



Research paper

The co-occurrence of diabetes and adverse childhood experiences and its impact on mortality in US adults



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ARTICLE INFO

Keywords:

Adverse childhood experiences

Diabetes

Mortality

Cohort

MIDUS

ABSTRACT

Background: Diabetes is a leading cause of death in the US. Adverse childhood experiences (ACEs) have also been linked to increased mortality. ACEs are associated with the development of diabetes however the amplified effect on mortality has not been studied.

Methods: Data from Midlife development in the United States (MIDUS), from 1995 to 1996 (Wave 1), 2004–2006 (Wave 2), and 2011–2014 (Wave 3) were used with a total of 3023 participants. Survey Cox proportional hazards regression models were used to calculate all-cause mortality. Univariate and multivariable Cox models were performed for the four combinations of diabetes and ACE categories, with estimation of hazard ratio completed for each.

Results: After adjusting for covariates and comorbidity burden, ‘ACE only’ was not significantly different in mortality compared to ‘no diabetes and no ACE’. ‘Diabetes only’ had a 78% higher mortality (HR 1.78, 95% CI 1.04–3.04) compared to ‘no diabetes and no ACE’. ‘Diabetes and ACE’ had a 132% higher mortality (HR 2.32, 95% CI 1.64–3.28) compared to ‘no diabetes and no ACE’.

Limitations: ACE and diabetes measures are self-report, and while longitudinal a temporal relationship cannot be established. Therefore, future research should collect prospective data to investigate mechanisms for this association based on observational data.

Conclusions: Results showed a strong association between ‘diabetes and ACE’ and mortality with a pronounced difference between both ‘ACE only’ and ‘diabetes only’ after 20-year follow-up. These results suggest an amplified effect of diabetes and ACE on mortality for adults who have experienced ACEs.

1. Introduction

Adverse Childhood Experiences (ACEs) encompass a broad range of negative experiences and events that can occur or co-occur in the first 18 years of life (Felitti et al., 1998). ACEs include various types of abuse and neglect, as well as, aspects of a child's living environment that may cause trauma or chronic stress (Felitti et al., 1998). It is well established that those with ACEs tend to have higher rates of morbidity and are more likely to engage in risky health behaviors compared to those who do not report ACEs (Anda et al., 2006; Bellis et al., 2015; Goodwin et al., 2004; Husarewycz et al., 2014; Campbell et al., 2016; Miller et al., 2011; Cohen et al., 2007). For example, individuals who experienced ACEs during childhood, have an increased risk of developing heart disease, diabetes, and chronic lower respiratory disease

(Felitti et al., 1998), three of the leading causes of death (CDC, 2018a). Additional studies have shown that ACEs significantly increase the risk of early adult mortality, and those experiencing multiple ACEs have more than double the risk of early mortality compared to those with only one ACE (Brown et al., 2009; Bellis et al., 2015; Kelly-Irving et al., 2013; Chen et al., 2016).

It is unclear if the co-occurrence of ACEs with a chronic disease, such as diabetes, explains the increased risk for mortality, or if the co-occurrence of ACEs and chronic disease amplifies risk of early mortality. Diabetes is the 7th leading cause of death and associated with a two to three-fold increase in all-cause mortality in adults worldwide (CDC, 2017; Roper et al., 2002; Barr et al., 2007; Seshasai et al., 2011). In addition to the physical burden, health expenditures associated with diabetes are an estimated \$245 billion in direct and indirect costs

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<https://doi.org/10.1016/j.jad.2019.02.016>

Received 24 October 2018; Received in revised form 1 February 2019; Accepted 5 February 2019

Available online 06 February 2019

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annually, and those with diabetes have approximately 2.3 times the health expenditures of those without diabetes (CDC, 2017). The literature to date has primarily focused on identifying and establishing the association between ACEs and diabetes, and has shown both a threshold and a dose-response effect of having ACEs and/or multiple ACEs on diabetes (Rich-Edwards et al., 2010; Lynch et al., 2013; Hypponen et al. 2008; Campbell et al., 2016; Felitti et al., 1998; Huang et al., 2015; Huffhines et al., 2016; Hughes et al., 2017). Specifically, evidence shows that a single endorsement of an ACE may increase risk for diabetes in adulthood by 11% (Lynch et al., 2013). Other studies have shown that this risk of developing diabetes may increase two-fold when endorsing greater than three ACEs (Huffhines et al., 2016).

