THE NEW MATH OF AMERICAN HEALTH CARE PAYMENT

Calculating cost, quality, and value

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Opposition to Cadillac Tax Creates Broad Alliance

By Frank Diamond

You could never describe the health insurance industry as sleepy even though employer-sponsored coverage may have at times been the butt of jokes similar to those aimed at accounting. However, as Virgil said, “The greatest wealth is health.” It trumps mere money. So in recent decades, since the time when employers turned to HMOs to contain costs, coverage debates have run like the bulls of Pamplona: movement aplenty resulting in a goreing now and then.

Our package about the ascendancy of value-based care (page 18) choreographs the latest moves in the insurer-provider cha-cha. Who assumes how much risk for what? Oh, and, who pays? Well, employers. Still. And they’re worried about the Cadillac tax, a 40% penalty starting in 2018 for packages that cost above $10,200 per individual and $27,500 per family per year.

Enter fight or flight, a response alluded to on cave walls and which Virgil used as a literary trope. As the New York Times reports, some companies want to replace Cadillac plans with “plans that could prove far more expensive for workers and their families.”

Proponents say the Cadillac tax might be “a way for the country to move away from the tax exclusion of health benefits, one reason there is such a heavy reliance on employers to provide health coverage,” according to the Times.

Well, the enemy of my enemy is my frenemy, and the issue manages to place employers and unions on the same side. But not just them. A web page sprang up recently. The Alliance to Fight the 40 includes unions, employers, politicians (there’s a bipartisan support), a representative of big pharma, Pfizer, and an erstwhile member of big insurance, Cigna, before it was gobbled up by Anthem (page 11)—antitrust regulators permitting.

As Virgil said: “Wherever the fates lead us, let us follow.”

CONTACT E-MAIL ADDRESSES:
Editorial: fdiamond@medimedia.com
Circulation: jott@medimedia.com
Advertising: mliberti@medimedia.com
Reprints: mecurry@medimedia.com

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Medicare Advantage Underutilizes Telehealth’s Potential

There’s a lot of support and momentum behind telemedicine, as the cover story in Managed Care’s July issue well documented. Videoconferencing, text messaging, and email mean that the treatment option might soon become common practice. Maybe.

There are still significant roadblocks, as Kaiser Health News pointed out last month. For instance, the population that’s most homebound and physically impaired—the demographic that could really benefit from this technology—lacks access.

Fewer than 1% of Medicare beneficiaries get care remotely. There are many reasons for that, but restrictions imposed by Congress and CMS are among them. One worry is that telehealth could encourage overutilization and actually add to costs.

Harvard expert Ateeq Mehrotra, MD, MPH, says that’s a legitimate concern. Mehrotra, who is a member of Managed Care’s editorial board, told Congress last year that telemedicine could lead to overutilization of Medicare benefits. “The very advantage of telehealth, its ability to make care convenient, is also potentially its Achilles’ heel,” he said.

“Telehealth may be too convenient.”

To no one’s surprise, the American Telemedicine Association (ATA) disagrees. “Currently, Medicare is failing its beneficiaries by its very restrictive rules,” Jonathan Linkous, the ATA’s leader, wrote to CMS in February. The ATA is gaining allies. The AARP, American Academy of Family Physicians, American Hospital Association, and the American Medical Association all want Medicare beneficiaries to tune into. Of course, the doctors also want to make sure that they’re fairly compensated for virtual care.

As of now, Medicare can offer telemedicine only in rural areas and only if the patient goes to a clinic. Medicare Advantage plans, on the other hand, avoid those restrictions because capitation means, in essence, that the insurer picks up the tab for the services. So far, though, only Anthem and the University of Pittsburgh Medical Center Health Plan offer telemedicine to Medicare Advantage beneficiaries.

Mehrotra tells Managed Care that “in a Medicare Advantage plan, the plan has an incentive to ensure appropriate use of care. If a MA plan sets up restrictions on when/where telemedicine is used to try to focus the care on patients who will most benefit, then that would be great. However, I have not seen MA plans act in this manner. They have relatively limited market power and, therefore, impact on provider behavior.”

Anthem officials insist that its program pays off in quality, patient satisfaction, and cost reduction. The insurer offers telemedicine to about 350,000 MA beneficiaries in 12 states. John Jesser, the general manager of Anthem’s LiveHealth Online (launched in the beginning of the year) tells Managed Care that “based on six months of experience, we have not seen overutilization. Our current challenge is actually the opposite—to make seniors more aware of telemedicine as an option. We recognize that it will take more education and an increased comfort level with telemedicine for seniors to adopt the technology.”

Jesser argues that if CMS lifts telemedicine restraints on all Medicare beneficiaries, more physicians would make telemedicine a routine part of their practice. “The basic value proposition of telehealth should be even more compelling to seniors, some of whom have to rely on friends, family or caregivers to provide them transportation to health care providers,” says Jesser.

“As more seniors use smartphones and gain more comfort with this technology, we believe that adoption rates will steadily increase, just as we’ve seen in our under-65 membership.”

Doctors In Dark About Opioid Abuse

The growing addiction to painkillers often starts at the doctor’s office, and health insurers could possibly stem this society-destroying tide with a little education—for primary care physicians (PCPs) as well as patients.

Researchers sent a survey to 1,000 primary care physicians and received responses from 420. All of the respondents said that addiction to prescribed opioids is at least a small problem in their communities, according to a study in the June 23, 2015, issue of the Journal of Clinical Pain.

Thirty-seven percent called it a moderate problem, while 53% described it as a big problem.

It is a big problem. In 2013, the latest year for which CDC statistics are available, 43,982 Americans died from drug overdoses, and about half—22,767—were overdoses of prescription drugs.
Death by prescription drug overdose has tripled in the United States since 1990, while the use of prescription painkillers nearly doubled between 2000 and 2010, researchers said.

PCPs, for the most part, don’t know that they exacerbate the situation. They also don’t understand how many people abuse these drugs and how addictive the medications can be.

“Only two thirds of physicians (66%) correctly reported that the most common route of abuse was swallowing pills intact while nearly one half (46%) erroneously indicated that abuse-deterrent opioid formulations were less addictive than their non-abuse-deterrent counterparts,” reported the researchers, most of who hail from the Johns Hopkins Bloomberg School of Public Health.

In April 2015, the FDA released the final version of a guidance about abuse-deterrent opioids that says the agency considers them “a high public health priority.” But the FDA also warns that deterrent formulations have failed so far to deter people from swallowing the pills intact, which the guidance, like the Hopkins researchers, says is the most common form of abuse. PCPs and patients need to be told just what abuse deterrence can and cannot do, says G. Caleb Alexander, MD, MS, the study’s main author and co-director of Bloomberg’s Center for Drug Safety and Effectiveness.

“As medical professionals, we have overestimated the effectiveness of opioids and underestimated their risks for far too long,” he tells Managed Care.

Only 13% of the PCPs surveyed between February and May 2014 correctly believed that relatives and friends give the drugs to non-prescribers, and 25% said that they were not at all or only slightly concerned about such diversions.

The problem begins in medical school, where the average student receives 11 hours of education about pain, and very little instruction about recognizing substance abuse, the study states, though a number of states mandate that prescribers be trained about the dangers of opioid addiction.

**Smoking Signals Reinterpreted**

The tendency for those suffering from a schizophrenic episode to be smokers has been long assumed to be an example of self-medication: Smoking might help counteract stressful symptoms or the side effects of antipsychotic medication.

What if, however, smoking is one of the causes of schizophrenia? That’s a question researchers at King’s College London’s Institute of Psychiatry took on in a study in *Lancet Psychiatry*.

Results were inconclusive. Researchers state that “daily tobacco use is associated with an increased risk of psychotic disorder and an earlier age at onset of psychotic illness. However, the effect of smoking seems to be modest.” Still, just the suggestion that the causal direction between smoking and schizophrenia might be the reverse of the usual self-medication explanation caused a stir.

The meta-analysis examined 15,000 tobacco users and 273,000 nonusers, comparing their relative rates of psychosis. They found that 57% of those enduring their first episode of psychosis were smokers. They were three times more likely to be smokers than those in the control groups.

Researchers posit that the genes for smoking overlap with those for psychosis and a commentary that accompanied the study agreed. There are 108 separate genetic loci associated with an increased risk of schizophrenia.

“One of these is located in a cluster of genes—CHRNA5, CHRNA3, and CHRN5B—one chromosome 15, and this region is associated with both early age at onset of smoking and heavy smoking,” say the authors of the commentary, Helen L. Alderson and Stephen M. Lawrie of the University of Edinburgh.

The authors also point out, however, that people typically begin smoking in their teens. People are usually about 25 years old when they are hit by a schizophrenic episode.

“Regular smoking is unlikely to take years to exert a psychotogenic effect but, then again, most smoking-related diseases only arise after prolonged exposure,” the commentators write.

Most studies end with “further research is needed” and that seemed to be the main goal for these authors. They took the first step, and want others to follow with large prospective studies.
Nearly 15 million women in the United States have only limited access to gynecologic cancer care, according to a study in *Gynecologic Oncology*. That's especially true for women residing in the Midwest and Mountain West regions, say researchers, noting that more than 7,000 women in those regions have difficulty getting care for uterine, ovarian, and cervical cancer because of the long distances they must travel.

Diabetes is costly and complicated, a fact borne out yet again in a study by the Health Care Cost Institute, a Washington, D.C., group that researches cost and utilization in the employer-sponsored insurance (ESI) market. In 2013, the annual health care costs for a person without diabetes was $4,305, the study says. The annual costs for an adult with diabetes was $10,700 more, or $14,999, and for children with diabetes, it was $15,456. The cost of new insulin analogs helped power the cost difference.

How well painkillers such as aspirin, ibuprofen, and other NSAIDs work depends on a patient's genotype, according to a study in *JAMA*. NSAIDs have long been associated with lower risk of colon cancer; researchers found that variations in a certain gene nullifies NSAIDs' effect.

How sick you are is everything when it comes to the value of follow-up visits after a hospital stay. Follow-up visits within seven days were associated with lower readmission rates among patients with the highest clinical complexity, according to a study in the *Annals of Family Medicine*. But most patients don't appear to benefit from such early follow-up visits. In fact, follow-up within 30 days of discharge had a negligible effect on readmission rates among people with no or just one chronic condition.

Cognitive impairment can be one of the side effects for men getting androgen-deprivation therapy for prostate cancer, according to researchers at Tampa's Moffitt Cancer Center. Men undergoing treatment can experience cognitive impairment within the first six months.

— Frank Diamond

### CDC: More than 1 in 10 Americans with HIV are undiagnosed

Approximately 1.2 million Americans were living with HIV in 2012, but 153,600 (12.8%) didn't know it, according to CDC researchers, who argue that health policymakers need to more fully implement HIV testing. The study, published in the June 26, 2015, issue of the CDC's *Morbidity and Mortality Weekly Report*, uses data from the National HIV Surveillance System to estimate how many people have undiagnosed HIV in each state and the District of Columbia.

The stakes are high. “Persons unaware of their [HIV] infection contribute nearly one third of ongoing transmission in the United States,” the study states. The U.S. Preventive Services Task Force recommends that Americans age 15 to 65 be tested for HIV at least once. People at increased risk—including men who have sex with men and people who inject drugs—should be tested at regular intervals.

The national goal is for 90% or more people who are infected with HIV to have a diagnosis, because early treatment lengthens the infected person's life and reduces the risk of transmission. “Because the percentage of persons with undiagnosed HIV varies by geographical area, efforts tailored to each area’s unique circumstances might be needed to increase the percentage of persons aware of their infection,” the study states.

Among men who have sex with men—who make up about 60% of Americans diagnosed with HIV each year—the percentage with HIV who had received an HIV diagnosis was as low as 75% in Louisiana. Only a handful of jurisdictions were above the goal of 90% or more.

#### Percentage of people living with HIV who had not yet been diagnosed (as of 2012)

- **US overall:** 12.8%
- **District of Columbia:** 10.6%
- **15–17%**
- **12–15%**
- **8–12%**
- **<8%**

* The estimated undiagnosed HIV prevalence was calculated by subtracting the estimated number of diagnosed HIV infections in living persons from the number of persons included in estimated overall HIV prevalence.

** Estimates for jurisdictions with fewer than 60 diagnoses per year (average) over the most recent five years (2008–2012) are considered numerically unstable.

Four of the big five commercial health plans have lined up suitors for merger. Aetna and Humana have paired up in a $37 billion cash-and-stock deal, and Anthem wants to buy Cigna for more than $54 billion. But Wall Street isn't too excited about these maneuvers, and that's a sign that investors think the regulatory landscape for health insurer tie-ups could be more of a minefield than a lovers’ lane.

How else to explain that Anthem is buying Cigna in a combination cash and stock deal equaling about $188 a share, when the Cigna stock was trading at about $30 less than that price? Or that Aetna's stock price has muddled around $115 despite some analysts projecting it would reach $150? Or that stocks of health insurance companies have remained flat overall since the Supreme Court's King v. Burwell ruling that upheld subsidies for policies sold on the federal government's version of the health exchanges?

For commercial plans, the ACA giveth and the ACA taketh away. Jay Angoff, former director of HHS's Office of Consumer Information and Insurance Oversight and now a Washington lobbyist, said at a briefing for reporters held a few days before the Supreme Court ruling that the Dow Jones Industrial Average has increased 67% since the passage of the ACA, but the top five publicly owned health insurers have seen their stocks rise an average of 250%.

"What a bonanza, what riches this law has created for the insurance industry," Angoff said—and who would disagree?

But that bonanza may be tapped out. Let's take a deeper dive into some of the regulatory issues these mergers will encounter.

David Balto, former policy director for the Federal Trade Commission and now a Washington attorney who specializes in consumer and public interest advocacy, thinks these health insurer mergers will face "a pretty tough reception" at the Department of Justice (DOJ)—and the ACA is why.

"The purpose of the Affordable Care Act was to attempt to rein in the anticompetitive practices and deceptive conduct by health insurers," he says. "It was based largely on the finding that health insurance markets were highly concentrated and that consumers suffered because of that. I don't think that's changed much."

Of course, the ACA is President Obama's signature legislation, and as long as his appointees are occupying the DOJ antitrust offices about seven blocks from the White House, any perceived threat to its objectives will get close scrutiny.

"Competition among health insurers and the availability of affordable health insurance has been one of the cornerstones of the Obama administration," says Barak D. Richman, a professor at Duke Law School. "To a large degree that's what the exchanges are all about, and in that sense the Obama administration, from the White House on down, would take this merger activity very seriously."

That's not to say the administration will block the activity outright, but "competition among health insurers will be a policy priority, as it has been," Richman says.

It's complicated

With these mergers, DOJ is in for a "very complicated set of analyses," Richman says. Commercial insurers do business in several states, and in many cases in different regional submarkets within those states. They sell different products in each state and submarket, in addition to the products they sell to nationwide employers. Moreover, as Richman notes, the nature of competition among insurers is complicated, and there are many possible entrants into the health insurance market: "Who knows? Maybe Wal-Mart or CVS will go into the market."
The Comcast-Time Warner deal that fell apart this year and the AT&T and T-Mobile merger that founderered in 2011 presented much easier antitrust questions, where the competitive harm was unquestionable and impossible to remedy, says Richman. The DOJ will likely find the competitive consequences of health insurance mergers more difficult to assess.

Innovative approaches

“It’s all about ease of entry for competitors and ease of exit for consumers,” says Richman. “We really don’t know whether and how the ACA’s exchanges will change the competitive landscape.”

Richman says increasing familiarity with buying health insurance on the web may allow innovative approaches—he points to Oscar Health Insurance as an example—to take hold and spread faster, shaking up the previously staid insurance market.

The DOJ and even state regulators will parse the motives behind these acquisitions. Anthem President and CEO Joseph Swedish says that an Anthem-Cigna merger—which analysts say will create about $115 billion in annual revenues—would generate around $2 billion in synergies within two years and add $17 earnings per share by 2018. Regulators will have to determine if $2 billion in purported synergies is enough for a $100 billion-plus corporation to justify a merger.

Michael Bernstein is skeptical. Now a private equity partner with Baird Capital, Bernstein is a former president of Cobalt Corporation, a managed care descendent of Blue Cross Blue Shield United of Wisconsin, which WellPoint, now Anthem, acquired in 2003.

