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Health Policy Analysis

Challenges with Forecasting Budget Impact: A Case Study of Six ICER Reports

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ABSTRACT

Background: Payers frequently rely on budget impact model (BIM) results to help determine drug coverage policy and its effect on their bottom line. It is unclear whether BIMs typically overestimate or underestimate real-world budget impact. **Objective:** We examined how different modeling assumptions influenced the results of 6 BIMs from the Institute for Clinical and Economic Review (ICER). **Study Design:** Retrospective analysis of pharmaceutical sales data. **Methods:** From ICER reports issued before 2016, we collected estimates of 3 BIM outputs: aggregate therapy cost (ie, cost to treat the patient population with a particular therapy), therapy uptake, and price. We compared these against real-world estimates that we generated using drug sales data. We considered 2 classes of BIM estimates: those forecasting future uptake of new agents, which assumed "unmanaged uptake," and those describing the contemporaneous market state (ie, estimates of current, managed uptake and budget impact for compounds already on the market). **Results:** Differences between ICER's estimates and our own were largest for forecasted studies. Here, ICER's uptake estimates exceeded real-world estimates by factors ranging from 7.4 (sacubitril/valsartan) to 54 (hepatitis C treatments). The "unmanaged uptake" assumption (removed from ICER's approach in 2017) yields large deviations between BIM estimates and real-world consumption. Nevertheless, in some cases, ICER's BIMs that relied on current market estimates also deviated substantially from real-world sales data. **Conclusions:** This study highlights challenges with forecasting budget impact. In particular, assumptions about uptake and data source selection can greatly influence the accuracy of results.

Keywords: budget impact analysis, economic modeling, healthcare costs, methodology

Introduction

As new healthcare technologies enter the market, private and public payers rely on budget impact models (BIMs) to forecast the likely cost of new technologies. Even if a therapy is deemed cost-effective, short-term affordability can pose challenges. BIMs help to guide coverage decisions and help payers ensure adequate funding to cover expected outlays.[1]

Budget impact modeling is inherently difficult, particularly for new therapies for which future usage or price is likely to be unknown. Although payers rely on BIMs to inform major formulary decisions, the general accuracy of these models is not well understood. Recent scholarship suggests that BIMs may be subject to systematic positive bias (overestimation).[2] To the extent that bias does exist, it may reflect inaccurate forecasting of price, future uptake, or both.

The Institute for Clinical and Economic Review (ICER) has developed several BIMs as part of their effort to evaluate new medical technologies in the United States. ICER is an independent organization that performs health technology assessments with the aim of informing negotiations between insurers and drug manufacturers.[3] Until mid-2017, ICER modeled budget impact assuming "unmanaged uptake," which it defined as "the potential uptake of a new intervention if insurers and provider groups exercise no restraint on utilization." In 2017, ICER revised its BIM methodology by replacing single-point estimates for uptake and cost with a range of potential budget impacts based on different price and uptake scenarios. This range would only include the original "unmanaged uptake" value if the budget impact calculated at that level of uptake and with a price that would yield an ICER of $50 000/QALY was less than or equal to the estimated budget threshold value for that year.[4,5]

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This report examines ICER's predictions developed under the previous framework. We believe that assessing these older reports is informative for larger discussions regarding the challenges of budget impact forecasting, because these reports have been influential,[6] because the data are available to do so (in contrast to newer studies), and because the analysis highlights general and ongoing BIM challenges for ICER and other health technology assessment bodies. In addition, ICER makes its methodology and results readily available; together, these attributes make its past reports useful case studies. In particular, we compare ICER BIM estimates of price, uptake, and aggregate therapy cost with companion values reflecting the analysis of real-world data.

Methods

Study Design Overview

We identified medical technologies reviewed by ICER for which we could measure real-world sales. For each identified ICER study, we recorded ICER's forecast or estimates of the therapy's price, uptake, and aggregate therapy cost. Next, we used market data to calculate the corresponding real-world values.

We then compared ICER estimates to our own real-world values graphically and by calculating mean and median percentage differences. Because of small sample sizes, we did not use formal statistical methods (eg, null-hypothesis significance testing).

We note that conventional BIMs (including ICERs) also include cost offsets in their calculations. Because we lacked cost offset data, we compared the aggregate therapy cost component of budget impact and did not consider offsets.

Inclusion Criteria

This study included new medical technologies if:

- they were pharmacologic in nature (ie, biologic or small-molecule);
- they were the subject of a previously released ICER review;
- the ICER review contained BIM estimates, at the state, regional, or national level, including detail on aggregate treatment cost;
- ICER released its final report for the new technology before December 31, 2015 (to allow sufficient follow-up time for the generation of real-world data).

