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BRIEF REPORT

Rising Mortality Associated With Hepatitis C Virus in the United States, 2003–2013

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In the United States, hepatitis C virus (HCV)–associated mortality is increasing. From 2003-2013, the number of deaths associated with HCV has now surpassed 60 other nationally notifiable infectious conditions combined. The increasing HCV-associated mortality trend underscores the urgency in finding, evaluating, and treating HCV-infected persons.

Keywords. hepatitis C; mortality trends; death certificates; causes of death.

Despite enthusiasm for the new curative, brief (12-week), all-oral antiviral treatments for hepatitis C virus (HCV) infection, the continued health burden [1] and increased mortality [2] for HCV-infected patients in the United States remain underappreciated. We examined national multiple-cause-of-death (MCOD) data from 2003 to 2013 to provide more current estimates of trends in hepatitis C–related mortality in the United States and compared these with trends in deaths associated with 60 other nationally notifiable infectious conditions (ONNICs) that are routinely reported to the Centers for Disease Control and Prevention (CDC).

METHODS

Death certificate information from the public-use MCOD data, obtained from the National Center for Health Statistics, was examined. Mortality codes for 2 disease categories, hepatitis C and ONNICs, as classified by the *International Classification of Diseases, 10th Revision* (*ICD-10*) [3], were examined. Deaths associated with hepatitis C were defined as having the *ICD-10* codes B17.1 and B18.2 listed in the "record axis" MCOD fields. Deaths associated with ONNICs [4] were defined as having any of the *ICD-10* codes associated with 60 conditions (see Supplementary Appendix) recorded in the "record axis" MCOD fields. To ensure mutual exclusivity between the 2 disease categories, any ONNIC-related death that also had a listing of hepatitis C was excluded from the ONNICs category, which was, on average, 1067 deaths (range, 936–1193) per year.

To calculate mortality rates, the number of deaths associated with HCV infection and ONNICs were divided by the total US census population for each year and then adjusted to the age distribution of the standard US population in 2000 by using the direct method [5]. Ninety-five percent confidence intervals (CIs) were calculated based on the gamma distribution to estimate the variance [6]. Trends in age-adjusted mortality rates were analyzed using joinpoint regression [7]. The resulting trends were described by the slope of the line segment or annual percentage change by applying the least-squares linear regression method.

RESULTS

From 2003 to 2013, the number of deaths associated with hepatitis C listed on death certificates increased from 11 051 in 2003 to 19 368 in 2013 (Figure 1). These deaths represented an average annual increase of 865 deaths per year, and the average annual percentage increase was 6.2% ($P < .05$). In comparison, the number of deaths associated with ONNICs, 60 conditions in all, decreased from 24 745 in 2003 to 17 915 in 2013 (see Supplementary Appendix for listing of deaths in 2013 by specific infectious condition). These deaths represented an average annual decrease of 718 deaths per year (Figure 1), and the average annual percentage decrease was 3.4% ($P < .05$). The decline in ONNIC-related deaths was mostly due to a decline in human immunodeficiency virus (HIV)–related deaths, and, to a lesser extent, a decline in pneumococcal disease–related and tuberculosis-related deaths. The number of HIV-related deaths declined by 41.8% from 15 168 deaths in 2003 to 8831 deaths in 2013. Pneumococcal disease–related deaths decreased by 31.0% from 1283 deaths in 2003 to 885 deaths in 2013; tuberculosis-related deaths decreased by 28.2% from 1382 deaths in 2003 to 992 deaths in 2013. When combined, these 3 conditions were associated with a 39.9% decline from 17 764 deaths in 2003 to 10 683 deaths in 2013.

