Center for American Progress

Comparing the Effectiveness of Prescription Drugs: The German Experience

By Daniel Bahr and Thomas Huelskoetter May 21, 2014

As federal minister of health in Germany, Daniel Bahr oversaw the implementation of wide-reaching reforms to Germany's prescription drug market. In this paper, he offers his unique perspective to explain these reforms and how the United States can learn from Germany's example.

Rising prescription drug prices have posed a challenge to health care systems all over the world. This is particularly true in the United States, which has the highest prescription drug prices among major countries, paying more than twice as much as countries such as Australia and the United Kingdom.[1] Although drugs continue to increase in price, we often know little about whether improvements in the effectiveness of these drugs are keeping pace. Many other countries evaluate drugs by funding comparative effectiveness research, or CER, which evaluates the clinical effectiveness of two or more medical treatments, drugs, or medical devices. Alternatively, some countries focus on cost-effectiveness and prefer cost-benefit analyses, which contrast the price of a drug against the added benefit to patients. While the consideration of cost is controversial in many countries, including the United States, CER considers only the differences in clinical benefit for patients between two or more treatments.[2]

Since the United States has traditionally underinvested in CER and consequently suffers from a lack of meaningful comparative information on medical treatments, the Affordable Care Act created the Patient-Centered Outcomes Research Institute, or PCORI, to publicly fund CER in the United States.[3] As PCORI decides how to allocate its substantial research funding, it should look abroad to see how other countries have successfully funded and utilized high-priority CER.

Germany reformed its prescription drug market in 2010 to incorporate a structured CER process to evaluate the effectiveness of new drugs, in order to reduce spending, improve competition and efficiency, and stay patient- and innovation-friendly. Germany's reform effort provides a useful example for the United States. The German model of universal health care is not a state-driven, single-payer system, but instead insures most people through nonprofit health insurance funds, often referred to as

"sickness funds."[4] Similar to the United States, Germany has traditionally had higher drug prices than the rest of Europe, but prioritizes patient choice and market availability for new drugs that receive safety approval.[5] Given these similarities, Germany's new model for CER offers a potential path forward for PCORI.

German policymakers felt a pressing need for action since spending on prescription drugs by the government and health insurance funds rose 6.03 percent per insured person in 2009.[6] This increase, amounting to about 1.6 billion euros—or $2.2 billion—followed previous years of high spending and contributed to total spending on pharmaceuticals of 30 billion euros—$41 billion—in 2009.[7] For new prescription drugs, the rise in spending was particularly high. Up until the 2010 reforms, manufacturers could set any price for their new drugs, with the knowledge that the health insurance funds would immediately have to reimburse them at this price. However, corresponding increases in effectiveness did not always accompany these price increases. By putting in place an organized CER process for assessing the added patient benefit of new drugs, Germany's reform has already resulted in financial savings without adversely affecting German access to new innovations.

The aims of the Pharmaceutical Market Restructuring Act

German policymakers wanted to maintain open market access for new drugs and ensure access to the best and most-effective medicine for patients in the event of illness. Similarly, they wanted to ensure that their reforms would not discourage innovation but rather create a reliable framework for the continued innovation of new prescription drugs. However, they also wished to ensure that higher drug prices were tied to improved effectiveness.

In short, German policymakers sought the right balance between preserving access to real innovations and reducing spending. As a result, the 2010 reform—the Pharmaceutical Market Restructuring Act, abbreviated in German as AMNOG—consists of a mixture of measures: short-term cost savings, reduction of overregulation, and long-term structural changes. Together, these elements enhance competitiveness within the German health system. The centerpiece of the law was the establishment of an organized process to assess the added benefit of new drugs through the use of CER.

Benefit assessment

In AMNOG's new system, manufacturers continue to set the initial price for new prescription drugs after approval by the European Medicines Agency or the German Federal Institute for Drugs and Medical Devices, the European and German regulatory bodies responsible for prescription drug safety—a role performed by the Food and

Drug Administration, or FDA, in the United States. Since the reform went into effect in 2011, however, this initial manufacturer price is only valid for the first 12 months after the drug's launch. As soon as the drug enters the market, a new process of benefit assessment begins. Manufacturers must submit a dossier that uses clinical CER studies to demonstrate proof of added benefit to the patient, compared to the previously existing standard treatment.[8] The dossier must also indicate and prove which group of patients the added benefit will affect.

