MAYO CLINIC PROCEEDINGS: INNOVATIONS, QUALITY & OUTCOMES

ORIGINAL ARTICLE

Association Between Educational Status and Mortality According to Diabetes Status Among US Adults

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Abstract

Objective: To examine differences in the association between educational attainment and mortality by the presence of diabetes and diabetic retinopathy (DR)—a major complication of diabetes.

Patients and Methods: We used a nationally representative sample of 54,924 US adults aged 20 years or older with diabetes from the National Health and Nutrition Examination Survey 1999-2018 and its mortality data through 2019. We applied the multivariable Cox proportional hazard models to investigate the associations between educational attainment (low, less than high school; middle, high school; and high, more than high school) and all-cause mortality according to diabetes status: nondiabetes, diabetes without DR, and diabetes with DR. Differences in the survival rate by educational attainment were evaluated using the slope inequality index (SII).

Results: Among the 54,924 participants (mean age, 49.9 years), adults in the low educational group reported an increased risk of all-cause mortality compared with those of the high educational group in any diabetes status (nondiabetes—hazard ratio [HR], 1.69; 95% CI, 1.56-1.82; diabetes without DR—HR, 1.61; 95% CI, 1.37-1.90; diabetes with DR—HR, 1.43; 95% CI, 1.10-1.86). SIIs among the diabetes without DR group and diabetes with DR group were 22.17 and 20.87 per 1000 person-years, respectively, which were 2 times greater than those among the nondiabetes group (SII=9.94).

Conclusion: The differences in the mortality risks owing to the educational attainment increased by the presence of diabetes regardless of the complication of DR. Our findings indicate that prevention of diabetes itself is critical to mitigate health disparities by socioeconomic status such as education status.

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Diabetes—one of the major chronic diseases—is the 7th leading cause of death in the United States.[1] Individuals with diabetes are likely to develop complications such as diabetic retinopathy (DR), which is reported to be the leading cause of blindness in the United States.[2] A previous review reported that one-third of patients with diabetes develop DR in their life.[3] Given the increased risk of mortality for such individuals with diabetes and DR,[4] it is crucial to provide individuals with equal opportunities and qualities of diabetes care in daily clinical practice.

Although prevention and management of diabetes and DR require long-term efforts, the education status is a key facet of an individual's socioeconomic status (SES) that determines the achievability of such an undertaking. That is, education promotes an individual's competency in aspects of independent health management (eg, health literacy) and governs the nature of other determinants of SES (eg, occupation and income). Several studies reported that those with low educational attainment were more likely to exhibit unhealthy behaviors such as smoking and physical inactivity,[5,6] which might lead to the development of diabetes.[7,8] Even among patients with diabetes, low educational attainment is associated with increased risk of complications such as DR.[9-11]

Moreover, educational attainment has been reported to be associated with increased mortality among patients with diabetes. A previous study found that patients with diabetes and low educational attainment (less than high school) experienced 503 excessive deaths of every 10,000 people each year compared with individuals with diabetes and high educational attainment (more than high school).[12] Another study assessed the relationships between low educational attainment (less than high school), glycated hemoglobin A1c (HbA1c) level, and mortality among US adults with self-reported diabetes. In their study, having both low educational attainment and a high HbA1c (≥7.0%) reported a large increase in mortality risks (hazard ratio [HR], 2.18) compared with those of individuals with high educational attainment (high school or more) and low HbA1c (<7.0%).[13] However, evidence is limited that fully covers the relationships between educational attainment and mortality across different stages of diabetes, such as nondiabetes, diabetes without complications, and diabetes with complications, simultaneously.

To address this knowledge gap, we used the most recent data of the representative sample of US. adults to examine the difference in mortality rates by educational attainment among individuals without diabetes, those with diabetes who did not present with DR, and those with diabetes who presented with DR. Quantifying survival differences by educational attainment among these groups would provide a better understanding of how the educational disparities change in each stage of diabetes and will give further insight into the clinical implications of a tailored approach toward equitable diabetes care.

PATIENTS AND METHODS

Data Sources and Study Population

This study used nationally representative data from the National Health and Nutrition Examination Survey (NHANES) and mortality data from the National Death Index (NDI), provided by the National Center for Health Statistics. NHANES includes stratified multistage probability samples that are randomly selected from the national population through a statistical process. The NHANES consists of demographic, dietary, examination, laboratory, and questionnaire data of the participants. The NDI is a data set that tracks their survival and cause of death. This study includes 10 cycles of NHANES cohorts (1999-2000, 2001-2002, 2003-2004, 2005-2006, 2007-2008, 2009-2010, 2011-2012, 2013-2014, 2015-2016, and 2017-2018) combined with NDI through December, 2019. The NHANES study was on the basis of a protocol approved by the National Center for Health Statistics institutional review board.

