eAppendix 1. Construction of the study sample, index dates, and treatment completion

Algorithm used to identify patients with hepatitis C virus

The details of the algorithm and diagnoses codes used to identify the study sample were described in eAppendix 1 of a previous publication cited below.[1]

Index date construction and robustness checks

We constructed an index date for each patient following a commonly used approach – we identified the first HCV claim after at least a one-year "wash-out" period with no HCV claim. Patients with an index date in 2014 had a one-year wash-out period, while the 2015 and 2016 cohorts had 2-year and 3-year wash-out periods, respectively. About 55% of the total sample had at least a two-year wash-out period. An analysis using only these patients with a longer wash-out period produced results consistent with the main study findings: the hazard ratio (HR) of dying between DAA users and non-users was 0.51 (95% CI, 0.44-0.59) in the cirrhosis group, and 0.65 (95% CI, 0.59-0.73) in the non-cirrhosis group.

We checked the index date based on our approach against the date of viral hepatitis diagnosis included in the Beneficiary File. This diagnosis date is not hepatitis C specific but is based on any hepatitis (hepatitis A, B, C, D and E), so it is subject to some measurement error. About 46% of the study sample – *in both DAA users and non-users* – had an index date that matched the hepatitis diagnosis date. Analyses with only these beneficiaries showed consistent results with the main study finding: the HR of dying between DAA users and non-users was 0.46 (95% CI, 0.38-0.55) in the cirrhosis group and 0.54 (95% CI, 0.48-0.60) in the non-cirrhosis group.

Definition of completion of treatment

Details of how we defined completion of direct-acting antivirals (DAAs) introduced before 2017, including elbasvir/grazoprevir, ledipasvir/sofosbuvir, ombitasvir/paritaprevir/ritonavir plus dasabuvir, sofosbuvir, and sofosbuvir/velpatasvir were described in eAppendix 2 of a previous publication cited below.[1] We also included the following DAAs that were approved in 2017 in this study: sofosbuvir/velpatasvir/voxilaprevir and glecaprevir/pibrentasvir.

DAA regimens vary by genotype and prior HCV treatment experience, which cannot be identified from Medicare claims. Based on the recommended duration of therapy indicated by package inserts, we considered 12 weeks of treatment with ofosbuvir/velpatasvir/voxilaprevir or glecaprevir/pibrentasvir as completion. If patients filled prescriptions for more than 12 weeks, we considered 16 weeks as completion for glecaprevir/pibrentasvir, and 24 weeks for sofosbuvir/velpatasvir/voxilaprevir. We considered an interval between fills of fewer than 60 days as continuation of the therapy.

References

1. Jung J, Feldman R, Kalidindi Y, et al (Accepted for publication). Association of direct acting antiviral therapy for hepatitis C with after treatment costs among Medicare beneficiaries. *JAMA Network Open*

eTable 1. Definitions and data sources of the covariates used in the study

The data sources and covariates used in this study have been defined in eTable 1 of a previous publication cited below.[1] In addition to the covariates used in the prior study, we included a variable for dual-eligibility status in this study. The definition and data source for dual-eligibility status are provided below:

	Definition	Data Source
Dual-eligible	Binary indicator that indicates whether a patient was eligible for both Medicare and Medicaid	Medicare master beneficiary summary file

References

1. Jung J, Feldman R, Kalidindi Y, et al (Accepted for publication). Association of direct acting antiviral therapy for hepatitis C with after treatment costs among Medicare beneficiaries. *JAMA Network Open*

eTable 2. Patient characteristics in the full unmatched sample[a]