The Federal Joint Committee—a nongovernmental body that includes insurer, provider, and patient representatives—is responsible for overseeing the benefit assessment. To facilitate the dossier submission process, the Federal Joint Committee has established standards for appropriate comparators and endpoints and also offers to consult with manufacturers on proper methods of preparation and submission.

For the actual technical evaluation of the dossier's research, the Federal Joint Committee commissions a report from another nongovernmental body, the Institute for Quality and Efficiency in Health Care, or IQWiG, which evaluates the rigor and scientific validity of the dossier's CER. IQWiG then determines whether the manufacturer has sufficiently proven that the new drug adds a patient-relevant benefit such as an improvement of health status, shortening of disease duration, extension of life expectancy, reduction of side effects, or improvement in quality of life. If the drug provides added benefit, then IQWiG categorizes this benefit into one of three levels: major, considerable, or minor added benefit.[9] As a rule, IQWiG's assessment of the dossier should be completed within three months of a drug's launch.

After reviewing IQWiG's findings, the Federal Joint Committee will then issue its decision on whether the drug provides added benefit within the subsequent three months or six months after the drug's introduction.

In addition to the structured process for new drugs, AMNOG also allows for discretionary research to evaluate existing medications and medical devices. Before AMNOG, the Federal Joint Committee had the voluntary authority to commission IQWiG to conduct its own CER studies on drugs. However, this was an ad hoc, discretionary power that was used on a much smaller scale—there was no structured process to assess the benefits of all new drugs. Under AMNOG, the Federal Joint Committee and IQWiG maintain this discretionary power for prescription drugs that went on the market before the reform went into effect and thus were not assessed for benefit. In addition, the Federal Joint Committee or drug manufacturers can request a follow-up study on a drug that was previously assessed. These additional benefit assessments, conducted by IQWiG, can then inform future reimbursement negotiations. While AMNOG did not include medical devices in the organized CER process, the law did empower the Federal Joint Committee to commission specific medical device studies from IQWiG on its own initiative.

Price negotiation and reference pricing

If the Federal Joint Committee finds that the drug provides no added benefit, then health insurance funds will reimburse for the new drug according to reference pricing—paying only up to the price of the current standard treatment for the relevant disease or condition. A patient still has the choice to buy the drug, but if the manufacturer does not reduce the price, then the patient would have to pay the difference out of pocket. With this system, manufacturers can no longer charge health insurance funds more expensive rates for new drugs that offer no real improvement upon existing medicine.

If the Federal Joint Committee does find an added benefit, then health insurance funds and the manufacturer will negotiate a discounted reimbursement amount. These negotiations are organized on a national basis, with the health insurance funds represented collectively by their national association, so that all health insurance funds will pay the same price for the drug. The level of added benefit determined by IQWiG serves as the basis for the negotiation. In addition, the final agreement contains provisions on volume amounts and quality standards.

In the rare cases in which added benefit is proven but the health insurance funds and the manufacturer fail to agree on a price within one year, an arbitration board decides the price and content of the agreement. The arbitration board includes two representatives from each of the contracting parties and three impartial members. The reimbursement price fixed by the arbitration board is then binding, although either party can challenge this price and apply to have a comprehensive cost-benefit analysis conducted. The Federal Joint Committee and the pharmaceutical manufacturer coordinate the preparation for a cost-benefit analysis, which IQWiG conducts and is eventually used directly with clinical studies as the basis for new negotiations. This is the only scenario under which IQWiG considers price and, notably, only influences the price negotiation itself, not the assessment of the drug's benefit.

