Trajectories of childhood adversity and mortality in early adulthood: A population-based cohort study

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Abstract

Background: Adverse events in childhood may have long-lasting effects on health. We aim to describe trajectories of adverse childhood experiences and relate these to overall and cause-specific mortality in early adult life. We distinguish between three different dimensions of childhood adversities: poverty and material deprivation; loss or threat of loss within the family; and aspects of family dynamics such as maternal separation.

Methods: We used unselected annually updated data from Danish nationwide registers covering more than 1 million children born between 1980 and1998. A group-based multi-trajectory clustering model was used to define the different trajectories between 0 and16 years of age. We assessed the associations between these trajectories and mortality rates using a Cox proportional hazards model and an Aalen hazards difference model between 16 to 34 years of age.

Findings: We identified five distinct trajectories of childhood adversities. Compared with those with a low adversity trajectory, children who had experienced early life material deprivation (HR=1.4; 95% CI 1.3-1.5), persistent deprivation (HR=1.8; 1.6-1.9), or loss or threat of loss (HR=1.8; 1.6-2.0) had a moderately higher risk of premature mortality. A small group of children (3%) experienced multiple adversities within all dimensions and throughout the entire childhood. This group had a 4.5 times higher all-cause mortality risk (95% CI: 4.1; 5.1) corresponding to 10.3 (95% CI: 9.0; 11.6) additional deaths per 10,000 person years. Accidents, suicides and cancer were the most common causes of death in in this population.

Interpretation: Almost half of Danish children experience some degree of adversity, and this is associated with a moderately higher risk of mortality in adulthood. Among these, a small group of children experiences multiple adversities across social, health and family-related dimensions and this group carries a markedly higher mortality risk than other children, which requires public health attention.

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Research in context

Evidence before this study

The health and mortality effects of childhood adversities may have been severely underestimated because previous studies have mainly focused on the effects of single stressors or have been limited by design (recall bias or selective participation). We did a comprehensive literature review in PubMed (from inception to September 5th 2019) using the search terms (‘adverse childhood events’ or ‘poverty’ or ‘bereavement’ or ‘adversity’ or ´stressors´ or [life change events]) and ([mortality] or ‘premature mortality’ or ‘death’ or ‘suicide’). We identified articles addressing childhood adversity and its effect on mortality in adult life. We also established an interdisciplinary expert panel consisting of experts in child health, child psychology, medicine, statistics and epidemiology to provide a strong theoretical and methodological foundation for the study.

Added value of this study

We used unselected annually updated nationwide register data covering more than 1 million Danish children to assess the complex and time-varying nature of childhood adversities by utilizing the full range of information on duration and timing of childhood adversities. Trajectories of childhood adversity across social, health, and family-related dimensions were identified from this high-resolution data. About half of the children experienced none or few isolated events and the mortality rate in early adulthood was lowest in this group. A small subset of children (3%) experienced high and accelerating numbers of adversities across their entire childhood and these children had a four-fold higher mortality risk in early adult life, which accounted for a substantial number of extra deaths. The elevated mortality was most pronounced for suicides and accidents, but a higher risk of somatic mortality including cancer was also observed.

Implications of all the available evidence

From a policy perspective, it is striking that such clear associations between childhood adversities and premature mortality are found even in the context of the Danish social security system that promotes economic stability for families. Presumably, childhood adversities have even stronger mortality effects in societies with less social security. Our findings indicate the critical importance of broader structural public health initiatives aimed at addressing the underlying social drivers of childhood adversities including prevention of childhood poverty and social inequalities in health. In addition, addressing the cumulative risks associated with multiple childhood adversities across social and family-related dimensions may help to identify vulnerable children who would benefit from targeted support.

Introduction

Childhood is a sensitive period with rapid bodily, neurological and cognitive development, and adversity in early childhood may lead to lifelong impairments in health.[1] Childhood adversities cover a broad range of factors, from economic hardship to an unfavorable family environment. Even in countries with a high level of social security, almost one in ten children experience more than three childhood adversities such as bereavement, poverty, parental divorce or parental alcohol abuse between early infancy and late adolescence.[2]

A number of studies have documented health effects of childhood adversity, including premature death.[3,4] However, the recent focus on risk 'syndemics' emphasises the importance of understanding the complex interaction of bio-social risks over the lifecourse.[5] Thus, to understand the health consequences of childhood adversities we need larger studies that can capture the clustering of multiple stressors in vulnerable groups of children over time. This is particularly important since the biological stress response system and coping mechanisms seem more likely to break down when confronted with multiple stressors over longer periods of time.[6]

In one of the few prospective studies to evaluate premature mortality related to multiple severe childhood adversities, Kelly-Irving et al. show that the accumulation of adverse childhood experiences was associated with a higher mortality risk.[7] Attrition could, however, be a problem in this and other longitudinal studies, since individuals with continued participation over many years may be different from those who leave the cohort. This potential selection bias may impact the assessment of the health effects of childhood adversities.[8] Concern has also been raised about the unhelpful conflation of conceptually different risks when considering childhood adversity, for example socioeconomic conditions and factors such as childhood abuse.[9]

To advance the existing literature, the aim of our study is twofold. First, we aim to describe distinct trajectories of childhood adversity using a unique unselected cohort constructed from nationwide registers covering more than 1 million Danish children. Second, we aim to relate these trajectories to overall and cause-specific mortality in early adult life. We will acknowledge the complexity and time-varying nature of childhood adversities by incorporating the full range of information on duration and timing of childhood adversities based on annually updated data. We also aim to distinguish between three different dimensions of adverse childhood experiences, i.e. poverty and material deprivation, loss or threat of loss within the family, and family dynamics.

