studies and in women relative to men. There were too few studies to explore the effect of care on other causes of mortality, such as cardiovascular disease and cancer.

Implications of all the available evidence

The steady rise in the prevalence of children in state care in several countries brings into sharp focus the need to understand its potential health consequences. The present synthesis of existing evidence found that the excess risk of adult mortality in this group was not attributable to other measures of adversity captured in included studies, suggesting that, in the countries represented (ie, Canada, the USA, western Europe, and Australia), child protection systems, social policy, and health services following care graduation are insufficient to mitigate the adverse experiences that might have preceded placement into care and those that might accompany it.

by country and ethnicity, the prevalence might be as high as 13%.¹⁰

The decision to transfer to state care is predicated upon providing a better opportunity for the child to flourish. However, there is growing evidence that these children continue to be disadvantaged in several ways. In the short term, children in substitute care tend to perform less well academically,^{11,12} are more prone to permanent school exclusion,¹³ are more likely to engage in illicit drug taking,¹⁴ and have a higher prevalence of a range of psychiatric disorders, than their unexposed peers.¹⁵ As looked-after children transition to independent living in early adulthood, there is a suggestion that mental health problems continue,^{13,16,17} in addition to there being an increased likelihood of socioeconomic disadvantage,^{17,18} homelessness,¹⁹ and engagement in harmful health behaviours.^{17,20} The burden of risk ascribed to these unfavourable characteristics raises the possibility that exposure to state care in childhood might be associated with an elevated occurrence of physical health problems later in the life course, most obviously in terms of total mortality, cardiovascular disease, and selected cancers.^{21–24} Furthermore, a correlation between childhood care exposure and risk factors for suicide—eg, mental health problems,¹³ substance use,²⁵ and unemployment²⁶—has been documented. Although some studies have found that placement into care is associated with an increased risk of total and suicide mortality, these are not universal findings.^{10,27–30}

To the best of our knowledge, there is no comprehensive and systematic synthesis of the evidence base for the potential effect of pre-adult care on later death, illness, and injury. As such, at least two fundamental issues require clarification. First, the extent to which any elevation in rates of adult mortality can be ascribed to care itself, as opposed to the circumstances that preceded it, is not well understood. Additional to this issue of confounding is the role of the timing of being taken into care in adult health. The notion of sensitive periods in this context posits that entering care in adolescence, as opposed to infancy when the perception of personal circumstances is less acute, could have the most pronounced effect as reflected by an elevated risk of ill health.³¹ Accordingly, the aims of this study were to, first, conduct a systematic review of all published findings on childhood state care and adult mortality; second, address any evidence gaps revealed by this process using individual participant analyses of unpublished (raw) data from long-term mortality surveillance of participants in two UK birth cohort studies; and third, aggregate both strands of results using a meta-analytical approach.

Methods

Search strategy, study selection, and results extraction for the published studies

This systematic review and meta-analysis was prospectively registered with the PROSPERO database (CRD42021254665).³² We followed the Meta-analysis of

Observational Studies in Epidemiology (MOOSE) guidelines³³ for the conduct of the review, and the Preferred Reporting Items for Systematic Reviews and Meta-analyses of Individual Participant Data (PRISMA-IPD) guidelines for preparing the manuscript.³⁴

The search strategy focused on four health outcomes hypothesised to be linked to exposure to early state care: total mortality, cardiovascular disease (including stroke and coronary heart disease), cancer (including specific malignancies), and suicide. We did a systematic search of the literature using the PubMed (MEDLINE) and Embase databases between their inception in 1966 and Jan 21, 2022. Without applying any restrictions, we used the terms “out-of-home care”, “out of home care”, “foster care”, “public care”, “looked-after-children”, and “looked after children” for the exposure; and “mortality”, “death”, “suicide”, “cardiovascular”, “stroke”, “heart disease”, and “cancer” for the outcomes. Additionally, we scrutinised the reference sections of retrieved publications for other reports. The literature search and article screening were independently done by GDB and PF. There were no substantial disagreements over inclusion.

We included a published paper provided it fulfilled all the following criteria: it was a prospective study in which the assessment of care was made up to 18 years of age; it included an unexposed comparator group; the focus of the study was temporary out-of-home care and not adoption; mortality surveillance was extended into adulthood; standard estimates of association (eg, relative risk, odds ratios, or hazard ratios) and variance (eg, CIs and SE) were provided; the study appeared in a peer-reviewed journal; and the study was published in English. When there were multiple reports featuring the same material (eg, Stockholm Birth Cohort study^{35–37}), the publication with the longest duration of follow-up, and therefore the greatest number of health events, was included on the basis that this offered the greatest statistical power.

