Case Study - Sovaldi

The Emergence of Cost-Effective yet Unaffordable Cures for Formerly Intractable Conditions

Key Takeaways:
Sovaldi, an innovative treatment for Hepatitis C, launched in 2013 with a list price of $84,000. Experts rated it as cost-effective in most cases, but its total cost rendered it unaffordable for much of the population.

Price, cost-effectiveness, and affordability often are conflated, but are distinct. Sovaldi's price was not among 2013's 15 most expensive drugs, and it was deemed cost-effective, but the combination of high price and pent-up demand made it the most disruptive drug for both private and government payers launched in the past decade.

The American healthcare system currently uses patchwork systems to expand access and create affordability for needed expensive treatments. Experts wonder whether these systems are sustainable.

To the extent cost-effectiveness is considered a proxy for fair pricing and could become a price management tool, America will be challenged in funding cost-effective yet unaffordable therapies -- pharmaceutical or otherwise -- in the future.

Background - Sovaldi

Growing pressure to control costs have led policy experts to ask: What's a reasonable price for a given therapy? One approach to answering this question is to connect price to effectiveness through a cost-effectiveness ratio. But what if a therapy generates so much demand in a given time frame that even if cost-effective it poses an unaffordable burden on payers? American healthcare is likely to face this challenge increasingly as innovators develop cures for previously untreatable diseases and base their pricing on cost-effectiveness arguments.

Sovaldi (sofosbuvir) was launched in late 2013 by Gilead Sciences as an oral therapy that cured most patients with the hepatitis C virus (HCV), an infection that can lead to severe liver damage. Because it was both more effective and more tolerable than prior therapies, Sovaldi generated

tremendous demand from both newly diagnosed and previously treated patients. However, this demand, coupled with a price tag of $84,000 for a course of therapy, strained payer budgets to an unprecedented degree.

Several sets of researchers determined Sovaldi to be cost-effective for many or most patients. This was little comfort to payers. More helpful was the advent of competition, starting in 2014 with similar therapies and continuing since then with superior ones. Sovaldi's sales peaked at $19.1 billion in 2015 and will fall to less than $4 billion in 2018 due to 1) successful cure of the majority of Americans diagnosed with hepatitis C, 2) price discounts due to increased competition, and 3) preference of providers and payers for newer treatments.

Sovaldi no longer poses a major financial challenge to the healthcare system but represents a harbinger of difficult decisions to come. Expensive therapies are continually being introduced, and some will be powerful cures for widespread conditions. Cost-effectiveness analysis (CEA) is a leading approach to help find a fair price for such therapies, but doesn't guarantee affordability. Cures can present a particular dilemma, since they might be quite cost-effective when considered over time but can't work within annual budgets. How should the healthcare system think about and manage cost-effective, unaffordable medical miracles?

Sovaldi: A High-Priced, Cost-Effective, Unaffordable Cure

Gilead knew that it had a blockbuster on its hands during its planning for Sovaldi's launch. The hepatitis C market was ripe for an effective treatment, since existing approaches didn't fully eliminate the disease in most patients and had significant side effects and drug-drug interactions. These drawbacks caused many patients to stop therapy, regardless of health consequences, increasing the patient pool nearly fourfold once Sovaldi launched.

Sovaldi's price -- $1,000 per pill, or $84,000 for a standard 12-week course of therapy – was eye-popping, but not unique. In fact, it barely made the list of the 20 most expensive drugs for 2013, coming in at #19. At the top of the list that year was Soliris, coming in at $537,000. The

10th most expensive drug that year was Revlimid, at $128,166. However, most of the drugs on the top 20 list that year were targeted at patient populations of fewer than 200,000. Thus their aggregate costs tended to be small, and any given payer would have relatively few patients receiving the drug. Sovaldi had both a high price and a large patient population hungry for an effective and tolerable new treatment – a recipe for an affordability crisis.

> "We priced the product at exactly the same as the existing standard of care, which worked about 50% of the time, and are providing a benefit that, based on real world experience, works about 95% of the time. From our perspective, it was a very good value. What happened was a failure to understand exactly how many people were direly ill and had come into care. That is, there were hundreds of thousands of people who needed this immediately. The surge into the system was very large, and that created a lot of anxiety around the payers and of course created an outcry against us for having mispriced the product."
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> - Gilead Sciences CEO John Milligan, December 2016

Gilead considered prices for Sovaldi ranging from $50,000 (which it thought would be acceptable but would leave money on the table that investors should capture) to $170,000 (which the company thought would be fair but would provoke an unacceptable public outcry – which occurred anyway.) Gilead President John Milligan claimed that "We priced the product at exactly the same as the existing standard of care, which worked about 50% of the time, and are providing a benefit that, based on real world experience, works about 98% of the time. From our perspective, it was a very good value." The company pointed out that $84,000 is a bargain compared with an estimated $270,000 for living with chronic liver disease for 10 years. Yet a given payer may find it easier to spend $27,000 every year than $84,000 in one year – particularly when pent-up demand causes previously diagnosed patients to seek therapy all at once. The company also noted that Sovaldi routinely would prevent the need for a liver transplant, which average $570,000.