Six ICER studies met these criteria (Table 1).[7-12]

The included ICER reports fell into 2 categories, which we termed "predictive" and "contemporaneous." Predictive studies forecasted future uptake and budget impact for newly approved drugs. Four of the 6 studies fell into this category. Contemporaneous studies measured current (managed) uptake and budget impact for compounds already on the market. These studies sought to inform policy makers on how changes in disease management models might affect population health outcomes and healthcare system costs; for example, ICER's BIM for school-aged children with ADHD on Medicaid in New England estimated how Medicaid spending would change if this population's treatment shifted away from a baseline mix of ADHD medications toward greater uptake of methylphenidate.

For predictive studies, we compared ICER's estimates of "unmanaged" uptake and aggregate therapy cost with our own estimates of these quantities. Because our estimates were calculated using real-world data, they implicitly reflect "managed" uptake; this distinction represents an important difference between ICER's results and our own.

For contemporaneous studies, we compared ICER's baseline estimates to our own real-world estimates. In these studies, ICER typically considered a shift in the treatment mix for some population of interest. By "baseline" we mean the status quo uptake and budget impact as estimated by ICER at the time of report publication, before a hypothetical shift in treatment mix. In theory, ICER's contemporaneous study baseline estimates should be directly comparable to our own real-world estimates because they did not incorporate the unmanaged uptake assumption. The Supplemental Materials include an expanded description of ICER's methodology (see Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.10.005).

Data Sources

The IQVIA National Sales Perspective (NSP) dataset and National Prescription Audit (NPA) dataset were the primary data sources for this study. The NSP contains national estimates of the total

Table 1 – Included ICER studies

Disease	Drugs	Population	Report year	Report type
ADHD[7]	Methylphenidate, mixed amphetamine salts, atomoxetine	School-aged children covered by Medicaid in New England	2012	Contemporaneous
Type 2 diabetes[8]	NPH insulin, insulin analogs	New England	2014	Contemporaneous
Hepatitis C (genotypes 1–3)[9]	Novel DAAs (sofosbuvir, simeprevir) and companion drugs (ribavirin and pegylated interferon)	California	2014	Predictive
Hepatitis C (genotype 1)[10]	Novel DAAs (sofosbuvir, simeprevir, ledipasvir/sofosbuvir) and companion drugs (ribavirin and pegylated interferon)	California Medi-Cal and Department of Corrections	2015	Predictive
ASCVD[11]	PCSK9is (alirocumab and evolocumab)	United States	2015	Predictive
Heart Failure[12]	Sacubitril/valsartan	United States	2015	Predictive

ADHD indicates attention-deficit hyperactivity disorder; ASCVD, atherosclerotic cardiovascular disease; DAA, direct-acting antiviral; ICER, Institute for Clinical and Economic Review; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor.

therapy units (eg, pills, tables, or milliliters) for individual pharmaceuticals sold in the United States and estimates of the total associated sales (revenues to manufacturers). Data are gathered from warehouse ship-to invoice data and sales revenue reported by manufacturers. The NPA contains national and regional estimates of total prescriptions dispensed in the United States. Both datasets are available on a monthly basis for the past 6 years (at the time of analysis, December 2010 through November 2016). In addition, NPA data document the payer (Medicaid, cash, third party) for the past 36 months and the state in which the prescription was dispensed during the past 24 months.[13]

Outcomes

This study's primary outcome is the real-world estimated annual aggregate treatment cost for drugs included in ICER's BIM analyses. Aggregate treatment cost is the product of the estimated therapy cost for a single patient, and total uptake for the course of 1 year. We constructed these variables for each therapy from the NSP data set by disease space and region or patient population (if applicable). At times, ICER conducted a budget impact analysis for particular patient groups, such as children, or for regions, such as California, or both (eg, children covered by Medicaid in New England).

We constructed real-world estimates to be consistent with the definitions used by ICER. For most reports, ICER did not state the year for which budget impact was modeled. In these cases, we generated estimates for the first calendar year after ICER's report publication.

Calculation of Drug Use, Revenue, and Price

We used NSP data to quantify aggregate therapy cost and prices for the population of interest. Although the NSP stratifies annual population revenues and units sold by therapy and calendar year, it aggregates this information over indications. We therefore had to disaggregate the data in cases when the therapy was indicated for more than one condition and ICER did not include all conditions in its budget impact estimates; for example, ICER estimated use of mixed amphetamine salts for ADHD but not for other diseases for which they are also indicated. We therefore had to net out revenue attributable to non-ADHD conditions to obtain estimates for ADHD alone.

The Appendix (see Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.10.005) describes calculation of indication-specific drug use, revenue, and price. For these calculations, we assumed the following: (1) indication-specific revenue is the product of total drug revenue and indication-specific use, (2) indication-specific use is the product of the FDA-label indicated dose and the number of individuals with the indication, (3) the number of individuals with each indication is proportional to indication-specific prevalence, and the number of individuals with each indication sum to the total number of individuals using the drug, and (4) the total number of individuals using the drug is total drug use divided by the indication-population–weighted average dose. With these estimates, we subtracted the revenue attributable to an indication not included in an ICER report from the revenue for the indication of interest. By calculating indication-specific values for revenue, price, and use, we were able to estimate analogs to indications addressed in ICER reports. In scenario analysis, we re-estimated endpoints under the assumption that all revenue was attributable to indications of interest.