When available, we extracted and tabulated a range of characteristics from each retrieved paper, including the name of the lead author, publication year, country of sample population, number of participants, year of birth of participants, number of participants exposed to childhood care, number of deaths, and effect estimates for both minimally adjusted and multivariable-adjusted results. Where clarification regarding results or additional analyses were required, we attempted to contact the authors with contrasting levels of success. Study data for all included papers were extracted by one reviewer (GDB) and for a random selection by a second (PF).

Individual participant data for the unpublished studies

We used individual participant data from two sources in the UK: the 1958 birth cohort study (also known as the National Child Development Study) and the 1970 birth

cohort study. Described in detail elsewhere,^{38,39} these are well established, ongoing, closed, geographically representative, prospective birth cohort studies, in which the investigators sampled all livebirths occurring during a single week in 1958 (17 634 babies) and 1970 (17 287) in the contiguous countries of the UK. Data collection was approved by the National Health Service Research Ethics Committee for the 1958 study,³⁸ and the London Central Research Ethics Committee for the 1970 study.³⁹ With the present data being anonymised, permissions for analyses were not required.

Involvement in state care by the study member was reported by the parent or carer in the first three childhood surveys and referenced all of the preceding period: ages 7, 11, and 16 years in the 1958 cohort study,^{17,40} and ages 5, 10, and 16 years in the 1970 cohort study.⁶ We created a binary variable denoting care mentioned at any of the three data collection points (yes or no). In basic analyses, we used the standard covariates of sex, parental socioeconomic position (as indexed by occupational social class), and mother’s age at birth of participant. Additional adjustments were made for adverse childhood experience (yes or no) as denoted by the presence of any of the following characteristics: physical neglect; child’s or family’s contact with the prison service; parental separation due to divorce, death, or other; family history of mental illness; family history of substance abuse; childhood disability; and psychological distress as measured at age 7 years in the 1958 cohort study using the teacher-rated Bristol Social Adjustment Guide,⁴¹ and at age 5 years in the 1970 cohort study using the Rutter Behaviour Scale.⁴² Vital status was derived from official death records of the National Health Service Central Register,⁴³ fieldwork, or cohort maintenance (<1% of deaths). Participants in the 1958 cohort were followed up for 42 years for total (all-cause) mortality, from March, 1974 (age 16 years), until December, 2016 (age 58 years), whereas participants in the 1970 cohort were followed up for 27 years, from March, 1986 (age 16 years), until December, 2013 (age 43 years).

Quality assessment

We used an adapted version of the Cochrane Risk of Bias Tool for cohort studies to assess study quality.⁴⁴ Comprising six domains of appraisal, including the exposure, confounding variables, outcome, and adequacy of the follow-up (appendix p 2), we regarded the quality of the study as high if the total score was at least 21 (maximum 24). One author (GDB) evaluated the quality of each study included in the review and scores were independently corroborated for a random 50% sample by another (PF).

See Online for appendix

Statistical analysis

In analyses of individuals without missing data in the 1958 and 1970 birth cohort studies, we ascertained whether the proportional hazards assumption had been

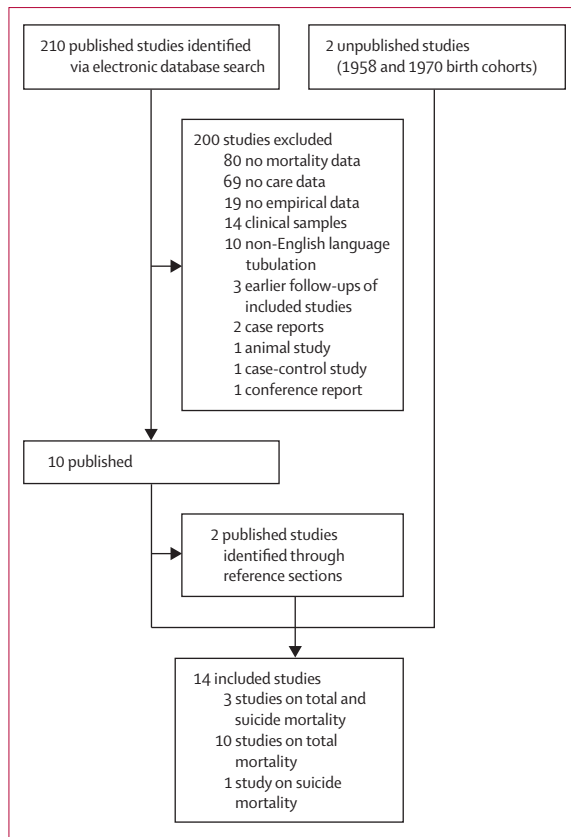


Figure 1: Study selection

violated by computing Schoenfeld residuals.⁴⁵ With no strong evidence that this was the case, we computed hazard ratios with accompanying 95% CIs for care and total (or suicide) mortality separately for each study. Next, we pooled the results from the analyses of raw data alongside published study-specific estimates using a random-effects meta-analysis,⁴⁶ an approach that incorporates the heterogeneity of effects in the computation of their aggregation. An I^2 statistic was computed to summarise the heterogeneity in estimates across studies. Lastly, we explored the magnitude of the care–mortality association according to different contexts, including sex, study quality, region, and complexity of covariate adjustment. All analyses were conducted using Stata, version 15.

