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Increasing Mortality Among Patients With Diabetes and Chronic Liver Disease From 2007 to 2017

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The age-standardized prevalence of diabetes increased from 9.8% in 1988–1994, to 10.8% in 2001–2002, to 12.4% in 2011–2012 in the United States.¹ According to the National Vital Statistics System data, diabetes-related mortality has remained stable as the seventh-leading cause of death nationally since 2006.² However, the age-standardized diabetes-related mortality decreased from 112.2 per 100,000 individuals in 2007 to 104.3 per 100,000 individuals in 2017.³ In terms of cause-specific mortality, the age-standardized mortality for cardiovascular disease, complications of diabetes, and cancer among individuals with diabetes declined annually by approximately 1%.³ In contrast, chronic liver disease–related mortality has been reported to be increasing in individuals with diabetes.^{4,5} However, the trends in mortality due to chronic liver disease in the setting of diabetes remain unknown. In this study, we estimated the trends in chronic liver disease–related mortality among individuals with diabetes from 2007 to 2017 in the United States.

Materials and Methods

We analyzed the de-identified mortality records from the National Vital Statistics System database, in which the cause of death was coded by International Classification of Diseases–Tenth Revision (ICD-10).³ We defined chronic liver disease–related deaths using underlying cause of death among individuals with diabetes (E10–E14). In a sensitivity analysis, we determined chronic liver disease–related deaths using the underlying or contributing cause of death. We used ICD-10 codes to define cirrhosis (K70.3, K74.0, K74.1, K74.2, K74.3, K74.4, and K74.6), portal hypertension (K76.6), or 1 of the complications of cirrhosis/portal hypertension: spontaneous bacterial peritonitis (K65.2), hepatic encephalopathy (K72.11 and

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Conflicts of interest

The authors disclose no conflicts.

K72.91), variceal bleeding (I85.0 and I85.1), or hepatorenal syndrome (K76.7). In addition, we identified chronic hepatitis C virus (HCV) infection (B17.1, B18.2, and B19.2), chronic hepatitis B virus (HBV) infection (B16, B17.0, B18.0, B18.1, and B19.1), alcoholic liver disease (ALD) (K70.0, K70.1, K70.2, K70.3, K70.4, and K70.9), nonalcoholic fatty liver disease (NAFLD) (K76.0 and K75.81), and hepatocellular carcinoma (HCC) (C22.0). Age-specific mortality was calculated by dividing the number of deaths by the total U.S. Census population for each year and were standardized according to age distribution of 2010 U.S. standard population. Trends were analyzed by Joinpoint Regression Program version 4.7.0.0 (National Cancer Institute, Bethesda, MD). For each trend segment, the annual percentage change (APC) and the average APC, which is a summary measure of trend and explanation for transitions within each trend segment, were calculated.

Results

Among 2,686,590 individuals with diabetes, we identified 48,761 with chronic liver disease as the underlying cause of death listed on death certificate. Individuals who died with chronic liver disease in the setting of diabetes were predominantly of younger age, male sex, and Hispanic race/ethnicity. Among individuals who had diabetes listed on their death certificate, the age-standardized mortality for cirrhosis and HCC as an underlying cause of death increased at an annual rate of 1.2% for cirrhosis (95% confidence interval [CI], 0.6% to 1.7%) and 1.9% for HCC (95% CI, 1.2% to 2.6%) (Figure 1A). Based on etiology, age-standardized mortality for HCV and HBV decreased at an annual rate of -4.4% (95% CI, -6.0% to -2.8%) and -5.1% (95% CI, -9.8% to -0.1%), respectively. In contrast, mortality in individuals with NAFLD increased at a rate of 11.6% (95% CI, 9.5% to 13.8%) and in individuals with ALD at a rate of 1.4% (95% CI, 0.5% to 2.2%). When we defined chronic liver disease as an underlying or contributing cause of death among individuals with diabetes listed on the death certificate, the overall results remained similar (Figure 1B). The age-standardized mortality for cirrhosis and HCC showed comparable trends for cirrhosis (APC, 2.3%; 95% CI, 1.6% to 3.0%) and for HCC (APC, 2.2%; 95% CI, 1.5% to 2.9%) (Figure 1B). For NAFLD, age-standardized mortality steadily increased during the 11 years (APC, 11.6%; 95% CI, 10.2% to 13.1%).

Discussion

Using nationally representative mortality data in the United States, we found that the age-standardized cirrhosis and HCC-related mortality among individuals with diabetes increased 1.2%–1.9% annually during the recent decade. While the age-standardized mortality decreased in individuals with viral hepatitis, mortality increased rapidly in NAFLD and modestly in ALD. Our study using death certificates and ICD-10 codes has the potential for misclassification and underestimation for diabetes and chronic liver disease-related mortality. However, the coding method has been constant over time, so it is unlikely to account for presented trends. Increasing obesity and associated insulin resistance likely explain the link between diabetes and NAFLD and end-stage liver disease through hepatic inflammation and various proinflammatory cytokines.⁶ While diabetes-related mortality has been reported to be decreasing due to improved awareness and management,^{7,8} our results

highlight the need to better address NAFLD and end-stage liver disease among individuals with diabetes.

