SHORT COMMUNICATION

Childhood adversity and risk of type 2 diabetes in early adulthood: results from a population-wide cohort study of 1.2 million individuals

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Abstract

Aims/hypothesis To examine whether childhood adversity is related to development of type 2 diabetes in early adulthood (16 to 38 years) among men and women.

Methods We used nationwide register data of 1,277,429 individuals born in Denmark between 1 January 1980 and 31 December 2001, who were still resident in Denmark and without diabetes at age 16 years. Individuals were divided into five childhood adversity groups based on their yearly exposure to childhood adversities (from age 0–15 years) across three dimensions: material deprivation, loss or threat of loss, and family dynamics. We estimated HR and hazard differences (HD) for type 2 diabetes according to the childhood adversity groups using Cox proportional hazards and Aalen additive hazards models.

Results During follow-up from age 16 to 31 December 2018, 4860 individuals developed type 2 diabetes. Compared with the low adversity group, the risk of type 2 diabetes was higher in all other childhood adversity groups among both men and women. For example, the risk was higher in the high adversity group characterised by high rates of adversity across all three dimensions among men (HR 2.41; 95% CI 2.04, 2.85) and women (1.58; 1.31, 1.91), translating into 36.2 (25.9, 46.5) additional cases of type 2 diabetes per 100,000 person-years among men and 18.6 (8.2, 29.0) among women.

Conclusions/interpretation Individuals who experienced childhood adversity are at higher risk of developing type 2 diabetes in early adulthood. Intervening upon proximal determinants of adversity may help reduce the number of type 2 diabetes cases among young adults.

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Abbreviations
DANLIFE   Danish life course cohort study
HD   Hazard difference

Research in context

What is already known about this subject?

- Childhood adversity is hypothesised to increase the risk of type 2 diabetes through activation of the physiological stress response and its influence on health behaviours

- The association between childhood adversity and type 2 diabetes in early adulthood (<40 years) remains to be examined in longitudinal studies

What is the key question?

- Is childhood adversity related to a higher risk of type 2 diabetes in early adulthood?

What are the new findings?

- The risk of type 2 diabetes in early adulthood was higher in individuals exposed to childhood adversity compared with individuals exposed to low adversity

- Among men, the association was most pronounced in those who had experienced high rates of adversity across multiple life dimensions during childhood

- Among women, the associated risks were equally elevated in those who had experienced persistent material deprivation throughout childhood, loss or threat of loss, or high rates of adversity across multiple life dimensions

How might this impact on clinical practice in the foreseeable future?

- Individuals who have experienced childhood adversity are at higher risk of developing type 2 diabetes in early adulthood, making this a target group for early intervention

Introduction

The worldwide prevalence of type 2 diabetes in adolescents and young adults has increased substantially over the last centuries, largely driven by changes in lifestyle and obesity prevalence [1]. This is worrying because early-onset type 2 diabetes (<40 years of age) is suggested to be a more aggressive pathological entity [1]. In addition, young adult-onset of type 2 diabetes has a major impact on individuals and society as it affects younger individuals who are of working age, potentially predisposing them to lifelong treatment and increasing the risk of complications [1]. Combined, this makes it of crucial importance for public health to identify potential risk factors for type 2 diabetes in early adulthood [2].

Childhood adversity, which entails experiences such as maltreatment, physical or mental illness in the family, and poverty, has been associated with diabetes, even in young adulthood [3–7]. Childhood adversity could trigger and dysregulate the physiological stress response and related bodily systems, such as the nervous system, hypothalamic-pituitary-adrenal axis, endocrine and immune system, and it could influence mental health and health behaviours, such as sleep, smoking, physical activity, sedentary behaviour and eating behaviour, which may eventually influence obesity and type 2 diabetes [1, 7–9]. However, evidence for an association

between childhood adversity and type 2 diabetes in young adulthood, specifically beyond maltreatment, is scarce [3–5] and sex-specific estimates are lacking [7, 8, 10]. In addition, there is a need for methodological improvements in this research area [4], including a need for prospective studies using objective and more comprehensive measures of childhood adversity [3, 4, 7–9]. We utilise detailed register-based data on childhood adversity and type 2 diabetes of over 1 million individuals to examine whether childhood adversity in multiple dimensions of life is associated with a higher risk of type 2 diabetes in young adult men and women.

Methods

The Danish life course cohort study (DANLIFE) includes data from various nationwide registers on childhood adversities and background information of children born in Denmark since 1 January 1980 [11]. The processing of personal data in the DANLIFE study is approved by the Faculty of Health and Medical Sciences at the University of Copenhagen (Copenhagen, Denmark) (record number 514-0641/21-3000) on behalf of the Danish Data Protection Agency, which ensures compliance with national and EU legislation. To allow for follow-up from age 16 years, the sample for the

current study was restricted to individuals born up until 31 December 2001 (n=1,357,808). Children who emigrated or died before age 16 were excluded (n=73,853). We further excluded children who were diagnosed with type 1 or type 2 diabetes before age 16 (n=5208). As 99.9% of these individuals had complete information on the covariates included in the main analysis, we further restricted the sample to those with complete information on these covariates, totalling 1,277,429 individuals in the study (electronic supplementary material [ESM] Fig. 1).