	Cirrhosis patients (N=14,491)			Non-cirrhosis patients (N=95,118)		
	DAA Treated (N=4,122)	DAA Untreated (N=10,369)	St.Diff,[b] %	DAA Treated (N=21,619)	DAA Untreated (N=73,499)	St.Diff,[b] %
Variable	No. (%)	No. (%)		No. (%)	No. (%)	
Age						
Age <65	2,357(57.1%)	5,454(52.6%)	9.2	14,344(66.4%)	4,5962(62.5%)	8.0
Age 65-70	9,31(22.6%)	1,966(19.0%)	8.9	4,144(19.2%)	1,1571(15.7%)	9.0
Age 70-75	4,58(11.1%)	1,351(13.0%)	-5.9	1,941(9.0%)	7,118(9.7%)	-2.4
Age >75	3,76(9.1%)	1,598(15.4%)	-19.3	1,190(5.5%)	8,848(12.0%)	-23.3
Female Gender	1,515(36.7%)	4,065(39.2%)	-5.0	8,994(41.6%)	31,684(43.1%)	-3.0
Race						
White	2,917(70.8%)	7,371(71.1%)	-0.7	14,358(66.4%)	51,078(69.5%)	-6.6
African American	872(21.2%)	1,733(16.7%)	11.4	5,823(26.9%)	16,250(22.1%)	11.2
Hispanic	145(3.5%)	587(5.7%)	-10.3	595(2.8%)	2,404(3.3%)	-3.0
Other	188(4.6%)	678(6.5%)	-8.6	843(3.9%)	3,767(5.1%)	-5.9
Dual eligibility[c]	2,733(66.3%)	7,190(69.3%)	-6.5	15,182(70.2%)	53,706(73.1%)	-6.3
Conditions						
Decompensated cirrhosis	1,248(30.3%)	4,620(44.6%)	-29.8	-		.
HIV/AIDS	109(2.6%)	356(3.4%)	-4.6	1,175(5.5%)	3,751(5%)	1.5
Hepatocellular cancer	239(5.8%)	947(9.1%)	-12.7	76(0.4%)	442(0.6%)	-3.6
Anemia	1,808(43.9%)	6,999(67.5%)	-49.0	5,572(25.8%)	30,989(42.2%)	-35.1
Lung Disease	1,166(28.3%)	4,413(42.6%)	-30.2	5,364(24.8%)	28,347(38.6%)	-29.9
Cancer	524(12.7%)	1,833(17.7%)	-13.9	2,208(10.2%)	10,775(14.7%)	-13.5
Cardiac disease	3,140(76.2%)	9,066(87.4%)	-29.5	14,742(68.2%)	57,938(78.8%)	-24.3
Dementia	254(6.2%)	1,796(17.3%)	-35.2	895(4.1%)	9,000(12.2%)	-29.9
Psychiatric conditions	1,810(43.9%)	5,869(56.6%)	-25.6	10,840(50.1%)	44,447(60.5%)	-20.9
Diabetes	1,554(37.7%)	5,279(50.9%)	-26.8	6,123(28.3%)	26,657(36.3%)	-17.1
Eye disease	675(16.4%)	1,729(16.7%)	-0.8	3,403(15.7%)	10,962(14.9%)	2.3
Kidney disorders	1,150(27.9%)	5,351(51.6%)	-49.9	4,160(19.2%)	25,728(35.0%)	-36.0
Drug and alcohol related disorder	2,052(49.8%)	6,531(63.0%)	-26.9	10,123(46.8%)	42,688(58.1%)	-22.7
Bone disease	1,520(36.9%)	4,567(44.0%)	-14.6	8,419(38.9%)	32,017(43.6%)	-9.4
ESRD	164(4.0%)	969(9.3%)	-21.6	703(3.2%)	6,244(8.5%)	-22.4
Time from index date[d] to DAA initiation						
<6 months	1,151(27.9%)	NA		7161(33.1%)	NA	
6-12 months	1,506(36.6%)			6907(31.9%)		
12-24 months	1,086(26.4%)			5195(24.0%)		
24-36 months	302(7.3%)			1866(8.6%)		
>36 months	77(1.9%)			490(2.3%)		

Abbreviations: AIDS, Acquired immunodeficiency syndrome; DAA, Direct-acting antiviral drug; ESRD, End-stage renal disease; HIV, Human immunodeficiency virus; St.Diff, Standardized difference

[a] Patient characteristics are measured at index date

[b] A standardized difference less than 10% is considered to denote balanced patient characteristics

[c] Dual eligibility is an indicator of whether a person is eligible for both Medicare and Medicaid

[d] Index date is the date when the patient first sought HCV care after a one-year wash-out period

eTable 3. Full results – adjusted hazard ratios[a] for mortality comparing direct-acting antiviral agent (DAA) treated and DAA untreated patients