Methods

The DANish LIFE Course (DANLIFE) cohort

We used data from a register-based life course cohort study (DANLIFE) based on continuously updated information from nationwide registers.[2] Access to Danish registers is granted by *Statistics Denmark* and the *Danish Health Data Authorities* in an anonymous and secure form. The DANLIFE cohort is registered with the Danish Data Protection Agency *(no. 514-0262/18-3000)* and all data linkage is performed according to Danish Law. Every Danish citizen is given a unique personal identification number at birth, which permits exact individual level linkage between registries in Denmark.[10] All children born in Denmark in 1980 or later have been included in the

DANLIFE cohort, which includes a total of 2,223,927 children born between 1980 and 2015. In order to cover trajectories for an entire childhood (0 to 16 years of age), we excluded 1,064,864 children born after 1998 and 11,161 children who died before their 16th birthday. Almost half of these deaths (45%) were neonatal deaths (within the first 28 days of life), and 68% of the deaths occurred in children less than 1 year old. Finally, we excluded 50,274 children who emigrated before their 16th birthday. This left us with a final sample of 1,097,628 children (Suppl Figure 1). The DANLIFE cohort is an open cohort, which means that we have continuously included new children born in Denmark from 1980 and onwards into the cohort. Thus, while we are able to follow the oldest children (i.e. those born in 1980) for 18 years, those children born later can only be followed for a shorter time span.[2]

Childhood adversities

The linkage between child, parents and siblings in the registers enables the measurement of a range of childhood adversities. Table 1 provides an overview of the 12 included childhood adversities and their definitions. A panel of experts in stress, child health and child psychology decided on the three predefined dimensions of childhood adversity after a thorough investigation of the literature. These dimensions included material deprivation (i.e. family poverty and parental long-term unemployment); loss or threat of loss within the family (i.e. parental severe somatic illness, sibling severe somatic illness, and death of a parent or a sibling); and family dynamics (i.e. maternal separation, being placed in foster care, parental psychiatric illness, sibling psychiatric illness, and parental alcohol or drug abuse). Direct information on child abuse/neglect or domestic violence was unfortunately not available in the registers.

Premature mortality

The study participants were followed from their 16th birthday and until emigration, death or end of follow-up on the 31st of December 2014, meaning that they are being followed between ages 16 and 34. Individuals emigrating during follow-up (n=69,412) were censored at the date of emigration. Cause-specific mortality was identified in the Danish Register of Causes of Death. Cancers, accidents and suicides were the three most common causes of death in this age group. Cause-specific mortality was thus divided into cancers (ICD-10 codes C00 to C97), accidents (ICD-10 codes V01 to X59), suicides (ICD-10 codes X60 to X84) and others (remaining ICD-10 codes for causes of death).

Covariates

Covariates included sex, birth weight (in grams), household's highest education at the time of birth (*low* $\leq$ 9 years, *middle* 10-12 years, and *high* >12 years), origin of parents (*European decent [Europe, North America, Australia and New Zealand], non- European decent* if at least one parent has another nationality), and parental age at time of birth (*<20 years, 20-30 years, >30 years*).

Statistical methods

We used a group-based multi-trajectory model to determine trajectory groups of adversities based on the three prespecified dimensions of material deprivation, loss or threat of loss, and family dynamics. This approach allowed us to incorporate the full range of information from the high-resolution longitudinal data. We used the package TRAJ for Stata to fit between 1 and 8 trajectory clusters using zero-inflated Poisson regressions with a quadratic trajectory function yielding a probability for each individual of being in each trajectory group[11] (see the technical appendix for

details). We visually judged that 5 trajectory groups divided the individuals optimally, as the vast majority of individuals had a very high probability of belonging to a specific group while still allowing for a reasonable number of trajectory groups (Suppl Figure 2 shows trajectories with 1 to 8 groups for comparison).

We first estimated the overall cumulative mortality for each trajectory group. We also estimated age-adjusted hazard ratios (HR) and 95% confidence intervals (CI) for all-cause mortality in a Cox proportional hazards model with the trajectory groups as exposure variable. Age was used as the underlying time scale. The assumption of proportional hazards was met. Hazard differences were estimated using Aalen's additive hazards model, in which the hazard is modeled as a linear function of the explanatory variables. This approach provides an estimate of the absolute burden of excess mortality in one trajectory group compared with another. The assumption of time-invariant associations was met. We also showed the cumulative mortality decomposed into the most common causes of death for each trajectory group using a multi-state survival analysis taking into account competing risks. All analyses were stratified by sex in a supplementary analysis.