We estimated price by dividing revenue by units sold (for the indication of interest only), and then multiplying by yearly indication-specific dosage. Because we derived price estimates from transactions between manufacturers and wholesalers, drug chains, and mail service pharmacies, they implicitly account for discounts given at these levels in the supply chain. Nevertheless, any direct-to-end-user rebates and discounts not included in the transaction price are not accounted for. We calculated aggregate treatment cost as the product of price and uptake.

Calculation of Regional-Specific and Payer-Specific Endpoints

In some cases, ICER produced regional-specific, payer-specific, and regional payer–specific budget impact estimates. We used the NPA data set to calculate corresponding real-world estimates. For regional estimates, we assumed that the fraction of a drug's revenue earned in a state (or region) was proportional to the fraction of that drug's prescriptions filled in that state (or region). Similarly, for payer-specific estimates, we assumed that the fraction of a drug's revenue covered by a payer was proportional to the fraction of covered prescriptions. For ICER studies that were both regional-specific and payer-specific, we estimated revenues as the product of total revenues, the region's estimated share of prescriptions, and the payer's estimated share of prescriptions; for example, to estimate direct-acting antiviral (DAA) revenue from California Medicaid sales, we multiplied the national revenue estimate by the proportion of DAA prescriptions filled in California and by the proportion of DAA prescriptions filled for Medicaid.

Scenario Analyses

We conducted 4 one-way scenario analyses to assess the robustness of our results. First, we included newer DAAs in the California-wide Hepatitis-C budget impact estimate. This scenario was included to address the significant possibility that some prescription activity for this class of drugs shifted to therapies introduced after ICER published its report; for example, if ledipasvir/sofosbuvir had not been approved the following year, it is likely that sofosbuvir sales would have been higher. This scenario analysis included ledipasvir/sofosbuvir and other DAAs with smaller market share, such as ombitasvir/paritaprevir/ritonavir and dasabuvir. Our scenario analysis included ledipasvir/sofosbuvir and other new DAAs in our *real-world* aggregate treatment cost estimates.

Our second scenario analysis altered the assumed distribution of drug use duration in our analysis of coverage of ledipasvir/sofosbuvir by the state Medicaid program and the Department of Corrections in California. This scenario was included to assess the extent to which differences between ICER's assumptions and our own—specifically regarding the distribution of patients to treatment durations—might affect base case results. Our base case assumed that patients take one of the dosages listed in the "Highlights of Prescribing Information / Dosage and Administration" section of the ledipasvir/sofosbuvir FDA label.[14] The base case assumed that 99% of patients took ledipasvir/sofosbuvir for 12 weeks and that other patients took it for 24 weeks, based on the methods described earlier. Our scenario analysis instead used ICER's estimates for the proportion of patients receiving the therapy for 8, 12, and 24 weeks (59%, 29%, and 12%, respectively).[10]

Our third scenario assumed that all units sold were for the indications analyzed in the ICER reports. This scenario was selected to address a limitation in our design; namely, for drugs indicated for 2 or more conditions, our base case model assumed that usage is proportional to population prevalence. This change was applicable for ADHD and type 2 diabetes drugs only. In contrast, the base case excluded indications not of interest (eg, NPH insulin usage for the treatment of type 1 diabetes or mixed amphetamine salts usage for the treatment of narcolepsy) from price, uptake, and aggregate treatment cost calculations. To address the possibility that the indication-specific number of individuals treated and hence indication-specific drug use were not

proportional to prevalence, which could bias the real-world estimates, we conducted a scenario analysis that assumed that all sales revenues were attributable to indications analyzed in the ICER reports; for example, this scenario assumed that all NPH insulin and insulin analogs were purchased for treating type 2 diabetes. We used the resulting revenue figure to calculate price and uptake.

Our final scenario analysis increased the assumed proportion of national usage and prescriptions covered by California and Medicaid by 50%. This scenario was included because our data are not sufficiently granular to permit calculation of the share of prescriptions that were covered by Medicaid *within* individual states. This scenario analysis addressed the potential study weakness that a higher proportion of hepatitis C prescriptions were covered by Medi-Cal in California than by Medicaid on a national level.

Results

Predictive Studies

ICER's estimated prices for predictive studies exceeded real-world estimates by an average of 15%. Differences ranged from 5% (ledipasvir/sofosbuvir, for hepatitis C) to 31% (glecaprevir/pibrentasvir, also for hepatitis C; Fig. 1, Table 2).

Summarizes ICER price estimates (vertical axis) and real-world price estimates (horizontal) for all predictive studies. Points on the dashed line represent cases for which the ICER's price equals the real-world price. Points above the line indicate that ICER's value exceeds the real-world value, whereas points below the line indicate the opposite.

ICER's estimates of unmanaged uptake exceeded real-world uptake by an average of 25-fold, with values ranging from a factor of 7.4 (sacubitril/valsartan, for heart failure) to 54 (aggregation of direct-acting agents, for hepatitis C) (see Appendix Fig. S1 and Table S2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.10.005).