Exceptions: Orphan drugs and vaccines

German policymakers included safeguards to promote the development of orphan drugs in the 2010 reform law, which target rare diseases and thus have small potential markets. The European Union gives orphan drug status to medications that treat diseases affecting only up to 5 in 10,000 people.[10] In Germany, manufacturers must submit a dossier for orphan drugs, but the new drug is considered to add benefit by virtue of its existence since these cases concern very rare diseases that may not yet have any adequate treatment. Thus, exemption from the benefit assessment helps promote the development of drugs to treat these diseases. However, to prevent manufacturers from

gaming the system by attempting to misclassify other drugs as orphan drugs, this exception does not apply to extremely profitable drugs. If total sales of an orphan drug exceed 50 million euros—$68.6 million—then a complete dossier must be submitted within 12 months to demonstrate added benefit.[11]

Vaccines fall into another special category. Rather than incorporate vaccines into the benefit assessment process, German policymakers chose to use reference pricing, tying reimbursement to vaccine prices in comparable European countries. The basis for fixing the vaccine price is currently the average price in the four European countries where the gross national product is closest to Germany's: France, the United Kingdom, Italy, and Spain.[12]

Impact of reform

AMNOG has already affected prescription drug reimbursement in Germany. Of the 66 early benefit assessments completed as of February 2014, 27 proved that no added benefit for the drug existed.[13] Out of the 39 drugs with added benefit, 13 offered a considerable added benefit, 20 offered a small improvement, and 6 offered a real but nonquantifiable improvement.[14] While some critics, including the pharmaceutical industry, argued that AMNOG would harm Germany's traditionally open market for new prescription drugs, these misgivings have not been borne out.[15] Even though the Federal Joint Committee ruled 27 prescription drugs to have no added benefit, only 5 of these drugs have left the German market as a result, and the remaining 22 drugs are referenced priced.[16] Similarly, there is no evidence that manufacturers have tried to game the system by drastically increasing their initial drug prices during the first 12 months. The national association for the health insurance funds has been strongly supportive of the law and has praised its impact, with the association's deputy chairman saying that AMNOG really "separates the wheat from the chaff."[17]

One example of the reform's impact is the case of Trobalt, a treatment for epileptic seizures from GlaxoSmithKline. The Federal Joint Committee accepted the findings from IQWiG and ruled in May 2012 that no added benefit was proven for Trobalt.[18] Faced with the prospect of reference pricing, GlaxoSmithKline withdrew Trobalt from the German market.[19] Later on, the European Medicines Agency decided that Trobalt should only be prescribed in a small minority of cases due to major risks found by new studies.[20] This shows that CER not only identifies whether new drugs fail to offer real improvements for patients but also serves as an additional layer of protection for patient safety.

Financially, the reform's effects have been limited thus far. Since the program did not begin until 2011—and the manufacturers' prices continue to hold for the first 12 months after the drugs enter the market—AMNOG did not begin to change prices until 2012. For the first 29 prices negotiated, the national association of the health insurance funds saw savings of 180 million euros—U.S. $247 million.[21] The negotiated discounts on prices ranged from 0 percent to 70 percent, with an average of 16 percent.[22]

However, this represents only a partial accounting of AMNOG's savings. Most notably, this value does not include any of the savings from the 22 drugs subjected to reference pricing or from the 10 approved drugs that were still in the price negotiation process as of January 2013. In addition, the initial two years saw a relatively small number of drugs submitted and reviewed, so fewer prices were negotiated than anticipated. Policymakers expect the savings to increase in the next few years due to the number of expensive, high-volume drugs that are expected to be released.

International comparisons

Compared to Germany's IQWiG, France, the United Kingdom, and Australia have similar institutes for benefit assessments. These agencies—France's National Authority for Health, or HAS; the U.K.'s National Institute for Health and Care Excellence, or NICE; and Australia's Pharmaceutical Benefits Advisory Committee, or PBAC—are each largely independent. The European institutes formally collaborate with a periodic workshop to share experience and expertise and generate media attention if they reach different conclusions on a particular drug.