While the aim of the paper is to describe multi-dimensional patterns of childhood adversities and how they relate to mortality patterns, an obvious next question is whether these associations are driven by other early life risk factors. Family adversity may impact the health of children already in utero, and birth weight was therefore perceived as a potential mediator and not included in the main analyses. Also, parental education, parental origin and teenage pregnancies are highly correlated with material deprivation making it difficult to disentangle causes from effects. To assess the impact of these factors, we also ran a supplementary analysis adjusting for these variables.

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Results

Trajectories of childhood adversities

We identified five distinct trajectory groups based on combinations of sub-trajectories within the three predefined dimensions (Figure 1). The *Low Adversity* trajectory group comprised 54% of the children. The trajectory group was characterized by a very low rate of adversities in all dimensions, meaning that some children in the trajectory may have experienced a few isolated adversities, but the annual rate was very low.

The *Early Life Material Deprivation* trajectory group comprised 20% of the children. This trajectory group was characterized by a high annual rate of material deprivation during the first 4-5 years of life after which the rate of material deprivation became very low. The annual rates of adversities in the other two dimensions were very low.

The *Persistent Material Deprivation* trajectory group comprised 13% of the children. This trajectory group was characterized by a high annual rate of material deprivation during the entire childhood, but with a low rate of adversities in the other two dimensions.

The *Loss or Threat of Loss* trajectory group comprised 10% of the children. The trajectory group was characterized by a relative high and increasing annual rate of loss or threat of loss during the course of childhood, while the rates of adversities in the two other dimensions were low.

The *High Adversity* trajectory comprised 3% of the children. The trajectory was characterized by a high and increasing annual rate of adversities in all three dimensions. The annual rate of adversities was high and increasing in the family dynamics dimension, especially during adolescence where the children on average experienced almost one adversity every year.

Background characteristics

Background characteristics are shown in Table 2. The proportion with low birth weight was lowest in the low adversity group (4.1%) and highest in the high adversity group (10%). There was also a clear education gradient with only 8.8% in the low adversity group being born into a household with low education, while this proportion was 54.1% in the high adversity group. Those with persistent material deprivation were more often born to parents of non-European origin (9%) compared with all other groups (<5%). Teenage mothers are uncommon in Denmark and only 1% of those in the low adversity group were born by teenage mothers while this proportion was markedly higher among those in the persistent material deprivation group (7.3%) and in the high adversity group (10.7%). The proportion of teenage fathers is even lower, but follows a similar pattern.

All-cause mortality

We recorded 3827 deaths during a mean follow-up time of 8.6 years, ranging from 1 day to 18 years. As expected, the crude mortality rate was low at this young age with only 2.9 deaths per 10,000 person years in the low adversity group (Figure 2). Compared with the low adversity group, the mortality rate was higher in the early life material deprivation group (HR=1.4; 95% CI 1.3-1.5), in the persistent material deprivation group (HR=1.8; 95%CI: 1.6-1.9) and in the loss group (HR=1.8; 95% CI; 1.6- 2.0). Most pronounced was a 4.5 times higher risk of premature mortality (95% CI: 4.1-5.1) in the high vs. low adversity group, corresponding to 10.3 (95% CI: 9.0; 11.6) additional deaths per 10,000 person years. The relative effects were similar in men and women, but the absolute effects were larger in men due to an overall higher mortality rate in young men than women (Suppl Fig 3). For example, being in the high vs. low adversity group was associated with 13.7 (95% CI: 11.7; 15.7) additional deaths in men and 6.1 (4.7; 7.6) additional deaths per 10,000 years in women. In a subpopulation with full information (n=1,043,495), we adjusted for sex, birth weight, household education, parental origin and parental age at birth (Suppl Fig 4). This adjustment resulted in a slight attenuation of the risk estimates in the high vs. low adversity group (the HR goes from 4.7 to 3.8 in this subsample). The risk estimates were almost identical in the other groups before and after adjustment.

Cause-specific mortality

Of the 3827 deaths, the majority (37%) were due to accidents. The mortality patterns for deaths due to accidents were similar to that of overall mortality (Figure 3) with a moderately higher mortality risk in the early life material deprivation group (HR=1.7; 95% CI 1.4-1.9), in the persistent material deprivation group (HR=2.0; 95% CI: 1.8-2.3) and in the loss group (HR=1.7; 95% CI; 1.4.-2.0). Again, a markedly higher risk of death due to accidents was found in the high vs. low adversity group (HR= 4.2; 95% CI; 3.5-5.1), which corresponds to 3.3 (95% CI: 2.6-4.1) extra deaths due to accidents per 10,000 person-years.

A total of 586 (15%) deaths were due to suicides with a very low risk among children in the low adversity group, a moderately higher risk among children in the early life material deprivation, persistent deprivation and loss groups. Again, a markedly higher risk of suicide was seen among persons in the high vs. low adversity group (HR=4.9; 95% CI 3.7-6.4), which corresponds to 1.8 (95% CI: 1.3-2.3) extra deaths due to suicide per 10,000 person-years.

