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Child maltreatment, early life socioeconomic disadvantage and all-cause mortality in mid-adulthood: findings from a prospective British birth cohort

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3 Child maltreatment, early life socioeconomic disadvantage and all-cause mortality in mid-
4 adulthood: findings from a prospective British birth cohort
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Abstract

Objectives: Early-life adversities such as child maltreatment (neglect and abuse) and socioeconomic disadvantage have been associated with adult mortality. However, evidence is sparse for specific types of early-life adversity. We aimed to establish whether specific early-life adversities (i.e. different types of child maltreatment and socioeconomic disadvantage) were associated independently with all-cause mortality in mid-adulthood and to examine potential intermediary pathways.

Design: Prospective cohort study

Setting: 1958 British birth cohort: a longitudinal, population-based sample of individuals born in Great Britain during a single week in March 1958.

Participants: 9310 males and females with data on child maltreatment and mortality (44/45y to 58y).

Outcome measures: Mortality follow-up from 2002/3 to 2016 when participants were aged 44/45y to 58y. Death was ascertained via the NHS Central Register (N=296) or cohort maintenance activities (N=16).

Results: Prevalence of early-life adversities ranged from 1.6% (sexual abuse) to 11% (psychological abuse). Several, but not all, early-life adversities were associated with increased risk of premature death, independent of covariates and other adversities; adjusted hazard ratios were 2.64(95%CI:1.52,4.59) for sexual abuse, 1.93(1.45,2.58) for socioeconomic disadvantage, 1.73(1.11,2.71) for physical abuse and 1.43(1.03,1.98) for neglect. After adjustment for covariates and other adversities, no associations with mortality were observed for psychological and witnessing abuse. Regarding potential intermediaries (including child-to-adult height growth, adult socioeconomic factors, behaviours, adiposity, mental health and cardio-metabolic

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3 markers), most associations attenuated after accounting for adult health behaviours (particularly
4 smoking). In addition, early-life socioeconomic disadvantage and neglect associations attenuated
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6 after accounting for adult socioeconomic factors. The association for sexual abuse and
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8 premature mortality was largely unaffected by potential intermediaries.
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13 **Conclusions:** Associations with premature mortality varied by type of early-life adversity:
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15 associations for sexual and physical abuse, neglect and socioeconomic disadvantage were
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17 independent of each other.
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25 **Keywords:** Birth cohort, Child maltreatment, Child abuse, Child neglect, Early-life socioeconomic
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27 disadvantage, Life course epidemiology, premature mortality
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34 Research Council and the Biotechnology and Biological Sciences Research Council
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Strengths and limitations of this study

- Data were from a large population-based cohort followed from birth, which allowed prospective ascertainment of child neglect, early-life socioeconomic disadvantage, important covariates and potential intermediary factors.
- Information on different types of child abuse was reported retrospectively at 45y.
- Data on cause-specific mortality was not available; however, mortality data was collected over 14 years.

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Background

Early-life adversities (ELAs) such as child maltreatment (neglect and abuse) and socioeconomic disadvantage are major public health issues[1,2]. These adversities are not uncommon, for example in the UK, approximately 9% of children and 22% of adolescents are estimated to experience neglect and/or physical, psychological or sexual abuse[3], and approximately 4.6 million children live in poverty[4]. Although a growing literature links child maltreatment (CM) to several poor health outcomes[5–7] in childhood through to older ages, evidence on links to mortality in adulthood is based primarily on adversity scores[8–11], which include other experiences such as living in a household with someone who has previously been imprisoned. While a more extensive literature including systemic reviews[2] demonstrates associations for early-life socioeconomic disadvantage, few studies[9] consider both CM and early-life socioeconomic disadvantage simultaneously in relation to mortality in adulthood. This omission is important because, although these ELAs are related, they represent distinct concepts[12] with potential differences in mortality risk. Clarifying the extent to which CM associates with later mortality independent of childhood socioeconomic background (and vice versa) would inform understanding of the role of different types of early-life exposures.

Moreover, it is possible that associations vary for *specific* types of CM and mortality in adulthood, given the differences reported for several outcomes in adulthood, including socioeconomic disadvantage[13,14], mental[15–17] and physical[6] health. Variation in associations with adult mortality cannot be determined from the sparse literature available to date for specific types of CM. One US study that combined multiple CMs together, found no risk of premature mortality although follow-up was limited to young adulthood[18]. In a second US study, associations were found in women but not men for physical and psychological abuse with all-cause mortality over 20-years of follow-up from ages 25y to 74y at baseline; information on sexual abuse and neglect was unavailable[9]. Thus, previous studies have investigated CM as a combined score of different types[9,18] or a limited number of types examined separately[9]. With such limitations of research conducted to date, possible differential associations for specific types of CM (i.e. their independence from each other as well as from early-life socioeconomic disadvantage) on mortality in adulthood are not well understood.

With respect to potential pathways from ELAs to adult mortality, it is well-established that, for example, CM is associated with detrimental factors in adulthood, including socioeconomic circumstances[13,14], risky health behaviors (e.g. smoking, drug misuse, problem drinking)[16,19,20], obesity[6], poor mental health[15–17] and poor physical health and development (e.g. child-to-adult height growth[21]). In turn,

1 these factors are linked to mortality[22–24]. Yet existing literature examining such intermediaries is
2 limited, particularly in relation to CM. Understanding pathways through which specific types of ELAs link to
3 mortality in mid-adulthood is important for developing appropriate interventions that aim to reduce
4 inequalities in mortality.
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8 Given current knowledge gaps, we aimed to establish in a general population sample followed from birth:
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10 (i) the extent to which CM and early-life socioeconomic disadvantage are associated with premature
11 mortality in midlife (from 44/45y to 58y) and whether associations vary by type of ELA; and (ii) whether
12 associations are explained by potential intermediaries including adult socioeconomic, behavioural,
13 adiposity, mental health, cardio-metabolic status and child-to-adult height growth.
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22 **Methods**

23 The 1958 British birth cohort consists of over 17,000 participants followed-up since birth during one week
24 of March 1958[25]. Respondents in mid-adulthood are broadly representative of the surviving cohort[26].
25 Ethical approval was given, including at 50y by the London Multicenter Research Ethics Committee and
26 participants gave informed consent at various sweeps. Of 11,971 invited at 44/45y, 9,310 completed
27 questions on CM and had information on mortality (44/45-58y) (see supplementary figure 1).
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34 *Early-life adversities:* Socioeconomic disadvantage was identified from prospectively recorded information
35 on father's occupation at the participant's birth. Those with a father in an unskilled manual occupation
36 were classified as disadvantaged. Child neglect was identified from prospectively collected information at
37 7y and 11y from interview questions to the child's mother and teacher. Eleven indicators of neglect were
38 selected to represent conventional definitions and were summed to create a score (range 0-11). A score ≥ 3
39 yielded a prevalence estimate in line with other UK estimates[1,3], and was used here to define child
40 neglect. Childhood (0-16y) physical, psychological, witnessing and sexual abuse was reported
41 retrospectively at 44/45y using a confidential computer-assisted data-entry questionnaire. Child neglect
42 and abuse measures have been used in several previous studies that, reassuringly, provide extensive
43 evidence of construct validity[27]. Details of all ELAs are given in Table 1.
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56 *All-cause mortality:* Information on deaths between 2002/3 and end of 2016 was ascertained from a
57 variety of sources, mostly (N=296) through receipt of death certificates (including date of death) from the
58 National Health Service Central Register. Information from relatives or close friends during survey
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activities/cohort maintenance allowed identification of 16 further deaths (details in Table 2 footnotes).

Cause-specific data were not available.

Covariates: were selected a-priori. All were prospectively recorded, including maternal age at birth, birthweight (adjusted for gestational age), birth order and 7y physical or cognitive impairment. Additional covariates for CM analyses included social class at birth and household factors (amenities, tenure and crowding) at 7y (details in Table 3 footnotes). Birthweight was ascertained from clinical records, parents reported all other factors.

Potential mid-adult intermediary factors: were selected based on established associations with both ELAs and premature mortality. Details of included factors are given in Table 4 footnotes, i.e. for adult (i) socioeconomic factors: social class and educational qualifications, (ii) behavioural factors: smoking, problem drinking and illegal drugs use in the last 12 months; (iii) adiposity: obesity and waist-hip ratio; (iv) mental health; (v) cardio-metabolic factors: glycated haemoglobin (HbA1c), triglycerides and low-density lipoprotein cholesterol (LDL-c), all adjusted for medications, and (vi) child-to-adult height trajectories. Cardio-metabolic factors, height, weight, hip and waist were measured by trained professionals; other factors were self-reported. Most considered intermediaries were associated with mortality in this cohort (Table S1).

Statistical analysis

Cox proportional hazard models were used to estimate hazard ratios and 95% confidence intervals (HR(95%CI)) for associations between each type of ELA and mortality. Survival time included the time from completion of the 44/45y questionnaire to the date of death, censoring (last date of contact) or the end of the study period (December 2016), whichever came first. Schoenfeld residuals were examined to test the assumption of proportional hazards for covariates and potential intermediaries; none violated the assumption (p -values ≥ 0.12).

We examined associations between each type of ELA and mortality in separate analyses for men and women and also tested interactions with sex in analyses of both sexes combined. There was little evidence of effect modification, hence in a first level of analyses we adjusted for sex (model 1). Second, to assess whether associations were independent of other early-life factors, we additionally adjusted for covariates listed above (model 2). Third, because different types of ELAs often cluster[28], we assessed two-way

1 correlations between examined ELAs. Most ELAs were weakly or only modestly correlated (phi coefficient
2 <0.50). Therefore, in model 3, we adjusted for all types of ELA simultaneously. To assess the role of
3 potential intermediaries (socioeconomic, behavioural, adiposity, mental health, cardio-metabolic factors
4 and child-to-adult height trajectories) in explaining ELA—mortality associations, we further adjusted model
5 3 for each potential intermediary separately.
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10 In sensitivity analyses, we checked whether restricting the sample to those completing the CM questions at
11 44/45y affected results, by repeating analyses using the larger sample available for child neglect and
12 socioeconomic disadvantage (N=15,092). Survival time included the time from completion of the 11y
13 survey to the date of death, censoring or the end of the study period, whichever came first. Main findings
14 were largely unaltered (Table S2) and we present findings for ELAs using the sample with complete data on
15 CM at 44/45y (N= 9,310). As an additional check on the independence of associations for different types of
16 ELAs from model 3, we examined associations with mortality for groups with only one specific type of ELA
17 vs no ELA. Findings were broadly similar (albeit with wider confidence intervals) to main results from
18 model 3 (Table S3).
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28 Missing data ranged from 0.3% (social class at birth) to 20.9% (LDL-c). Data loss was minimized, by
29 imputing missing data using multiple imputation chained equations. Imputation models included all model
30 variables and main predictors of missingness[26]. Regression analyses were run across 20 imputed datasets
31 and overall estimates obtained. Imputed results were similar to those obtained using observed values; the
32 former are presented.
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37 38 **Patient and public involvement**

39 Patients and the public were not involved in the design of the study, or in the interpretation or writing up
40 of the manuscript.
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45 46 **Results**