In 2012, the number of deaths associated with hepatitis C surpassed that of 60 ONNICs that are routinely reported to CDC (Figure 1). The mortality rate, as opposed to the crude number of deaths, associated with hepatitis C increased from 3.72 (95% CI, 3.65–3.79) deaths per 100 000 population in 2003 to 5.03 (95% CI, 4.96–5.11) deaths per 100 000 population in 2013. These mortality rates represent an average annual increase of 0.14 deaths per 100 000 population per year, and the average annual percentage increase was 3.4% ($P < .05$). In comparison, the mortality rate associated with ONNICs decreased from 8.51 (95% CI, 8.41–8.62) deaths per 100 000 population in 2003 to 5.25 (95% CI, 5.17–5.33) deaths per 100 000

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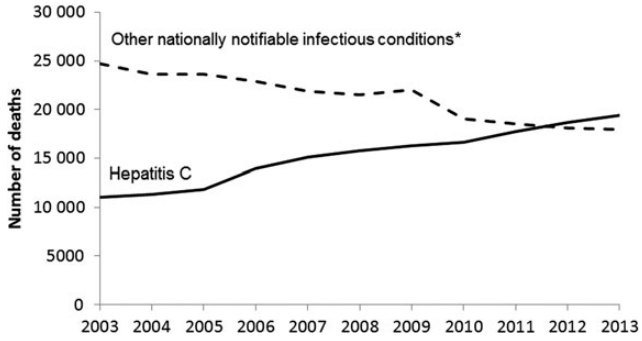

Figure 1. Annual number of deaths associated with hepatitis C virus and all other nationally notifiable infectious conditions* listed as multiple causes of death in the United States between 2003 and 2013. *Identified in the absence of hepatitis C. The list of 60 other nationally notifiable infectious conditions was obtained from the Centers for Disease Control and Prevention National Notifiable Diseases Surveillance System website (http://wwwn.cdc.gov/nndss/conditions/notifiable/2013/infectious-diseases/).

population in 2013. These mortality rates represented an average annual decrease of 0.34 deaths per 100 000 population per year, and the average annual percentage decrease was 4.9% ($P < .05$). In 2013, 51.1% (n = 9899) of HCV-related deaths occurred among persons aged 55–64 years (mean age, 59.7 years).

DISCUSSION

Despite improving therapies [8], our study found that deaths associated with HCV continued to rise while deaths associated with 60 ONNICs that are routinely reported to CDC declined. The great decline among deaths associated with HIV, pneumococcal disease, and tuberculosis from the ONNICs category were likely due to implementation of effective public health programs and policies.

One explanation for the increasing HCV-related mortality could be that many HCV-infected persons are not receiving antiviral therapy and achieving a sustained virologic response indicative of a cure. In fact, one study found that only 19% of HCV and 16% of HCV/HIV-coinfected patients were eligible for and advanced to treatment [9]. Furthermore, only 13% and 11%, respectively, completed treatment and 3% and 6%, respectively, achieved a sustained virologic response [9]. Data from our study and from previous analyses showed that HCV-related deaths occurred mainly among those aged 55–64 years [2], indicating the premature loss of life and economic burden with HCV infection. The largest extant analysis of approximately 1600 well-characterized HCV-infected patients in the United States who died found that only 19% of them had HCV listed anywhere on their death certificate, although 75% had premortem indications of substantial or extensive liver disease at time of death [10]. Even among HCV-infected patients whose death certificate listed a liver-related cause of death, 59% did not have HCV listed as a cause of death [10]. Therefore, we believe these data greatly underestimate the true hepatitis C mortality burden.

There are many putative reasons why there remains underappreciation of the seriousness of HCV infection, an infection among an estimated 3.2 million US residents [1], and continuing deficiencies in the decades-long asymptomatic incubation period that may make clinicians and patients discount the importance of the infection; the lack of cohesive and vocal advocacy groups as many patients were former injection drug users; "compassion fatigue" from HIV/AIDS and other large acute public health problems; and, currently, a new therapeutic nihilism not about the efficacy of antivirals but about their perceived cost, despite evident cost-effectiveness [12]. The unabated increasing trend in the number of hepatitis C–related deaths documented from 1999 to 2013, predominantly among middle-aged persons, underscores the urgency in finding, evaluating, and treating patients in the largest infectious disease epidemic in the United States.

Supplementary Data

Supplementary materials are available at http://cid.oxfordjournals.org. Consisting of data provided by the author to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the author, so questions or comments should be addressed to the author.

Notes

Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention (CDC).

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Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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