ICER's aggregate treatment cost estimates exceeded real-world values by an average of 36-fold, with values ranging from a factor of 9 (sacubitril/valsartan) to 85 (DAAs; Fig. 2,[16] Table 2).

Some and perhaps much of the difference between the ICER estimates and our own may reflect different modeling assumptions—specifically whether uptake is assumed to be unmanaged, as in the ICER reports, or implicitly managed, as in our analyses. The remaining differences are attributable to other unmeasured quantities in forecasting: predicting the future is difficult. Nevertheless, these quantities cannot be estimated from available data. Fortunately, as we have noted, the 2 ICER contemporaneous studies do not incorporate the unmanaged uptake assumption and thus afford an opportunity for an "apples-to-apples" comparison.

Contemporaneous Studies

Comparing ICER's contemporaneous report estimates and real-world based estimates avoids the inconsistency introduced by ICER's use of an "unmanaged uptake" assumption and the "managed uptake" assumption implicitly built into our estimates. Because the ICER contemporaneous estimates and our estimates both reflect "managed" uptake, any remaining differences can be attributed to other factors.

For drugs evaluated in ICER's contemporaneous studies, we found that price estimates were on average 24% lower than our own real-world estimates. Differences ranged from −77% (methylphenidate for ADHD) to 55% (atomoxetine, also for ADHD; see Fig. 3[15]).

Uptake estimates for ICER's contemporaneous studies were closer to real-world estimates than they were for predictive studies, but the gap remained large. On average, the ICER estimates of aggregate treatment cost for drugs assessed in

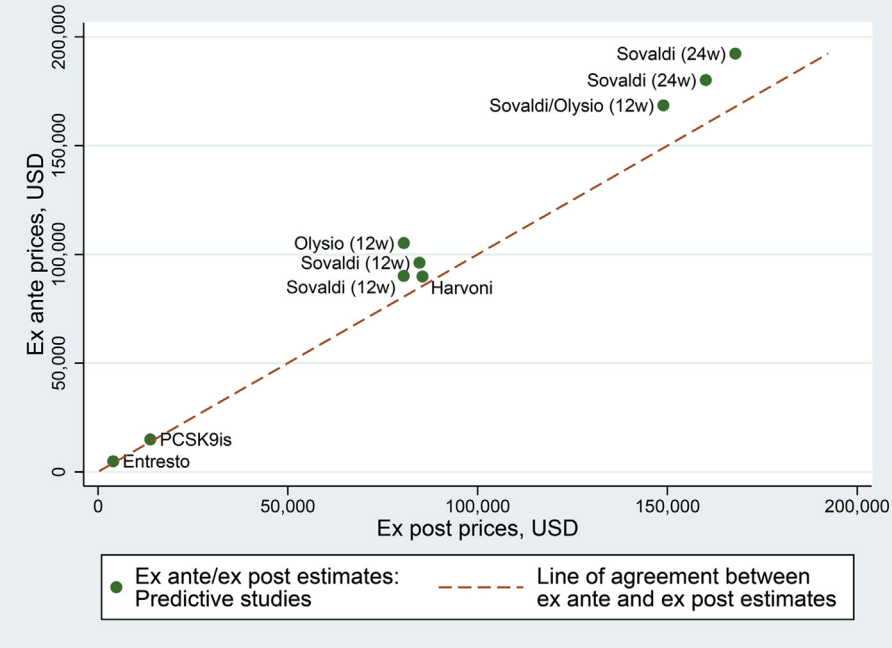

Fig. 1 – Comparison of ICER and real-world price estimates, predictive studies. (1) All prices are in 2016 US dollars, adjusted using medical CPI.[15] (2) "12w" indicates a 12-week course of treatment; "24w" indicates 24 weeks. (3) ICER estimated price for more than one drug in each report; all figures compare the ICER and real-world estimates by drug. The exception is PSCK9 inhibitors, where price was aggregated across class. CPI indicates consumer price index; ICER, Institute for Clinical and Economic Review.

Table 2 – Comparison of real-world and ICER outcomes by study type

Outcome	Study type	Average difference, %	Range of differences, %	Median difference, %
Price	Predictive	15	5 to 31	13
Uptake	Predictive	2500	740 to 5400	1400
Aggregate treatment cost	Predictive	3600	920 to 8500	2100
Price	Contemporaneous	−24	−77 to 55	−29
Uptake	Contemporaneous	760	89 to 2400	280
Aggregate treatment cost	Contemporaneous	860	−12 to 3700	85

Note: (1) All numbers are listed to 2 significant figures. (2) Positive percentages indicate that ICER's estimates were larger than those produced by real-world data. Negative percentages indicate that ICER's estimates were smaller than those produced by real-world data. (3) ICER's predictive studies developed BIM estimates with an "unmanaged uptake" assumption, which is defined as "the potential uptake of a new intervention if insurers and provider groups exercise no restraint on utilization".[18]
ICER indicates Institute for Clinical and Economic Review.

contemporaneous studies exceeded ex-post values by 8.6-fold (Fig. 4, Table 2). The closest pair of estimates was for the use of NPH insulin in New England, for which the ICER uptake was 89% larger than the real-world value. On average, ICER's uptake estimates exceeded our market-based estimates by 7.6-fold (see Appendix Fig. S2 and Table S2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.10.005).