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48 The prevalence of ELAs varied from 1.6% (sexual abuse) to 11% (psychological abuse) with 10% classified as
49 socioeconomically disadvantaged in early-life (Table 2). The majority of participants reported no ELA (71%)
50 with 19% reporting one and 10% reporting two or more types of ELA. Between 44/45y and 58y, 3.4% of the
51 sample died (N=312).
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58 All types of ELA were associated with risk of death (44/45y-58y) after controlling for covariates (Model 2;
59 Table 3), for example HR for neglect was 1.49(1.08,2.07) and for physical abuse was 2.15(1.54,3.02). In
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1 models simultaneously adjusted for all other types of ELA (Model 3; Table 3) associations remained for all
2 except psychological and witnessing abuse, namely for neglect (HR:1.43(1.03,1.98)), physical abuse
3 (HR:1.73(1.11,2.71)), sexual abuse (HR:2.64(1.52,4.59)) and socioeconomic disadvantage
4 (HR:1.93(1.45,2.58)). The reduction in HRs between Models 2 and 3 was seen consistently for all ELAs,
5 although modest in some instances, for example, for early-life socioeconomic disadvantage the HR reduced
6 from 2.12(1.60,2.82) to 1.93(1.45,2.58) after adjusting for all CMs.
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14 In regard to potential intermediaries, associations between ELAs and death in mid-adulthood were largely
15 unaffected by adjustment for the range of factors examined (Table 4). However, most associations
16 attenuated after adjustment for adult health behaviors, for example HRs for physical abuse attenuated
17 from 1.73(1.11,2.71) to 1.50(0.96,2.34). Separate adjustment for each health behavior in turn showed a
18 predominant attenuating effect of smoking (Table S4). Additionally, associations for neglect and early-life
19 socioeconomic disadvantage attenuated after controlling for adult socioeconomic factors. For sexual abuse
20 and early-life socioeconomic disadvantage reductions in the strong associations with mortality in mid-
21 adulthood were negligible after accounting for intermediaries.
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31 Discussion

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33 In this large population-based study on different types of ELA and mortality in mid-adulthood we showed
34 several important findings. First, some ELAs, but not all, were associated with higher risk of premature
35 mortality in mid-adulthood. That is, findings varied by type of adversity. Child sexual abuse was strongly
36 associated with mortality with a 2.6 times higher risk of premature death in mid-adulthood, although it
37 was the least prevalent adversity. Whilst for early-life socioeconomic disadvantage, an approximate
38 doubling in risk of premature mortality applied to one in 10 of the population. For physical abuse and
39 neglect the estimated elevated risk of death was more modest (73% and 43% higher respectively), whereas
40 no associations were observed for psychological and witnessing abuse. Second, observed associations were
41 independent of potential confounding factors and the other adversities examined. Importantly, the specific
42 CM associations were mostly robust when accounting for early-life socioeconomic disadvantage and vice
43 versa. Third in relation to potential intermediaries, associations for all types of ELA attenuated after
44 controlling for adult health behaviours, in particular smoking. But, in some instances this attenuation was
45 minor, such that for sexual abuse the association was largely unaltered. Associations for early-life
46 socioeconomic disadvantage and neglect were also attenuated by adult socioeconomic factors. Whereas,
47 other examined intermediaries including cardio-metabolic markers did little to explain observed
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1 associations between specific CMs and mortality in mid-adulthood or for early-life socioeconomic
2 disadvantage.
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4 Our study has several notable strengths. The range of data available on different types of ELA facilitated
5 simultaneous analysis to inform on their independent effects. This is essential for investigating distinct
6 effects of CM on mortality, i.e. separate from those of socioeconomic background and also, in regard to
7 specific types of CMs. Inclusion of child neglect is particularly important given that it is often ignored in
8 research on CM[29]. A follow-up of approximately 14y is a further study strength, as is use of linked
9 mortality data, which is independent of ongoing study participation. Alongside the 14y mortality follow-up
10 there are advantages of using a single-age sample in reducing the range of possible causes of premature
11 death and related underlying pathways. However, study limitations are acknowledged. Ascertainment of
12 childhood maltreatment is not straightforward, with limitations noted for all methods[1], including those
13 used here. While, child neglect indicators were measured prospectively and included many aspects of the
14 conventional definition (e.g. failure to ensure a child's basic physical, emotional and educational needs),
15 there were some omissions (e.g. failure to ensure a child's safety). However, our measure uses information
16 from different sources (parents and teachers) which may reduce misclassification and rather than relying
17 on individual items, we used a composite score. Abuse by a parent was reported retrospectively and does
18 not include abuse by others possibly leading to an underestimate of prevalence. Nonetheless, prevalence
19 estimates of CM were generally in keeping with previous approximates for the UK[1,3]. An exception is
20 child sexual abuse where prevalence is low and estimates may be under-powered. Thus, we have used
21 both prospective (neglect and early-life socioeconomic disadvantage) and retrospective (abuse) measures
22 and we acknowledge that these may identify different groups of individuals[30]. However, it is reassuring
23 that a broad range of studies based on our measures of child neglect and abuse provide extensive evidence
24 of construct validity[27]. As with any long-term study, selection bias needs to be considered: by 45y, when
25 information was collected on child abuse, not all in the cohort had survived (6.7% had died); however over
26 half of these deaths had occurred before 7y (mostly in the first months of life)[26]. Selection bias may
27 affect findings reported here, but only if patterns of association with mortality differ in the surviving and
28 deceased populations. Relatedly, sensitivity analysis for child neglect and socioeconomic disadvantage in a
29 larger sample with longer follow-up from 11y suggests that study results are robust. Finally, cause-specific
30 mortality data was unavailable, restricting understanding of possible mechanisms linking ELAs to different
31 causes of premature death.
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57 Our main finding of varying associations for specific types of ELAs with risk of premature mortality is novel
58 largely because there is a dearth of literature that focuses on such variations. The large population and
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1 range of ELA measures examined in our study compared with two previous studies[9,18] has facilitated this
2 novel finding. Notably, in respect of CMs, we found that sexual and physical abuse and also neglect were
3 associated with elevated mortality in mid-adulthood in the 1958 birth cohort, but there were no
4 associations for psychological and witnessing abuse. The strong association for child sexual abuse, 2.6
5 times higher risk of premature mortality, is particularly important given the lack of evidence to date. One
6 previous study of CM and mortality did not include sexual abuse[9] and a second study considered sexual
7 abuse, physical abuse and neglect as a composite measure[18]; thus comparison with our findings for
8 specific types of CMs is not possible. The latter composite measure study reported no association with
9 mortality in young adulthood[18] whereas, our focus is on premature mortality for the age range 44/45y to
10 58y. The life-stage examined might explain discrepant findings i.e. associations with mortality were not
11 present in young adulthood[18] but may emerge by mid-adulthood as suggested here. Whereas for
12 physical abuse, our finding of a 73% higher risk of premature mortality is consistent with a previous
13 estimate of 58% higher risk of death for severe physical abuse in US women aged over 45y to 94y at the
14 end of follow-up[9]. This broad similarity in estimates for physical abuse was unexpected given the wider
15 age range of US study participants compared with our range 44/45y to 58y for mortality follow-up.
16 Nonetheless, discrepant with our findings was the lack of a physical abuse association with mortality in US
17 men[9], possibly due to known variations in main causes of death by age and gender[31]. For child neglect
18 we are unable to compare our finding of an independent association, with a 43% higher risk of premature
19 death in mid-adulthood, as neither of the two previous CM—mortality studies investigated this exposure
20 separately[9,18]. Thus, our finding provides new evidence for an important component of CM where
21 knowledge of long-term outcome is particularly sparse[29]. For witnessing abuse in childhood we are not
22 aware of any previous study with which to confirm our null finding in relation to premature mortality;
23 whereas for psychological abuse, findings for the US (weak association in women only[9]) and our UK (null)
24 study are discrepant. Possible reasons for discrepancies include differences in age at death, abuse
25 measurement and also, the extent to which other ELAs were taken into account. In respect of the latter, it
26 is noteworthy that our findings for specific CM associations with elevated mortality in mid-adulthood were
27 independent of other types of CM as well as childhood socioeconomic circumstances, highlighting the
28 potential for long-term harm associated with specific CMs.

29 A further novelty of our study is the demonstration that the early-life socioeconomic disadvantage
30 association of an approximate doubling in risk of premature all-cause mortality was independent of specific
31 CMs. While links between early-life socioeconomic disadvantage and mortality in adulthood are well-
32 established[2] and consistent with previous work in this cohort[32], few studies[9] consider both CM and
33 early-life socioeconomic disadvantage simultaneously. By suggesting that, notwithstanding the utility of

1 understanding the long-term impact of CM, the latter does not appear to undermine or explain the strong
2 and robust findings relating to childhood socioeconomic disadvantage our study adds new knowledge to
3 the literature. This is important in a policy context as the recent emphasis on adverse childhood
4 experiences may displace attention away from the early socioeconomic environment, as argued
5 elsewhere[12].
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10 Our findings suggest that adult smoking is a consistent and in some instances important explanatory factor
11 across observed associations. This was expected because smoking remains one of the most common
12 preventable causes of premature death in adults[33]; and, CM[6,20] and early-life socioeconomic
13 disadvantage[34] are associated with subsequent smoking patterns. Thus, interventions to reduce smoking
14 prevalence in specific ELA groups, either by reducing initiation or promoting cessation, might be
15 considered as possible strategies to lessen differences in premature mortality. Interestingly, while specific
16 CMs in this cohort were associated with the wide range of potential intermediary factors examined, these
17 did not appear to explain associations with mortality. In particular, the strong association for sexual abuse
18 was little explained by examined factors. Nonetheless, the potential intermediary factors considered here
19 may play a role in pathways to mortality at older ages. Whereas in relation to the focus here on premature
20 mortality, further insight into pathways from sexual abuse and other ELAs might be gained in future studies
21 of cause-specific mortality.
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33 In summary, our findings of independent associations for specific types of CM (sexual and physical abuse
34 and neglect) and early-life socioeconomic disadvantage with increased risk of premature mortality in mid-
35 adulthood highlight the long-lasting consequences of these ELAs. Smoking may be a particularly important
36 intermediary for physical abuse, neglect and early-life socioeconomic disadvantage associations; adult
37 socioeconomic factors may be an additional intermediary for neglect and early-life socioeconomic
38 disadvantage. These findings are relevant for public health because, for example, an estimated 3.1 million
39 adults in England and Wales reported being victims of sexual abuse before 16y[35] and approximately 4.6
40 million children in the UK live in poverty[4]. Moreover, relative child poverty is projected to rise from
41 29.7% to 36.6% in the UK between 2018 to 2022[36]. Given these stark projections and our study findings
42 of a strong relationship between childhood disadvantage and an early adult death, policies focused on
43 improving socioeconomic opportunities and assistance to adopt and maintain positive health behaviors for
44 individuals from disadvantaged backgrounds may reduce the burden of premature mortality.
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56 **Conclusions**

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1 In sum, our findings highlight the potential of specific types of CMs (i.e. sexual abuse, physical abuse and
2 neglect) for long-term harm. Notwithstanding this important finding, childhood socioeconomic
3 disadvantage associations with premature mortality are strong and not explained by associations with CM.
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10 Abbreviations

11 **CM:** Child maltreatment

12 **ELA:** Early-life adversity
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Contributors

CP and SMPP conceived the study. NTR carried out the analysis and drafted the paper. All authors contributed to the interpretation of data, revision of the manuscript, and approved its final version.

Declaration of interests

We declare no competing interests.

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Ethical declarations

Ethical approval was given, including at 50y by the London Multicenter Research Ethics Committee. Participants gave informed consent at various sweeps.

