

eAppendix Table 1. 2014-2015 Criteria for approval and denial of reimbursement of hepatitis C medications at Harvard Pilgrim Health Care

Inclusion-criteria common to most medications	
Age	
All medications	18 years old
Diagnosis	
All medications	Chronic hepatitis C genotype 1 or 1b, 2, 3, 4, 5 or 6
Required concomitant therapies	
7 out of 8 medications (not including daclatasvir dihydrochloride (Daklinza))	Ribavirin
Liver disease/liver transplant status	
Daclatasvir dihydrochloride (Daklinza), ledipasvir/sofosbuvir (Harvoni), simeprevir sodium (Olysio), sofosbuvir (Sovaldi), ombitasvir/paritaprevir/ritonavir (Technivie), ombitasvir/paritaprevir/ritonavir/dasabuvir sodium (Viekira Pak)	Patient's liver disease been staged using either an invasive or non-invasive testing method (e.g., liver biopsy confirming METAVIR score, Ishak score, transient elastography (Fibroscan) score, FibroTest/FibroSURE score, or radiological imaging) within the past 3 years
6 out of 8 medications Daclatasvir dihydrochloride (Daklinza), ledipasvir/sofosbuvir (Harvoni), sofosbuvir (Sovaldi), and ombitasvir/paritaprevir/ritonavir/dasabuvir sodium (Viekira Pak))	Evidence of stage 2 or greater hepatic fibrosis: <ul style="list-style-type: none"> • Liver biopsy confirming a METAVIR score of F2, F3 or F4 • Ishak Score ≥ 3 • Transient elastography (Fibroscan) score ≥ 7.5 kPa • FibroTest (FibroSURE) score ≥ 0.48 • Radiological imaging demonstrating cirrhosis (e.g., evidence of portal hypertension or ascites)
4 out of 8 medications	
Other requirements	
All medications	Prescribed by a gastroenterologist, infectious disease specialist, or a physician specializing in the treatment of hepatitis (e.g. hepatologist)
Daclatasvir dihydrochloride (Daklinza), ledipasvir/sofosbuvir (Harvoni), sofosbuvir (Sovaldi) (not mention in 2014), ombitasvir/paritaprevir/ritonavir (Technivie), ombitasvir/paritaprevir/ritonavir/dasabuvir sodium (Viekira Pak)	The provider attested that the patient is not currently participating in illicit substance abuse or alcohol abuse, or that the patient is receiving substance or alcohol abuse counseling services as an adjunct to HCV treatment
5 out of 8*	

Ombitasvir/paritaprevir/ritonavir/dasabuvir sodium (Viekira Pak), ombitasvir/paritaprevir/ritonavir (Technivie), Sofosbuvir (Sovaldi)	Prescriber indicated that treatment with Harvoni would be clinically inappropriate, or that the patient was, or will be, unable to tolerate treatment with Harvoni
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3 out of 8 medications

Exclusion-criteria common to most medications

Liver disease/liver transplant status

Daclatasvir dihydrochloride (Daklinza), ledipasvir/sofosbuvir (Harvoni), sofosbuvir (Sovaldi), ombitasvir/paritaprevir/ritonavir (Technivie), and ombitasvir/paritaprevir/ritonavir/dasabuvir sodium (Viekira Pak)	End stage renal disease, or required dialysis
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5 out of 8 medications

Ombitasvir/paritaprevir/ritonavir (Technivie), Ombitasvir/paritaprevir/ritonavir/dasabuvir sodium (Viekira Pak), Daclatasvir (Daklinza)	Recurrent hepatitis C post liver transplant
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3 out of 8 medications

All medications	Decompensated cirrhosis
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Pre-treatment and response

All medications	Currently taking: a strong inducer of CYP3A (e.g., carbamazepine, phenobarbital, phenytoin, rifampin, or St. John's Wort)
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Other criteria for denial

Boceprevir (Victrelis), telaprevir (Incivek), simeprevir sodium (Olysio), ledipasvir/sofosbuvir (Harvoni)	Co-infection with HIV or hepatitis B or a history of previous solid organ transplant
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4 out of 8 medications

