AUTHOR	Upadhyaya, Subina; Tolmunen, Tommi; Elomaa, Antti-Pekka; Ruohomäki, Aleksi; Kraav, Siiri-Liisi; Kauhanen, Laura; Kaplan, George; Kauhanen, Jussi; Lehto, Soili M.
TITLE	Parental Alcohol Problems, Parental Divorce, and Type 2 Diabetes in Adulthood: A Longitudinal Prospective Cohort Study in Middle-Aged Men
YEAR	2020
DOI	10.1097/PSY.0000000000000865
VERSION	Author's accepted manuscript
CITATION	Upadhyaya, Subina MPH; Tolmunen, Tommi MD, PhD; Elomaa, Antti-Pekka MD, PhD; Ruohomäki, Aleksi MD; Kraav, Siiri-Liisi MSc; Kauhanen, Laura MD, PhD; Kaplan, George PhD; Kauhanen, Jussi MD, PhD; Lehto, Soili M. MD, PhD Parental Alcohol Problems, Parental Divorce, and Type 2 Diabetes in Adulthood: A Longitudinal Prospective Cohort Study in Middle-Aged Men, Psychosomatic Medicine: 11/12 2020 - Volume 82 - Issue 9 - p 817-822 doi: 10.1097/PSY.0000000000000865

Parental Alcohol Problems, Parental Divorce, and Type 2 Diabetes in Adulthood: A Longitudinal Prospective Cohort Study in Middle-Aged Men

Subina Upadhyaya, MPH, Tommi Tolmunen, MD, PhD, Antti-Pekka Elomaa, MD, PhD, Aleksi Ruohomäki, MD, Siiri-Liisi Kraav, MSc, Laura Kauhanen, MD, PhD, George Kaplan, PhD, Jussi Kauhanen, MD, PhD, and Soili M. Lehto, MD, PhD

ABSTRACT

Objective: Type 2 diabetes is a chronic disease and a serious global public health concern increasing both mortality and morbidity. Previous studies have found evidence for an association between early psychological stress and diabetes later in life.

Methods: This study examined the association between parental alcohol problems and parental divorce and the incidence of type 2 diabetes in Finnish men aged 42 to 61 years ($n = 754$) in a prospective setting. Information on parental alcohol problems and parental divorce was derived from school records and subjective experiences of the same events from self-rated questionnaires. The average follow-up time for the participants until the first type 2 diabetes diagnosis was 23.3 years (25th–75th percentile, 21.2–27.9 years).

Results: Cox regression analyses revealed that parental alcohol problems (hazard ratio = 3.09, 95% confidence interval = 1.38–6.88) were associated with an increased risk of type 2 diabetes during the follow-up, even after adjustment for age, marital status, education, Human Population Laboratory Depression Scale scores, smoking, alcohol consumption, body mass index, and serum high-sensitivity C-reactive protein. In a similar model, parental divorce (hazard ratio = 1.69, 95% confidence interval = 0.40–7.05) was not associated with an increased risk of type 2 diabetes during the follow-up.

Conclusions: Our findings suggest that not all adverse childhood experiences contribute equally to the risk of type 2 diabetes. Parental alcohol problems, but not parental divorce, were associated with an increased risk of type 2 diabetes in men. These findings highlight the need for early interventions targeting parents with excessive alcohol consumption to reduce their offspring's risk of life-style–related disorders.

Key words: diabetes, early adversity, risk factors, prospective, parental alcohol, parental divorce.

INTRODUCTION

Adverse childhood experiences (ACEs) such as childhood trauma, a dysfunctional household, parental separation, and exposure to domestic violence have a profound impact on the health of individuals as they reach adulthood (1). Exposure to early adverse experiences can damage a child's development and is associated with poor outcomes across different phases of life (2). Not only do ACEs affect an individual's psychosocial well-being (3,4), but they are also associated with mortality and morbidity, that is, serious chronic health conditions (5).

