*AHRQ Healthcare Horizon Scanning System*

# Report of a Pilot Project: Rapid Cost Analyses of Selected Potential High-Impact Intervention Reports

**Prepared for:**
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This report incorporates data collected during implementation of the Agency for Healthcare Research and Quality (AHRQ) Healthcare Horizon Scanning System by ECRI Institute under contract to AHRQ, Rockville, MD (Contract No. 290-2010-00006-C). The findings and conclusions in this document are those of the authors, who are responsible for its content, and do not necessarily represent the views of AHRQ. No statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

This report's content should not be construed as either endorsements or rejections of specific interventions. As topics are entered into the System, individual topic profiles are developed for technologies and programs that appear to be close to diffusion into practice in the United States. Those reports are sent to various experts with clinical, health systems, health administration, and/or research backgrounds for comment and opinions about potential for impact. The comments and opinions received are then considered and synthesized by ECRI Institute to identify interventions that experts deemed, through the comment process, to have potential for high impact. Please see the methods section for more details about this process. This report is produced twice annually and topics included may change depending on expert comments received on interventions issued for comment during the preceding 6 months.

A representative from AHRQ served as a Contracting Officer's Technical Representative and provided input during the implementation of the horizon scanning system. AHRQ did not directly participate in horizon scanning, assessing the leads for topics, or providing opinions regarding potential impact of interventions.



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# Preface

The purpose of the AHRQ Healthcare Horizon Scanning System is to conduct horizon scanning of emerging health care technologies and innovations to better inform patient-centered outcomes research investments at AHRQ through the Effective Health Care Program. The Healthcare Horizon Scanning System provides AHRQ a systematic process to identify and monitor emerging technologies and innovations in health care and to create an inventory of interventions that have the highest potential for impact on clinical care, the health care system, patient outcomes, and costs. It is also a tool for the public to identify and find information on new health care technologies and interventions. Any investigator or funder of research can use the AHRQ Healthcare Horizon Scanning System to select potential topics for research.

The health care technologies and innovations of interest for horizon scanning are those that have yet to diffuse into or become part of established health care practice. These health care interventions are still in the early stages of development or adoption, except in the case of new applications of already-diffused technologies. Consistent with the definitions of health care interventions provided by the National Academy of Medicine (formerly the Institute of Medicine) and the Federal Coordinating Council for Comparative Effectiveness Research, AHRQ is interested in innovations in drugs and biologics, medical devices, screening and diagnostic tests, procedures, services and programs, and care delivery.

Horizon scanning involves two processes. The first is identifying and monitoring new and evolving health care interventions that are purported to or may hold potential to diagnose, treat, or otherwise manage a particular condition or to improve care delivery for a variety of conditions. The second is analyzing the relevant health care context in which these new and evolving interventions exist to understand their potential impact on clinical care, the health care system, patient outcomes, and costs. In 2014, nearly 4 years after initiation of the horizon scanning system, AHRQ requested some exploratory and simple cost analyses be performed to illuminate the known or potential costs of new interventions that had been identified, tracked, and eventually deemed to have potential for high impact in the Potential High-Impact Intervention Reports of December 2013 and June 2014. Topics selected had a moderate or high designation within the high-impact-potential range.

We welcome comments on this report on the rapid cost analyses. Send comments by mail to the Task Order Officer named in this report to: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to: effectivehealthcare@ahrq.hhs.gov.

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# Report of a Pilot Project: Rapid Cost Analyses of Selected Potential High Impact Intervention Reports

## Structured Abstract

**Background.** Health care horizon scanning is an activity undertaken to identify technological and system innovations (pharmaceuticals, medical devices, diagnostic tests, procedures, therapeutic interventions, rehabilitative interventions, behavioral health interventions, public health, and health promotion activities) that could have important impacts or bring about paradigm shifts in the health care system. The Agency for Healthcare Research and Quality (AHRQ) established a national Healthcare Horizon Scanning System to identify interventions that purport to address important unmet needs and are up to 3 years out on the horizon and then to follow them up to 2 years after initial entry into the health care system. At any given time, between 500 and 650 topics meeting the criteria are being actively tracked in the system. About 15 to 20 percent of these interventions are developed enough (e.g., have late-phase data available) to consider for inclusion in a Potential High Impact Intervention report, which AHRQ publishes twice a year. In 2014, AHRQ requested exploratory, rapid, cost analyses to elucidate the potential 1-year spend of 53 selected interventions deemed to have potential for high impact on the health care system.

**Methods.** To estimate potential costs of these new and emerging interventions, medical librarians performed searches to identify data that analysts could use in the following categories: prevalence of the disease or condition targeted by each intervention; actual or projected 1-year adoption of the new intervention; costs of the intervention; costs of a similar intervention; and costs of an alternative intervention used for the disease or condition.

**Results.** The high-end of the 1-year health care cost estimate for these 53 potential high-impact interventions was about $96.5 billion. This scenario assumed availability and implementation of all interventions in the estimated patient populations in a theoretical 1-year timeframe. The 53 interventions span 14 priority condition areas and 1 cross-cutting priority area. New drugs for treating one disease—direct-acting oral antivirals for interferon-free treatment of hepatitis C virus (HCV)—represented about $17 billion in 1-year health care expenditures if used to treat about 10 percent of the 3.2 million U.S. population estimated to have HCV infection. When considering categories of these interventions, such as drugs, devices, and procedures, new pharmaceuticals/biotechnologies and new off-label uses of existing pharmaceuticals constituted about 60 percent of estimated costs. Thirty-six interventions with an estimated annual spend of $500,000 to $1 billion each totaled about $11.4 billion. Eleven interventions with an estimated annual spend of more than $1 billion each totaled $35 billion in estimated spend (including the new oral drugs for treating hepatitis C).

**Conclusions.** Limitations of these rapid cost analyses include the short timeframe to produce them, limited available information requiring many assumptions, and a near-term view. Nonetheless, they do suggest that estimating short-term cost impacts is possible for novel health care interventions in development or just entering the market that purport to address unmet needs.

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# Background

Health care horizon scanning is an activity undertaken to identify technological and system innovations that could have important impacts or bring about paradigm shifts in the health care system. The activity pertains to identifying new (and new uses of existing) pharmaceuticals, medical devices, diagnostic tests, procedures, therapeutic interventions, rehabilitative interventions, behavioral health interventions, public health, and health promotion activities. In early 2010, the Agency for Healthcare Research and Quality (AHRQ) identified the need to establish a national Healthcare Horizon Scanning System to generate information to inform comparative-effectiveness research investments by AHRQ and other interested entities. AHRQ makes those investments in 14 priority areas. For purposes of horizon scanning, AHRQ's interests are broad and encompass drugs, devices, procedures, treatments, screening and diagnostics, therapeutics, surgery, programs, and care delivery innovations that address unmet needs. Thus, we refer to topics identified and tracked in the AHRQ Healthcare Horizon Scanning System generically as "interventions." The implementation of a systematic horizon scanning protocol began on December 1, 2010, for the AHRQ Healthcare Horizon Scanning System. The system is intended to identify interventions that purport to address an unmet need and are up to 3 years out on the horizon and then to follow them up to 2 years after initial entry into the health care system. Since that implementation, review of more than 18,500 leads about potential topics has resulted in identification and tracking of about 2,050 topics across the 14 AHRQ priority areas and 1 cross-cutting area. At any given time, between 500 and 650 topics are being actively tracked in the system, and about 15 percent to 20 percent of these interventions are developed enough to enable us to obtain expert comments for consideration in a Potential High Impact Intervention report.

In 2014, AHRQ requested that exploratory analyses be performed to elucidate known or potential costs (i.e., potential 1-year spend) of certain interventions that had been identified, tracked, and eventually deemed to have potential for high impact. This set of analyses considered topics in the Potential High-Impact Intervention Reports of December 2013 and June 2014 that were designated moderate or high within the potential high impact range.

# Methods

We completed 53 rapid cost analyses on 55 topics over a period of 4 months from July through November 2014. The topics consisted of selected Potential High Impact Intervention reports published in 2013 and 2014. These 55 topics had a designation of moderate or high potential for high impact in those reports. To estimate potential costs of these new and emerging interventions, we sought to identify data on the following: prevalence of the disease or condition targeted by each intervention; actual or projected adoption of the new intervention; costs of the intervention; costs of a similar intervention; and costs of an alternative intervention used for the disease or condition. Of note, however, is the fact that ongoing development of two of the interventions was questionable at the time of the analyses because of unexpected phase III data (Symplicity™ Renal Denervation System for treatment-resistant hypertension) or financial difficulties of the company (RenalGuard device for preventing contrast-induced nephropathy). Also of note is that costs for 2 of the 55 interventions, a program and an infrastructure intervention, could not be estimated by these rapid methods because too many variables are associated with the interventions.

After collecting available data, we estimated costs of each new intervention for the estimated adoption rate, and we estimated costs of one or two of the main interventions used for the current standard of care or alternative interventions. We also sought to determine whether the new intervention would replace or add to existing standard of care. These rapid cost analyses did not consider effectiveness of interventions in any depth, because performing systematic effectiveness reviews is not part of the horizon scanning activity. In some cases, we referred to clinical results reported in article abstracts to provide context.

These rapid analyses also took a short-term view for the most part—for many we estimated what costs would be for the interventions adopted over a 1-year period. The analyses typically did not consider how much the cost of the new interventions might be offset by replacing other interventions or other downstream effects. In a small number of cases in which published cost-effectiveness models had been published on one of the topics, we reported their findings, some of which provide longer-term cost-impact projections. Further details of our methods are below.

To identify data for these analyses, ECRI Institute medical librarians performed topic-specific searches of peer-reviewed clinical literature, business literature, public resources providing retail cost information on drugs, and proprietary databases of cost information for medical equipment and supplies that ECRI Institute collects from more than 1,500 hospitals across North America. (See Table 1). These search strategies were also used to supply ECRI Institute subcontractor Truven Health Analytics (Ann Arbor, Michigan) with source documents and information used in four Truven Health Cost Models on selected topics. ECRI Institute horizon scanning analysts and Truven Health analysts used these search results to identify data they used to perform their analyses.

**Table 1. Sources searched for cost data**

| Source |
|---|
| Embase® |
| Lexis-Nexis® |
| Pharma and MedTech Business Intelligence (Grey Sheet, Pink Sheet, In Vivo, Start-up, Medtech Insight) |
| GoodRX (drugs) |
| PriceGuide ECRI Database (searches for implant and disposable prices paid by hospitals) |
| PricePaid ECRI Database (searches for capital equipment prices paid by hospitals) |
| Health Technology Assessment Information Service ECRI Database (information on clinical, safety, cost, and reimbursement for health care interventions) |
| Cochrane (cost studies) |
| The Wall Street Journal |
| HCUP |
| Google |
| NICE (if no U.S. information found) |

To identify possible costs of interventions not yet on the market in the United States, we identified existing interventions to serve as proxies for the new intervention. For example, in considering a new transcathether cardiac valve in development for a new clinical indication, we considered as a proxy the average cost of new and novel cardiac valves or devices that entered the U.S. market within the past 2–3 years. In some cases, devices have entered the European market 1 or more years before entering the U.S. market and European costs were available. Although European costs are not recognized as a direct proxy for U.S. costs, they provide some sense of pricing in industrialized countries adopting the device. For emerging pharmaceuticals or biotechnologies that have not yet reached market and lack cost information, we used as proxies novel pharmaceuticals or biotechnologies entering the market within the past 2–3 years for the same or similar conditions. For example, we used data on the retail cost of new targeted oncology drugs over the past 4 years as a proxy for targeted oncology drugs in development.

For each topic, we also conducted searches to identify costs of one or two interventions used as the current standard of care for the clinical condition that the new intervention is intended to treat. Again, we did not attempt to calculate long-term costs and effectiveness.

Understanding potential costs also requires understanding the disease or condition prevalence (the number of patients in the target population eligible for the new intervention) and estimating what proportion of that target population might use the intervention in question. For most topics, our projections of possible cost impacts are for 1 year of the technology's use. Typically, a target population is a subset of the population with the disease or condition. Most new interventions are not adopted by 100 percent of the patient population with the disease or condition because many factors affect adoption, such as patient and clinician acceptance, access or availability, affordability, and patient preference. For some diseases and conditions, reliable prevalence information has not been collected or published. Companies also publish projections of anticipated market share and marketing plans for product launch. While these projections are typically optimistic, in the absence of information on prevalence and adoption rates, we considered this information, but with a degree of skepticism. We compared prevalence data we found with market share projections to ascertain gaps or discrepancies between what we found and what companies projected. We also tempered our adoption estimates with the expert comments we received when preparing the Potential High-Impact Intervention report about patient and clinician acceptance and adoption factors.

The types of information we gathered for each cost analysis are as follows:

- Brief description of the topic (fuller description is in High Impact report)
- Prevalence of the condition (if known or best available estimate)
- Estimated adoption rates (best available data)

- Anticipated cost per patient
- Costs of similar interventions for the same or other conditions
- Costs of alternative interventions for the disease/condition (if alternatives exist)
- Infrastructure and capital equipment costs (if applicable and available)
- Cost impact of replacement of existing interventions (if the intervention is a replacement)
- Cost impact of adding this intervention to existing interventions (if this intervention is going to be added to existing interventions)
- Potential overall cost impact

# Results

There were 55 interventions designated as having moderate to high potential for high impact in the December 2013 and June 2014 Potential High Impact Reports. We calculated an estimate of the 1-year spend (based on data available in 2014) for 53 of these interventions. Costs for one program and one infrastructure intervention could not be estimated, as noted above; for spend estimates on some interventions, we provided a range or high and low estimates. The two interventions whose costs we could not estimate because of the wide range of variables affecting their adoption and implementation were the Lazarus opioid prevention program and building senior-specific emergency departments.

The high-end of the 1-year health care cost estimate for 53 of these 55 potential high-impact interventions was about $96.5 billion. This scenario assumed availability and implementation of all interventions in the estimated patient populations in a theoretical 1-year timeframe—which, realistically, is not possible because some of the interventions are still in development and on the horizon. These interventions included many that recently entered the market (in 2013 and 2014) and many that remain on the horizon and may enter clinical care in the next 1 to 3 years. The 53 interventions span 14 priority areas and 1 cross-cutting priority area. (Topics for multiple, similar interventions that were addressed as a group—rolled up—in the December 2013 and June 2014 High Impact reports are also rolled up in these cost analyses). Table 2 below shows the number of rapid cost analyses performed on interventions in each AHRQ priority area.

**Table 2. Number of cost analyses in each of 14 priority areas**

| Priority Area | Number of Topics With Cost Analysis |
|---|---|
| Arthritis and nontraumatic joint disease | 3 |
| Cancer | 13 |
| Cardiovascular Disease | 5 |
| Dementia, including Alzheimer's disease | 1 |
| Depression and other mental health disorders | 3 |
| Developmental delays, attention deficit hyperactivity disorder, and autism | 1 |
| Diabetes mellitus | 2 |
| Functional limitations and disability | 8 |
| Infectious disease, including HIV | 9 |
| Obesity | 3 |
| Peptic ulcer and dyspepsia, including bowel diseases | 2 |
| Pregnancy and preterm birth: no topics were of moderate or high impact | 0 |
| Pulmonary disease | 2 |
| Substance abuse | 2 |
| Cross-cutting | 1 |
| **Total** | 55 |

## Breakdown of Potential High-Impact Intervention Costs

Tables summarizing key information on each intervention's cost estimate can be found in Appendix A of this report (see Table A-1 through Table A-14). The interventions are grouped alphabetically by AHRQ priority area. These rapid cost analyses did not typically consider downstream cost impacts (i.e., savings or cost offsets). The key information in these tables notes the

U.S. Food and Drug Administration (FDA) status of products subject to FDA regulation at the time the cost calculations were performed in the second and third quarters of 2014.

Table A-15 presents estimated 1-year costs (health care spend) for each topic covered in this report. In addition to these cost expenditure estimates, we asked Truven Health Analytics to perform more detailed cost models on four topics to understand downstream impacts. These models were performed taking a payer perspective. Table A-16 through Table A-19 summarize results of these cost models.

