



Borrowing for the Cure

Debt Financing of Breakthrough Treatments

Soeren Mattke and Emily Hoch

Recent market entries of breakthrough pharmaceutical products have reignited the debate about the affordability of high-priced specialty drugs for public and private payers worldwide. Payers had voiced concerns about such drugs before but, faced with a possible outcry of patients and advocates, grudgingly accepted them. In the UK, for example, the National Health Service (NHS) set up the Cancer Drugs Fund in 2010 to ensure access to oncology medicines, such as the leukemia drug ofatumumab (Arzerra®), that would not meet its usual standards for cost-effectiveness. This arrangement was viable because the drugs were prescribed for only a limited number of patients. But as more high-cost drugs reach the market and treat more-prevalent conditions, medical professionals and government ministers have complained that this “blank check” might not be sustainable.¹

The High Cost of Breakthrough Treatments

Today’s lightning rod is Gilead’s hepatitis C drug Sovaldi® (sofosbuvir) with its \$1,000-per-pill (average wholesale) price tag in the United States and a typical 12-week course of treatment costing in excess of \$80,000.² Unlike previous treatments, which had success rates of 40 percent, more than 95 percent of patients on Sovaldi in clinical trials experienced sustained viral response and are essentially cured.³ The prevalence of hepatitis C—the Centers for Disease Control and Prevention (CDC) estimates that 3.2 million people in the United States have chronic hepatitis C infection, with an additional 17,000 new cases annually⁴—implies that treatment for a single disease will have tangible effects on overall drug spending. Express Scripts, a leading pharmacy benefit manager, projects that domestic specialty prescription drug spending will increase by

63 percent by 2017, fueled by the 1,800-percent spending increase on hepatitis C alone.⁵

Sovaldi's 2014 sales projections range from \$8 billion to nearly \$11 billion, on par with past sales of Pfizer's Lipitor® (atorvastatin), the best-selling drug of all time.⁶ In spite of the cost, the effectiveness of the drug means that payers and policymakers do not regard Sovaldi as poor value. European countries universally opted to cover it, albeit at a lower list price than in the United States, such as \$66,000 in Germany⁷ and \$59,000 in the UK per course of treatment.⁸ But they are concerned about the short-term budget impact. Recently, NHS draft guidance stated that the expected spending prohibited giving the drug to all eligible patients, even though it met its cost-effectiveness criteria and could lead to savings in later years.⁹

Similarly difficult decisions are on the horizon. A vaccine for dengue fever is likely to come to market in 2015, having met its end points in two large trials. It can rid emerging economies of a deadly and costly scourge, but vaccinating the 2.5 billion people living in 100 endemic countries¹⁰ at a cost of as much as \$100 per person might be unaffordable for most national health systems. To illustrate, total health spending in Brazil, a middle-income country that is severely affected by dengue, is \$210 billion (as of 2012) annually, and vaccinating its 203 million citizens would cost as much as \$20 billion, half of its ministry of health budget.¹¹

The Policy Dilemma: Short-Term Budget Discipline or Long-Term Investment?

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vaccines aim to cure or prevent, respectively, the targeted disease and are administered only until the intended effect has been achieved. Antibiotics are given for a defined number of days, and vaccines require up to three to four injections. In contrast, for treatment of noncommunicable diseases, such as heart failure or asthma, drugs attempt only to control the disease and its symptoms rather than to cure it, meaning that lifelong treatment is typically required.¹² Thus, for infectious diseases, companies will sell only a limited number of doses per patient and argue that they need to set unit prices high in order to recoup their investments with such a limited number of doses.

More worrisome is the prospect that the Sovaldi effect could extend into the realm of treatment for common chronic conditions. Take congestive heart failure, a disease affecting 5.1 million patients in the United States and 23 million worldwide, with poor prognosis under currently available treatment options.¹³ Recently published trial results for the Novartis drug LCZ696 suggest that it could displace established treatments,¹⁴ and promising gene therapy approaches are in the research pipeline. Given the clinical value of such innovations relative to available therapies, we expect prices to be high. The short-term cost of switching even a subset of patients to those new treatments might eclipse the cost impact of Sovaldi and create a very uncomfortable situation for policymakers

and payers: Make treatment accessible and accept high short-term costs with the expectation of long-term savings, or insist on budget discipline, forgo clinical benefit and long-term savings, and anger affected populations.

Many payers might find it impossible to defend their budgets against pressure from advocacy groups and providers, even in European countries that typically have policies to constrain prices or overall spending on prescription drugs. In middle-income countries, citizens will question why their governments are unwilling to invest in innovations, such as dengue vaccines, with clear long-term benefits for population health and economic growth. And pressure will mount on multilateral agencies, such as Gavi, a global vaccine alliance, to support expanded vaccine and treatment programs for low-income countries.