Scenario Analyses

Our results proved to be robust in our 4 scenario analyses. Once ledipasvir/sofosbuvir and other new DAAs were included in our calculations, real-world aggregate treatment cost estimates grew, indicating that there was substantial substitution from older DAAs to newer ones. In the baseline analysis, we found that the ICER uptake and aggregate treatment cost estimates exceeded real-world estimates by 54- and 85-fold, respectively. In this scenario analysis, these differences fell to 5.2-fold and 9.2-fold, respectively.

Results for other scenario analyses also indicated that ICER uptake and aggregate treatment cost estimates substantially exceeded corresponding values based on market data. When we included a potential 8-week treatment duration for ledipasvir/sofosbuvir in our California-wide DoC and Medicaid analysis, our real-world uptake estimates increased, whereas our price estimates decreased, resulting in no net change in aggregate therapy cost. Including indications not analyzed by ICER and increasing the proportion of prescriptions attributable to California and Medicaid likewise had no qualitative impact on our findings. Tables S2 to S4 of the Appendix summarize our findings (see Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.10.005).

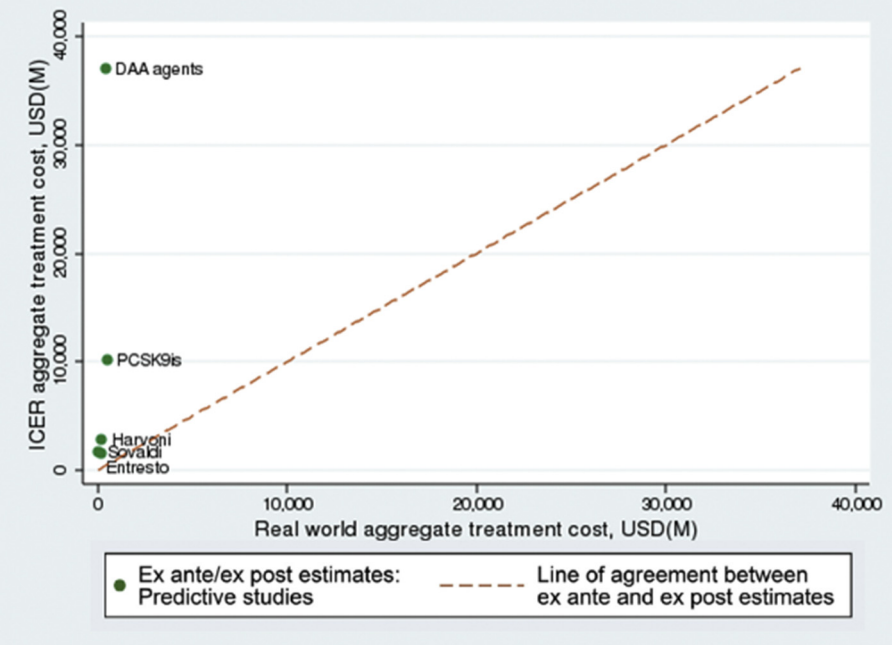

Fig. 2 – Aggregate treatment cost estimates, predictive studies. (1) Harvoni and Sovaldi estimates are for California Medicaid ("Medi-Cal") and the California Department of Corrections (DOC). (2) "DAA agents" estimates are for California. (3) ICER estimated uptake by class, or drug, if there was only a drug studied individually in the ICER report. (4) ICER's predictive studies developed budget impact model estimates with an "unmanaged uptake" assumption, which is defined as "the potential uptake of a new intervention if insurers and provider groups exercise no restraint on utilization".[18] CPI indicates consumer price index; ICER, Institute for Clinical and Economic Review.