While the benefit assessment approach applied by IQWiG, NICE, HAS, and PBAC are similar in many respects, there are also major differences. While Germany allows the manufacturer to set the price for an initial period during the benefit assessment, most other European countries will only reimburse for new drugs after assessing the added benefit and negotiating the price.[23] Australia allows drugs to be sold immediately after safety approval, but the government will not pay for the drug until a cost-benefit analysis is complete and a price negotiated—so patients who want the drug immediately have to pay out of pocket.[24]

Another major difference is the consideration of price. Germany and France use CER to focus on clinical benefits, while the United Kingdom and Australia add cost-benefit analyses to their processes to focus on cost effectiveness.[25] IQWiG does not consider price during benefit assessments, only whether a treatment has an added benefit over the comparator. As a result, Germany has no hard limit for treatment prices. Similarly, France does not explicitly consider price through cost-benefit analyses, although it may use budget impact estimates showing a particular drug's overall volume cost to the government to implicitly inform decisions.[26]

On the other hand, in the United Kingdom, NICE considers price in all cases. While NICE focuses on drugs that are expected to have a large budget impact and thus formally evaluates only about 40 percent of new drugs, it strictly quantifies the benefits of these drugs to generate a cost-quality ratio.[27] NICE's measure of quality, called the QALY, is based on the number of years that the medical treatment would add to a patient's life. The cost/QALY limit in the United Kingdom ranges from 20,000 pounds to 30,000 pounds—$34,000 to $50,000—depending on the condition involved, meaning that the British National Health Service is willing to pay up to a maximum of 30,000 pounds—$50,000—for an added year of life expectancy by the treatment or drug.[28] While Australia does perform cost-benefit analyses on all drugs, it does not adhere to a fixed maximum cost-effectiveness ratio as the United Kingdom does, instead opting for a more flexible determination process.[29]

Among the countries using either CER or cost-benefit analysis, the consideration of price emerges as the primary dividing line. Yet even within each category exists substantial variation. While the U.K.'s approach, also adopted by the Netherlands, has been effective in controlling costs and has a transparent methodology, some other countries that consider cost such as Australia consider it to be overly restrictive. Instead, they—much like countries such as Germany that use CER instead—prefer more flexible arrangements that maintain higher levels of patient choice.

TABLE 1

Prescription drug pricing in France, the United Kingdom, Germany, and Australia

	Centralized price negotiations	International price referencing	National price referencing	Early benefit assessment	Cost-benefit assessment	Budget impact analysis
France	Yes, with government agency	Yes, formal and informal. Prices compared to Germany, Spain, Italy, and the United Kingdom	Yes, informally, by comparators	Yes, by HAS. Comparator is standard treatment.	No	Yes
United Kingdom	Yes, with Health Ministry	No	Implicitly by cost/QUALY comparison	Yes, by NICE, for about 40 percent of drugs—those with large budget impact. In Scotland, every drug is assessed for benefit.	Yes, conducted by NICE with cost/QUALY ratio	Yes, by NICE or a local authority if desired
Germany	Yes, initial price set by manufacturer, then health insurance funds negotiate with manufacturer	Only for vaccines or as part of the arbitration process for failed negotiations	Yes, for drugs without added benefit	Yes, by IQWiG, for every new prescription drug within a period of six months after launch. Comparator is standard treatment.	No, not for benefit assessment. Only done if requested during arbitration process for failed negotiations.	No
Australia	Yes, with Department of Health	No	Yes, for drugs without added benefit	Yes, by PBAC. Comparator is standard treatment.	Yes, although no strict cutoff threshold	Yes

Sources: Joshua Cohen, Ashley Malins, and Zainab Shahpurwala, "Compared To US Practice, Evidence-Based Reviews In Europe Appear To Lead To Lower Prices For Some Drugs," *Health Affairs*, 32 (4) (2013): 762–770, available at http://content.healthaffairs.org/content/32/4/762.full.html; Ruth Lopert and Adam G. Elshaug, "Australia's 'Fourth Hurdle' Drug Review Comparing Costs And Benefits Holds Lessons For The United States," *Health Affairs* 32 (4) (2013): 778–787, available at http://content.healthaffairs.org/content/32/4/778.full.html.