* In 2014 PA for Sofosbuvir (Sovaldi) attestation by a medical professional regarding alcohol or substance abuse was not mentioned and then added in during later years

Notes:

All medications refers to: Boceprevir (Victrelis), telaprevir (Incivek), daclatasvir dihydrochloride (Daklinza), ledipasvir/sofosbuvir (Harvoni), simeprevir sodium (Olysio), sofosbuvir (Sovaldi), ombitasvir/paritaprevir/ritonavir (Technivie), ombitasvir/paritaprevir/ritonavir/dasabuvir sodium (Viekira Pak)

eAppendix Table 2. Codes Used to Create Comorbidities

Comorbidities	Codes
Hepatic decomposition	ICD-9-CM: 070.41, 070.44, 070.49, 070.6, 155.0, 456.0, 456.1, 456.2x, 567.0, 567.2x, 567.8x, 567.9, 570, 572.2, 572.3, 572.4, 572.8, 789.5x
Liver cirrhosis	ICD-9-CM: 571.2, 571.5
Liver Transplant	ICD-9-CM: V42.7, 996.82, ICD-9-CM Procedure: 505
HIV	ICD-9-CM: 042, V08
Substance abuse alcohol	ICD-9-CM: 291.xx, 303.x, 305.0, 535.3, 571.0, 571.1, 571.2, 571.3
Substance abuse opioid	ICD-9-CM: 304.0
Substance abuse other drugs	ICD-9-CM: 292.xx, 304.1, 304.2, 304.3, 304.4, 304.5, 304.6, 304.7, 304.8, 304.9, 305.2, 305.3, 305.4, 305.5, 305.6, 305.7, 305.8, 305.9, 648.3
Severe mental illness	ICD-9-CM: 296.4, 296.5, 296.6, 296.7, 296.8x, 294.0, 294.8, 294.9, 295.x, 296.9x, 297.x, 298.x, 299.8, 299.9
Major and other depression	ICD-9-CM: 296.2, 296.3, 300.4, 311
Other mental illness	ICD-9-CM: 294.1, 296.0, 296.1, 300.0x, 300.1x, 300.2x, 300.3, 300.5, 300.6, 300.7, 300.8x, 300.9, 301.x, 302.x, 306.x, 307.x, 308.x, 309.0, 309.1, 309.2x, 309.3, 309.4, 309.8x, 309.9, 312.xx, 313.xx, 314.xx, 316
Chronic pulmonary disease	ICD-9-CM: 416.8, 416.9, 490.x–505.x, 506.4, 508.1, 508.8
Any malignancy, including lymphoma and leukemia, except malignant neoplasm of skin	ICD-9-CM: 140.x–172.x, 174.x–195.8, 200.x–208.x, 238.6
Metastatic solid tumor	ICD-9-CM: 196.x–199.x
Congestive heart failure	ICD-9-CM: 398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4–425.9, 428.x
Myocardial infarction	ICD-9-CM: 410.x, 412.x
Diabetes, uncomplicated	ICD-9-CM: 250.0–250.3
Diabetes, complicated	ICD-9-CM: 250.4–250.9

eAppendix Table 3. Inflation-adjusted average yearly spending per member with chronic hepatitis C virus infection, 2012-2015* (2015 US \$)

	Year 2012	Year 2013	Year 2014	Year 2015
Number of members with chronic hepatitis C, n	2,299	2,447	2,363	2,091
Total months of enrollment among members with chronic hepatitis C, n	25,046	26,087	23,382	18,759
Health plan costs per member with chronic hepatitis C				
Total pharmacy costs	\$7,908.08	\$5,173.66	\$16,217.10	\$24,342.73
Pharmacy costs for HCV medications	\$3,878.63	\$1,482.67	\$12,336.43	\$19,912.88
Pharmacy costs for non-HCV medications	\$4,029.45	\$3,690.99	\$3,880.67	\$4,429.85
Medical costs	\$12,877.68	\$12,127.76	\$12,554.13	\$12,561.32
Total health plan costs (pharmacy, medical)	\$20,785.76	\$17,301.42	\$28,761.23	\$37,904.05
OOP costs per member with chronic hepatitis C				
Total pharmacy OOP	\$568.20	\$547.87	\$548.05	\$575.73
Pharmacy OOP for HCV medications	\$41.48	\$24.64	\$59.11	\$95.98
Pharmacy OOP for non-HCV medications**	\$526.72	\$523.23	\$488.94	\$479.75
Medical OOP	\$655.18	\$663.21	\$661.88	\$669.33

