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COMING SOON FROM THE GLOBAL LEADER
IN RENAL THERAPY.
EDITOR’S MEMO

Achieving Price Transparency Is in the Realm of the Possible
By John Marcille

U
we Reinhardt, PhD, in our Q&A on page 21, says — somewhat tongue in cheek — “... that is another miracle of American health care: We don’t know prices. We know Medicare prices — at least you could know them — because they are in the public domain. But prices negotiated between hospitals and doctors are trade secrets. So if you don’t know prices, competition can’t work.”

There has always been a need for price transparency, and now might be our best opportunity yet to achieve it. Our cover story on page 16 by contributing editor Joseph Burns warns that even with the help of the Affordable Care Act, transparency won’t come easily. In fact, some of the ACA’s efforts in this area are making some consumers more confused.

And it’s easy to get confused, as even savvy customers note. A Viewpoint on page 7 by John Sung Kim, who runs a health technology company, includes this interesting tidbit regarding a recent hospital stay.

“While the hospital charged $49,675, my insurer paid only $34,772. The rest was ‘forgiven’ by the hospital.” That was for one night, with no surgery. “Just a CT scan, eight shots of Dilaudid, cable TV (no HBO), bed, and a bland continental breakfast.” Sobering, but health plans still see an opportunity. Rick Weisblatt, PhD, a vice president at Harvard Pilgrim Health Care, says in our cover story, “If we can drive more volume to lower-cost providers, then, in theory, we should be able to save on health insurance premiums. If the market becomes more competitive and providers are forced to be more efficient and then improve their cost structure and lower their prices, that should mean we could lower the cost of insurance.”

What was that word Reinhardt used? Miracle? Almost everything we’ve achieved thus far was once considered a miracle, so we might be on the right course.!

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Clear Need for Price Transparency

What consumers have for comparing physicians and hospitals is woefully inadequate today, yet price transparency is more imperative than ever. Could it be that health plans have sufficient tools for the job?

Q&A: Professor Reinhardt’s Rosy Prognosis

The noted Princeton health care economist Uwe Reinhardt, PhD, sees a bright future. Growth in costs is slowing, and if the industry tackles administrative overhead, things should be fine in five years.

Private Exchanges Elbow Their Way In

It always pays to keep a close eye on employers. They like options. Private exchanges might prove especially attractive to businesses that are self-insured.

Clopidogrel, Prasugrel, or Ticagrelor?

Which of the three drugs is the best oral antiplatelet medication? Clopidogrel is the least expensive, and that is important, but there are significant clinical differences.

Get a Handle on Echocardiography

Utilization management for outpatients cuts testing rates significantly, according to a review of claims for over 2 million patients. Use declined the most in low- and medium-risk groups.

DEPARTMENTS

Editor’s Memo........................................1
Transparency: Worth the effort.

News & Commentary..........................4
Mammography debate continues.

Viewpoint .........................................7
Tough to get a straight answer on bills.

Medication Management...............8
Heart failure meds hard to find.

Formulary Files ................................44
Varicella vaccine advance.

Ad Index .............................................44
Plan Watch.................................45
Metabolic syndrome program tested.

Snapshot .........................................46
Employers liking CDHPs more.

Tomorrow’s Medicine..................47
Test finds multidrug-resistant TB fast.

Outlook ............................................49
Slowdown in drug spending won’t last.
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Does Mammography Screening Need to Start Earlier?

The 2009 recommendation by the U.S. Preventive Services Task Force that routine mammography screening begin at 50 did not put the issue to rest. In fact, it pushed it to the forefront of the debate about overtesting and overscreening, where it has remained.

Now comes a study in the journal Cancer reporting that more than two-thirds of breast cancer deaths occur in younger women who have either never had a mammogram or had them at intervals of two years or more.

The study, “A Failure Analysis of Invasive Breast Cancer,” published online in September, states, “To maximize mortality reduction and life-years gained, initiation of regular screening before age 50 years should be encouraged.”

The authors know they are throwing water on a grease fire: “In the presence of conflicting evidence, national recommendations for screening mammography have become a point of contention.”