A total of 491 (13%) deaths were due to cancers. While the differences were smaller, we still observed a moderately higher risk of cancer mortality in the persistent material deprivation group (HR=1.3; 95 % CI: 1.1-1.7) and in the high adversity group (HR=1.8; 95% CI: 1.2-2.6) compared with the low adversity group.

The remaining 1317 (34%) deaths were due to a combination of other causes, and even though the patterns were similar to those for overall mortality, it was difficult to make cause-specific comparisons due to small numbers. The two most common causes of death among the remaining causes were diseases of the nervous system (191 cases) and circulatory system (178 cases) (Suppl Table 1).

Discussion

In an unselected sample of more than 1 million Danish children, we identified five distinct trajectories of childhood adversities. About half of the children experienced none or few isolated events and the mortality rate in early adulthood was lowest in this group. However, a substantial proportion of children (~45%) experienced childhood adversities in specific dimensions, such as material deprivation or loss in the family. These children experienced a moderately higher mortality risk in early adult life. A small group of children (3%) experienced a high and increasing rate of adversities in all three dimensions during their entire childhood. This group of disadvantaged children had more than four times higher risk of premature mortality in early adult life. Accidents and suicides constituted the most common causes of death and the mortality patterns for these events followed that of overall mortality. Cancer was the third most common cause of death, and while less pronounced, a moderately higher risk of cancer mortality was also found in the high vs. low adversity group.

Our findings corroborate a number of smaller studies[7,12 13–17] We add to this literature by utilizing high-resolution data to distinguish between different dimensions of childhood adversities and by studying premature deaths in young adulthood. We document how the accumulation and interrelation between these dimensions are important to fully understand the mortality risk associated with childhood adversities. Our findings are pertinent to the ongoing discussion in life course epidemiology about sensitive periods vs. accumulation of risk.[18] Using annually repeated measures, which cover entire childhoods, we have shown that these two concepts are highly intertwined and that they cannot be understood independently of each other. For example, if we had focused solely on material deprivation in early childhood, children in three of the five identified trajectory groups (i.e. the early life material deprivation, the persistent deprivation and the high adversity group) would have been lumped into one group. This would have hidden the very different trajectories these children follow.

The concept of syndemics has recently been taken up in the medical literature as a conceptual framework for understanding intertwined and cumulated effects of social and biomedical factors and how they shape distributions of diseases across populations.[5] Our results point to a potential childhood adversity syndemic in a small subset of children with high and accelerating adversities across various dimensions, ending in a negative biosocial feedback loop associated with a markedly higher mortality risk in early adult life. While we have studied the dynamic interplay between different types of adversities and their effects on mortality, the underlying interacting and mutually reinforcing social and health conditions generating this higher mortality needs further investigation.

Our study population is nested within a social welfare system with universal child care and a social security system that promotes economic stability for families. It is striking that such clear associations between childhood adversities and premature mortality are found even within this social structure, and even stronger effects may be found in societies with less social security. Investigation into how effects of underlying structures materialize, and whether the trajectories through childhood adversity dimensions are mutually causal, synergistically interacting or serially causal for the effect on premature mortality needs to be further explored.[19]

An eco-bio-developmental framework underscores how early experiences can leave a lasting signature on emerging brain architecture and long-term health.[1] The theoretical framework highlights the fundamental importance of the early years, where the brain is particularly sensitive to elevated levels of stress hormones, which can interfere with its developing architecture. Shonkoff et al. argues that toxic stress may produce physiological disruptions in the development of the body's response system and affect the developing brain, immune, cardiovascular and metabolic systems with associated long-lasting effects on health.[1] The child's intrafamilial environment is important for coping and learning, and children exposed to a cumulative toxic stress may also be more likely than other children to adapt unhealthy behaviors such as excessive alcohol drinking or drug abuse,[20,21] which may partly explain the higher risk of accidents observed in the high adversity group.

Accidents and suicides accounted for the majority of deaths in our study, and there is an extensive literature on the association between exposure to childhood adversities and suicide, which supports our findings.[22] [23] By contrast there are few or no large studies on childhood events and accidents to the best of our knowledge. Again, we add to this literature by showing that childhood adversities accumulate over time and across social, health and family-related dimensions, which indicates that multi-faceted interventions are needed to address the problem.

Cancer was the third most common cause of death in the current study. We found a moderately higher risk of cancer mortality in the persistent material deprivation and high adversity groups. A few studies have addressed the effect of single major stressors, such as bereavement, on cancer mortality and they generally find no overall effect or a very small effect of childhood adversities on cancer mortality risk.[24] The effect of childhood adversities on the incidence and survival of various subtypes of cancer with different underlying etiology needs to be addressed in future studies.