Childhood adversity DANLIFE includes information on 12 different childhood adversities, which are divided into the dimensions of material deprivation (family poverty and parental long-term unemployment), loss or threat of loss (parental somatic illness, sibling somatic illness, parental death, sibling death) and family dynamics (foster care placement, parental psychiatric illness, sibling psychiatric illness, parental alcohol abuse, parental drug abuse and maternal separation) (ESM Table 1).

In a previous study [12], we allocated children to five childhood adversity groups based on annual counts of their exposure to childhood adversities in each of the three dimensions from 0 to 15 years using group-based multi-trajectory modelling (using the *traj* package in Stata, version 2016) [13]. In these five groups children experience: (1) relatively low levels of adversity across childhood (54%); (2) material deprivation specifically in early childhood (20%); (3) material deprivation throughout childhood and adolescence (13%); (4) relatively high levels of somatic illness or death in the family (9%); and (5) relatively high levels of adversity across all three dimensions (3%) (ESM Fig. 2).

Diabetes Diagnosis and date of diagnosis of type 2 diabetes, as well as of type 1 diabetes, was determined by combining information from three Danish registers, i.e. the National Patient Register (NPR), the Danish National Prescription Registry (DNPR), and the Danish Adult Diabetes Registry (DADR), in line with the approach used by Carstensen et al (2020) (see ESM Methods) [14].

Covariates Potential confounders included parental origin (Western/non-Western), maternal age at birth (<20 years, 20–30 years, >30 years), parental diabetes (yes/no) and year of birth. In additional analyses, we adjusted for parental education at the time of birth (<10 years, 10–12 years, and >12 years), size for gestational age (birthweight-for-age <10th, ≥10th–≤90th, and >90th percentile of age- and sex-specific intrauterine growth reference curves) [15] and preterm birth (<37 weeks/≥37 weeks of gestation) in a sample with information on all covariates (n=1,231,654).

Statistical analysis We first estimated the cumulative risk of type 2 diabetes across the five groups using a spline with 6 df. Second, we estimated adjusted HR and hazard differences (HDs) per 100,000 person-years for type 2 diabetes in the different childhood adversity groups, compared with the low adversity group, using Cox proportional hazards models and Aalen additive hazards models. We used age as the underlying time scale. Individuals were followed from age 16 until diagnosis of type 2 diabetes, emigration, death, diagnosis of type 1 diabetes or the end of follow-up (31 December 2018). Analyses were stratified by sex. In a sensitivity analysis, we restricted the population to those without parental diabetes

Table 1 Adjusted HRs and HDs per 100,000 person-years for type 2 diabetes

Childhood adversity groups	Type 2 diabetes (n)	Rate[a]	aHR (95% CI)	aHD (95% CI)
Men				
Low adversity	759	20.9	1 (ref)	0 (ref)
Early life material deprivation	513	34.2	1.45 (1.30, 1.63)	9.5 (6.2, 12.8)
Persistent material deprivation	593	52.3	1.66 (1.49, 1.86)	17.1 (12.7, 21.5)
Loss or threat of loss	262	44.3	1.76 (1.53, 2.03)	16.4 (10.9, 21.9)
High adversity	173	67.6	2.41 (2.04, 2.85)	36.2 (25.9, 46.5)
Women				
Low adversity	940	27.6	1 (ref)	0 (ref)
Early life material deprivation	586	41.4	1.34 (1.21, 1.49)	9.5 (5.7, 13.3)
Persistent material deprivation	627	58.5	1.51 (1.36, 1.68)	17.0 (12.1, 21.9)
Loss or threat of loss	283	50.3	1.46 (1.28, 1.67)	13.5 (7.4, 19.6)
High adversity	124	57.9	1.58 (1.31, 1.91)	18.6 (8.2, 29.0)

Analyses are adjusted for parental origin, maternal age at birth, parental diabetes and year of birth (n=1,277,429)