The sheer size of these mergers is mind-boggling, Bernstein says. “At this scale, I have a very difficult time imagining that going from the size that they already are individually, which is giant, to the size that they’re going to be, actually stimulates meaningful administrative savings—certainly not on a scale that would actually support reasons for doing the deal,” he says.

Bernstein sees strategic reasons for the mergers but believes the “unspoken motive would be to eliminate a big competitor.”

If that’s how DOJ’s antitrust lawyers see it, the Aetna and Humana merger may unravel and Anthem and Cigna end in a whimper. Don’t forget the grenades that state governments may lob into the regulatory minefield.

In 2009, Pittsburgh-based Highmark and Philadelphia-based Independence Blue Cross walked away from a merger because Joel Ario, the Pennsylvania insurance commissioner, imposed a condition that the two not-for-profit Blues would not accept.

Now David Jones, California’s insurance commissioner, is raising questions about the Anthem-Cigna deal. “Generally speaking, further consolidation in the health insurance industry is not a good thing for consumers, employers, or medical providers,” he told the Los Angeles Times.

Richman, at Duke, points out that even in a rigorous antitrust enforcement climate, there are ways to fix problematic mergers by selling off pieces. Divestiture has been an option for mergers too big for regulators to swallow, but the Comcast-Time Warner debacle is making that strategy seem dubious.

“I think it shows that the agencies are becoming very skeptical about whether divestitures will work,” says Balto, the former Federal Trade Commission official. “Many people may believe that you can cure the tremendous amount of market power Aetna will have by acquiring Humana through some kind of divestiture, but the agency will be very skeptical about whether divestiture will be adequate to resolve the substantial competitive concerns risked in the merger.”

There’s also the central purpose of the ACA itself, which as Chief Justice Roberts wrote in the King v. Burwell majority opinion, was designed to improve health insurance markets, not to destroy them.

Less competition

Consolidation of the top five insurance companies into three behemoths maybe wouldn’t destroy health insurance markets.

But it would probably render them a good deal less competitive, says Balto: “Permitting these mergers would be like prescribing ice cream for somebody who’s obese. This would be a giant step backward for many of the things that have been achieved through the Affordable Care Act.”

And so far it seems that Wall Street is not the least bit interested in putting its money on going backward.
There are at least two sides to every story, including the one involving the PCSK9 inhibitors. Oftentimes, one side of a story can overshadow the other, and that seems to be the case with the new anticholesterol agents evolocumab (Repatha), made by Amgen, and alirocumab (Praluent), a joint effort by Sanofi and Regeneron.

These new lipid fighters are coming onto the market under a cloud of worry and criticism about their exorbitant costs and inadequate outcomes data. They are expected to cost between $5,000 and $12,000 annually per prescription. Other reports have highlighted the lack of safety and cardiovascular outcomes data. The drugs have been evaluated by the FDA for their impact on low-density lipoprotein (LDL), a surrogate outcome, and one-year safety profiles.

By some estimates, 3.5 million Americans might eventually be prescribed a PCSK9 inhibitor. The FDA approved alirocumab on July 24 as a treatment for familial hypercholesterolemia and for people at high risk for a cardiovascular event, such as a heart attack, who need LDL-lowering therapy in addition to whatever diet and aggressive statin therapy can accomplish in that department. But the approved indications and use of alirocumab and its PCSK9 inhibitor colleagues could broaden.

Say that 3.5 million estimate proves to be accurate. The annual tab for PCSK9 inhibitors at their anticipated prices would range from $17.5 billion to $42 billion.

But the other side of the PCSK9 inhibitor story sets costs aside and looks at the phenomenal impact these agents have in lowering LDL cholesterol. “They may present an opportunity to more clearly understand the true potential of low cholesterol in reducing cardiovascular events,” notes Elliott Antman, MD, a professor at Harvard Medical School and the immediate past president of the American Heart Association. When alirocumab and evolocumab are added to existing anticholesterol therapy, they can cut LDL levels by another 60%.

Atorvastatin (Lipitor) alone can reduce LDL by between 39% and 50%, and adding a PCSK9 inhibitor may lower LDL levels much further. The FDA’s advisory panel briefing document shows that with a statin plus evolocumab, it is possible to achieve LDL levels below 50 mg/dL, which is far below 100 mg/dL, the optimum level in the current federal cholesterol guidelines.

Antman notes that in the first year of life, a healthy infant’s cholesterol level is about 30 mg/dL—an indication that human beings can get their LDL levels down to much lower levels—and also that triple digit levels are not normal but the consequence of bad diets and sedentary ways. Moreover, as Antman points out, people with an inherited PCSK9 defect have very low lifelong LDL levels and almost never have vascular disease.

If pushing down LDL levels translates into less cardiovascular disease, then the cost-benefit math of the PCSK9 inhibitors could put the high price of the drugs in a more favorable light, argues Antman. The direct costs of cardiovascular disease are well over $300 billion a year. Add in disability and lost wages, and the dollar figures get much higher. About 200,000 of the heart attacks that Americans have each year are repeat heart attacks, and secondary prevention efforts, including therapy to ratchet down LDL levels to much lower levels, might reduce that number by a lot. The same might be true for stroke.

How low should we go?

Antman is not alone in suggesting a more aggressive approach to cholesterol management. In 2013, the cholesterol guidelines from the...
American College of Cardiology and the American Heart Association started to move away from absolute cholesterol targets. Instead, they target percentage reductions in LDL, and those percentage reductions may translate into LDL reductions well below 100 mg/dL.

**22% reduction in cardiovascular events**
The current evidence is that a 40 mg/dL reduction in LDL cholesterol is associated with a 22% reduction in cardiovascular events. In two of the clinical trials of evolocumab, there was an absolute reduction of at least 70 mg/dL in patients with a median LDL of 120 mg/dL. If the relationship between cholesterol reduction and risk reduction is linear, then evolocumab could, in theory, reduce cardiovascular events by 38.5%.

Studies of other agents have also suggested that perhaps we haven’t gone nearly far enough in lowering cholesterol levels. The IMPROVE-IT trial of ezetimibe (Zetia) showed a statistically significant benefit in driving cholesterol lower than the 100 mg/dL benchmark. The study included 18,144 high risk patients taking ezetimibe plus a simvastatin (the treatment group) or a placebo plus simvastatin (the control group). After a year, the mean LDL level in the treatment group was 53.2 mg/dL vs. 69.9 mg/dL in the control group.

The seven-year event (cardiovascular death, heart attack, and so on) rate was 32.7% in the treatment group and 34.7% in the control group, a 2% percentage point difference and a relative difference of about 6%. These results indicate that about 50 patients would need to be treated for seven years to prevent one CVD event.

While the risk difference was statistically significant, IMPROVE-IT has not generated that much excitement. One reason, perhaps, is that the study’s results identify a factor that must be taken into consideration when evaluating new therapies: poor adherence. It is definitely a barrier to achieving lasting cholesterol reductions. In the IMPROVE-IT trial, 42% of patients in each arm discontinued their study regimen before the end of the trial.

All of the stories surrounding the PCSK9 inhibitors present a real management challenge for health insurers and PBMs. The additive power of the PCSK9 inhibitors in driving LDL levels down means they will be attractive to some patients and clinicians.

The high cost of PCSK9 inhibitors means that they may not be the best means, even if very low LDL cholesterol levels—by today’s standards—turn out to be the desired end. Chronis Manolis, RPh, vice president of pharmacy at UPMC Health Plan in Pittsburgh, notes that the current arsenal of statins is often capable of getting patients well below 100 mg/dL.

However, there is considerable play yet in what PCSK9 inhibitors will actually end up costing. As they have with sofosbuvir (Sovaldi) and other new hepatitis C drugs, the national PBMs may have enough clout to negotiate discounts, rebates, and formulary placement so that the actual price to plan sponsors will be considerably lower than the sticker price.

Still, there are unresolved questions about the safety and outcomes of the PCSK9 inhibitors. Multiple phase 3 cardiovascular outcome studies are underway for both evolocumab and alirocumab, but the results will not be available until 2017 or 2018. These large-scale trials in diverse populations are intended to prove longer term safety and clearly demonstrate the impact of these drugs on cardiovascular outcomes, since the initial review relied upon LDL as a surrogate outcome.

**Pay attention to adherence**
An article last month on the American College of Cardiology’s website acknowledged that definitive safety and outcomes data are not available, so the role that PCSK9 inhibitors will play in cardiovascular disease prevention is hazy right now. The piece went on to say, though, that the excitement surrounding the new medications was warranted because they “may potentially change the paradigm surrounding the treatment and management of patients for years to come.”

Manolis argues for a measured response. While it’s an important development to have an effective medication for cholesterol management, he says clinicians need to pay close attention to adherence, partly because PCSK9 inhibitors are expensive. And it needs to be confirmed that there has been a thorough attempt at statin therapy. “Clinicians shouldn’t bring out the big guns unless they are truly indicated,” he says. NC
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Orkambi’s Slick Unveiling Puts Insurers in a Bind

Makers of this expensive new cystic fibrosis medication manage to sidestep controversy. Health plans may not be as lucky as they weigh cost against value.

By Ed Silverman

How is this for shrewd maneuvering?

Earlier this summer, Vertex Pharmaceutical received FDA approval for its Orkambi medication for treating people age 12 and older who have a gene mutation found in about 50% of those who suffer from cystic fibrosis. But instead of pricing the treatment at nearly the same $311,000 price point for its older Kalydeco medication, the drugmaker is selling Orkambi for $259,000, a 17% difference.

This is still a considerable sum for a medication that must be taken each year. Yet at that price, Vertex managed to defuse several charged issues at once. First, the move appeased investors. Most Wall Street analysts expected Orkambi to be priced slightly higher, but given the patient population, Vertex will be able to charge less than some had anticipated and still earn a return on its investment.

The Cystic Fibrosis Foundation estimates that 30,000 Americans have cystic fibrosis, an inherited condition that leads to a buildup of sticky mucus primarily in the airways of the lungs, but also in the pancreas and organs of the digestive system. About half of those people have the gene mutation that would be addressed by Orkambi, which combines Vertex’s older Kalydeco treatment and an investigational compound, lumacaftor. For now, the population that Vertex plans to target with the new medicine amounts to about 8,500 people.

At the same time, the decision was politically deft. Instead of inciting still more outcry about the high cost of a new drug, Vertex was able to sidestep that sort of criticism because patients and lawmakers now see a lower price, at least compared to Kalydeco. Although Kalydeco treats a small number of patients, its cost has helped fuel the ongoing controversy over prescription drug pricing. Earlier this year, for instance, Arkansas Medicaid officials settled litigation with three cystic fibrosis patients who claimed the state violated their civil rights by denying them access to Kalydeco.

“But if more patients are taking the new drug, Orkambi, you can charge less, which is a smart way to deal with a politically potent problem,” says Randy Vogenberg, a partner at Access Market Intelligence, a consulting firm that specializes in managed care issues, and a member of MANAGED CARE’s editorial board.

“Now, everyone is happy, or at least not as upset. Investors see a return and Congress thinks [Vertex is] wonderful because they charged a lower price than the existing drug,” says Vogenberg.

Physicians, meanwhile, may decide Orkambi offers a good value, according to Vogenberg. He points to the recent Drugabacus.org website for assessing cancer medicines as a good example of how value
can be weighed and calculated with software and an appealing online tool. Although the older Kalydeco treatment is actually more effective in improving lung function, Orkambi may still be seen as the better choice, he notes. With comparable safety and a lower price, the newer Vertex drug may seem like a good value in the eyes of many.

But payers still face a daunting choice. Orkambi is plenty expensive, and the benefit for many patients may end up being pretty modest. A review by FDA staffer notes that Orkambi only offered a small improvement in lung function and did not compare as favorably when it came to decreasing hospitalizations or infections.

**Breaking the bank**

One pharmacy benefits manager believes Orkambi’s pricing is not low enough to provide good value. Patrick Gleason, who is director of health outcomes at Prime Therapeutics, calculates that covering Orkambi will add 1% to all pharmacy benefit costs, an increase which he argues is unsustainable.

Not every new drug adds such costs, but if enough do, that level of pricing “can become unaffordable in a few years,” he says.

A recent Prime analysis found that 1,067 of its approximately 13 million commercially insured members had a claim indicating cystic fibrosis. Of these, 76% were age 12 and older, and of those, 47% are expected to have the gene mutation that means they would be candidates to be treated with Orkambi. This works out to 382 commercially insured members, which at $259,000 per year comes to a total annual cost of nearly $100 million.

“At this rate, such [pricing] would break the big bank,” Gleason says. “Does the health insurance industry need to provide the revenues at the level we’re seeing for the benefit of drug manufacturers? Does this drug need to cost $259,000?” He adds that it will likely be difficult to negotiate rebates since there is no competition for Orkambi.

Such sentiments suggest an open question remains concerning payer strategies, according to Sanford Bernstein analyst Geoff Porges. He believes payers may suspend reimbursement if patients fail to benefit or possibly require a certain level of disease severity for reimbursement to be granted, although Gleason notes the label does not say whether Orkambi works better at various stages of the disease.

“Because Orkambi has only very modest benefit in many patients, payers will likely require lung function or other tests after a short period of therapy,” says Roger Longman, chief executive at Real Endpoints, a research firm that tracks reimbursement issues. “If there’s no improvement, they will have to require lots of special authorizations or exceptions to continue paying for it.” In other words, payers may want to limit their financial exposure by restricting usage, rather than openly fighting over the price. In fact, this is the tactic that payers took with Sovaldi, the hepatitis C drug that became the poster child for high-priced drugs, since there was no competition to the Gilead Sciences treatment for nearly a year after it was launched. During that time, restricting access became the primary tool for keeping a lid on costs.

Meanwhile, public payers may feel more of the brunt with Orkambi than with the older Kalydeco treatment. Specifically, Medicaid patients are likely to account for a greater portion of Orkambi patients—an estimated 35% to 40%, compared with the low- to mid-20% range for Kalydeco, according to Porges at Sanford Bernstein.

As for Medicaid managed care plans, Vogenberg notes these have a negotiated discount built in and amounts to the same rates offered Medicaid. “If they get a deeper discount, that’s based on negotiating,” he says. “But we will have another product that costs more. We have a rational way to use it that makes sense, but still haven’t answered the question about how we can afford it.”

**CF Foundation got royalties**

For anyone who thinks patient advocacy groups may somehow turn the tide, this is unlikely. Over the past 20 or so years, the Cystic Fibrosis Foundation gave Vertex about $150 million in exchange for a share of the royalties for any treatment emanating from Vertex research. Late last year, the foundation sold its royalty rights to an investment company for $3.3 billion.

A statement issued by the foundation at the time that Vertex won approval for the drug in early July did not mention price at all. A foundation spokeswoman declined to say specifically whether there was any concern about the price Vertex is charging for Orkambi but did send a statement saying its research shows that nearly a quarter of people with cystic fibrosis delay or skip care due to cost, in general.

“This is of great concern to us,” she wrote. “That’s why we address the financial burden of living with cystic fibrosis through a variety of patient access and advocacy resources. We also communicate to payers and pharmaceutical companies our serious concerns about the burden that the cost of treatments and care places on people with cystic fibrosis and their families.”

Ed Silverman founded the Pharmalot blog and has covered the pharmaceutical industry for 20 years.
American health care is the most expensive health care in the world, gobbling up over 16% of GDP. It may also be the global leader in coining buzzwords and catchphrases. The current fav: value-based—as in value-based care, value-based payment, value-based reimbursement. It seems like everything good and wholesome in health care these days is value-based.

CMS has been leading the charge, with dozens of programs and pilot projects that involve valued-based care. In January of this year, HHS Secretary Sylvia Mathews Burwell announced that her department had set a goal of having 85% of traditional Medicare payments linked to quality or value by 2016 and 90% by 2018. Last month, CMS started to make good on that promise with a plan that would mean about a quarter of the 400,000 hip and knee replacements that Medicare beneficiaries receive each year would be paid for with bundled payments, which seem like this year's go-to value-based payment.

At about the same time that federal health officials were trumpeting their goals—the Health Care Transformation Task Force, a provider, payment, and purchaser organization that includes heavyweights like Aetna and Partners Healthcare in Boston—said its members would shoot for having 75% of their business operating under value-based payment arrangements by 2020.