Strengths and limitations

Relying on register-based information ensured a very large sample size and prevented problems with selective inclusion and exclusion from the cohort. However, it came at the cost of a limited selection of childhood adversities available in the registers. For example, we did not have direct information on child physical or sexual abuse, which is also associated with higher mortality.[25] The

same goes for domestic violence and child neglect. Although we lacked this kind of information, the very severe cases are likely to have been captured by information on foster care. Furthermore, we derived information on alcohol abuse from hospitalizations and medication use related to alcohol abuse, but it is well-known that the majority of alcohol abuses is never registered. The same goes for a number of other indicators, where we only catch the tip of the iceberg. Divorce and parental psychiatric illness are used as indicators of family dynamics, while a home environment with a high conflict level or even violence will not necessarily have been captured by these measures. By using many and repeated indicators of childhood adversities we hope to have captured some general patterns, but we may have underestimated the true effect of childhood adversities to some degree.

We excluded children who died before the age of 16 years. The majority of these children died within the first year of life due to e.g. neonatal complications, congenital anomalies or preterm birth. The drivers of these deaths are mainly established prior to the child being born and constitute a related but different question that is not within the scope of this paper. Although the child mortality rate is very low in Denmark, some children die between 1 and 16 years and those deaths may be related to childhood adversities. For example, Grey et al. recently found that the experience of 4+ childhood adversities vs. none was associated with child mortality.[26] Thus, we may have underestimated the effect of childhood adversities on mortality by excluding childhood mortality.

Conclusions

We have identified five distinct trajectories of childhood adversity, which are clearly associated with mortality risk in early adult life. A small group of children experienced a high and accelerating rate of adversities across intertwined dimensions of deprivation, loss and family dynamics during the entire childhood and carried a very high mortality risk, particular from suicide and accidents, but also from somatic conditions such as cancer. These findings also suggest a significant burden of underlying morbidity that will likely translate into a significant public health problem as the cohort ages. Our findings indicate the critical importance of broader structural public health initiatives as well as help to identify vulnerable children who would benefit from targeted support.

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Author contributions

NHR, AR, DTR, ND and AMNA conceived the idea and designed the study. JB performed the data linkage and data cleaning for DANLIFE. AR, EBJ and CCJ performed the trajectory analyses. NHR, JB, EBJ and AR had access to all the data. NHR wrote the first draft of the manuscript. All authors discussed the results and contributed to the final manuscript. All authors have seen and approved of the final text.

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484 **Table 1. Dimensions and definition of adverse childhood experiences**

Dimension	Adversity	Definition	Registers
Material deprivation	Family poverty	1 count each year of life when the family income is below 50% of the median national family income	The Income Statistics Register
	Long-term unemployment	1 count each year of life for each parent being unemployed for at least 12 months	The Integrated Database for Labour Market Affiliation
Loss or threat of loss	Death of a parent	1 count in the year a parent dies	The Danish Civil Registration System
	Death of a sibling	1 count for each death of a sibling	The Danish Civil Registration System
	Parental somatic illness	1 count each year of life for each parent diagnosed with one of the illnesses related to mortality included in the Charlson comorbidity index	The Danish National Patient Register
	Sibling somatic illness	1 count each year of life for each sibling diagnosed with one of the seven most common somatic illnesses related to mortality in children aged 0-18 years in Denmark: malignant neoplasm; congenital anomalies of the heart and circulatory system; congenital anomalies of the nervous system; cerebral palsy; epilepsy cardiomyopathy; congenital disorders of lipid metabolism	The Danish National Patient Register
Family dynamics	Foster care	1 count each year of life, which overlaps with a calendar year, where the child was registered as placed in out-of-home care	The Register of Support for Children and Adolescents
	Parental psychiatric illness	1 count each year of life for each parent with a hospital admission with a diagnosis related to psychiatric illness (excluding main diagnoses related to alcohol and drug abuse)	The Danish Psychiatric Central Research Register; The Danish National Patient Register
	Sibling psychiatric illness	1 count each year of life for each sibling with a hospital admission with a diagnosis related to psychiatric illness	The Danish Psychiatric Central Research Register; The Danish National Patient Register
	Parental alcohol abuse	1 count each year of life for each parent diagnosed with an illness related to alcohol abuse or receiving a prescription of a drug used in treatment of alcohol addiction	The Danish Psychiatric Central Research Register; The Danish National Patient Register; The Danish National Prescription Registry
	Parental drug abuse	1 count each year of life for each parent diagnosed with an illness related to drug abuse or receiving a prescription of drugs used in treatment of drug addiction	The Danish Psychiatric Central Research Register; The Danish National Patient Register; The Danish National Prescription Registry
	Maternal separation	1 count each year of life, which overlaps with a calendar year, where the mother gets separated from a partner	The Danish Civil Registration System

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Table 2. Background characteristics at time of birth for 1,097,628 Danish children by the five estimated trajectory groups.