Total OOP (pharmacy, medical)	\$1,223.38	\$1,211.08	\$1,209.93	\$1,245.15
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OOP costs per HCV medication user

Individuals with chronic hepatitis C receiving a HCV medication, n	212	89	267	409
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Pharmacy OOP for HCV medications	\$449.86	\$677.56	\$523.11	\$490.70
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Pharmacy OOP for non-HCV medications	\$588.86	\$614.54	\$552.29	\$548.04
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Medical OOP	\$828.57	\$1018.79	\$833.25	\$782.85
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Total OOP (pharmacy and medical)	\$1867.30	\$2310.89	\$1908.66	\$1821.59
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OOP costs per member not receiving any HCV medication in any of the study years

Individuals not receiving a HCV medication in any of the study years, N	1711	1796	1674	1432
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Pharmacy for OOP non-HCV medications	\$507.32	\$514.40	\$470.90	\$455.70
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Medical OOP	\$651.06	\$658.15	\$636.31	\$656.80
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Total OOP (pharmacy and medical)	\$1158.38	\$1172.55	\$1107.21	\$1112.50
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OOP costs per member not receiving any HCV medication in the respective calendar year

Individuals not receiving a HCV	2087	2358	2096	1682
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medication in the calendar year,*** N				
Pharmacy for OOP non-HCV medications	\$520.40	\$519.78	\$480.87	\$463.14
Medical OOP	\$637.57	\$649.79	\$640.05	\$641.73
Total OOP (pharmacy and medical)	\$1157.97	\$1169.58	\$1120.92	\$1104.87

*Test for trend using time series regression. No significant trend detected unless otherwise noted.

** P value <.05

*** Members may have received HCV medication in other study years

eAppendix Table 4. Inflation-adjusted median (25th and 75th percentile) yearly spending per member with chronic hepatitis C virus infection, 2012-2015 (2015 US \$)