The assessment and treatment of ACEs and diabetes has historically been relegated to single areas of specialty and disciplines. However, as evidence suggests experiencing ACEs increases risk for developing diabetes in adulthood, understanding whether an acceleration of poor health occurs, leading to early mortality when both ACEs and diabetes are present over time, is highly warranted and has implications for a multidisciplinary approach to treatment. Specifically, secondary and tertiary prevention efforts to prevent the development of diabetes in individuals with a history of ACEs and efforts to prevent further complications and poor health outcomes among individuals with a history of ACEs who have developed diabetes.

Further elucidating the relationship between ACEs and diabetes will allow for better understanding to inform the development of interventions to simultaneously address ACEs and diabetes at both a secondary and tertiary level. Therefore, this study aims to build on the current literature on ACEs and diabetes by addressing this gap in knowledge by examining the impact of co-occurring diabetes and ACEs on mortality in a longitudinal cohort of US adults.

2. Methods

2.1. Sample and study population

This analysis uses three waves of data from the national longitudinal survey of Midlife development in the United States (MIDUS), which was conducted in 1995–1996 (Wave 1), 2004–2006 (Wave 2), and 2011–2014 (Wave 3). MIDUS is based on a nationally representative random-digit-dial (RDD) sample of noninstitutionalized, English-speaking adults, aged 25–74, selected from working telephone banks in the United States (MIDUS, 2011). MIDUS wave 1 is comprised of 7108 adults who participated in a phone interview and then were invited to complete a self-administered questionnaire (MIDUS, SAQ). MIDUS wave 2 repeated baseline assessments (e.g., phone interview and extensive self-administered questionnaire), and expanded data collection to include biomarker measurements. 4963 participants from the initial cohort were successfully contacted to participate in wave 2 phone interview. 3294 of those who participated in the Wave 2 phone interview were again successfully contacted to participate in Wave 3 phone interview.

Only the main RDD sample included population weighting information, and therefore was chosen to incorporate in this analysis. There are 3034 participants who answered both telephone and mail questionnaires as part of the national random digit dialing sample (Main RDD sample), two participants without weight information were excluded. We further excluded seven participants who did not report diabetes status and two participants who had no age information, the final analysis cohort for this study is 3023.

2.2. Mortality outcome

Mortality information was collected during Wave 2 and Wave 3. We used the mortality statistics from Wave 3 and verified status against information from Wave 2. The mortality status was collected from three general source categories: 1. Tracing conducted by University of

Wisconsin Survey Center (UWSC) before, during, and after fielding; 2. Formal National Death Index (NDI) searches; and 3. Longitudinal sample maintenance. The MIDUS Administrative Core obtains information about decedents by sending birthday cards and newsletters to MIDUS participants which generates contacts from family and friends of decedents, and returned mailings marked ‘Deceased’. These notifications are routinely verified via SSDI (Social Security Death Index) and online obituary searches. The mortality outcome of interest in this analysis includes all-cause death.

2.3. Diabetes

Participants were asked the following two questions during each wave's self-administered survey. “in the past 12 months, have you experienced or been treated for diabetes or high blood sugar”; “during the past 30 days, have you taken prescription medicine for diabetes”. Diabetes is defined as ‘yes’ to either of the above questions.

Diabetes status was defined as a time varying variable and was allowed to change from ‘no diabetes’ to ‘diabetes’ during Wave 2 or Wave 3.