Two infrastructure topics for which we could estimate costs (i.e., single-patient intensive care rooms and copper surfaces in patient rooms to aid infection prevention) totaled $13.67 billion if implemented nationwide in most hospitals. If we exclude the cost estimates for these infrastructure interventions, the total estimate for the drugs, devices, and procedures in this report is a maximum (high end of the range) of about $82.8 billion. The lower range of the cost estimate is $46.2 billion (again, without the two infrastructure topics).

Also, of note is that not all of the interventions were available for clinical use at the time of the cost estimates—some remain in development, and further development of a few interventions may be in limbo because of funding issues or late-phase trials failing to meet anticipated outcomes. Depending on the success of the development pathway for some of the interventions, such as catheter-based renal denervation technology for hypertension or deep-brain stimulation for major depressive disorder, some might not reach clinical use if late-phase development is not successfully completed and FDA approval or clearance is not received. In addition, the infrastructure and program interventions would not be built or implemented nationally within a 1-year timeframe.

Of interest is that new drugs for treating one disease—direct-acting oral antivirals, which provide ribavirin and interferon-free treatment regimens for hepatitis C virus (HCV)—represent about $17 billion in 1-year health care expenditures if used to treat about 10 percent of the 3.2 million U.S. population estimated to have HCV infection. (Note: The health care system does not have sufficient resources, i.e., health care providers and financial resources, to treat all infected patients in a 1-year timeframe.) This area of treatment and pricing for these drugs is a dynamic situation with frequent changes due to additional FDA approvals that bring competition and payer demands to negotiate lower pricing. However, as pricing discounts have been announced, payers have also broadened the eligibility for treatment to include infected individuals with earlier stage HCV disease.

When considering the cost of interventions by category, such as drugs, devices, and procedures, we find that new pharmaceuticals/biotechnologies and new off-label uses of existing pharmaceuticals constitute about 60 percent of estimated costs of the interventions discussed in this report. The new all-oral drug regimens for HCV treatment represent about 30 percent of that pharmaceutical cost estimate. Pharmaceuticals constitute about 75 percent of the topics being actively tracked in the horizon scanning at any given time. Devices constitute about 19 percent of the topics actively tracked in the horizon scanning system at any given time.

When excluding program and infrastructure innovations from this list of high potential impact interventions, and grouping a few similar interventions together (like direct-acting antiviral drugs for HCV infection or a cancer drug used for two types of cancer), 47 drugs, devices, and procedures remain. To gain a high level view of the proportion of interventions that constitute high costs versus lower costs, we then categorized interventions into two groups: those with an annual estimated spend (cost) of more than $1 billion and those with an estimated annual spend of $500,000 to $1 billion (no intervention had an annual spend estimate of less than $500,000). Of these 47 interventions, 36 had an estimated annual spend between $500,000 and $1 billion each, for a total estimate of about $11.4 billion. We further divided this group of 36 interventions into those with an

annual spend of less than $250 million and those with an estimated annual spend of $250 million to $1 billion. Of these 36 interventions, 20 had an estimated annual spend of less than $250 million each, and 16 had an estimated annual spend of $250 million to $1 billion each. See Figure 1 for details.

In grouping interventions with an estimated annual spend of more than $1 billion, 11 interventions hit this mark and totaled an estimated spend of $35 billion. Of these 11 interventions, 1 had an estimated annual spend of $17 billion (i.e., direct-acting hepatitis C drugs) and 10 had an estimated annual spend of $1 billion to $2.4 billion. See Figure 2 for details.

We also roughly estimated how much 2015 health care costs might increase over 2014 health care costs if all 47 interventions were available in clinical care and could achieve maximum expected utilization in 2015. For the many interventions that recently already entered the market in 2014, we considered only the additional spend that would occur in 2015 if full clinical deployment were achieved. We then added to that figure the estimated 1-year spend for the interventions that were *not* commercially available in 2014 under a scenario assumption that all would be available and fully deployed in 2015. The incremental increase in health care spend for these interventions from 2014 to 2015, if all were available and used at maximum estimated utilization rates would be an estimated $32.5 billion. If we considered only those interventions that were commercially available and deployed into clinical care in 2014, and estimated how much more would be spent on them in 2015 than was spent on them in 2014, the estimated that amount would be $9.5 billion.

**Figure 1. 36 interventions with annual estimated average cost ~$500,000 to ~$1 billion each (~$11.4 billion total)**

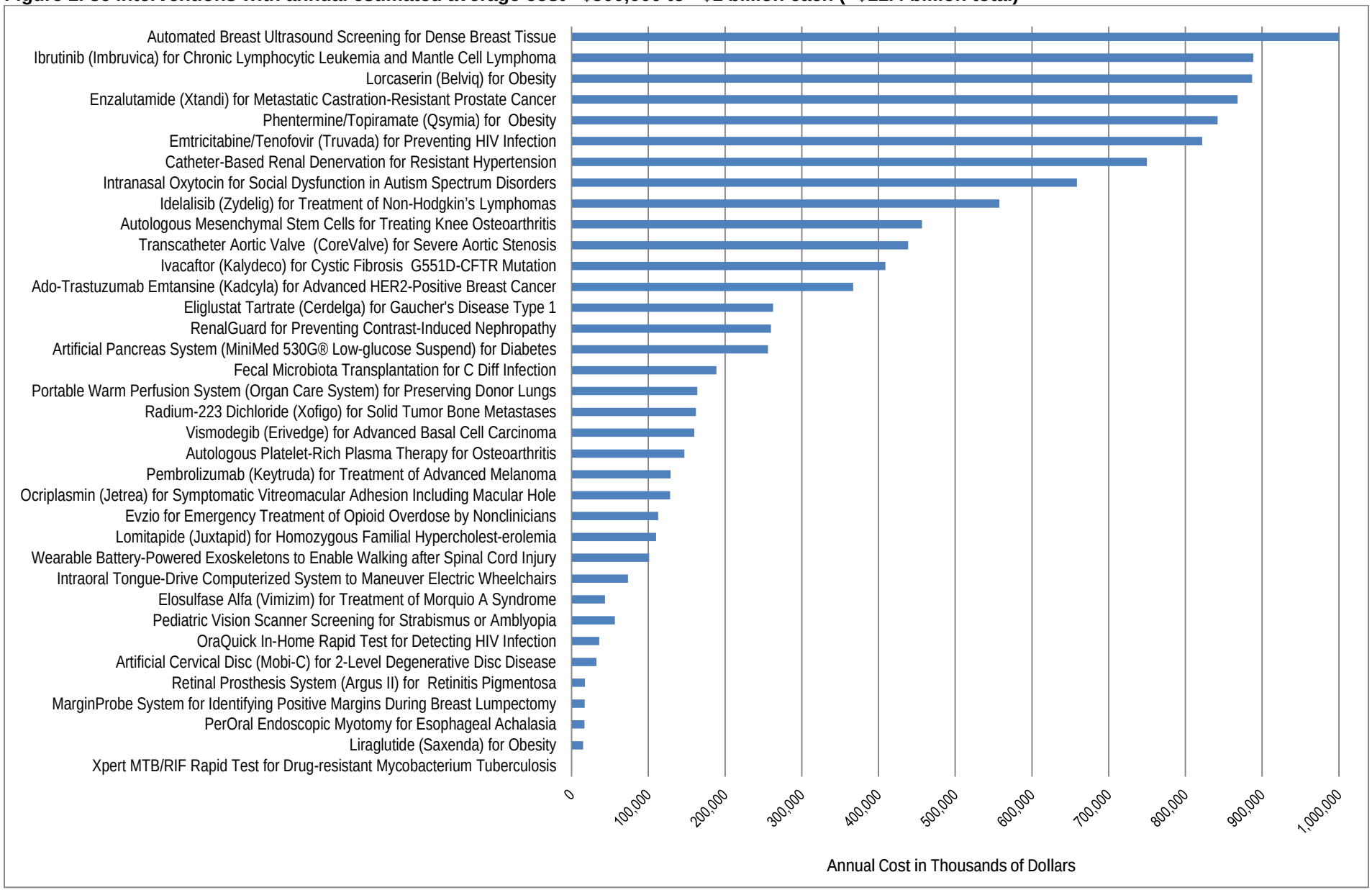
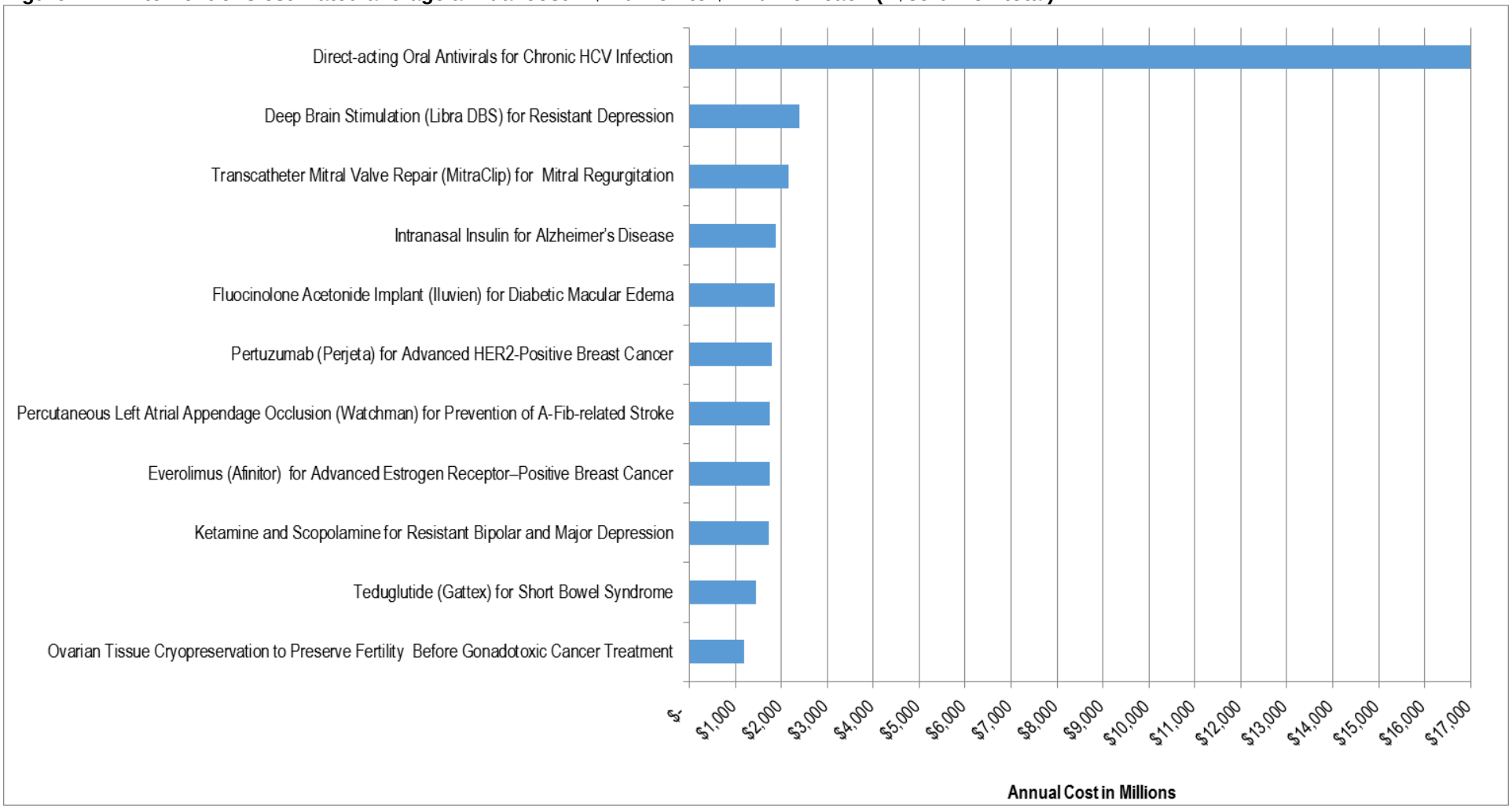


**Figure 2. 11 interventions estimated average annual cost > $1 billion to $17 billion each (~$35 billion total)**



# Discussion

The interventions discussed in this report were deemed to have moderate-to-high potential for high impact. These interventions are a small subset of all interventions in the horizon scanning system and represent less than 10 percent of the interventions being tracked in the system at any given time. (Not all interventions initially tracked are deemed through subsequent expert opinion processes to have potential for high impact.) Thus, the costs of the interventions described herein represent only a small portion of costs of novel interventions or innovations in development and entering the market that purport to address an unmet need.

Published estimates of 2013 expenditures on U.S. health care were about $3 trillion. The clinical use of the small number of new interventions profiled in this report would represent about 2 percent to 3 percent of $3 trillion, using the lower and upper range of estimates. Some of the costs of these interventions would presumably be offset by avoidance of other health care costs in some cases and by gains in health benefits. Each intervention would require its own detailed cost-effectiveness analysis once on the market to determine the value of the interventions over time, which was beyond the scope of these rapid cost analyses. Nonetheless, some observations can be offered and trends identified.

## New Era of High-Cost Pharmaceuticals

The proportion of costs attributable to new specialty pharmaceuticals and biotechnologies, many of which are also called "targeted" or "precision" therapies, strongly indicates a new era of high-cost pharmaceuticals and biotechnologies in the 21st century. The interventions identified and tracked in the horizon scanning system, by definition, address important unmet needs that had not been adequately addressed by existing health care interventions. Thus, the interventions are intended to offer potential health benefits not otherwise obtainable. Overall, the growing number of these interventions taken together with their costs suggests that pharmaceuticals and biologics will constitute a growing proportion of all health care spending.

Most of these new drugs were granted one or more special designations by FDA, such as breakthrough, orphan, or fast-track status. They address serious, and often life-threatening disorders in fields such as oncology (especially lung, skin, or breast cancer), infectious disease (e.g., HCV infection), autoimmune diseases, and rare, inherited diseases (e.g.,cystic fibrosis; familial hypercholesterolemia). The HCV treatment landscape is quickly changing with new regimens continuing to reach market after the initial blockbuster sofosbuvir led the way in early 2014. By late 2014, all-oral interferon/ribavirin-free HCV drugs offering high cure rates had entered the market and signaled the start of competition among different manufacturers. Payers began negotiating with manufacturers to reduce the $83,000 and higher costs of these regimens. However, even if competition reduces oral HCV drug prices by 20 percent to 30 percent (e.g., to an estimated $65,000 per patient treated); treating all currently infected HCV patients would cost more than $200 billion.

The health care infrastructure (e.g., physician availability) is not sufficient to treat every HCV-infected patient at once, so the patient population would need to be treated over a number of years. This estimate also does not include any need for retreatment or new cases of chronic HCV infection. For example, we estimated that treating all chronic HCV-infected patients who are candidates for one of these regimens (i.e., genotypes 1, 2, 3, and 4) could take as long as 15 years if about 215,000 patients per year are treated, and that estimate does not include newly infected HCV patients. One approach to treatment taken by some third-party payers is to treat only those patients in advanced

stages of infection (stage 3 and 4). However, some data have emerged suggesting that treatment earlier in the disease course leads to better outcomes, less morbidity, and less HCV transmission to others. In November 2104, the California Technology Assessment Forum released a draft report indicating that the all-oral sofosbuvir/ledipasvir (Harvoni) combination pill has high efficacy and is cost-effective by "conventional standards," but that the added cost to treat all patients with genotype 1 infection "(even if only 50 percent of them are aware of their infection) are substantial; when added to the additional expenditures required for genotypes 2 and 3, this represents a per-member per-month premium increase that is five-fold higher than frequently discussed manageable thresholds for new interventions." Furthermore, in Philadelphia, PA, a large employer (Southeastern Transportation Authority) filed a lawsuit in 2014 against the sofosbuvir manufacturer over the drug's high cost.

Our observations since the initiation of the U.S. horizon scanning program in late 2010 are that new thresholds for pharmaceutical price tolerance have been reached in the United States with the advent of genetically targeted, personalized drug therapies. In oncology, the average price of a new targeted oral therapy for any type of cancer is about $10,000 per patient per month—or about $333 per day. Targeted therapies addressing rare orphan diseases or an underlying disease mechanism such as an oral enzyme replacement therapy or a genetic–defect–correcting therapy, command a price of about $30,000 per patient per month—or about $1,000 per day.