There were 55,081 participants aged 20 years or older at enrollment. We excluded 157 participants without information on physicians' diagnosis of diabetes (refused, do not know, or missing), resulting in 54,924 participants. Participants who presented with diabetes were also asked for a previous diagnosis of DR (yes or no). We categorized the participants into the following 3 groups on the basis of this self-reported information: (1) without diabetes, (2) diabetes without DR, and (3) diabetes with DR. We also categorized them using HbA1c (details are described further in the Sensitivity Analyses section). HbA1c was measured on the basis of the NHANES laboratory procedure guideline.[14]

Exposure Ascertainment

In NHANES, the educational attainment was self-reported during the household interview. Following a previous study's methods,[12] we categorized participants into 3 groups of educational attainment: less than 11th grade, such as 12th grade with no diploma (low education group); high school degree or equivalent (middle education group); and college graduate or above (high education group).

Outcome Ascertainment

The primary outcome of this study was all-cause mortality. The mortality data were obtained from the NDI records matched by social security number, date of birth, race/ethnicity, sex, state of birth, and state of residence. Time to event was calculated by the period between the NHANES interview date and the end of follow-up or the death date. As the secondary outcome, we defined cardiovascular mortality on the basis of the following International Classification of Diseases, Tenth Version codes: I00-09, I11, I13, I20-51, and I60-69.

Covariates

Other variables, such as demographic characteristics (age, sex, and race/ethnicity), income, smoking status, and physical activity status,

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TABLE. Baseline Characteristics

Characteristic	Educational attainment		
	Higher than high school	High school or equivalent	Lower than high school
Participants (n)	27,079	12,727	15,118
Age (y)	47.82 ± 17.69	49.90 ± 18.86	53.55 ± 18.74
Sex			
Male	12,576 (46.4)	6279 (49.3)	7550 (49.9)
Female	14,503 (53.6)	6448 (50.7)	7568 (50.1)
Race			
Mexican American	2370 (8.8)	1798 (14.1)	5398 (35.7)
Other Hispanic	1855 (6.9)	886 (7.0)	1753 (11.6)
Non-Hispanic White	13,897 (51.3)	6329 (49.7)	4033 (26.7)
Non-Hispanic Black	5514 (20.4)	2885 (22.7)	3086 (20.4)
Other race	3443 (12.7)	829 (6.5)	848 (5.6)
PIR			
>3.5	11,554 (42.7)	2534 (19.9)	1190 (7.9)
>1.3 to ≤3.5	8820 (32.6)	5109 (40.1)	4995 (33.0)
≤1.3	4574 (16.9)	3854 (30.3)	7049 (46.6)
NA	2131 (7.9)	1230 (9.7)	1884 (12.5)
Smoking			
Nonsmoker	16,205 (59.8)	6226 (48.9)	7481 (49.5)
Ex-smoker	6608 (24.4)	3192 (25.1)	3760 (24.9)
Current smoker	4257 (15.7)	3300 (25.9)	3853 (25.5)
NA	9 (0.0)	9 (0.1)	24 (0.2)
Physical activity			
At least once in the past 30 d	13,561 (50.1)	6098 (47.9)	5253 (34.7)
No activity in the past 30 d	13,234 (48.9)	6389 (50.2)	9353 (61.9)
NA	284 (1.0)	240 (1.9)	512 (3.4)
BMI (kg/m^2)	28.73 (6.84)	29.26 (6.93)	29.09 (6.62)
eGFR (mL/min/1.73 m^2)			
<60	1650 ± 6.1	1005 ± 7.9	1301 ± 8.6
≥60	20,568 ± 76.0	9189 ± 72.2	10,509 ± 69.5
NA	4861 ± 18.0	2533 ± 19.9	3308 ± 21.9
HbA1c (%)			
<6.5	22,576 (83.4)	10,264 (80.6)	11,301 (74.8)
≥6.5 to ≤7.0	797 (2.9)	455 (3.6)	719 (4.8)
>7.0	1332 (4.9)	752 (5.9)	1437 (9.5)
NA	2374 (8.8)	1256 (9.9)	1661 (11.0)
Self-reported diabetes status			
No diabetes	24,497 (90.5)	11,240 (88.3)	12,530 (82.9)
Diabetes only	2069 (7.6)	1150 (9.0)	1944 (12.9)
Diabetes and diabetic retinopathy	513 (1.9)	337 (2.6)	644 (4.3)