They looked at 7,300 women diagnosed with breast cancer between 1990 and 1999 and tracked them until 2007.

Of the 609 deaths from breast cancer, 71% had not been screened or had been screened at intervals of two or more years. The median age of diagnosis for fatal cancer was 49. The median age for women who died of breast cancer, 71% had not been screened to 4,200 patients between 2002 and 2008. The categories are:

- Errors of commission
- Errors of omission
- Errors of communication
- Errors of context
- Errors in diagnoses

James’s baseline estimate is 210,000 preventable deaths at hospitals each year. But because not all the data, such as diagnostic errors, are captured, the number could be more than twice as high.

Lucian Leape, MD, sat on the committee that wrote To Err Is Human. He tells ProPublica that James’s estimate is on target. Leape and other experts think it’s time to put the IOM’s 98,000 figure to rest.

The American Hospital Association disagrees, telling ProPublica that the screening method James used (the Global Trigger Tool) cannot really make a nationwide estimate.

James writes: “In a sense, it does not matter whether the deaths of 100,000, 200,000, or 400,000 Americans each year are associated with PAEs at hospitals. Any of the estimates demands assertive action on the part of providers, legislators, and people who will one day become patients.”

Care Management Strikes Out in Study

The recidivism rates for alcohol and drug addiction are heartbreaking, and efforts to help people crawl out of their private hells have mostly failed. It doesn’t look as if the patient-centered medical home (PCMH), one of the bulwarks of the Affordable Care Act, will help much either, according to a study in the Journal of the American Medical Association (JAMA).

Chronic care management (CCM) will be one of the goals of PCMHs, note the authors of “Chronic Care Management for Dependence on Alcohol and Other Drugs,” in the Sept. 18 issue.

About 560 people in Boston were recruited from an urban teaching hospital, detoxification units, and via advertisements to participate in a randomized study from September 2006 to September 2008.

Of those, 282 received CCM and 281 were simply given a primary care appointment and a list of resources that included phone numbers of counselors.

“Chronic care management included longitudinal care coordi-
nated with a primary care clinician; motivational enhancement therapy; relapse prevention counseling; and on-site medical, addiction, and psychiatric treatment, social work assistance, and referrals (including mutual help),” the study states. “The no CCM (control) group received a primary care appointment and a list of treatment resources, including a telephone number to arrange counseling.”

After a year, 44% of the CCM group reported abstinence from opioids, stimulants, or heavy drinking. For the control group, it was 42%.

Briefly Noted

Patient-centered medical homes increase patient satisfaction, according to a study in JAMA Internal Medicine (“Patient-Centered Medical Home Intervention Makes Some Progress”), but they actually seem to increase admission to hospitals. Emergency department use for PCMH patients was the same as for the control group.... Even if the electronic health record system that a physician practice installs does not meet the government’s meaningful use standards, it could still be effective, according to the Office of the National Coordinator for Health IT. Seventy-nine percent of physicians using EHRs that do not meet meaningful use standards say that their systems help their clinical efforts....

Private practice is dead? Not so, according to the American Medical Association. The majority of physicians own their own practices, says an AMA study that disputes all the talk of provider consolidation (http://tinyurl.com/AMA-practice-study). About 53% of surveyed physicians described themselves as self-employed in 2012.... Not only has the use of medications to treat attention-deficit/hyperactivity disorder in children soared the last five years, but now the stimulant drugs are being used to treat other neurological disorders, according to a study in the Journal of Child and Adolescent Psychopharmacology (http://tinyurl.com/meds-article).  

— Frank Diamond

Employers look to create a culture of wellness

And good luck with that. Businesses appreciate the benefits of keeping employees healthy, but many are flummoxed about just how to do it, according to a survey by Towers Watson and the National Business Group on Health. Employers are beginning to understand that more “health programs without an articulated strategy may not be an effective approach to affect behavior change. Instead, most now point to establishing a culture of health as their top priority...” to tackle major lifestyle problems like stress, obesity, and lack of physical activity.