Type 2 diabetes is a severe chronic disease and has become a major public health concern in the last few decades (6). In global terms, approximately 8.8% of the adult population is affected by diabetes (with type 2 diabetes accounting for 90% of all diabetes cases), and it is projected to increase up to 10% by 2045 (7). The tendency to develop type 2 diabetes has been attributed to genetic heredity and personal life-style factors, including diet and smoking (8). The existence of type 2 diabetes doubles the risk for a wide range of vascular diseases, such as coronary ischemia and stroke (9). ACEs may lead to type 2 diabetes through their adverse effects on mental well-being and various life-style factors, including diet, smoking, and physical activity (10). Nevertheless, knowledge on the role of early adverse experiences in the development of adult-onset diabetes remains scarce, although ACEs seem to induce physiological changes very similar to those observed in diabetes (11).

ACEs = adverse childhood experiences, **BMI** = body mass index, **CRHC** = Care Register for Health Care, **hsCRP** = high-sensitivity C-reactive protein

SDC Supplemental Content

From the Research Centre for Child Psychiatry (Upadhyaya), University of Turku, Turku; Department of Psychiatry (Tolmunen), Kuopio University Hospital; Department of Neurosurgery (Elomaa), Kuopio University Hospital; Institute of Clinical Medicine/Psychiatry (Tolmunen, Ruohomäki, Kraav) and Department of Social Sciences (Kraav), University of Eastern Finland, Kuopio, Finland; School of Medicine (Kauhanen), Vilnius University, Vilnius, Lithuania; Center for Social Epidemiology and Population Health (Kaplan), University of Michigan, Ann Arbor, Michigan; Institute for Integrative Health (Kaplan), Baltimore, Maryland; Institute of Public Health and Clinical Nutrition (Kauhanen), University of Eastern Finland, Kuopio, Finland; Institute of Clinical Medicine (Lehto), University of Oslo, Oslo; R&D Department, Division of Mental Health Services (Lehto), Akershus University Hospital, Lørenskog, Norway; and Department of Psychiatry (Lehto), University of Helsinki and Helsinki University Hospital, Helsinki, Finland.

Address correspondence to Soili M. Lehto, MD, PhD, Institute of Clinical Medicine, University of Oslo, Oslo, Norway. E-mail: s.m.lehto@medisin.uio.no

Received for publication March 17, 2020; revision received August 12, 2020.

DOI: 10.1097/PSY.0000000000000865

A few cross-sectional (1,5,12–18) and longitudinal (19,20) studies have examined the associations between ACEs (including parental alcohol problems and/or parental divorce) and diabetes (regardless of the type) in adulthood. The previous studies assessing the relationship between ACEs and diabetes in adulthood have combined ACEs into a single summed construct that represents the number of ACEs experienced by an individual, and most often have focused on childhood abuse and neglect as a measure of ACEs. Five studies have evaluated the independent effect of parental alcohol problems and parental divorce (as measures of ACEs) on adult-onset diabetes (regardless of the type); only one of these studies reported a significant association between parental divorce and diabetes (16), the others having nonsignificant findings (5,12,18,20). However, all the previous studies have used retrospective self-reporting to identify ACEs, which has a potential for recall bias, and furthermore, have combined both type 2 and type 2 diabetes as the outcome. No previous studies have examined the relationship between parental alcohol problems, parental divorce, and exclusively type 2 diabetes in adulthood using both participant-reported and official school record-based data.

The aim of this study was to examine the associations between official school record-based and participant-reported accounts of two ACEs, that is, parental alcohol problems and parental divorce, and the subsequent risk of type 2 diabetes in adulthood. This study used data from two different sources: a) school health records of the participants maintained by school nurses and doctors during childhood and b) retrospective questionnaires completed in adulthood. The associations of parental alcohol problems and parental divorce with type 2 diabetes were examined in a prospective setting. We hypothesized that both parental alcohol problems and parental divorce would exert an adverse impact later in life, such as an increased incidence of type 2 diabetes in adulthood.

METHODS

Study Population

The Kuopio Ischemic Heart Disease Risk Factor Study is a population-based study focusing on risk factors for ischemic heart disease and other outcomes among middle-aged men in the Kuopio region of Eastern Finland (21). A total of 2682 participants aged from 42 to 60 years were recruited for the baseline examination, which occurred between March 1984 and December 1989. The information on ACEs such as parental alcohol problems and parental divorce was derived from school health records, which were available for 800 participants. Those participants who reported type 1 or type 2 diabetes mellitus or had a serum high-sensitivity C-reactive protein (hsCRP) score of ≥10 at baseline were excluded. Consequently, the final number of participants was 754. All participants provided written informed consent, and the Research Ethics Committee of the University of Eastern Finland approved the study protocol.