	Cirrhosis patients (N=8,240)		Non-cirrhosis patients (N=43,238)	
Variable	**HR (95% CI)**	**P**	**HR (95% CI)**	**P**
DAA treatment as time-varying exposure	0.51 (0.46-0.57)	<.001	0.54 (0.50-0.58)	<.001
Age (ref. Age<65)				
Age 65-70	1.24 (1.09-1.40)	<.001	1.40 (1.28-1.53)	<.001
Age 70-75	1.37 (1.16-1.61)	<.001	1.40 (1.24-1.58)	<.001
Age >75	1.59 (1.33-1.90)	<.001	2.13 (1.86-2.43)	<.001
Gender (ref. Male)				
Female	0.85 (0.76-0.94)	0.002	0.68 (0.64-0.73)	<.001
Race (ref. White)				
African American	1.03 (0.91-1.17)	0.59	0.88 (0.81-0.95)	0.00
Hispanic	0.76 (0.58-1.01)	0.06	0.53 (0.40-0.70)	<.001
Other	0.81 (0.63-1.03)	0.09	0.66 (0.54-0.81)	<.001
Dual eligibility[b]	1.06 (0.95-1.18)	0.31	1.16 (1.07-1.26)	0.002
Cirrhosis type (ref. Compensated cirrhosis)				
Decompensated cirrhosis	1.90 (1.72-2.09)	<.001	.	.
Conditions				
HIV/AIDS	0.73 (0.51-1.04)	0.08	1.06 (0.92-1.22)	0.42
Hepatocellular cancer	2.31 (2.00-2.67)	<.001	3.76 (2.76-5.12)	<.001
Anemia	1.46 (1.32-1.62)	<.001	1.53 (1.42-1.64)	<.001
Lung Disease	1.22 (1.10-1.35)	<.001	1.49 (1.38-1.59)	<.001
Cancer	0.98 (0.85-1.12)	0.74	1.24 (1.13-1.36)	<.001
Cardiac disease	1.06 (0.93-1.21)	0.37	1.21 (1.11-1.32)	<.001
Dementia	1.28 (1.07-1.54)	0.01	1.69 (1.50-1.90)	<.001
Psychiatric conditions	0.93 0.84-1.03()	0.15	1.06 (0.98-1.38)	0.12
Diabetes	0.96 (0.86-1.06)	0.38	1.15 (1.07-1.23)	<.001
Eye disease	0.88 (0.77-1.01)	0.07	0.88 (0.80-0.96)	0.001
Kidney disorders	1.21 (1.08-1.35)	<.001	1.71 (1.58-1.85)	<.001
Drug and alcohol related disorder	1.39 (1.24-1.55)	<.001	1.32 (1.22-1.42)	<.001
Bone disease	0.88 (0.80-0.98)	0.02	0.90 (0.84-0.96)	0.007
ESRD	1.14 (0.92-1.42)	0.24	1.55 (1.36-1.76)	<.001

Abbreviations: AIDS, Acquired immunodeficiency syndrome; CIs, Confidence intervals; DAA, Direct-acting antiviral drug; ESRD, End-stage renal disease; HR, Hazard ratios; HIV, Human immunodeficiency virus

[a] Adjusted for patient characteristics and risk factors summarized in eTable2

[b] Dual eligibility is an indicator of whether a person is eligible for both Medicare and Medicaid

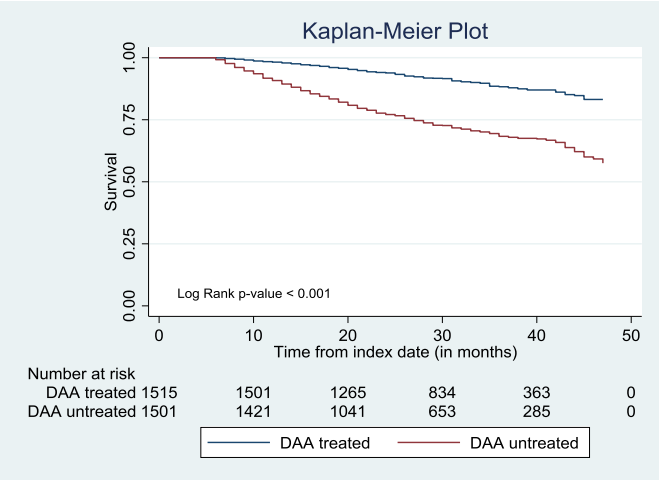
eTable 4. Interaction tests to assess significance of treatment effects across subgroup