Now, “low usage rates show that the programs are not working as well as they could.”

The authors recommend:
- Developing a strategy that recognizes the needs and desires of the employee population
- Tailoring programs to individuals and specific demographic groups
- Communicating to employees and giving them incentives to change behavior
- Consistently measuring the effectiveness of the strategy and individual programs, and making changes that evolve with the progress of the workforce

What U.S. employers consider main lifestyle challenges for workers

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress</td>
<td>78%</td>
</tr>
<tr>
<td>Obesity</td>
<td>75%</td>
</tr>
<tr>
<td>Lack of physical activity</td>
<td>73%</td>
</tr>
<tr>
<td>Poor nutrition</td>
<td>57%</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>32%</td>
</tr>
<tr>
<td>Presenteeism</td>
<td>21%</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>13%</td>
</tr>
</tbody>
</table>

Top priorities for health and productivity programs

<table>
<thead>
<tr>
<th>Priority</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Develop a workplace culture where employees are responsible for their health and understand its importance</td>
<td>70%</td>
</tr>
<tr>
<td>Improve employee engagement in health and productivity programs</td>
<td>63%</td>
</tr>
<tr>
<td>Educate employees to be more informed consumers of health care</td>
<td>44%</td>
</tr>
<tr>
<td>Improve employee awareness of health and risks</td>
<td>29%</td>
</tr>
<tr>
<td>Improve the physical health of employees</td>
<td>28%</td>
</tr>
<tr>
<td>Improve the emotional/mental health of employees by lessening stress and anxiety</td>
<td>15%</td>
</tr>
</tbody>
</table>

Note: Based on a survey of 199 employers taken between May and July 2013.

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*Communicate. Connect. Rule your world…*
The Problem With Our Health Care Cost Crisis?  
Hint: It Has Nothing to Do With Providers

By John Sung Kim

As an executive at a leading health technology company in San Francisco, I often view both patients and medical providers as a bit whiny. As they rail against “Obamacare” or “intolerable patient families,” I’m often thinking, “Oh, do you need me to take you for a ride on your Whaaambulance?”

After all, we live in a system where hospitals don’t turn patients away and being a nurse or doctor still has plenty of social esteem. And when you’re dealing with health care technology on a large scale (we have 12,000 providers servicing nearly 5 million patients on our secure mobile messaging platform), getting caught up in individual provider or patient stories can seem like a waste of time.

That is, until you end up in the hospital yourself....

I crashed my motorcycle. I broke my arm, and got a bill. Because my humerus was shattered, surgery wasn’t necessary. Just a CT scan, eight shots of Dilaudid, cable TV (no HBO), bed, and a bland continental breakfast. Guess what the bill for that one-night stay was?

While the hospital charged $49,675, my insurer paid only $34,772. The rest was “forgiven” by the hospital. I called both the insurer and the hospital; the insurer told me that I was fully covered, and the hospital made it nearly impossible to get an itemized list.

The bill that’s not a bill

When I asked why that location sending me a bill wasn’t answering their phones, she told me “that branch is now closed. You won’t receive any more bills.”

This entire experience has further reinforced my belief that the “problem” with our health care cost crisis has nothing to do with the medical providers. In fact, the care I received throughout was exceptional.

So one does start to wonder if these organizations create a degree of separation between corporate management and billing so that if someone gets accused of fraud, management can feign ignorance. I’m not saying that’s true, but it does make a skeptic more skeptical, if you get my drift. If only getting a straight answer were as simple as a phone call.
The clinical guidelines for the treatment of heart failure were completely revised by the American College of Cardiology Foundation and the American Heart Association (ACCF/AHA), to emphasize the role of medication therapy as the foremost approach to managing this high profile condition. Approximately 5.1 million people in the United States have heart failure and it is the leading cause of hospitalization among people over age 65. The Agency for Healthcare Research and Quality projects there were 928,000 heart failure admissions in 2012, far exceeding those for heart attack (594,000), coronary artery disease (480,000) or atrial fibrillation (466,000). Hospitalization for acute heart failure is prognostic of a 50% risk for readmission within six months and a one-year mortality rate of approximately 30%, according to the ACCF/AHA.