Role of the funding source

There was no funding source for this study.

Results

Our database search identified 210 published studies; 14 met our inclusion criteria, two of which were unpublished (figure 1). There was a sufficiently large number of studies reporting on the association between care and total mortality (11 published reports^{10,27–29,47–53} and two unpublished datasets^{38,39}) and the association between

care and suicide mortality (four published reports^{29,30,47,48}) to facilitate meta-analyses, whereas the frequency of the presentation of other outcomes, such as cancer²⁹ and vascular disease,¹⁰ was too low for a meta-analysis to be viable.

Of the 13 cohort studies featured in analyses of total mortality, four were from Finland,^{10,28,48,53} three were from Sweden,^{47,49,51} three were from the UK⁵² (of which two were unpublished^{38,39}), one was from the USA,⁵⁰ one was from Canada,²⁹ and one was from Australia²⁷ (table). These studies comprised 15 analytical independent samples and 3 223 580 individuals (sample size range: 1242 to 989 871)^{49,50} born across eight decades (1933–2003).^{27,28} The maximum age at follow-up was 78 years.²⁸ Two studies used participants who were part of a wartime intercountry foster-care programme,^{10,53} whereas the remainder were based on within-country movement. Seven studies were generated solely from linkage of participants to population registers,^{27–29,47–49,53} with a further six also involving field work (four published^{10,50–52} and two unpublished). Where the number of people in the study sample with a history of care during childhood was reported alongside the population at risk, the prevalence ranged between 1·6%⁵² and 13·4%.¹⁰

Although heterogeneity was high across individual studies ($I^2=98%$; $p<0\cdot001$)—study-specific risk ratios varied between 1·04 and 5·77—all risk ratios indicated elevated rates of mortality in adults who, as children, had experienced care (figure 2). However, for two studies (three samples) from Finland,^{10,28} the increased risk attributable to care exposure was marginal. Pooling of effect estimates revealed that adults with experience of previous state care had around twice the risk of mortality than those without (risk ratio 2·21 [95% CI 1·62–3·02]).

An association between early-life care and adult mortality that was significant at conventional levels persisted across all population subgroups (figure 3). Although mortality rates were similarly elevated by sex, region, and exposure ascertainment, there were more marked differentials for high-quality studies (3·13 [2·35–4·18]) than for low-quality studies (1·76 [1·36–2·27]), and for those with short-term follow-up (3·07 [2·11–4·48]) than for those with long-term follow-up (1·62 [1·17–2·25]). The greatest differential in effect estimate—and the only null result—was apparent for studies that sampled war-era evacuees (1·06 [0·99–1·14]) compared with those that did not (2·69 [2·06–3·51]). This finding also explains the lack of a care–death association in study members born in 1933–52, which is entirely comprised of these two evacuee-based studies.^{10,28}

We also carried out analyses according to age at entry to the care system. In comparison with the no-care group, the magnitude of the association with death was lowest among adults who, as children, had been placed in care in early childhood (1·75 [1·25–2·45]) relative to those placed in care in middle (2·75 [1·52–4·96]) or late

	Year of birth	Number of participants	Proportion of women (%)	Age at baseline (years)	Proportion in care (%)	Age at follow-up (years)	Total deaths	Suicides
Unpublished studies								
1958 birth cohort (UK)	1958	17 670	49%	16	4.5%	16–58	1101	0
1970 birth cohort (UK)	1970	16 418	48%	16	3.7%	16–43	357	0
Published studies								
Thompson and Newman (Canada, 1995) ²⁹	1962–80	20 471	NR	1–18	NR	18–25	29	24
Vinnerljung and Ribe (Sweden, 2001) ⁴⁷	1969–76	13 100	NR	1–12	NR	19–26	103	26
Kalland et al (Finland, 2001) ⁴⁸	1973–97	13 371	NR	0–18	NR	18–24	68	35
Hjern et al (Sweden, 2004) ⁴⁹	1973–82	989 871	NR	13–17	NR	13–27	2365	0
Alastalo et al (Finland, 2012) ³⁰	1934–44	12 915	47%	2–11	13.4%	37–69	1640	0
Juon et al (USA, 2014) ⁵⁰	1960	1242	51%	6–7	1.9%	19–44	87	0
Santavirta (Finland, 2014) ²⁸	1933–44	66 053	49%	2–11	3.0%	38–78	16 294	0
Wall-Wieler et al (Sweden, 2018) ³⁰	1973–80	487 948	53%	1–18	2.9% (women); 2.6% (men)	18–40	..	130 women and 264 men
Jackisch et al (Sweden, 2019) ⁵¹	1953	14 004	49%	0–18	9.0%	19–65	1354	0
Murray et al (UK, 2020) ⁵²	1953–2001	353 601	49%	1–18	1.6%	18–60	8814	0
Segal et al (Australia, 2021) ²⁷	1986–2003	331 254	49%	0–16	2.0%	16–33	980	0
Sariaslan et al (Finland, 2022) ⁵³	1986–2000	885 662	49%	0–15	3.4%	15–32	3901	0