		Low adversity	Early life material deprivation	Persistent material deprivation	Loss or threat of loss	High adversity
		(n = 590,161)	(n = 218,327)	(n = 147,895)	(n = 105,164)	(n = 36,081)
Sex, n (%)						
	Boys	302,800 (51.3)	111,655 (51.1)	75,654 (51.2)	53,511 (50.9)	19,560 (54.2)
	Girls	287,361 (48.7)	106,672 (48.9)	72,241 (48.9)	51,653 (49.1)	16,521 (45.8)
Birth weight, n (%)						
	< 2500 g	24,340 (4.1)	10,933 (5.0)	8,290 (5.6)	6,725 (6.4)	3,619 (10.0)
	2500-4500 g	543,076 (92.0)	200,603 (91.9)	135,337 (91.5)	94,818 (90.2)	31,552 (87.5)
	>4500 g	15,661 (2.7)	4,763 (2.2)	2,744 (1.9)	2,410 (2.3)	470 (1.3)
	Missing	7,084 (1.2)	2,028 (0.9)	1,524 (1.0)	1,211 (1.2)	440 (1.2)
Highest household education, n (%)						
	Low	51,666 (8.8)	49,768 (22.8)	49,489 (33.5)	22,524 (21.4)	19,534 (54.1)
	Medium	288,448 (48.9)	120,351 (55.1)	71,179 (48.1)	52,615 (50.0)	12,654 (35.1)
	High	247,506 (41.9)	47,377 (21.7)	26,100 (17.7)	29,570 (28.1)	3,497 (9.7)
	Missing	2,541 (0.4)	831 (0.4)	1,127 (0.8)	455 (0.4)	396 (1.1)
Parental origin, n (%)						
	Others	7,440 (1.3)	9,233 (4.2)	13,265 (9.0)	3864 (3.7)	1,106 (3.1)
	European	581,705 (98.6)	209,054 (95.8)	134,580 (91.0)	101,275 (96.3)	34,963 (96.9)
	Missing	1,016 (0.2)	40 (<0.1)	50 (<0.1)	25 (<0.1)	12 (<0.1)
Maternal age, n (%)						
	< 20 years	5,832 (1.0)	8,184 (3.8)	10,774 (7.3)	3,671 (3.5)	3,847 (10.7)
	20-30 years	394,592 (66.9)	162,869 (74.6)	105,764 (71.5)	68,285 (64.9)	24,655 (68.3)
	> 30 years	189,214 (32.1)	47,261 (21.7)	31,338 (21.2)	33,195 (31.6)	7,573 (21.0)
	missing	523 (0.1)	13 (<0.1)	19 (<0.1)	13 (<0.1)	6 (<0.1)
Paternal age, n (%)						
	< 20 years	1,281 (0.2)	1,649 (0.8)	2378 (1.6)	784 (0.8)	838 (2.3)
	20-30 years	280,555 (47.5)	123,566 (56.6)	81,123 (54.9)	48,243 (45.9)	18,239 (50.6)
	> 30 years	292,420 (49.6)	82,975 (38.0)	57,344 (38.8)	52,357 (49.8)	13,009 (36.1)
	missing	15,905 (2.7)	10,137 (4.6)	7050 (4.8)	3,780 (3.6)	3,995 (11.1)

Figure 1. Estimated trajectory groups of childhood adversities among 1,097,628 Danish children