Data sharing statement Cohort data comply with ESRC data sharing policies, readers can access these data via the UK Data Archive at <http://www.data-archive.ac.uk/>

Table 1. Definition of early-life adversities (child maltreatment and early-life socioeconomic disadvantage) and representative variables from the 1958 British Birth cohort

	Definition ^a	1958 cohort variables	Age of ascertainment (method) ^b
Prospective report, birth to 11y			
Socioeconomic disadvantage (birth)		Based on father's occupation at birth ^c , using the Registrar General's Classification. Fathers with an unskilled manual occupation or households with no male head were classified as disadvantaged.	Birth (P)
Neglect ^d (7y & 11y)	Failure to meet a child's basic physical, emotional, medical/dental, or education need; failure to provide adequate nutrition, hygiene, or shelter; or failure to ensure a child's safety	- Child looks undernourished, scruffy or dirty	7 & 11y (T)
		- Mother never, or hardly ever takes child out ^e	7 & 11y (P)
		- Father never, or hardly ever takes child out ^e	7 & 11y (P)
		- Mother shows little or no interest in child's educational progress	7 & 11y (T)
		- Father shows little or no interest in child's educational progress	7 & 11y (T)
		-Mother and Father never, or hardly ever read to, or reads with the child	7y (P)
Retrospective report at 44/45y			
Physical abuse (0-16y)	Intentional use of physical force or implements against a child that results in, or has the potential to result in, physical injury.	I was physically abused by a parent – punched, kicked or hit or beaten with an object, or needed medical treatment	45y (S)
Psychological abuse ^f (0-16y)	Intentional behaviour that conveys to a child that s/he is worthless, flawed, unloved, unwanted, endangered, or valued only in meeting another's needs. <i>UK definition^g includes harmful (unintentional) parent-child interactions: 'the persistent emotional maltreatment of a child such as to cause severe and persistent adverse effects on the child's emotional development'</i>	- I was verbally abused by a parent (or parent-figure) - I suffered humiliation, ridicule, bullying or mental cruelty from a parent (or parent-figure) - Mother (or mother-figure) and father (or father-figure) were not at all affectionate	45y (S)
Witnessing abuse (0-16y)	Any incident of threatening behaviour, violence, or abuse (psychological, physical, sexual, financial, or emotional) between intimate partners or adult family members, irrespective of sex or sexuality	I witnessed physical or sexual abuse of others in my family	45y (S)
Sexual abuse (0-16y)	Any completed or attempted sexual act, sexual contact, or non-contact sexual interaction with a child by a caregiver	I was sexually abused by a parent (or parent-figure)	45y (S)

1 a: Gilbert et al. Lancet. 2009;373; b: (S): self-report; (T): teacher-report; (P): parent-report; c: socioeconomic position was classified as missing for fathers' who were unemployed or sick; d: Questions relating to child neglect at 7y and 11y
2 were answered by the child's teacher and mother (or father if the mother was unavailable). The 11 neglect indicators were summed to create a score (range 0–11); those scoring > 3 were classified as neglected (see text for further
3 details); e: e.g. walks, outings, picnics, visits, shopping; [†]In the 1958 cohort psychological abuse was defined as experiencing at least one of the three listed variables; g: Department for Education. Working together to safeguard children.
4 Her Majesty's Government, 2006.
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For peer review only

Table 2. Prevalence of early-life adversities and mortality^a in the 1958 British birth cohort (N=9310).

Early-life adversity	Population sample N ^b	Total cases N (%)	Males (%)	Females (%)	Deaths N (%)
Socioeconomic disadvantage	9033	925 (10.2)	9.63	10.8	61 (6.59)
Neglect ^c	8460	878 (10.4)	11.1	9.69	49 (5.58)
Physical abuse	9308	562 (6.04)	5.93	6.14	40 (7.12)
Psychological abuse	9310	1000 (10.7)	8.87	12.6	50 (5.00)
Witnessing abuse	9308	559 (6.01)	4.42	7.57	33 (5.90)
Sexual abuse	9308	149 (1.60)	0.48	2.71	17 (11.4)
Deaths 44/45y-58y ^a	9310	312 (3.35)	3.68	3.03	

^a Date of death was ascertained through receipt of death certificates to the Centre for Longitudinal Studies from the National Health Service Central Register (N=296) i.e. data missing for 16 individuals (see: National Child Development Study Deaths Dataset, 1958-2016 UK Data Service for details). Using survey/cohort maintenance data we determined if the deceased died between 45-50y (N=7), 50-55y (N=5) and 55-58y (N=4). Date of death was estimated as the mid-point between these ages.

^b N varies due to missing data.

^c Those with complete data on 6 or more of 11 neglect items.

Table 3: Hazard ratios (95% confidence intervals) for early-life adversities in relation to all-cause mortality in 1958 birth cohort participants aged 44/45y to 58y (N=9310).

	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Socioeconomic disadvantage	2.22(1.68,2.94)	2.12(1.60,2.82)	1.93(1.45,2.58)
Neglect	1.71(1.26,2.33)	1.49(1.08,2.07)	1.43(1.03,1.98)
Physical abuse	2.35(1.69, 3.27)	2.15(1.54,3.02)	1.73(1.11,2.71)
Psychological abuse	1.64(1.21,2.22)	1.55(1.14,2.10)	0.99(0.66,1.47)
Witnessing abuse	1.94(1.35,2.79)	1.81(1.26,2.62)	1.15(0.73,1.80)
Sexual abuse	4.12(2.51,6.77)	3.60(2.18,5.96)	2.64(1.52,4.59)

Model 1: Adjusted for sex only.

Model 2: Additionally adjusted for maternal age at birth, birthweight (adjusted for gestational age), birth order and 7y physical or cognitive impairment (yes/no). For associations with neglect, physical abuse, psychological abuse, witnessing abuse and sexual abuse (but not for early-life disadvantage) models additionally adjusted for social class at birth (or if missing, at 7y), 7y household amenities (sharing or lack a bathroom, lavatory or hot water), 7y housing tenure (owner/occupier, renter or other), and 7y household crowding (1+ person/room).

Model 3: Model 2 plus simultaneous adjustments for all other early-life adversities.

Table 4. Early-life adversities and risk of all-cause mortality (Hazard ratio (95% CI)) in adults (44/45y to 58y) adjusted for mid-adult (i) socioeconomic (ii) behavioural, (iii) adiposity, (iv) mental health, (v) cardio-metabolic factors and (vi) child-to-adult height trajectories^a.

	Socioeconomic disadvantage	Neglect	Physical abuse	Sexual abuse
Model 3	1.93(1.45,2.58)	1.43 (1.03,1.98)	1.73(1.11,2.71)	2.64(1.52,4.59)
+ mid-adult socioeconomic factors	1.82(1.36,2.43)	1.28(0.91,1.79)	1.74(1.11,2.73)	2.54(1.46,4.42)
+ mid-adult behavioural factors	1.75(1.31,2.34)	1.32(0.95,1.83)	1.50(0.96,2.34)	2.43(1.40,4.23)
+ mid-adult adiposity	1.90(1.42,2.53)	1.39(1.00,1.93)	1.75(1.12,2.73)	2.71(1.56,4.73)
+ mid-adult mental health	1.91(1.43,2.55)	1.37(0.99,1.91)	1.70(1.09,2.64)	2.54(1.46,4.42)
+ mid-adult cardio-metabolic factors	1.89(1.42,2.53)	1.39(1.00,1.93)	1.65(1.05,2.57)	2.71(1.56,4.72)
+ child-to-adult height trajectories	1.93(1.45,2.58)	1.42(1.03,1.98)	1.73(1.11,2.71)	2.63(1.51,4.58)

Model 3 (adjustments shown in Table 3 footnotes)

^a Models were adjusted for each intermediary group of factors separately (not simultaneously). Socioeconomic factors include: 33y social class (professional/managerial, skilled non-manual, skilled manual and partly skilled/unskilled) and 33y educational qualifications (none, CSE/O-level, A-level, degree level or higher); behavioural factors include: 42y smoking (never, ex, light/moderate, heavy), 45y problem drinking (4 categories using AUDIT scale: low-risk, risky or hazardous behaviour, high risk and almost certainly dependent), 42y illegal drugs use (ecstasy, amphetamines, LSD, popper, magic mushrooms, cocaine, temazepan, crack, ketamine, heroin or methadone in last 12 months); adiposity included: 45y obesity (BMI ≥ 30 kg/m²) and 45y waist-to-hip ratio; mental health factors included: 42y psychological distress assessed using the malaise inventory (see Geoffroy et al. PLoS One 2013;8(11) for details); cardio-metabolic factors included: 45y HbA1c, triglycerides and LDL-c, all adjusted for medications (see Li et al. BMJ Open 2019;9(3) for details); child-to-adult height trajectories included: 7y and 45y measured height (see Denholm R et al. Int J Epidemiol 2013;42(5) for details).

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Supplementary tables

Table S1. Potential intermediary variables and risk of all-cause mortality (44/45y to 58y) adjusted for sex

Intermediary variable	HR (95%CI)
Socioeconomic	
33y social class ^a	1.21(1.09,1.34)
33y educational qualifications ^a	1.28(1.16,1.41)
Behavioural	
42y smoking ^a	3.01(2.32,3.89)
45y problem drinking ^a	3.04(1.65,5.62)
42y illegal drug use	2.59(1.62,4.14)
Adiposity	
45y obesity ^a	1.38(1.08, 1.75)
45y waist-hip ratio ^b	2.32(0.44,12.2)
Mental health	
42y mental health ^c	1.11(1.07,1.15)
Cardio-metabolic factors	
45y glycated haemoglobin (mmol/L)	1.02(1.01,1.03)
45y triglycerides (mmol/L)	1.00(1.00,1.01)
45y low-density lipoprotein cholesterol (mmol/L)	1.00(1.00,1.01)
Child to adult height growth ^d	
7y height	0.89(0.76, 1.04)
7-45y height growth ^d	1.00(0.76, 1.32)

^a For categorical variables, extreme category groups are compared (e.g.: lowest vs highest (reference group) social class)

^b per 0.01 unit increase in waist/hip ratio

^c per increase on 15-point malaise scale

^d 7y height and growth (7y-45y) modelled simultaneously

Table S2: Hazard ratios (95% confidence intervals) for childhood socioeconomic disadvantage and neglect in relation to all-cause mortality in 1958 birth cohort participants aged 11y to 58y (N=15,092).

	Model 1 HR (95%CI)	Model 2 HR (95%CI)
Socioeconomic disadvantage	1.65(1.40,1.94)	1.55(1.31,1.83)
Neglect	1.72(1.46,2.01)	1.46(1.23,1.73)

Model 1: Adjusted for sex only.

Model 2: Additionally adjusted for maternal age at birth, birthweight (adjusted for gestational age), birth order and 7y physical or cognitive impairment (yes/no). For associations with neglect models additionally adjusted for social class at birth (or if missing, at 7y), 7y household amenities (sharing or lack a bathroom, lavatory or hot water), 7y housing tenure (owner/occupier, renter or other), and 7y household crowding (1+ person/room).

Table S3 Hazard ratios (95% confidence intervals) for distinct non-overlapping early-life adversities (versus none) in relation to all-cause mortality in 1958 birth cohort participants aged 44/45y to 58y.

Early Life adversities vs no Early life adversities	N ^a (%)	Model 1 HR (95%CI)	Model 2 HR (95%CI)
No Early life adversities	5968 (78.5)	ref	ref
Socioeconomic disadvantage only	544 (7.16)	2.34(1.63,3.37)	2.30(1.59, 3.32)
Neglect ^b only	522 (7.26)	2.11(1.44,3.08)	2.01(1.34, 3.02)
Physical abuse only	66 (0.87)	1.73(0.60, 5.02)	1.66(0.57, 4.83)
Psychological abuse only	342 (4.50)	1.16(0.63,2.13)	1.17(0.63,2.15)
Witnessing abuse only	108 (1.42)	0.66(0.16,2.66)	0.65(0.16, 2.61)
Sexual abuse only	23 (0.30)	3.62(0.90,14.6)	3.70 (0.91, 15.0)

^a N varies due to missing data.

^b Those with complete data on 6 or more of 11 neglect items.

Model 1: Adjusted for sex only.