This policy dilemma calls for creative approaches to financing access to breakthrough pharmaceuticals. In other industries, suppliers commonly adapt their commercial models to make investment goods affordable, such as through equipment leases or supplier-financed credit. Publicly financed health care could learn from creative financing approaches in the private sector and adapt them to make purchases of high-impact, high-cost drugs more affordable in the short run.

Borrowing to Invest in Breakthrough Treatments

We propose a debt-financing model for breakthrough medical innovations as a means to overcome such short-term budget and cash-flow constraints and enable investments with long-term benefits. Instead of paying for those products outright, an institution, such as the NHS or a *Krankenkasse* (sickness fund) in Germany, would issue a debt instrument to the manufacturer to cover the

acquisition cost. Those instruments could be structured in various ways: as a bond, in which the manufacturer would receive only interest payments until the maturity date and then a balloon payment for the principal; as a mortgage with fixed monthly payments and a self-liquidating schedule; or as a credit line with payments at agreed-upon milestones. Interest rates on those instruments would reflect the respective institution's credit rating. Ideally, the structure of the instrument would reflect the trajectory over which the value of the treatment materializes. Box 1 illustrates the concept with a hypothetical example.

Linking Repayment to Real-World Value Generation

Importantly, the debt arrangements should have covenants that link repayment to real-world treatment effectiveness. Pricing agreements between pharmaceutical companies and payers are commonly based on health economics models that estimate the impact of the drug or vaccine on health outcomes and cost at the population level. Those estimates are compared to an absolute standard, such as marginal cost per quality-adjusted life-year saved, or a relative standard, such as incremental cost and benefit relative to current standard of care.

The assumptions for impact on outcomes are usually based on the *efficacy* of the drug or vaccine in clinical trials because those trials provide detailed and validated data. There is, however, the

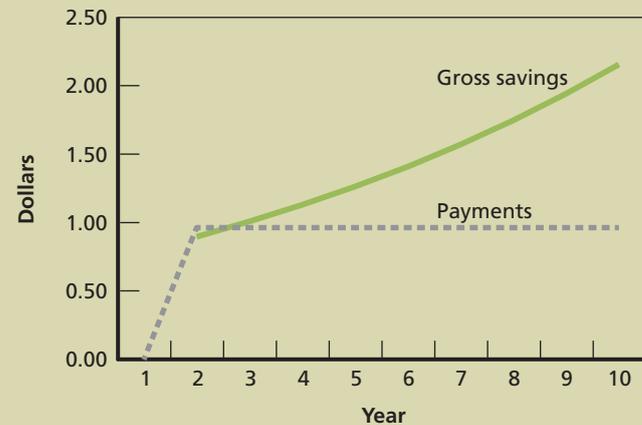
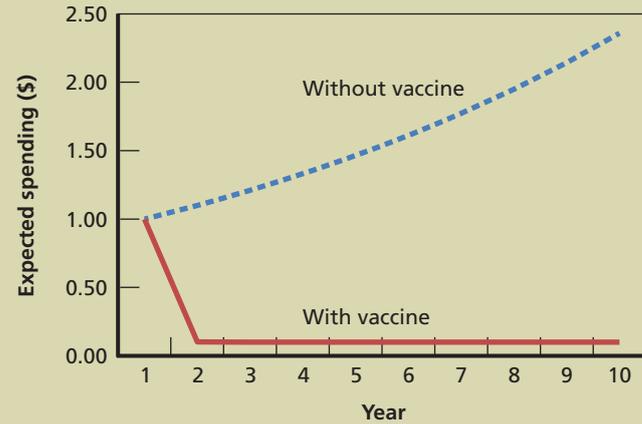
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Box 1: Financing a Vaccination Program

Here is a hypothetical example: An emerging-market country contracts with a manufacturer to supply a vaccine for its population over ten years. Assume that the country's birth rate is about 2 percent per year and that the vaccine is given in year 1 and will be 90 percent effective as of year 2, implying that the entire population needs to be vaccinated in year 1 and only the newborns in the subsequent years. The country's health care cost inflation rate is 8 percent, and its market interest rate for a ten-year bond is 12 percent.

Let us assume that the country currently spends about \$1 billion per year on care for the disease against which the vaccine protects and that the cost of vaccinating the entire population in year 1 is \$5 billion. In nominal terms, the vaccination campaign would lead to more than \$8 billion in net savings to the country based on health care cost alone (top figure), but it might not be able to afford the \$5 billion up-front investment.

A debt-financed arrangement could be structured as follows: The manufacturer provides the vaccine in year 1 in exchange for a promissory note of nine payments of \$760 million each, starting in year 2. This schedule would pay off the principal with a 12-percent interest rate. In addition, the country pays the \$100 million required to vaccinate all newborns directly as of year 2. As illustrated in the bottom figure, the country would be able to realize gross savings as of year 3 and reduce cumulative net spending by about \$4.5 billion.



risk that real-world *effectiveness* of the product is lower. Patients in clinical trials are carefully selected; they receive treatment at leading institutions; and their adherence to the care plan is tightly monitored. Under real-world conditions, patients might have more comorbidities that interfere with treatment and lower adherence. For example, CVS Health researchers recently reported that about 8 percent of patients did not complete the recommended 12-week

course of Sovaldi, endangering the drug's effectiveness.¹⁵ Thus, the actual impact on cost and outcomes might be less than expected. A neutral arbiter, such as the UK's National Institute for Health and Care Excellence (NICE), would determine the actual effectiveness of the drug or vaccine; if effectiveness fell short of the agreed-upon target, the repayment rates would decline.