Abbreviations: BMI, body mass index; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin A1c; PIR, poverty income ratio

Data are reported n (%) for categorical variables and mean ± SD for continuous variables.

were self-reported. Race/ethnicity was classified as Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and others. We classified the income levels of the participants by poverty income ratio: ≤1.3 (low income); >1.3 and ≤3.5 (middle income); and >3.5 (high income). The smoking status of the participants was categorized into 3 categories: smoked at least 100 cigarettes in life and smoked every day or some days (current smoker); smoked at least 100 cigarettes in life and do not smoke currently (ex-smoker); and have not smoked 100 cigarettes in life (nonsmoker). Physical activity status was determined on the basis of whether participants did moderate or vigorous physical activity in the past 30 days (otherwise not considered physical activity). Body mass index (BMI) was calculated from measured weight and height. Estimated glomerular filtration rate (eGFR) was computed from the serum creatinine concentrations.[15]

Statistical Analyses

First, to investigate the association between educational attainment and diabetes status, we applied multinomial logistic regression models to estimate the odds ratio (OR) of diabetes status (nondiabetes [outcome reference group], diabetes without DR, and diabetes with DR) according to the education groups (low, middle, and high).

Second, we applied the multivariable Cox proportional hazard models to estimate the HR of all-cause mortality and cardiovascular-related mortality associated with educational attainment among each diabetes status group. In both multinomial logistic regression models and Cox proportional hazard models, we adjusted for age, sex (male or female), and race/ethnicity (Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and others).

Finally, we calculated the slope inequality index (SII) to assess the absolute difference in mortality risk by educational attainment across our 3 groups defined by diabetes and DR status (ie, nondiabetes, diabetes without DR, and diabetes with DR). SII was computed by taking the difference in mortality rates (per 1000 person-years) between the high education group and the low education group, on the basis of the Poisson regression model adjusting for age, sex, and race/ethnicity.[16] The 95% CI of SII were calculated using 1000 bootstrap samples. All analyses were conducted with R version 4.0.2. The NHANES sampling weights were applied following the official guidance of NHANES to compute national estimates adjusted for oversampling, survey nonresponse, difference in study design, and poststratification.[17]

Sensitivity Analyses

We conducted the following 3 sensitivity analyses. First, to minimize the residual confounding bias, we additionally adjusted for income, smoking status, physical activity status, and BMI in our logistic and Cox regression models. We did not include these variables in our main model because they are likely to be mediators between educational attainment and health outcomes. Second, to minimize the information bias due to self-report of physicians' diagnosis, we reanalyzed the data among the 3 groups using HbA1c and self-report of diabetes: (1) HbA1c of $<$6.5% and no self-reported diabetes; 2) HbA1c of $\geq$6.5% to $\leq$7.0% or self-reported diabetes; and 3) HbA1c of $>$7.0%. Third, we used the presence of chronic kidney disease (CKD) as a complication of diabetes instead of DR. In this additional analysis, we categorized the participants into 3 diabetes status: (1) no self-reported diabetes; (2) no CKD and self-reported diabetes; and (3) CKD (eGFR $<$60 mL/min/1.73 m^2) and self-reported diabetes.

RESULTS

Baseline Characteristics of the Study Population

Among 54,924 participants included in our study, the mean age was 49.9 years (SD, 18.4 years) and women were 51.9% [Table]. Compared with participants with high educational attainment, those with low educational attainment were more likely to be older, Mexican American, smokers, less physically active and have low income. They were more likely to exhibit lower eGFR, higher HbA1c, diabetes, and retinopathy.

Educational Attainment and the Presence of Diabetes/DR

After adjusting for demographic characteristics, the low education group (lower than high school degree) was associated with an increased prevalence of diabetes (OR, 1.23; 95% CI, 1.12-1.36) and DR (OR, 1.93; 95% CI, 1.61 to 2.30) compared with those of the

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high education group (higher than high school) (Figure 1). The middle education group (high school or equivalent) also tended to exhibit a higher risk of diabetes (OR, 1.06; 95% CI, 0.95 to 1.18) and DR (OR, 1.53; 95% CI, 1.26 to 1.86), whereas the magnitude of the association was smaller than the low education group, and the 95% CI for diabetes included the null.