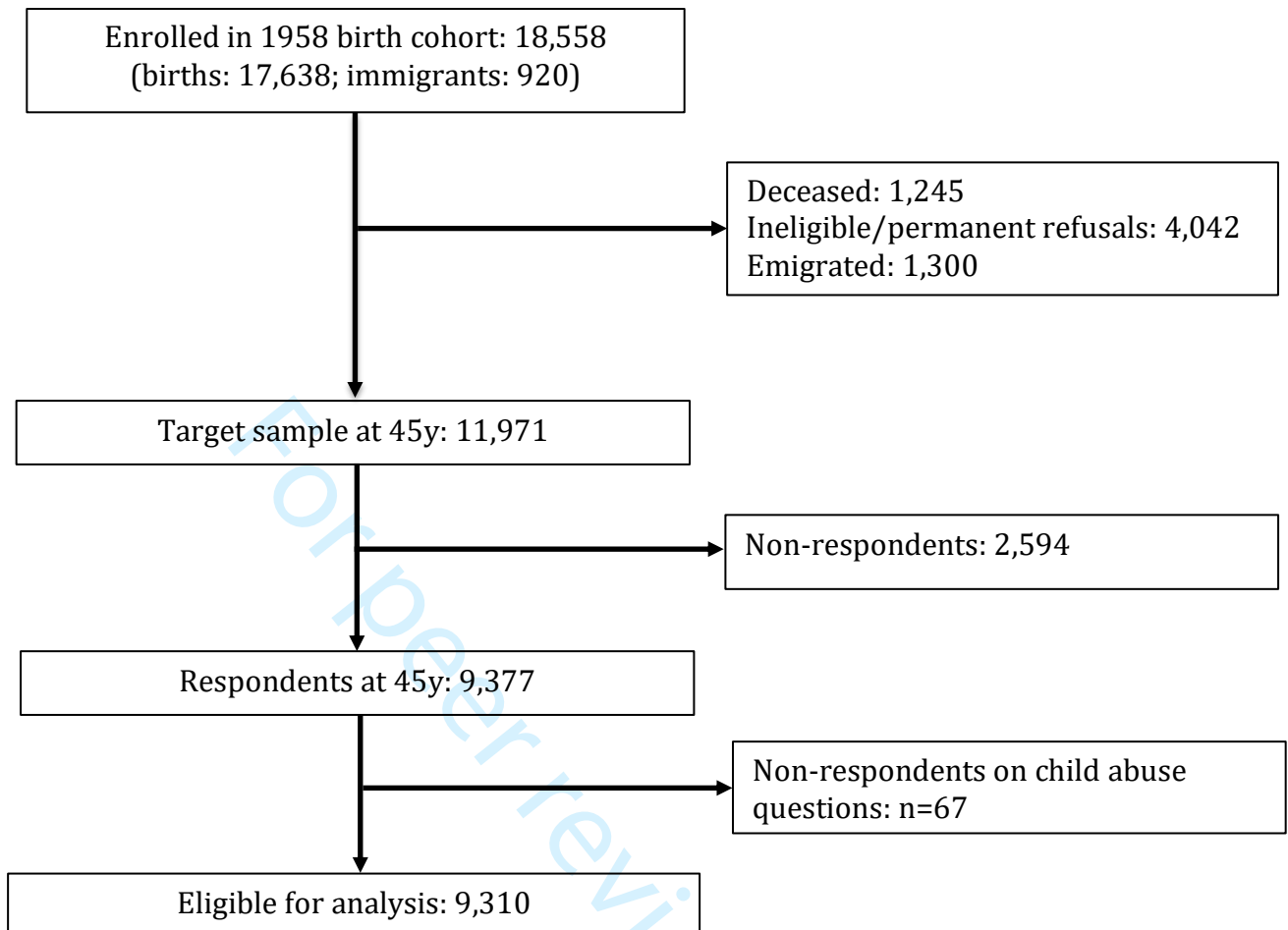
Model 2: Additionally, adjusted for maternal age at birth, birthweight (adjusted for gestational age), birth order and 7y physical or cognitive impairment (yes/no). For associations with neglect, physical abuse, psychological abuse, witnessing abuse and sexual abuse (but not for early-life disadvantage) models additionally adjusted for social class at birth (or if missing, at 7y), 7y household amenities (sharing or lack a bathroom, lavatory or hot water), 7y housing tenure (owner/occupier, renter or other), and 7y household crowding (1+ person/room).

Table S4 Hazard ratios (95% confidence intervals) for early-life adversities and risk of premature death (44/45y to 58y) adjusted separately for potential intermediaries^a.

	Socioeconomic disadvantage	Neglect	Physical abuse	Sexual abuse
Model 3 ^b	1.96(1.47,2.61)	1.45 (1.04,2.03)	1.72(1.10, 2.70)	2.60(1.49, 4.52)
Socioeconomic				
+ 33y social class	1.89(1.42,2.53)	1.37(0.98,1.91)	1.74(1.11,2.73)	2.57(1.48,4.48)
+ 33y educational qualifications	1.82(1.36, 2.43)	1.29(0.92,1.80)	1.74(1.11,2.72)	2.56(1.48,4.45)
Behavioural				
+ 42y smoking,	1.75(1.31,2.34)	1.29(0.93,1.80)	1.57(1.00,2.45)	2.33(1.34,4.05)
+45y problem drinking	1.91(1.42,2.55)	1.45(1.04,2.01)	1.69(1.08,2.63)	2.78(1.60,4.83)
+42y illegal drug use	1.92(1.44, 2.57)	1.43(1.03,1.98)	1.68(1.07,2.62)	2.61(1.50,4.55)
Adiposity				
+ 45y obesity	1.92(1.44,2.56)	1.42(1.02, 1.97)	1.72(1.10,2.69)	2.63(1.51,4.58)
+ 45y waist-hip ratio	1.89(1.42,2.53)	1.39(1.00,1.92)	1.75(1.12,2.73)	2.73(1.57,4.76)
Mental Health				
+42y psychological distress	1.91(1.43,2.55)	1.37(0.98,1.91)	1.70(1.09,2.64)	2.54(1.46, 4.42)
Cardio-metabolic factors				
+ 45y glycated haemoglobin	1.89(1.41,2.52)	1.39 (1.00,1.93)	1.65(1.05, 2.58)	2.72(1.57, 4.73)
+ 45y triglycerides	1.92(1.44,2.57)	1.42(1.02,1.96)	1.72(1.10, 2.70)	2.67(1.53, 4.64)
+ 45y low-density lipoprotein cholesterol	1.93(1.45,2.58)	1.43 (1.03,1.98)	1.72(1.10, 2.69)	2.61(1.50, 4.54)
Child and adult height				
+ 7y height	1.93(1.44,2.58)	1.43(1.03,1.98)	1.73(1.11,2.71)	2.63(1.51,4.58)
+ 45y height	1.93(1.45,2.58)	1.43(1.03,1.98)	1.73(1.11,2.71)	2.64(1.52,4.59)

^a For each pathway, models were adjusted for factors separately (not simultaneously). See text and Table 4 for details on intermediary factors.

^b Model 3 (adjustments shown in Table 3 footnotes)



Supplementary Figure 1: Flow diagram of participants from birth who were eligible to be included in analytical sample

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	8
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	8

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	9
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9-10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Child maltreatment, early life socioeconomic disadvantage and all-cause mortality in mid-adulthood: findings from a prospective British birth cohort

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3 Child maltreatment, early life socioeconomic disadvantage and all-cause mortality in mid-
4 adulthood: findings from a prospective British birth cohort
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Abstract

Objectives: Early-life adversities (ELAs) such as child maltreatment (neglect and abuse) and socioeconomic disadvantage have been associated with adult mortality. However, evidence is sparse for specific types of ELA. We aimed to establish whether specific ELAs (i.e. different types of child maltreatment and socioeconomic disadvantage) were associated independently with all-cause mortality in mid-adulthood and to examine potential intermediary pathways.

Design: Prospective cohort study

Setting: 1958 British birth cohort: a longitudinal, population-based sample of individuals born in Great Britain during a single week in March 1958.

Participants: 9310 males and females with data on child maltreatment and mortality (44/45y to 58y).

Outcome measures: Mortality follow-up from 2002/3 to 2016 when participants were aged 44/45y to 58y. Death was ascertained via the NHS Central Register (N=296) or cohort maintenance activities (N=16).

Results: Prevalence of ELAs ranged from 1.6% (sexual abuse) to 11% (psychological abuse). Several, but not all, ELAs were associated with increased risk of premature death, independent of covariates and other adversities; adjusted hazard ratios were 2.64(95%CI:1.52,4.59) for sexual abuse, 1.93(1.45,2.58) for socioeconomic disadvantage, 1.73(1.11,2.71) for physical abuse and 1.43(1.03,1.98) for neglect. After adjustment for covariates and other adversities, no associations with mortality were observed for psychological and witnessing abuse. Regarding potential intermediaries (including adult socioeconomic factors, behaviours, adiposity, mental health and cardio-metabolic markers), most associations attenuated after accounting for adult health behaviours (particularly smoking). In addition, early-life socioeconomic disadvantage and

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3 neglect associations attenuated after accounting for adult socioeconomic factors. The
4
5 association for sexual abuse and premature mortality was largely unaffected by potential
6
7 intermediaries.
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10 **Conclusions:** Associations with premature mortality varied by type of ELA: associations for sexual
11
12 and physical abuse, neglect and socioeconomic disadvantage were independent of each other.
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14 Different types of ELAs could influence premature mortality via different pathways; this requires
15
16 further research.
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25 **Keywords:** Birth cohort, Child maltreatment, Child abuse, Child neglect, Early-life socioeconomic
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27 disadvantage, Life course epidemiology, premature mortality
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Strengths and limitations of this study

- Data were from a large population-based cohort followed from birth, which allowed prospective ascertainment of child neglect, early-life socioeconomic disadvantage, important covariates and potential intermediary factors.
- Information on different types of child abuse was reported retrospectively at 45y.
- Data on cause-specific mortality was not available; however, mortality data was collected over 14 years.

For peer review only

Background

1
2
3 Early-life adversities (ELAs) such as child maltreatment (neglect and abuse) and socioeconomic
4 disadvantage are major public health issues[1,2]. These adversities are not uncommon, for example in the
5 UK, approximately 9% of children and 22% of adolescents are estimated to experience neglect and/or
6 physical, psychological or sexual abuse[3], and approximately 4.6 million children live in poverty[4].
7
8 Although a growing literature links child maltreatment (CM) to several poor health outcomes[5–7] in
9 childhood through to older ages, evidence on links to mortality in adulthood is based primarily on adversity
10 scores[8–12], which include other experiences such as living in a household with someone who has
11 previously been imprisoned. While a more extensive literature including systemic reviews[2] demonstrates
12 associations for early-life socioeconomic disadvantage, few studies[9] consider both CM and early-life
13 socioeconomic disadvantage simultaneously in relation to mortality in adulthood. This omission is
14 important because, although these ELAs are related, they represent distinct concepts[13] with potential
15 differences in mortality risk. Clarifying the extent to which CM associates with later mortality independent
16 of childhood socioeconomic background (and vice versa) would inform understanding of the role of
17 different types of early-life exposures.

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19 Moreover, it is possible that associations vary for *specific* types of CM and mortality in adulthood, given the
20 differences reported for several outcomes in adulthood, including socioeconomic disadvantage[14,15],
21 mental[16–18] and physical[6] health. Variation in associations with adult mortality cannot be determined
22 from the sparse literature available to date for specific types of CM. One US study that combined multiple
23 CMs together, found no risk of premature mortality although follow-up was limited to young
24 adulthood[19]. In a second US study, associations were found in women but not men for physical and
25 psychological abuse with all-cause mortality over 20-years of follow-up from ages 25y to 74y at baseline;
26 information on sexual abuse and neglect was unavailable[9]. Thus, previous studies have investigated CM
27 as a combined score of different types[9,19] or a limited number of types examined separately[9]. With
28 such limitations of research conducted to date, possible differential associations for specific types of CM
29 (i.e. their independence from each other as well as from early-life socioeconomic disadvantage) on
30 mortality in adulthood are not well understood.