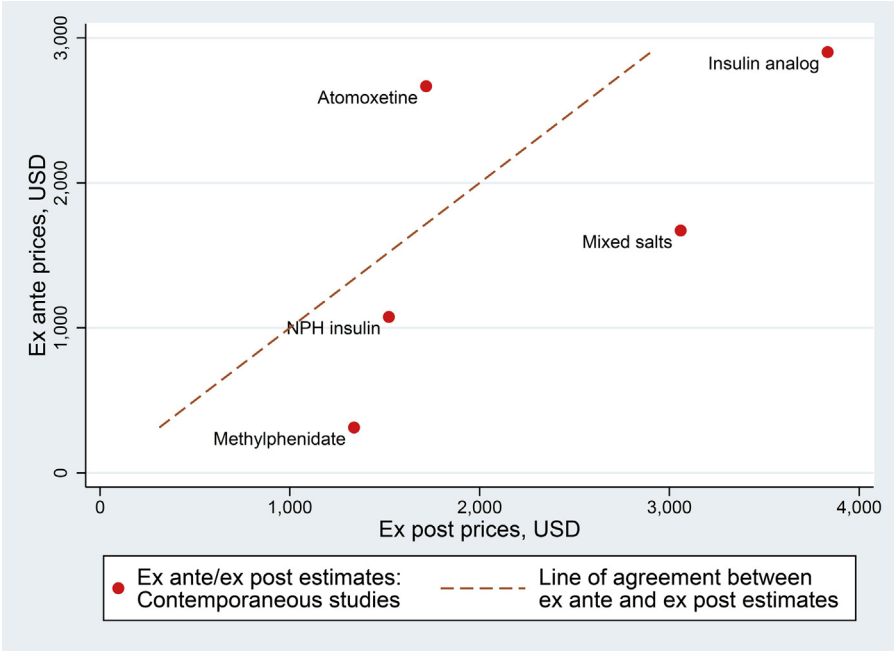

Fig. 3 – Comparison of ICER and real-world price estimates, contemporaneous studies. (1) All prices are in 2016 US dollars, adjusted using medical CPI.[15] (2) ICER estimated price for more than one drug in each report; all figures compare ICER and real-world estimates by drug. The exceptions are PSCK9 inhibitors, insulin analogs, and NPH insulin, where price was aggregated across class. ICER indicates Institute for Clinical and Economic Review.

Discussion

Among predictive studies, we find that ICER's real-world aggregate treatment cost estimates substantially exceed our own ex-post, market-based estimates by 36-fold on average. Most of this difference reflects ICER's overestimation of uptake by an average of 25-fold. ICER price estimates, although exceeding real-world

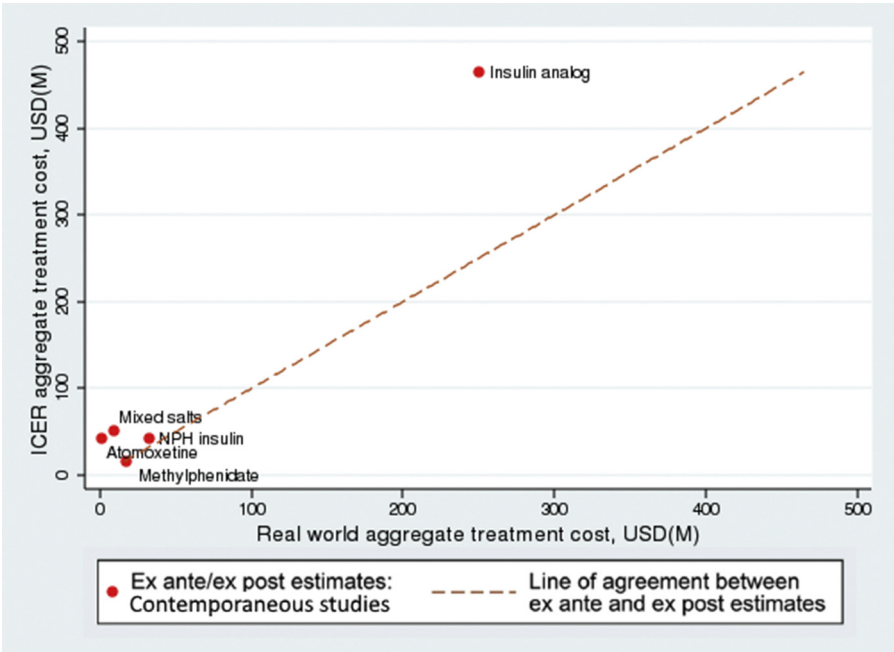

Fig. 4 – Aggregate treatment cost estimates, contemporaneous studies. (1) ADHD uptake (ie, methylphenidate, atomoxetine, mixed amphetamine salts) is estimated for school-aged children covered by Medicaid in New England. (2) Type 2 diabetes estimates (ie, NPH insulin, insulin analog) are for New England. (3) ICER estimated uptake by class, or drug, if there was only a single drug studied in the ICER report. ADHD indicates attention-deficit hyperactivity disorder; ICER, Institute for Clinical and Economic Review.

prices on average, were considerably closer to the values we obtained from market data.

ICER's overestimation of uptake largely reflects the fact that ICER's predictive studies deliberately assumed unmanaged uptake (ie, that payers would not restrict patient uptake) as a way of alerting the marketplace to potentially large increases in future drug spending. These estimates likely provide a signal to payers regarding potential areas of future financial risk. In contrast, our market-based estimates reflect actual, managed uptake as it occurred in the real world. Unfortunately, it is not possible to assess how much of the observed differences in uptake is attributable to this methodological difference versus other factors. Nevertheless, the 2 contemporaneous studies that we analyzed should be informative because they did not rely on the unmanaged uptake assumption and hence should be definitionally consistent with our own.