Studies are ordered according to ascending publication year. In studies where data are not reported, the authors of the study compared mortality rates in a care group with the general population (the unexposed) by computing a standardised mortality rate. The number of events and people at risk in the latter group are typically not given. Hjern and colleagues (2004)⁴⁹ also reported on suicide mortality but their study is superseded by the study by Wall-Wieler and colleagues (2018),³⁰ which is based on the same sample but with more events owing to the longer duration of follow-up. NR=not reported.

Table: Characteristics of included studies

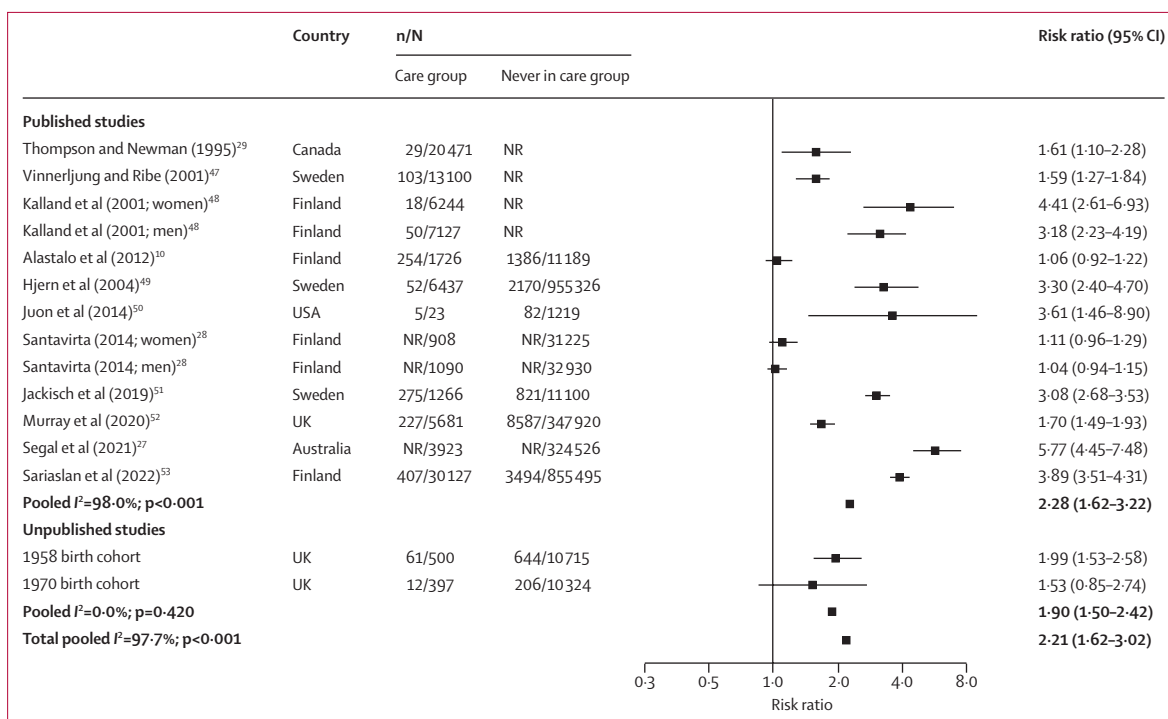


Figure 2: Association between state care in childhood and total mortality in adulthood

Studies are ordered according to ascending publication year. Risk ratios are minimally adjusted, ranging between zero and four covariates (appendix p 6). NR=not reported.

childhood (2.47 [0.98–6.52]). Study-specific results according to each of the 11 characteristics depicted in figure 3 are presented in the appendix (pp 3–13).

