

Direct-Acting Antiviral Therapy for Hepatitis C Virus Decreases All-Cause Mortality and Decompensated Cirrhosis: Treat (Virtually) Everyone



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This summary reviews Ogawa E, Chien N, Kam L, et al. Association of Direct-Acting Antiviral Therapy with Liver and Nonliver Complications and Long-term Mortality in Patients with Chronic Hepatitis C. JAMA Intern Med 2023; 183(2):97-105.

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STRUCTURED ABSTRACT

Question: Are direct-acting antiviral agents (DAA) associated with decreased mortality and decreased liver outcomes (e.g., decompensated cirrhosis, hepatocellular carcinoma) among individuals with hepatitis C virus (HCV)?

Design: A retrospective cohort study from January 2014 to March 2021.

Setting: Optum Clinformatics Data Mart database of administrative claims from individuals with commercial and Medicare Advantage Health Plans.

Patients: Patients infected with HCV.

Interventions/Exposure: Treatment with DAAs.

Outcome: Primary endpoints were: (1) incidence of liver outcomes, including hepatocellular carcinoma (HCC) and decompensated cirrhosis; and (2) all-cause mortality. Secondary endpoints were incidence of non-liver outcomes, including non-liver

cancer, chronic kidney disease, cardiovascular disease, and diabetes.

Data Analysis: Cumulative HCC incidence and mortality was calculated with the Kaplan-Meier method. Log-rank test was used to compare differences between DAA-treated HCV patients and non-treated patients. Cox proportional hazards regression was used to estimate adjusted hazard ratios (aHRs).

Funding: Stanford Center for Population Health Sciences and the National Institute of Health.

Results: A total of 245,596 patients with HCV (mean age 59; 59% men; 57% White; 17% Black) were included in data analysis, with 17% receiving at least 1 prescription for DAA and 83% with no prescriptions. Compared to untreated patients, patients receiving DAAs were slightly older (59.9 years vs 58.5 years), male (61.6% vs 58.5%), and had compensated cirrhosis (44% vs 29%).

The incidence (per 1,000 person-years) was significantly lower in DAA-treated patients vs untreated patients for developing decompensated cirrhosis (28.2 vs 40.8), HCC among the sub-group with compensated cirrhosis (20.1 vs 41.8), and all-cause mortality (36.5 vs 64.7). The difference in all-cause mortality was demonstrated in sub-groups of individuals without baseline cirrhosis, with compensated cirrhosis at baseline, and with decompensated cirrhosis at baseline (**Figure 1**).

In multi-logistic regression analysis, DAA treatment was independently associated with a decreased risk of decompensated cirrhosis (aHR 0.36; 95% confidence interval [CI]: 0.35-0.38), HCC (aHR 0.73; 95% CI: 0.68-0.77), diabetes (aHR 0.74; 95% CI: 0.70-0.77), and all-cause mortality (aHR 0.43; 95% CI: 0.42-0.45).

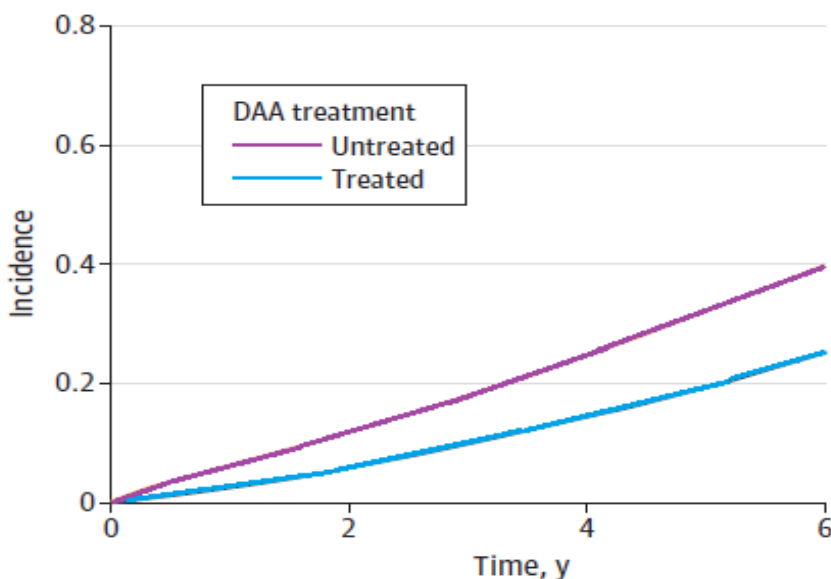


Figure 1. All-cause mortality among patients with hepatitis C virus treated with direct-acting antiviral agents (DAAs) vs untreated (total cohort). $P < .001$.

COMMENTARY

Why Is This Important?

HCV is a public health crisis. Over 2.4 million Americans are estimated to be infected with HCV, and Centers for Disease Control and Prevention data indicate that acute HCV infection has increased 400% from 2010 to 2020 with the highest infections rates among 20–39-year-olds. However, as many as 40% are unaware that they are infected.¹ Yet, the severe morbidity and mortality due to HCV can be decreased with the breakthrough antiviral agents approved in the past 10 years. Oral DAA regimens of 8–12 weeks are over 95% effective at eradicating HCV and extremely well-tolerated. This success has been demonstrated regardless of prior treatment failure, presence of cirrhosis, advanced age, or comorbidities. Thus, treatment is appropriate for virtually all populations unless they already have a very short life expectancy.

Unfortunately, only a minority of HCV-infected individuals have been treated and as many as 40% of these individuals are unaware that they are even infected. This has led to recommendations from the American Association for the Study of Liver Disease and the Infectious Disease Society of America for universal HCV screening and DAA treatment for all infected patients. The importance of these recommendations is affirmed by this excellent study from Ogawa et al, which estimates efficacy of DAAs when

prescribed in a large, insured community-based group of patients. Specifically, the adjusted risk reduction for all-cause mortality was greater than 50% and decompensated cirrhosis was greater than 60% when DAAs were prescribed.

Key Study Findings

The incidence (per 1,000 person-years) was significantly lower in DAA-treated patients vs untreated patients for developing decompensated cirrhosis (28.2 vs 40.8), HCC among the sub-group with compensated cirrhosis (20.1 vs 41.8), and all-cause mortality (36.5 vs 64.7).

Caution

Achieving sustained virologic response was not a primary outcome of the study. However, given the efficacy of DAAs, most patients prescribed DAAs probably achieved sustained virologic response. Study patients had private insurance or Medicare Advantage and may differ from non-insured individuals. Consistent with large database studies, misclassification bias is possible despite using *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* and *ICD-10-CM* codes to identify outcomes.

My Practice

At our Veterans Affairs Medical Center, we offer DAAs to all HCV-infected patients unless they have a very short life expectancy or if their mental illness/polysubstance abuse is so severe that establishing compliance with follow-up visits or adherence to medication is hopeless. Overall, our treatment approach has

become much more inclusive, and we actively seek to screen all veterans for HCV and actively pursue HCV-infected veterans to initiate treatment.

For Future Research

Further research should focus on expanding HCV screening, diagnosis, and treatment since the consequences of untreated HCV infection are clear and since DAAs have demonstrated their efficacy and safety.

Conflict of Interest

Dr. Schoenfeld reports no potential conflicts of interest.

Note: The authors of the article published in *JAMA Internal Medicine* are active on social media. Tag them to discuss their work and this EBGI summary!

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