2.4. Adverse childhood experiences (ACEs)

We used the ACE Study Questionnaire (Felitti et al., 1998) as a template to construct measures of adverse events experienced during childhood, in addition to variables defined by the MIDUS collaborators to measure childhood adversity. The MIDUS surveys collected information on abuse (emotional abuse; physical abuse), household dysfunction (not lived with biological parents including parental divorce or never lived together, death of a parent, adopted; lack of male head in the household; parental alcohol or drug use; parental mental illness), and financial strain (receipt of welfare; reported of being ‘worse off’ than other families; less than a high school education for father, or mother where father was not present). Items covering the emotional and physical abuse were derived from childhood family background regarding abuse questions completed by participants at wave 1, a dichotomous variable was recoded indicating experience of given adversity, reported “often” was coded as 1. Items covering the household dysfunction were derived from childhood background questions at wave 1. Items covering the financial strain were derived from childhood background and childhood family background questions at wave 1. The final constructed measures for ACEs in this analysis are as follows:

2.4.1. Emotional abuse

During your childhood how often did [mother, father, sibling, anyone else] insult you or swore at you; sulked or refused to talk to you; stomped out of the room; did or said something to spite you; threatened to hit you; smashed or kicked something in anger.

2.4.2. Physical abuse

During your childhood how often did [mother, father, sibling, anyone else] pushed, grabbed, or shoved you; slapped you; threw something at you; kicked, bit, or hit you with a fist; hit or tried to hit you with something; beat you up.

2.4.3. Household dysfunction

Experienced any of the following during childhood: (1) Not living with biological parent while growing up, including (1a) parental divorce during childhood or parents never lived together, (1b) death of a parent, (1c) adopted, (1d) other reason; (2) lack of male head in the household; (3) parental alcohol or drug use; (4) parental mental illness.

2.4.4. Financial strain

Experienced any of the following during childhood: (1) family received welfare; (2) reported ‘worse off’ than other families; (3) father had less than a high school education, or mother had less than a high

school education if father was not present.

2.5. Covariates

Covariates included gender, age (grouped as 20–39 years; 40–54 years; 55–74 years), race (grouped as white; black; and other minority), education (dichotomized as high school diploma or less and higher education), marital status (dichotomized as married and not married), household total income (grouped as less than 25k; 25k - < 75k; and 75k +) and comorbidity burden based on comorbidity count (low comorbidity (0–1), moderate comorbidity (2–4) and high comorbidity (5+)). Comorbidity burden was based on self-reported chronic conditions collected at wave 1 based on the following question: “In the past 12 months, have you experienced or been treated for any of the following conditions/illnesses?”. All the demographic variables and comorbidity were collected from baseline MIDUS Wave 1.

Some missing values existed for covariates, however, none reached a level that would indicate possibility of bias from missingness (largest percent was for income which only had 3% of the sample missing).

2.6. Follow-up time line variables

The start date of follow-up is the date the self-administered survey was received for MIDUS baseline Wave 1. Death date only includes year and month, so we used day 15 in the month of death for calculations. Censor date is defined by individual participation in the self-administered portion of each wave. Those who only participated in wave 1, were censored at the beginning of wave 2 (January 1, 2004); those who participated in wave 1 and wave 2 only, were censored at the beginning of wave 3 (May 1, 2013); and those who participated every wave, then censored at end of follow-up date (May 15, 2015). Each individual's end of follow-up date is the earlier date of death date or censor date, with mortality event defined as end of follow-up as death date.

2.7. Statistical analysis

MIDUS developed a total of six weights that adjusted for differences in probability of selection and differential nonresponse to increase representativeness of the sample, and used the product of these weights to create a final summary weight that can be used in analysis (MIDUS, 2017). The final summary weights were used in all analyses to reflect a nationally representative population. Cox proportional hazards regression models for survey data were used to calculate all-cause mortality (MIDUS, 2017). Diabetes was treated as time-varying variable, with diagnosis date as the beginning of the survey in which diabetes was reported. We completed a sensitivity analysis by defining diabetes diagnosis date as the end of prior survey and found no differences in significance of findings.