Information on Parental Alcohol Problems and Parental Divorce

School Health Records

We obtained data regarding parental alcohol problems and parental divorce from school health records that had been completed by school health nurses and doctors in the 1930s to 1950s and archived by the schools or the municipalities. The school health program, which started in the late 1920s, is mandatory throughout Finland. The collected records were based on the school health nurse's personal observations at school and during home visits performed by school nurses. The nurses gathered information on issues such as the health status, school performance, behavior at school, general parenting practices and the hygiene/cleanliness of the child, and socioeconomic circumstances, including poverty and neglect. The nurses did not specifically ask about possible ACEs but noted down everything they observed at school or while visiting children's homes. Detailed information on the school health records has been presented elsewhere (22,23).

Questionnaire-Based Data

Questionnaire-based data were derived from the Kuopio Ischemic Heart Disease Risk Factor Study Baseline Questionnaire. The participants were asked about their a) father's alcohol problems (yes versus no), b) mother's alcohol problems (yes versus no), and c) parental divorce (yes versus no) (23).

In this study, parental alcohol problems were reported as present (yes) if a participant reported that either of the parents had an alcohol problem in a self-reported questionnaire and/or the problems were identified from school health records. Similarly, parental divorce was reported as present (yes) if a participant reported parental divorce in a self-reported questionnaire and/or the same event was identified from school health records.

Baseline Covariates

Depression Measures

Depressive symptoms were assessed at baseline with the 18-item Human Population Laboratory Depression Scale, which was developed for screening general population samples (24). Conceptually, it resembles other brief symptom checklists such as the Center for Epidemiological Studies Depression Scale (25,26).

Socioeconomic and Health-Related Background Variables

Participants completed questionnaires that enquired about their sociodemographic background and health-related factors. Marital status (married or living with a partner versus living alone) and educational level (years of formal education received) were recorded. At baseline, a history of diabetes was assessed with the question "Have you been diagnosed by a physician as having diabetes?" including type 1 and/or type 2 diabetes. A research nurse measured the weight and height of the participants, and the body mass index (BMI; in kilograms per meter squared) was calculated.

Smoking and Alcohol Use

The current number of cigarettes, cigars, and pipefuls of tobacco smoked daily and the duration of regular smoking in years were recorded in the self-administered questionnaire. The lifelong exposure to smoking was converted into pack years. Alcohol consumption (in grams per week) was assessed with a structured quantity-frequency method using the Nordic Alcohol Consumption Inventory for drinking behavior over the previous 12 months (27).

Blood Samples

Participants were requested to fast overnight, abstain from smoking for 12 hours, and avoid alcohol use for 3 days before providing blood samples. Copper-free needles and tubes were used for collecting and storing blood. The participants rested in a supine position for 30 minutes before blood sampling.

Serum hsCRP was measured with an immunometric assay, the Immulite High Sensitivity CRP Assay (Diagnostic Products Corporation, Los Angeles, CA), which has been standardized against the World Health Organization International Reference Standard for CRP immunoassay 85/506. At the level of 3.2 mg/L, the within-run coefficient of variation was 2.8% and the total coefficient of variation was 3.1%.

Outcome Variables

In the follow-up setting, the Care Register for Health Care (CRHC) was used to extract information on the diagnoses of type 2 diabetes. All diagnoses registered in the CRHC as type 2 diabetes until 2014 were included. The CRHC, formerly known as the Hospital Discharge Register, contains nationwide linkable data on all inpatient hospital discharges with personal identity codes since 1969 and outpatient primary care visits since 2011. The register contains general information including the area of residence, hospital identifier, admission and discharge dates, and patient diagnoses (28). We excluded those who self-reported that they were experiencing diabetes at baseline. The average follow-up time for the participants until the first type 2 diabetes diagnosis was 23.3 years (25th–75th percentile, 21.2–27.9 years).

Statistical Analyses

Differences between the participants having or not having type 2 diabetes were assessed using the χ^2 test or Fisher exact test for the dichotomous variables, and Mann-Whitney *U* test for nonparametric continuous variables.

