Predicted vs Actual Drug Spending for Interferon-Free Direct-Acting Antiviral Therapies in Hepatitis C: A Case Study on Drug Spending Forecasts

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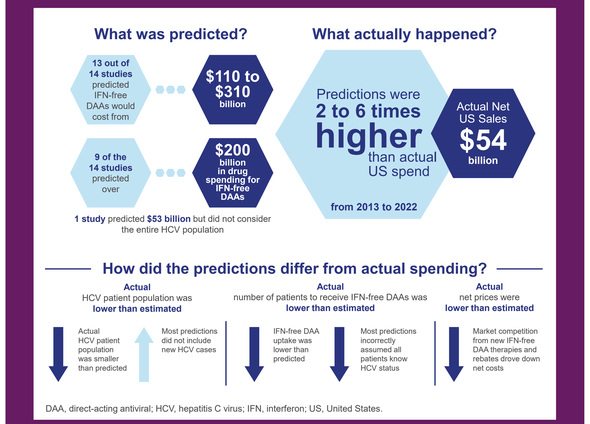
Key Findings

Predicted spending for DAAs in 13 of 14 studies was 2 to 6 times higher than actual spending. Main factors impacting overestimation were inaccurate estimates of the number of patients with a known HCV infection, the number of HCV patients who received treatment, and the net drug price over time



Background

- Forecasts are frequently used to predict drug spending in the United States (US) and inform stakeholder decision-making, focusing on novel therapies across a wide range of indications
- Interferon-free direct-acting antivirals (DAAs) have been used for more than a decade for the treatment of hepatitis C virus (HCV), thus making it an attractive model for assessing the accuracy of early estimates of treatment costs
  - HCV, which affects an estimated 3.2 million individuals in the US, was transformed by the introduction of DAAs that had initial list prices of $84,000 to $189,000 for a 12- to 24-week treatment course[1-4]
- Despite the ability of these novel therapies to address critical unmet needs in the lives of patients, peer-reviewed publications and mainstream journalists/media outlets focused heavily on costs and predicted these treatments would substantially impact the US healthcare system budget, potentially costing hundreds of billions of dollars[5-7]
- Understanding the accuracy of forecasts for interferon-free DAAs in HCV could inform the development of forecasts currently being used to predict drug spending on therapies such as glucagon-like peptide-1 (GLP-1) therapies for weight loss,[8] amyloid-targeted therapies for Alzheimer's disease,[9] and single-administration cell and gene therapies across numerous conditions[10,11]

Objective

- Using interferon-free DAA therapies approved to treat HCV infection as a case study, this study investigated the accuracy of historical drug spending predictions with a focus on attributes that may have contributed to over- or underestimations

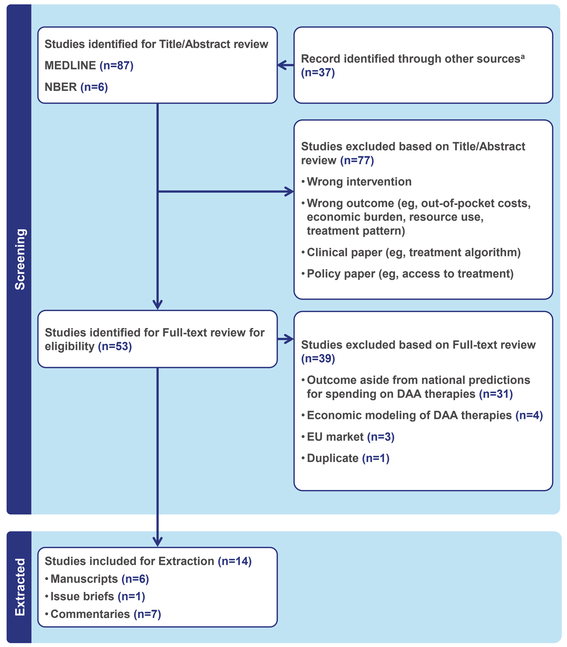
Methods

- In June 2023, a targeted literature review (TLR) was conducted to identify publicly available analytical predictions of national US sales for interferon-free DAA therapies that were approved for treatment of patients infected with HCV from 2013 through 2022
  - Since 2013, approved interferon-free DAA therapies include: sofosbuvir, ledipasvir/sofosbuvir, ombitasvir/paritaprevir/ritonavir with dasabuvir, ombitasvir/paritaprevir/ritonavir, daclatasvir, elbasvir/grazoprevir, sofosbuvir/velpatasvir, ombitasvir/paritaprevir/ritonavir/dasabuvir, sofosbuvir/velpatasvir/voxilaprevir, and glecaprevir/pibrentasvir[4,12-16]
- Actual US net sales over time were derived from corporate financial reports (Forms 10-K) between 2013 and 2022 for comparison with national sales predictions extracted from the TLR
  - Total spending was not adjusted for inflation
- Ten, 1-hour, in-depth interviews were conducted with US payers in October 2023 to validate and further inform analysis findings

Results

- Fourteen analytical predictions for total US spending on interferon-free DAA therapies in HCV were identified in the TLR (**Figure 1**)

Figure 1 *PRISMA diagram for targeted literature review*

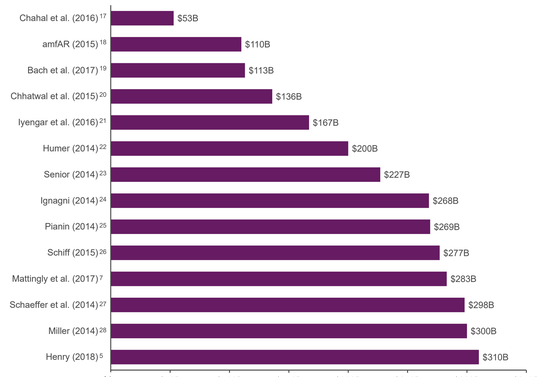


[a]Other sources were identified through review of citations for identified studies or additional hand searching, and included journal articles, conference proceedings, news articles, blog posts, and other reports.
DAA, direct-acting antiviral; EU, European Union; NBER, National Bureau of Economic Research; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

Results (cont.)