The sustainability of such pricing paradigms for new drugs was called into question recently by Peter B. Bach, M.D., MAPP, from the Health Outcomes Research Group, Memorial Sloan-Kettering Cancer Center, New York, NY. In an October 22, 2014, editorial on oncology drug pricing (JAMA. 2014;312(16):1629-1630. doi:10.1001/jama.2014.13235), he proposed that value be considered in new drug pricing with respect to the expected health benefit a drug provides for a specific indication. Bach points out that a given drug used for treating many cancers can offer a markedly different health benefit for each cancer—from a median progression-free survival benefit of weeks to a benefit of months or years, depending on the indication. Bach notes, "The American Society of Clinical Oncology recently announced that it will develop scorecards of different cancer treatments, ranking them by their benefits, adverse effects, and costs. The National Comprehensive Cancer Network, a prominent publisher of cancer treatment guidelines, is also planning to publish treatment costs along with their conventional measures of treatment efficacy, toxicity, and the quality of the underlying clinical research data (Robert Carlson, M.D., oral communication, September 4, 2014)." At the 2015 meeting of the American Society of Clinical Oncology, a value-based model for oncology drug pricing was introduced. Whether these initiatives will alter drug pricing is unclear at this time, although Dr. Bach noted that the objections made by his institution to the pricing of one new high-cost/low-benefit oncology drug resulted in a virtually immediate pricing cut by the manufacturer.

Although anti-obesity drugs are not part of the high-cost paradigm seen with specialty pharmaceuticals, the high prevalence of the condition increases the overall cost impact of these drugs. The demand for new antiobesity drugs has been addressed in large part by three new oral drugs approved by FDA since 2012. Their cost (about $2,500 to $2,600 per patient per year) overall, even if used by only 1 percent (1 million) of the overweight and obese population, approaches $3 billion a year. In December 2014, an injected drug long used for treating type 2 diabetes received FDA approval for weight management (liraglutide [Saxenda]), but its cost is expected to be up to four times higher than oral antiobesity medications. For individuals with type 2 diabetes however, Saxenda may address two needs: weight loss and blood glucose control. The question is whether these drugs can produce a benefit sufficient to offset obesity-associated

morbidity, such as diabetes. The evidence for these longer-term outcomes will need to be collected over time.

## Novel, Minimally Invasive but Complex and Costly Implanted Cardiovascular and Neurologic Devices

Novel device implants offering minimally invasive treatment options appear to have established their own pricing paradigm. Several novel implanted devices have become available or are in late-phase development for conditions not previously treatable, such as cardiovascular conditions in patients who are not candidates for open surgery. These include complex devices such as heart valves deployed through transcatheter approaches for various conditions and deep brain stimulators for conditions like treatment-resistant depression. They appear to follow a pricing trend of about $25,000 to $30,000 per implant plus procedure, physician, and hospital costs. Implantation of many of these new devices also requires sophisticated, costly infrastructure in the form of hybrid operating rooms or hybrid catheterization laboratories. Such infrastructure improvements cost about $3 million to $4 million in equipment for one hybrid operating room. Total procedure costs average about $75,000 per patient (without complications) for a minimally invasive procedure using a novel cardiac or neurologic implant. These procedures have not been envisioned as cures, but rather as potential life-extending options to better manage symptoms and improve quality of life in the face of failed medical therapies.

With regard to devices, ECRI Institute is aware of new strategies being employed by some health systems regarding pricing for medical devices and supplies. Health system supply-chain and value-analysis groups indicate prices they are willing to pay for certain classes of devices and refuse to consider products from companies that are unwilling to meet the price point they have established. Companies making claims about the superiority of their devices and asking for a higher price must show clear evidence of incremental benefit to merit consideration by the health system for that higher price. This strategy is used more often for device classes that have many competitors in the field, but as additional high-priced implants emerge on the market and as reimbursement falls short of the health system's costs for the device and procedure, this value-based purchasing approach could migrate to novel devices without competitors.

## Other Novel Devices

An interesting device with a significant cost targets a relatively small patient population: patients in need of a lung transplant. The portable warm blood perfusion system (Organ Care System) is intended to maintain donor lungs in a more viable state for transplantation, which would add about $49,000 to each lung transplantation procedure if used for all patients on the waitlist in 1 year. This assumes that its use would make lesser-quality donor lungs that are currently discarded viable for transplantation, fully addressing the need of all on the wait list. The cost model created by Truven Health Analytics indicates that use of the technology could actually be cost saving and improve quality of life when the high costs of care for the very ill patients on the waitlist are considered. Another similar device intended for the same purpose has also been developed recently and entered the market (XVIVO Perfusion System [XPS] with STEEN Solution).

A device intended to reduce the rate of second surgeries for patients undergoing lumpectomy for breast cancer has not yet gained the traction its developer had hoped for since its FDA approval. MarginProbe, used during breast cancer lumpectomy to identify clear margins and avert the need for a second surgery, has not been adopted in large part because third-party payers are not providing additional coverage yet. It appears they are awaiting further evidence of benefit. Hospitals adopting

this technology in the absence of coverage incur additional costs by using MarginProbe while also seeing a declining revenue stream by averting second surgeries, if the device does in fact help to avert second surgeries.

## Low-Tech Procedures

In terms of procedures, one low-tech, low-cost procedure has emerged as having both a high potential clinical and cost benefit. Fecal microbiota therapy (also called bacteriotherapy) has gained greater acceptance for treating recurrent *Clostridium difficile* infection (CDI)—a prevalent, debilitating, and even life-threatening condition that incurs high costs for inpatient care. The procedure is about half the cost of the newest CDI antibiotic, fidaxomicin (Dificid®), and reported results thus far have garnered wide support from the clinical community, as well as the attention of FDA, the lay press, and patients desperately seeking relief from debilitating CDI recurrences. In more than 4 years of tracking in the horizon scanning system, the intervention has diffused from one or two centers to hundreds of clinics across the United States. The horizon scanning system is also tracking this intervention for other novel indications, such as treatment of Crohn's disease and ulcerative colitis.

## Infrastructure and Care Process Innovations

Some infrastructure and care process interventions, such as antimicrobial copper surfaces in intensive care units, although having a high initial outfitting cost, can purportedly save money within a relatively short timeframe by reducing risk of hospital-acquired infections. Again, formal studies are needed to determine the cost-effectiveness.

Concern about infection control, infectious diseases in the hospital, and difficult-to-treat or resistant microbes has increased interest in single-patient rooms, especially in intensive care units. The equipment costs of outfitting one such patient room are an estimated $270,000 according to ECRI Institute hospital consultants who have outfitted such rooms.

Senior-specific emergency department (ED) design also appears to be gaining momentum, as the number of self-identified senior EDs has increased from a handful in 2010 to scores we identified in 2015. This growth appears to be a result of the increasing number of elderly people, special care considerations necessary to meet their needs and avoid complications, and the frequency with which they access ED services. Robust studies measuring outcomes such as reduced admissions, reduced returns to the ED, and reduced adverse events while in the ED are needed to determine the cost-effectiveness of these special care environments. The cost of these EDs is difficult to calculate generally for purposes of this report because of the number of variables that make each senior-specific ED project unique: number of ED beds desired, new construction vs renovation, geriatric specialty staffing needs, geriatric equipment needs.

The cost of one care process innovation, the Lazarus Opioid Overdose Prevention and Treatment Program, could not be calculated because the program was piloted in one geographic area and costs were not reported for any aspects of the program. The program involves engagement between health care providers and the community to identify signs that place an individual at risk of overdose, and educating and equipping lay persons and emergency personnel regarding the equipment (e.g., naloxone kits) to quickly reverse an overdose. These costs and approaches can be highly variable, even if they are eventually reported.

## Conclusions

In the absence of major changes in preventive care and the financing of health care in the United States, costs will continue to rise with the advent of new specialty pharmaceuticals, biologics, and devices, and the increasing longevity of more people who eventually develop a chronic disease, such as heart failure, diabetes, or cancer. Pharmaceuticals will command a greater proportion of overall health care expenditures because of advances that yield a better understanding of genetics, which enables development of targeted therapies not only for common diseases, but for less common inherited disorders, such as cystic fibrosis, familial hypercholesterolemia, or rare enzyme disorders. These advances are resulting in more and better treatment options, sometimes where none previously existed. Yet, these new options carry a hefty price tag, with many patients requiring lifelong drug therapy. Thus, diseases that previously killed at earlier ages are becoming chronic diseases to manage over a much longer period, with attendant health care costs.

Targeted therapies, by definition, usually address a small subset of a patient population with a disease or condition. Thus, we are living in an era in which more research and development costs are incurred to develop therapies to address unmet needs in target populations. These costs inevitably transfer to employers, private and government health insurers, and consumers.

A relatively small proportion of the 47 interventions discussed in this report—about 23 percent—account for 75 percent of the overall estimated costs. Most of the innovations add to care—they do not replace existing care. Exceptions to that may be the new direct-acting antivirals for chronic HCV infection, which are intended to reduce the viral load to an undetectable level in 90 percent of patients who adhere to the medication regimen. The promise of these drugs is prevention of liver failure, its high treatment costs, and avoidance of a need for liver transplantation. Whether the short-term efficacy of these drugs turns into a permanent cure remains to be seen because the data are relatively short-term (i.e. the longest follow up before their FDA approval was about 1 year).

The question arises, “how often will a situation such as a $17 billion annual expenditure for one type of drug for one condition arise?” The pharmaceuticals in development being tracked in the horizon scanning system indicated that the answer is likely to be more often than we may want to acknowledge—and not just for drugs—but also for new minimally invasive devices. Similar costs are accruing to new targeted cancer and heart disease therapies such as the PCSK9 inhibitors under development for hypercholesterolemia. The American Cancer Society estimates that cancer is diagnosed in more than 1.6 million Americans each year, adding to the population of millions of cancer survivors who continue to need and receive care, often with new, high-cost targeted therapies in succession over many years as cancer cells mutate to necessitate new targeted therapies. The U.S. Centers for Disease Control and Prevention (CDC) estimates that more than 5 million Americans have heart failure. Costly drugs and implantable devices recently approved or on the horizon offer the hope of extending life for these patients.

The AHRQ Healthcare Horizon Scanning System and its outputs (Potential High Impact Intervention Reports published twice a year and Status Update Reports published five times a year) enable those who use its resources to see and plan for the next big health care intervention and the anticipated impacts of soon-to-emerge innovations across broad clinical landscapes. The system also affords a high-level view over vast areas of development to enable one to see gaps—the absence of innovation in areas of significant unmet need. The system empowers providers, payers, consumers, and policy makers to understand, strategize, plan, prepare for, and inform their decision making about health care innovations in advance of the innovations entry into clinical care.

# Appendix A. Summary Tables

**Table A-1. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: arthritis priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 1. Artificial Cervical Disc (Mobi-C) for Treatment of Two-Level Degenerative Disc Disease | The American Association of Neurological Surgeons estimates about 200,000 surgical procedures are performed for treating cervical degenerative disc disease (DDD) in the United States annually. Assuming about 5% of surgical procedures are cervical disc replacement surgeries, about 10,000 cervical disc replacements would be performed in the United States annually. Because multilevel cervical disc replacement is considered investigational by 3rd-party payers, we estimated that no more than 10% of patients (1,000) with DDD who undergo cervical disc replacement would have the interest and means to pay out-of-pocket for 2-level disc replacement. If 2-level TDR costs are about $30,380, an estimated $30.4 million could be spent by patients on 2-level cervical disc replacement annually. However, some part of those costs might be paid by insurers with coverage policies for single-level total disc replacement (TDR), depending on how the procedure is coded and billed. The estimated costs reported for single-level anterior cervical discectomy and fusion (ACDF) are about $19,811 per patient. Additional analysis is needed to determine cost savings of 2-level TDR using Mobi-C compared with 2-level ACDF; however in a randomized clinical trial, the success rate for patients treated with 2-level Mobi-C was 69.7% compared with 37.4% for 2-level ACDF at 24-month followup ($p<0.0001$). Additionally, the reoperation rate for Mobi-C recipients was 3.1% compared with 11.4% in ACDF recipients ($p<0.05$), suggesting the potential for longer-term cost savings for 2-level DDD Mobi-C over ACDF. 2-level Mobi-C was recently FDA approved, but major insurers consider the procedure investigational or experimental at this time and do not reimburse for it. |
| 2. Autologous Mesenchymal Stem Cells for Treatment of Knee Osteoarthritis | We estimated that adoption of mesenchymal stem cell (MSC) therapy by 20% of patients (48,600) with knee osteoarthritis (OA) who receive 1 to 3 MSC injections at an average cost of $4,700 per injection could cost on average, from $228 million to $685 million. These costs are likely to be borne out of pocket by patients with severe knee OA who do not want to avoid or delay knee replacement; major insurers consider the procedure investigational or experimental at this time and do not reimburse for it. |
| 3. Autologous Platelet-Rich Plasma Therapy for Osteoarthritis | In 2006, experts valued the market value of platelet rich plasma (PRP) therapy for OA at $45 million and estimated it would increase to $126 million by 2016. Our estimates indicate the market could be slightly higher than that. If we assume that about 20% of 243,000 OA patients (~49,000 patients) receive an average of 3 PRP injections at an average cost of $1,000 each, the cost would add about $147 million to costs of treating OA. PRP is not regulated by FDA, and major insurers consider the procedure investigational or experimental at this time and do not reimburse for it. |

**Table A-2. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: cancer priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| Automated Breast Ultrasound (Invenia Automated Breast Ultrasound System, Formerly Called somo•v) for Screening Dense Breast Tissue | This device recently received FDA approval for screening dense breasts in conjunction with mammography screening. Assuming that 4 million of 20 million women who have dense breast tissue in the United States have a mammogram with normal results and are prescribed additional screening with automated breast ultrasound (ABUS) at a cost of $180 to $300 per scan, the total estimated cost of ABUS breast cancer screening for this patient population would range between $720 million and $1.2 billion per year, assuming women have annual mammograms. If this same population were screened with magnetic resonance imaging (MRI), which has a reported per procedure cost of about $3,000, the cost would be about $12 billion. If ABUS accuracy proves to be similar to MRI accuracy for dense breasts, ABUS could offer a much less costly option for screening dense breast tissue. |
| Enzalutamide (Xtandi) for Treatment of Metastatic Castration-Resistant Prostate Cancer | Enzalutamide was recently FDA approved for mCRPC treatment. We estimated that the adoption of enzalutamide for treating metastatic castration-resistant prostate cancer (CRPC) will add approximately $28,000 to the cost of care per patient over the duration of the patient's treatment. With an estimated 31,000 patients in whom mCRPC is diagnosed each year who could receive enzalutamide, this would represent an additional cost of approximately $900 million. |
| Everolimus (Afinitor) for Treatment of Advanced Estrogen Receptor–Positive Breast Cancer | Everolimus was recently FDA approved for ER+ breast cancer treatment. Advanced ER+ breast cancer constitutes about 75% of all diagnosed breast cancers; therefore in 2014, about 176,300 cases will be ER+ breast cancer. ER+ breast cancer has limited treatment options, and clinical data have shown everolimus has potential to improve quality of life by overcoming endocrine resistance. We estimated that more than 75% of this patient population will use everolimus as second-line treatment. The cost of adding 14 weeks of daily everolimus in combination with exemestane to the treatment regimen in patients whose ER+ breast cancer has progressed after aromatase inhibitor therapy would cost between $1.2 billion and $2.3 billion. |
| Ibrutinib (Imbruvica) for Recurrent or Treatment - Refractory Non-Hodgkin's Lymphomas (chronic lymphocytic leukemia and mantle cell lymphoma) | Ibrutinib is a first-in-class, orally administered drug that was recently FDA approved for treating 2 types of recurrent or treatment-refractory NHL: chronic lymphocytic leukemia (CLL) and mantle cell lymphoma (MCL). Estimates of the prevalence of these conditions and recurrent/refractory disease in various treatment settings are not widely available. The drug developer provided estimates of the prevalence of chronic lymphocytic leukemia and mantle cell lymphoma based on prescription data from July 2013 to June 2014. For chronic lymphocytic leukemia, Pharmacyclics estimates that 121,200 patients are living with the disease and that during the year 10,300 underwent treatment in the second-line setting and 7,000 underwent treatment in the 3rd-line or greater setting. For mantle cell lymphoma, they estimate that 13,300 patients are living with the disease and that during the year, 1,400 underwent treatment in the second-line setting and 1,000 underwent treatment in the 3rd-line or greater setting. We estimated costs associated with adopting ibrutinib for treating chronic lymphocytic leukemia to be between $130 million and $220 million per year, assuming adoption rates between 36% and 60% in the recurrent/refractory setting. We estimated costs associated with adopting ibrutinib for treating mantle cell lymphoma will be between $51 million and $76 million per year, assuming adoption rates between 40% and 60% in the recurrent/refractory setting. |