Based on responses to diabetes and ACE questions, four population groups were defined: 1) no Diabetes, and no ACE; 2) ACE only; 3) Diabetes only; 4) both Diabetes and ACE. Univariate and multivariable survey Cox regression models were used to estimate the hazard ratio for the four combinations based on ACE and Diabetes interaction, adjusting for demographic variables including age, gender, race, education, marital status, household income; and comorbidity variable. Statistical significance (i.e. alpha level) was set at 0.05.

3. Results

The longitudinal sample included 3023 adults, ages 25–74 years, which represented 151,986,954 US adults, ages 25–74 years. Table 1 provides sample baseline demographics. The cohort's median age was 46 (inter-quartile range of 36–57), of which 51.4% were female, 86.3% were non-Hispanic white, and 21.6% reported less than \$25,000 annual income. 57.8% reported having at least one ACE, and 13.4% reported having diabetes.

Table 1
MIDUS Main RDD Cohort Descriptions (n = 3023).

Gender	
Male	48.56%
Female	51.44%
Median age in years at interview	46
Age group	
20–39	33.08%
40–54	35.89%
55–74	31.03%
Race	
White	86.30%
Black	6.72%
Other	5.43%
Education level	
High school diploma or less	39.07%
Higher education	60.87%
Marital status	
Married	64.04%
Not Married	35.96%
Household total income category	
Less than \$25k	21.60%
\$25k–< \$75k	44.72%
\$75k+	30.23%
Comorbidity category	
Low comorbidity (0–1)	55.01%
Moderate comorbidity (2–4)	37.05%
High comorbidity (5+)	7.77%
Diabetes and ACE category	
No diabetes No ACE	37.45%
ACE only	49.16%
Diabetes only	4.76%
Diabetes and ACE	8.63%

Table 2 provides information on univariate and multivariable weighted cox proportional hazard models. The univariate models indicate hazard ratios for each variable independently (i.e. *P*-values indicate significance for the singular variable in relation to mortality). The multivariable models indicate the hazard ratio for ACE/Diabetes categories with adjustment for all covariates (i.e. *P*-values indicate significance for the variable adjusted for all other variables in the model). After adjusting for gender, age, race, education, income, marital status, and comorbidity burden, ‘ACE only’ was not significantly different in mortality compared to ‘no diabetes and no ACE’. ‘Diabetes only’ had a 78% higher mortality (HR 1.78, 95% CI 1.04–3.04) compared to ‘no diabetes and no ACE’. ‘Diabetes and ACE’ had a 132% higher mortality (HR 2.32, 95% CI 1.64–3.28) compared to ‘no diabetes and no ACE’.

Fig. 1 shows the survival function by weighted Kaplan-Meier estimates for the four groups overtime. There is strong association between ‘diabetes and ACE’ and mortality with a pronounced difference between both ‘ACE only’ and ‘diabetes only’ after 20 years follow-up, supporting an amplified effect of diabetes and ACE on mortality.

4. Discussion

In this longitudinal analysis examining the effect of diabetes and ACEs on mortality in 3023 US adults, results show that over the 20-year follow-up period, adults with both diabetes and ACEs have a mortality rate 2.3 times that of adults who have neither diabetes, nor experienced an ACE. In addition, the increased mortality for those with both diabetes and ACE is higher than that of either diabetes alone or adults who have ACEs alone. The existing literature examining mortality with ACEs and with diabetes has not examined the co-occurring impact of the two on mortality. These results suggest that for adults who have experienced an ACE, the co-occurrence of diabetes can lead to an increased risk of mortality above that of individuals that did not experience an ACE. This relationship is important from both a clinical and public health standpoint given the growing epidemic of diabetes in the US.

Prior studies have investigated the association between ACEs and

Table 2
Weighted Cox proportional hazard models for mortality.

	Unadjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Diabetes and ACE category		< 0.0001		< 0.0001
No diabetes No ACE	Ref		Ref	
ACE only	1.34 (1.03–1.75)		1.03 (0.78–1.37)	
Diabetes only	3.69 (2.33–5.83)		1.78 (1.04–3.04)	
Diabetes and ACE	5.18 (3.81–7.03)		2.32 (1.64–3.28)	
Gender		0.2496		0.0002
Male	Ref		Ref	
Female	0.88 (0.71–1.09)		0.64 (0.51–0.81)	
Age group		< 0.0001		< 0.0001
40–54	Ref		Ref	
20–39	0.32 (0.19–0.54)		0.28 (0.16–0.48)	
55–74	5.22 (4.01–6.80)		4.23 (3.20–5.59)	
Race		0.1031		0.8117
White	Ref		Ref	
Black	1.20 (0.79–1.81)		0.99 (0.64–1.54)	
Other	0.53 (0.27–1.02)		0.80 (0.40–1.58)	
Education level		< 0.0001		0.7316
High school diploma or less	Ref		Ref	
Higher education	0.54 (0.43–0.66)		0.96 (0.76–1.21)	
Marital status		0.0063		0.1645
Married	Ref		Ref	
not Married	1.36 (1.09–1.71)		1.21 (0.93–1.57)	
Household total income category		< 0.0001		< 0.0001
Less than \$25k	Ref		Ref	
\$25k–< \$75k	0.45 (0.35–0.57)		0.63 (0.48–0.83)	
\$75k +	0.23 (0.17–0.32)		0.39 (0.27–0.55)	
Comorbidity category		< 0.0001		0.0028
Low comorbidity (0–1)	Ref		Ref	
Moderate comorbidity (2–4)	1.83 (1.44–2.34)		1.10 (0.85–1.42)	
High comorbidity (5 +)	3.36 (2.39–4.71)		1.91 (1.31–2.79)	

Note:
 1. Diabetes and ACE category is the estimate of the interaction of diabetes and ACE, Diabetes as a time-varying variable, and its diagnosis date assumed as the beginning of the reporting survey.
 2. Unadjusted HR is the estimate of univariate Cox model of each listed variable.
 3. Adjusted HR is the estimate of multivariable Cox model of all listed variables.

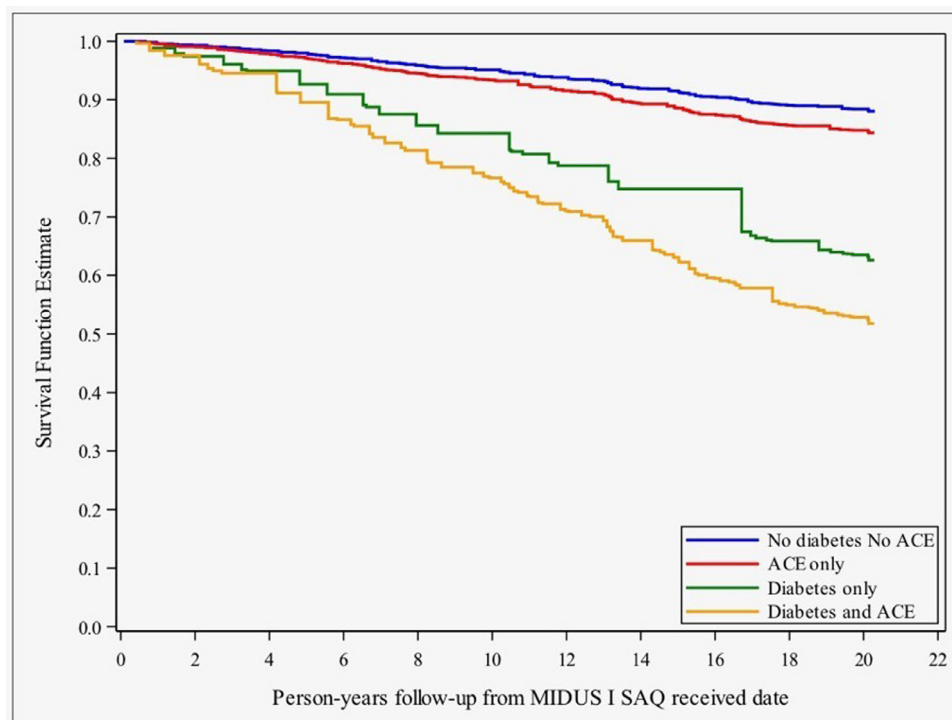


Fig. 1. Weighted Kaplan-Meier estimates by diabetes and ACE status.