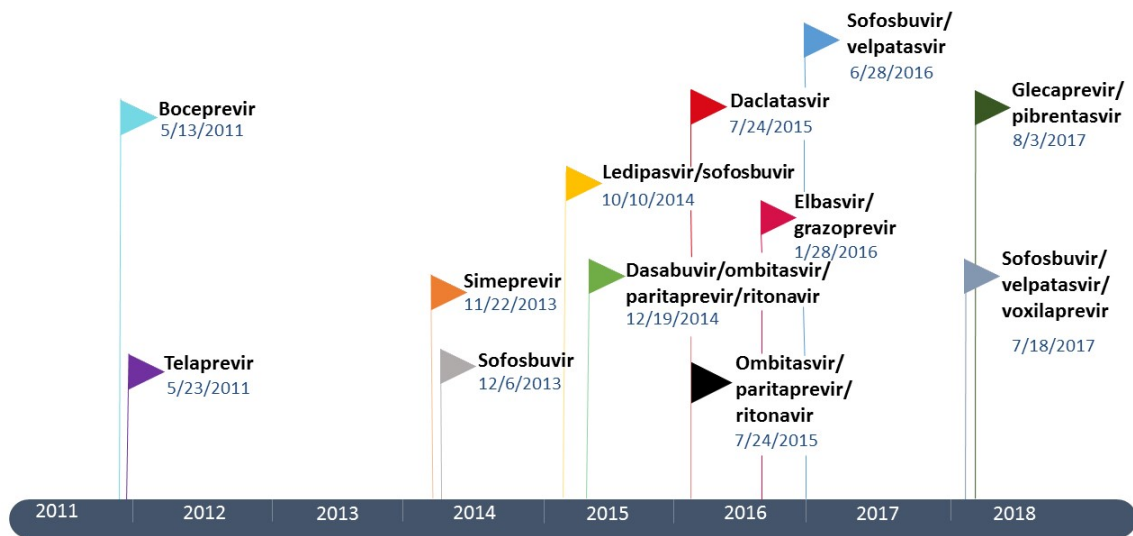
	Year 2012	Year 2013	Year 2014	Year 2015
Number of members with chronic hepatitis C, n	2,299	2,447	2,363	2,091
Total months of enrollment among members with chronic hepatitis C, n	25,046	26,087	23,382	18,759
Health plan costs per member with chronic hepatitis C				
Total pharmacy costs	\$626.72 (\$27.03, \$3,999.67)	\$374.49 (\$13.86, \$2,853.73)	\$527.39 (\$27.66, \$4,746.14)	\$1,067.71 (\$40.27, \$13,135.35)
Pharmacy costs for HCV medications	\$0.00 (\$0.00, \$0.00)	\$0.00 (\$0.00, \$0.00)	\$0.00 (\$0.00, \$0.00)	\$0.00 (\$0.00, \$0.00)
Pharmacy costs for non-HCV medications	\$456.13 (\$21.54, \$2,676.86)	\$332.99 (\$12.19, \$2,426.58)	\$336.43 (\$17.0, \$2,518.64)	\$360.45 (\$18.12, \$2,760.05)
Medical costs	\$3,421.64 (\$1,050.50, \$9,010.23)	\$2,765.38 (\$889.88, \$8,616.72)	\$2,829.19 (\$907.08, \$8,609.88)	\$2,845.45 (\$900.24, \$8,099.82)
Total health plan costs (pharmacy, medical)	\$5,709.59 (\$1,733.92, \$19,552.05)	\$4,660.75 (\$1,425.99, \$15,139.59)	\$5,384.43 (\$1,491.51, 22556.99)	\$7,241.43 (\$1,702.32, \$40,444.59)
OOP costs per member with chronic hepatitis C				
Total pharmacy OOP	\$335.17 (\$91.92, \$756.90)	\$293.67 (\$168.17, \$713.20)	\$302.22 (\$81.96, \$701.77)	\$300 (\$89.67, \$702.07)
Pharmacy OOP for HCV medications	\$0.00 (\$0.00, \$0.00)	\$0.00 (\$0.00, \$0.00)	\$0.00 (\$0.00, \$0.00)	\$0.00 (\$0.00, \$0.00)
Pharmacy OOP for non-HCV medications	\$302.78 (\$81.10, \$702.89)	\$283.18 (\$62.93, \$691.90)	\$270.79 (\$71.71, \$660.79)	\$260.00 (\$70.00, \$640.00)
Medical OOP	\$346.04 (\$94.33, \$821.10)			\$300.00 (\$90.00, \$790.00)

		\$314.65 (\$90.3, \$830.67)	\$307.34 (\$97.33, \$823.05)	
Total OOP (pharmacy, medical)	\$829.78 (\$335.22, \$1,654.48)	\$760.40 (\$304.37, \$1,582.45)	\$763.65 (\$307.34, \$1,628.88)	\$778.14 (\$330.00, \$1,598.7)

OOP costs per HCV medication user

Individuals with chronic hepatitis C receiving a HCV medication, n	212	89	267	409
Pharmacy OOP for HCV medications	\$302.78 (\$151.39, \$454.17)	\$241.23 (\$104.88, \$419.53)	\$225.39 (\$97.33, \$338.08)	\$90.00 (\$60.00, \$180.00)
Pharmacy OOP for non-HCV medications	\$415.24 (\$132.46, \$857.87)	\$418.46 (\$110.13, \$887.30)	\$332.96 (\$102.45, \$778.61)	\$339.00 (\$98.76, \$708.42)