**Table A-2. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: cancer priority area (continued)**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| Idelalisib (Zydelig) for Recurrent or Treatment – Refractory Non-Hodgkin's Lymphomas | Non-Hodgkin's lymphoma (NHL) comprises a set of malignancies that arises from lymphocytes of the immune system. Idelalisib (Zydelig™) is a first-in-class, orally administered, small-molecule inhibitor of the delta isoform of phosphatidylinositide-3 kinase (PI3K), an enzyme that plays multiple roles in regulating B lymphocytes. Idelalisib is being studied in treating a wide array of B-cell lymphomas and was recently FDA approved for treating three types of recurrent/refractory NHL: chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), and follicular lymphoma (FL). Adoption of idelalisib-containing regimens for treating recurrent/refractory CLL, SLL, and FL would lead to drug costs of approximately $417 million to $698 million per year. By disease, the cost breaks down this way: assuming 15% to 25% of patients with recurrent/refractory CLL (1,950–3,250 patients per year) undergo treatment with idelalisib plus rituximab at a cost of $110,000 per patient, this would represent a cost of about $214 million to $360 million per year. Assuming 15% to 25% of patients with recurrent/refractory SLL (645–1,075 patients per year) undergo treatment with idelalisib at a cost of $60,000 per patient, this would represent a cost of approximately $39 million to $65 million per year. Assuming 30% to 50% of patients with recurrent/refractory FL (2,730–4,550 patients per year) undergo treatment with idelalisib at a cost of $60,000 per patient, this would represent a cost of approximately $164 million to $273 million per year. Some of these drug costs would be offset by obviating the need for other therapies, which could reduce the incremental cost of idelalisib adoption to approximately $31 million to $50 million. Clinical trials of idelalisib and ibrutinib in combination with current standard-of-care regimens for B-cell lymphomas are ongoing and future costs could increase as these drugs are incorporated into combination therapy regimens in earlier lines of treatment. |
| MarginProbe System for Intraoperatively Identifying Positive Margins During Breast Cancer Lumpectomy | FDA approved MarginProbe in early January 2013 for use during intraoperative lumpectomy to identify positive tumor margins and avoid the need for second surgeries that are performed in 20% to 25% of patients undergoing lumpectomy because clear margins were not obtained initially. We estimated that each year, about 139,000 patients undergo lumpectomy in the United States. When added to standard intraoperative assessment during lumpectomy for early stage breast cancer, MarginProbe increases the cost by approximately $700 to $1,700 per patient for providers performing the procedure. Payers do not currently reimburse for use of the system. If used in 10% of women undergoing lumpectomy each year, this would add approximately $10 million to $24 million per year to provider costs of performing these procedures. Thus far, the use of MarginProbe is not reimbursed separately from the bundled payments provided for lumpectomy procedures. Institutions using MarginProbe to reduce second surgeries would also lose the revenue stream they had from those re-excision surgeries; however payers could benefit by saving on reimbursement for re-excision surgeries. Patients could save co-pays and improve quality of life by avoiding re-excision surgery. |
| Novel Targeted Therapies for Breast Cancer: Ado-Trastuzumab Emtansine (Kadcyla); Pertuzumab (Perjeta) for Advanced HER2-Positive Breast Cancer | Both of these agents have recently received FDA approval for advanced HER2+ breast cancer. HER2-positive cancer makes up approximately 20% to 25% of all diagnosed breast cancers, which means that between 47,000 and 58,800 of cases in 2014 would be HER2-positive. Out of all the HER2-positive breast cancer cases in the United States, we estimated approximately 43,700–54,700 patients might receive pertuzumab as neoadjuvant therapy, and 3,300–4,100 patients could receive it as 1st-line therapy for metastatic breast cancer, which would bring the cost of adopting pertuzumab for both indications to $1.6 billion to $2 billion. If metastatic breast cancer progresses after 1st-line treatment at an average rate of 65%, between 2,100 and 2,700 patients could receive ado-trastuzumab emtansine treatment. Based on these data, we estimated adopting agent ado-trastuzumab emtansine as 2nd-line treatment for advanced metastatic HER2-positive breast cancer could cost between $321 million and $413 million. |

**Table A-2. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: cancer priority area (continued)**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| Ovarian Tissue Cryopreservation for Fertility Preservation in Women Undergoing Gonadotoxic Cancer Treatment | If we use 58% as the benchmark for the proportion of patients who would seek any type of fertility preservation treatment (based on a published study), we then estimate that ovarian tissue cryopreservation use would not exceed about 20% of that population, or 44,600 patients. Ovarian tissue cryopreservation is in early adoption and is considered by 3rd-party payers to be investigational. The adoption rate could increase if reimbursement by 3rd-party payers becomes available. If implemented today, we estimated ovarian tissue cryopreservation would cost about $1.2 billion, assuming that approximately 44,600 female patients of reproductive age who have survived cancer treatment would undergo the procedure for approximately $27,000 before receiving gonadotoxic chemotherapy. Whether patients would bear all these costs or 3rd-party payers would reimburse some part of costs is unclear at this time because evidence on effectiveness of the procedure is limited at this time. This procedure is not subject to FDA regulatory approval. |
| Pembrolizumab (Keytruda) for Treatment of Advanced Melanoma | Programmed cell death protein 1 (PD-1) is a central player in immune checkpoints thought to prevent runaway immune responses. PD-1 is a therapeutic target that could potentially induce an immune response to cancer by "releasing a brake" placed on the immune response through the PD-1 signaling pathway. Pembrolizumab (Keytruda®) is a humanized monoclonal antibody highly specific for PD-1. As a PD-1 checkpoint inhibitor, it reportedly prevents activation of an immune checkpoint and leads to an increase in anticancer immune response against melanoma. Pembrolizumab is administered by intravenous infusion. Pembrolizumab was FDA approved in September 2014 for treating advanced melanoma in patients whose disease has progressed after treatment with ipilimumab (Yervoy) or a *BRAF* inhibitor if the melanoma is $BRAF^{V600}$ positive. Out of all the ipilimumab-resistant melanoma cases in the United States each year, we estimated approximately 640–1,500 patients would receive 17 cycles of pembrolizumab as treatment for nonresectable melanoma, which would cost between $77 million and $181 million per year. Analysts estimate that by 2025, pembrolizumab could generate sales of about $6 billion. However, this estimate assumes pembrolizumab receives an additional indication as first-line treatment for advanced melanoma. Conversely, additional antibodies against PD-1 and PD-L1 are under clinical development and could receive FDA approval by 2025, which would decrease pembrolizumab's market share and revenue. |
| Radium-223 Dichloride (Xofigo) for Treatment of Solid Tumor Bone Metastases | Radium-223 was FDA approved recently and will be used in place of existing treatments in some patients and as an addition to treatment in other patients. Based on worldwide sales of $55 million per quarter, and assuming an even split between U.S. and non-U.S. sales and a cost of $69,000 per patient treated, we estimated that about 1,600 patients per year are currently treated with radium-223. We used this figure as the low end of the potential radium-223 adoption rate in the United States. For the high end, we estimated that 35% of patients with advanced prostate cancer with symptoms related to bone metastases will be treated with radium-223, which we estimated to be about 3,500 patients. Based on these assumptions, we estimated that adopting radium-223 would add between $69 million and $151 million to the annual cost of treating patients with prostate cancer in the United States. This is based on the assumption that 50% would use it as a replacement and 50% would use it as an adjunctive therapy. |
| Vismodegib (Erivedge) for Treatment of Advanced Basal Cell Carcinoma | FDA recently approved vismodegib for treating advanced basal cell carcinoma. Firm prevalence estimates of advanced basal cell carcinoma (BCC) are not available or formally tracked by the National Cancer; therefore, only estimates of BCC incidence and prevalence are available. A 2006 study suggested that about 2.2 million individuals would be diagnosed with nonmelanoma skin cancers in the United States each year, with about 1.8 million of these cancers being BCCs. Vismodegib's manufacturer estimated that about 28,000 patients in the United States could be eligible for treatment each year; however, it is unclear whether this estimate reflects the labelled indication, which requires locally advanced basal cell carcinoma to be ineligible for surgery or radiation therapy, or if it represents all patients with metastatic/locally advanced basal cell carcinoma. We estimated that approximately 1,500 to 2,000 patients with inoperable basal cell carcinoma would be treated with vismodegib in the United States each year. At a drug cost of about $9,000 per patient per month for 10 months, we estimated approximately $140 million to $180 million per year in costs of this new drug for the labeled indication. Vismodegib use in operable BCC has the potential to substantially increase the cost of vismodegib to the health care system; however, recent disappointing results in this setting suggest that this is unlikely to be an off-label treatment option in the near future and, therefore, we did not include these costs in our overall cost impact. |

**Table A-3. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: cardiovascular diseases priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 4. Catheter-Based Renal Denervation (Symplicity System) for Treatment-Resistant Hypertension | The Symplicity system is not FDA approved in the United States, but has been on the market in the European Union for a few years. A next-generation version of the device is in development in the United States. Based on potential initial adoption of about 10% (i.e., about 800,000 patients) of the eligible patient population the first year the technology would be available, at an estimated cost of $12,500 per case, the increase in short-term treatment costs would be about $10 billion plus facility costs to purchase and maintain Symplicity systems. Assuming a 50% decrease in the need for antihypertensive medications after catheter-based renal denervation, the estimated 1-year cost savings for antihypertensive pharmacotherapy for 800,000 patients could range from $153 million to $414 million. The overall cost-effectiveness of the technology will depend on whether it improves clinical outcomes compared with medical management alone. 2 cost-effectiveness models based on results from the Symplicity HTN-2 trial suggested that the procedure is a cost-effective strategy for treatment-resistant hypertension that might result in lower cardiovascular morbidity and mortality. Further study of cost-effectiveness is needed, because Symplicity HTN-3, a 530-patient, phase III trial intended to support an FDA premarket approval application for the Symplicity system, surprisingly failed to meet its primary efficacy endpoint. Nonetheless, development is continuing to identify and address the short-comings of the HTN-3 trial. |
| 5. Lomitapide (Juxtapid) for Treatment of Homozygous Familial Hypercholest-erolemia | FDA approved lomitapide in December 2012 for treating homozygous familial hypercholesterolemia (HoFH), a rare disease with an estimated prevalence of 1 of every 1 million people in the United States (i.e., about 316 people). Despite the availability of lipid-lowering pharmacotherapies, many patients with HoFH do not achieve acceptable lipid levels and remain at increased risk of having early coronary events, needing liver transplantation, and experiencing sudden death. The retail cost is about $29,000 per patient per month. Lomitapide would have to be taken daily for life by HoFH patients. We estimate the annual cost of treating 316 adults at about $110 million. Switching all patients from injectable mipomersen sodium, also approved for HoFH treatment, to oral lomitapide would increase drug costs by about $32 million a year. If lomitapide obviates the need for apheresis in 10% of this patient population, that savings will offset a small portion of the cost of lomitapide by about $8.9 million a year. After 20 months of treatment, lomitapide would be more costly than the half-million dollar cost of liver transplantation. |
| 6. Percutaneous Left Atrial Appendage Occlusion (Watchman) for Prevention of Atrial Fibrillation–Associated Stroke | The Watchman device is a permanent implant that is placed in the left atrial appendage (LAA) to prevent strokes in patients with atrial fibrillation (AF). Stroke prevention is accomplished by occluding the LAA opening to prevent clots that have formed in the LAA from entering circulatory system. The Watchman LAA Closure Technology consists of three components: a delivery catheter and transseptal access sheath, which is used to access the LAA and serves as a conduit for the delivery catheter; a self-expanding nitinol frame with a permeable polyester fabric that is preloaded within the delivery catheter; and fixation barbs on the frame that allow the device to be secured in the LAA. Once the device is expanded, the fabric covers the atrium-facing surface of the device. The device is not yet approved, but a premarket application is under review at FDA. About 1.1 million to 2.4 million (40%) of the estimated 2.7 million to 6.1 million patients who currently have AF have one or more contraindications to anticoagulants. About half of the patients with contraindications to anticoagulants (550,000 to 1.2 million) are at high risk of experiencing a stroke and could be eligible for an LAA closure procedure. If 10% (55,000 to 120,000) of these patients undergo the Watchman procedure in the first full year of its availability, at a cost of $20,000 each, the cost would be $1.1 billion to $2.4 billion.<br>Thereafter, about 160,000 new cases of AF are expected to be diagnosed each year, and if 40% (64,000) of these new cases have contraindications to anticoagulants, about 10% (6,400) might choose the Watchman device, which would cost about $128 million per year for the procedure and implant. |

**Table A-3. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: cardiovascular diseases priority area (continued)**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 7. Transcatheter Aortic Valve Implantation (CoreValve) for Treatment of Severe Aortic Stenosis | FDA recently approved CoreValve, the 2nd valve of this type to reach the U.S. market. Assuming that the CoreValve System captures about 20% of the projected TAVI market share of 20,350 implants expected to be sold in 2015, we estimated that CoreValve System will be used in 4,070 patients in that year. We estimated that about 75% of those 4,070 CoreValve procedures will be performed in inoperable patients (i.e., about 3,053 patients) and the other 25% will be performed in patients at high risk for surgical complications (i.e., about 1,017 patients). If 3,053 inoperable patients previously treated with medical therapy undergo transfemoral TAVI in 2015, the cost would be an estimated $165 million. If 1,017 patients at high risk for surgical complications undergo transfemoral TAVI rather than open surgery in 2015, overall 1-year costs may decrease by about $1 million. Several cost-effectiveness studies indicate that TAVI is likely to be cost-effective for patients ineligible for open aortic valve replacement; however, the cost-effectiveness in patients at high risk for open aortic valve replacement is still under debate. Although CMS has accepted a request to establish specific higher-paying DRGs for TAVI in 2015, Medicare reimbursement rates might not fully cover costs for the procedure, device, and hospitalization, and hospitals would have to absorb those costs, as they have been to this point. Also, for centers that are not equipped with a hybrid OR, infrastructure investments ranging between $3.5 million and $5 million would be required to construct and outfit a hybrid OR; these costs must be absorbed by the facility as general operating costs. |
| 8. Transcatheter Mitral Valve Repair (MitraClip) for Treatment of Mitral Regurgitation | FDA recently approved MitraClip for treatment of degenerative mitral valve regurgitation (MR), but not for functional mitral valve regurgitation. Performing transcatheter mitral valve repair in patients with degenerative MR who are ineligible for open mitral valve repair would likely increase short-term treatment costs. Estimated costs for performing 30,000 transcatheter mitral valve repairs are expected to be about $3.24 billion in 1 year (~$108,000 per patient for the procedure and first-year post-procedure costs, although costs could be higher depending on the number of MitraClip devices implanted—up to 4 are used in some procedures). However, if the procedure is safe and effective, substantive long-term cost savings would likely offset the first-year procedure and follow-up costs because of decreased need for medication, fewer emergency department visits, fewer hospitalizations for acute MR symptoms, and decreased mortality in this patient population. To date, no U.S. cost-effectiveness studies comparing transcatheter mitral valve repair with medical therapy have been published, but several are in clinical trials. Although CMS approved a new technology add-on payment for MitraClip System in fiscal year 2015 and announced that the agency will cover transcatheter mitral valve repair for functional MR under its Coverage with Evidence Development program, Medicare reimbursement rates might not cover the total costs for the procedure, device, and hospitalization Also, for centers that are not equipped with a hybrid OR, costs ranging between $3.5 million and $5 million to construct and outfit such an OR must be absorbed by the facility as a general operating cost. |