- Base case prediction estimates of the total national budget impact ranged from $53 billion to $310 billion (**Figure 2**)
  - Nearly two-thirds (9/14) predicted total US spending of at least $200 billion

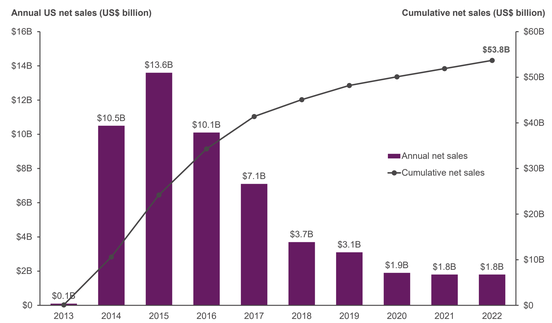
Figure 2 *Predicted US national spending for interferon-free DAA therapies to treat patients infected with HCV*



The graphic displays base case US national spending predictions for interferon-free DAA therapies approved in the US to treat HCV infection. For Iyengar et al. (2016),[21] the base case estimate for treatment with sofosbuvir is visualized. For Schiff (2015),[26] the estimate to treat all HCV-infected individuals is visualized.
B, billion; DAA, direct-acting antiviral; HCV, hepatitis C virus; US, United States.

- Between 2013 and 2022, total actual US net sales (derived from 22 corporate financial reports [Forms 10-K]) summed to $54 billion (**Figure 3**)
  - Sales increased in 2014, coinciding with the approval of ledipasvir/sofosbuvir and ombitasvir/paritaprevir/ritonavir with dasabuvir[12,16]
  - Annual sales peaked in 2015, which is the same year as approvals of ombitasvir/paritaprevir/ritonavir and daclatasvir[13]
- With the exception of the lowest-spending prediction, actual US net sales ranged from 17% to 49% of the other published predictions

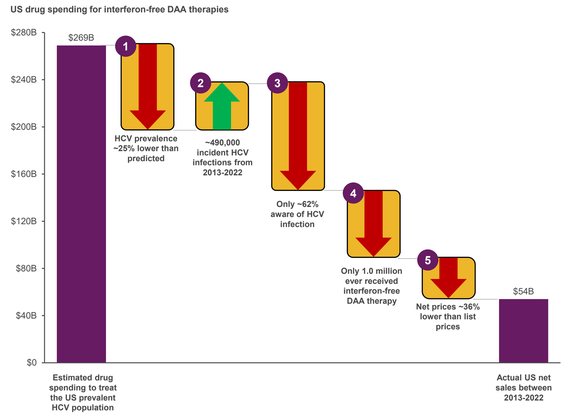
Figure 3 *Actual US net sales for interferon-free DAA therapies approved to treat HCV (2013-2022)*



The graphic displays yearly net sales of interferon-free DAA therapies approved in the US to treat HCV.
B, billion; DAA, direct-acting antiviral; HCV, hepatitis C virus; US, United States.

- During the interviews with 10 US payers, 5 factors related to HCV prevalence, awareness of HCV infection, estimation of treatment uptake, and drug prices were identified that may have resulted in the differences observed between predicted and actual spending (**Figure 4**)

Figure 4 *Differences in predicted vs actual US spending for interferon-free DAA therapies approved to treat HCV*



Explanatory factors for differences in predicted vs actual US spending:	
1	Overestimating HCV prevalence due to reliance, in part, on NHANES 1999-2002 data, which overestimated true prevalence by 0.8 million
2	Most predictions underestimated HCV prevalence by not accounting for new (incident) HCV cases over time
3	Overestimating those aware of their HCV infection, thus inflating the pool of potential patients
4	Despite some predictions estimating a range of treatment uptake scenarios (range, 10% to 100%), the majority of predictions overestimated and assumed a 100% uptake rate
5	Overestimating drug prices over time by using list prices instead of likely net prices, which may be affected by rebates/discounts and not anticipating competitive pricing dynamics

Estimated drug spending to treat the US prevalent HCV population calculated based on the branded list price of sofosbuvir per treatment course ($84,000) and US HCV prevalence estimates from the 1999-2002 NHANES survey (3.2 million individuals). This estimate is consistent with the estimated spending published by Pianin (2014).[25] Directional estimates do not include any payer- or plan-specific information or proprietary data. All estimates are derived from publicly available data and literature based on directional input from discussions with US payers.
B, billion; DAA, direct-acting antiviral; HCV, hepatitis C virus; NHANES, National Health and Nutrition Examination Survey; US, United States.

Conclusions

- Most public predictions overestimated actual US spending for interferon-free DAA therapies in HCV
- While predictions can be useful for estimating the budget impact of therapies on future healthcare spending, this assessment underscores the challenges and necessity of factoring in nuances related to the disease, its treatment, and the affected population when developing healthcare spending forecasts

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