	Cirrhosis patients (N=8,240)		Non-cirrhosis patients (N=43,238)	
Variable	**Coefficient**	**P**	**Coefficient**	**P**
Subgroup: Gender				
DAA treatment as time-varying exposure	-0.63	<0.001	-0.60	<0.001
Female	-0.13	0.03	-0.38	<0.001
Interaction - DAA treatment as time-varying exposure and female	-0.13	0.27	-0.03	0.71
Subgroup: Dual-eligibility[a]				
DAA treatment as time-varying exposure	-0.69	<0.001	-0.77	<0.001
Dual-eligible	0.05	0.45	0.08	0.09
Interaction - DAA treatment as time-varying exposure and dual-eligible	0.03	0.80	0.22	0.02

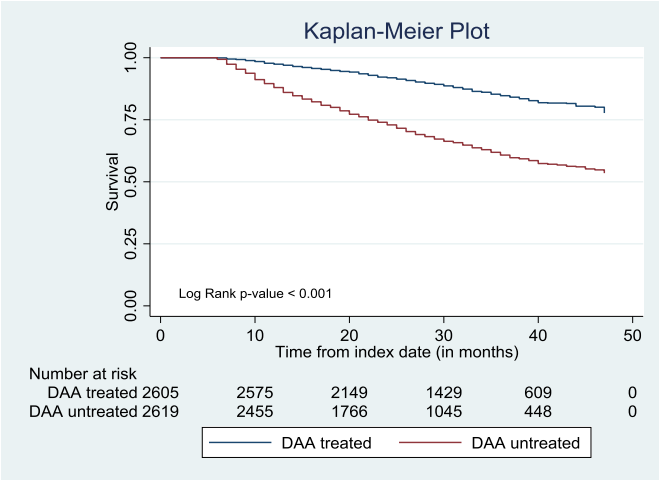
[a] Dual eligibility is an indicator of whether a person is eligible for both Medicare and Medicaid

eFigure 1. Cirrhosis patients – Survival stratified by receipt of Direct-Acting Antiviral (DAA) therapy (by patient sub-group)

