



Economic burden and healthcare utilization in nonalcoholic fatty liver disease

Eric R. Yoo¹, Aijaz Ahmed², Donghee Kim²

¹Department of Internal Medicine, Santa Clara Valley Medical Center, San Jose, CA, USA; ²Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Stanford, CA, USA

Correspondence to: Donghee Kim, MD, PhD. Division of Gastroenterology and Hepatology, Stanford University School of Medicine, 300 Pasteur Drive, Stanford, CA 94304, USA. Email: dhkimmd@stanford.edu.

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In the United States (US), the shift in the treatment paradigm following the introduction of second generation direct-acting antiviral (DAA) agents for hepatitis C virus (HCV) infection has favorably transformed the landscape of end-stage liver disease (ESLD) with a rapid decline in HCV-related liver transplantation; HCV had been the leading indication for liver transplantation for the last two decades (1). While the rate of liver transplantation in patients with HCV infection has plummeted in the US following the widespread application of DAA-based regimens in the pre-transplant setting, the rise in alcohol use disorder and obesity has catapulted alcoholic liver disease (ALD) to become the leading indication for liver transplantation in the US in 2016 followed closely by nonalcoholic steatohepatitis (NASH), a progressive subset of nonalcoholic liver disease (NAFLD) (1). Despite the decline in HCV-related liver transplantation in the US, the total number of liver transplants per year are on an upward trajectory as a result of marked increase in ESLD associated with ALD and NASH—an ominous trend.

The approval of second generation DAA agents in late 2013 heralded a revolutionary era in the treatment of HCV infection. This was portrayed in our recent population-based study in which we showed that prior to the DAA-era between 2007 and 2014, there was a marked increase in HCV-related mortality [annual percent change (APC): +2.0% per year], but a marked decrease in HCV-related mortality in the DAA-era from 2014 through 2016 (APC: -6.4% per year) (2). While HCV-related mortality decreased with the introduction of DAA agents, mortality

from ALD and NAFLD has steadily increased from 2007 to 2016. Another study reported that in NAFLD-related cirrhosis, age-standardized mortality rates increased significantly between 2007 and 2016 (APC: +15.4%; 95% confidence interval: 14.1–16.7%) (3). These findings further support the observations reported in a previous population-based study projecting an ongoing increase in the burden of NAFLD between 1988 and 2008 fueled by an unconstrained obesity epidemic in the US (4). While it is likely that NAFLD has a substantial economic impact, complete representative data are still lacking in the US. Based on data from a random sample of national outpatient claims of Medicare beneficiaries, a study noted that the number of outpatient visits for NAFLD increased from 2005 to 2010, and the mean yearly charge and payment increased significantly from \$2,624 and \$561 in 2005 to \$3,608 and \$629 ($P < 0.05$), respectively (5). Recently, Allen *et al.* analyzed the annual cost of care and resource utilization per patient with and without NAFLD between 2010 and 2014 using OptumLabs Data Warehouse, a national claims database of individuals enrolled in private and Medicare Advantage health plans (6). The authors matched 108,420 adults with a first claim for NAFLD to non-NAFLD controls by age, sex, race, geographic region, year of diagnosis, metabolic comorbidities, length of follow-up, and insurance type (6). The authors demonstrated that the highest annual cost occurs around a new diagnosis of NAFLD, reaching \$7,804 per individual with private insurance and \$9,062 per individual with Medicare Advantage, both of which are significantly

higher than the total annual cost of \$2,298 in the matched control group. Annual costs for long-term management decreased to \$3,789 and \$5,363 per individual with private insurance and Medicare Advantage, respectively, but remained considerably higher than those of the control group. The average rate of overall outpatient visits at 5 years following diagnosis was 40% higher among patients with NAFLD compared with controls. However, this study only considered patients with private insurance and Medicare Advantage health plans. Patients experiencing difficulties with healthcare access are less likely to have private insurance or Medicare Advantage and may be diagnosed with NAFLD at a later stage; as such, there may be a considerable difference in healthcare costs associated in the management for these populations. A follow-up study looking at the healthcare cost and resource utilization in the management of patients with NAFLD without private insurance or Medicare Advantage [i.e., original Medicare (parts A and B), Medicare supplemental insurance, and Medicaid, and uninsured patients] would be interesting. This topic is relevant in light of recent findings that in the US, minority populations (non-Hispanic blacks, non-Hispanic Asians, and Hispanics) have a disproportionately higher burden of mortality related to chronic liver disease (2), ESLD-related mortality and HCC-related mortality (3). Likewise, studies on Asian-American and Hispanic American sub-cohorts have further demonstrated disproportionate association between ethnicity and chronic liver disease-related mortality (7,8). These findings may be derived from disparities in linkage to care and healthcare access which are likely contributing to the increased burden of chronic liver disease seen among minorities and minority subgroups.

Finally, Allen *et al.* reported that the largest portion of healthcare utilization are represented by liver biopsies and imaging. A population-based study evaluated the association of noninvasive fibrosis markers with mortality and demonstrated that patients with advanced fibrosis had an increased risk of overall mortality compared to patients without advanced fibrosis (9). Issues with healthcare access bring to light the question whether or not it would be more beneficial to increase efforts on utilizing noninvasive measures and increase efforts on screening for NAFLD. This last point is especially poignant in light of Allen *et al.*'s interesting finding that about 95.4% to 97% of total office visits in the study were conducted by primary care clinics.

It is evident that the burden of NAFLD on healthcare

costs and resource utilization remains significant, and that this chronic liver disease will predominantly impact minorities and patients who experience health disparities. As such, healthcare providers and policy makers may need to shift and prioritize their focus towards addressing NAFLD in high-risk sub-populations and minorities.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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