Lessons for the United States

Similar to Germans, U.S. citizens want to have unrestricted patient choice. But at the same time, the United States faces the challenge of rising prescription drug prices.[30] The consideration of price as in the United Kingdom or Australia would be highly controversial in the United States. CER studies comparing clinical benefit, however, can help inform and improve patient and physician choice instead of restricting it. While France's more regulated, state-driven process offers fewer clear parallels to the current U.S. approach, Germany's more market-friendly use of CER to inform private-sector price negotiations holds greater potential for adaptation by the United States.

Germany does not control prescription drug prices through a government bureaucracy. The Federal Joint Committee and IQWiG are both nongovernmental bodies, and private-sector negotiations determine prices. Similarly, in the United States, private insurance companies negotiate with manufacturers over drug prices. However, most U.S. insurers contract with pharmacy benefit manufacturers, companies that aggregate the market power of multiple insurers in order to conduct price negotiations with drug manufacturers. Although these negotiations are not as standardized as the nationally based price negotiations in Germany, some pharmacy benefit managers represent more people than the collective health insurance funds in Germany. The largest U.S. pharmacy benefit manager, Express Scripts, now handles prescription drugs for an estimated 155 million covered lives, while the German health insurance funds insure 69.8 million people.[31] While price negotiation is the norm in the private sector, federal law forbids Medicare Part D from negotiating prescription drug prices with manufacturers.[32] As a result, price negotiations in the United States are more fragmented than in Germany, giving drug manufacturers greater leverage.

In the United States, these pharmacy benefit managers can use CER to inform their price negotiations, and some already do.[33] However, the lack of quality CER studies in the United States hampers these efforts. To address this, the Affordable Care Act, or ACA, provides a basis for more publicly funded CER with the Patient-Centered Outcomes Research Institute, or PCORI. Similar to Germany's IQWiG, PCORI is a nongovernmental, nonprofit institute. The law forbids PCORI from considering cost or mandating coverage decisions, so it shares IQWiG's focus on comparative clinical effectiveness rather than price.[34] This is not necessarily a weakness; given the current lack of useful comparative effectiveness data, CER alone has the potential to make a meaningful impact. Similar to the pre-AMNOG iteration of IQWiG, PCORI currently funds CER on a purely discretionary basis rather than as part of a structured process as IQWiG does now. As a result, PCORI's effectiveness in improving our understanding of which treatments add benefit for patients depends largely on how well its funding is targeted.

The example of IQWiG shows that if targeted wisely, PCORI's research grants could identify which drugs are truly innovative and which provide no real added benefit, allowing patients and physicians to make better-informed treatment decisions. To date, however, PCORI has allocated less than 3 percent of its research funding to studies involving prescription drugs and has not funded a single study of medical devices.[35] Although its recent announcement of a large-scale pragmatic trials initiative holds promise, it is imperative that PCORI focus its funding on meaningful drug and device research.[36] While the growth rate of U.S. health care costs has slowed in recent years, a worrying recent study identified the primary driver of this cost slowdown as the relative lack of new, high-priced medical technology launches over this period.[37] Given the expected surge in diffusion of expensive medical devices over the next few years, using CER to ensure that we are truly receiving value for our money is essential if the cost slowdown is to continue.

IQWiG's evolution from conductor of discretionary research to key actor in a structured process for evaluating all new drugs holds important lessons for PCORI. In the future, policymakers should carefully consider how PCORI could be integrated into an organized CER process for drugs in the United States. PCORI's existing purview even offers policymakers the opportunity to expand upon the IQWiG model by including medical devices in this framework. While PCORI's existence is currently term-limited through 2019, the potential for the institute to play a broader, more structured role could provide a strong rationale for reauthorizing PCORI for another term or making it permanent.

Conclusion

Although the financial impact has yet to fully take root, Germany's approach to prescription drug reform shows great promise and offers an intriguing example for U.S. policymakers. With the United States only now beginning to establish a framework for publicly funded CER, IQWiG's evolving role in Germany's structured process for evaluating all drugs holds important lessons for PCORI. While PCORI has disappointingly neglected to fund many studies of prescription drugs or any of medical devices, it is not too late to focus its research funding on meaningful, high-impact CER. The German example demonstrates that by using CER to identify truly innovative drugs and devices, it is possible to establish an evidence-based framework for lowering prices without sacrificing quality or patient choice.