In addition, control for an array of early-life covariates led to a degree of attenuation of the care–death association (1.72 [1.21–2.44]) relative to minimal adjustment (2.21

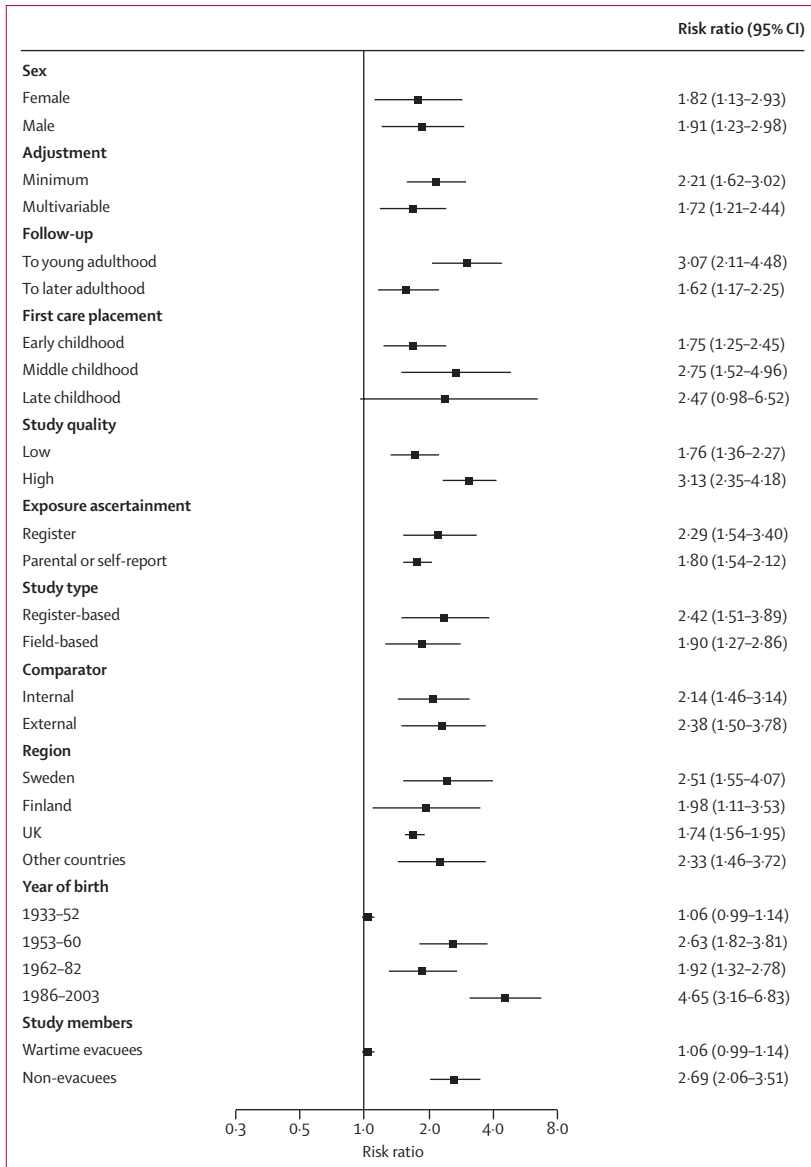


Figure 3: Association between public care in childhood and total mortality in adulthood, according to context

For analyses of follow-up, young adulthood is broadly denoted by ages 18–31 years, and later adulthood by up to age 65 years. For first care placement, early childhood is broadly denoted by ages 0–6 years, middle childhood by ages 7–12 years, and late childhood by ages 13–19 years. There is variation across studies in the variables comprising minimal and multivariable adjustment. Gao et al (2017),⁵⁴ based on an earlier follow-up of the Jakisch et al (2019)⁵¹ sample, was included in analyses of age at care placement.

[1.62–3.02]; figure 3). With the several published reports on care and total mortality providing only rudimentary statistical control (largely age and sex), we used the 1958 and 1970 birth cohort studies to explore in greater detail the effect of individual and collective control for adverse childhood experiences other than care, such as childhood disability or poor mental health, and parental health problems (appendix p 14). Relative to a comparator model (1958 study: 1.99 [1.53–2.58]; 1970 study: 1.53 [0.85–2.74]) in which effect estimates were adjusted for

parental socioeconomic occupational social class, mother’s age at birth, and sex (adjustment for age was made indirectly given all study members were born in the same week), we found that taking into account adversity and psychological distress led to some attenuation of the care–death association in the 1958 birth cohort only, whereas adjustment for disability had no impact on the risk ratios in either study. Multiple adjustment for these covariates led to an attenuation of almost 50% in the 1958 study (1.54 [1.17–2.03]), whereas the 1970 study (1.46 [0.81–2.64]) was largely robust to such statistical treatment. In related analyses using these data, we also examined if the strength of the association between care and later mortality was equivalent to that for individuals who had a disadvantaged socioeconomic background (as indexed by parental occupational social class) but no experience of care (appendix p 15). Although statistical precision was hampered by a low number of deaths in the 1970 cohort, findings from both studies suggested a stronger association between care and mortality than was apparent for early-life poverty. In separate analyses of the relative effect sizes for care and any other childhood adversity in relation to all-cause mortality, a higher magnitude was also apparent for care (appendix p 16).