Multivariate analyses were conducted with Cox regression to examine the association of parental alcohol problems and parental divorce with the incidence of type 2 diabetes during the follow-up. The model was adjusted for life-style and socioeconomic variables. The following covariates were chosen based on their earlier reported associations with either the outcome variable or the predictors, that is, marital status (married versus living alone) (29,30), education (in years) (29,31), Human Population Laboratory Depression Scale scores (32,33), smoking (cigarette packs per year) (34,35), alcohol per week (in grams) (23,36), BMI (37,38), and serum hsCRP (39,40). We also investigated whether any observed significant associations between either of the examined ACEs and adulthood type 2 diabetes would remain present when individuals reporting the other investigated ACE were excluded. Associations were measured using hazard ratios and two-sided 95% confidence intervals.

Two-tailed p values <.05 were considered statistically significant in all analyses. All statistical analyses were performed using SPSS/PASW software (version 24.0; SPSS Inc., Chicago, IL).

RESULTS

Baseline Characteristics

The baseline characteristics of the study population are presented in Table 1. The individuals with type 2 diabetes had higher BMI values and serum hsCRP levels than did the individuals who did not develop type 2 diabetes during the follow-up period. Altogether, 10.3% of participants with type 2 diabetes had parents with parental alcohol problems compared with 3.4% of participants without type 2 diabetes, whereas 2.9% of participants with type 2 diabetes had parents who had divorced compared with 2.2% of participants without type 2 diabetes (Table 1).

Cox Regression Modeling

In the model examining the role of parental alcohol problems as a risk factor for future type 2 diabetes, we observed that parental alcohol problems were associated with a threefold increase in the risk of developing type 2 diabetes. In the same model, an individual's baseline BMI value was also associated with his/her risk of developing type 2 diabetes in adulthood (Table 2).

In the model examining the role of parental divorce in future type 2 diabetes, no association was observed between parental divorce and type 2 diabetes in adulthood. However, as in the previous model, baseline BMI displayed an association with type 2 diabetes in adulthood in this model (Table 3).

When we excluded individuals with parental divorce from the Cox regression analysis, the results remained unaltered (Table S1, Supplemental Digital Content, http://links.lww.com/PSYMED/A684).

DISCUSSION

Summary of Main Findings

Parental alcohol problems were associated with a 3.1-fold higher incidence of type 2 diabetes over a 23-year follow-up, even after adjusting for a number of confounding factors. This association remained significant when we excluded individuals with parental divorce from the model. Parental divorce did not SEEM to be associated with type 2 diabetes in adulthood.

Comparison With Previous Studies

This is the first study identifying an association between parental alcohol problems and type 2 diabetes in adulthood. In contrast

TABLE 1. Baseline Characteristics of the Study Sample With Respect to Type 2 Diabetes at the Follow-Up

	Type 2 Diabetes *n* (%) or Median (IQR)			
	Yes (*n* = 68)	No (*n* = 686)	Test Statistics	*p*
Parental alcohol problems	7 (10.3)	23 (3.4)	7.80	.005[a]
Parental divorce	2 (2.9)	15 (2.2)	0.16	.69[a]
Living alone	13 (19.1)	99 (14.4)	1.07	.30[a]
Age, y	54.33 (48.2–54.5)	54.25 (42.9–54.5)	−0.79	.43[b]
Years of education	8 (6–11)	8 (7–10)	−0.80	.42[b]
HPL Depression Scale scores	1 (0–2)	1 (0–2)	−0.70	.48[b]
Smoking, cigarette pack/y	0 (0–14.1)	0 (0–5.7)	−0.26	.79[b]
Alcohol consumption, g/wk	40.0 (6.5–97.3)	36.5 (7.8–95.5)	−0.11	.91[b]
Body mass index, kg/m^2	28.6 (26.2–31.2)	26.05 (24.2–28.5)	−5.25	<.001[b]
Serum hsCRP, mg/L	1.79 (0.93–3.46)	1.14 (0.65–2.13)	−3.63	<.001[b]

IQR = interquartile range; HPL = Human Population Laboratory; hsCRP = high sensitivity C-reactive protein.

[a] χ^2 Test.

[b] Mann-Whitney *U* test.