Is this all aspirational talk without any real-world walk? It doesn't seem that way. UnitedHealthcare executives have boasted that $36 billion of the company's spend last year involved some kind of value-based arrangement and that the amount will increase to over $43 billion this year. Anthem is in the same ballpark. The company's CEO, Joe Swedish, told Wall Street analysts during an earnings report earlier this year that $38 billion of the company's spend was done under value-based contracts.

Catalyst for Payment Reform, an employer group pushing for “a higher-value health care system” hasn't yet come out with its 2015 report card. The 2014 version, based on answers from 39 health plans, showed that 40% of commercial in-network payments were “value-oriented,” which the group defines as payment tied to performance metrics or designed in some way to cut waste. That's a big jump from the group's 2013 report card, which showed just 11% of payments coming with value-base strings attached.

Not all the signs point to so much value-based payment. When 146 financial officers at hospital-based provider systems were asked about value-based payment in a survey conducted earlier this year, they reported that a relatively measly 12% of the commercial insurance payments to their employers was value-based.

On the other hand, the financial officers said that they expected that proportion to grow to 50% in the next three years.

### WHAT’S GETTING TRACTION

Methodologies used for value-oriented payments in 2013 and 2014, compiled by Catalyst for Payment Reform from a national sampling of plans.

<table>
<thead>
<tr>
<th>Methodology</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full capitation</td>
<td>1.6%</td>
<td>15.0%</td>
</tr>
<tr>
<td>FFS-based pay + P4P</td>
<td>1.6%</td>
<td>12.8%</td>
</tr>
<tr>
<td>Other</td>
<td>0.8%</td>
<td>6.7%</td>
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<tr>
<td>FFS + shared savings</td>
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<tr>
<td>Partial or condition-specific capitation</td>
<td>1.3%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Shared risk</td>
<td>1.2%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Non-FFS non-visit payments</td>
<td>0.6%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Non-FFS shared savings</td>
<td>0.2%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Bundled payment</td>
<td>0.1%</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

FFS=fee for service.

Source: Catalyst for Payment Reform
The value-based care ratio
What value means in value-based care varies, depending on who is using the term and for what purpose. But fundamentally, it’s a ratio, with quality and outcomes in the numerator and cost in the denominator.

If you want to be aphoristic about it, value-based care is really nothing more than getting the biggest health bang for the health care buck. The bang, or numerator, can include anything from HEDIS scores to mortality rates to results of patient experience surveys. How exactly the cost, or denominator, is calculated is unlimited. The ratio can be improved in 1 of 3 ways: Beef up that numerator by improving quality and outcomes, slim down that denominator by cutting costs, or, ideally, do both at the same time.

The payment mechanisms—how exactly the money flows—for achieving value-based care are now jockeying for position. Experts agree that we’re in a period of experimentation, sorting out how to deploy health care dollars to the maximum effect.

If you want certainty, there is this: Defenders of fee-for-service are few and far between.

Different payment mechanisms
Pay for performance goes back well over a decade and is so familiar that in payer and provider circles, it goes by a three-character moniker: P4P. Pay for performance’s virtue is also its shortcoming: It can be implemented without expensive IT or the hard work of care coordination and with relatively little change to the fee-for-service revenue cycle. The equation remains volume X intensity = more money for the provider, albeit with bonuses for meeting performance measures that are supposed to nudge the care toward better quality and outcomes.

With bundled payments, providers get paid a set amount for all the services related to a specific condition or procedure. If care is delivered for less than the set amount, they keep the difference as reward for managing the surgery or condition in a cost-effective manner. If it costs more, and the contract includes downside risk, they pay a penalty. Bundled payments are widely seen as the pragmatic, user-friendly version of value-based payment. In fact, the retrospective version leaves fee-for-service payment pretty much intact with a reconciliation process afterward determining whether savings goals were met.

Conceptually, bundled payments are descendants of the diagnosis-related group (DRG) for hospital services, which were supposed to allow hospitals to manage care and costs by diagnosis instead of by each and every service. Some of the same problems inherent in DRGs may be lurking within bundled payments: For the individual provider, bundled payments may not alter the incentive to pursue volume and could, in fact, heighten it. But if the providers who chase volume are also those who have mastered cost-effective care under a bundled payment system, that could be good for value-based care and for the health care system as a whole.

Capitation is familiar to anyone who knows managed care’s 1990s origin stories. There’s a belief that other value-based payment mechanisms are simply warm-up acts for when capitation retakes the stage and full risk moves to providers. Andrei Gonzales, MD, of McKesson Health Solutions, says that judging from what commercial health plans executives are telling him and the signals coming out of CMS, there’s a general desire to go to capitation but to go slowly because many providers aren’t ready for the full risk.

For some, memories of the furious backlash against the ’90s version of capitation have lingered. This time around it will be different, say the proponents. Providers are both more ready and more willing because they’re more sophisticated about managing population health, have better financial systems, vastly improved IT, and terabytes of data at their disposal.

In the meantime, shared savings (and risk, if the contract includes the downside) is a kind of hedged capitation bet, with payers and providers agreeing to divvy up money saved by delivering care more
Yes, it failed to uproot the volume and intensity incentives of fee-for-service medicine. But P4P deserves credit for getting the world ready for today’s value-based payment.

When Doug Moeller, MD, a medical director at McKesson Health Solutions who specializes in coding compliance, assessed just what role pay for performance plays these days, he had to reach. “I’m not hearing the same level of energy around it,” says Moeller. Studies show that for an incentive or penalty to be effective, it needs to involve nearly 20% of annual salary, he says, and “P4P never got close to that.”

But in addition to having a tweet-friendly nickname way ahead of its time, pay for performance paved the way for the current surge toward value-based payment that may finally wean American health care off fee-for-service that rewards volume and intensity over quality and cost. P4P changed the mindset by attaching strings to payment. And at a practical level, many of the quality measures developed for P4P programs have been applied to today’s value-based payment systems.

“Yes, it failed to uproot the volume and intensity incentives of fee-for-service medicine. But P4P deserves credit for getting the world ready for today’s value-based payment.”

**PAY FOR PERFORMANCE**

**Losing Mojo But Getting Props**

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rated specialists and low-cost labs. Lisa McDonnel, a United senior vice president, says only primary care physicians who have at least 100 of the company’s beneficiaries in their panels are allowed to participate so the financial incentives—bonus payments based on PMPM cost savings—have some punch. “We are trying to make it a meaty enough carrot to get the behavior change,” she says.

Flexibility is another important feature. McDonnel says UnitedHealthcare’s philosophy is to meet providers “where they are. Even if I had the perfect payment scenario, it would still take a provider on the other side who is ready to manage the population in that way,” she says.

Finally, some experts believe that the Mr. Nice Guy-era of health care we’re in, during which many value-based payment arrangements have been limited to upside risk and bonuses, is wholly inadequate for pushing American health into value-based care. Two-sided risk and penalties are needed if the system is to leave its fee-for-service days behind and give up on its volume and intensity ways, they say.

**P4P in to 2 types**

HCI3’s website calls P4P a misnomer because fee for service can be characterized as a type of pay for performance: It pays for every service, and the performance sought is production of volume. But that kind of thinking is for insiders and wordsmiths. In everyday health care parlance, P4P is used to describe payment systems that link a portion of a clinician’s or hospital’s payment to certain performance criteria. The performance criteria vary and can be endlessly tinkered with, but traditionally they have been process measures—how many patients have received the appropriate cancer screenings, for example—because they are the easiest to measure.

Although P4P is old news, it remains the dominant...
A mode of value-based payment, according to Andrei Gonzales, MD, a colleague of Moeller’s at McKesson Health Solutions and the company’s director of value-based reimbursement. (Whether P4P really should be counted as value-based payment can be debated, but that’s an argument for another day.)

P4P programs can be devised in any number of ways, but Gonzales says they typically fall into two categories. In one, if providers meet the performance criteria, they get a small percentage increase on their FFS payments the next year. In the other, providers are ranked on performance measures and are paid bonuses according to where they fall in the rankings. For example, providers in the 90th percentile of the performance measures might earn larger bonuses than those in the 80th percentile. In essence, this is P4P grading on a curve.

Gonzales says it’s not clear which approach is more effective, although as behavioral economists like to say, the lump sum may be more salient—it grabs people’s attention. On the other hand, a 1% or 2% increase in FFS payments adds up. Gonzales says large medical groups have recognized that it’s enough money to make it worthwhile to hire someone to make sure the performance measures are recorded and reported, which is often half the battle.

Dollars short, years too early
Still, his colleague believes P4P often hasn’t put quite enough money on the table. “I think doctors were curious about pay for performance and I think that if the money had been bigger, they would have been a lot more curious,” says Moeller. A practice that gets 70% of its patients with diabetes to get an eye exam might get a bonus, but it needed to be “a large enough bonus, because chasing down those diabetics and getting them to have eye exams is some real work.”

It hasn’t helped matters that P4P programs have typically been the brainchildren of payers, especially when the providers and payers were like a couple in a bad marriage and not making nice like they are now. “Physicians are appropriately focused on how they’re getting paid, what they’re getting paid, and whether it’s adequate to meet their needs to provide high quality care,” says Jeffrey Rideout, MD, president and CEO of the Integrated Healthcare Association, a not-for-profit group in California with an agenda similar to de Brantes’s national organization. Any incentive program works better if it’s been developed or endorsed by the physician leadership, says Rideout. “It gets very, very difficult when somebody outside the clinical enterprise is throwing expectations at you.”

But even benchmarks developed by physician leadership don’t guarantee buy-in among those on the front lines of delivering care, notes Rideout. “Physicians spend most of their time practicing, they don’t spend most of their time creating performance standards,” he says. “There’s a lot of physician involvement in performance standard creation. Every organization that issues standards has lots of physicians. Does that represent the rank and file in a way that the rank and file believes in? Probably not.”

Another reason why P4P programs haven’t made as much of a difference as their proponents had hoped is that a great percentage of money still gets pumped through the fee-for-service system, with P4P getting a relative trickle of dollars for care that is supposed to result in better outcomes. Little wonder that volume and intensity win out. “Pay for performance pays people a little more or a little less but the fundamental system is still based on fee-for-service,” comments Rideout.

But there’s another way to look at the P4P programs. The fault is not so much in P4P but in the times when many of the programs were introduced. P4P was an attempt to revamp health care payment and delivery when the health care system wasn’t ready for rethinking payment, de Brantes, Moeller, and Rideout agree.

What’s changed? A lot, and the sway of CMS is the reason. “When CMS finally says we’re going to do some things differently, they’re the only payer in the country, in my opinion, that has the clout to just start making changes,” says Moeller. “Everybody else has to sort of play ball. Even United and Aetna and some of the jumbos rarely have more than 20% or 30% in any single region.”

De Brantes credits the ACA with shaking things up enough to start wrestling the system from fee-for-service. The exchanges have created an impetus to reduce costs in order to have competitive premiums,
although it looks like there will be large increases in rates in 2016. CMS’s ACOs, bundled payment programs, and the Comprehensive Primary Care program “all have very significant incentives in overall payment that is related to provider performance,” he says.

The providers are listening this time, de Brantes adds. “The ACA has changed provider mindsets and focused them on accepting that old-style, fee-for-service payments are on their way out and will be replaced. Providers aren’t rebelling against accountability anymore. They’re trying to find ways to cope with it and the inevitable full transparency in price and quality that is coming.”

Expect hospitals and physicians to invest more in technology. “I’ve said for many years that until payment changed, the desire by providers to invest in technology systems that will link them together with patients and provide important feedback on patient outcomes would be lacking,” says de Brantes. “And now that payment has finally changed, I think you will see some very rapid adoption of new technologies to help providers vastly improve their efficiency.”

Paying for care by the episodes may be the shortest path to value-based care. But administration is tricky, and early results raise questions about the savings achieved.

Health care researchers are typically a sober bunch, not given to angry online contretemps on the intricacies of their often dry and arcane topic. So it was a little surprising to see some strongly worded back-and-forth on the Health Affairs blog last year debating whether the concept of bundled payments has proven its worth.

A pair of Rand Corp. researchers had just published a review of a bundled payment demonstration in California that they said had “failed” because it was not able to attract enough physician participants. Their dismissal of the program got under the skin of the nation’s foremost proponent of bundled payments, François de Brantes, whose nonprofit Health Care Incentives Improvement Institute (HCI3) has been a leading innovator in payment reform.

De Brantes complained in his own blog that the Rand review reflected “vague conjecture and the deliberate choice to ignore the truth and spread falsehoods.” The Rand researchers felt compelled to fire back on the Health Affairs blog about “ad hominem” attacks.

New software
McKesson, of course, is happy to oblige, as are hundreds of other companies. “Recent releases of claims-auditing software … are creating a new context for claims processing,” says Moeller. “In addition to helping enforce correct coding guidance, new software logic can use claims history to count the number of rewardable events in P4P programs, such as vaccine administration, diabetic eye exams, and other codable events in a health plan database.”

The Supreme Court’s King v. Burwell decision means that more ACA provisions will be implemented, says Moeller. “We’re just starting to see the cost-saving initiatives that were articulated in that legislation. I think it’s a little soon, oddly enough, to really evaluate the impact other than to say everybody is clear that it’s time to change.”

P4P will probably not be a crucial part of the conversation, Moeller predicts. “It did not make the difference that the advocates for that approach thought it would. It helped, but the increase in cost of care hasn’t subsided because of P4P.” — Frank Diamond

BUNDLED PAYMENTS
Value in Bite Sizes

Paying for care by the episodes may be the shortest path to value-based care. But administration is tricky, and early results raise questions about the savings achieved.

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of care. It is similar conceptually to the diagnosis-related group (DRG) that CMS has used for years, but the DRG includes only inpatient care, while bundles can encompass a variety of providers. Bundles can be designed in many ways, by nearly any player in the health care system—insurers, hospital systems, medical groups, even employers.

In contrast to other value-based payment concepts such as ACOs and patient-centered medical homes, the idea of bundling the provider payments for an episode is more targeted and flexible because it is on a smaller scale, involving a given procedure or diagnosis and a smaller group of patients. Bundled payments are seen as a transitional payment method that moves the American health care system toward more efficient coordination of care without physicians having to learn complex financial models for managing all the care for a group of patients.

“Bundles are little bite-sized nuggets of episodes that you can plug into an ACO or a medical home,” says Elaine Daniels, who worked with bundles for 7 of her 20 years at Blue Cross Blue Shield of North Carolina before joining Aver, an informatics company. “To me, it’s an easy segue into managing costs in ACOs and medical homes.”

Rob Lazerow, a practice manager for the Advisory Board Co., agrees that the methods can be used together, noting that they have different purposes: “An ACO tries to reduce or avoid utilization, whereas bundled payments try to make an episode more efficient.”

Lili Brillstein, director of the episodes of care program for Horizon Blue Cross Blue Shield of New Jersey, sees the value-based payment models—bundles, ACOs, medical homes—as synergistic. “What’s really nice about the episodes approach is that it’s a microcosm of these bigger models, and it’s easier to get up and running. Episodes don’t require the same kind of infrastructure and you can get there fast, but the concepts are exactly the same. You create this medical neighborhood and have this cadre of providers who can deliver services effectively and efficiently across the spectrum of care.”

Proponents of bundling tend to be enthusiastic, even evangelical about the potential for bundling to finally take the health care system where it needs to go. “I would bundle everything if I could,” says Daniels, only partly in jest. They find it frustrating that some published studies have painted a less optimistic picture of how bundling works in actual practice.

Skepticism about bundled payments centers on concern that bundles won’t save much money if they are variations on fee for service and don’t require providers to take on risk. Critics also argue that bundling is administratively difficult. It requires one party to take financial responsibility and have the expertise to understand how much the whole episode should cost and how much each participant should earn. That expertise can be hard to come by, as can the information systems and algorithms required to carry it out.

How bundles work
Many of the early bundled payment initiatives have been retrospective with upside risk. The providers bill just as they have under fee for service, but when the episode of care is over there is a reconciliation process. If financial goals are met or exceeded, a bonus is paid. If they aren’t and the bundled payment arrangement included downside risk, a penalty is assessed. Andrei Gonzales, MD, a value-based payment expert at McKesson Health Solutions, says there’s often a lead provider, or “quarterback,” in bundled payment arrangements who earns the bonus or pays the penalty. For a bundled payment for a surgical episode, the quarterback would typically be the surgeon; for congestive heart failure, it would probably be a cardiolo-
Texas Medicaid insurer bundles pregnant moms, bundles of joy

When Community Health Choice (CHC), a regional HMO in southeast Texas, decided to try a bundled payment pilot, pregnancies were the natural place to start. The nonprofit insurer covers 300,000 lives, two-thirds of them in Medicaid, and maintains a specialty with Children’s Health Insurance Program (CHIP) perinatal patients. CHC manages more than 25,000 births each year.