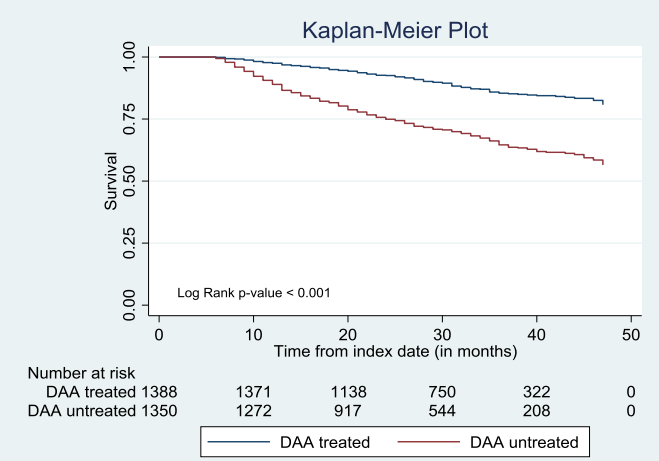
A. Female



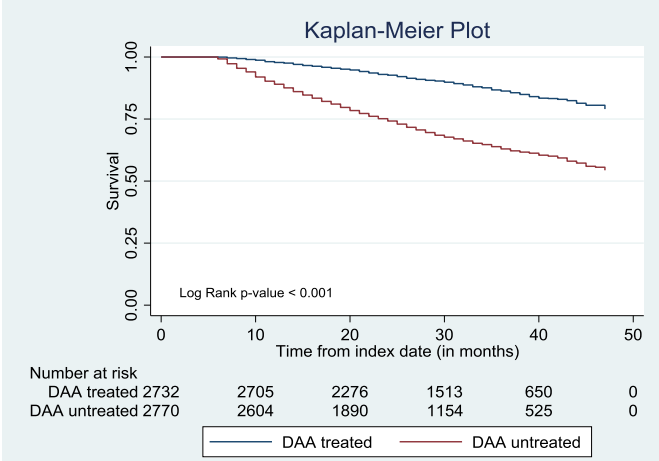
B. Male



C. Non-dual-eligible[a]



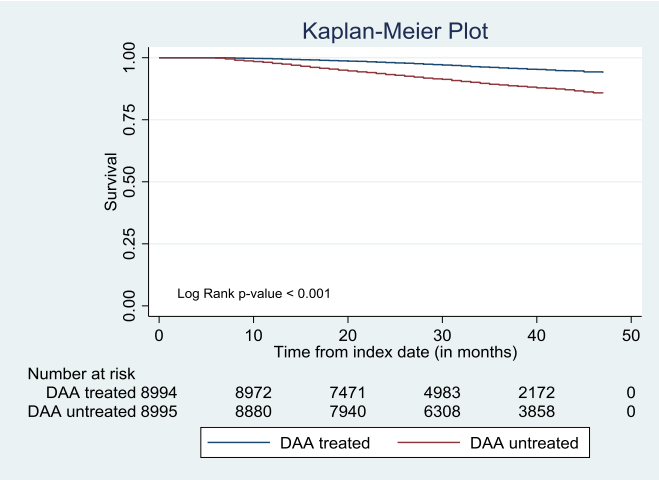
D. Dual eligible[b]



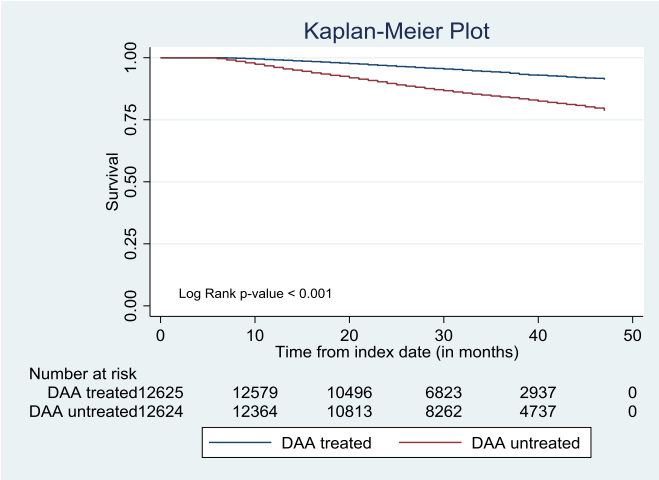
Abbreviations: DAA, Direct-acting antiviral agent
[a] Non dual eligibles are eligible for Medicare only
[b] Dual eligibles are eligible for Medicare and Medicaid

eFigure 2. Non-cirrhosis patients – Survival stratified by receipt of Direct-Acting Antiviral (DAA) therapy (by patient sub-group)