**Table A-4. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: dementia and Alzheimer's disease priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 9. Off-label Intranasal Insulin for Treatment of Alzheimer's Disease | Intranasal insulin is not FDA approved for treating Alzheimer's disease (AD), but has been under study for this indication, though not by a manufacturer. Thus, its use is off-label for this indication. If adopted, insulin could either replace some AD medication use or be used as an add-on therapy, thereby adding to costs of medical therapy. Assuming positive results from larger ongoing clinical trials, we anticipate that 520,000 to 1.3 million patients could initially use this intervention. If 3rd-party payers do not cover it, patients would bear the cost out of pocket, although the cost could be low relative to other drug therapies for AD. Based on projected per-patient costs between $375 and $3,750 annually, we estimated an initial overall cost impact of about $195 million to $4.9 billion annually on patients' out of pocket costs for those who choose this intervention. Ongoing clinical trials will clarify treatment protocols, including dosages and treatment initiation and duration; interactions with approved AD medications; how these interactions are affected by genetic markers or disease severity; and the extent, if any, of intranasal insulin's disease-modifying properties. |

**Table A-5. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: depression and other mental health disorders priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
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| 10. Deep Brain Stimulation (Reclaim DBS Therapy or Libra DBS) for Treatment-Resistant Depression | One manufacturer halted development of the Reclaim device for this indication; however, another manufacturer continues to develop the Libra device for this indication. We estimated initial adoption rates of 40,200 to 133,600 patients (2% to 4% of the population with treatment-resistant MDD). It is not yet FDA approved. Based on per-patient treatment costs between $60,000 and $80,000, we estimated use of DBS could cost $2.4 billion to $10.7 billion; but if proven effective, those costs could be offset over the long term if they obviate the need for other therapies that are required ongoing, including hospitalizations and other intensive care regimens. Comparatively, the National Alliance on Mental Illness estimates that depression accounts for $34 billion in direct and indirect workplace costs. |
| 11. Off-Label, Fast-Acting Drugs (Ketamine, Scopolamine) for Treatment-Resistant Bipolar Depression and Major Depressive Disorder | Our estimated initial adoption rates projected that between 822,000 and 2.2 million patients with treatment-resistant depression (TRD) could use ketamine or scopolamine for treatment-resistant depression. Adoption rates could increase if additional evidence of effectiveness accumulates and payers reimburse for use. In the immediate future, however, we expect patients would have to cover these treatment costs, unless 3rd-party payers reimburse on a case-by-case basis in the absence of a general coverage policy. Sales of oral anti-depressants have been falling over the past 10 years and are projected to continue declining to an expenditure of $6 billion by 2016 based on claims data from IMS and Thomson Reuters. These declines are attributable to generics and also lack of efficacy for TRD. However, costs of fast-acting drugs for TRD could mediate the decline in drug expenditures for depression. Based on annual per-patient treatment costs of between $2,100 and $5,000 for infusions of these medications, we estimated that use of these fast-acting antidepressant drugs could be $1.7 billion to $10.9 billion. The National Alliance on Mental Illness estimates that depression accounts for $34 billion in direct and indirect workplace costs annually. We note that, even if we underestimated ketamine and scopolamine adoption rates, their combined cost impact still represents a significant potential savings from current costs related to treatment-resistant depression. |

**Table A-6. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: developmental delays, ADHD and autism priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 12. Off-Label Intranasal Oxytocin for Treatment of Social Dysfunction in Autism Spectrum Disorders | Assuming positive results from larger ongoing clinical trials, we anticipate 930,000 to 1.39 million patients would initially adopt this intervention at a cost of $217 million to $1.1 billion per year, based on current pricing ($234 to $836 per patient per year) from markets outside the United States. These costs would be borne by patients or their caregivers unless 3rd-party payers reimbursed for this off-label use. Previously, health care experts calculated that treating ASD patients costs more than $35 billion annually. Oxytocin, if proven sufficiently effective, could reduce the need for ongoing behavioral therapy, which is a more costly treatment. |

**Table A-7. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: diabetes priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 13. Artificial Pancreas Device System (Medtronic MiniMed 530G® Low-glucose Suspend System with Enlite Sensors) for Treatment of Diabetes | A true artificial pancreas device system has not been FDA approved yet, but the first step in that direction was FDA approved in September 2013, a low-glucose suspend system with sensors. Based on potential adoption of the MiniMed 530G system with Enlite sensor in 2015 by an estimated 3%, or 27,525 people with type 1 diabetes mellitus, overall average patient costs to adopt the technology would be about $256 million, or an average of $9,300 per patient. About 95% of patients using pumps have private insurance and copays of up to 50% of the costs. Thus, patients and insurers would each bear a portion of the costs. This estimate does not include consideration of savings from positive health impacts if tighter blood glucose control is achieved and costs of treating complications are avoided; a formal cost-effectiveness analysis would be needed. The overall cost-effectiveness of the technology will depend on whether the integrated system improves clinical outcomes compared with other available methods of intensive insulin management. Marketing of competing systems and improvements in sensor technology will likely decrease overall costs. |
| 14. Fluocinolone Acetonide Implant (Iluvien) for Treatment of Diabetic Macular Edema | The Iluvien implant was FDA approved in September 2014. Assuming that the Iluvien implant will be used to provide an option for the 100,000 people with chronic diabetic macular degeneration (DME) who have not responded sufficiently to laser photocoagulation therapy and/or anti-VEGF drugs, health care costs to treat chronic DME could increase if the cost of the implant is similar to other intravitreal implants ($18,630 per implant for a total of $1.86 billion). These costs could be partially offset (by up to $955 million) because we assume that patients would not be receiving intravitreal injections of triamcinolone which would cost $27.4 million to treat 100,000 patients, and anti-VEGF drugs (i.e., ranibizumab), which cost about $955 million for 100,000 patients in a given year. If Iluvien proves to be a long-term efficacious solution to DME, the offset in costs could be greater because these other interventions are given each year, ongoing for up to several years, compared to Iluvien which is intended to last up to 3 years. |

**Table A-8. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: functional limitations priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 15. Eliglustat Tartrate (Cerdelga) for Treatment of Gaucher's Disease Type 1 | Gaucher's disease is a rare hereditary deficiency of glucocerebrosidase, which leads to enlarged and malfunctioning organs, skeletal disorders, and painful neurologic complications due to accumulation of glucocerebroside. Estimated prevalence has been reported as between 1 in 40,000 and 1 in 60,000. Based on a U.S. population of 316 million people, this suggests that between 5,300 and 7,900 persons are living with the disease in United States. Standard treatment is enzyme-replacement therapy (ERT). 3 ERTs for treating Gaucher's disease are available in the United States, but have unwanted side effects and/or inconvenient administration routes. Eliglustat tartrate is a new, orally administered therapy recently approved by FDA for use in all patients with Gaucher's disease, irrespective of ERT eligibility. We estimated that adoption of eliglustat would increase cost of care per year for this patient population by between $10 million and $16 million over other available therapies. This increase assumes that a proportion of patients will switch from other therapies (intravenous imiglucerase or miglustat) to this more convenient oral administration route, especially if it has a better side effect profile. |
| 16. Elosulfase Alfa (Vimizim) for Treatment of Morquio A Syndrome | Morquio A syndrome is a rare, potentially fatal metabolic disorder that primarily affects bone development. Patients with this syndrome may require multiple surgeries to alleviate posture, motion, and cardiovascular symptoms. Symptoms typically increase as the disorder progresses, and a patient's mobility may become significantly impaired; most adult patients with this disorder are reliant on wheelchairs. Elosulfase alfa (Vimizim™), a purified recombinant human N-acetylgalactosamine-6-sulfatase enzyme, is a treatment for patients with Morquio A syndrome that was approved recently by the U.S. Food and Drug Administration (FDA). Before the 2014 approval, no nonsurgical treatments existed for this disorder; therefore, elosulfase alfa has potential to meet an unmet need for nonsurgical interventions for patients with Morquio A syndrome. The U.S. prevalence of Morquio A syndrome is about 800–1,580 patients, with an estimated 13 to 20 new cases each year. The drug cost for a pediatric patient weighing 49 lb would be about $119,800 annually and the cost for an adult patient weighing 150 lb would be about $359,400 annually. According to the manufacturer, about 120—or 8% of the 1,500 U.S. patients eligible for treatment—were identified as of May 2014. The manufacturer expects elosulfase alfa revenue to be about $70 million in 2014. Assuming the U.S. market is responsible for 25% of the projected revenue, the U.S. could spend $17.5 million on elosulfase alfa in 2014 on the estimated 120 patients. Children with Morquio A syndrome are typically identified by 5 years of age and are often insured. Thus, sales of the drug in the United States will likely more than double in 2015, bringing the spending to about $43.5 million. If U.S. spending continues to account for about 25% of elosulfase alfa revenue and the manufacturer reaches its projected $800 million in elosulfase alfa sales globally by 2023, the U.S. could spend up to $200 million on the drug annually. |
| 17. Intraoral Tongue-Drive Computerized System to Aid Quadraplegic Patients in Maneuvering Electric Wheelchairs | The Tongue Drive System (TDS) is a computerized, assistive neurotechnology designed for integration with electrically powered wheelchairs. The technology is being developed and manufactured by Bionic Sciences and the Georgia Institute of Technology (both of Atlanta, GA), in collaboration with other national academic and medical institutions. TDS is intended for use by patients with quadriplegia. The technology consists of a titanium magnetic tracer/stud affixed to the patient's tongue, and a headset with magnetic field sensors located near the cheeks. TDS sensors detect tongue movement and wirelessly transmit output signals to a receiving device, such as a smartphone; these receiving devices then communicate with electrically powered wheelchairs. Receiving devices can also transmit information to a computer, allowing patients to perform daily tasks, while a standby mechanism enables additional functionality without using the TDS. Patients also must complete computer training so that the TDS software can properly interpret and calibrate their tongue movements. The technology is not yet FDA cleared for marketing. We estimated TDS's adoption rate to be between 6,975 and 14,940 patients annually. Based on developer statements, TDS could enter the U.S. health care market as early as 2015. At an anticipated price of $6,000 to $7,000 per patient, our estimated peak adoption rate represents a cost of $42 million to $105 million in 1 year. |

**Table A-8. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: functional limitations priority area (continued)**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 18. Ocriplasmin (Jetrea) for Treatment of Symptomatic Vitreomacular Adhesion Including Macular Hole | Jetrea was recently FDA approved. Average retail price is about $4,270 for a single-use vial (0.2 mL of 2.5 mg/mL ocriplasmin) injected by an ophthalmologist into the patient's eye. Ocriplasmin's reported total procedure costs are $9,000 to $11,000 per patient. Although industry analysts' peak sales projections initially suggested nationwide adoption rates approaching 139,000–153,000 patients annually, initial sales reports indicate that actual adoption rates fall short of these estimates with only 23% market penetration reported at present. Recent ECRI Institute searches of 11 representative, private, 3rd-party payers that publish their coverage policies online identified only 4 payers—Aetna, Blue Cross/Blue Shield Alabama, CIGNA, and Humana—with policies providing coverage for ocriplasmin use in treating symptomatic VMA. The U.S. Centers for Medicare & Medicaid Services has not issued a national coverage determination for ocriplasmin for symptomatic VMA; coverage is left to discretion of local carriers. We identified 14 local coverage determinations, although lack of a published policy does not mean ocriplasmin is not covered. Patients might bear some co-pay cost depending on their level of insurance coverage. Based on our estimated patient pool and the manufacturer's peak adoption rates, we calculate ocriplasmin's prospective population to be 7,000 to 17,600 patients annually. Given these estimates, this intervention's potential cost impact is between $63 million and $194 million per year, with costs carried in part by health insurers, Medicare, and patients co-pays. We also note that this potential impact could be lowered by concerns regarding reduced sales estimates, and ocriplasmin's treatment efficacy compared to the standard of care. |
| 19. Retinal Prosthesis System (Argus II) for Treatment of Retinitis Pigmentosa | Argus II is an FDA-approved implantable device intended to treat patients with severe retinitis pigmentosa. Based on available prevalence data, severe cases number 15,000 or fewer Americans. As of mid-2014, fewer than 10 patients had received the device since its approval, and fewer than 50 patients overall (including those in clinical trials) have received it, suggesting a limited overall cost impact on the health system. In October 2013, Medicare approved a new technology add-on payment (inpatient) and a transitional pass-through payment (outpatient) to facilitate payment; however this does not mean that local Medicare carriers necessarily provide coverage and reimbursement. There is no Medicare national coverage determination for the implant, so coverage is at the discretion of local carriers. Our searches of major 3rd-party payer coverage polices found few payers that cover artificial retinal devices for treating RP as of mid-2014; most consider it investigational. Those that do cover it require certain age and medical characteristics for coverage. As this technology matures and additional long-term safety and efficacy data are available, we anticipate 3rd-party payer coverage may expand. In the absence of coverage, patients will have high out-of-pocket costs for the technology. Given Argus II's listed cost of $115,000 to $145,000 for the procedure, as well as reported patient adoption rates of 5–10 patients yearly, we estimated a cost of $575,000 to $1.45 million per year, and assume that post-implantation fittings and trainings are included. If broader 3rd-party payer coverage becomes available, we conservatively project peak adoption rates of 50 to 200 patients annually at a cost of between $5.8 million and $29 million per year, with the majority of costs borne by payers and the remainder borne by patient co-pays. |

**Table A-8. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: functional limitations priority area (continued)**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 20. Pediatric Vision Scanner Screening for Strabismus or Amblyopia | As a diagnostic intervention, the potential overall cost impact of pediatric vision (PVS) screenings can be evaluated at direct and secondary levels. Direct per-patient PVS costs are anticipated to be comparable to available screening options. Considering our estimated provider adoption and patient utilization rates in the 3- to 5-year old population, we estimated that 600,000 to 1.5 million screenings per year would be conducted, at a cost of $10 to $25 per patient. We calculated direct patient costs of $6 million to $38 million annually. If the screening were applied to infants to 3-year-olds, the cost impact would be about double, or about $75,000,000. Based on diffusion of commercially available screening devices, we estimated peak provider adoption rates of 250 to 1,000 scanners purchased per year. If competitively priced against comparable devices, with an average price of $5,000, we estimated the PVS' peak direct provider cost impact to be $1 million to $5 million annually. Average annual provider costs are anticipated to be lower than this range, because the PVS and similar devices are designed for long-term use, with minor recurring maintenance costs. Secondary cost impacts for this intervention will originate from increased amblyopia detection, and associated patient treatment; these costs will be borne by patients and 3rd-party payers. Previously published cost-effectiveness studies note that if detected by age 3, amblyopia is often successfully treated by age 10, at an average annual cost of $1,240 per patient. The average amblyopia detection rate across all current pediatric screening methods is approximately 65%, while comprehensive eye exams detect 95% of amblyopia cases. Subsequently, 23% of screening-detected and 57% of comprehensive exam-detected amblyopia cases are successfully treated. If PVS screening is as effective as comprehensive eye exams, and is used to screen 600,000 to 1.5 million children annually, we estimated that PVS screening will detect 5,700 to 57,000 amblyopia cases, at current prevalence rates. These figures represent an additional 1,800 to 18,000 amblyopia cases compared with current pediatric screening. Assuming a median successful treatment rate of 40% for the 5,700 to 57,000 detected amblyopia cases at $1,240 each, we anticipate the PVS' annual average secondary cost impact to be $3 million to $28 million per year. |
| 21. RenalGuard for Prevention of Contrast-Induced Nephropathy | The RenalGuard System has been in development to reduce the risk of contrast-induced nephropathy (CIN) in patients with chronic kidney disease (CKD) or who have known risk factors for CIN and who need to undergo imaging that requires use of contrast media. No other treatment is available to prevent CIN. Assuming that 650,000 patients who are at risk of developing CIN after cardiac catheterization procedures, use of a $500 disposable RenalGuard device while undergoing a contrast imaging procedure would add $325 million to costs of the procedure, which would likely have to be absorbed by the institution performing the imaging examinations. However, these costs might be offset by the number of CIN cases prevented, but this would require more complex cost-effectiveness analysis that is beyond the scope of this report. On September 26, 2014, the developer of this technology for the U.S. market, PLC Medical Systems, merged with Viveve, and the RenalGuard business was sold to PLC's debt holder, which is calling the business RenalGuard Solutions. The debt holder is a subsidiary of Genesis Capital Advisors. While the CIN-RG RenalGuard pivotal trial was underway in the U.S. and was intended to support a regulatory filing with FDA, it is not clear at this time how further development will proceed under the debt holder. |