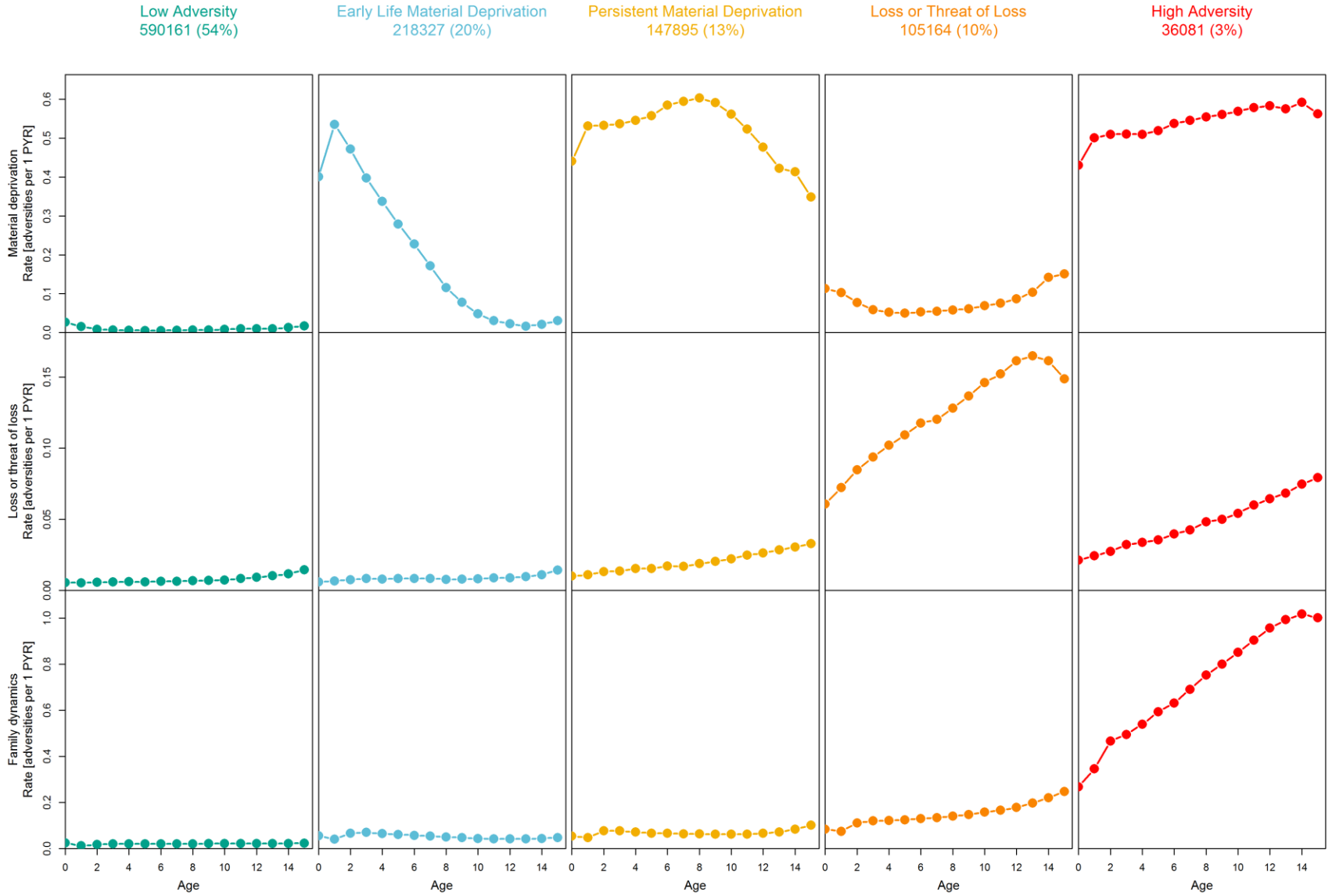


Figure 2. Cumulative all-cause mortality among 1,097,628 Danish children divided into the five estimated trajectory groups of childhood adversities.