Daniel Bahr is the former federal minister of health in Germany and is a Visiting Senior Fellow at the Center for American Progress. Thomas Huelskoetter is the Special Assistant for Health Policy at the Center.

Endnotes

1 Panos Kanavos and others, "Higher US Branded Drug Prices And Spending Compared To Other Countries May Stem Partly From Quick Uptake Of New Drugs," *Health Affairs,* 32 (4) (2013): 753–761, available at http://content.healthaffairs.org/content/32/4/753.full.html.

2 National Bureau of Economic Research, "Can Comparative Effectiveness Research Help Reduce Health Care Costs" (2011), available at http://www.nber.org/bah/2011no3/w16990.html.

3 *The Patient Protection and Affordable Care Act*, Public Law 148, 111th Cong., 2d sess. (March 23, 2010), Section 6301.

4 Olga Khazan, "What American Healthcare Can Learn From Germany," *The Atlantic*, April 8, 2014, available at http://www.theatlantic.com/health/archive/2014/04/what-american-healthcare-can-learn-from-germany/360133/.

5 Kavanos and others, "Higher US Branded Drug Prices."

6 Federal Ministry of Health, Germany, "Kennzahlen und Faustformeln" (2011), available at http://www.bmg.bund.de/fileadmin/dateien/Downloads/Statistiken/GKV/Kennzahlen_Daten/Kennzahlen_und_Faustformeln_GKV_2000-2010_111129.pdf.

7 Ibid.

8 German Federal Ministry of Health, "The Act on the Reform of the Market for Medicinal Products," available at http://www.bmg.bund.de/ministerium/english-version/health/amnog.html (last accessed March 2014).

9 Sophia Schlette and Rainer Hess, "Early Benefit Assessment for Pharmaceuticals in Germany: Lessons for Policymakers" (New York: The Commonwealth Fund, 2013), available at http://www.commonwealthfund.org/~/media/Files/Publications/Issue%20Brief/2013/Oct/1711_Schlette_early_benefit_assessment_Rx_Germany_Intl_brief.pdf.

10 European Medicines Agency, "Orphan designation," available at http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000029.jsp& (last accessed May 2014).

11 German Federal Joint Committee, "Questions and Answers about the Procedure," available at http://www.english.g-ba.de/benefitassessment/information/faq/ (last accessed March 2014.

12 Jürgen Barth and others, "Mechanics and Effects of European Reference Pricing for Vaccines in Germany According to §130a Abs. 2 SGB V: An Analysis Using the Example of Influenza," *Gesundheitswesen* 76 (4) (2013), available at http://www.ncbi.nlm.nih.gov/pubmed/24081570.

13 *Apotheke Adhoc*, "Hecken: AMNOG trennt Spreu vom Weizen," March 20, 2014, available at http://www.apotheke-adhoc.de/nachrichten/nachricht-detail/nutzenbewertung-amnog-hecken-zieht-positives-fazit/.

14 Ibid.

15 Kevin Grogan, "Germany policy hurting pharma innovation - Lilly CEO," Pharma Times, July 11, 2011, available at http://www.pharmatimes.com/article/11-07-11/German_policy_hurting_pharma_innovation_-_Lilly_CEO.aspx.

16 *Apotheke Adhoc*, "Hecken: AMNOG."

17 Sunna Gieseke, "GKV feiert, vfa beklagt Strafmodell," Ärzte *Zeitun,* May 30, 2013, available at http://www.aerztezeitung.de/politik_gesellschaft/arzneimittelpolitik/nutzenbewertung/article/839721/jahr-amnog-gkv-feiert-vfa-beklagt-strafmodell.html.

18 Federal Joint Committee, "Resolutions" (2012), available at http://www.english.g-ba.de/benefitassessment/resolutions/.

19 "First Price Negotiation Successful As Product Withdrawals Multiply in Germany," IHS, June 1, 2012, available at http://www.ihs.com/products/global-insight/industry-economic-report.aspx?id=1065968289.