We do indeed find these estimates to be closer to our own. Nonetheless, they are still much larger, exceeding our estimates by an average of 7.6-fold. ICER's contemporaneous study aggregate treatment cost estimates exceed our corresponding estimates by an average of 8.6-fold. Although much less than the 36-fold difference observed between ICER's predictive study and our market-based aggregate cost estimates, the gap remains large.

The observed differences may in part be due to an "ICER effect," in which the release of ICER's reports depresses real-world drug uptake. Specifically, payers may respond to ICER's publications by implementing formulary policies intended to reduce access to the reviewed drugs. Indeed, several payers have indicated that their coverage decision making takes ICER's reports into account.[17,18] Nevertheless, there is also reason to believe that the magnitude of this effect may be limited. If this factor were the primary explanation for the deviation between the ICER and real-world sales and uptake figures, then we would not expect to see the overestimation of uptake that we documented in ICER's contemporaneous studies. Ultimately, further disentangling the response of payers to ICER's reports from modeling error was beyond the scope of this study; it remains an interesting area for future research.

This study has several other limitations. First, it considers only 6 ICER BIM estimates and thus has limited generalizability to other studies. Second, some of the therapies of interest have more than one indication, and our market data report uptake only at the therapy (as opposed to the therapy and indication) level. To estimate disease-specific usage, we assumed that usage was proportional to disease prevalence in the general US population. This limitation did not apply to drugs with only one indication or in cases where ICER included all indications in the budget impact (making it unnecessary for us to decompose and subtract indications not included by ICER). Nevertheless, attributing all revenue to the indications analyzed by ICER did not substantially alter the base case results (see Appendix Tables S2 to S4 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.10.005).

Third, we assumed that all patients used products in accordance with their FDA labels. In one case (ledipasvir/sofosbuvir, for hepatitis C), ICER assumed a shorter treatment duration than we assumed in our analysis. A scenario analysis using the shorter treatment duration indicated that if patients took the drug as ICER assumed, real-world aggregate treatment costs remained orders of magnitude lower than ICER's estimates. Nor did we consider off-label use, a factor that may be salient in the context of ADHD and type 2 diabetes, but less so for PCSK9 inhibitors, sacubitril/valsartan, or novel DAAs because payers have carefully managed use of those drugs. Therefore, off-label use seems unlikely to account for the gap between ICER's estimates and our own.

Fourth, ICER in some cases modeled budget impacts for specific regions and payers—for example, the California Medicaid population. Nevertheless, the NPA does not provide data at this level of granularity. Therefore, real-world estimates of region and payer-specific uptake and costs depended on our estimating payer and regional revenue shares. To address the possibility that we underestimated these proportions, we conducted a scenario analysis that simultaneously increased the Medicaid and California shares by 50% above their base case values. Results did not qualitatively change.

Fifth, we calculated aggregate treatment cost for the specific drugs mentioned in ICER's reports. Nevertheless, in some cases, new class entrants came to market shortly after report publication. By drawing demand away from the drugs included in ICER's analysis, these new entrants could make it appear that ICER had overstated uptake for the original drugs. This potential problem likely only applied to ICER's first hepatitis C study, as ledipasvir/sofosbuvir, a major DAA, launched shortly after publication. In the technical Appendix (see Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.10.005) we present results of a sensitivity analysis that includes uptake of ledipasvir/sofosbuvir and other new DAAs in the comparative analysis. As we discuss in the Appendix (see Supplemental Materials found at https://doi.org/10.1016/j.jval.2018.10.005), this inclusion significantly increases our estimated uptake but does not alter the qualitative conclusion that ICER's estimate substantially overstates values suggested by real-world market data.

This study is among the first to compare ICER's BIM estimates to estimates based on real-world data. Broder et al. recently conducted an analysis comparing BIM estimates from several sources (including but not limited to ICER) to market data from corporate financial statements.[2] Although that study considered only 2 of the 6 ICER reports included here (sacubitril/valsartan and alirocumab/evolocumab), it reached the same qualitative conclusions regarding the large discrepancy between ICER's BIM estimates and estimates based on real-world data.

This study's comparative analysis provides useful lessons for future budget impact modeling efforts. Budget impact analyses are important because they can potentially affect patient access to treatments and consequently influence health outcomes. They can also influence innovation because they address relatively common conditions. It is important to reiterate that in 2017 ICER changed its budget impact methodology so that they now calculate a budget "alert" based on a range of assumptions regarding a drug's price and level of use.[4]

In recent years, ICER has changed its BIM methodology to acknowledge and address limitations in its prior approach and to add flexibility.[5] First, ICER now uses prices net of discounts. Second, ICER now models a range of uptake scenarios rather than a single estimate. Interestingly, this range does not include a scenario in which uptake is "unmanaged"—a decision possibly motivated by an awareness that report users did not fully appreciate that these values were not intended to be predictions. We do believe that this change will add some measure of clarity to the budget impact estimates because—as ICER has noted—there has been considerable confusion in the research community as to whether these unmanaged uptake scenarios are predictions of the future. Precisely how ICER's readership will interpret these new ranges of estimates remains to be seen.