TABLE 2. Cox Regression Model Examining Associations Between Parental Alcohol Problems and Type 2 Diabetes During the Follow-Up (n = 754), Adjusting for Covariates

	Type 2 Diabetes		
	HR	95% CI	p
Parental alcohol problems (yes)	3.09	1.38–6.88	.006
Age	1.03	0.98–1.08	.21
Smoking	1.02	1.0–1.04	.051
HPL Depression Scale scores	1.03	0.91–1.16	.61
Alcohol consumption	1.00	0.99–1.00	.94
Years of education	0.96	0.88–1.04	.31
Marital status (living alone)	1.35	0.72–2.55	.34
Body mass index	1.16	1.09–1.22	<.001
Serum hsCRP	1.11	0.99–1.26	.070

HR = hazard ratio; CI = confidence interval; HPL = Human Population Laboratory; hsCRP = high-sensitivity C-reactive protein.

with our results, Pisto et al. (20) observed no associations between parental alcohol problems and type 2 diabetes in adulthood in a Finnish survey with a follow-up time of 8 years (i.e., from 1998 to 2006). They used a random sample of the working population (N = 24,057; age, 20–55 years) and categorized the diagnosis of diabetes according to the medication being used (insulin, tablet, combination, and drug-naïve), and included both type 1 and type 2 diabetes. Furthermore, in a cross-sectional community survey of adults in 10 countries, there was no evidence of any association between parental substance use disorder (including parental alcohol and drugs abuse) and diabetes in adulthood; instead, parental divorce was associated with an increased risk of diabetes in adulthood (16). In that study, the diagnosis of diabetes was based on a self-reported questionnaire and the type of diabetes was not specified. In the United States, two recent studies reported no associations between parental alcohol problems and diabetes in adulthood (regardless of the type). These studies comprised a cross-sectional telephone survey of US adults in five states (5,12) and an annual cross-sectional survey of US adults in 14 states (18). The associations did not vary by sex (12). These US survey studies included adults aged ≥18 years and used data gathered from the Behavioral Risk Factor Surveillance System, an annual cross-sectional telephone survey conducted by the Centers for Disease Control and Prevention and US states. The diabetes types were not differentiated in these studies.

Possible Mechanisms

Stressful life events may have long-term effects on a child's development. A longitudinal study suggested that perceived stress was associated with a 2.3-fold increase in the odds of developing type 2 diabetes (41). Stressful life events have been associated with poor metabolic control (42). Furthermore, stress activates the sympathetic nervous system, which releases stress hormones such as epinephrine and cortisol. These hormones increase glucose production in the liver, inhibit insulin secretion in the pancreas, and elevate insulin resistance (43). Furthermore, the Biological Embedding of Childhood Adversity Model might explain the mechanisms involved in the development of chronic illness through exposure to early life stress (44,45).

Maternal alcohol consumption during pregnancy may also have adverse effects on the offspring's metabolic regulation. Animal studies have indicated that prenatal exposure to alcohol impairs glucose tolerance in the offspring by inducing insulin resistance and β-cell dysfunction (46). However, in our study, we had no information available regarding possible maternal alcohol consumption during pregnancy and were therefore unable to examine the potential contribution of maternofetal factors to our findings. Nonetheless, it has been reported that mothers who exhibit risky drinking behavior before pregnancy display an increased risk of drinking alcohol when pregnant (47).

In addition to possible causal factors explaining our observations, it is crucial to recognize that prospective associations do not necessarily imply causality. It is possible that shared environmental or genetic factors may contribute to both the style of parental alcohol consumption and likelihood of type 2 diabetes developing in the offspring (48).

Strengths and Limitations

The main strength of this study is the access to prospective and retrospective measures of parental alcohol problems and parental divorce. We were able to combine self-reported, questionnaire-based data with information collected from school health records. Recall bias may, however, affect self-rated responses and lead to underestimating the impact of childhood circumstances. Furthermore, we controlled for a diabetes diagnosis at baseline and used clinician-reported type 2 diabetes diagnoses from national registers with a long follow-up period. We were also able to adjust for several important confounders, including serum hsCRP.