Karen Love, the HMO’s senior vice president for strategic planning and partnerships, had been hearing about bundled payments as a concept of increasing interest to the state Medicaid agency, and she started attending a yearly national bundled payments summit to learn more. CHC ended up hiring the summit’s sponsor, the Health Care Incentives Improvement Institute (known as HCI3), to help launch a pregnancy-related bundle with two physician groups with an interest in trying new payment models. HCI3 helped the insurer examine claims data to provide target budgets and develop the pitch to the providers. “It’s helpful to have a third party facilitate when you’re having those conversations,” says Love.

The two-year program was launched in March with the first year including just upside risk, meaning that CHC will share any savings 50–50 with the physician groups at the end of year one if they come in under budget. The second year will involve some type of downside risk that has not yet been decided. It will also include quality metrics (such as rates of sepsis, breastfeeding, and postpartum depression screening) that are being benchmarked during the first year. The physicians helped choose the quality metrics and select their own methods of adjusting clinical care to meet the financial and quality goals.

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CHC was interested in pursuing bundled payments as a new way to reduce medical costs while at the same time improving the quality of care for its pregnant patients. “We consider ourselves cutting-edge and like to do things that are novel and out there in the literature,” says Love.

If the pilot is successful, the insurer would like to have it inform future contracts with the provider groups, with a shared savings component built in; the concept could be expanded to other provider groups that do high volumes of particular medical services. CHC will also monitor quality measures and patient experience through surveys.

One unique thing about this bundle, Love says, is that it includes care and outcomes for the baby as well as the mother. “We really like that focus,” she says. “Those kiddos become ours down the line. We believe in that whole thread...improving birth outcomes leads to better health outcomes. The kid is healthier, gets a better education, a better job and someday doesn’t need Medicaid services at all.”
sophisticated incarnations, such as bundling patients with multiple comorbidities together—the connection being not their specific diagnoses, but the way providers need to organize to care for them.

Bundled payments make up less than 1% of all commercial insurance payments, according to a 2014 report by the Catalyst for Payment Reform, an employer group pushing for value-based payment. It’s unclear exactly how many bundles are currently in use. Lazerow at the Advisory Board is tracking a couple of dozen commercial insurer bundling pilots around the country, though there are undoubtedly more running under the radar. Blue Cross Blue Shield insurers in North Carolina and New Jersey are both enthusiastic adopters of bundles; the North Carolina Blue reported saving 8% to 10% on a bundled payment arrangement for knee replacements back in 2011.

In 2013, CMS launched the Bundled Payments for Care Improvement initiative, which offers 1 of 4 models and 48 different episodes to choose from. The agency says providers are currently participating in its bundling pilots. An evaluation of the initial participants released earlier this year was more an outline for future evaluation and drew few conclusions. Jeff Goldsmith, a health care consultant and member of the Managed Care editorial board, likes the “elegance” of the ideas behind bundled payments, but found the CMS results troubling because he didn’t see them as showing any cost savings. If you add in the report from the Rand researchers, says Goldsmith, there’s enough recent bad news about bundled payments to sow serious doubts about whether an attractive idea can be implemented successfully.

State Medicaid agencies are also innovating with bundled payments, particularly in Arkansas, which has launched an initiative involving bundled payments and medical homes with its Medicaid program, along with two major commercial insurers. Initial results showed that more providers gained from the program than lost, though there were substantial penalties for those that did not meet financial goals. It is hoped that will change as providers adjust their practice to meet financial and quality metrics.

Large national employers are experimenting with the idea, focusing on contracting with providers for specific services. For instance, Wal-Mart has a program for employees who need cardiac, spine and certain other surgery that encourages them to use 1 of 6 providers with high volumes and good outcomes.

**To-do list for bundles**

So, what needs to happen to bring bundling into the mainstream and convince skeptics? Several things:

**Providers must become willing to take risk.** That way, these models can go from retrospective to prospective and reap more savings. They also need to move ahead with hiring care coordinators, collecting data and sharing information with other providers in an episode of care.

**Definitions must be agreed upon.** Differences in how bundles are defined could cause trouble down the road, as providers have to manage several versions of a given episode of care. HCI3’s Prometheus project has provided a starting point for episode definitions, says Daniels, adding “but payers and providers need to work collaboratively to come to a comfort level on what a definition should be and what services should be included in that time period.”

**Payers must invest in analytics systems to manage bundles and track savings and quality.** Seventies-era information systems used by some Medicaid administrators and other payers are a real roadblock to managing innovative payment systems, argues de Brantes. And insurers run the risk of becoming irrelevant if providers contract directly with employers to act as centers of excellence.

**Insurers and employers need to work together to design benefits to encourage consumers to use services packaged for efficiency and quality.** The insurers that have led the way into bundling see several advantages, beyond just the need to take part in an inevitable change in the marketplace. One important plus, says Brillstein, is that the process of designing bundles gives insurers and physicians an opportunity to work closely together to support high-quality, patient-centered care, which can improve a relationship that has often been adversarial. “These programs are changing the spirit of the relationship between providers and payers,” says Brillstein. “It’s very collaborative.”

Once providers get on board, payers have analytic and payment systems in place to manage bundles, and employers encourage patients to use bundled services (through steerage mechanisms), “the sky’s the limit,” says Daniels, who led early adoption at Blue Cross Blue Shield of North Carolina. “We’re right on the cusp, and you’re going to see a lot of stuff happening in the bundled space. The future of health care is going to be bundled payment.” — Jan Greene
Of all the “value-based” provider payment methodologies, this one’s the classic. And it may be mounting a comeback.

The Macarena has yielded the dance floor, the TV hospital show E.R. is long gone, and the president is no longer named Clinton—for the moment, anyway. But the payment methodology that was white-hot in health care in 1996 seems to be warming up once more. Of course, it’s capitation.

Capitation—paying providers upfront on a per-member, per-month basis to give their covered panel of patients all necessary medical services to make and keep them well—lost ground when the public came to believe it was too stingy with needed care and many providers blamed it for a hemorrhage of red ink. But it hasn’t disappeared. And some in the industry say the problem then wasn’t that capitation was a faulty tool but that doctors, hospitals, and consumers simply weren’t ready for managed care’s prime time.

Now, two decades later, perhaps they are.

Gaining currency
Capitation reached its high-water mark in 1996, according to Dave Gans, senior fellow for industry affairs at the Medical Group Management Association (MGMA). That year, 68.3% of multispecialty medical groups reported that they had capitated contracts. By 2013, that proportion had fallen to 27.4%.

In the ’90s, capitation was seen as a way of controlling utilization through the use of a primary care gatekeeper to, in effect, ration care, says Gans. Today, the primary care physician is supposed to coordinate the care, not gainsay it, he explains. Patients may self-refer to a specialist, but that specialist, if the system is running right, sends information back to the primary care doctor to complete the medical record.

Of course, capitation can apply at different levels. It can mean the way a hospital or medical group is paid by an insurer, or the way that hospital or group in turn remunerates individual physicians, either primary care doctors or specialists. Partial capitation is used to describe an arrangement whereby the provider takes on financial responsibility for just part of the patient care—for example, just outpatient care.

Certainly the capitation tide has receded—and not just because of misunderstanding. Writing in the Journal of General Internal Medicine back in 2001, Thomas Bodenheimer, MD, a member of MANAGED CARE’s editorial board, noted with regret that “capitation has been sorely misused to the benefit of for-profit plans and physician entrepreneurs.” He decried “embarrassing” studies showing that, just as capitation’s critics charged, mechanisms of payment to individual doctors sometimes influenced their clinical decisions. “Capitation payment is waning, [and] fee-for-service is enjoying a resurgence,” Bodenheimer wrote. But he still saw a future for capitation as a system for paying institutions, which would then turn around and remunerate individual physicians and other providers with whatever mixture of capitation and fee for service worked best.

The Catalyst for Payment Reform, an employer group campaigning for value-based health care, said in its 2013 National Scorecard on Payment Reform that just 1.6% of payments are made through contracts that call for “full capitation with quality”—
that is, capitation contracts that allow for what Executive Director Suzanne Delbanco calls “payment adjustments based on measured performance and payment risk.” The group’s 2014 scorecard said 15% of commercial in-network payments were through full capitation and 1.6% through partial or condition-specific capitation.

The role of IBNR
“The difference between the 1990s and today is that back then there was essentially only capitation, while today there’s a broad continuum of value-based methodologies,” says Gary Greensweig, DO, vice president and chief physician executive for physician integration at Dignity Health in San Francisco, the nation’s fifth largest health care delivery system. The ‘90s version was all about lowering costs, he adds. “There’s nothing wrong with that,” says Greensweig “but today our focus is more broad, and it includes building substantial infrastructure around population health management.”

By about 2000, he says, more than 90% of the California medical groups that had accepted capitation were insolvent—partly because they’d failed to allocate sufficiently for a financial category called IBNR—“incurred but not reported” expenses.

“Groups that were taking capitation thought, ‘Boy, we’re doing great!’” says Greensweig. “But when a patient is in the hospital, you might not get the bill for six months. Six, eight, 12, 24 months later, they realized they were out of money because they hadn’t reserved enough for the downstream price.”

Of Dignity Health’s $9.5 billion in patient revenue last year, as Modern Healthcare has reported, 15% came under value-based contracts such as ACOs and bundled-payment systems, but only 3% was capitation. Still, the magazine said, “Dignity’s capitation contracts let the system hedge by allowing it to default to fee-for-service rates if there is ‘material deterioration’ in financial performance.”

Greensweig foresees growth for capitation, but says it won’t become “the be-all and the end-all,” just one tool in the value-based toolbox. His group is preparing to succeed with capitation not only by putting enough aside for IBNR, but also with the investments it’s making in population health management. These include care and case management, “health information exchanges,” electronic data systems with data warehouses and portals for patients and physicians, and analytics.

“If you’re managing half a million or a million patients,” he says, “you need special tools that can comb through the data and help pull out those people who need our attention so that we can focus on them in a systematic way. Those kinds of tools we didn’t have in the 1990s [when Dignity’s predecessor organization was known as Catholic Healthcare West]. We have some of them now, but not all of them, and we are building them as we speak.”

Old letterhead
Mention capitation’s possible comeback to Ruth Benton, and you may elicit a barely suppressed chuckle. She’s the CEO of the Denver-area group New West Physicians. “I signed a capitated Medicare Advantage contract with Pacificare out of California in 1995, and we’ve managed that downside risk ever since,” she says. “I still have the same contract—it has 25 amendments. And it’s still on Pacificare paper, even though United bought that company more than 10 years ago!”

How has this physician owned and governed group thrived where others stumbled? Benton cites “great” doctors and board members and a “brilliant” medical director and president. But she adds that she “grew up in the insurance industry” and knew, when she started the group two decades ago, two things about signing a risk contract that many similar groups didn’t grasp: “First, you need to reinsure it,” she says. “Second, you need to create your own stop-loss protection for IBNR. And I set that up from day one. So when the bottom fell out in 1998 with many of these HMOs and all the risk they’d let out to providers, many physician organizations went out of business. But we didn’t. We did incur expenses, but we burned through our internal reserves and claimed everything we could on our reinsurance, so we never lost any money.”

In the ‘90s, she recalls, capitation accounted for 60% of the group’s revenue—if you include primary care capitation. But then “the managed care companies just stopped doing capitation,” she says.

Today, Benton’s group has 70 primary care physi-
cians (about a 3–2 mix in favor of family practice over internal medicine) and 33 midlevel providers. It doesn't accept traditional Medicare; its capitated Medicare Advantage contract has continued to generate incremental revenue for the group practice. There are a 13 to 35 “quality gates” that New West Physicians must clear, but that has been true since the beginning, and the group is used to it, says Benton.

“There’s no quality withhold,” she explains. “The plan takes the professional fee part of the Medicare premium and pays that in a calculation to us. And we’ve been doing it for so long, between their financial people and my financial people, we predict it pretty damn closely. We’re paid a capitation amount monthly, and we capitate our primary care physicians and pay fee-for-service to our specialists.”

Like Greensweig, Benton attributes much of her group’s success to applying methods of population health—she calls them “a managed care engine of clinical people who know how to do population management.” She is bullish about capitation being the most promising value-based payment method and regards a capitated medical group as the best answer to the consumer’s need for connection. “There isn’t a consumer out there who’s really sick who wouldn’t greatly benefit from a long-term relationship with a primary care physician advocate who can help him or her with the right access to care in the scary health care system,” she says.

Benton adds: “I want the commercial ACOs to evolve into capitation. The insurers have this many covered lives and need someone to manage their health care risk, and I’m willing and able to take that on,” she says. “As far as jumping over quality gates, that’s not a new idea—we’ve been doing it for 20 years. It’s just coming back around the mulberry bush.”

Whether or not every medical group is ready to embrace this once-unpopular payment mechanism quite that wholeheartedly, it seems clear that capitation’s story isn’t finished. “There are opportunities for practices through capitation,” says the MGMA’s Gans.

To work successfully with capitated payments, he warns, a practice needs to “have enough patients to be sure to avoid adverse selection and to capitalize the cost of the information systems necessary to manage capitation patients.”

— Timothy Kelley

**SHARED SAVINGS**

**Way Station to Shared Risk**

Without shared risk, shared savings might not be strong enough medicine for what ails American health care.

Sharing—that’s a good thing. And who can object to savings?

So shared savings certainly doesn’t have an image problem, and it’s one of the most popular payment mechanisms in this fledgling period of value-based health care. But winning popularity contests doesn’t mean you’re without flaws or critics, who are more than happy to point them out. Shared savings has been knocked for rewarding expensive providers with historically high spending patterns and simply being a tricked-up version of pay-for-performance lacking horsepower to drive change in American health care.

Even those with less harsh opinions see shared savings as merely being a transition to payer–provider arrangements in which providers shoulder more of the burden if the health care costs they rack up are too high.

“Shared saving is viewed as a way station,” says Michael Bailit, MBA, a payment reform expert and founder and president of the Massachusetts health care consulting firm that bears his name. The next phase after shared savings is shared-risk arrangements, says Bailit, and then eventually full risk.

Bailit gave two reasons for shared savings’s status as a mere stopover. First, providers who have some success with shared savings will have fewer and fewer savings opportunities as time goes by. What do you do after you have squeezed—and squeezed again—the low-value care out of your practice, clinic, or hospital? People in health care management often talk metaphorically about low-hanging fruit—early accomplishments deceive because easier problems tend to yield to solutions faster than tougher ones. Bailit’s point is that shared savings efforts may lead to the corollary circumstance of only the high-hanging fruit being left to pick.
Reason number two is what decision theorists call loss aversion; without some downside risk attached, shared savings may not give hospital executives, doctors, physician assistants, nurses—anyone involved in the provision of health care—enough of a reason to take on the hard work of providing true value in health care. “Fear of loss,” says Bailit, “gives more motivation than the opportunity to gain.”

Even if shared savings is all about the journey, not the destination, it’s an important phase and would probably deserve its own chapter if yakked-about value-based health care actually comes to be. The basic concept is easy to grasp—and it’s easier still if you take the payer’s point of view. The shared-savings arrangement starts with the payer and provider organization agreeing upon some kind of financial benchmark for a population of patients—say, the cost of outpatient care for a year for a thousand people with Acme Health Insurance. That benchmark can be based on past spending patterns or comparisons with other providers in the same market—or both. A year goes by. If the provider spends less than that benchmark—the namesake savings, as far as the payer is concerned—then the provider and the payer divvy up that money. That is the shared savings. In arrangements when only savings are at stake, the provider–payer split is usually 50-50.

In shared-risk arrangements—also called two-sided risk—the provider agrees to write a check to the payer if spending goes over the financial benchmark. (In the fee-for-service mode, that overspending looks like revenue to the provider, not overspending.) Typically, explains Bailit, in shared risk arrangements the 50-50 split changes to a ratio that gives the provider a greater proportion of any savings. That’s the trade-off for taking on the risk.