Such performance-linked payment would reward manufacturers for improving real-world effectiveness of their products. For example, they could design and implement robust patient-education programs; they could monitor treatment adherence and maintain registries to ensure that patients return for all required doses of a vaccine. As we argued in an earlier report, value-based payment models would allow companies to monetize the value that such investments create.¹⁶

Precedents for performance-linked payment already exist. Johnson and Johnson negotiated an agreement with the Scottish Medicines Consortium for its hepatitis C drug Olysio® (simeprevir), under which it would rebate the cost for patients who did not respond to treatment, dubbed “pay for clear.”¹⁷ Similarly, the Velcade® (bortezomib) Response Scheme states that the NHS of England and Wales will receive a rebate if a patient’s tumor does not shrink after treatment. Italy has introduced comparable outcome-based payments for several oncology drugs.¹⁸

Schemes that are based on the response of *individual* patients are challenging for health care agencies. They have to pay the full cost of the drug in advance and have to provide positive and conclusive proof of nonresponse to obtain a rebate. In other words, they need to track each patient and make sure that all required tests are conducted at prespecified intervals, document cases of treatment failure, and submit the information for review by the manufacturer, a substantial administrative burden. Even if a patient did not respond, he or she might have moved to another jurisdiction or not reported to follow up, making it hard for the agency to obtain the required data. Although formal evaluations of such schemes have not, to our knowledge, been published, we were told anecdotally that several European payers were giving up on rebate schemes.

Clearly, operating such individual-level schemes for treatments that are used in large numbers of patients seems impossible.

As an alternative, we propose to ascertain effectiveness based on a population-level sample. The neutral arbiter would obtain a stratified random sample representative for the treated population and estimate impact based on it. Proper weighting and statistical techniques would allow generating valid estimates, even if some patients were lost to follow-up. The details of the estimation procedure and the potential penalties would be documented in the covenants of the debt arrangements so that both sides would have a clear and shared understanding of the implications. Box 2 describes a hypothetical example.

Summary

Debt-financing schemes for breakthrough pharmaceutical products might offer a win-win-win for patients, payers, and manufacturers. Patients would obtain access to medicines; payers could ensure such access while remaining fiscally prudent. For pharmaceutical companies, entering into such a scheme would clearly be a better business and public relations strategy than fighting discounts and coverage denials. Such schemes could even bridge budget silos between different government agencies and funding pools: If a drug’s value were mainly to reduce long-term disability, the agency in charge of financing disability payments, rather than a health agency, could incur part of the debt. Similarly, if a drug’s value were in allowing someone to avoid hospital care, part of the payback might come from the hospital’s budget.

Importantly, the envisioned scheme assumes that the same payer is responsible for a patient at least for the time frame in which the debt is repaid or that a transfer scheme is in place, under which

Box 2: Financing Value-Based Cholesterol Treatment

The European Medicines Agency approved a highly effective drug to reduce low-density lipoprotein (LDL) cholesterol in patients for whom established treatments had failed. In subsequent discussions with the ministry of health of a southern European country, the manufacturer's market-access experts presented convincing data that the drug could reduce overall cost of care in spite of its high price. Ministry officials, however, were concerned that most of the savings would materialize in about five years because the drug would lower the risk of heart attacks and stroke in the treated patients, whereas treatment cost would be incurred immediately. Given austerity measures, the ministry could cover the drug for only a small segment of the eligible patients each year.

To ensure broader access and maximize clinical benefit, the ministry and the manufacturer agreed on the following arrangement: The government issued a bond with five-year maturity and market-level interest rates to the manufacturer to finance the acquisition cost of the drug. An independent research institute developed a statistical model to predict the risk of stroke and heart attack in treated patients relative to that under the current standard of care. The parties agreed that the bond would have to be paid in full if the treatment effect were 90 to 110 percent of the projected effect based on a 5,000-patient sample. A two-sided gain-sharing scheme provided for additional incentive payments, if the estimated effect were higher, or penalties, if lower.

the responsibility to repay the debt follows the patient to a different payer.

Without a doubt, implementing such sophisticated finance models is not an easy task. Structuring the debt correctly requires robust capabilities in cost-of-illness modeling and understanding of financial products; designing a gain-sharing

component requires deep expertise in outcome research, sampling designs, and statistical analysis. But an effort to craft demonstration programs to test their feasibility could spur new financing instruments that resolve the tension between cost and innovation posed by recently introduced breakthrough pharmaceutical products.

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