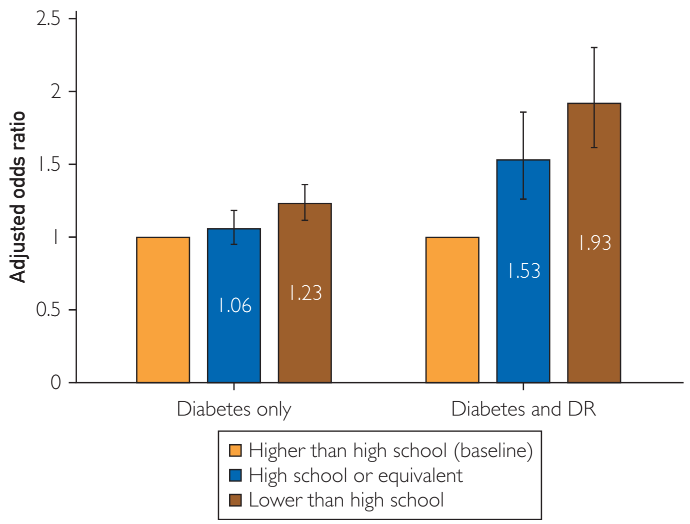

FIGURE 1. Adjusted odds ratios of diabetes status according to educational attainment. The multinomial logistic regression models included age, sex, and race/ethnicity.

Educational Attainment and Mortality

Over the median follow-up period of 9.2 years, there were 8886 events of death from any cause, including 2814 cardiovascular disease—related mortality. Among participants without diabetes, the low education group and the middle education group reported an increased risk of all-cause mortality compared with those of the high education group after adjusting for age, sex, and race/ethnicity (low education group, HR, 1.69; 95% CI, 1.56 to 1.82; middle education group, HR, 1.33; 95% CI, 1.24 to 1.44) (Figure 2). The association for low education group was also found among those with diabetes without DR (HR, 1.61; 95% CI, 1.37 to 1.90) and those with diabetes and DR (HR, 1.43; 95% CI, 1.10 to 1.86). We found similar results for cardiovascular mortality although some of the estimates included the null owing to the limited number of events.

When we calculated the mortality rate in 1000 person-years, the mortality rate was the highest among the low education group with diabetes and DR (67.66; 95% CI, 58.81-76.98) and the lowest among the high education group without diabetes (13.47; 95% CI, 12.78-14.23) (Figure 3 and Supplementary Table 1, available online at http://www.mcpiqojournal.org). SIIs for all-cause mortality were 9.94 (95% CI, 8.60 to 11.35) among participants without diabetes, 22.17 (95% CI, 15.94 to 28.80) among those with diabetes but without DR, and 20.87 (95% CI, 7.58 to 33.44) among those with diabetes and DR (Supplementary Table 2, available online at http://www.mcpiqojournal.org). We found a similar pattern for cardiovascular-related mortality rate, but it was less clear because of a limited number of events. SIIs for cardiovascular mortality were 2.99 (95% CI, 2.25 to 3.74) among participants without diabetes, 11.53 (95% CI, 7.56 to 15.82) among those with diabetes but without DR, and 8.17 (95% CI, 0.40 to 15.94) among those with diabetes and DR.

Sensitivity Analysis

When we additionally adjusted for income, physical activity, smoking, and BMI, the low education group was still associated with the increased prevalence of diabetes and DR compared with the high education group (Supplementary Figure 1, available online at http://www.mcpiqojournal.org). After adjusting for these variables, the association between educational attainment and all-cause mortality also remained among participants without diabetes but not among those with diabetes but without DR and those with diabetes and DR (Supplementary Figure 2, available online at http://www.mcpiqojournal.org). When we used HbA1c to define diabetes status and its severity, we observed similar trends with our main analysis: for example, the low education group was associated with an increased prevalence of diabetes with HbA1c of >7.0% (OR, 1.50; 95% CI, 1.34 to 1.68) (Supplementary Figure 3, available online at http://www.mcpiqojournal.org and increased risk of all-cause mortality (HR, 1.62; 95% CI, 1.31 to