To guard against shoddy care delivered in pursuit of shared-saving dollars, the payer usually requires the provider to meet some quality metrics before the organization gets shared savings. Most shared-savings arrangements protect providers against costly outliers. The payer may simply agree to cover those cases or, in some cases, the providers purchase separate insurance against them. Some shared-savings arrangements set a threshold above the financial benchmark at which the shared savings start.

When Bailit and a colleague wrote a report on shared savings for the Commonwealth Fund in 2011, most of the 27 programs they assessed were primary care medical homes and “ACO-like” arrangements involving broader provider organizations. But since that report came out, CMS has launched its ACO programs, and shared savings is a prominent feature of those programs. CMS did not invent shared savings and nor is it the sole purveyor, but Bailit says CMS put “booster rockets” on the payment mechanism, and many payers are designing their programs using the CMS chassis.

The federal agency’s largest ACO program has shared savings in its name. As designed, the Medicare Shared Savings Program (MSSP) was supposed to wean the participating 400 participating organizations off of one-sided risk and move them into the discipline of the two-sided risk. But under new regulations that came out earlier this year, the participants will be allowed to sign up for another three-year hitch of one-sided risk at a 50-50 shared savings rate, provided they have met quality standards. One criticism of shared savings is that it doesn’t go much beyond penny-pinching—that’s not disruptive enough when it comes to reforming the delivery of health care and tilting the system toward value. The extension of one-sided risk in MSSP confirms that low opinion.

CMS’s other ACO programs do include two-sided risk. The Pioneer ACO Model program has a menu of five payment arrangements with shared saving and losses of up to 60% to 75% and adjusted based on quality scores. The New Generation ACO Model, which was just announced this year and isn’t up and running yet, has two proposed tracks: shared savings and losses up to 80% and another one with full risk—shared savings and losses of up to 100%. But by design, these are experimental programs, the products of the CMS’s Innovation Center, so there’s some question about how much sway they have, notwithstanding the surprising influence that CMS has come to have as a trendsetter.

That’s one small step for value…

Faulting shared savings as milquetoast may be missing the point, say some experts. Given how entrenched fee-for-service is and all the interests and behaviors that have grown up around it, incremental change may be more realistic and sustainable than anything root and branch. In that way, shared savings may be like the ACA. Moreover, shared savings isn’t really a stand-alone program but a concept and payment mechanism that can be used with pay-for-performance, bundled payments, or capitation. How it will be viewed in a few years will depend on the fate of value-based care. —Peter Wehrwein
While Gay Couples Say ‘I Do,’ Health Care Often Says ‘We Don’t’

Ruling in same-sex marriage case extends insurance coverage, but problems with discrimination and lack of access persist.

By Joseph Burns
Contributing Editor

A

merican marrieds marry for love, happiness, family—and sometimes the added benefit of one person getting new or better health insurance through the other’s employer. The Supreme Court ruling on June 26 that legalized same-sex marriage throughout the country was a landmark decision with many implications. One practical effect may be health insurance coverage for thousands of previously uninsured and unmarried people in same-sex relationships.

At the same time, legal experts note that neither this year’s Obergefell v. Hodges decision legalizing gay marriage nor the 2013 United States v. Windsor decision that found the Defense of Marriage Act was unconstitutional cleared up the matter entirely. Those are constitutional, not employment law decisions, and they don’t explicitly address the obligations of employers, notes Jennifer Kates, director of global health and HIV policy at the Kaiser Family Foundation.

“The EEOC just issued a major ruling which, for the first time, said that sexual orientation is inherently a sex-based consideration,” says Jennifer Kates of the Kaiser Family Foundation.

Experts on lesbian, gay, bisexual, and transgender health issues say extending health insurance is one thing, eliminating disparities in health care services for gay Americans and others in the LGBT community is another. Among the problems they talk about are medical care for transgender Americans, adverse tiering for people with high-cost conditions such as HIV, and failure to offer insurance coverage for in vitro fertilization for gay and lesbian couples. The Obergefell decision may bring some needed attention to these shortcomings and inequities, says Michael A. Horberg, MD, one of the nation’s foremost experts on LGBT health care and the executive director of research, community benefit, and Medicaid strategy for the Mid-Atlantic Permanente Medical Group in Rockville, Md. Many people who work in health care don’t understand what it means to be a gay man or woman, and “that means there are major gaps in care,” says Horberg.

Consequential decision

Still, no one is saying that the Supreme Court’s same-sex marriage decision was inconsequential. The Williams Institute, a think tank at UCLA’s law school that concentrates on sexual orientation and gender identity issues, estimates that about 150,000 same-sex couples live in the 13 states that did not allow same-sex marriage before the court said those bans violate the 14th Amendment. Just under half of those couples—70,000 or so—are expected to marry in the next few years, according to the institute. Putting aside for the moment the legal contingencies, many of those marriages should mean employer-sponsored health insurance coverage for spouses. Marrying will also
mean the extension of Medicare coverage to some same-sex spouses. Before the Obergefell decision, same-sex marriage had become legal in 37 states, so many same-sex couples were already getting health insurance benefits. The Williams Institute estimates that the number of married same-sex couples had reached about 390,000.

Edging up
Exactly how many people will gain employer-sponsored health insurance because of Obergefell is difficult to predict. A brief research piece published by JAMA on the day of the Supreme Court decision—presumably so it would get the maximum attention—showed that the end of the ban on same-sex marriage in New York State in 2011 led to a small but notable increase in employer-sponsored coverage among gay New Yorkers.

The proportion of men ages 26 to 64 in same-sex marriages with employer-sponsored insurance edged up from 77.4% to 83.9% during the 18 months after same-sex marriage was legalized in New York, while the number of men in opposite-sex marriages with employer-sponsored insurance slid slightly, from 76% to 73.8%. The pattern was the same for women: an increase (78.1% to 83.6%) among those in same-sex marriages and a decrease (76.7% to 74.4%) among those in opposite-sex marriages. Gilbert Gonzales, a University of Minnesota graduate student who did the research, also found a decline in Medicaid coverage among New Yorkers in same-sex marriages.

Legal weapon
The Obergefell decision will certainly give same-sex couples an important legal weapon if employers that offer opposite-sex coverage don’t extend it to them. But even before the decision, CMS had issued guidance based on a clarification of ACA regulations that said all health plan issuers need to offer spousal coverage to same-sex married couples if they offer spousal coverage to opposite-sex married couples. It didn’t matter what the state law was on same-sex marriage, as long as the couple was married. But, as Kates explains, just because issuers had to offer the coverage doesn’t mean that employers were legally required to buy it, although as a practical matter most did in the states where same-sex marriage was legal. In fact, even employers in the states that banned gay marriage often purchased coverage for their employees that included same-sex spousal coverage, she says. Large employers have long done so in order to attract and retain employees.

Some courts and the Equal Employment Opportunity Commission are construing Title VII of the Civil Rights Act that bans discrimination on the basis of

Stats about same-sex couples

- Approximately 1 million same-sex couples (married and unmarried) live together in the United States.
- The number of married same-sex couples in the United States has tripled since 2013. An estimated 390,000 same-sex couples are currently married.
- About 122,000 same-sex couples are raising 210,000 children under age 18, of whom 58,000 are adopted or foster children.
- Same-sex couples are nearly three times as likely as their opposite-sex counterparts to raise an adopted or foster child.
- Approximately 150,000 same-sex couples live in the 13 states that did not previously allow same-sex marriage. An estimated 70,000 of those couples are expected to marry in the next three years.

Source: The Williams Institute at the UCLA School of Law, 2015.
sex by employers as also applying to discrimination on the basis of sexual orientation, according to Kates: “The EEOC just issued a major ruling which, for the first time, said that sexual orientation is inherently a sex-based consideration.”

But in one of those twists of legal and historical irony, some same-sex couples could end up losing health insurance coverage in this new era of legalized gay marriage. Employers have been offering health insurance to couples, same- and opposite-sex, in domestic partnerships since the early ’80s. In many instances, it was a tactic for extending coverage to gay couples when marriage was not a possibility.

But when courts and legislatures at the state level began overturning the prohibition on same-sex marriage, employers began dropping domestic partner insurance coverage. To continue to be covered, those couples need to marry, employers said. After the Supreme Court’s decision in June, Kaiser Health News reported that employers may do as Verizon did last year when it told same-sex partners in states where gay marriage is legal that they had to tie the knot if they wanted to qualify for benefits.

**Similarities**

Despite the legal obstacles and, until recently, the country’s marriage laws, federal health surveys don’t show large differences between gay and straight Americans in some important health-related areas, including the

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**Transgender people face obstacles but coverage is expanding**

LGBT advocates and health experts say that their community faces discrimination in myriad ways but that the problem may be more severe for transgender people. The discrimination is two-pronged. Physicians and other providers frequently turn away these patients, says M. Dru Levasseur, national director of the Transgender Rights Project at Lambda Legal. “There’s a range of discrimination among providers which could result in trouble accessing preventive care or they might face outright mistreatment,” he adds.

Health insurers also discriminate, Levasseur says. The Human Rights Campaign lists insurers in every state that offer health plans that cover care related to transgender health issues, but many insurers are not on that list. Even if a plan does provide coverage, the claims approval staff often don’t know the rules and deny care incorrectly, requiring appeals, says Levasseur. Moreover, insurers may have transgender-friendly plans but employers have to actively ask for them—and often insurers remove transgender health exclusions only from their priciest offerings, according to Anand Kalra, the health program manager at the Transgender Law Center in Oakland.

But there is good news. A growing number of insurers are covering counseling, hormone therapy, and surgery for transgender members, according to Levasseur. Ten states and Washington, D.C., have rules prohibiting insurers from discriminating against transgender men and women in the administration of health benefit plans. Of the 47 employers who responded to a 2013 National Business Group on Health survey, 60% said they would cover at least some nonsurgical gender reassignment costs in 2014, and 50% said they would offer at least one plan that covers gender reassignment surgical care, compared with just 5% in 2007.

The ACA requires essential health benefits to include coverage for all regardless of sexual orientation. Last year the Federal Employees Health Benefit Plan required all of its health insurers to cover care for members with gender dysphoria. Also, Medicare lifted its exclusion on coverage of gender-transition surgeries. It did not specify how plans should administer the benefit, instead leaving the details up to its contractors, which have been slow to act, notes Kalra.

Costs have not been as high as many thought they might be. A report from Oregon’s Health Evidence Review Commission last year showed that if the state Medicaid program covered such services, only about 175 Oregonians would seek such treatment each year, and the total annual costs would be about $150,000. The commission said this amount would be “a few thousandths of 1% of the state’s $1 billion health budget.”

In January, the Oregon Medicaid program began covering care for transgender beneficiaries, including gender reassignment surgery. In 2013, a Williams Institute survey found that employers reported low costs after adding transition-related coverage. A year earlier, the California Department of Insurance reported that after the University of California eliminated transgender discrimination in its benefit plans in 2005, its insurers did not charge the university system an additional premium. The health plan with the largest enrollment said the maximum claim costs over the first 6.5 years of the program were 20 cents per member per month.
Spend any amount of time with LGBT women, men and transgender, and for some of these statistics, the LGBT numbers are not so favorable, especially when it comes to health status itself.

The big LGBT tent may make sense for political, social, and other reasons, but when it comes to health status the subgroups often go their separate ways. Earlier this year, the Kaiser Family Foundation published a report, Health and Access to Care and Coverage for Lesbian, Gay, Bisexual, and Transgender Individuals in the U.S. Spend any amount of time with the report and it becomes apparent that sweeping generalizations about LGBT health status don’t hold up. For example, obesity rates are higher among lesbian and bisexual women compared with straight women but lowest among gay men. With smoking, the pattern is similar: higher rates among lesbians and bisexual women whereas the rates are similar for gay and straight men. Bisexual women are more likely to have been a victim of rape, sexual violence other than rape, and intimate partner violence than either lesbians or straight women.

HIV/AIDS still disproportionately affects gay and bisexual men and is relatively rare among lesbians. The Kaiser report cites CDC figures showing that while gay, bisexual, and other men who have sex with men make up about 2% of the American population, they account for more than half (56%) of the Americans living with an HIV infection and about two thirds of new infections. Surveys indicate that roughly 1 in 4 transgender women are HIV-positive and, to make matters worse, don’t know it, so they don’t get early treatment that can control the infection and reduce the risk of transmission.

Edging up

The Kaiser report blames “challenges and barriers to accessing needed health services” for poor (at least in some areas) LGBT health status. “These challenges,” says the report, “can include stigma, discrimination, violence, and rejection by families and communities, as well as other barriers, such as inequality in the workplace and health insurance sectors, the provision of substandard care, and outright denial of care because of an individual’s sexual orientation or gender identity.”

Discrimination outside of health care can also adversely affect people’s health, notes Jeff Goodman, DrPH, a core faculty member in George Washington University’s graduate LGBT Health Policy and Practice program. According to Goodman, workplace discrimination based on sexual orientation is still allowed in 18 states and housing discrimination is legal in 28 states. Such discrimination contributes to poor health, particularly poor mental health, and may also discourage some LGBT people from marrying and perhaps gaining access to health insurance, says Goodman. “Someone might not want to get a state-issued document that he or she is married if it means getting fired or being homeless within 24 hours.”

Tears for tiers

One pressing issue for the LGBT population is the cost of medications, particularly for those with HIV. Some insurers have been accused of “adverse tiering”—putting most, if not all, HIV drugs on the uppermost and costly tier of their formularies. Last year, a civil rights complaint was filed in Florida against four insurers accusing them of adverse tiering of HIV drugs which, in addition to making drugs costly, may also feed adverse selection to plans that don’t make their HIV drugs expensive.

After the complaint was filed, the Florida insurance commissioner negotiated some quick fixes with the insurers that, among other changes, limited cost sharing for HIV/AIDS drugs. Cigna and Aetna also ended up changing their formularies. “Obviously, access without tiering for patients who are HIV-positive has a strong impact on the LGBT population,” notes Horberg, at the Permanente Group.

In vitro fertilization (IVF) is another area where LGBT groups see discrimination. For many couples, IVF is the best choice for insemination. A recent New York Times story reported that many insurers exclude IVF treatment for same-sex couples. The Obergefell decision may lead to legal challenges of those exclusions.

Despite increased coverage under the ACA and the Obergefell ruling, Goodman fears discrimination will continue. Many LGBT Americans qualify for Medicaid, which in many states is not very good insurance but is better than nothing. “If some states don’t expand Medicaid, then they may exacerbate the gaps in care for the LGBT population,” says Goodman. “Contrary to the popular perception, not everyone in the LGBT community is rich with excess disposable income. In fact, most are not.”
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**Medical Devices Predicted to Keep Americans Living Longer, Healthier**

Costly now, but as uses proliferate and prices come down, apps have potential for consumer motivation, medical school uptake, and health care cost reductions.

Wearable technology designed to monitor health status and provide opportunities for timely healthcare interventions is no longer a novelty. Just as smartphones are now integral to most people’s lives, so too will be the wearables — the Apple Watch and Google Fit, for example. Only the price is a drawback—for now. The 18-carat, gold-encased Apple Watch sells directly from Apple for $10,000 and up, depending on the model. Although an Apple Watch can be bought on Craigslist, the price is not much lower there. Medscape reports that 1 million Apple Watches were sold in the first 24 hours they became available, and 6% of adults now say they will purchase one.

Consumers do want “smarter” tracking of their medical information, according to any number of surveys. And younger consumers are more in tune with tracking than, say, people over 55—a characteristic that generally applies to physicians as well. A MetaData Group survey found that doctors younger than 40 are more in agreement with a fully connected health care environment within the next five years than those who are older. Stands to reason, given that medical schools nationally are just now beginning to absorb medical apps into their curricula. The University of California–Irvine School of Medicine has created a program to implement medical apps into its curriculum, and other medical schools are sure to follow. Doctors at Brigham and Women’s Hospital in Boston are testing the PMC 320 app, which prompts patients at least once a day to answer questions about their pain levels, mood, activity levels, and other metrics. Developers say the app will help patients and their doctors better manage chronic pain—which affects more than 100 million Americans—potentially reducing the $635 billion in medical costs spent annually on pain.