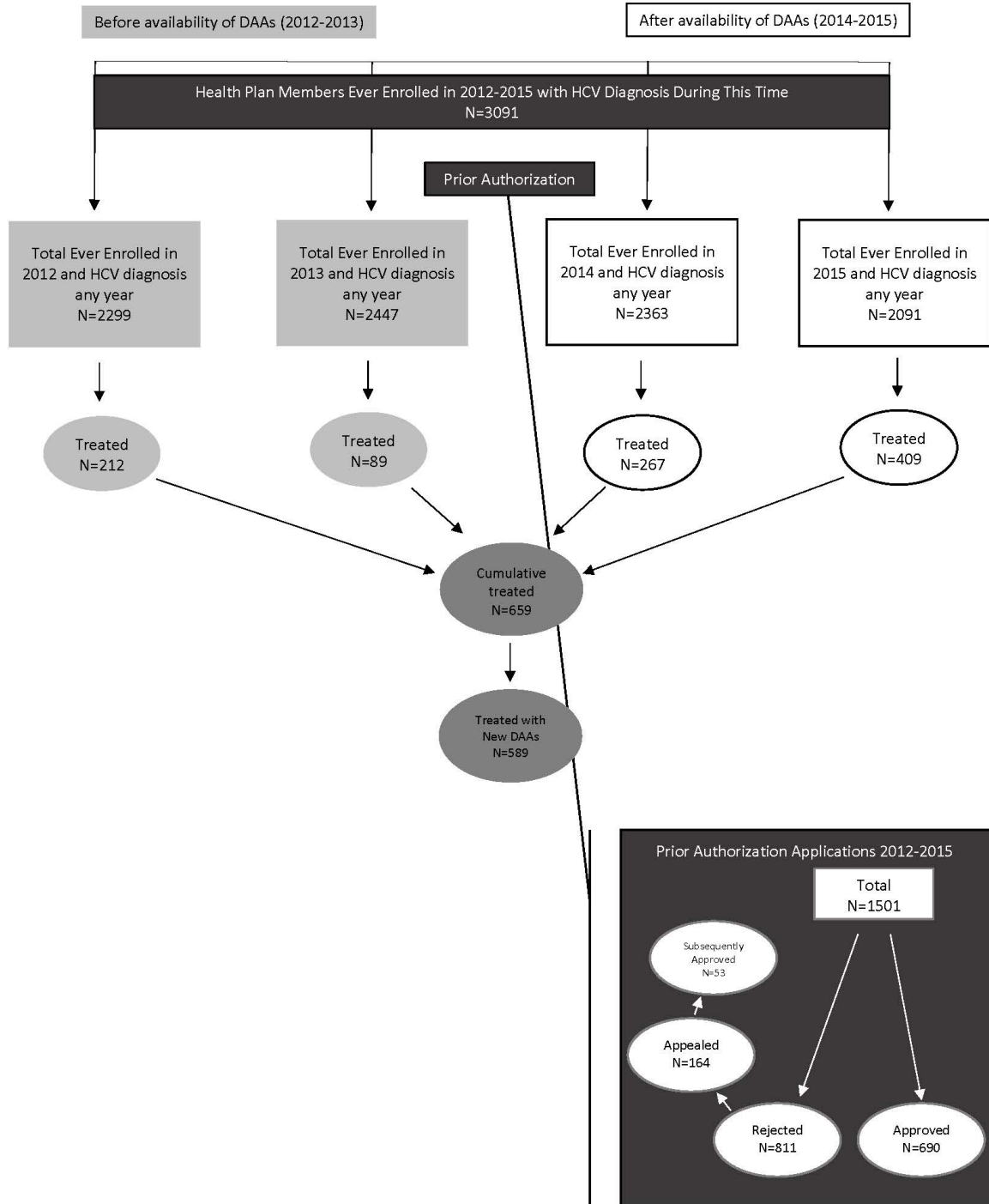
eAppendix Figure 1. FDA approvals of DAAs for hepatitis C