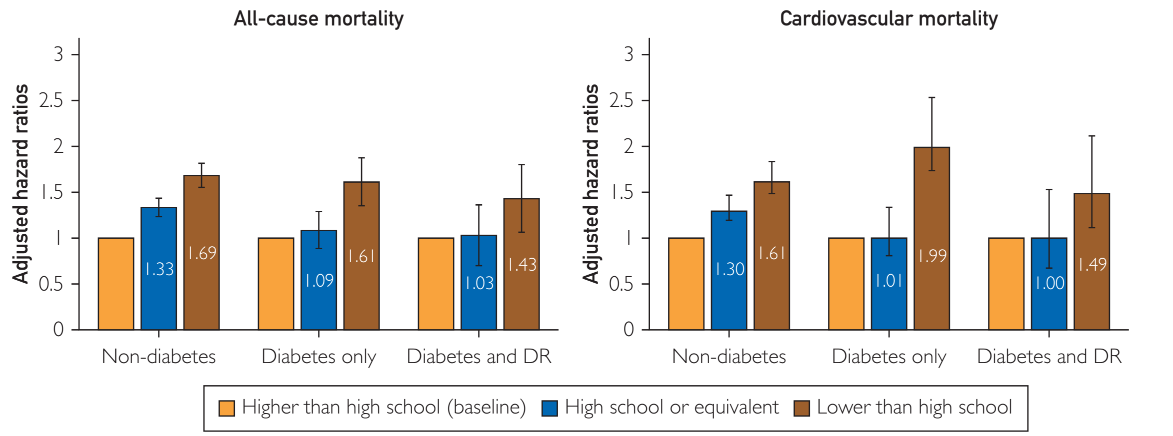

FIGURE 2. Adjusted hazard ratios of all-cause—related and cardiovascular-related mortality according to educational attainment and diabetes status. The multivariable Cox regression models included age, sex, and race/ethnicity for all-cause—related mortality (left) and cardiovascular-related mortality (right).

2.01) (Supplementary Figure 4, available online at http://www.mcpiqojournal.org). SIIs for all-cause mortality were 9.08 (95% CI, 7.72 to 10.47) among participants without diabetes (HbA1c, <6.5%), 16.41 (95% CI, 9.53 to 23.69) among those with moderate diabetes (HbA1c, 6.5% to 7.0%), and 20.12 (95% CI, 13.28 to 26.13) among those with severe diabetes (HbA1c, ≥7.0%), respectively (Supplementary Table 3, available online at http://www.mcpiqojournal.org). When we classified participants by diabetes status using CKD, we observed similar trends of mortality rates in 1000 person-years; the mortality rates were 99.73 (95% CI, 87.42-112.64) among the low education group with diabetes and CKD, and 11.59 (95% CI, 10.90-12.32) among the high education group without diabetes or CKD (Supplementary Table 4, available online at http://www.mcpiqojournal.org).

DISCUSSION

Among the general population of US adults, low educational attainment was associated with the increased prevalence of diabetes and DR and the increased risk of all-cause and cardiovascular mortality. The difference in the mortality rate by educational attainment was larger among patients with diabetes than those without, whereas the difference did not differ by the complication of DR. A similar pattern was observed when we categorized participants on the basis of HbA1c levels. These findings highlighted that the prevention of diabetes itself is critical from the perspective of health disparities by education status.

To our knowledge, this is one of the first studies that estimated differences in mortality rate by educational attainment according to diabetes status and its severity, simultaneously. Low educational attainment is a well-known risk factor for incident diabetes and its development, such as complications and death.[18] Using 3312 adults from the Health and Retirement Study in 2006, 2008, and 2010, Dupre et al[13] reported that the association between educational attainment and mortality increased with the presence of diabetes. However, this study evaluated the health disparities by educational attainment on the relative scale and not on the absolute scale. To obtain public health implications, estimating the absolute difference is important because it considers the actual effect of health disparities across educational levels in the real-world.[19] Dray-Spira et al in 2010[12] investigated the absolute disparities among patients with diabetes using 86,867 samples from the National Health Interview Survey between 1986 and 1996. However, they did not assess the disparities according to diabetes severity such as the presence of complications and