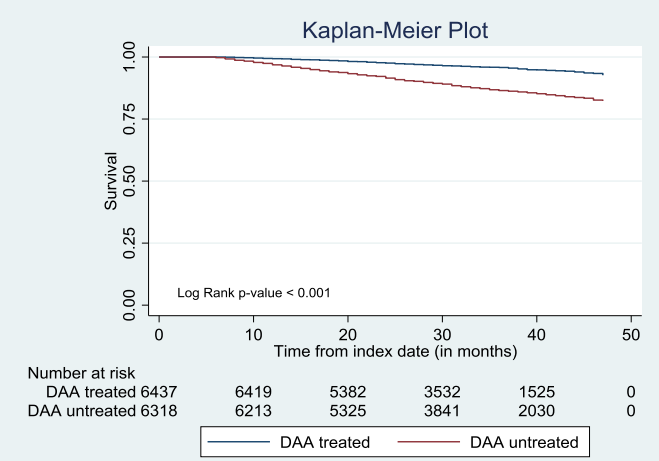
A. Female



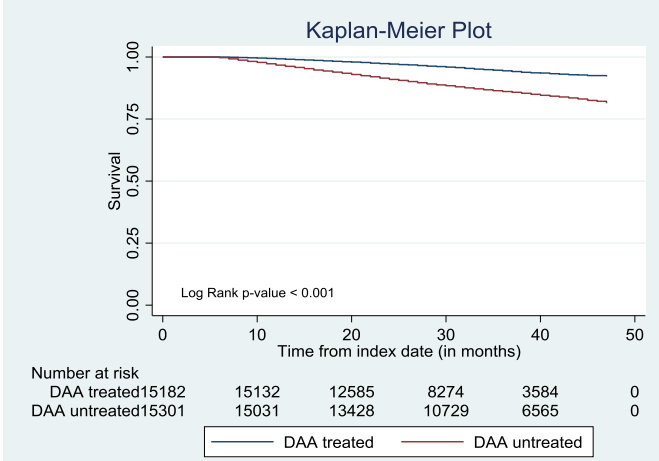
B. Male



C. Non-dual-eligible[a]



D. Dual eligible[b]

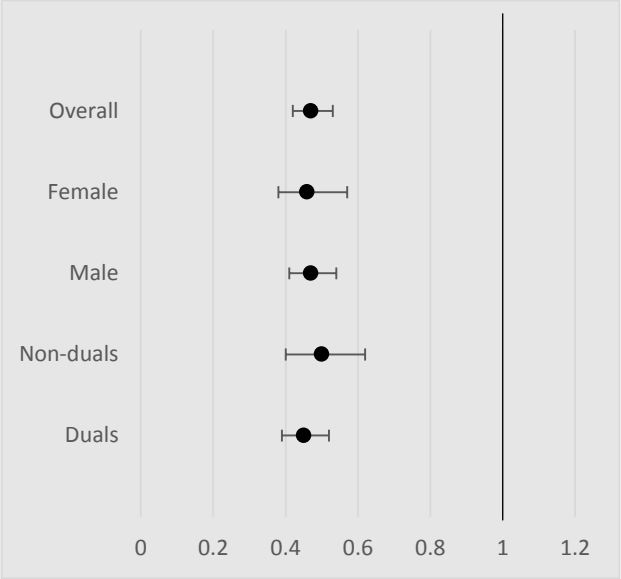


Abbreviations: DAA, Direct-acting antiviral agent
[a] Non dual eligibles are eligible for Medicare only
[b] Dual eligibles are eligible for Medicare and Medicaid

eFigure 3. Adjusted hazard ratios[a] for mortality comparing direct-acting antiviral (DAA) treated and DAA untreated (patients alive for one year)

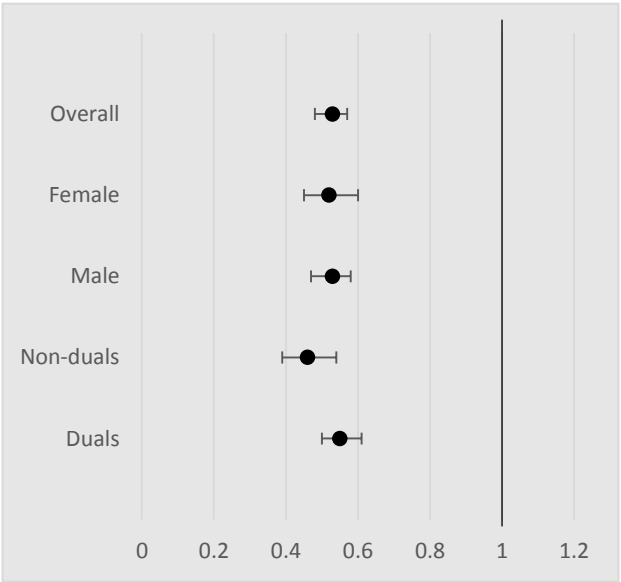
A Among cirrhosis patients

	N	HR (95% CIs)	P value
Overall	8,060	0.47 (0.42-0.53)	<0.001
Female	3,002	0.46 (0.38-0.57)	<0.001
Male	5,058	0.47 (0.41-0.54)	<0.001
Non dual eligibles[b]	2,678	0.50 (0.40-0.62)	<0.001
Dual eligibles[c]	5,382	0.45 (0.39-0.52)	<0.001



B Among non-cirrhosis patients

	N	HR (95% CIs)	P value
Overall	42,956	0.53 (0.48-0.57)	<0.001
Female	17,967	0.52 (0.45-0.60)	<0.001
Male	24,989	0.53 (0.47-0.58)	<0.001
Non dual eligibles[b]	12,668	0.46 (0.39-0.54)	<0.001
Dual eligibles[c]	30,288	0.55 (0.50-0.61)	<0.001



Abbreviations: CIs, Confidence intervals; HR, Hazard ratios
[a] Adjusted for patient characteristics and risk factors summarized in eTable1
[b] Non dual eligibles are eligible for Medicare only
[c] Dual eligibles are eligible for Medicare and Medicaid