Health apps are also gaining traction in other medical areas. Google’s life sciences group has created a health-tracking wristband that could be used in clinical trials and for drug tests to provide researchers and physicians minute-by-minute data on patients’ pulse, heart rhythm, and skin temperature, as well as light exposure and noise levels. The experimental device, developed within the company’s Google X research division, would not be available for direct consumer use, but rather will be prescribed for patients, or it could be used in clinical trials. An advantage over other health-tracking methods, says Google, is that the device, by continuously collecting information, would not have to rely on patient compliance or data garnered in a laboratory. The company says it will collaborate with academic researchers and drugmakers to test the wristband’s accuracy.

Novartis, meanwhile, has released new features for its ViaOpta applications. The hands-free app can be used with wearable devices, such as Apple Watch and Android Wear. ViaOpta allows a person who is visually impaired or blind to move independently to a destination and to facilitate their orientation while moving. In Novartis’ words, people with impaired vision will be able to “walk to a nearby cafe, go to the pharmacy, and pick up their grandchildren at the kindergarten, helping to increase confidence and independence and maintaining discretion.”

Do the wearables presage a healthier, fitter, and more independent population in the years ahead? Only time will tell, but one thing is now certain: Americans are living longer, and they will need all the help they can get to stay healthy.

**Utility of balloon up in air**

Compared with conventional angioplasty, the FDA-approved Lutonix 035 drug-coated balloon showed superior primary patency—the interval from balloon angioplasty until the next intervention—at one year, according to LEVANT 2 study results. Coated with a therapeutic dose of paclitaxel, the balloon uses standard mechanical dilatation of a vessel to restore blood flow for patients with peripheral arterial disease in the femoropopliteal arteries. Study results were published in the July 9 issue of the *New England Journal of Medicine.*

For another important endpoint, target-lesion revascularization, however, LEVANT 2 found no significant difference between the two trial groups. Moreover, with respect to primary patency, FDA briefing documents made note of
## Selected FDA medical device approvals, May 1–July 2, 2015

<table>
<thead>
<tr>
<th>Date</th>
<th>Manufacturer</th>
<th>Device name</th>
<th>Use and notes</th>
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<tr>
<td>May 8</td>
<td>Nevro</td>
<td>Senza Spinal Cord Stimulation (SCS) System</td>
<td>Implantable/rechargeable spinal cord system to treat intractable chronic pain in body trunk and/or limbs. Implanted through a small incision in a patient's back to provide electrostimulation, the device is the first SCS system that does not require paresthesia to be effective, eliminating the need for paresthesia mapping during the procedure.</td>
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<tr>
<td>May 18</td>
<td>Silk Road Medical</td>
<td>Enroute Transcarotid Stent</td>
<td>Implanted directly into the carotid artery. Used with the Enroute Transcarotid Neuroprotection System in patients with a likelihood of complications due to other medical problems, body abnormalities, or who have had a recent stroke with moderate blockage in the neck.</td>
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<tr>
<td>May 20</td>
<td>Vertiflex</td>
<td>Superion InterSpinous Spacer</td>
<td>Small H-shaped implant fits in the lower back to reduce symptoms of moderate degenerative lumbar spinal stenosis. In a clinical study, the overall success rate was 95 out of 183 patients (52.7%), compared with 93 of 187 patients (50.2%) in the control group (a different approved spacer) at 24 months.</td>
</tr>
<tr>
<td>June 12</td>
<td>St. Jude Medical</td>
<td>Brio Neurostimulation System</td>
<td>Battery-powered rechargeable electrical pulse generator implanted under the skin with electrodes attached to the brain to treat Parkinson's disease or essential tremor. Two clinical studies in patients whose tremors were inadequately controlled by medication demonstrated effectiveness vs. medication alone.</td>
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<tr>
<td>June 17</td>
<td>Edwards Lifesciences</td>
<td>Sapien 3 Transcatheter Heart Valve (THV)</td>
<td>Third generation of Sapien THV, originally approved in 2011, to treat aortic valve stenosis. The device has a major design change that adds a skirt at the base of the valve to minimize leakage around the valve.</td>
</tr>
<tr>
<td>June 18</td>
<td>Wicab</td>
<td>BrainPort V100</td>
<td>Orient people who are blind by helping them to process visual images through their tongues. Components include a video camera mounted on a pair of glasses and electrodes that the user holds against the tongue. Software converts images captured by the camera to electrical signals that are perceived as vibrations on the tongue. User learns to interpret the signals to determine the location, position, size, and shape of objects, and whether they are in motion. In studies, 69 of 74 patients successfully completed an object recognition test after using the device for 1 year.</td>
</tr>
<tr>
<td>June 23</td>
<td>Medtronic</td>
<td>Evolut R System</td>
<td>First recapturable and repositionable system device for transcatheter aortic valve replacement. Self-expanding device is used in severe aortic stenosis patients at high surgical risk.</td>
</tr>
<tr>
<td>July 2</td>
<td>Proteus Digital Health</td>
<td>Ingestible sensor</td>
<td>Expanded indication for ingestible sensor, first approved in 2012, for measuring medication adherence. Sensors embedded in tablets log actual time of intake, which is communicated through a skin patch to a mobile device. In clinical studies, the system demonstrated 99% positive detection accuracy. Proteus says the device has the potential to speed clinical trials and to improve the real-world effectiveness of medications by promoting better adherence.</td>
</tr>
</tbody>
</table>

Sources: FDA, manufacturers' news releases
a diminished treatment effect at 24 months—data that were not published in the New England Journal article. In their paper, the researchers acknowledged that LEVANT-2 did not provide definitive guidance on the use of the paclitaxel-coated balloon. Longitudinal follow-up, they wrote, will be useful in determining the long-term benefit of the intervention.

Good news on pain relief

Boston Scientific’s Precision Spectra Spinal Cord Stimulator System, used in conjunction with Illumina 3D neural targeting software, provided 1.5 times better overall pain relief and 2 times better low-back pain relief than the previous generation of its system, according to data presented at the International Neuromodulation Society’s 12th World Congress in Montreal.

Stimulation of the dorsal root ganglion (DRG) with the St. Jude Medical Axium Neurostimulator System provided greater pain relief and treatment success versus traditional spinal cord stimulation—81.2% versus 55.7%—for treatment of chronic pain in the lower limbs, according to data from the ACCURATE study. The DRG processes pain signals as they travel to the brain. Designed to support U.S. approval of DRG stimulation, ACCURATE is the medical device industry’s largest-ever study to evaluate patients suffering from chronic lower limb pain associated with nerve damage.

FDA issues UDI guidelines

The FDA has launched its unique device identification (UDI) initiative, emphasizing the September deadline for the direct marking of high-risk class III devices. Class III devices are generally those requiring premarket approval from the FDA. In direct marking, a UDI number is permanently placed on the device rather than on its label. The guidance requires direct marking for devices that will be used more than once and are reprocessed between uses. It also allows exemptions on a case-by-case basis if direct marking is not technologically feasible, if a device was previously marked, or if marking would interfere with its safety and effectiveness.

The FDA states that for devices classified through the de novo process or cleared in a 510(k) submission, “We expect you to conduct analysis and/or testing to determine whether direct marking could significantly affect the safety or effectiveness of the device.” Class II devices face a 2018 deadline for compliance (see table).

The United States is the largest medical device market in the world, with a market size of $110 billion and which is growing quickly. American exports of medical devices in key product categories identified by the Department of Commerce exceeded $44 billion in 2012, a greater than 7% increase over the previous year.

—Katherine T. Adams

<table>
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<td><strong>Device</strong></td>
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<tr>
<td>--------------------------------------</td>
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<tr>
<td>Class III (including class III LS/LS) Devices licensed under the Public Health Service Act</td>
</tr>
<tr>
<td>Implantable (class II, class I &amp; unclassified)</td>
</tr>
<tr>
<td>Class II (other than I/LS/LS)</td>
</tr>
<tr>
<td>Class I or unclassified (other than I/LS/LS)</td>
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*Direct mark requirements apply to products that are intended to be used more than once and intended to be reprocessed before each use. Direct mark compliance dates are in addition to label/GUID/date format compliance dates.

Heart failure has been with us for a long time. It was described in ancient Egypt, Greece, and India. The Romans figured out that it could be treated with foxglove, the source of digoxin. Some notable developments over the last several hundred years that helped with the understanding include William Harvey’s description of the relation of heart failure to the circulatory system in 1628, the invention of the stethoscope by René Laënnec in 1819, and the invention of the X-ray by Wilhelm Röntgen in 1895 and electrocardiogram technology shortly thereafter.

But most of our knowledge about treating heart failure has come in the past half century. Although early—and quite toxic—forms of diuretics were in use in the ’20s, modern diuretics were not discovered until the ’50s. We’ve seen a parade of other new therapy classes added since the diuretics, including loop diuretics, beta blockers, ACE inhibitors, and ARBs.

But, remarkably, despite all of the research over the past half century, we are still learning more about this ancient disease. Now a new medicine that combines one of the most commonly prescribed ARBs, valsartan, with an enzyme, neprilysin, is set to change how heart failure is treated in this country.

Giving some of neprilysin’s back story might be helpful in appreciating the excitement about this new medication, because it wasn’t that long ago that it seemed like it would end up on the dust heap rather than in the medicine cabinet. (If you want the full history, I recommend a review written by Eugene Braunwald, the prominent Harvard cardiologist, published in the March 2015 issue of the Journal of the American College of Cardiology.) Congestive heart failure is typically treated with compounds like ACE inhibitors and ARBs that stymie the renin–angiotensin–aldosterone system. In the ’70s, a second path to treating heart failure started to open up when scientists discovered an enzyme that degrades endogenous vasoactive peptides. It went by various names but in cardiology the name neprilysin won out. Researchers first tried compounds that inhibited just neprilysin, but they had little effect on blood pressure or heart failure because they affected both vasoconstrictive and vasodilatory peptides, according to Braunwald’s account. Then researchers tried combining neprilysin inhibition with ACE inhibition—omapatrilat was the name of the leading compound—but angioedema was a serious side effect. The quest to take advantage of the understanding of neprilysin seemed to have hit a dead end.

At last, the right combination
The breakthrough came when researchers tried combining a neprilysin inhibitor, called sacubitril, with an ARB, valsartan, because ARBs stifle the breakdown of bradykinin—and that was expected to reduce the risk of angioedema. The pivotal trial of the new compound—experimental name, LCZ696; brand name, Entresto—was stopped early after a median follow-up of 27 months because it compared so favorably against the control medication, enalapril (Vasotec), an ACE inhibitor. The primary endpoints of the industry-sponsored trial, called PARADIGM-HF, were cardiovascular death or hospitalization for heart failure. The results were persuasive: Cardiovascular death was 20% lower in the treatment group; heart failure hospitalizations

Thomas Morrow, MD, is the chief medical officer of Next IT. He has been the founding medical director of five HMOs and a disease management company, a medical director at Genentech, and president of the National Association of Managed Care Physicians. You can contact him at TMorrow@ManagedCareMag.com.
were lower by about the same amount, and all-cause mortality was 16% lower than the control group taking enalapril.

Importantly, the adverse event rate was low, with angioedema occurring in just 0.1% of patients. Another good sign is that more people discontinued therapy in the control arm than in the treatment arm.

**Entresto will cost about $12.50 per day less discounts adding about $4,500 to the cost of treating a patient with heart failure.**

Comes in three doses
The FDA approved Entresto with the indication “to reduce the risk of cardiovascular death and hospitalization for heart failure in patients with chronic heart failure (NYHA II-IV) and reduced ejection fraction. Entresto is usually administered in conjunction with other heart failure therapies, in place of an ACE inhibitor or other ARB.”

The combination tablet is available in three dosages: 24 mg sacubitril/26 mg valsartan; 49 mg sacubitril/51 mg valsartan; and 97 mg sacubitril/103 mg valsartan. In the pivotal study, these dosages were referred to as 50 mg, 100 mg, and 200 mg, respectively—but this nomenclature was not carried into the package insert, so it is important to clarify the exact dosage when prescribing.

The recommended starting dose for Entresto is 49/51 mg (sacubitril/valsartan) twice daily. The dose is doubled after two to four weeks to the target maintenance dose of 93/103 mg (sacubitril/valsartan) twice daily, as tolerated by the patient.

Lower doses are suggested for several groups of patients, including those with severe renal impairment, those not currently taking an ACE inhibitor or ARB, those previously only taking a low dose of an ACE inhibitor or an ARB, and finally, for those with moderate liver impairment. (Note that Entresto is not recommended for those with serious cases of liver impairment.)

Entresto is contraindicated in patients with a history of angioedema related to ACE inhibitors or ARB therapy. It also is contraindicated for concomitant use of ACE inhibitor and patients with diabetes who are taking aliskiren, a direct renin inhibitor. Entresto also comes with a list of drug interactions that include potassium-sparing diuretics, NSAIDs, and lithium. It also is contraindicated during pregnancy as it can cause fetal harm.

An issue that needs to be clarified in future studies is that neprilysin is one of multiple enzymes involved in the clearance of beta amyloid from the brain and spinal fluid. Beta amyloid has been implicated as a cause of Alzheimer’s disease so, in theory, prolonged use of a drug like Entresto that inhibits beta amyloid clearance may increase the risk of Alzheimer’s. During the PARADIGM-HF trial, cerebrospinal fluid levels of beta amyloid were higher in the treatment group than in the control group, but the cognition changes were not mentioned in the package insert. The clinical relevance of this finding is unknown at the present time and will be subject to future study.

**Managed care implications**
According to a *Forbes* article, Entresto will cost about $12.50 per day less discounts, adding about $4,500 to the cost of treating a patient with heart failure. Executives at Novartis, the drug’s maker, have stated that they are interested in working closely with payers. CEO Joe Jimenez told the *Wall Street Journal* that the company was “looking hard” at going to insurers with add-on services intended to improve outcomes for patients taking Entresto. The article went on to discuss the potential use of remote monitoring devices and other e-health measures to improve overall patient care.

Entresto, focusing on a treatment strategy that was decades in the making, is likely to become an important new medication for heart failure patients, again adding to the hope of Tomorrow’s Medicine.

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INTRODUCTION
Chronic obstructive pulmonary disease (COPD) exacerbations are defined as episodes of worsening in respiratory symptoms that necessitate a change in regular medication (Pauwels 2004). Frequent exacerbations may lead to reduced lung function; exacerbations are strongly associated with reduced quality of life and high rate of hospitalization (Donaldson 2006, Solem 2013). Exacerbations are a substantial contributor to the economic burden of COPD; a recent retrospective study estimated the cost of a severe exacerbation to be as high as $18,000 per severe exacerbation (Abudagga 2013).

Prevention and adequate treatment of COPD exacerbations is a cornerstone in COPD management. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines recommended that long-acting formulations of β2-agonist (LABA) and long-acting muscarinic antagonists (LAMA), alone or with an inhaled corticosteroid (ICS), be used for patients with high risk of exacerbation. Additionally, combined use of LABA and LAMA may be considered if symptoms do not improve, and ICS, phosphodiesterase-4 (PDE4) inhibitors, or theophylline may also be added for severely ill patients (GOLD 2014).

Roflumilast was the first PDE4 inhibitor drug approved by the US Food and Drug Administration (FDA) as a treatment to reduce the risk of COPD exacerbations. Approved in February 2011 and sold under the brand name Daliresp, roflumilast has been incorporated into the GOLD guidelines for severe COPD associated with chronic bronchitis and a history of exacerbations (GOLD 2014, Daliresp 2011). Evidence from large, international, multicenter, randomized placebo-controlled trials of 6–12 months’ duration shows that roflumilast decreased COPD exacerbations in patients with severe chronic bronchitis (Calverley 2009, Fabbri 2009). But COPD is a highly heterogeneous disease. Posthoc analysis of pooled clinical trial data has shown that roflumilast is effective in reducing exacerbations for specific subpopulations (Rennard 2008, Rennard 2011). These results, in conjunction with the GOLD recommendations, emphasize the need to understand
the characteristics of patients who are treated with roflumilast in the real world. In addition, in spite of the efficacy shown in randomized, placebo-controlled trials, little is known about the impact of roflumilast use on health care resource utilization and costs relative to other COPD treatments in a real-world setting.

The objectives of this study were to describe characteristics of COPD patients using roflumilast and compare their characteristics, health care utilization, and associated costs to those of patients on other combination medications among COPD patients with a history of exacerbations.