There are some limitations that need to be considered while interpreting our findings. First, our population consisted of middle-aged men, and thus, the results may not be generalizable to women and individuals representing other age groups. Second, information from school health records was only available for 28% of the total study population. Third, because there were few cases with a combination of both diabetes and parental alcohol problems, the

TABLE 3. Cox Regression Model Examining Associations Between Parental Divorce and Type 2 Diabetes During the Follow-Up (n = 754), Adjusting for Covariates

	Diabetes		
	HR	95% CI	p
Parental divorce (yes)	1.69	0.40–7.05	.47
Age	1.03	0.98–1.07	.22
Smoking	1.01	0.99–1.03	.78
HPL Depression Scale scores	1.03	0.91–1.17	.56
Alcohol consumption	1.00	0.99–1.00	.96
Years of education	0.96	0.88–1.04	.32
Marital status (living alone)	1.48	0.79–2.77	.22
Body mass index	1.15	1.09–1.22	<.001
Serum hsCRP	1.12	0.99–1.26	.061

HR = hazard ratio; CI = confidence interval; HPL = Human Population Laboratory; hsCRP = high-sensitivity C-reactive protein.

possibility of a type 1 error, that it, a chance finding, should also be considered while interpreting the findings regarding parental alcohol problems and diabetes. Fourth, because the number of individuals reporting parental divorce in our sample was limited, the possibility of a type 2 error should be taken into consideration when interpreting the findings regarding parental divorce. Finally, although school health nurses and doctors completed the school health records, we do not know what instructions were given to them regarding the collection and reporting of information on parental alcohol and parental divorce, as these data were not collected to be used in a research study.

CONCLUSIONS

Our findings suggest that parental alcohol problems may increase the risk of type 2 diabetes in men. These observations highlight the need for early interventions targeting the children of parents with excessive alcohol use to prevent the offspring's risk of life-style–related illness later in life. Future studies with larger sample sizes and high-risk samples are required to replicate the findings.

Source of Funding and Conflicts of Interest: The study was supported by the Finnish Medical Foundation (S.M.L.), the Signe and Ane Gyllenberg Foundation (S.L.K.), and the University of Turku Graduate School (S.U.). There are no conflicts of interests to declare.