31
32 With respect to potential pathways from ELAs to adult mortality, it is well-established that, for example,
33 CM is associated with detrimental factors in adulthood, including socioeconomic circumstances[14,15],
34 risky health behaviors (e.g. smoking, drug misuse, problem drinking)[17,20,21], obesity[6], poor mental
35 [16–18] and physical health[22]. In turn, these factors are linked to mortality[23–25]. Yet existing
36 literature examining such intermediaries is limited, particularly in relation to CM. Understanding pathways

1 through which specific types of ELAs link to mortality in mid-adulthood is important for developing
2 appropriate interventions that aim to reduce inequalities in mortality.
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5 Given current knowledge gaps, we aimed to establish in a general population sample followed from birth:
6 (i) the extent to which CM and early-life socioeconomic disadvantage are associated independently with
7 premature mortality in midlife (from 44/45y to 58y) and whether associations vary by type of ELA; and (ii)
8 whether associations are explained by potential intermediaries including adult socioeconomic,
9 behavioural, adiposity, mental health and cardio-metabolic status.
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18 **Methods**

19 The 1958 British birth cohort consists of over 17,000 participants followed-up since birth during one week
20 of March 1958[26]. Respondents in mid-adulthood are broadly representative of the surviving cohort[27].
21 Ethical approval was given, including at 50y by the London Multicenter Research Ethics Committee and
22 participants gave informed consent at various sweeps. Of 11,971 invited at 44/45y, 9,310 completed at
23 least one question on CM and had information on mortality (44/45-58y) (see supplementary figure 1).
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30 *Early-life adversities:* Socioeconomic disadvantage was identified from prospectively recorded information
31 on father's occupation at the participant's birth. Those with a father in an unskilled manual occupation
32 were classified as disadvantaged. Child neglect was identified from prospectively collected information at
33 7y and 11y from interview questions to the child's mother and teacher. Eleven indicators of neglect were
34 selected to represent conventional definitions and were summed to create a score (range 0-11). A score ≥ 3
35 yielded a prevalence estimate in line with other UK estimates[1,3], and was used here to define child
36 neglect. Childhood (0-16y) physical, psychological, witnessing and sexual abuse was reported
37 retrospectively at 44/45y using a confidential computer-assisted data-entry questionnaire. Child neglect
38 and abuse measures have been used in several previous studies that, reassuringly, provide extensive
39 evidence of construct validity[28]. Details of all ELAs are given in Table 1.
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52 *All-cause mortality:* Information on deaths between 2002/3 and end of 2016 was ascertained from a
53 variety of sources, mostly (N=296) through receipt of death certificates (including date of death) from the
54 National Health Service Central Register. Information from relatives or close friends during survey
55 activities/cohort maintenance allowed identification of 16 further deaths (details in Table 2 footnotes).
56 Cause-specific data were not available.
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3 *Covariates:* were selected a-priori. All were prospectively recorded, including maternal age at birth,
4 birthweight (adjusted for gestational age), birth order and 7y physical or cognitive impairment. Additional
5 covariates for CM analyses included social class at birth and household factors (amenities, tenure and
6 crowding) at 7y (details in Figure 1 footnotes). Birthweight was ascertained from clinical records; parents
7 reported all other factors.
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14 *Potential mid-adult intermediary factors:* were selected based on established associations with both ELAs
15 and premature mortality. Details of included factors are given in Table S1 (supplementary file), i.e. for
16 adult (i) socioeconomic factors: 33y social class and educational qualifications, (ii) behavioural factors: 42y
17 smoking, 45y problem drinking and 42y illegal drugs use in the last 12 months; (iii) adiposity: 45y obesity
18 and waist-hip ratio; (iv) 42y mental health; and (v) cardio-metabolic factors: 45y glycated haemoglobin
19 (HbA1c), triglycerides and low-density lipoprotein cholesterol (LDL-c), all adjusted for medications. Cardio-
20 metabolic factors, height, weight, hip and waist were measured by trained professionals; other factors
21 were self-reported. Most considered intermediaries were associated with mortality in this cohort (Table
22 S2).
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34 **Statistical analysis**

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37 Cox proportional hazard models were used to estimate hazard ratios and 95% confidence intervals
38 (HR(95%CI)) for associations between each type of ELA and mortality. Survival time included the time from
39 completion of the 44/45y questionnaire to the date of death, censoring (last date of contact) or the end of
40 the study period (December 2016), whichever came first. Schoenfeld residuals were examined to test the
41 assumption of proportional hazards for covariates and potential intermediaries; none violated the
42 assumption (p-values \geq 0.12).
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49 We examined associations between each type of ELA and mortality in separate analyses for men and
50 women and also tested whether associations differed using an interaction term (i.e. type of ELA and
51 mortality by sex) in analyses of both sexes combined. There was little evidence of effect modification
52 ($p_{\text{sex*ELA}} \geq 0.28$ and Table S3), hence in a first level of analyses we adjusted for sex (model 1). Second, to
53 assess whether associations were independent of other early-life factors, we additionally adjusted for
54 covariates listed above (model 2). Third, because different types of ELAs often cluster[29], we assessed
55 two-way correlations between examined ELAs (Table S4). Most ELAs were weakly or only modestly
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1 correlated (ϕ coefficient ≤ 0.50). Therefore, in model 3, we adjusted for all types of ELA simultaneously.
2 For associations that remained in model 3, we assessed the role of potential intermediaries
3 (socioeconomic, behavioural, adiposity, mental health and cardio-metabolic factors) in explaining
4 ELA—mortality associations, by further adjusting model 3 for each potential intermediary (in groups as well
5 as for each factor separately).
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10 In sensitivity analyses, we checked whether restricting the sample to those completing the CM questions at
11 44/45y affected results, by repeating analyses using the larger sample available for child neglect and
12 socioeconomic disadvantage (N=15,092). Survival time included the time from completion of the 11y
13 survey to the date of death, censoring or the end of the study period, whichever came first. As an
14 additional check on the independence of associations for different types of ELAs from model 3, we
15 examined associations with mortality for groups with only one specific type of ELA vs no ELA.
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22 Missing data ranged from 0.02% (physical, sexual and witnessing abuse) to 21% (LDL-c) (Table S5). Data
23 loss was minimized, by imputing missing data on all substantive model variables (i.e. all variables included
24 in models 1, 2 and/or 3) using multiple imputation chained equations. Imputation models included all
25 substantive model variables and main predictors of missingness[27]. Regression analyses were run across
26 20 imputed datasets and overall estimates obtained. Imputed results were similar to those obtained using
27 observed values (Table S6); the former are presented.
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34 **Patient and public involvement**

35 Patients and the public were not involved in the design of the study, or in the interpretation or writing up
36 of the manuscript.
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42 **Results**

43 The prevalence of ELAs varied from 1.6% (sexual abuse) to 11% (psychological abuse) with 10% classified as
44 socioeconomically disadvantaged in early-life (Table 2). The majority of participants reported no ELA (71%)
45 with 19% reporting one and 10% reporting two or more types of ELA. Between 44/45y and 58y, 3.4% of the
46 sample died (N=312).
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53 All types of ELA were associated with risk of death (44/45y-58y) after controlling for covariates (Model 2;
54 Figure 1 and Table S6), for example HR for neglect was 1.49(1.08,2.07) and for physical abuse was
55 2.15(1.54,3.02). In models simultaneously adjusted for all other types of ELA (Model 3) associations
56 remained for all except psychological and witnessing abuse, namely for neglect (HR:1.43(1.03,1.98)),
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1 physical abuse (HR:1.73(1.11,2.71)), sexual abuse (HR:2.64(1.52,4.59)) and socioeconomic disadvantage
2 (HR:1.93(1.45,2.58)). The reduction in HRs between Models 2 and 3 was seen consistently for all ELAs,
3 although modest in some instances, for example, for early-life socioeconomic disadvantage the HR reduced
4 from 2.12(1.60,2.82) to 1.93(1.45,2.58) after adjusting for all CMs.
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10 In regard to potential intermediaries, associations between ELAs and death in mid-adulthood were largely
11 unaffected by adjustment for the range of factors examined (Table 3). However, most associations
12 attenuated after adjustment for adult health behaviors, for example HRs for physical abuse attenuated
13 from 1.73(1.11,2.71) to 1.50(0.96,2.34). Separate adjustment for each health behavior in turn showed a
14 predominant attenuating effect of smoking (Table S7). Additionally, associations for neglect and early-life
15 socioeconomic disadvantage attenuated after controlling for adult socioeconomic factors. For sexual abuse
16 and early-life socioeconomic disadvantage reductions in the strong associations with mortality in mid-
17 adulthood were negligible after accounting for intermediaries.
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26 In sensitivity analysis using the larger sample available for child neglect and socioeconomic disadvantage
27 (N=15,092), main findings were largely unaltered to those presented in Figure 1 (Table S8). Checks on the
28 independence of associations performed for groups with only one specific type of ELA (vs no ELA) showed
29 broadly similar mortality associations (albeit with wider confidence intervals) to main results in Figure 1
30 model 3 (Table S9).
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39 Discussion

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41 In this large population-based study on different types of ELA and mortality in mid-adulthood we showed
42 several important findings. First, some ELAs, but not all, were associated with higher risk of premature
43 mortality in mid-adulthood. That is, findings varied by type of adversity. Child sexual abuse was strongly
44 associated with mortality with a 2.6 times higher risk of premature death in mid-adulthood, although it
45 was the least prevalent adversity. For early-life socioeconomic disadvantage, experienced by 10% of the
46 population, there was an approximate doubling in risk of premature mortality. For physical abuse and
47 neglect the estimated elevated risk of death was more modest (73% and 43% higher respectively), whereas
48 no associations were observed for psychological and witnessing abuse. Second, observed associations were
49 independent of potential confounding factors and the other adversities examined. Importantly, the specific
50 CM associations were mostly robust when accounting for early-life socioeconomic disadvantage and vice
51 versa. Third in relation to potential intermediaries, associations for all types of ELA attenuated after
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controlling for adult health behaviours, in particular smoking. But, in some instances this attenuation was minor, such that for sexual abuse the association was largely unaltered. Associations for early-life socioeconomic disadvantage and neglect were also attenuated by adult socioeconomic factors. Other examined intermediaries including cardio-metabolic markers did little to explain observed associations between specific CMs and mortality in mid-adulthood or for early-life socioeconomic disadvantage.