Gilead's arguments implied that Sovaldi was a cost-effective therapy. Cost-effectiveness analysis is a widely used approach to determine the value of a therapy. Several countries, such as Great Britain and Australia, require evidence of cost-effectiveness before agreeing to public funding of a drug. One of the most common CEA techniques involves measuring years of life saved due to a treatment, and then adjusting those life-years for quality. (For example, living

while blind or in chronic pain is X% as desirable as living in full health.) Researchers have quantified and validated this approach over decades. While there is no universal threshold for cost-effectiveness, most estimates among wealthier countries are in the range of $50,000 - $150,000 per quality-adjusted life-year (QALY) gained. Presumably, therapies in this cost-effectiveness range represent acceptable value for the healthcare system. For Sovaldi, several independent research teams found it to be cost-effective under this approach.

Cost-effective or not, Sovaldi was a budget-buster. If when Sovaldi was first launched it had been used to treat all 3 million patients in the US with hepatitis C, the total cost would have been about $300 billion. That's about the same amount as was spent that year on all other drugs combined. CMS estimated that total spending on Sovaldi and the two main competing drugs in 2014 was up 11.3 % for private payers, 16.9 % in Medicare, and 24.3 % in Medicaid; hepatitis C drugs were named as a factor in each sector. Spending on these drugs also contributed to the rise in Medicare Part D spending per beneficiary, which rose by just 2 % in 2013, but by more than 8 % in both 2014 and 2015.

Because hepatitis C is concentrated among intravenous drug users and lower-income Americans, the cost burden was particularly acute for state Medicaid programs. In New Mexico in 2015, Sovaldi was restricted to only the sickest HCV patients, allowing only about 1,800 patients to be covered. This still represented a cost of $140 million per year. Because it was restricted for Stage 3 or 4 fibrosis patients, many already had permanently damaged their livers, which means they may still have incurred such future health costs as liver transplants that run about $250,000 per surgery. Treating everyone with hepatitis C in the nation's Medicaid and state prison systems would have cost $55 billion. The double whammy of the higher need for HCV treatment in the Medicaid and prison populations and the greater budget limitations among those payers exacerbated inequities in access to this breakthrough therapy.

Sovaldi must be used in combination with pegylated interferons and/or ribavirin. The drug's price hasn't changed since launch. However, Gilead began offering discounts and rebates as soon as competitors emerged, typically in the range of 40%-50% of list price. Many payers that

complained bitterly at the $84,000 price admitted that Sovaldi was much more reasonably priced at $40,000-$50,000.

Cost-Effectiveness as a Payment Criterion

Sovaldi is prototypical but not unique. More therapies – both pharmaceutical and non-pharmaceutical – are in the pipeline that may be priced to value and yet threaten payer solvency. Some of today's treatments are spectacularly expensive yet still cost-effective. Moreover, many widely accepted therapies are well beyond the cost-effective range. Some academics and policy experts argue that cost-effectiveness analysis should play a specified role in setting drug prices and reimbursing for expensive services. That said, there are many ways that CEA could be incorporated into reimbursement policies, all of them challenging.

Cost (price), cost-effectiveness, and the relationship between the two vary widely. This holds true for both common and rare therapies, and for pharmacological and non-pharmacological treatments and tests. (See box below for examples.)

Though CEA is used in some countries as a basis for negotiating drug prices, it has not gained much traction in the US. The Veterans Administration, which has one of the most restrictive drug formularies of any large payer in the country, announced in 2017 that it would begin using drug assessment reports from the non-profit Institute for Clinical and Economic Research (ICER) in coverage and price negotiations with the pharmaceutical industry. More broadly, however, the Food and Drug Administration doesn't consider price or cost-effectiveness in its drug approval decisions. The Medicare program is not allowed to negotiate drug prices directly, and so has little opportunity to employ CEA for those purposes.

CEA for non-pharmaceutical therapies is rarely used in coverage decisions. Pricing for a given test or procedure varies widely from provider to provider, as do treatment criteria, complicating research and analysis into cost-effectiveness. However, Medicare has used CEA for determining coverage of preventive services. These have included pneumococcal vaccine, HIV

screening, and behavioral counseling for alcohol misuse, all of which were found to be cost-effective prior to coverage being granted.

If a key goal for the healthcare system is to provide value for money spent, CEA provides an excellent framework for decision-making. However, the analysis is resource-intensive to conduct and practically and politically difficult to apply. Given public reluctance to have government or private payers set clear limits on treatment, it could be hard to marshal support for using the abstract, technical rules of CEA to influence coverage and payment.