METHODS

Study Design and Data Source

For this retrospective observational study, medical, pharmacy, and eligibility claims data were extracted from the HealthCore Integrated Research Database (HIRD), which consists of claims from 14 geographically dispersed US health plans representing 30 million lives at the time this study was conducted. HIRD is one of the largest datasets of a commercially insured US population. Overall, it is comparable with US Census data (American Community Survey) by age and gender, with the HIRD population being slightly younger because all members are commercially insured.

All personally identifiable data used in this observational study were de-identified and accessed with protocols compliant with the Health Insurance Portability and Accountability Act (HIPAA). Patient confidentiality was preserved and the anonymity of all patient data was safeguarded throughout the study. This study was exempt from institutional review board (IRB) approval, as it was compliant with HIPAA and with federal guidance on Public Welfare and the Protection of Human Subjects. Specifically per the Code of Federal Regulations (45 CFR 46 §46.101(b)(4)), IRB review was not needed for a study of this nature because “subjects cannot be identified, directly or through identifiers linked to the subjects . . . .”

Study Patients

Medical, pharmacy, and eligibility claims data for the designated study period, March 1, 2010, to Nov. 30, 2012, were extracted and analyzed. Study patients were identified from March 1, 2011 (after roflumilast was approved in the US) to Nov. 30, 2012, which was regarded as the patient-identification period.

Patients were identified for the study if they had at least 1 medical claim for COPD (International Classification of Disease, Ninth Revision, Clinical Modification [ICD-9-CM] codes 491.xx, 492.xx, 496.xx) during the study period and had at least 1 pharmacy claim for a COPD medication class of interest, including roflumilast, LAMA, LABA, ICS, theophylline, or LABA-ICS, during the patient-identification period. Additional requirements were applied while defining the roflumilast and nonroflumilast cohorts, as elaborated below.

Cohort Definition

Roflumilast is indicated for severe COPD and is recommended as an add-on to other combination therapy. Therefore, to make cohorts comparable, the nonroflumilast cohort was identified as patients with no pharmacy claims for roflumilast and with at least 2 pharmacy claims of different COPD medication classes occurring within a 90-day window during the patient-identification period. If the patient received combination therapy on the same day, the index date was defined as that fill date. If the first medication class (drug A) was filled, followed by a different medication class (drug B and/or C) within 90 days, then the index date was defined as the first fill date of the last occurring medication class (drug B or C).

Patients were assigned to the roflumilast cohort if they had at least 1 pharmacy claim for roflumilast during patient-identification period. If a patient had a pharmacy claim for any other COPD medication on or
90 days before the first fill date of roflumilast, then the first fill date of roflumilast was assigned as the index date. On the other hand, if a patient had a pharmacy claim for any other COPD medication within 90 days after the first fill date of roflumilast, the index date was defined as the fill date of the last occurring medication class.

Inclusion/Exclusion Criteria
Patients included in the study were aged 40 years on the index date, had at least 12 months of continuous health insurance enrollment prior to the index date (preindex period) and at least 3 months of continuous enrollment after the index date (follow-up period), were commercially insured or had Medicare Advantage.

Patients were also required to have at least 1 treatment-based exacerbation (Seemungal 2009) during the preindex period. With claims data, exacerbation was defined as: (1) an inpatient or emergency room (ER) admission with a primary diagnosis of COPD acute exacerbation (ICD-9 codes 491.21, 491.22, 493.22) or emphysema (ICD-9 code 492.8x) or a primary diagnosis of respiratory failure combined with a secondary diagnosis of COPD acute exacerbation or emphysema (Lindenauer 2010, Rothberg 2010); (2) a physician office visit with qualifying diagnosis for pulmonary conditions of interest (eg, pneumonia or pulmonary insufficiency) (Mapel 2011); (3) a pharmacy claim for qualifying drug therapy, (ie, systemic steroids or antibiotics commonly used for respiratory infection such as β2-lactamase inhibitors, second- or third-generation cephalosporins, macrolides, and doxycycline) (Mapel 2011).

Patients were excluded from the study if they had a medical claim for cystic fibrosis (ICD-9-CM code 277.0x), respiratory tract cancer (ICD-9-CM codes 160.xx–164.xx, or 231.xx), active tuberculosis (ICD-9-CM codes 010.xx–018.9x), interstitial lung disease diagnosis (ICD-9-CM codes 516.3x), or α1-antitrypsin deficiency (ICD-9-CM codes 273.4x) during the entire study period.

Matching
Patients receiving newly approved medication, such as roflumilast, may be sicker, more likely to have failed existing therapies, or have more generous health plan benefits than patients in the nonroflumilast group (Schneeweiss 2011). Use of the propensity score facilitates the construction of matched sets with similar distributions of covariates, without requiring close or exact matches on all the individual variables (Stuart 2010). However, there are reasons to believe some confounders play an important role in the assignment of patients to the treatment and comparison groups and outcomes of interest (Calieno 2008, Brookhart 2006).

Roflumilast is recommended for patients with severe exacerbation and, therefore, is likely to be initially prescribed to patients who are severely ill, have already failed on existing therapies, or have generous health plan benefits. As time passes and roflumilast’s market share increases, it is expected that it will be prescribed to patients with less severe exacerbations as its market share increases. If patients were matched solely on the basis of a propensity score that included the number of severe exacerbations and time since the FDA’s approval of roflumilast, it is possible that a patient with a greater number of exacerbations closer to the FDA approval date—thereby defeating the purpose of the matching exercise. Therefore, based on methods proposed by Lechner (2002), propensity
score (generated on the basis of demographic characteristics, preindex Deyo-Charlson comorbidity index [DCI], preindex COPD exacerbation, preindex COPD severity proxy, and preindex all-cause total costs) was used as a partial balancing score and then complemented with exact matching on the preindex number of inpatient or ER exacerbations (categorized as 0, 1, 2, 3, and ≥4 exacerbations), number of COPD maintenance medication classes in combination therapy (classified as 2 vs 3–4 combinations), time of the index date since approval of roflumilast (expressed as sequential quarterly indicator), and 75 categories of the estimated propensity score (Lechner 2002).

Outcome Measures

Patient Characteristics

Patient characteristics were examined during the 12 months prior to the index date. Demographic characteristics included age, gender, type of health insurance plan (PPO, HMO, or other insurance plan type), and geographic region of patients’ residence (as determined by the US Census classification). Clinical characteristics included comorbidity burden, as measured by DCI, and specific comorbid conditions of interest (eg, asthma, acute bronchitis, bronchitis) during the preindex period. DCI consists of 19 diagnoses identified by ICD-9-CM codes with a scoring weight from 1 to 6 identified for each diagnosis. The final summary DCI score consists of a sum of weighted values for existing comorbidities, ranging from 0 to 33, with higher scores indicating a greater comorbidity burden (Deyo 1992).

Severity of COPD during the preindex period was evaluated using measures to approximate COPD complexity (Wu 2006), including number of hospitalization days due to acute exacerbation of chronic bronchitis (AECB), episodes for AECB, spirometry test, pulmonologist visit, and use of COPD medications (anticholinergics, oral corticosteroids, ICS, short-acting β₂-agonists [SABA], or LABA) (Wu 2006). The preindex number of COPD exacerbations also was evaluated. Furthermore, patients who had an ER- or inpatient-associated exacerbation were considered as having severe exacerbation, whereas those with a qualifying drug therapy were considered as having moderate exacerbations.

Healthcare Resource Utilization and Costs

Outcomes were measured within the entire follow-up period on a per-patient, per-month (PPPM) basis in any health care setting (including inpatient admissions, ER visits, and outpatient visits). Postindex all-cause health care resource utilization was defined as the use of any health care service associated with any condition identified from medical claims. Postindex all-cause health care costs were calculated using health plan allowed amounts, which are the full fees contractually allowed by health plans (inclusive of the amount paid by the health plan and the patient), and were considered as the direct health care cost associated with any condition identified from medical and pharmacy claims.

Statistical analysis

For unmatched cohorts, the unadjusted differences between 2 cohorts were assessed using χ² test for categorical variables, Wilcoxon-Mann-Whitney test for discrete/nonnormal continuous variables, and 2 sample t-test for continuous variables. For unadjusted differences between matched cohorts, the McNemar test for categorical variables, the Wilcoxon signed-rank test for discrete/non-normal continuous variables, and paired t test for continuous variables were used. Adjusted differences in number of hospitalizations and total costs between matched cohorts were estimated using a Poisson regression and generalized linear model with log link and gamma variance function, respectively, controlling for statistically and/or clinically important demographic and clinical characteristics, COPD-related resource utilization and costs. Differences were considered statistically significant at P<.05. All data...
analyses were conducted using SAS version 9.2 (SAS Institute, Cary, NC) and STATA version 12 (StataCorp, College Station, TX).

**RESULTS**

**Unmatched Cohorts**

**Demographic and Clinical Characteristics**

Of the 116,247 patients with at least 1 medical claim for COPD and 1 pharmacy claim for a medication class of interest, 31,237 (84.6%) patients met all study criteria and were used in the analyses, of whom 695 patients were classified in roflumilast cohort and 30,542 patients were in nonroflumilast cohort (Figure 1).

More than half of the study patients were female, with mean age of about 63 years for both cohorts (Table 1). Patients in the roflumilast cohort had higher mean DCI score (2.3 vs 2.1; \(P<.01\)) than the nonroflumilast cohort, indicating an overall relatively higher baseline comorbidity burden for patients with roflumilast. In addition, among the comorbid conditions examined in this study, the roflumilast cohort showed greater proportions of acute bronchitis and bronchitis, cardiovascular disease, diabetes, anxiety, and depression diagnoses than the nonroflumilast cohort (Table 1).

Patients in the roflumilast cohort showed a significantly higher number of episodes of AECB and hospitalizations due to AECB or chronic bronchitis, had more visits to a pulmonologist, underwent a greater number of spirometry tests, and used more oral corticosteroids than the nonroflumilast cohort (\(P<.05\) for all above measures), indicating that patients with roflumilast were in more severe condition than those without roflumilast at baseline (Table 1). The roflumilast cohort also experienced a greater number of severe (\(P<.05\)) and moderate (\(P<.05\)) exacerbations than the nonroflumilast cohort during the baseline period (Table 1).

Among the roflumilast cohort, 18.7% (n=130) of patients had roflumilast as monotherapy. Nearly 42% (n=289) patients were on a combination of 4 medication classes (ie, roflumilast plus 3 other classes), followed by 21.4% (n=149) with 3 classes, 13.8% (n=96) with 2 classes, and <5% (n=31) having roflumilast with 4 other classes as the index medication. In contrast, among the nonroflumilast cohort, 89.2% of patients were on a combination of 2 medication classes, 10.5% with 3 classes, and 0.3% with 4 medication classes as the index medication (Table 2).

**Matched cohorts:**

**Demographic and Clinical Characteristics**

To make these 2 cohorts more comparable for outcome evaluation, patients in the roflumilast cohort were matched (M) with patients in the nonroflumilast cohort, with a match rate of 61.4%.

After matching on preindex number of severe exacerbations, number of medication classes, 6 quarters since the approval month of roflumilast, and 75th deciles of estimated propensity score, the roflumilast (M) and nonroflumilast (M) cohorts consisted of similar proportions of males, with equivalent mean age and follow-up time (Table 3). In general, comorbidity burden and COPD severity were similar between the roflumilast (M) cohort and the nonroflumilast (M) cohort, although a higher percentage of patients with asthma diagnosis (41.2% vs 32.3%; \(P=.01\)) and higher number of SABA prescription fills (3.4 vs 2.7; \(P=.03\)) were still observed for roflumilast cohort during the 12 months prior to the index date (Table 3).

**Health Care Resource Utilization and Costs**

During the postindex period, utilization of all-cause inpatient admissions, ER visits, and outpatient visits was not significantly different between the roflumilast (M) cohort and the nonroflumilast (M) cohort (Table 4). Compared to the nonroflumilast (M) cohort, the roflumilast (M) cohort had significantly higher unadjusted PPPM all-cause pharmacy costs ($702 vs $608; \(P<.001\)) but did not show statistically significant difference in medical and total (pharmacy + medical) costs (Table 4).

The adjusted numbers of hospitalizations were not significantly different between the 2 cohorts (relative risk, 0.86 [95% CI, 0.46–1.62]; \(P=.65\))

### TABLE 2

**Numbers of combination medications occurring within a 90-day window prior to matching**

<table>
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<th>Category</th>
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<th>Nonroflumilast group</th>
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<tbody>
<tr>
<td></td>
<td>(N)</td>
<td>%</td>
</tr>
<tr>
<td>695</td>
<td>100.0%</td>
<td>30,542</td>
</tr>
<tr>
<td>2</td>
<td>96</td>
<td>13.8%</td>
</tr>
<tr>
<td>3</td>
<td>149</td>
<td>21.4%</td>
</tr>
<tr>
<td>4</td>
<td>289</td>
<td>41.6%</td>
</tr>
<tr>
<td>5</td>
<td>31</td>
<td>4.5%</td>
</tr>
<tr>
<td>Roflumilast monotherapy</td>
<td>130</td>
<td>18.7%</td>
</tr>
</tbody>
</table>
### TABLE 3
Patient characteristics of roflumilast vs nonroflumilast exact matched (M) cohorts

<table>
<thead>
<tr>
<th></th>
<th>Roflumilast (M) (n=328)</th>
<th>Nonroflumilast (M) (n=328)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female (n, %)</strong></td>
<td>182 55.5%</td>
<td>169 51.5%</td>
<td>.32</td>
</tr>
<tr>
<td><strong>Age (mean ± SD)</strong></td>
<td>63.5 ± 10.2</td>
<td>63.0 ± 9.8</td>
<td>.56</td>
</tr>
<tr>
<td><strong>Health plan type (n, %)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HMO</td>
<td>104 31.7%</td>
<td>92 28.0%</td>
<td>.48</td>
</tr>
<tr>
<td>PPO</td>
<td>212 64.6%</td>
<td>219 66.8%</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>12 3.7%</td>
<td>17 5.2%</td>
<td></td>
</tr>
<tr>
<td><strong>Geographic region (n, %)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>44 13.4%</td>
<td>41 12.5%</td>
<td>.58</td>
</tr>
<tr>
<td>Midwest</td>
<td>130 39.6%</td>
<td>119 36.3%</td>
<td></td>
</tr>
<tr>
<td>South</td>
<td>121 36.9%</td>
<td>138 42.1%</td>
<td></td>
</tr>
<tr>
<td>West</td>
<td>33 10.1%</td>
<td>30 9.1%</td>
<td></td>
</tr>
<tr>
<td><strong>Pre-index Deyo-Charlson comorbidity index (mean ± SD)</strong></td>
<td>2.4 ± 2.0</td>
<td>2.4 ± 1.9</td>
<td>.97</td>
</tr>
<tr>
<td><strong>Pre-index period comorbidities of interest (n, %)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>135 41.2%</td>
<td>106 32.3%</td>
<td>.01</td>
</tr>
<tr>
<td>Acute bronchitis and bronchitis</td>
<td>124 37.8%</td>
<td>134 40.9%</td>
<td>.43</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>33 10.1%</td>
<td>30 3.0%</td>
<td>.69</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>66 20.1%</td>
<td>61 18.6%</td>
<td>.61</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>103 31.4%</td>
<td>94 28.7%</td>
<td>.43</td>
</tr>
<tr>
<td>Hypertension</td>
<td>225 68.6%</td>
<td>222 67.7%</td>
<td>.79</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>90 27.4%</td>
<td>85 25.9%</td>
<td>.65</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease</td>
<td>82 25.0%</td>
<td>98 29.9%</td>
<td>.17</td>
</tr>
<tr>
<td>Anxiety</td>
<td>77 23.5%</td>
<td>57 17.4%</td>
<td>.06</td>
</tr>
<tr>
<td>Depression</td>
<td>52 15.9%</td>
<td>50 15.2%</td>
<td>.82</td>
</tr>
<tr>
<td><strong>Pre-index COPD severity proxy (mean ± SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of hospitalization days due to AECB or CB</td>
<td>1.4 ± 5.1</td>
<td>1.2 ± 3.7</td>
<td>.38</td>
</tr>
<tr>
<td>Number of episodes for AECB</td>
<td>0.9 ± 1.2</td>
<td>1.0 ± 1.4</td>
<td>.90</td>
</tr>
<tr>
<td>Number of spirometry tests</td>
<td>0.9 ± 1.4</td>
<td>0.8 ± 1.7</td>
<td>.38</td>
</tr>
<tr>
<td>Number of pulmonologist visits</td>
<td>1.1 ± 1.9</td>
<td>1.2 ± 2.1</td>
<td>.40</td>
</tr>
<tr>
<td>Number of anticholinergics prescription fills</td>
<td>2.5 ± 3.2</td>
<td>2.3 ± 3.5</td>
<td>.31</td>
</tr>
<tr>
<td>Number of oral corticosteroids prescription fills</td>
<td>2.6 ± 3.2</td>
<td>2.2 ± 3.2</td>
<td>.05</td>
</tr>
<tr>
<td>Number of ICS prescription fills</td>
<td>0.4 ± 1.4</td>
<td>0.3 ± 1.1</td>
<td>.26</td>
</tr>
<tr>
<td>Number of SABA prescription fills</td>
<td>3.4 ± 4.2</td>
<td>2.7 ± 4.1</td>
<td>.03</td>
</tr>
<tr>
<td>Number of LABA prescription fills</td>
<td>0.2 ± 1.2</td>
<td>0.2 ± 1.0</td>
<td>.31</td>
</tr>
</tbody>
</table>

AECB=acute exacerbation of chronic bronchitis, CB=chronic bronchitis, HMO=health maintenance organization, ICS=inhaled corticosteroids, LABA=long-acting β₂-agonists, LAMA=long-acting muscarinic antagonist, PPO=preferred provider organization, SABA=short-acting β₂-agonists, SD=standard deviation.