Our study has several notable strengths. The range of data available on different types of ELA facilitated simultaneous analysis to inform on their independent effects. This is essential for investigating distinct effects of CM on mortality, i.e. separate from those of socioeconomic background and also, in regard to specific types of CMs. Inclusion of child neglect is particularly important given that it is often ignored in research on CM[30]. A follow-up of approximately 14y is a further study strength, as is use of linked mortality data, which is independent of ongoing study participation. Alongside the 14y mortality follow-up there are advantages of using a single-age sample in reducing the range of possible causes of premature death and related underlying pathways. However, study limitations are acknowledged. Ascertainment of childhood maltreatment is not straightforward, with limitations noted for all methods[1], including those used here. While child neglect indicators were measured prospectively and included many aspects of the conventional definition (e.g. failure to ensure a child's basic physical, emotional and educational needs), there were some omissions (e.g. failure to ensure a child's safety) and neglect after age 11y may be missed. However, our measure uses information from different sources (parents and teachers) and at two ages (7y and 11y) which may reduce misclassification and rather than relying on individual items, we used a composite score. Abuse by a parent (up to 16y) was reported retrospectively and does not include abuse by others possibly leading to an underestimate of prevalence. Nonetheless, prevalence estimates of CM were generally in keeping with previous approximates for the UK[1,3]. An exception is child sexual abuse where prevalence is low and estimates may be under-powered. Thus, we have used both prospective (neglect and early-life socioeconomic disadvantage) and retrospective (abuse) measures and we acknowledge that these may identify different groups of individuals[31]. However, it is reassuring that a broad range of studies based on our measures of child neglect and abuse provide extensive evidence of construct validity[28]. As with any long-term study, selection bias needs to be considered: by 45y, when information was collected on child abuse, not all in the cohort had survived (6.7% had died); however over half of these deaths had occurred before 7y (mostly in the first months of life)[27]. Selection bias may affect findings reported here, but only if patterns of association with mortality differ in the surviving and deceased populations. Relatedly, sensitivity analysis for child neglect and socioeconomic disadvantage in a larger sample with longer follow-up from 11y suggests that study results are robust. The analytic approach used allows insights into possible mechanisms underlying ELA associations with premature mortality, but it

1 is not possible to determine the most important intermediaries without considering confounding between
2 mediator—outcome associations or the interrelationship between the mediators. Mortality data were
3 available till age 58y and thus results apply to premature mortality; we are unable to infer whether
4 associations will be stable through to later life. Finally, cause-specific mortality data was unavailable,
5 restricting understanding of possible mechanisms linking ELAs to different causes of premature death.
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11 Our main finding of varying associations for specific types of ELAs with risk of premature mortality is novel
12 largely because there is a dearth of literature that focuses on such variations. The large population and
13 range of ELA measures examined in our study compared with two previous studies[9,19] has facilitated this
14 novel finding. Notably, in respect of CMs, we found that after accounting for confounders and all other
15 ELAs, sexual and physical abuse and also neglect were independently associated with elevated mortality in
16 mid-adulthood in the 1958 birth cohort, but there were no associations for psychological and witnessing
17 abuse. The strong association for child sexual abuse, 2.6 times higher risk of premature mortality, is
18 particularly important given the lack of evidence to date. One previous study of CM and mortality did not
19 include sexual abuse[9] and a second study considered sexual abuse, physical abuse and neglect as a
20 composite measure[19]; thus comparison with our findings for specific types of CMs is not possible. The
21 latter composite measure study reported no association with mortality in young adulthood[19] whereas,
22 our focus is on premature mortality for the age range 44/45y to 58y. The life-stage examined might explain
23 discrepant findings i.e. associations with mortality were not present in young adulthood[19] but may
24 emerge by mid-adulthood as suggested here. For physical abuse, our finding of a 73% higher risk of
25 premature mortality is consistent with a previous estimate of 58% higher risk of death for severe physical
26 abuse in US women aged over 45y to 94y at the end of follow-up[9]. This broad similarity in estimates for
27 physical abuse was unexpected given the wider age range of US study participants compared with our
28 range 44/45y to 58y for mortality follow-up. Nonetheless, there was a discrepancy between our observed
29 association for physical abuse and mortality and the lack of an association in US men[9]. The most common
30 cause of death for men between 20y to 49y is due to external causes (e.g. accidents and suicides),
31 whereas, from 50y, cancer, heart disease and strokes and respiratory diseases are the most common
32 causes of death[32]. These variations in main cause of death may explain the noted discrepancy in findings.
33 For child neglect we are unable to compare our finding of an independent association, with a 43% higher
34 risk of premature death in mid-adulthood, as neither of the two previous CM—mortality studies
35 investigated this exposure separately[9,19]. Thus, our finding provides new evidence for an important
36 component of CM where knowledge of long-term outcome is particularly sparse[30]. For witnessing abuse
37 in childhood we are not aware of any previous study with which to confirm our null finding in relation to
38 premature mortality; whereas for psychological abuse, findings for the US (weak association in women
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only[9]) and our UK (null) study are discrepant. Possible reasons for discrepancies include differences in age at death, abuse measurement and also, the extent to which other ELAs were taken into account. In respect of the latter, it is noteworthy that our findings for specific CM associations with elevated mortality in mid-adulthood were independent of other types of CM as well as childhood socioeconomic circumstances, highlighting the potential for long-term harm associated with specific CMs.

A further novelty of our study is the demonstration that the early-life socioeconomic disadvantage association of an approximate doubling in risk of premature all-cause mortality was independent of specific CMs. While links between early-life socioeconomic disadvantage and mortality in adulthood are well-established[2] and consistent with previous work in this cohort[33], few studies[9] consider both CM and early-life socioeconomic disadvantage simultaneously. By suggesting that, notwithstanding the utility of understanding the long-term impact of CM, the latter does not appear to undermine or explain the strong and robust findings relating to childhood socioeconomic disadvantage our study adds new knowledge to the literature. This is important in a policy context as the recent emphasis on adverse childhood experiences may displace attention away from the early socioeconomic environment, as argued elsewhere[13].

Our findings suggest that adult smoking may be a consistent and in some instances important explanatory factor across observed associations. This was expected because smoking remains one of the most common preventable causes of premature death in adults[34]; and, CM[6,21] and early-life socioeconomic disadvantage[35] are associated with subsequent smoking patterns. Thus, interventions to reduce smoking prevalence in specific ELA groups, either by reducing initiation or promoting cessation, might be considered as possible strategies to lessen differences in premature mortality. Interestingly, while specific CMs in this cohort were associated with the wide range of potential intermediary factors examined, these did not appear to explain associations with mortality. In particular, the strong association for sexual abuse was little explained by examined factors. Nonetheless, the potential intermediary factors considered here may play a role in pathways to mortality at older ages. Whereas in relation to the focus here on premature mortality, further insight into pathways from sexual abuse and other ELAs might be gained in future studies of cause-specific mortality.

In summary, our findings of independent associations for specific types of CM (sexual and physical abuse and neglect) and early-life socioeconomic disadvantage with increased risk of premature mortality in mid-adulthood highlight the long-lasting consequences of these ELAs. Smoking may be a particularly important intermediary for physical abuse, neglect and early-life socioeconomic disadvantage associations; adult socioeconomic factors may be an additional intermediary for neglect and early-life socioeconomic

1 disadvantage. These findings are relevant for public health because, for example, an estimated 3.1 million
2 adults in England and Wales reported being victims of sexual abuse before 16y[36] and approximately 4.6
3 million children in the UK live in poverty[4]. Moreover, relative child poverty is projected to rise from
4 29.7% to 36.6% in the UK between 2018 to 2022[37]. Given these stark projections and our study findings
5 of a strong relationship between childhood disadvantage and an early adult death, policies focused on
6 improving socioeconomic opportunities and assistance to adopt and maintain positive health behaviors for
7 individuals from disadvantaged backgrounds may reduce the burden of premature mortality.
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15 **Conclusions**

16 In sum, our findings highlight the potential of specific types of CMs (i.e. sexual abuse, physical abuse and
17 neglect) for long-term harm. Notwithstanding this important finding, childhood socioeconomic
18 disadvantage associations with premature mortality are strong and not explained by associations with CM.
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26 **Abbreviations**

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28 **CM:** Child maltreatment

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30 **ELA:** Early-life adversity
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Contributors

CP and SMPP conceived the study. NTR carried out the analysis and drafted the paper. All authors contributed to the interpretation of data, revision of the manuscript, and approved its final version.

Declaration of interests

We declare no competing interests.

Acknowledgments

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Ethical declarations

Ethical approval was given, including at 50y by the London Multicenter Research Ethics Committee. Participants gave informed consent at various sweeps.

Data sharing statement Cohort data comply with ESRC data sharing policies, readers can access these data via the UK Data Archive at <http://www.data-archive.ac.uk/>

Table 1. Definition of early-life adversities (child maltreatment and early-life socioeconomic disadvantage) and representative variables from the 1958 British Birth cohort

	Definition ^a	1958 cohort variables	Age of ascertainment (method) ^b
Prospective report, birth to 11y			
Socioeconomic disadvantage (birth)		Based on father's occupation at birth ^c , using the Registrar General's Classification. Fathers with an unskilled manual occupation or households with no male head were classified as disadvantaged.	Birth (P)
Neglect ^d (7y & 11y)	Failure to meet a child's basic physical, emotional, medical/dental, or education need; failure to provide adequate nutrition, hygiene, or shelter; or failure to ensure a child's safety	<ul style="list-style-type: none"> - Child looks undernourished, scruffy or dirty - Mother never/hardly ever takes child out^e - Father never/hardly ever takes child out^e - Mother shows little/no interest in child's educational progress - Father shows little/no interest in child's educational progress - Mother and Father never/hardly ever read to, or reads with child 	7 & 11y (T) 7 & 11y (P) 7 & 11y (P) 7 & 11y (T) 7 & 11y (T) 7y (P)
Retrospective report at 44/45y			
Physical abuse (0-16y)	Intentional use of physical force or implements against a child that results in, or has the potential to result in, physical injury.	I was physically abused by a parent – punched, kicked or hit or beaten with an object, or needed medical treatment	45y (S)
Psychological abuse ^f (0-16y)	Intentional behaviour that conveys to a child that s/he is worthless, flawed, unloved, unwanted, endangered, or valued only in meeting another's needs. <i>UK definition^g includes harmful (unintentional) parent-child interactions: 'the persistent emotional maltreatment of a child such as to cause severe and persistent adverse effects on the child's emotional development'</i>	<ul style="list-style-type: none"> - I was verbally abused by a parent (or parent-figure) - I suffered humiliation, ridicule, bullying or mental cruelty from a parent (or parent-figure) - Mother (or mother-figure) and father (or father-figure) were not at all affectionate 	45y (S)
Witnessing abuse (0-16y)	Any incident of threatening behaviour, violence, or abuse (psychological, physical, sexual, financial, or emotional) between intimate partners or adult family members, irrespective of sex or sexuality	I witnessed physical or sexual abuse of others in my family	45y (S)
Sexual abuse (0-16y)	Any completed or attempted sexual act, sexual contact, or non-contact sexual interaction with a child by a caregiver	I was sexually abused by a parent (or parent-figure)	45y (S)

a: Gilbert et al. Lancet. 2009;373; b: (S): self-report; (T): teacher-report; (P): parent-report; c: socioeconomic position was classified as missing for fathers' who were unemployed or sick; d: Questions relating to child neglect at 7y and 11y were answered by the child's teacher and mother (or father if the mother was unavailable). The 11 neglect indicators were summed to create a score (range 0–11); those scoring > 3 were classified as neglected (see text for further details); e: e.g. walks, outings, picnics, visits, shopping; ^fIn the 1958 cohort psychological abuse was defined as experiencing at least one of the three listed variables; g: Department for Education. Working together to safeguard children. Her Majesty's Government, 2006.

Table 2. Prevalence of early-life adversities and mortality^a in the 1958 British birth cohort.

Early-life adversity	Population sample N ^b	Total cases N (%)	Males (%)	Females (%)	Deaths N (%)
Socioeconomic disadvantage	9033	925 (10.2)	9.6	10.8	61 (6.6)
Neglect ^c	8460	878 (10.4)	11.1	9.7	49 (5.6)
Physical abuse	9308	562 (6.0)	5.9	6.1	40 (7.1)
Psychological abuse	9310	1000 (10.7)	8.9	12.6	50 (5.0)
Witnessing abuse	9308	559 (6.0)	4.4	7.6	33 (5.9)
Sexual abuse	9308	149 (1.6)	0.5	2.7	17 (11.4)
Deaths 44/45y-58y ^a	9310	312 (3.4)	3.7	3.0	

^aDate of death was ascertained through receipt of death certificates to the Centre for Longitudinal Studies from the National Health Service Central Register (N=296) i.e. data missing for 16 individuals (see: National Child Development Study Deaths Dataset, 1958-2016 UK Data Service for details). Using survey/cohort maintenance data we determined if the deceased died between 45-50y (N=7), 50-55y (N=5) and 55-58y (N=4). Date of death was estimated as the mid-point between these ages; ^bN varies due to missing data;

^cThose with complete data on 6 or more of 11 neglect items (as detailed in Power C et al. Longit Life Course Stud. 2020).