20 European Medicines Agency, "European Medicines Agency recommends restricting Trobaltto last-line therapy in partial epilepsy," Press release, May 31, 2013, available at http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2013/05/news_detail_001802.jsp&mid=WC0b01ac058004d5c1.

21 *Aerzteblatt.de*, "Regierung: AMNOG hat bislang 180 Millionen Euro eingespart," January 3, 2013, available at http://www.aerzteblatt.de/nachrichten/57096/Regierung-AMNOG-hat-bislang-180-Millionen-Euro-eingespart.

22 Ibid.

23 Joshua Cohen, Ashley Malins, and Zainab Shahpurwala, "Compared To US Practice, Evidence-Based Reviews In Europe Appear To Lead To Lower Prices For Some Drugs," *Health Affairs* 32 (4) (2013): 762–770, available at http://content.healthaffairs.org/content/32/4/762.full.html.

24 Ruth Lopert and Adam G. Elshaug, "Australia's 'Fourth Hurdle' Drug Review Comparing Costs And Benefits Holds Lessons For The United States," *Health Affairs* 32 (4) (2013): 778–787, available at http://content.healthaffairs.org/content/32/4/778.full.html.

25 Cohen, Malins, and Shahpurwala, "Compared To US Practice."

26 Ibid.

27 Robert Steinbrook, "Saying No Isn't NICE — The Travails of Britain's National Institute for Health and Clinical Excellence," *New England Journal of Medicine* 359 (2008): 1977–1981, available at http://www.nejm.org/doi/full/10.1056/NEJMp0806862.

28 NICE, "Measuring effectiveness and cost effectiveness: the QALY," available at http://www.nice.org.uk/newsroom/features/measuringeffectivenessandcosteffectivenesstheqaly.jsp. (last accessed March 2014).

29 Lopert and Elshaug, "Australia's 'Fourth Hurdle.'"

30 Anne B. Martin and others, "National Health Spending In 2012: Rate Of Health Spending Growth Remained Low For The Fourth Consecutive Year," *Health Affairs* 33 (1) (2014): 67–77, available at http://content.healthaffairs.org/content/33/1/67.full.html.

31 Fred Gebhart, "Medco and Express Scripts: Could this merger put your business at risk?", *Drug Topics*, September 25, 2011, available at http://drugtopics.modernmedicine.com/drug-topics/news/modernmedicine/modern-medicine-feature-articles/medco-and-express-scripts-could-mer; Federal Ministry of Health, " Kennzahlen und Faustformeln."

32 *Medicare Prescription Drug, Improvement, and Modernization Act of 2003*, Public Law 173, 108th Cong., 1st sess. (December 3, 2003), Section 1860D–11

33 Sarah Collins, "Payer Perspectives on Federally Funded Comparative Effectiveness Research," *Biotechnology Healthcare* 7 (1) (2010): 19–22.

34 *The Patient Protection and Affordable Care Act*, Public Law 148, 111th Cong., 2nd sess. (March 23, 2010), Section 6301.

35 CAP Analysis of PCORI grants, including Pilot Projects, Cycles I-III, and August 2013 awards through December 2013. For more on this topic, see Neera Tanden and others, "Comparing the Effectiveness of Health Care: Fulfilling the Mission of the Patient-Centered Outcomes Research Institute" (Washington: Center for American Progress, 2014), available at http://www.americanprogress.org/issues/healthcare/report/2014/01/24/82775/comparing-the-effectiveness-of-health-care/.

36 PCORI, "Pragmatic Clinical Studies and Large Simple Trials to Evaluate Patient-Centered Outcomes," March 10, 2014, available at http://www.pcori.org/funding-opportunities/funding-announcements/pragmatic-clinical-studies-and-large-simple-trials-to-evaluate-patient-centered-outcomes/.

37 Amitabh Chandra, Jonathan Holmes, and Jonathan Skinner, "Is This Time Different? The Slowdown In Healthcare Spending." Working Paper 19700 (National Bureau of Economic Research, 2013), available at http://www.nber.org/papers/w19700.pdf.