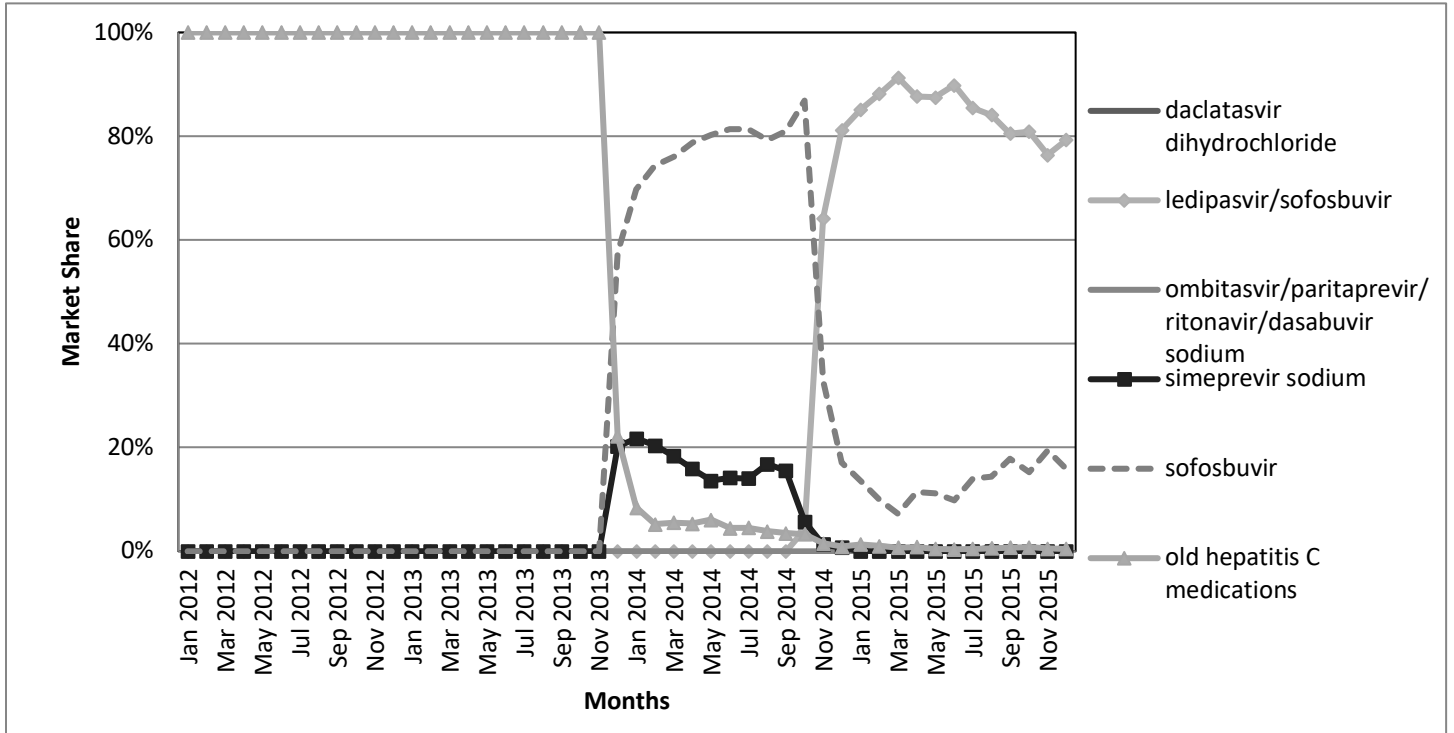
Note: DAAs=direct acting antivirals; FDA=Food and Drug Administration, information from

<https://www.accessdata.fda.gov/scripts/cder/drugsatfda/>

eAppendix Figure 2. Cascading flow chart for the analytical cohort



eAppendix Figure 3. Market share of new DAAs among all hepatitis C medications, based on pharmacy spending



Footnote: Old hepatitis C medications include: boceprevir (Victrelis), telaprevir (Incivek), peginterferon, and ribavirin

eAppendix Figure 4. Market share of individual DAAs based on numbers of patients treated by these medications