**Note:** Paired t test was used to compare differences in continuous variables and McNemar test was used to compare differences in categorical variables between the 2 study cohorts.
after controlling for patient characteristics, including demographics, health plan characteristics, baseline comorbidities, Medicare Advantage enrollment, proxies for the severity of COPD complexity, and resource utilization, including preindex COPD-related costs. The adjusted all-cause health care costs showed a similar pattern. After controlling for the same patient characteristics, the roflumilast (M) cohort exhibited lower adjusted total health care costs on a PPPM basis (ratio, 0.9858 [95% CI, 0.84–1.16] compared with the nonroflumilast (M) cohort, although this comparison did not reach statistical significance (P=.86).

**DISCUSSION**
There is limited real-world evidence of the demographic and clinical characteristics, as well as resource utilizations and associated costs, among COPD patients who were on roflumilast vs other maintenance combination medications. Results from this study indicate that, at baseline, most patients in the roflumilast cohort use roflumilast along with other maintenance medications as combination therapy. The roflumilast cohort showed a larger proportion of patients with >3 drug classes in their combination therapy, a greater comorbidity burden, more severe COPD conditions, and higher exacerbation history compared with the nonroflumilast cohort.

These results are not unexpected. Roflumilast is a relatively new drug indicated for the treatment of severe COPD, and previous research has suggested that newer drugs are more likely to be prescribed to patients who have failed to respond to other treatments, tend to be sicker, or both (Schneeweiss 2011). In addition, the GOLD guidelines recommend adding roflumilast to a combination therapy for severely ill patients (GOLD 2014). Therefore, it is expected that patients using roflumilast would be more severely ill. These results imply that when evaluating the impact of the use of roflumilast, careful attention should be given to verify that the cohorts being evaluated are comparable. If the cohorts are not well matched, the comparison may not be meaningful. This study used propensity score as a partial balancing score. We exactly matched patients on number of severe exacerbations and medication classes, quarters since approval month of roflumilast, and 75th categories of estimated propensity score. This approach produced a roflumilast cohort that was very similar to the nonroflumilast cohort in terms of demographic and clinical characteristics. Therefore, results based on the matched cohorts were robust. Because of large differences between the 2 groups, the match rate was 61.4%.

As expected, this study found that patients in the roflumilast (M) group had higher PPPM pharmacy costs than those in nonroflumilast (M) cohort. However, despite higher pharmacy costs, the roflumilast (M) cohort had similar total costs relative to the nonroflumilast (M) cohort. Additionally, this study found that the roflumilast (M) cohort had lower health care resource utilization although the comparison did not reach statistical significance. The adjusted results that control for the baseline demographic and clinical characteristics convey the same message.

Previous studies have shown that COPD exacerbations increase health care resource use (Blasi 2014). Treatment strategies that lead to the reduction of COPD exacerbations, therefore, have the potential to improve quality of life and mitigate use of limited health care resources. Roflumilast has been shown to decrease the occurrence of exacerbations in randomized, placebo-controlled trials (Calverley 2009, Fabbri 2009). This study provides evidence, using the real-world data, that affirms the findings from those trials. The non-significant results could be due to a

### TABLE 4

<table>
<thead>
<tr>
<th>Unadjusted health care resource utilization and costs of roflumilast vs nonroflumilast exact matched (M) cohorts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PPPMM all-cause health care resource utilization</strong></td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>Hospitalizations</td>
</tr>
<tr>
<td>Emergency room visits</td>
</tr>
<tr>
<td>Outpatient visits</td>
</tr>
</tbody>
</table>

**PPPMM all-cause health care costs**

<table>
<thead>
<tr>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient admissions</td>
<td>$1252 ±$3696</td>
<td>$1316 ±$3525</td>
<td>.77</td>
<td></td>
</tr>
<tr>
<td>Emergency room visits</td>
<td>$76 ±$280</td>
<td>$62 ±$207</td>
<td>.66</td>
<td></td>
</tr>
<tr>
<td>Outpatient visits</td>
<td>$651 ±$870</td>
<td>$815 ±$1231</td>
<td>.12</td>
<td></td>
</tr>
<tr>
<td>Medical</td>
<td>$1980 ±$3994</td>
<td>$2193 ±$4,42</td>
<td>.41</td>
<td></td>
</tr>
<tr>
<td>Pharmacy</td>
<td>$702 ±$464</td>
<td>$608 ±$646</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Total (Medical + pharmacy)</td>
<td>$2682 ±$4061</td>
<td>$2802 ±$4229</td>
<td>.90</td>
<td></td>
</tr>
</tbody>
</table>

**PPPMM=per-patient, per-month, SD=standard deviation.**
limited follow-up period (average of 9 months) and a limited sample. Even with these limitations, this study found that total costs of care in the rofilumast (M) cohort were no higher than in the nonrofilumast (M) group, despite use of a costlier brand-name drug in the treatment group. In fact, most of the numerical estimates of health care utilization and costs are lower, except for pharmacy costs. The higher pharmacy cost is to be expected for a brand-name drug, but it is offset by lower health care utilization and medical costs. The net results are comparable total costs of care, with lower numerical estimates for rofilumast users.

Most physicians regard balancing costs with effectiveness as an appropriate component of clinical decision making (Ginsburg 2000). This study suggests that total health care costs are less of a concern for rofilumast use. For physicians and policy makers, a critical point when considering rofilumast as an add-on therapy may be the effectiveness of rofilumast for the appropriate severe chronic bronchitis patients with history of exacerbation and inadequate control. In the rofilumast population in this study, total costs of care and health care utilization were comparable between users and nonusers, with the lower point estimates in majority of the outcomes for rofilumast users. A longer-term evaluation with larger sample size is needed to warrant or manifest the current findings in this study.

Limitations
This study presented and compared the patient characteristics of a rofilumast cohort and a nonrofilumast cohort and estimated the impact of the use of rofilumast on healthcare resource utilization and costs. As such, confidence intervals were used to quantify the uncertainty pertaining to these estimated effects; therefore, it is possible that sample size may have influenced the estimated uncertainty. Additionally, the results are applicable only for a relatively short duration follow-up. In this study, we assigned index medications based on prescription use as observed through the pharmacy claims. For patients to be assigned to a combination therapy, a 90-day window before and after the first observed pharmacy claim was allowed. This identification strategy may have misclassified a “switching” from one drug treatment to another as being a combination therapy use. However, it is unlikely that a patient may switch from drug A to drug B and then switch back to drug A (or similar combinations of >2 drug classes); we believe the risk of this type of misclassification is very low.

Similar to other retrospective database studies, this study is subject to limitations, including coding errors of omission and commission, incomplete claims, unreliable clinical coding, and unobservable factors that may also have influenced the outcomes. Only direct costs that were billed and reimbursed by insurance claims were evaluated. Other costs outside of administrative data, such as over-the-counter drug cost, were not considered. Indirect costs were also ignored. Finally, study results were derived from commercial health plans in the US; therefore, results may not be generalized to people with other forms of insurance coverage. Nonetheless, the data used in this study were derived from a large, geographically diverse population, which enhances the generalizability of the results.

CONCLUSION
Findings from this study offer data to health plans regarding the characteristics of COPD patients on rofilumast in the real-world setting. This study found that, in general, patients in the rofilumast cohort were sicker and had more severe COPD. In most cases, rofilumast was prescribed as an add-on therapy to at least 2 other COPD maintenance medications. Therefore, this result implies that, in retrospective studies, attention needs to be given to defining a comparable group when evaluating the impact of rofilumast on health or economic outcomes of COPD patients.

Although the statistical evidence was not strong enough to show significance, the study found that despite higher pharmacy costs in the rofilumast group, total health care costs were lower than in the nonrofilumast group, and health care resource utilization was lower in the rofilumast cohort as well. Future research with a longer follow-up period and larger sample size is needed to evaluate health care resource utilization and costs with rofilumast treatment in long-term management of severe COPD patients.

Disclosure: Jain, Cai, and Tan are employed by HealthCore, a consultancy whose activities for this project were funded by Forest Research Institute. Sun is an employee of Actavis, the sponsor of the study and the maker of rofilumast, and owns Actavis stock and stock options.

Corresponding author: Rahul Jain, PhD
Research Manager
HealthCore Inc.
800 Delaware Avenue, 5F
Wilmington, DE 19801
Phone: (978) 247-6643
Email: rjain@healthcore.com

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Rennard SI, Calverley PM, Goehring UM, et al. Reduction of exacerbations by the PDE4 inhibitor rolflumilast—the importance of defining different subsets of patients with COPD. Respir Res. 2011;12:18.


TABLE 1
Patient characteristics of roflumilast vs nonroflumilast cohorts

<table>
<thead>
<tr>
<th></th>
<th>Roflumilast (n=695)</th>
<th>Nonroflumilast (n=30,542)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, (mean ± SD)</strong></td>
<td>62.6 ±9.3</td>
<td>63.2 ±11.4</td>
<td>.12</td>
</tr>
<tr>
<td><strong>Female (n, %)</strong></td>
<td>382 55.0%</td>
<td>17,503 57.3%</td>
<td>.22</td>
</tr>
<tr>
<td><strong>Health plan type (n, %)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HMO</td>
<td>177 25.5%</td>
<td>9165 30.0%</td>
<td>.02</td>
</tr>
<tr>
<td>PPO</td>
<td>484 69.6%</td>
<td>19,755 64.7%</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>34 4.9%</td>
<td>1622 5.3%</td>
<td></td>
</tr>
<tr>
<td><strong>Geographic region (n, %)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>90 12.9%</td>
<td>6904 22.6%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Midwest</td>
<td>262 37.7%</td>
<td>10,814 35.4%</td>
<td></td>
</tr>
<tr>
<td>South</td>
<td>281 40.4%</td>
<td>9050 29.6%</td>
<td></td>
</tr>
<tr>
<td>West</td>
<td>62 8.9%</td>
<td>3774 12.4%</td>
<td></td>
</tr>
<tr>
<td><strong>Pre-index Deyo-Charlson Comorbidity Index (mean ± SD)</strong></td>
<td>2.3 ±1.9</td>
<td>2.1 ±1.8</td>
<td>.003</td>
</tr>
<tr>
<td><strong>Pre-index comorbidities of interest (n, %)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>298 42.9%</td>
<td>13,768 45.1%</td>
<td>.25</td>
</tr>
<tr>
<td>Acute bronchitis and bronchitis</td>
<td>269 38.7%</td>
<td>10,654 34.9%</td>
<td>.04</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>69 9.9%</td>
<td>1761 5.8%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>133 19.1%</td>
<td>4257 13.9%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>211 30.4%</td>
<td>7233 23.7%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>474 68.2%</td>
<td>19,711 64.5%</td>
<td>.05</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>204 29.4%</td>
<td>7435 24.3%</td>
<td>.002</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease</td>
<td>192 27.6%</td>
<td>7009 22.9%</td>
<td>&lt;.004</td>
</tr>
<tr>
<td>Anxiety</td>
<td>183 26.3%</td>
<td>4900 16.0%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Depression</td>
<td>146 21.0%</td>
<td>4608 15.1%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Pre-index COPD severity proxy (mean ± SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of hospitalization days due to AECB or CB</td>
<td>2.3 ±6.4</td>
<td>0.7 ±3.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Number of episodes for AECB</td>
<td>1.1 ±1.4</td>
<td>0.4 ±0.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Number of spirometry test</td>
<td>1.0 ±1.6</td>
<td>0.7 ±1.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Number of pulmonologist visit</td>
<td>1.5 ±2.5</td>
<td>0.7 ±1.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Number of anticholinergics</td>
<td>3.4 ±4.1</td>
<td>1.3 ±2.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Number of oral corticosteroids</td>
<td>3.2 ±3.7</td>
<td>1.5 ±2.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Number of ICS use</td>
<td>0.5 ±2.0</td>
<td>0.3 ±1.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Number of SABA use</td>
<td>4.2 ±5.0</td>
<td>2.2 ±3.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Number of LABA use</td>
<td>0.4 ±1.8</td>
<td>0.2 ±1.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Pre-index COPD exacerbation (mean ± SD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inpatient exacerbation (severe exacerbation)</td>
<td>0.4 ±0.8</td>
<td>0.1 ±0.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Emergency room exacerbation (severe exacerbation)</td>
<td>0.1 ±0.6</td>
<td>0.04 ±0.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Exacerbation by qualifying diagnosis (moderate exacerbation)</td>
<td>2.0 ±2.3</td>
<td>1.2 ±1.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Exacerbation by qualifying drug therapy (moderate exacerbation)</td>
<td>2.3 ±2.6</td>
<td>1.6 ±1.9</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

AECB=acute exacerbation of chronic bronchitis, CB=chronic bronchitis, HMO=health maintenance organization, ICS=inhaled corticosteroids, LABA=long-acting β₂-agonists, LAMA=long-acting muscarinic antagonist, PPO=preferred provider organization, SABA=short-acting β₂-agonists, SD=standard deviation.

Note: Two-sample Student’s test was used to compare differences in continuous variables and χ² test was used to compare differences in categorical variables between the 2 study cohorts.
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Progress made, but still not enough in America’s long war on cancer

The war on cancer was declared in 1971 with passage of the National Cancer Act. We were putting men on the moon so beating cancer forever in a relatively short time seemed plausible. Though fantastic strides have been made, that’s not quite how things worked out.

Consider a study in the July issue of Preventing Chronic Disease, a peer-reviewed journal published by the CDC. The researchers, led by Hannah Weir of the CDC, used trends from 1975 to 2009 to project deaths and death rates from cancer through 2020.

By their reckoning, the total number of cancer deaths will increase by more than 10% among men and black women between 2007 and 2020, but level off to an increase of 4.4% among white women partly because of declines in breast, cervical, and colorectal cancer deaths. If their predictions prove to be accurate, more than 335,000 American men will die of cancer in 2020 and more than 290,000 American women.

That war on cancer—it’s hardly won.

The increase in total deaths from cancer is partly explained by demographics, particularly an aging population. When Weir and her colleagues calculated age-standardized cancer death rates, the picture brightens. Between 2007 and 2020, they figure Americans will see declines in the rates for lung and bronchus (21.3%), female breast (19.6%), cervix uteri (12.5%), colon and rectum (22.5%), oral cavity and pharynx (16.0%), prostate (26.4%), and melanoma (7.4%). The rate for those seven sites combined is projected to decrease by 15.6%. In fact, the pitch of the declines for the individual cancer sites is steep enough that, with the exception of melanoma, goals set in the federal government’s Healthy People 2020, a health planning document, are likely to be met.

Explanations for declining rates vary with the cancer. Lung cancer rates are going down because lung cancer incidence is decreasing, a reflection of declining smoking rates. Screening—and to a lesser extent risk factor reduction—explain the favorable trends in the death rate from colon cancer.

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**Observed (2007) and predicted (2020) age-standardized death rates per 100,000 population**

Source: Weir HK et al., Preventing Chronic Disease, July 2015