ICER has also clarified the purpose of its budget impact analysis, explaining that rather than suggesting a budget cap for a particular therapy or category of spending, it instead characterizes when "the amount of added health care costs associated with a new service may be difficult for the health system to absorb over the short term without displacing other needed services or contributing to rapid growth in health care insurance costs that threaten sustainable access to high-value care for all patients".[4] Finally, ICER has also begun to use market data in recent studies to estimate price, a step forward that we believe is integral to producing accurate BIM parameter estimates.[19]

Our study demonstrated that, for each of the 6 BIMs we assessed, uptake estimates were significantly higher than ex-post market-based estimates of use. Differences were largest for predictive BIMs, reflecting an assumption of "unmanaged uptake." More broadly, we hope that this report highlights challenges involved in forecasting budget impact and provides guidance for future researchers engaging in budget impact modeling.

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Julia Thornton Snider holds the position of senior director and owns equity at Precision Health Economics (PHE), a health economics consultancy providing services to the life science industry. Jesse Sussell holds the position of research economist at PHE. Alicia Gonzalez holds the position of associate research scientist at PHE. Mahlet Gizaw Tebeka held the position of research scientist at PHE at the time this research was conducted. Joshua T. Cohen and Peter Neumann are consultants to PHE.

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Supplemental Materials

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2018.10.005.

REFERENCES

1. Mauskopf JA, Sullivan SD, Annemans L, et al. Principles of good practice for budget impact analysis: report of the ISPOR Task Force on good research practices—budget impact analysis. Value Health 2007;10:336–47.
2. Broder MS, Zambrano JM, Lee J, Marken RS. Systematic bias in predictions of new drugs' budget impact: analysis of a sample of recent US drug launches. Curr Med Res Opin 2017;34:765–73.
3. Institute for Clinical and Economic Review. What does ICER do? ICER video. icer-review.org. [Accessed 1 June 2018].
4. Institute for Clinical and Economic Review. Overview of the ICER Value Framework and Proposals for an Update for 2017-2018. 2017. https://icer-review.org/wp-content/uploads/2016/02/ICER-VAF-Update-Proposals-020117.pdf. [Access 13 February 2018].
5. Pearson SD. The ICER value framework: integrating cost effectiveness and affordability in the assessment of health care value. Value Health 2018;21:258–65.
6. Loftus P. Rising U.S. drug prices are focus of research grant, July 21, 2015. https://www.wsj.com/articles/rising-u-s-drug-prices-are-focus-of-research-grant-1437433550. [Accessed 25 May 2018].
7. Institute for Clinical and Economic Review. Attention Deficit Hyperactivity Disorder: Effectiveness of Treatment in At-risk Preschoolers & Long-term Effectiveness in All Ages. Boston: ICER; 2012. https://icer-review.org/wp-content/uploads/2016/01/Final-MASTER-Report-6.26.20123.pdf. [Accessed 13 February 2018].
8. Institute for Clinical and Economic Review. Controversies in the Management of Patients with Type 2 Diabetes. Boston: ICER; 2014. https://icer-review.org/wp-content/uploads/2015/03/CEPAC-T2D-Final-Report-December-22.pdf. [Accessed February 13, 2018].
9. Institute for Clinical and Economic Review. The Comparative Clinical Effectiveness and Value of Simeprevir and Sofosbuvir in the Treatment of Chronic Hepatitis C Infection. Boston: ICER; 2014.
10. Institute for Clinical and Economic Review. The Comparative Clinical Effectiveness and Value of Novel Combination Therapies for the Treatment of Patients with Genotype 1 Chronic Hepatitis C Infection. Boston: ICER; 2015.
11. Institute for Clinical and Economic Review. PCSK9 Inhibitors for Treatment of High Cholesterol: Effectiveness, Value, and Value-Based Price Benchmarks. Boston: ICER; 2015.
12. Institute for Clinical and Economic Review. CardioMEMS™ HF System (St. Jude Medical, Inc.) and Sacubitril/Valsartan (Entresto™, Novartis AG) for Management of Congestive Heart Failure: Effectiveness, Value, and Value-Based Price Benchmarks. Boston: ICER; 2015.
13. IMS. IMS MVP Solutions User Guide.
14. Gilead. Highlights of Prescribing Information—Harvoni. 2017.
15. Bureau of Labor Statistics. Consumer Price Index. Washington, DC: Bureau of Labor Statistics; 2017.
16. Institute for Clinical and Economic Review. Overview of the ICER value assessment framework and update for 2017-2019. Boston: ICER; 2017.
17. Schafer J, Galante D, Shafrin J. Value tools in managed care decision making: current hurdles and future opportunities. J Manag Care Spec Pharm 2017;23:S21–7.
18. Pizzi LT. The Institute for Clinical and Economic Review and its growing influence on the US healthcare. Am Health Drug Benefits 2016;9:9.
19. Institute for Clinical and Economic Review. Poly ADP-Ribose Polymerase (PARP) Inhibitors for Ovarian Cancer: Effectiveness and Value. Boston: ICER; 2017.