Table 3. Early-life adversities and risk of all-cause mortality (Hazard ratio (95% CI)) in adults (44/45y to 58y) adjusted for mid-adult (i) socioeconomic (ii) behavioural, (iii) adiposity, (iv) mental health and (v) cardio-metabolic factors^a (N=9310).

	Socioeconomic disadvantage	Neglect	Physical abuse	Sexual abuse
Model 3	1.93(1.45,2.58)	1.43 (1.03,1.98)	1.73(1.11,2.71)	2.64(1.52,4.59)
+ mid-adult socioeconomic factors	1.82(1.36,2.43)	1.28(0.91,1.79)	1.74(1.11,2.73)	2.54(1.46,4.42)
+ mid-adult behavioural factors	1.75(1.31,2.34)	1.32(0.95,1.83)	1.50(0.96,2.34)	2.43(1.40,4.23)
+ mid-adult adiposity	1.90(1.42,2.53)	1.39(1.00,1.93)	1.75(1.12,2.73)	2.71(1.56,4.73)
+ mid-adult mental health	1.91(1.43,2.55)	1.37(0.99,1.91)	1.70(1.09,2.64)	2.54(1.46,4.42)
+ mid-adult cardio-metabolic factors	1.89(1.42,2.53)	1.39(1.00,1.93)	1.65(1.05,2.57)	2.71(1.56,4.72)

Model 3 (adjustments shown in Figure 1 footnotes); ^a Models were adjusted for each intermediary group of factors separately (not simultaneously). See details of intermediary factors in Table S1.

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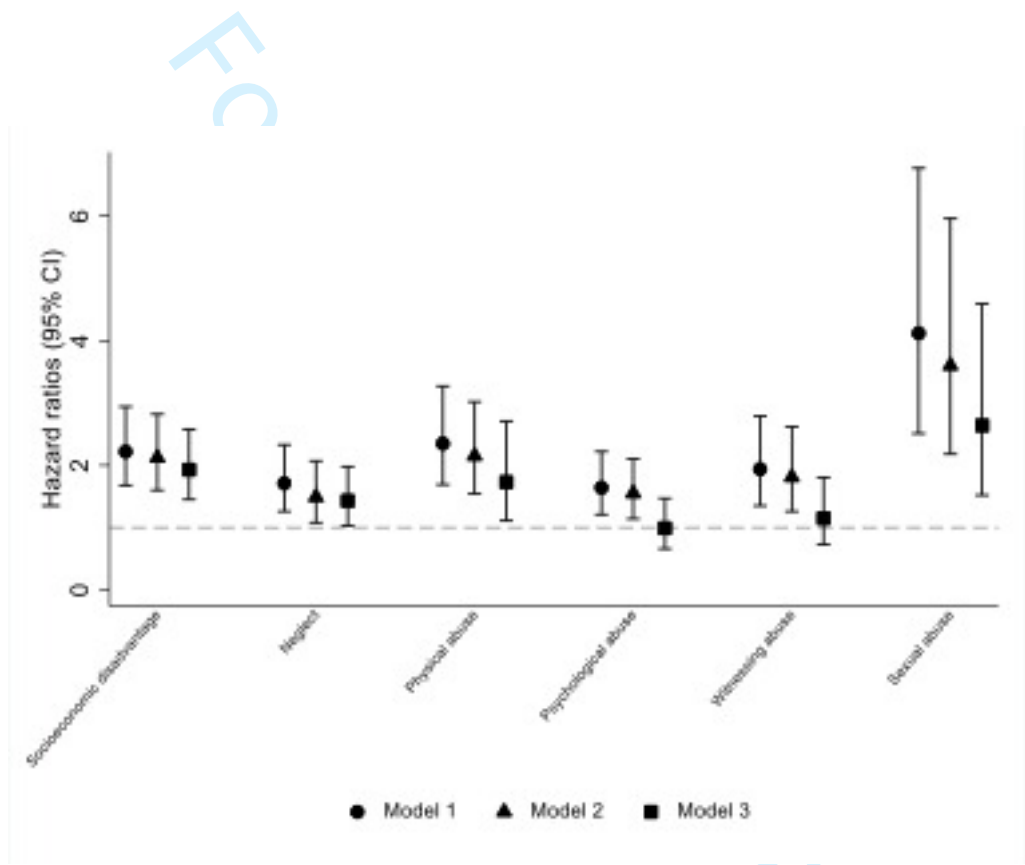
Figure Legend:

Figure 1: Model 1: Adjusted for sex only; Model 2: additionally adjusted for maternal age at birth, birthweight (adjusted for gestational age), birth order and 7y physical or cognitive impairment (yes/no). For associations with neglect, physical, psychological, witnessing and sexual abuse (but not for early-life disadvantage) models additionally adjusted for socioeconomic factors: social class at birth (or if missing, at 7y), 7y household amenities (sharing or lack a bathroom, lavatory or hot water), 7y housing tenure (owner/occupier, renter or other), and 7y household crowding (1+ person/room); Model 3: Model 2 plus simultaneous adjustments for all other early-life adversities

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3 **Supplementary tables**
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5 Table S1. Distribution of potential intermediary variables (observed values)
6

7 Intermediary variables	8	9 N(%)/Mean(SD)
Socioeconomic		
33y social class ^a		
	I/II	3757 (42.2)
	III non-manual	1938 (21.8)
	III manual	1727 (19.4)
	IV/V	1476 (16.6)
33y educational qualifications		
	None	1765 (21.8)
	O-levels	2797 (34.5)
	A-levels	2424 (29.9)
	Degree	1123 (13.9)
Behavioural		
42y smoking		
	Never	4127 (45.8)
	Ex-smoker	2709 (30.1)
	Current	2180 (24.2)
45y problem drinking		
	Low risk	6262 (72.9)
	Risky/hazardous behaviour	1981 (23.1)
	High risk	213 (2.48)
	Almost certainly dependent	131 (1.53)
	42y illegal drug use ^f	230 (2.56)
Adiposity		
	45y obesity	2269 (24.5)
	45y waist-hip ratio	0.87 (0.09)
Mental health		
	42y psychological distress* ^g	2 (0,4)

Cardio-metabolic factors^β

45y glycated haemoglobin (mmol/L)	5.25 (0.69)
45y triglycerides (mmol/L)*	1.6 (1.1,2.5)
45y low-density lipoprotein cholesterol (mmol/L)	3.45 (0.93)

N varies due to missing data. ^αclasses I and II (professional/managerial), class III non-manual (skilled non-manual), class III manual (skilled manual) and classes IV and V (partly/unskilled manual); ^εuse of ecstasy, amphetamines, LSD, popper, magic mushrooms, cocaine, temazepan, crack, ketamine, heroin or methadone in last 12 months; *median(inter-quartile range); ^εassessed using the malaise inventory (see Geoffroy et al. PLoS One 2013;8(11) for details); ^βall adjusted for medications (see Li et al. BMJ Open 2019;9(3) for details)

Table S2. Potential intermediary variables and sex-adjusted risk of all-cause mortality (44/45y to 58y; N=9310)

Intermediary variable	HR (95%CI)
Socioeconomic	
33y social class ^a	1.21(1.09,1.34)
33y educational qualifications ^a	1.28(1.16,1.41)
Behavioural	
42y smoking ^a	3.01(2.32,3.89)
45y problem drinking ^a	3.04(1.65,5.62)
42y illegal drug use	2.59(1.62,4.14)
Adiposity	
45y obesity	1.38(1.08, 1.75)
45y waist-hip ratio ^b	2.32(0.44,12.2)
Mental health	
42y mental health ^c	1.11(1.07,1.15)
Cardio-metabolic factors	
45y glycated haemoglobin (mmol/L)	1.02(1.01,1.03)
45y triglycerides (mmol/L)	1.00(1.00,1.01)
45y low-density lipoprotein cholesterol (mmol/L)	1.00(1.00,1.01)

^a For categorical variables, extreme category groups are compared (e.g.: lowest vs highest (reference group) social class);

^b per 0.01 unit increase in waist/hip ratio; ^c per increase on 15-point malaise scale

Table S3. Hazard ratios (95% confidence intervals) for early-life adversities in relation to all-cause mortality in 1958 birth cohort participants aged 44/45y to 58y, men and women separately (N=9310)

	Model 1	Model 2	Model 3
	HR (95%CI)	HR (95%CI)	HR (95%CI)
Men			
Socioeconomic disadvantage	1.89 (1.26,2.84)	1.85 (1.22,2.78)	1.69 (1.12,2.57)
Neglect	1.81 (1.22,2.70)	1.49 (0.97,2.30)	1.45 (0.94,2.23)
Physical abuse	2.16 (1.36,3.45)	2.01 (1.25,3.23)	1.81 (1.00,3.29)
Psychological abuse	1.54 (0.98,2.40)	1.46 (0.93,2.28)	0.95 (0.54,1.68)
Witnessing abuse	1.82 (1.04,3.21)	1.66 (0.94,2.95)	1.13 (0.58,2.22)
Sexual abuse	5.41 (2.01,14.58)	5.51 (2.01,15.07)	4.37 (1.53,12.47)
Women			
Socioeconomic disadvantage	2.60 (1.76,3.85)	2.44 (1.64,3.63)	2.23 (1.49,3.34)
Neglect	1.59 (0.98,2.57)	1.49 (0.89,2.48)	1.41 (0.84,2.35)
Physical abuse	2.57 (1.60,4.12)	2.33 (1.44,3.78)	1.67 (0.85,3.28)
Psychological abuse	1.73 (1.14,2.61)	1.66 (1.09,2.51)	1.02 (0.58,1.79)
Witnessing abuse	2.03 (1.27,3.26)	1.92 (1.19,3.10)	1.17 (0.64,2.14)
Sexual abuse	3.80 (2.15,6.73)	3.21 (1.79,5.75)	2.30 (1.18,4.49)

Adjustments as in Figure 1 footnotes.

Table S4. Correlation between early-life adversities (using Cramér's phi, observed data)

	Socioeconomic disadvantage	Neglect	Physical abuse	Psychological abuse	Witnessing abuse	Sexual abuse
Socioeconomic disadvantage		0.11	0.04	0.05	0.07	0.05
Neglect			0.07	0.04	0.07	0.04
Physical abuse				0.50	0.44	0.21
Psychological abuse					0.39	0.22
Witnessing abuse						0.25
Sexual abuse						

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Table S5. Proportion of missing data (ascending order) in sample and distribution of observed and imputed analysis samples

Variable	Missing N(%)	Data distribution	
		Observed sample %/Mean	Imputed sample* %/Mean
Sex	0 (0)		
Males		49.6	49.6 [€]
Females		50.4	50.4 [€]
Psychological abuse	0 (0)	10.7	10.7 [€]
Physical abuse	2 (0.02)	6.04	6.04
Sexual abuse	2 (0.02)	1.60	1.60
Witnessing abuse	2 (0.02)	6.01	6.01
45y obesity	61 (0.66)	24.5	24.6
45y waist-to-hip ratio	64 (0.69)	0.87	0.87
Social class ^α at birth	277 (2.98)		
I/II		19.1	19.1
III non-manual		10.0	10.0
III manual		48.7	48.7
IV/V/No male head		22.2	22.2
42y smoking	294 (3.16)		
Never		45.8	45.7
Ex		30.1	30.0
Current		24.2	24.3
42y Malaise inventory	332 (3.57)	2.46	2.47
42y Illegal drug use	335 (3.60)	2.56	2.60
33y Adult social class ^α	412 (4.43)		
I/II		42.2	41.7
III non-manual		21.8	21.7
III manual		19.4	19.5
IV/V		16.6	17.1
Maternal age at birth (years)	496 (5.33)	27.5	27.5
45y Problem drinking	723 (7.77)		
Low risk		72.9	73.2
Risky/hazardous behaviour		23.1	22.8
High risk		2.48	2.47