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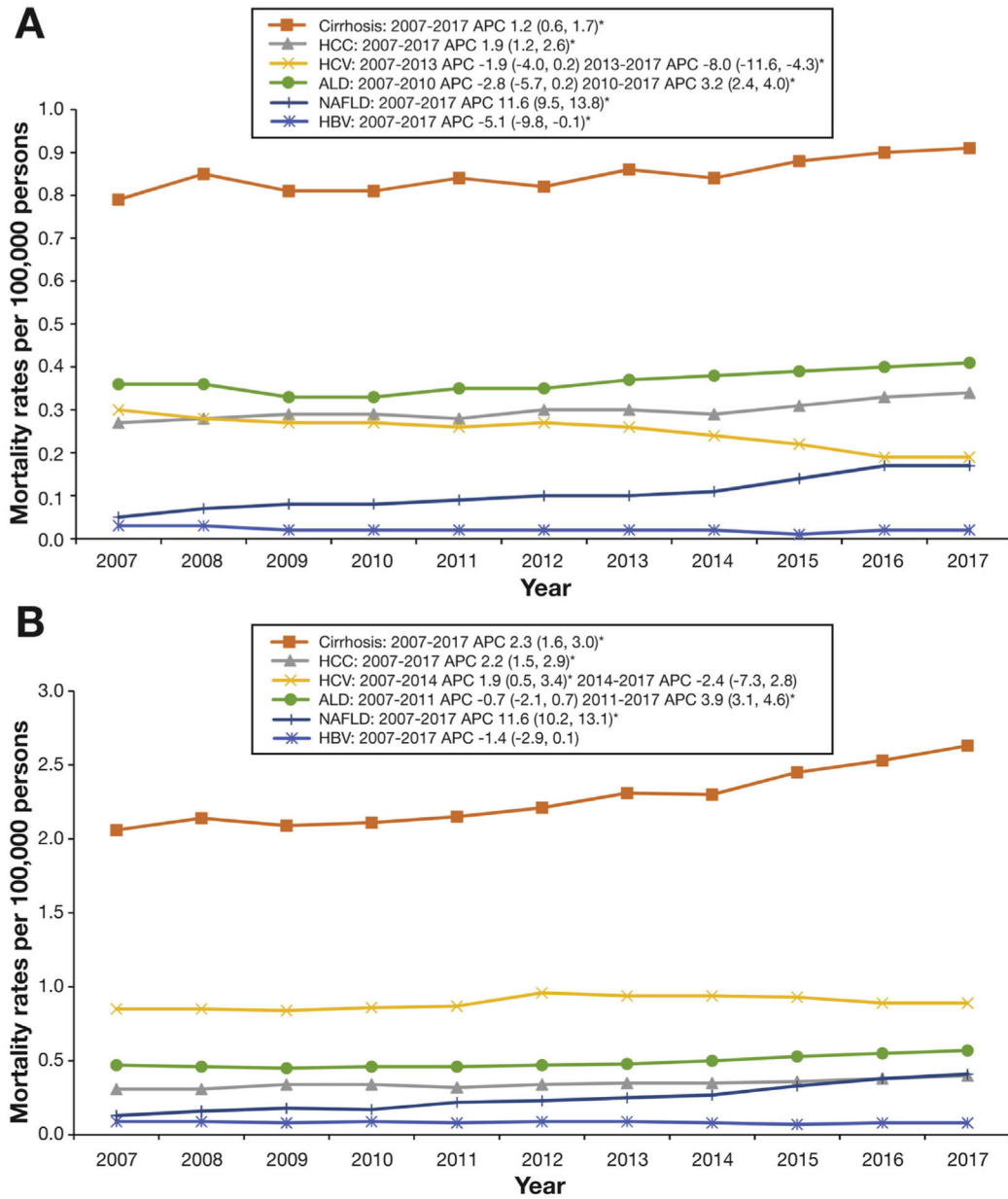


Figure 1. Annual age-standardized chronic liver disease–related mortality among individuals with diabetes listed on death certificates in the United States, from 2007 through 2017. Trends in chronic liver disease–related mortality as (A) the underlying cause of death or (B) the underlying or contributing cause of death. ALD, alcoholic liver disease; APC, annual percentage change; HBV, hepatitis B virus infection; HCC, hepatocellular carcinoma; HCV, hepatitis C virus infection; NAFLD, nonalcoholic fatty liver disease. * $P < .05$.