**Table A-8. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: functional limitations priority area (continued)**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 22. Wearable Battery-Powered Exoskeletons (ReWalk and Ekso Systems) to Enable Walking after Spinal Cord Injury | Each year, about 5,160 patients with a new diagnosis of incomplete or complete paraplegia may be candidates for a wearable powered exoskeleton as part of physical gait training in an institutional setting or for personal use in a community or home setting. Also, some of the estimated 116,000 patients living with incomplete or complete paraplegia may choose to be evaluated for wearable exoskeletons use. Powered exoskeletons are commercially available in FDA-cleared institutional and personal versions. The ReWalk Rehabilitation is available for rehabilitation centers (in the United States, European Union, and Israel) and ReWalk Personal for personal use (in the United States and European Union). The Ekso GT system is available for rehabilitation centers (in the United States, European Union, and South Africa) and a personal version was anticipated to be available in late 2014, according to the company. Purchase of wearable powered skeletons by 25 rehabilitation centers in 2015 would increase their equipment costs by an estimated $2 million to $3 million. Rehabilitation centers that currently own wearable powered exoskeletons will incur costs for service as warranties expire. If 1,400 patients purchase a system for personal use in 2015 as complements to their existing wheelchairs, estimated patient costs would increase by $97 million to $105 million; these devices are not a replacement for powered wheelchairs and are not expected to be reimbursed by 3rd-party payers. Data on the cost and health impact of long-term use of the technology are not yet available. |

**Table A-9. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: infectious disease priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 23. Antimicrobial Copper Surfaces in the Intensive Care Unit for Prevention of Hospital-Acquired Infections | Implementing antimicrobial copper surfaces to reduce hospital acquired infections (HAIs) requires capital investment, generally between a 10% to 30% increase in costs compared to items with standard surfaces in hospital patient rooms. However, based on published analyses available, the intervention is expected to be cost saving. The cost of converting about 15 item classes (surfaces such as bed rails, counters, sinks) in a 420-bed hospital is reportedly about $7,700 to $15,000 per room (about $3.2 million to $6.3 million for the entire renovation). If the intervention were confined to conversion of touch surfaces in critical care units, with about 70,000 adult intensive care beds (cardiac, medical/surgical, other ICUs and burn care) and 21,000 pediatric ICU beds (neonatal and pediatric) in the United States, the cost of conversion would range from about $637 million to $1.37 billion. Assuming a 5% HAI rate and a 20% reduction in HAIs after implementing copper surfaces, an annual cost savings that is as much as or slightly more than the investment could be realized. Thus, the renovation may be cost effective within 1 year, and could save as much as $66 million over 10 years. In some published reports, the cost of converting 6 item classes to antimicrobial copper surfaces in a 20-bed, single-patient-room ICU design was calculated to be cost effective in less than 2 months, assuming a 25% incidence of all HAIs and a 20% reduction in HAIs after copper surfaces were implemented. Copper surfaces could provide even greater reduction in HAIs: Salgado et al. (2013) reported patients in rooms with 6 items fitted with copper surfaces had 58% fewer HAIs than patients in rooms with standard surfaces. Smaller facilities or facilities with limited budgets can do some retrofitting. One 25-bed facility retrofitted 1,100 low-cost touch surfaces for a reported $7,000. HAIs add between $28 billion and $45 billion to annual U.S. health care costs. Contracting 1 of the 5 most common HAIs costs an additional $896 to $45,814 per case to treat, and the costs must be borne by the provider when the infection is contracted in the health care setting. If copper surfaces diffuse at a rate of 20% of U.S. hospitals and reduce HAI incidence by 20%, about $1.1 billion to $1.8 billion would be saved by health care facilities annually. If copper surfaces diffuse at a rate of 40% of hospitals and reduce HAI incidence by 58%, about $6.5 billion to $10.4 billion would be saved annually. |

**Table A-9. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: infectious disease priority area (continued)**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 24. Emtricitabine/Tenofovir (Truvada) for Prevention of HIV Infection | The U.S. Centers for Disease Control and Prevention (CDC) recommends pre-exposure prophylaxis (PrEP) for males who have sex with males (MSM) without using condoms; heterosexuals with partners at high risk (e.g., people who inject drugs or male bisexuals who have unprotected sex; people who regularly have sex with someone with confirmed HIV infection; and anyone who shares needles or injects drugs). If all people who are recommended to initiate PrEP did so, the number of emtricitabine/tenofovir prescriptions would increase from about 10,000 to 500,000 annually, according to one estimate. The per-patient cost would be about $16,440 per year. The total cost of providing PrEP from the current level of diffusion to all individuals recommended PrEP would increase from about $164 million to $8.2 billion, annually. If PrEP uptake reached a rate of 10% among the 500,000 persons recommended by the CDC to take it, it could cost about $822 million annually. In the absence of PrEP, about 491,800 new HIV infections are expected to occur during the next 20 years among MSM aged 13–64 years in the United States, revealed one dynamic model of HIV transmission combined with economic analysis. Assuming PrEP has a real-world efficacy of reducing HIV transmission by 44%, and if 20% of MSM in the United States took PrEP, about 13% of new infections (about 62,760 HIV infections) over the next 20 years would be prevented, compared with no change in HIV prevention policy. In the first year of widespread PrEP use among MSM, if 20%, 50% or 100% of MSM receive PrEP, HIV incidence would be reduced by 10%, 24%, and 45%, respectively. Preventing secondary HIV transmission with PrEP is expected to cause the percentage reduction in HIV incidence to increase over time. After 20 years, annual HIV incidence could be reduced by 17%, 37%, and 60% if 20%, 50%, and 100% of MSM received PrEP, respectively. Juusola and co-authors estimated that if PrEP was 44% effective and used by 20% of MSM over 20 years, it would cost an incremental $4.9 billion annually or $95 billion ($98 billion for PrEP minus $3 billion in savings related to HIV care) in lifetime health care–related costs compared with current prevention and treatment paradigms, or nearly $2 million per HIV infection prevented. However, the number they used for cost of PrEP ($776 for a 30-day supply) was much lower than current retail pricing of PrEP. Furthermore, if all MSM in the United States were to receive PrEP for 20 years, health care-related costs would increase by an estimated $480 billion. By targeting MSM who are considered at high risk for HIV infection, Juusola and associates suggest cost-effectiveness could be improved. Assuming 20% of MSM are at high risk (defined as having an average of five partners annually), an initial HIV prevalence of 20%, and an initial annual HIV incidence of 2.3%, the costs for 20% of high-risk MSM to take PrEP over 20 years would be about $828 million per year or $16.6 billion in total health care-related costs compared with current prevention and treatment paradigms, which would cost about $14.2 billion in total. PrEP in 20% of MSM at high risk could cost about $460,000 per infection prevented. If all high-risk MSM receive PrEP for 20 years, total incremental health care–related costs would increase by $76 billion compared with current prevention and treatment paradigms, or approximately $600,000 per HIV infection prevented. Some insurers cover PrEP, so costs and cost savings would be borne by 3rd-party payers, government assistance programs, and some uninsured patients. However, currently low uptake levels suggest that lack of awareness regarding HIV risk and potential cost barriers likely exist. Most long-term health care savings would be likely realized by 3rd-party payers and government assistance pograms. |

**Table A-9. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: infectious disease priority area (continued)**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
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| 25. Fecal Microbiota Transplantation To Treat Recurrent Clostridium Difficile Infection | As a 3rd-line therapy for recurrent *Clostridium difficile* infection (CDI), the estimated annual cost of performing fecal microbiota transplantation (FMT) would average a total of $188.6 million (98,000 cases at an average cost of $1,925 per case). The cost of 3rd-line treatment with the new antibiotic fidaxomicin (Dificid) would cost about $328.3 million ($3,350 per case), so FMT could save $139.7 million in direct treatment costs for 3rd-line therapy. 1st-line treatment with FMT could, if efficacious, save the cost of two courses of vancomycin (average per patient cost of $540 per 2-week regimen), one course of fidaxomicin ($3,350) and estimated costs of excess health care costs for hospital onset cases of CDI ($6,000 per case) that require at least three courses of CDI treatment. Thus, using FMT as 1st-line therapy could save about $8,500 per hospital onset case of recurrent CDI. If CDI incidence continues to increase as it has over the past 10 years at a rate of about 5% more cases per year, the number of candidates would also increase. For example, the overall expenditure for FMT as a 3rd-line treatment would increase by $48.1 million if 25,000 additional patients needed treatment in 1 year. These costs do not include adjustments for inflation. Although cost information is not yet available, oral microbiome-based therapeutics (i.e., capsules) being studied in clinical trials, may cost substantively less than existing FMT options. |
| 26. Interferon-free Oral Therapies for Chronic Hepatitis C Infection | At least 3.2 million Americans are living with chronic hepatitis C virus (HCV) infection (some estimates are as high as 5.7 million). Interferon (IFN)-free oral regimens available for treatment of HCV infection include sofosbuvir-based regimens (e.g., Harvoni® and simeprevir [Olysio™] with sofosbuvir) and a 3-drug (3-D) combination consisting of ABT450/ritonavir/ombitasvir/dasabuvir (Viekira™ Pak). These regimens are intended for treating genotype 1 HCV infection, the most prevalent genotype (i.e., affecting about 70% of patients). These and other combinations are also used for other HCV genotypes. FDA approvals for these new regimens have been given between December 2013 and 2014. Sofosbuvir was FDA approved in December 2013 for use with IFN and RBV; the sofosbuvir/ledipasvir combination (Harvoni) was FDA approved in October 2014 as the first IFN-free regimen, followed by ABT450/ritonavir/ombitasvir/dasabuvir (Viekira Pak) in December 2014. IFN-free regimens are for oral administration for 8 or 12 weeks depending on the regimen used and HCV genotype being treated. The retail costs of the IFN-free regimens range from about $83,300 to $94,500, although manufacturers were negotiating discounts with various payers at the time of our cost analysis.<br>The health care system is unable to accommodate providing treatment for all infected patients at the same time because of the limited number of clinicians available to treat and the financial resources needed to treat. An estimated 5% (about 160,000 patients) of HCV infected patients were expected to have been prescribed treatment in 2014 at a cost of more than $13 billion. The number being prescribed treatment is expected to increase further in 2015 with availability of new regimens and negotiated pricing discounts. Thus we estimated that an additional 8% (256,000) patients could be treated in the next year. If the cost of the interferon-free regimens are discounted by 20% from current lowest pricing to a cost of about $66,600 per patient, about $17 billion would be expended in 2015. |
| 27. OraQuick In-Home Rapid Test for Detection of HIV Infection | The OraQuick In-Home HIV Test is a rapid, home-based HIV test that is available without prescription, over the counter. It is intended to improve HIV-screening rates in people at risk of HIV exposure by removing barriers to screening. The test provides easy access to first-line testing that is affordable, safe, simple, rapid, painless, and anonymous. Assuming OraQuick could prevent 8,000 new HIV infections annually, and the annual cost of treating HIV is about $23,000 (in 2010 dollars), home-based HIV testing with OraQuick could reduce HIV treatment costs in the United States by about $184 million annually. Assuming a population of individuals who regularly engage in high-risk activities has an HIV prevalence of about 3.6%, which numbers about 111,111 people, and each individual uses the OraQuick kit twice annually, it would cost about $9 million out-of-pocket for home testing kits. According to the manufacturer, about 9,000 new HIV carriers would be identified for every 1 million people who use the test. For an estimated 8,000 infections to be detected, about 888,900 people would need to be tested, resulting in about $36 million in out-of-pocket costs for home HIV testing. |

**Table A-9. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: infectious disease priority area (continued)**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 28. Retrofitted Private Intensive Care Rooms To Reduce Hospital-Acquired Infections | On average, HAIs add an estimated 19.2 hospital days and $43,000 in additional costs for each patient who contracts one. Assuming a 30-bed ICU with an infection rate of 10% and an admission rate of 40 patient stays per bed per year, the unit will have about 120 HAIs annually. Those infections would add more than $5 million in costs and 2,300 additional days in length-of-stay (LOS). Results from a trial conducted in Montreal, Quebec, Canada, suggested that renovating ICU rooms to single-patient rooms reduced the adjusted combined rate of *C. difficile*, vancomycin-resistant *Enterococcus* species, and methicillin-resistant *Staphylococcus aureus* acquisition by 54%. Patients in renovated, private ICU rooms had a 10% reduction in the adjusted LOS compared with LOS for patients treated in the ICU before the renovation. Using these figures, a 10% reduction in LOS (and approximate total cost of HAI) would save the 30-bed ICU $520,000 per year. If the reduction in bacterial infections is closer to the 54% reduction in bacterial infections observed in the Montreal study, about $3 million could be saved annually, which could make the renovations cost saving in about 3–5 years. There are about 6,000 ICU units with about 91,000 beds in U.S. hospitals. Some researchers purport that building single-patient ICU rooms can cost millions of dollars, and the renovation may not be cost-saving for several years. According to one estimate provided by ECRI Institute's Applied Solutions group, which assists hospitals in building and renovation planning and construction, the cost of all capital medical equipment items for a single ICU room is about $270,000; construction costs would be additive. If we assumed that half the 91,000 ICU beds needed to be converted to single-patient ICU rooms, the costs for equipment alone could be about $12.3 billion (45,500 rooms at $270,000 each for equipment). Such conversions would not likely all take place in 1 year—but over several years as ICUs are converted. Whether other, much less costly interventions such as copper surfaces in hospital rooms can achieve similar reductions in HAIs needs more study to determine the most cost-effective hospital room design approach for reducing HAIs. |
| 29. Xpert MTB/RIF Test for Simultaneous Detection and Drug-Sensitivity Testing of Mycobacterium Tuberculosis | The *Mycobacterium tuberculosis*/rifampicin test (Xpert MTB/RIF) is a nucleic acid–based test run on the GeneXpert real-time polymerase chain reaction (PCR) system. The test simultaneously detects the presence of *M. tuberculosis* complex species and determines whether the identified bacterium is susceptible to rifampicin, the first-line TB drug. Assuming that about 20% of patients suspected of having TB test positive with microscopy or molecular methods, and 9,582 cases of TB were reported in the United States in 2013, about 47,900 patients in the United States may be suspected and tested for TB annually. Assuming about 10% of TB tests in the United States are performed with Xpert MTB testing at a cost of $98 per test, about $470,000 could be spent on Xpert MTB testing in the United States annually, once GeneXpert testing has been established at regional care centers. |

**Table A-10. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: obesity priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 30. Controlled-Release Phentermine/ Topiramate (Qsymia) for Treatment of Obesity | Controlled-release phentermine/topiramate (Qsymia) combines the appetite suppressant phentermine (approved for short-term weight loss) and topiramate (an approved antiepileptic agent with known weight-loss side effects). It is a controlled-release pill that is intended to be taken once daily and in trials reportedly resulted in more weight loss by more patients than other available antiobesity drugs. The approved dosage is phentermine 3.75 mg/topiramate 23 mg extended release for 14 days followed by phentermine 7.5 mg/topiramate 46 mg extended release daily. The overall weight-loss drug market is about 100 million in the United States, but given historical use of weight loss drugs, only a small minority of eligible patients opt to take a long-term weight loss drug. However, if 1% of eligible patients were prescribed a long-term weight loss drug, this would represent 1 million treated patients (approximately 12 million 30-day prescriptions per year). A 30-day supply of phentermine/topiramate (7.5 mg/46 mg daily) costs an average of $211). At this price, the cost of 1 year of phentermine/topiramate treatment would be about $2,530. The manufacturer reported that about 121,000 phentermine/ topiramate prescriptions were filled in the first quarter of 2014, in an unspecified mix of first-time and refill prescriptions. If about 1/3 of 1 million patients (333,000) were prescribed phentermine/topiramate for 1 year, the direct drug cost for patients who have to pay out of pocket for the entire cost would be about $842 million per year for phentermine/topiramate. Some health insurance drug prescription plans are starting to pay for antiobesity drugs, and thus costs would be shared between patient co-pays for a brand name drug and the remaining cost paid by the insurer. |
| 31. Liraglutide (Saxenda) for Treatment of Obesity | Liraglutide is a synthetic analog of the peptide hormone glucagon-like peptide-1 (GLP-1) that has been shown to suppress appetite and energy intake and delay gastric emptying, which may induce a feeling of satiety. The drug was FDA approved for treatment of type 2 diabetes in 2010, and was FDA approved for treating obesity in late December 2014. Liraglutide is administered once daily via subcutaneous injection using an automatic injection pen. Patients who opt for treatment with liraglutide would generate an incremental cost associated with liraglutide treatment (approximately $12,100 per year). About 100 million individuals in the United States meet the criteria for treatment with liraglutide or other antiobesity drugs, but only a small fraction of these patients are expected to try treatment with liraglutide because other weight loss drugs are available that do not require injection. Even if just 1% of eligible patients (approximately 1 million individuals) were prescribed a weight loss drug, and if liraglutide captured 1/3 of those patients (333,000), the cost would be about $4 billion per year. Some of this cost could be offset by improved weight control and reduction in health costs associated with being overweight or obese. Additionally, the cost could be offset if a substantial proportion of those patients opting for use of liraglutide for weight loss already require treatment for type 2 diabetes. Relative to the 1-year cost of other antiobesity drugs, which are oral, liraglutide would be about 4 times as expensive unless pricing for its use for treating obesity is different from its pricing for diabetes indications. |