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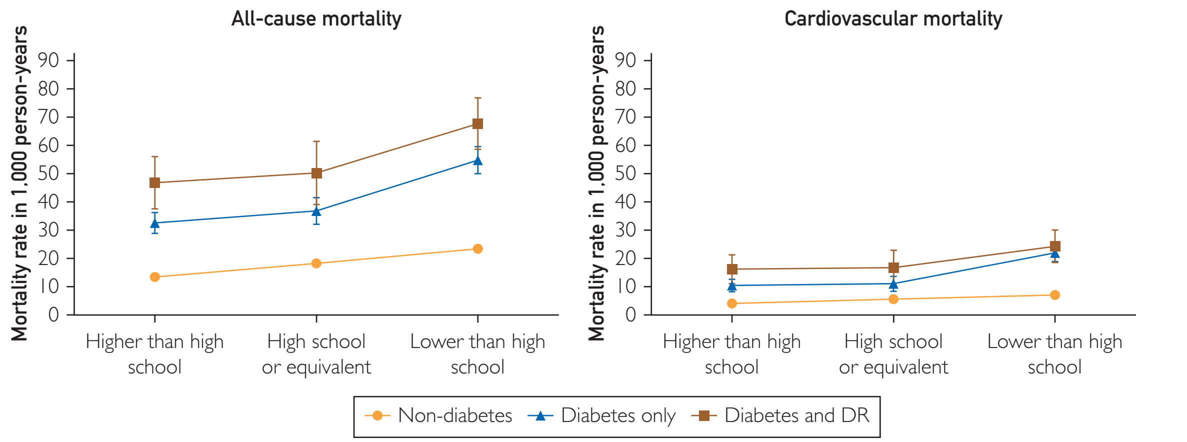

FIGURE 3. Mortality rates according to educational attainment and diabetes status. The multivariable Poisson regression models included age, sex, and race/ethnicity to calculate adjusted mortality rate for all-cause–related and cardiovascular-related mortality according to educational attainment and diabetes status. 95% CIs are computed from 1000 bootstrap samples.

HbA1c. In this context, our results using the most recent data until 2019 advance the current state of knowledge on this topic by providing a comprehensive assessment of health disparities owing to educational attainment according to diabetes status and its severity on an absolute scale.

Although the underlying mechanisms are not clear, the disparities reported in this study are likely to be present in (1) seeking diabetes care, (2) reaching to diabetes care providers such as primary care physicians and endocrinologists, (3) undergoing diabetes treatment, (4) adherence to long-term diabetes management, (5) increased allostatic load due to socioeconomic pressure, or (6) any combination of these.[20] Given that the HR of all-cause mortality for low educational attainment substantially decreased after adjusting for income, physical activity, smoking status, and BMI regardless of their diabetes status, these factors are not only the major risk factors of mortality but also the contributing factors for the existing health disparities due to educational attainment in diabetes care. In fact, previous studies reported that those with low SES often exhibit a lower tendency to complete diabetes management, which requires patients to control their life habits such as physical activity and smoking status, in the long run.[21,22] Future studies should address how formal or informal care and community-level health care support can mitigate the disparities.

Several limitations in this study should be acknowledged. First, because the diabetes status and DR were self-reported, our findings might be subjected to the misclassification of diabetes status. However, we obtained consistent results using a major objective biomarker for diabetes and its severity (ie, HbA1c) to define diabetes status in our sensitivity analysis. Second, the NHANES did not allow us to identify the type of diabetes (type 1 and type 2) in this study, whereas we believe that most of the adults included in this study would be type 2 diabetes given the epidemiology of diabetes in the United States.[23] Third, we used the diabetes status at the survey enrollment, and thus, our study did not evaluate the trend of diabetes status over the follow-up period. Fourth, although we aimed to describe the health disparities by education and did not aim to establish causality, our findings might experience confounding: that is, some unmeasured variables such as residential area, medical expense, and a family history of diabetes may partially explain the observed association. Finally, we did not measure other aspects of health disparities by educational attainment such as the quality of life of study participants. The mortality rate does not solely reflect the disparity that patients experience in general clinical practice and diabetes care.

CONCLUSION

In conclusion, we found the elevated risk of all-cause and cardiovascular mortality by low educational attainment when individuals presented with diabetes. The degree of health disparity by educational attainment was similar between individuals with diabetes without DR and those with diabetes and DR. Future studies should address mechanisms behind these health disparities relating to educational attainment in diabetes prevention and management and build an effective strategy to achieve equitable diabetes care.

POTENTIAL COMPETING INTERESTS

All authors state that they have no conflict of interest.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mcpiqojournal.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **BMI**, body mass index; **CKD**, chronic kidney disease; **DR**, diabetic retinopathy; **HbA1c**, glycated hemoglobin A1c; **HR**, hazard ratio; **OR**, odds ratio; **SII**, slope inequality index; **SES**, socioeconomic status; **NDI**, The National Death Index; **NHANES**, The National Health and Nutrition Examination Survey

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