Ethical Standards: The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

REFERENCES

1. Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, Koss MP, Marks JS. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE). Am J Prev Med 1998;14:245–58.
2. Anda RF, Fleisher VI, Felitti VJ, Edwards VJ, Whitfield CL, Dube SR, Williamson DF. Childhood abuse, household dysfunction, and indicators of impaired adult worker performance. Perm J 2004;8:30–8.
3. Afifi TO, Mather A, Boman J, Fleisher W, Enns MW, MacMillan H, Sareen J. Childhood adversity and personality disorders: results from a nationally representative population-based study. J Psychiatr Res 2011;45:814–22.
4. Elliott JC, Stohl M, Wall MM, Keyes KM, Goodwin RD, Skodol AE, Krueger RF, Grant BF, Hasin DS. The risk for persistent adult alcohol and nicotine dependence: the role of childhood maltreatment. Addiction 2014;109:842–50.
5. Campbell JA, Walker RJ, Egede LE. Associations between adverse childhood experiences, high-risk behaviors, and morbidity in adulthood. Am J Prev Med 2016; 50:344–52.
6. World Health Organization. Global Report on Diabetes. Geneva, Switzerland: World Health Organization; 2016.
7. International Diabetes Federation. IDF Diabetes Atlas. 8th ed. Brussels, Belgium: International Diabetes Federation; 2017;2019.
8. Wu Y, Ding Y, Tanaka Y, Zhang W. Risk factors contributing to type 2 diabetes and recent advances in the treatment and prevention. Int J Med Sci 2014; 11:1185–200.
9. Emerging Risk Factors Collaboration, Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio E, Ingelsson E, Lawlor DA, Selvin E, Stampfer M, Stehouwer CD, Lewington S, Pennells L, Thompson A, Sattar N, White IR, Ray KK, Danesh J. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet 2010;375:2215–22.
10. Hughes K, Bellis MA, Hardcastle KA, Sethi D, Butchart A, Mikton C, Jones L, Dunne MP. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. Lancet Public Health 2017;2:e356–66.
11. Hackett RA, Steptoe A. Type 2 diabetes mellitus and psychological stress—a modifiable risk factor. Nat Rev Endocrinol 2017;13:547–60.
12. Campbell JA, Farmer GC, Nguyen-Rodriguez S, Walker R, Egede L. Relationship between individual categories of adverse childhood experience and diabetes in adulthood in a sample of US adults: does it differ by gender? J Diabetes Complications 2018;32:139–43.
13. Bellis MA, Hughes K, Leckenby N, Hardcastle KA, Perkins C, Lowey H. Measuring mortality and the burden of adult disease associated with adverse childhood experiences in England: a national survey. J Public Health (Oxf) 2015; 37:445–54.
14. Chanlongbutra A, Singh GK, Mueller CD. Adverse childhood experiences, health-related quality of life, and chronic disease risks in rural areas of the United States. J Environ Public Health 2018;2018:7151297.
15. Gilbert LK, Breiding MJ, Merrick MT, Thompson WW, Ford DC, Dhingra SS, Parks SE. Childhood adversity and adult chronic disease: an update from ten states and the District of Columbia, 2010. Am J Prev Med 2015;48: 345–9.
16. Scott KM, Von Korff M, Angermeyer MC, Benjet C, Bruffaerts R, de Girolamo G, Haro JM, Lépine JP, Ormel J, Posada-Villa J, Tachimori H, Kessler RC. Association of childhood adversities and early-onset mental disorders with adult-onset chronic physical conditions. Arch Gen Psychiatry 2011;68:838–44.
17. Shields ME, Hovdestad WE, Pelletier C, Dykxhoorn JL, O'Donnell SC, Tonmyr L. Childhood maltreatment as a risk factor for diabetes: findings from a population-based survey of Canadian adults. BMC Public Health 2016; 16:879.
18. Monnat SM, Chandler RF. Long term physical health consequences of adverse childhood experiences. Sociol Q 2015;56:723–52.
19. Deschênes SS, Graham E, Kivimäki M, Schmitz N. Adverse childhood experiences and the risk of diabetes: examining the roles of depressive symptoms and cardiometabolic dysregulations in the Whitehall II cohort study. Diabetes Care 2018;41:2120–6.
20. Pisto L, Vadén A, Sillanmäki L, Mattila K. Childhood adversities are associated with diabetes management in working age in Finland. Int J Family Med 2014; 2014:1–7.
21. Salonen JT. Is there a continuing need for longitudinal epidemiologic research? The Kuopio Ischaemic Heart Disease Risk Factor Study. Ann Clin Res 1988; 20:46–50.
22. Leino J, Kauhanen L, Hokkinen L, Kurl S, Toriola AT, Voutilainen S, Lynch JW, Kauhanen J. Psychosocial problems in childhood and later alcohol consumption: a life course approach with historical information. Scand J Public Health 2011; 39:749–56.
23. Kauhanen L, Leino J, Lakka HM, Lynch JW, Kauhanen J. Adverse childhood experiences and risk of binge drinking and drunkenness in middle-aged Finnish men. Adv Prev Med 2011;2011:478741.
24. Kaplan GA, Roberts RE, Camacho TC, Coyne JC. Psychosocial predictors of depression. Prospective evidence from the human population laboratory studies. Am J Epidemiol 1987;125:206–20.
25. Roberts RE. Prevalence of depressive symptoms among Mexican Americans. J Nerv Ment Dis 1981;169:213–9.
26. Roberts RE, O'Keefe SJ. Sex differences in depression reexamined. J Health Soc Behav 1981;22:394–400.
27. Kauhanen J, Julkunen J, Salonen JT. Coping with inner feelings and stress: heavy alcohol use in the context of alexithymia. Behav Med 1992;18:121–6.
28. Sund R. Quality of the Finnish Hospital Discharge Register: a systematic review. Scand J Public Health 2012;40:505–15.
29. Font SA, Maguire-Jack K. Pathways from childhood abuse and other adversities to adult health risks: the role of adult socioeconomic conditions. Child Abuse Negl 2016;51:390–9.
30. Whisman MA, Li A, Sbarra DA, Raison CL. Marital quality and diabetes: results from the Health and Retirement Study. Health Psychol 2014;33:832–40.
31. Kim SH. Educational attainment moderates the associations of diabetes education with health outcomes. Int J Nurs Pract 2016;22:444–50.
32. Chapman DP, Whitfield CL, Felitti VJ, Dube SR, Edwards VJ, Anda RF. Adverse childhood experiences and the risk of depressive disorders in adulthood. J Affect Disord 2004;82:217–25.
33. Roy T, Lloyd CE. Epidemiology of depression and diabetes: a systematic review. J Affect Disord 2012;142(Suppl 142):S8–21.
34. Anda RF, Croft JB, Felitti VJ, Nordenberg D, Giles WH, Williamson DF, Giovino GA. Adverse childhood experiences and smoking during adolescence and adulthood. JAMA 1999;282:1652–8.
35. Yeh H, Duncan BB, Schmidt MI, Wang N, Brancati FL. Smoking, smoking cessation, and risk for type 2 diabetes mellitus: a cohort study. Ann Intern Med 2010; 152:10–7.
36. Holst C, Becker U, Jørgensen ME, Grønbæk M, Tolstrup JS. Alcohol drinking patterns and risk of diabetes: a cohort study of 70,551 men and women from the general Danish population. Diabetologia 2017;60:1941–50.
37. Gray N, Picone G, Sloan F, Yashkin A. Relation between BMI and diabetes mellitus and its complications among US older adults. South Med J 2015; 108:29–36.
38. Meadows AL, Strickland JC, Kerr MS, Rayapati AO, Rush CR. Adverse childhood experiences, tobacco use, and obesity: a crowdsourcing study. Subst Use Misuse 2019;54:1743–9.
39. Li A, Tu MT, Sousa AC, Alvarado B, Kone GK, Guralnik J, Zunzunegui MV. Early life adversity and C-reactive protein in diverse populations of older adults:

a cross-sectional analysis from the International Mobility in Aging Study (IMIAS). BMC Geriatr 2015;15:102.
40. Lontchi-Yimagou E, Sobngwi E, Matsha TE, Kengne AP. Diabetes mellitus and inflammation. Curr Diab Rep 2013;13:435–44.
41. Harris ML, Oldmeadow C, Hure A, Luu J, Loxton D, Attia J. Stress increases the risk of type 2 diabetes onset in women: a 12-year longitudinal study using causal modelling. PLoS One 2017;12:e0172126.
42. Helgeson VS, Escobar O, Siminerio L, Becker D. Relation of stressful life events to metabolic control among adolescents with diabetes: 5-year longitudinal study. Health Psychol 2010;29:153–9.
43. Kramer JR, Ledolter J, Manos GN, Bayless ML. Stress and metabolic control in diabetes mellitus: methodological issues and an illustrative analysis. Ann Behav Med 2000;22:17–28.
44. Weaver ICG, Cervoni N, Champagne FA, D'Alessio AC, Sharma S, Seckl JR, Dymov S, Szyf M, Meaney MJ. Epigenetic programming by maternal behavior. Nat Neurosci 2004;7:847–54.
45. Miller GE, Chen E, Parker KJ. Psychological stress in childhood and susceptibility to the chronic diseases of aging: moving toward a model of behavioral and biological mechanisms. Psychol Bull 2011;137:959–97.
46. Chen L, Nyomba BLG. Effects of prenatal alcohol exposure on glucose tolerance in the rat offspring. Metabolism 2003;52:454–62.
47. Ethen MK, Ramadhani TA, Scheuerle AE, Canfield MA, Wyszynski DF, Druschel CM, Romitti PA. Alcohol consumption by women before and during pregnancy. Matern Child Health J 2009;13:274–85.
48. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol 2018;14:88–98.

Supplemental Digital Content 1. Cox regression model examining associations between parental alcohol problems (excluding parental divorce, n = 17) and type II diabetes during follow-up (n = 733), adjusting for covariates.

	Type II diabetes		
	HR	**95% CI**	***p***
Parental alcohol problems (yes)	3.57	1.59–8.02	0.002
Age (years)	1.03	0.98–1.08	0.19
Smoking (cigarette pack years)	1.02	1.00–1.04	0.052
HPL depression scale scores	1.02	0.91–1.16	0.66
Alcohol consumption (grams/week)	0.99	0.99–1.00	0.68
Years of education	0.96	0.88–1.04	0.34
Marital status (living alone)	1.22	0.63–2.35	0.55
Body mass index	1.14	1.08–1.21	<.001
Serum hsCRP	1.13	1.006–1.27	0.040

HPL = Human Population Laboratory; HR = hazard ratio; hsCRP = high-sensitivity C-reactive protein.