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 32. Lorcaserin (Belviq) for Treatment of Obesity | Lorcaserin is an FDA-approved oral therapy intended for use in conjunction with diet, exercise, and behavior modifications in patients who are overweight or obese. Lorcaserin was FDA approved for use with a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial BMI of 30 $kg/m^2$ or more (obese), or 27 $kg/m^2$ or greater (overweight) in the presence of at least one weight related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes mellitus). Lorcaserin is administered at a dosage of 10 mg twice daily. Patients who do not achieve at least 5% weight loss after 12 weeks taking the recommended dose should discontinue treatment.[2] Lorcaserin is intended to be administered ongoing. Recent retail pricing for a 30-day supply (10 mg daily) averaged $222. At this price, the cost of 1 year of lorcaserin treatment would be about $2,640. In a phase III trial, only 55% of patients randomly assigned to receive lorcaserin completed a full year of therapy (compared to 45% of patients randomly assigned to placebo). Therefore, the per-patient cost for individuals initiating lorcaserin therapy will likely be lower than that for a full year's treatment. 110,000 lorcaserin prescriptions were filled in the second quarter of 2014, which represents an unspecified mix of first-time and refill prescriptions. The overall weight-loss drug market is about 100 million in the United States, but given historical use of weight loss drugs, only a small minority of eligible patients opt to take a long-term weight loss drug. However, if 1% of eligible patients were prescribed a long-term weight loss drug, this would represent 1 million treated patients. Lorcaserin competes with at least 3 other long-term prescription weight-loss drugs (i.e., orlistat, phentermine/topiramate, bupropion/naltrexone) and potentially up to four drugs (pending approval of liraglutide). If lorcaserin captured one-third of this potential market, the cost would be about $887 million annually. But if half of patients stopped taking it at some point during the year, the cost would be lower, although they might switch to an alternate antiobesity drug. |

**Table A-11. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: peptic ulcer and bowel disease priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 33. PerOral Endoscopic Myotomy for Treatment of Esophageal Achalasia | Peroral endoscopic myotomy (POEM) is a novel endoscopic surgical procedure that uses a natural orifice in the patient as an entry point for surgical instruments, with the intention of reducing the total number of incisions needed, thus reducing the overall invasiveness of surgery for treating esophageal achalasia. A retrospective cost comparison study by researchers at The Ohio State University, compared costs of POEM, laparoscopic Heller myotomy, and pneumatic dilation. The reported cost for POEM was about $41,700. They reported that standard laparoscopic Heller myotomy was about $15,500 less costly. We estimated that if 400 of the 2,000 patients undergoing surgery adopted POEM for treating esophageal achalasia, it would cost about $16,680,000 but save about $6.2 million overall in a given year by having this procedure instead of laparoscopic Heller myotomy. However, more data on patient outcomes would be needed to know whether POEM is as safe and effective as laparoscopic Heller myotomy in both the short and long term. |
| 34. Teduglutide (Gattex) for Treatment of Short Bowel Syndrome | Teduglutide was recently FDA approved to treat short bowel syndrome (SBS) intended to provide several critical actions throughout the gastrointestinal tract for treating SBS. Estimates of prevalence of SBS are difficult to make and, not well studied or reported in the literature. SBS purportedly affects males and females about equally. Most estimates are based on data describing patients requiring long-term home parenteral nutrition (PN) for SBS. According to the manufacturer, the addressable population in the United States for teduglutide use is a portion of the SBS population, or an estimated 3,000 to 5,000 patients with SBS. According to one online New York State registered pharmacy, RxUSA Pharmacy, the retail price of teduglutide is $30,000 for a 30-day supply, or about $360,000 annually per patient. The annual cost for 5,000 patients would be about $1.8 billion and its use would not obviate the need for PN for many patients. |

**Table A-12. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: pulmonary disease priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 35. Ivacaftor (Kalydeco) for Treatment of Cystic Fibrosis in Patients with G551D-CFTR Mutation | Patients with cystic fibrosis (CF) have various mutant alleles of the cystic fibrosis transmembrane conductance regulator (CFTR) protein. These mutant CFTR versions can be grouped into three general classes: proteins that are defective in proper subcellular trafficking to the cell membrane, in gating or ion and fluid flow, and in both trafficking and gating/flow. Ivacaftor was recently FDA approved and is a CFTR modulator that improves the function of the *CFTR* gene by targeting the defective protein that causes CF. The drug is intended as 1st-line treatment for the 4% (1,260) of patients with CF who have the G551D mutation in the United States. If all patients with the G551D mutation receive ivacaftor at the retail cost of about $324,600 per patient annually, about $409 million would be spent on ivacaftor in the United States annually. In 2013, ivacaftor sales were $371.3 million; which suggests that about 1,140 patients were treated and that ivacaftor had diffused to about 90% of the intended patient population in 2013. Most of these costs would be charged to third-party payers, because 99% of patients with CF have health insurance. If ivacaftor were to be approved for treating patients with another mutation for which it is under study, the F508del mutation, ivacaftor could be prescribed to about 87% of CF patients, or about 26,100 people. According to one estimate, if ivacaftor were approved for use in combination with another CF drug in development, lumacaftor, for treating patients with the F508del mutation, the price for the combination, estimated at about $150,000 to $200,000 per patient, would be lower than the current price of ivacaftor alone. This would cost the health care system between about $3.9 billion and $5.2 billion annually for use of both drugs, assuming 100% diffusion. If ivacaftor is shown to reduce the rate of hospitalizations, some of its costs could be offset, because the average annual cost of a hospital stay for a child with CF is about $109,000. |
| 36. Portable Warm Blood Perfusion System (Organ Care System) for Lung Transplantation | Only about 10% to 30% of donated lungs are considered to be suitable for transplantation, and in 10% to 20% of patients who have undergone lung transplantation, donor lungs have been so severely damaged by the time of transplantation, that the patient requires additional supportive therapies (i.e., ventilation, pharmacologic interventions). The Organ Care System (OCS) Lung is an investigational device in the United States (though approved for marketing in several other countries). It is an integrated and portable ex-vivo lung perfusion system intended to assess and improve marginal lungs and potentially to preserve or improve the condition of routine donor lungs by maintaining lungs in a warm, perfused state until transplantation. In 2012, 1,754 lung transplantations were performed in the United States with 1,616 patients awaiting transplantation on the national waiting list. The number of transplantations performed was limited by the number of suitable donor lungs available. Warm perfusion donor lung preservation could double the number of lung transplants available per year, enabling all patients on the waiting list in a given year to receive a lung transplant (about 3,370 transplantations). If 3,370 lung transplants were performed and 100% of procedures used the OCS Lung, equipment and service costs would be about $27 million for all 61 centers plus $151.6 million for the disposable sets used for 3,370 lung transplants (i.e., assuming all patients on the wait list receive a transplant) for an overall total of $178.6 million. The OCS developer has some volume discounts for purchasing perfusion sets to enable centers to have the OCS console at no cost. In this scenario, the cost of the sets and service would total about $163.8 million for 3,370 lung transplants. Estimates of impact on downstream, post-transplant costs of care and outcomes would require much more in-depth, complex cost modeling. |

**Table A-13. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: substance abuse priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 37. Community-Based Opioid Overdose Prevention Program (Project Lazarus) | Initiated in Wilkes County, NC, in 2008, Project Lazarus is a coordinated, community-based, integrative opioid-overdose prevention program and care model. It is designed to operate as a secular, nonprofit public health organization based on five central tenets: 1) activating the community and building coalitions, 2) monitoring and analyzing epidemiologic health data, 3) preventing overdose through medical education and other means, 4) providing community members with naloxone kits to reverse overdoses, and 5) regularly evaluating and adjusting project components. After successful implementation in Wilkes County, this program was expanded across North Carolina. Costs per year for nationwide implementation of this program cannot be calculated with available data. This intervention's potential costs depend, in part, on the perceived patient need and the degree of infrastructure required to support component services in a given geographic area. We can assume that in locales where opioid abuse rates are higher, program costs will be higher; additionally, costs during implementation and large-scale expansion periods may be greater than average costs for maintaining stable operating levels. Project Lazarus annual operating costs have not been published. However, a similar statewide program, Massachusetts' OEND project, published some operating cost data. In a separate report published by the Agency for Healthcare Research and Quality, OEND reported estimated annual total operating costs of $300,000, which excluded costs for community-level staff. Although similar in approach and implementation, the OEND project's potential patient population is less than 70% that of Project Lazarus. Given comparable listed costs and projecting additional expenses based on larger and more-developed infrastructure, we estimated Project Lazarus' potential overall cost to be between $430,000 and $850,000 per year in the area in which it operates. We expect that these costs would be offset by decreased costs from reduced emergency room visits and hospitalizations for overdoses, but these more complex analyses are beyond the scope of this rapid cost analysis. We also note that costs for Project Lazarus are carried entirely by private donors and public agencies providing public health services through financial, material, and personnel donations. |
| 38. Evzio for Emergency Treatment of Opioid Overdose by Nonclinicians | Evzio™ (kaléo, Inc., Richmond, VA) is a naloxone auto-injector, intended to rescue individuals who have experienced an opioid overdose. It is intended for use by nonmedical people, i.e., laypersons, in an administration manner that is similar in some ways to an Epipen. The single-use device is designed to deliver 0.4 mg naloxone, a dose typically used by medical professionals to reverse known or suspected opioid overdoses. FDA approved Evzio in April 2014 for emergency treatment of known or suspected opioid overdose and it became commercially available in August 2014. Overdose is characterized by respiratory system depression, central nervous system depression, or both. We estimated a potential national at-risk population between 665,000 and 836,000 patients annually who could experience an opioid overdose. As the only naloxone formulation FDA-approved for layperson use, Evzio could potentially have moderate to high peak adoption rates among patients, people in their support system, and even clinicians. However, peak adoption will depend highly on having clinicians who recommend it and write a prescription for its use. We anticipate that wide diffusion would need to be driven by clinicians prescribing Evzio to patients concurrently with prescribing higher doses of opioids for long-trerm pain relief, patients known to abuse opioids, or people known to be in close contact with patients at increased risk for opioid overdose. Because overdose is an acknowledged national public health issue, additional diffusion could potentially be propelled by initiatives mandating concomitant Evzio prescriptions for these same patient groups. We estimated Evzio's peak adoption rate to be between 66,500 and 293,000 patients annually, with the understanding that most people acquiring Evzio may never need to use it. Growing pressure to expand generic naloxone kit access (i.e. kits now used by emergency medical technicians, law enforcement, and community antiopioid abuse programs), an in-development intranasal naloxone spray, and social stigma associated with opioid abuse could all limit this intervention's adoption. At a current price of $588 to $636 per carton, our estimated peak adoption represents an approximate potential annual spend of $39.1 million to $186.4 million. Given the Evzio manufacturer's proposed prescription copayment assistance program and third-party payer coverage, the true direct cost impact for patients could be far lower. |

**Table A-14. Summary of 1-year health care spend estimates of December 2013 and June 2014 moderate- and high-impact topics: cross-cutting priority area**

| Intervention | Estimated Annual Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 39. Senior Specific Emergency Departments | The proportion of the U.S. population that is elderly is increasing each year, and emergency departments (EDs) are seeing more individuals aged 65 years or older seeking care. However, EDs are typically not optimally equipped to handle this population's unique needs. The ED's physical layout may pose a risk of falls for elderly patients, narrow and thin mattresses increase the risk of developing pressure ulcers, fluorescent lights and a lack of windows foster disorientation in cognitively impaired older adults, and noise pollution from alarms, staff, and patients contributes to communication difficulties in elderly patients who may be more likely to have hearing impairment than younger patients. Thus, since the advent of the first reported senior-specific ED in 2008, more health systems have been building or renovating EDs targeted just to seniors. The prevalence of senior-specific EDs is steadily growing because of the health care reform law's rules on readmissions, reported improvement in patient satisfaction and anticipated increased use of emergency services by the aging population. Costs to renovate an existing or construct a new senior-specific ED can range from $150,000 to several million dollars, depending on the number of beds, retrofitted and structural modifications, and new processes, protocols and staffing required. However, these costs might be offset by reduced admissions and return visits to the ED, reduced adverse events, and improved health outcomes. Two of the earliest adopters have reported significant decreases in geriatric hospital admissions from the ED after creating senior-specific EDs. Given the mean cost of a U.S. hospital admission is $10,000, reducing unnecessary admissions in the Medicare population could significantly decrease overall costs for Medicare and hospitals. Estimated direct savings attributed to fewer geriatric admissions in the year after creating a senior-specific ED may range from $29,000/100 visits to $82,000/100 visits, according the small amount of recently reported data from institutions tracking and publishing their data. Costs per year for nationwide implementation of senior EDs cannot be calculated because of the wide number of variables that affect the cost of their renovation or construction. |

**Table A-15. Aggregate annual estimated costs of potential high-impact interventions (December 2013 and June 2014)**

| Priority Area | Topic | Intervention Category | High-End Estimate (estimated annual cost at estimated adoption rate) | Low-End Estimate |
|---|---|---|---|---|
| **Arthritis** | Artificial Cervical Disc (Mobi-C) for Treatment of Two-Level Degenerative Disc Disease | Implant | $34,400,000 | $34,400,000 |
| | Autologous Mesenchymal Stem Cells for Treatment of Knee Osteoarthritis | Procedure | $685,000,000 | $228,000,000 |
| | Autologous Platelet-Rich Plasma Therapy for Osteoarthritis | Procedure | $147,000,000 | $147,000,000 |
| **Cancer** | Ado-Trastuzumab Emtansine (Kadcyla) for Advanced HER2-Positive Breast Cancer | Pharmaceutical | $413,000,000 | $321,000,000 |
| | Automated Breast Ultrasound (Invenia Automated Breast Ultrasound System, Formerly Called somo•v) for Screening Dense Breast Tissue | Diagnostic device | $1,200,000,000 | $720,000,000 |
| | Enzalutamide (Xtandi) for Treatment of Metastatic Castration-Resistant Prostate Cancer | Pharmaceutical | $868,000,000 | $868,000,000 |
| | Everolimus (Afinitor) for Treatment of Advanced Estrogen Receptor–Positive Breast Cancer | Pharmaceutical | $2,300,000,000 | $1,200,000,000 |
| | Ibrutinib (Imbruvica) for Treatment of Chronic lymphocytic leukemia | Pharmaceutical | $761,200,000 | $761,200,000 |
| | Ibrutinib (Imbruvica) for Treatment of mantle cell lymphoma | Pharmaceutical | $127,200,000 | $127,200,000 |
| | Idelalisib (Zydelig) for Treatment of Non-Hodgkin's Lymphomas | Pharmaceutical | $698,000,000 | $417,000,000 |
| | MarginProbe System for Intraoperatively Identifying Positive Margins During Breast Cancer Lumpectomy | Diagnostic device | $24,000,000 | $10,000,000 |
| | Ovarian Tissue Cryopreservation for Fertility Preservation in Women Undergoing Gonadotoxic Cancer Treatment | Procedure | $1,200,000,000 | $1,200,000,000 |
| | Pembrolizumab (Keytruda) for Treatment of Advanced Melanoma | Pharmaceutical | $181,000,000 | $77,000,000 |
| | Pertuzumab (Perjeta) for Advanced HER2-Positive Breast Cancer | Pharmaceutical | $2,000,000,000 | 1,600,000,000 |
| | Radium-223 Dichloride (Xofigo) for Treatment of Solid Tumor Bone Metastases | Pharmaceutical | $243,000,000 | $81,000,000 |
| | Vismodegib (Erivedge) for Treatment of Advanced Basal Cell Carcinoma | Pharmaceutical | $180,000,000 | $140,000,000 |
| **Cardiovascular Disease** | Catheter-Based Renal Denervation (Symplicity System) for Treatment-Resistant Hypertension | Therapeutic device | $1,000,000,000 | $500,000,000 |
| | Lomitapide (Juxtapid) for Treatment of Homozygous Familial Hypercholest-erolemia | Pharmaceutical | $110,000,000 | $110,000,000 |
| | Percutaneous Left Atrial Appendage Occlusion (Watchman) for Prevention of A-Fib-related Stroke | Therapeutic device | $2,400,000,000 | $1,100,000,000 |