Results for exposure to early-life state care and suicide mortality in adult life were available in four published cohort studies (six analytical samples; figure 4);^{29,30,47,48} cause-specific death data are not publicly available for the 1958 and 1970 birth cohorts. One study was drawn from Canada,²⁹ one from Finland,⁴⁸ and a further two from Sweden (table).^{30,47} These studies comprised 534 890 individuals (sample size range: 13 100–487 948)^{30,47} born in 1962–97,^{29,48} the maximum age at follow-up being 40 years.³⁰ In all studies, care was associated with increased rates of death by suicide and effect estimates were less heterogeneous ($I^2=72\%$; $p=0.003$)—ranging between 2.42 and 5.85—than those apparent in analyses of total mortality. The pooled risk ratio indicated that people with experience of care in childhood have a risk of death by suicide in adulthood that is more than three times that of unexposed people (3.35 [2.41–4.68]).

With there being fewer studies of suicide risk, opportunities for analyses according to context were diminished; the link between care and death by suicide was typically evident across population subgroups (figure 5). However, it was stronger in women (5.34 [3.64–7.82]) than in men (3.37 [1.79–6.37]), and in high-quality studies (5.08 [3.93–6.56]) than in low-quality studies (2.51 [2.00–3.15]). There was also an indication that adjustment for a wider array of covariates (1.70 [0.85–3.43]) yielded considerable attenuation in comparison to more basic efforts (5.08 [3.93–6.56]).

Discussion

Children with experience of state care had double the risk of total mortality and three times the risk of suicide in adulthood than did unexposed children. The association

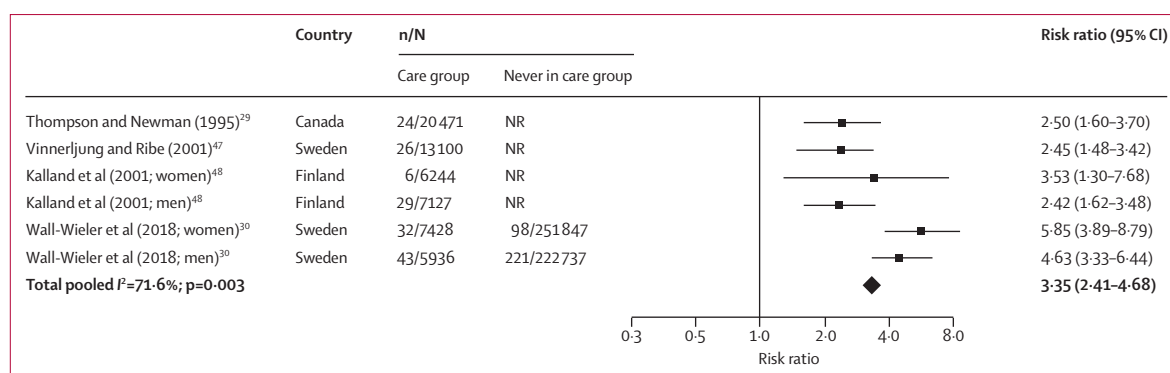


Figure 4: Association between public care in childhood and suicide mortality by middle age

Wall-Wieler et al (2018; baseline 1973–80)³⁰ and Vinnerljung and Ribe (2001; 1969–76)⁴⁷ study samples are partially overlapping. In the sensitivity analysis, the pooled effect was largely unchanged after omission of the latter sample (3.59 [2.46–5.22]). NR=not reported.

between care and total mortality was apparent into later adulthood, such that it did not exclusively occur during the period immediately following care graduation; it was also of higher magnitude in higher-quality studies and of similar strength in men and women. Although attenuated, this association remained following statistical adjustment for other early-life characteristics known to be related to both entry into care and risk of mortality in later life.^{42,55} Importantly, in selected published studies^{27,51} and also individual participant analyses of the UK birth cohort studies, these covariates included an array of indicators of early-life adversity additional to care, including physical neglect, parental contact with the prison service, parental separation due to divorce or death, a family history of mental illness or substance abuse, and poor socioeconomic circumstances. The approximate doubling of risk of total mortality for people with pre-adult exposure to care is broadly commensurate with that apparent for early-life socioeconomic disadvantage,⁵⁶ poor social engagement,⁵⁷ low mental ability,^{58,59} psychological distress,^{42,60} and obesity.⁶¹