mortality, for example, the original ACE study demonstrated that adults reporting 6 or more ACEs experienced mortality at a rate nearly 25 years earlier than those reporting zero ACEs and had a two-fold increase risk of dying at age 65 years or younger (Brown et al., 2009). Additionally, in a cohort of more than 17,000 adults, women who experienced at least one ACE had a 66% increased risk of mortality (Kelly-Irving et al., 2013). Experiencing at least two or more ACEs increased the risk of mortality to 80% and 57% for women and men, respectively (Kelly-Irving et al., 2013). In addition, the relationship between diabetes and mortality is well known (CDC, 2017). The results of this study suggest the effect of experiences in childhood and diabetes in adulthood amplifies the risk of mortality. Such findings suggest a number of relevant implications. Namely, research continues to show that ACEs are significantly associated with the development of diabetes in adulthood (Huang et al., 2015; Rich-Edwards et al., 2010; Huffhines et al., 2016; Duncan et al., 2015). The current findings now add to our understanding, by suggesting that the co-occurrence of both diabetes and ACEs may accelerate the risk of mortality known to exist for these conditions independent of each other. While additional research is highly warranted to understand the mechanisms that underlie the relationship, and whether it is the accumulation of adverse experiences or specific exposures that may exacerbate the effects of having diabetes, ultimately leading to early death, these findings highlight the importance of addressing diabetes risk among those who have experienced ACEs, as well as who have experienced ACEs who have developed diabetes.

Despite the large sample size and longitudinal nature of the data, this study has some limitations worth mentioning. First, ACE and diabetes data is self-report and therefore may be subject to recall bias. However, it has been shown that self-report measures for chronic conditions as well as significant life events (Edwards et al., 1994; Bowlin et al., 1996), such as trauma and adversity, have higher recall. Additionally, this data set did not allow to examine diabetes by type, however given that approximately 90% of the diabetes population have type 2, it may be suggested that this population with diabetes is primarily type 2 (CDC, 2018b). Second, there may be some forms of abuse and childhood adversity that are important factors to consider when examining ACEs that were not included in this dataset, such as sexual abuse. Thirdly, this analysis did not look at mortality differences between men and women. The literature looking at ACE mortality suggests that there may be a gender interaction, and should be taken into consideration in the future, particularly with larger datasets that would allow stratification without influencing power if interactions were found. Additionally, the study sample in this analysis represents 3023 individuals out of the original 7108 at Wave 1 and may not be fully generalizable based on selection bias and lack of sample diversity. Finally, this analysis examined the total effect of ACEs with diabetes and did not look at the individual effect of ACE categories with diabetes and whether this impacted mortality, nor were additional comorbidities included from Waves 2–3. It is therefore recommended that future research consider ACE categories with diabetes to better understand if this relationship is being driven by specific experiences.

Overall, this study showed that in a longitudinal sample of US adults that the co-occurrence of diabetes and ACEs significantly increases risk of mortality compared to having diabetes or ACEs alone. Further understanding of the mechanisms that underlie this relationship will allow to develop prevention efforts that may inform interventions across disciplines. Future studies should evaluate whether this relationship varies by gender and whether specific ACE categories drive this association more than others.

Author contributions

LEE obtained funding for the study. LEE, JAC, and RJW designed the study and developed the analysis. EG acquired and analyzed the data. LEE, JAC, RJW, EG, and EMJ contributed to interpretation and

critically revised the manuscript for important intellectual content. All authors approved the final manuscript.

Funding

This study was supported by the National Institute of Diabetes and Digestive and Kidney Diseases (Grant K24DK093699, Principal Investigator -LEE).

Competing interests

The authors declare that they have no competing interests.

Conflicts of interest and source of funding

No financial, consultant, institutional or other conflicts of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2019.02.016.

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