**Table A-15. Aggregate annual estimated costs of potential high-impact interventions (December 2013 and June 2014) (continued)**

| Priority Area | Topic | Intervention Category | High-End Estimate (estimated annual cost at estimated adoption rate) | Low-End Estimate |
|---|---|---|---|---|
| | Transcatheter Aortic Valve Implantation (CoreValve) for Treatment of Severe Aortic Stenosis | Implant | $438,750,000 | $438,750,000 |
| | Transcatheter Mitral Valve Repair (MitraClip) for Treatment of Mitral Regurgitation | Implant | $3,240,000,000 | $3,240,000,000 |
| **Dementia** | Off-label Intranasal Insulin for Treatment of Alzheimer's Disease | Off-label drug | $4,900,000,000 | $195,000,000 |
| **Depression** | Deep Brain Stimulation (Reclaim DBS Therapy or Libra DBS) for Treatment-Resistant Depression | Implant | $10,700,000,000 | $2,400,000,000 |
| | Off-Label, Fast-Acting Drugs (Ketamine and Scopolamine) for Treatment-Resistant Bipolar Depression and Major Depressive Disorder | Off-label drug | $10,900,000,000 | $1,700,000,000 |
| **Developmental Disorders, ADHD, Autism** | Off-Label Intranasal Oxytocin for Treatment of Social Dysfunction in Autism Spectrum Disorders | Off-label drug | $1,100,000,000 | $217,000,000 |
| **Diabetes** | Artificial Pancreas Device System (Medtronic MiniMed 530G® Low-glucose Suspend System) for Treatment of Diabetes | Implant | $256,000,000 | $256,000,000 |
| | Fluocinolone Acetonide Implant (Iluvien) for Treatment of Diabetic Macular Edema | Drug/device combo | $1,860,000,000 | $1,860,000,000 |
| **Functional Limitations** | Eliglustat Tartrate (Cerdelga) for Treatment of Gaucher's Disease Type 1 | Pharmaceutical | $262,500,000 | $262,500,000 |
| | Elosulfase Alfa (Vimizim) for Treatment of Morquio A Syndrome | Pharmaceutical | $43,500,000 | $43,500,000 |
| | Intraoral Tongue-Drive Computerized System to Maneuver Electric Wheelchairs | Therapeutic device | $105,000,000 | $42,000,000 |
| | Ocriplasmin (Jetrea) for Treatment of Symptomatic Vitreomacular Adhesion Including Macular Hole | Pharmaceutical | $194,000,000 | $63,000,000 |
| | Retinal Prosthesis System (Argus II) for Treatment of Retinitis Pigmentosa | Implant | $29,000,000 | $5,800,000 |
| | Pediatric Vision Scanner Screening for Strabismus or Amblyopia | Diagnostic device | $75,000,000 | $38,000,000 |
| | RenalGuard for Prevention of Contrast-Induced Nephropathy | Therapeutic device | $325,000,000 | $325,000,000 |
| | Wearable Battery-Powered Exoskeletons (ReWalk and Ekso Systems) for Rehabilitation Centers and Home Use to Enable Walking after Spinal Cord Injury | Therapeutic device | $105,000,000 | $97,000,000 |
| **Infectious Disease** | Antimicrobial Copper Surfaces in the Intensive Care Unit for Prevention of Hospital-Acquired Infections | Device | $1,370,000,000 | $ 637,000,000 |
| | Emtricitabine/Tenofovir (Truvada) for Prevention of HIV Infection | Pharmaceutical | $8,200,000,000 | $822,000,000 |

**Table A-15. Aggregate annual estimated costs of potential high-impact interventions (December 2013 and June 2014) (continued)**

| Priority Area | Topic | Intervention Category | High-End Estimate (estimated annual cost at estimated adoption rate) | Low-End Estimate |
|---|---|---|---|---|
| | Fecal Microbiota Transplantation To Treat Recurrent Clostridium Difficile Infection | Procedure | $188,600,000 | $188,600,000 |
| | Interferon free all oral regimens for HCV infection | Pharmaceutical | $17,000,000,000 | $17,000,000,000 |
| | OraQuick In-Home Rapid Test for Detection of HIV Infection | Dx blood test | $36,000,000 | $36,000,000 |
| | Retrofitted Private Intensive Care Rooms To Reduce Hospital-Acquired Infections | Infrastructure | $12,300,000,000 | $12,300,000,000 |
| | Xpert MTB/RIF Test for Simultaneous Detection and Drug-Sensitivity Testing of *Mycobacterium tuberculosis* | Dx blood test | $470,000 | $470,000 |
| **Obesity** | Controlled-Release Phentermine/Topiramate (Qsymia) for Treatment of Obesity | Pharmaceutical | $842,000,000 | $842,000,000 |
| | Liraglutide (Saxenda) for Treatment of Obesity | Pharmaceutical | $4,000,000,000 | $4,000,000,000 |
| | Lorcaserin (Belviq) for Treatment of Obesity | Pharmaceutical | $887,000,000 | $887,000,000 |
| **Peptic Ulcer** | PerOral Endoscopic Myotomy for Treatment of Esophageal Achalasia | Surgery | $16,680,000 | $16,680,00 |
| | Teduglutide (Gattex) for Treatment of Short Bowel Syndrome | Pharmaceutical | $,800,000,000 | $1,800,000,000 |
| **Pulmonary** | Ivacaftor (Kalydeco) for Treatment of Cystic Fibrosis in Patients with G551D-CFTR Mutation | Pharmaceutical | $409,000,000 | $409,000,000 |
| | Portable Warm Blood Perfusion System (Organ Care System) for Lung Transplantation | Therapeutic device | $163,800,000 | $163,800,000 |
| **Substance Abuse** | Evzio for Emergency Treatment of Opioid Overdose by Nonclinicians | Drug/device combo | $186,400,000 | $39,100,000 |
| | Lazarus Opioid Overdose Prevention/Treatment Program | Program | No cost estimate provided | No cost estimate provided |
| **Cross-cutting** | Senior-specific Emergency Departments | Infrastructure | No cost estimate provided | No cost estimate provided |
| | **Total estimated annual costs of these therapies** | | **$96,505,000,000** | **$59,967,000,000** |

**Table A-16.Truven Health cost model cancer topic**

| Intervention | Estimated Cost of New Treatment for Estimated Adoption Rate |
|---|---|
| 1. Margin Probe System for Achieving Clear Margins during Lumpectomy | Margin Probe is used intraoperatively during lumpectomy to achieve clear tumor margins in an effort to avoid second re-excision surgeries. We adopted a conservative estimate of 100,000 women undergoing lumpectomy each year. The cost of MarginProbe to the entire health care system from the payer's perspective will depend on several factors: whether payers start to reimburse hospitals separately when MarginProbe is used (they do not now reimburse for its use); how widely the device is used; and the proportion of individuals insured privately, by Medicaid, or by other sources. We will assume the moderate figure of 25 percent market share for MarginProbe. Any change to that figure will linearly raise or lower the total by the same proportion.<br>The case of MarginProbe is very unusual among new medical technologies because it does not change the course of follow-up care beyond re-excision, nor life expectancy. This leaves a simple trade-off between cost and the probability of re-excision. The net cost or savings associated with MarginProbe comes from three elements:<br>• An absolute reduction in re-excision rate between 5 and 21 percentage points with a middle figure of 7.1 points<br>• The savings associated with avoiding re-excision surgery, which is approximately $10,065 for privately insured individuals and $1,643 for people on Medicaid<br>• After the initial purchase price of $40,000, we assume a cost of $1,020 per patient for disposables. MarginProbe's cost to payers is currently zero; we could find no evidence that public or private insurers cover it. Providers are therefore purchasing it at their own expense. If payers decide to reimburse some part of that cost in future after more evidence accumulates, then provider costs would decline commensurately.<br>Multiplying the clinical benefit (a 7.1% effect or 0.071) by the associated savings yields a savings-per-use in original lumpectomies of $715 for privately insured individuals and $117 for those covered by Medicaid. At present, when payers do not reimburse hospitals for MarginProbe, payers receive this net savings. In the future providers, may be able to negotiate a payment for MarginProbe based on savings enjoyed by payers. Depending on their insurance coverage and whether re-excision is required, patients could pay more or less in the long run with MarginProbe.<br>If insurers reimburse hospitals $1,020 per surgery for MarginProbe (i.e., the cost of disposables), the net cost of MarginProbe to payers is $305 per use for privately insured individuals and $903 per use for Medicaid enrollees. Market share will be affected by alternatives. Similar devices are in development that, and if FDA approved, could easily prevent MarginProbe from reaching a 25% market share. They could also lead to price competition, which will reduce the extra costs associated with all of the technologies. For these reasons, the true economic impact of MarginProbe may need to be re-evaluated annually for several years. |

**Table A-17.Truven Health cost model infectious disease topic**

| Intervention | Estimated Cost of New Treatment for Estimated Adoption Rate |
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| 2. Oral Interferon-free Treatment Regmens for Hepatitis C Virus | Viekira Pak is an oral combination therapy (ombitasvir, paritaprevir, ritonavir and dasabuvir) taken as several pills a day for treating HCV genotype-1; Harvoni is an oral combination (ledipasvir and sofosbuvir [Sovaldi]) in 1 pill taken daily. These regimens were compared in this cost model; both provide similar survival outcomes. Pricing for these regimens has been in flux because of discounting deals that large retail pharmacy benefits management companies have negotiated. At the time of the cost model calculations for this report, Viekira Pak retail cost was listed at about $14,000 less than Harvoni on GoodRx. Nearly all of the cost over a 6-month period is related to the medication cost. Sensitivity analysis shows relatively little variation beyond what is accounted for by the two medications. Both are very new regimens and do not have full market penetration yet. If Viekira Pak is prescribed mostly to people who would otherwise have received Harvoni, total insurance spending will likely go down. Conversely, if Viekira Pak is mostly prescribed to other individuals, then total spending could rise dramatically—perhaps exceeding $10 billion per year for Viekira alone. Over the longer run, competition from new formulations and shorter treatment periods could moderate total spending, although we expect that it will still be measured in the billions of dollars per year across all HCV medications given the estimated 3.2 million individuals with HCV infection currently.<br><br>Health care costs related to HCV totaled about $24,500 over 6 months for the average privately insured person, or $49,000 per year. Successful treatment should reduce these costs essentially to zero. With an average 6-month treatment cost of $83,074 and a successful treatment rate of 95% or greater for treatment-naïve patients, the cost of Viekira Pak is likely to be recouped in future savings within 2 years on average.<br>Many unknowns at this time affect making accurate estimates of insurance payments for Viekira Pak. For example, whether Viekira Pak will largely displace Sovaldi, Harvoni, or other new medications is unclear. How quickly private insurers will pay for Viekira Pak or Harvoni is unclear. A few state Medicaid agencies are discussing coverage limits, but it appears that Viekira Pak is widely covered under Medicaid programs. Private insurers have similarly leveled severe criticism at manufacturers but it appears that most or all insurers have agreed to pay. Competition could eventually lower the price of of these treatments. For example, a large national pharmacy benefits manager, Express Scripts, has indicated at this time that Viekira Pak is its preferred HCV regimen over Harvoni because of discounts received. Competition may also come from other medications and from new formulations. |

**Table A-18.Truven Health cost model pulmonary disease topic**

| Intervention | Estimated Cost of New Treatment for Estimated Adoption Rate |
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| 3. Organ Care System for Preserving Donor Lungs | A double-lung transplant is a last resort for patients with end-stage lung disease. The Organ Care System (OCS) technology could provide an opportunity to treat more patients without greater risk and produce better clinical outcomes and less costly follow-up care. The extra costs of purchasing the OCS may level out over time. However, long-term results are still being evaluated. OCS would increase the number of acceptable donor lungs, which in turn would increase in the number of transplants performed. If we assume that OCS will be used in only 5% of transplants performed under standard donation criteria, and that OCS leads to an 8 percentage-point increase in transplants, then the total impact over a 3-year horizon is estimated at $107.2 million in additional expenditure. With a 25% market share and an increase of 11% in donated lungs, the total impact rises to $177.1 million. It rises to $255.3 million if OCS captures 50% market share and there is a 14 percentage-point increase in transplants. The estimation of net cost is complicated by the likely entry of close competitors. Two preservation systems are in clinical trials: The Toronto Technique and Vivoline. A 4th system, Xvivo Perfusion System received FDA approval in August 2014. Xvivo is similar to OCS in cost, with similar advantages of allowing the organ to spend more time outside of a living body, thus extending the standard donor criteria. If most or all of these machines come to market and have similar or better performance than OCS, a new economic analysis will be necessary. |

**Table A-19.Truven Health cost model substance abuse topic**

| Priority Area: Substance Abuse | Estimated Cost of New Treatment for Estimated Adoption Rate |
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| 4. Naloxone Evzio, Auto-Injector for Treatment of Opioid Overdose by Non-Clinicians | FDA approved a Evzio™ a naloxone auto-injector kit in April 2014 intended for use by non-clinicians. Evzio is the first auto-injector that uses voice-instruction technology to prompt the user to appropriately administer the medication. The primary benefits of Evzio over a standard naloxone kit are the voice-instruction technology and auto-injector. These features reduce the chance of human error and ensure that a proper dose is administered. They are designed to enable non-clinicians to use Evzio before medical professionals arrive.<br>The cost impact of prescribing a naloxone auto-injector for use in the event of overdose in persons prescribed opioids has not been investigated. Such information would be useful for health care providers, insurers, and health care policymakers as they make health care choices related to overdose risk policies and procedures. This cost model compared probabilities of survival, the use of health care services, and associated health care costs of overdose patients under four scenarios: (1) Evzio administration followed by emergency medical services (EMS) care, (2) naloxone administration from a standard kit followed by EMS, (3) EMS care without prior naloxone (which we term *usual care*), and (4) neither naloxone nor EMS care.<br>We limit our model to prescribed opioids for two reasons: (1) a person using opioids without a prescription is very unlikely to be prescribed a take-home naloxone kit and (2) a clear majority of deaths from opioid overdose occur in people with prescribed opioids. The Evzio naloxone auto-injector could have a moderate impact on spending by insurers, one that depends on many factors. In particular it will depend critically on the willingness of physicians to prescribe it to people who have a very low risk of mortality from overdose. The number of units sold per year in the near future may range from 50,000 to more than 550,000, making it a relatively common technology. Using a variety of observed costs and assumptions, we estimated that the likely impact on health care costs from a payer perspective will be between $123 million and $1.8 billion per year over a 6-month horizon. The true cost could be larger or smaller after taking account of variation observed in the sensitivity analyses and if the differential insurance costs in public insurance programs were taken into account.<br><br>Widespread use of Evzio could lead to as many as 591 lives saved nationally per 6-month period. While any life saved is important, the total number is relatively low for a potentially life-saving medication considering the number of prescriptions that could be filled. The low impact on survival results from two factors: the very high survival rate under the status quo (witnessed overdose leading to EMS call) and the unusual situation that Evzio will go unused by nearly everyone who fills a prescription for it. |