Although based on analyses of fewer studies, the magnitude of the association between childhood care and adult risk of death by suicide was higher than that with total mortality. This association was also not completely explained by other measured early-life covariates. Our overall results for care and death by suicide accord with those from studies of attempted suicide.^{62–64} Given that suicide was often a secondary outcome in retrieved publications owing to the lower number of events, as well as there being a general paucity of studies, there was typically insufficient reporting by context to facilitate analyses, including for age at follow-up, age at entry to substitute care, and care era. However, there was a suggestion of a weaker care–suicide association in men, which supports findings for childhood adversity in relation to later serious mental health illness,⁶⁵ although this is not a universal observation.⁶⁶ The tripling of risk in the suicide analyses suggest that the overall result for total mortality is, in

part, being generated by a stronger effect for suicide than for other causes of death in the included studies, which will include chronic illnesses such as cancer and cardiovascular disease. As indicated, too few studies offered results for these other mortality outcomes to facilitate aggregation.

Rarely for epidemiological investigations, there was some suggestion of sensitive periods of exposure, whereby individuals who entered state care for the first time later in childhood had greater rates of total mortality than those doing so earlier in the life course. It might be that the increased mortality risk apparent for adolescence care is, in fact, simply attributable to a more extended duration of exposure to a dysfunctional home environment. However, that several of the published studies controlled for childhood socioeconomic circumstances,^{27,51,52} and our own analyses of the two birth cohort studies took into account an array of early-life adversities (eg, physical neglect and a family history of mental illness or substance abuse), indicates that there might be some risk specifically ascribed to care experience. Imaging studies have revealed that there is a striking acceleration in brain growth during adolescence with marked development of both cortical and subcortical structures.⁶⁷ Perception of precarious personal circumstances will be more acute at these ages relative to, for instance, an individual being moved into care in infancy. Moreover, separation from family of origin later in childhood might also mean removal from the familiar social environments of school and neighbourhood, a change that might trigger adverse health behaviours such as illicit drug use and mental health problems.

That the link for substitute care to both total and suicide mortality did not appear to be fully explained by measured confounding variables implicates direct and indirect mechanisms. Indirect mechanisms include known links between care and unfavourable levels of future sociodemographic,²⁶ behavioural,²⁰ and health characteristics.^{13,16} A potential direct mechanism is the embodiment of the experience of state care, whereby

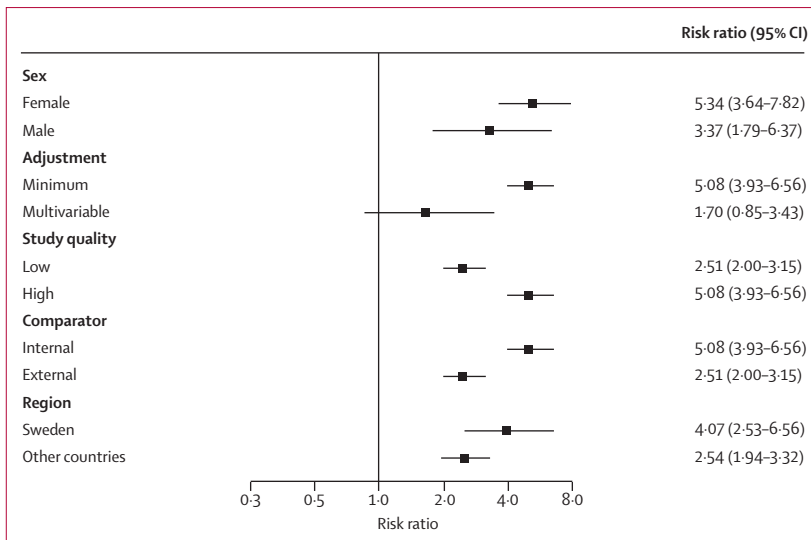


Figure 5: Association between public care in childhood and suicide mortality by middle age, according to context

In the minimally adjusted analyses, there was variability in the complexity of adjustment across studies, ranging from no adjustment³⁰ to age.^{29,47,48} In multivariable-adjusted analyses, the single study³⁰ in that group adjusted for age, education, residency, employment status, welfare, parental hospitalisation, and violence.

there is a biological response to this potentially chronic stressor that elevates mortality risk. Mediation by indicators of inflammatory, haemostatic, and metabolic function—known to be associated more broadly with early childhood adversity^{68,69}—could occur, although in recent analyses of two UK studies, there was no suggestion of an association between care and an array of such biomarkers.^{6,40} By contrast, as adults, childhood wartime evacuees had altered responsiveness of the hypothalamic–pituitary–adrenal axis—a system implicated in the stress response and the neurobiology of several mood disorders and functional illnesses—relative to their more geographically stable peers.⁷⁰ To further explore mediation by biological factors would require a study with data on care on the one hand, and mediators and mortality outcomes on the other. Although we are unaware of such data, as existing cohort studies mature, such analyses will become possible. In analyses of data from the Stockholm Birth Cohort Study,⁵⁴ socioeconomic and mental health factors appear to partially mediate the link between state care and total mortality.³⁶ An understanding of the role of other candidate mediators, including unhealthy behaviours (eg, smoking and heavy alcohol intake) given their associations with care²⁰ and trajectories of physical diseases and death,⁷¹ would be useful.