Where a breakthrough therapy is cost-effective, high-priced, and widely applicable, it will – as Sovaldi did – threaten payer budgets. One obvious strategy is to negotiate the price down – but this approach applies equally to expensive but cost-*ineffective* treatments, and is equally difficult to implement. Some experts have suggested alternative financing models for cost-effective therapies that are unaffordable over the near term. Just as individuals finance houses, cars, and educations over time, expensive treatments with long-term benefits – especially cures – might be financed over several years. Both the payer and patient payments could be financed.

Though CEA has yet to play a major role in drug pricing, some experts believe that this could change when and if a presidential administration gets serious about containing drug costs. The idea is that if the pharmaceutical industry becomes concerned about centrally imposed pricing – or even Medicare negotiations – the industry might be willing to compromise on cost/QALY thresholds (or similar standards) to avoid price controls.

Examples of Cost and Cost-Effectiveness

Cost, cost-effectiveness, and the relationship between the two vary widely. Some expensive therapies are cost-effective, while some inexpensive treatments are not. The Institute for Clinical and Economic Research generally uses the range of $50,000-$150,000 per quality-adjusted life-year (QALY) as a marker of cost-effectiveness.

Chimeric antigen receptor T-cell (CAR-T) therapy for pediatric relapsed/refractory acute lymphoblastic leukemia is priced at $475,000 and has a cost/QALY of $56,300.
A single lung transplant in the US cost an average of $561,200 and had a cost/QALY of $103,500 in 2010.

Non-small cell lung cancer accounts for approximately 85% of all lung cancer in the US. Tyrosine kinase inhibitors cost about $90,000 per year and have cost/QALYs in the range of $111,000 to $147,000 in treating NSCLC. PD-1 immunotherapies cost about $150,000 per year and have cost/QALYs ranging from $219,000 to $416,000 for NSCLC.

Medical tests can be assessed using CEA. Asymptomatic patients at high risk of CAD are screened using one of a variety of cardiac nuclear imaging techniques. In a hypothetical cohort of 60 year-old men with Type 2 diabetes and no symptoms of CAD, all of the techniques studied had cost/QALYs below $40,000. However, single-photon emission computerized tomography (SPECT), which costs between $500 and $1,500, had an incremental cost-effective ratio vs. ECHO of $326,000/QALY. Notably, a different analysis that included both men and women 45-65 years of age quantified the incremental cost/QALY of SPECT vs. ECHO at $75,000. This difference highlights the challenge of using CEA for clinical and reimbursement decisions.

Disease-modifying therapies for multiple sclerosis range in price from $33,500 to $103,500. With the exception of Lemtrada (alemtuzumab), the other 14 agents studied had cost/QALYs ranging from $227,000 to $942,000.

Soliris (eculizumab), a drug treating the rare condition of paroxysmal nocturnal hemoglobinuria (PNH), costs more than $500,000 and has cost/QALY of just under $2,000,000.

Learning from Sovaldi

Cost-effectiveness analysis can clarify the value a therapy of test offers to the healthcare system. However, some high-value interventions, due to their price and the patients they target, may be unaffordable over a short time frame. Sovaldi is a prime example of a novel

therapy that cured an important disease but threatened many payers with financial hardship, even bankruptcy. It's probable, and even desirable, that more innovative treatments are launched that can cure widespread conditions. It's also probable that such treatments will be, like Sovaldi, expensive, cost-effective, and difficult to pay for.

CEA offers a framework for pricing drugs that strikes a balance between sellers charging whatever they can get and government price controls. Though CEA isn't widely used by US payers, this could change as both political and market pressures on drug prices intensify.

Discussion Questions

- Does it matter that Sovaldi was rated as cost-effective, or is this just another story of an overpriced drug?
- What's the likelihood that we'll see more breakthrough therapies that are expensive, cost-effective, and unaffordable over a short time frame? Which diseases might be the most likely targets?
- Should strategies to control drug prices vary by a product's cost-effectiveness, or should total aggregate cost be the primary issue?
- Payers were greatly relieved when competitors to Sovaldi were launched, affording them some negotiating leverage. How can market competition be maximized for innovative therapies? Should the FDA play an active role?
- How can the healthcare system minimize inequities created by the launch of expensive therapies?
- Does CEA present a realistic opportunity to bring rationality to drug prices without regulation? How could that play out?
- If CEA were incorporated into pricing decisions, how should payers deal with products that are cost-effective but still unaffordable?
- Are there opportunities to use novel financing arrangements for expensive therapies whose cost is incurred up front but whose value extends for years?
- Should FDA require CEA as an element of drug approval? Would it be better to have a government or independent private agency conduct these analyses?
- Could (and should) CEA be used in reimbursement for non-pharmaceutical treatments and tests?
- What can we learn from the use of CEA in coverage and reimbursement in other countries?

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