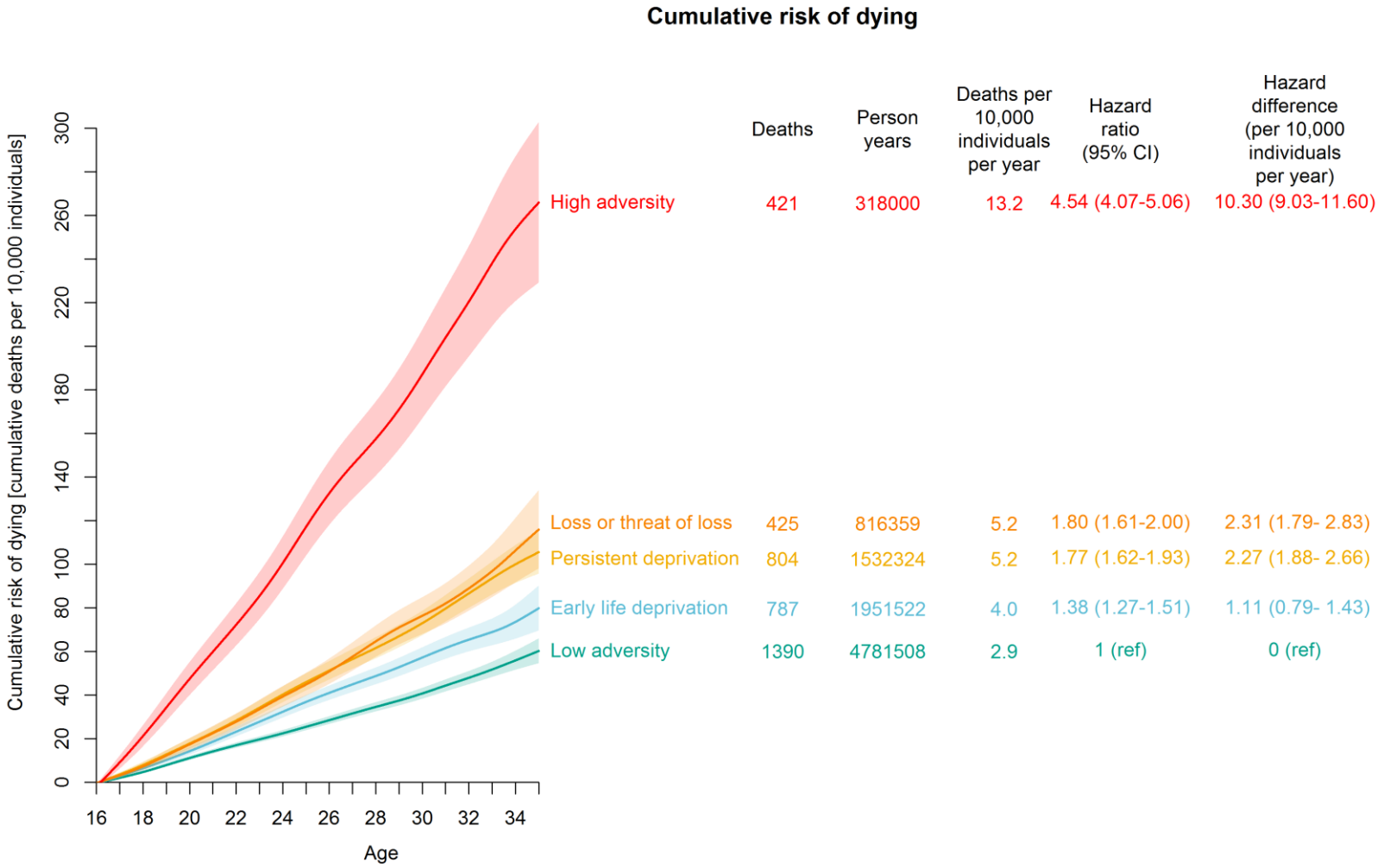
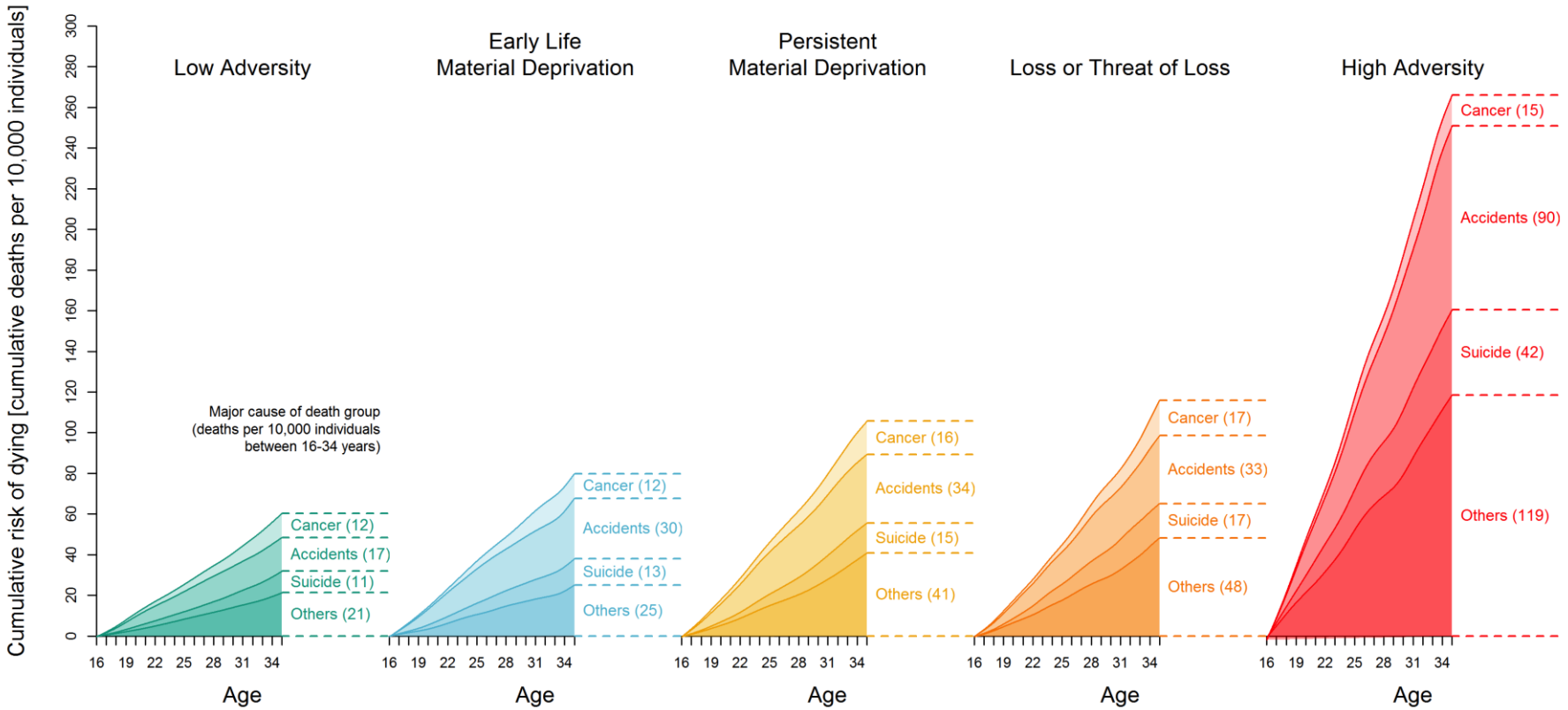


Figure 3. Cumulative cause-specific mortality among 1,097,628 Danish children, divided into the five estimated trajectory groups of childhood adversities.



Cause-specific hazard ratios (95% CI)

Cancer	1 (ref)	1.1 (0.9-1.4)	1.3 (1.1-1.7)	1.2 (0.8-1.6)	1.8 (1.2-2.6)
Accidents	1 (ref)	1.7 (1.4-1.9)	2.0 (1.8-2.3)	1.7 (1.4-2.0)	4.2 (3.5-5.1)
Suicide	1 (ref)	1.4 (1.1-1.7)	1.5 (1.2-1.9)	1.9 (1.5-2.5)	4.9 (3.7-6.4)
Others	1 (ref)	1.2 (1.0-1.4)	1.8 (1.6-2.1)	2.2 (1.8-2.6)	6.0 (5.1-7.2)