Although the present review has some strengths, including the use of unpublished individual-level data to complement the findings from published studies, interpretation of our findings inevitably requires consideration of various limitations. Firstly, a meta-analysis is only as methodologically robust as the studies it comprises; all results in the present review originate

from observational data and so raise concerns about unmeasured or residual confounding. As described, statistical adjustment for an array of confounding factors in individual participant analyses—multiple adversities, psychological distress, disability—attenuated the association between care and death by around 50% in the 1958 birth cohort study, but the association in the 1970 study held. There are some approaches that, in principle, have the capacity to further deal with the problem of confounding. One option would be an extension of these birth cohort studies included in the present review to those offering an even greater array of collateral data, including biological characteristics, with which to quantify the pathophysiological effect of state care. Although these studies exist,⁷² they have not yet yielded sufficient numbers of deaths to facilitate the same analyses as those conducted here. A further option is a natural experiment whereby the effect of changes in care policy on mortality, such as legislation to reduce the number of children being placed out of the home, are explored. An in-kind approach has been taken in extended mortality surveillance of Finnish children who, during World War 2, were evacuated into foster care in other ostensibly safer countries.^{10,28} Featured in this Article, the theoretical advantage of such studies is that these individuals were not subject to the family dysfunction that might necessitate care and, as such, these experiences cannot be confounding factors. However, there were socioeconomic differences according to evacuation status, whereby evacuees came from more disadvantaged circumstances than their geographically stable counterparts.¹⁰ More importantly, mortality surveillance in these studies did not commence until study members were aged between 27 and 38 years.¹⁰ With the peak incidence of suicide occurring in early adulthood,⁷³ a substantial number of such cases would have been missed. If suicide is largely generating the association between care and total mortality, as seems probable, this might explain the null result for care and total mortality in both studies.^{10,28}

Secondly, our meta-analysis featured only studies from Europe and North America, which means that extrapolation of our findings to other countries, particularly when care policies differ, is not possible. We only searched for English language publications. Although we are aware of very few birth cohort studies globally that are sufficiently mature and well characterised to examine the association between childhood state care and adult mortality, the two studies with individual participant data that we included are nonetheless based on a convenience sample, to the extent that they were already familiar to the authors,^{24,74} publicly available, and do not have an extended permissions process. It is of course possible that other unpublished data with the capacity to explore the present research question do exist. Thirdly, the characteristics of placement into state care in childhood, including type (foster care *vs* institution), duration, and stability, have been identified as being

potentially important in the context of adverse outcomes.⁷⁵ These data were not reported with sufficient frequency in the published studies to facilitate a meta-analysis, nor were they collected prospectively in the unpublished datasets. Fourthly, childhood protection and state care policies in several of the countries featured in this Article have evolved in recent years to provide better protection for this population. However, in analyses of total mortality, there was some suggestion of higher effect estimates in more contemporary cohorts. Relatedly, comprehensive health surveillance of contemporary children with care exposure continues to suggest multiple unfavourable outcomes that are consistent with earlier eras.⁵³ The potential importance of care era notwithstanding, the long-term impact of care policies from many decades ago on people currently in middle and older age should not be diminished. In studies using an external comparison group from the general population,^{29,47,48} this group would have contained individuals with care experience and, as such, cannot be regarded as being truly unexposed. Therefore, the lower risk ratios for care and mortality in those studies are likely to be an underestimation of the true effect. Lastly, either because the necessary data on ethnicity were not collected, or because the cohorts in question were not ethnically diverse even when representative of the general population (eg, the 1958 birth cohort study), we were not able to explore the impact, if any, of stratification of analyses by this characteristic.

In conclusion, our systematic review and meta-analysis showing excess rates of total and suicide mortality in children exposed to state care from the UK, Sweden, Finland, the USA, and Canada suggests child protection systems, social policy, and health services following care graduation are insufficient to mitigate the adverse experiences that might have preceded placement into care and those that might accompany it. These results add to an array of unfavourable social, psychological, and behavioural outcomes linked to state care in early life.

Contributors

GDB generated the idea for this work, conducted the literature search and data extraction, and drafted the manuscript. PF contributed to the literature search and data extraction, carried out the data analyses, prepared the figures and tables, and edited the manuscript. GDB and PF accessed and verified the data. MK edited the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

Individual participant data from the 1958 and 1970 birth cohort studies are freely available to download from the UK Data Archive (<https://ukdataservice.ac.uk/>).

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