	Almost certainly dependent	1.53	1.52	
1	Child neglect	850 (9.13)	10.4	10.5
2	7y physical or cognitive impairment	1128 (12.1)	4.40	4.72
3	Birth order	1150 (12.4)		
4	1 st born		38.5	38.8
5	2 nd -4 th		54.4	54.0
6	5th or more		7.17	7.18
7	7y tenure	1161 (12.5)		
8	Owner occupied		44.6	44.8
9	Council rented		37.6	37.5
10	Private rented		11.9	11.7
11	Other		5.87	5.99
12	7y Lacking household amenities	1190 (12.8)	17.0	16.9
13	33y educational attainment	1201 (12.9)		
14	None		10.0	10.8
15	Some		11.8	12.1
16	O-levels		34.5	34.4
17	A-levels		29.9	29.3
18	Degree		13.9	13.5
19	7y household crowding	1448 (15.6)	39.8	40.0
20	45y glycated haemoglobin (mmol/L) [£]	1478 (15.9)	165.1	165.2
21	45y Triglycerides (mmol/L) [£]	1545 (16.6)	52.6	52.9
22	Birthweight (adjusted for gestational age) [¥]	1581 (17.0)	0.03	0.02
23	45y low-density lipoprotein cholesterol (mmol/L) [£]	1950 (21.0)	120.1	120.9

24 *averaged over 20 imputed datasets; [£]No missing data on these variables; ^αclasses I and II (professional/managerial),
25 class III non-manual (skilled non-manual), class III manual (skilled manual) and classes IV and V (partly/unskilled
26 manual); [£]glycated haemoglobin and all lipids are presented (and modelled in imputation models) as 100*ln(x) (to
27 ensure data is normally distributed); [¥]standardised scale
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Table S6. Hazard ratios (95% confidence intervals) for early-life adversities in relation to all-cause mortality in 1958 birth cohort participants aged 44/45y to 58y

	Model 1	Model 2	Model 3
	HR (95%CI)	HR (95%CI)	HR (95%CI)
Imputed data (N=9310)			
Socioeconomic disadvantage	2.22(1.68,2.94)	2.12(1.60,2.82)	1.93(1.45,2.58)
Neglect	1.71(1.26,2.33)	1.49(1.08,2.07)	1.43(1.03,1.98)
Physical abuse	2.35(1.69, 3.27)	2.15(1.54,3.02)	1.73(1.11,2.71)
Psychological abuse	1.64(1.21,2.22)	1.55(1.14,2.10)	0.99(0.66,1.47)
Witnessing abuse	1.94(1.35,2.79)	1.81(1.26,2.62)	1.15(0.73,1.80)
Sexual abuse	4.12(2.51,6.77)	3.60(2.18,5.96)	2.64(1.52,4.59)
Complete case analysis ^a			
Socioeconomic disadvantage	2.22(1.68,2.94)	1.99(1.41,2.82)	1.78(1.25,2.54)
Neglect	1.72(1.27,2.34)	1.72(1.16,2.56)	1.68(1.13,2.50)
Physical abuse	2.35(1.69, 3.27)	2.40(1.59,3.64)	1.53(0.88,2.67)
Psychological abuse	1.64(1.21,2.22)	1.81(1.26,2.61)	1.08(0.67,1.75)
Witnessing abuse	1.94(1.35,2.79)	2.51(1.64,3.84)	1.56(0.92,2.62)
Sexual abuse	4.12(2.51,6.77)	5.64(3.10,10.26)	3.70(1.90,7.19)

^aN varies from 8460 (neglect) to 9310 (psychological abuse) in Model 1 and 6645 (CMs) to 6922 (socioeconomic disadvantage) in Model 3 due to missing data. Adjustments as in Figure 1 footnotes.

Table S7. Hazard ratios (95% confidence intervals) for early-life adversities and risk of premature death (44/45y to 58y) adjusted separately for potential intermediaries^a (N=9310).

	Socioeconomic disadvantage	Neglect	Physical abuse	Sexual abuse
Model 3 ^b	1.96(1.47,2.61)	1.45 (1.04,2.03)	1.72(1.10, 2.70)	2.60(1.49, 4.52)
Socioeconomic				
+ 33y social class	1.89(1.42,2.53)	1.37(0.98,1.91)	1.74(1.11,2.73)	2.57(1.48,4.48)
+ 33y educational qualifications	1.82(1.36, 2.43)	1.29(0.92,1.80)	1.74(1.11,2.72)	2.56(1.48,4.45)
Behavioural				
+ 42y smoking,	1.75(1.31,2.34)	1.29(0.93,1.80)	1.57(1.00,2.45)	2.33(1.34,4.05)
+45y problem drinking	1.91(1.42,2.55)	1.45(1.04,2.01)	1.69(1.08,2.63)	2.78(1.60,4.83)
+42y illegal drug use	1.92(1.44, 2.57)	1.43(1.03,1.98)	1.68(1.07,2.62)	2.61(1.50,4.55)
Adiposity				
+ 45y obesity	1.92(1.44,2.56)	1.42(1.02, 1.97)	1.72(1.10,2.69)	2.63(1.51,4.58)
+ 45y waist-hip ratio	1.89(1.42,2.53)	1.39(1.00,1.92)	1.75(1.12,2.73)	2.73(1.57,4.76)
Mental Health				
+42y psychological distress	1.91(1.43,2.55)	1.37(0.98,1.91)	1.70(1.09,2.64)	2.54(1.46, 4.42)
Cardio-metabolic factors				
+ 45y glycosylated haemoglobin	1.89(1.41,2.52)	1.39 (1.00,1.93)	1.65(1.05, 2.58)	2.72(1.57, 4.73)
+ 45y triglycerides	1.92(1.44,2.57)	1.42(1.02,1.96)	1.72(1.10, 2.70)	2.67(1.53, 4.64)
+ 45y low-density lipoprotein cholesterol	1.93(1.45,2.58)	1.43 (1.03,1.98)	1.72(1.10, 2.69)	2.61(1.50, 4.54)

^a For each pathway, models were adjusted for factors separately (not simultaneously). See text and Table S1 for details on intermediary factors.

^b Model 3 (adjustments shown in Figure 1 footnotes)

Table S8: Hazard ratios (95% confidence intervals) for childhood socioeconomic disadvantage and neglect in relation to all-cause mortality in 1958 birth cohort participants aged 11y to 58y (N=15,092).

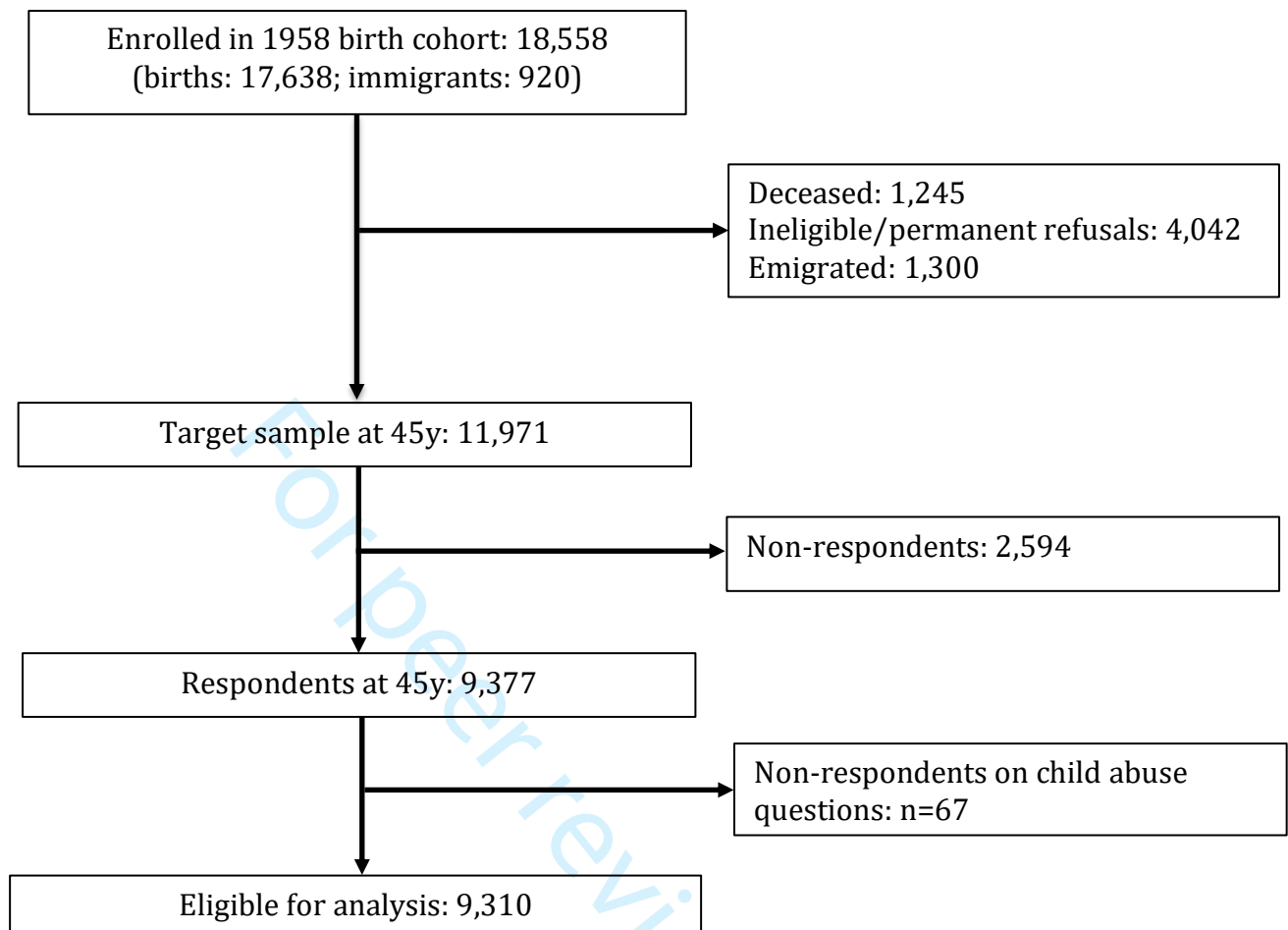
	Model 1 HR (95%CI)	Model 2 HR (95%CI)
Socioeconomic disadvantage	1.65(1.40,1.94)	1.55(1.31,1.83)
Neglect	1.72(1.46,2.01)	1.46(1.23,1.73)

Adjustments as in Figure 1 footnotes.

Table S9. Hazard ratios (95% confidence intervals) for distinct non-overlapping early-life adversities (versus none) in relation to all-cause mortality in 1958 birth cohort participants aged 44/45y to 58y.

Early Life adversities vs	N ^a (%)	Model 1 HR (95%CI)	Model 2 HR (95%CI)
no Early life adversities		ref	ref
No Early life adversities	5968 (78.5)	ref	ref
Socioeconomic disadvantage only	544 (7.16)	2.34(1.63,3.37)	2.30(1.59, 3.32)
Neglect ^b only	522 (7.26)	2.11(1.44,3.08)	2.01(1.34, 3.02)
Physical abuse only	66 (0.87)	1.73(0.60, 5.02)	1.66(0.57, 4.83)
Psychological abuse only	342 (4.50)	1.16(0.63,2.13)	1.17(0.63,2.15)
Witnessing abuse only	108 (1.42)	0.66(0.16,2.66)	0.65(0.16, 2.61)
Sexual abuse only	23 (0.30)	3.62(0.90,14.6)	3.70 (0.91, 15.0)

^a N varies due to missing data; ^b Those with complete data on 6 or more of 11 neglect items; Adjustments as in Figure 1 footnotes.



Supplementary Figure 1: Flow diagram of participants from birth who were eligible to be included in analytical sample

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	8
Study size	10	Explain how the study size was arrived at	8
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	8
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	9
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	9
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9-10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.