[a] Per 100,000 person-years

aHD, adjusted HD; aHR, adjusted HR

Fig. 1 Cumulative risk of type 2 diabetes in the five childhood adversity trajectory groups among men (**a**) and women (**b**). T2DM, type 2 diabetes
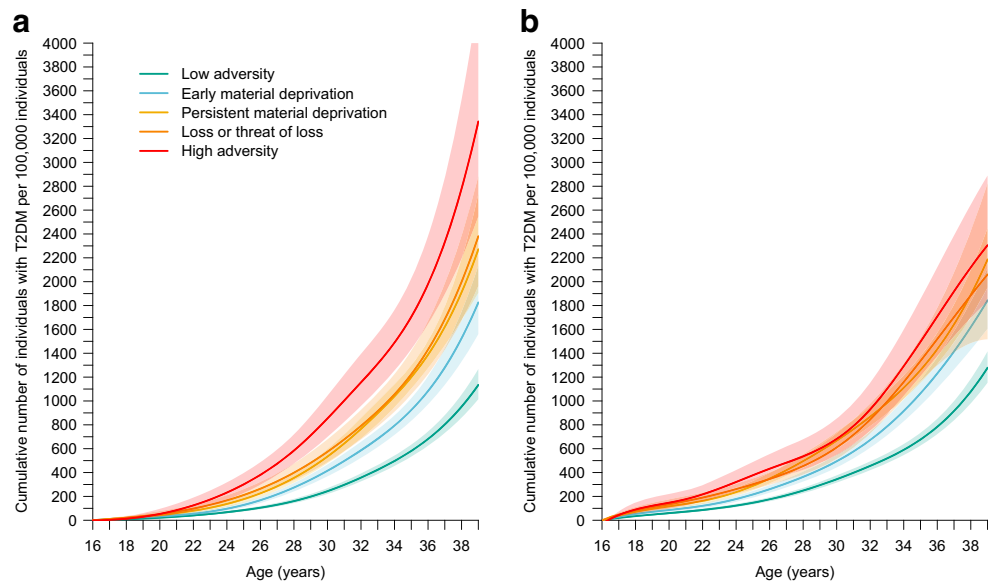
(n=1,094,686). Data preparation and analyses were done in Stata (version 14) and R (version 4).

Results

In total, 2560 women and 2300 men developed type 2 diabetes during follow-up. Individuals were followed up for a mean (SD) of 10.8 (6.2) years (total follow-up time: 13,782,218 person-years).

Background characteristics of the study population, overall and according to the five childhood adversity trajectory groups, are in ESM Table 2. Compared with the low adversity group, the cumulative number of individuals with type 2 diabetes per 100,000 individuals from age 16 to 38 years was higher in all other childhood adversity groups (Fig. 1). In adjusted analyses, the risk of type 2 diabetes was higher in all these groups, compared with the low adversity group, among both men and women (Table 1).

Effect estimates were attenuated when the associations were further adjusted for parental educational level, size for gestational age and preterm birth (ESM Table 3), specifically for women in the high adversity group vs the low adversity group (HR 1.23; 95% CI 1.00, 1.50 and HD 6.4; 95% CI −4.4, 17.3 additional cases per 100,000 person-years) and mainly due to adjustment for parental educational level.

Among individuals whose parents did not have a diagnosis of diabetes, the relative risks of diabetes associated with childhood adversity seemed somewhat higher than in the main analysis, particularly for men, while the absolute risks were lower, in line with the lower cumulative number of type 2 diabetes cases per 100,000 individuals in this subpopulation (ESM Table 4 and ESM Figure 3).

Discussion

In this large population-based study that does not suffer from selection or recall bias, we found that individuals who experienced different levels and types of adversity in childhood were at higher risk of type 2 diabetes in early adulthood than individuals who experienced low levels of adversity in childhood. Parental education is closely related to the experience of childhood adversity and explains some of the observed association.

Our findings are in line with previous studies reporting an association between childhood adversity and diabetes, as well as related physical and mental health conditions, in young [3, 5, 16] and middle adulthood [17, 18]. Disentangling underlying mechanisms, such as overweight, obesity, health behaviours, mental health and biological pathways, calls for further attention [5, 17, 18]. We add to the current evidence by using a comprehensive measure of a wide array of register-based childhood adversities, by distinguishing between type 1 and type 2 diabetes and by adjusting for parental diabetes. We additionally add to the evidence by showing that relative risks of type 2 diabetes following childhood adversity were lower among women than men. While the absolute effects of experiencing loss or threat of loss and high adversity during childhood were also lower among women than men, the absolute effects of experiencing material deprivation in early life or persistently throughout childhood were comparable between men and women.

While examining the association between childhood adversity and type 2 diabetes in young adulthood is an important contribution of this study, a limitation is that type 1 and type 2 diabetes diagnosis may be mixed up at this early age. We do, however, believe that by using multiple registers we have increased the likelihood of correctly classifying type 1 diabetes and type 2 diabetes cases.

Conclusion Individuals exposed to childhood adversity, such as poverty, illness or death in the family, and a dysfunctional household, are at higher risk of developing type 2 diabetes in young adulthood compared with individuals who experience low levels of adversity in childhood. This study shows that a share of the type 2 diabetes cases in young adulthood could likely be prevented by intervening on the fundamental causes generating childhood adversity.

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