Of the proportion of people under age 65 who were hospitalized for any reason, those hospitalized for heart failure rose from 23% in 2000 to 29% in 2010. “One of the most important updates is the formal definition of the concept of guideline-directed medical therapy, GDMT,” says Mariell Jessup, MD, vice chairwoman of the writing committee that wrote the guideline and professor of medicine at the University of Pennsylvania. “GDMT is the current optimal therapy for each stage of heart failure.”

The focus on GDMT reflects the advances that have been made in medical therapy for many cardiovascular disorders, and the ACCF/AHA intends to use this term throughout its long list of guidelines.

GDMT for heart failure has progressed from digitalis and diuretics to vasodilators and to the current neurohormonal agents in which rennin-angiotensin-aldosterone system antagonists are the drugs of choice. There have been no novel heart failure medications for decades.

Furthermore, existing therapies reduce morbidity or mortality only in 50% of heart failure patients — those affected by heart failure with reduced ejection fraction, HFrEF. Disease modifying medication therapy that has not yet been demonstrated conclusively for individuals with heart failure with preserved ejection fraction, HFrEF. Ejection fraction is the percent of the ventricular volume that is pumped out with each heartbeat. The revised guidelines define HFrEF as an ejection fraction ≤ 40% and HFpEF as an ejection fraction ≥ 50%. Borderline HFpEF has an ejection fraction of 41% to 49%.

Problems for health plans
Heart failure is expensive for Medicare Advantage plans. A recent article in Health Affairs reports that heart failure generates higher per-patient Medicare expenditures than diabetes or chronic obstructive pulmonary disease. A study reported online by the American Journal of Managed Care says the average annual cost for Medicare members is $33,000 with hospitalizations accounting for more than half of those costs. Late-stage heart failure patients may face substantial hospital costs in the form of implantation of expensive cardioverter defibrillators or ventricular-assist devices.

In addition, Medicare Advantage plans are penalized for readmissions, and in 2010 the heart failure readmission rate was 24.7%. Part D plans are able to escape penalties for readmissions, many of which are related to inadequate medication therapy.

“CMS is starting to have issues around readmissions in stand-alone Part D programs because they are not assigned financial responsibility in the same way health plans are.
penalized,” says Brian Solow, MD, chief medical officer at OptumRX, UnitedHealthcare’s captive PBM. CMS has finally realized it needs to start to look at this.” Solow says CMS has not figured out if or how it will deal with this issue.

Part D plans face another important challenge in heart failure. In 2013, 95% of Part D programs targeted heart failure for a medication therapy management program. In 2014, CMS will include a star rating for the completion of comprehensive medication reviews, CMRs, thus encouraging Part D plans to get them done for heart failure patients. The American College of Cardiology says in 2009 heart failure patients had an average of 5.91 comorbidities which increase the number of medications and greatly complicate CMRs.

The guideline revision pays special attention to HFrEF, which affects approximately 50% of patients and lacks proven effective pharmacological therapies. It received increased attention for several reasons.

The diagnosis of HFrEF is more challenging than the diagnosis of HFrEF because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of heart failure. Patients with HFrEF are usually older women with a history of hypertension, atrial fibrillation, obesity, and diabetes mellitus.

HFrEF poses serious therapeutic challenges, as drugs that are efficacious in HFrEF — angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs), and beta blockers — have produced disappointing results for morbidity and for mortality.

These patients are often treated for underlying risk factors and comorbidities, using GDMT similar to that used in patients with HFrEF.

Medications may affect the comorbidities surrounding heart failure but they do not improve heart failure morbidity and mortality.

The challenge in HFrEF is Stage C, which entails structural heart disease and symptoms. The pharmacologic treatment recommendations vary by New York Heart Association (NYHA) functional classification, which describes exercise capacity and the symptomatic status of the disease. Treatment in this stage includes blood pressure medications, diuretics, management of atrial fibrillation, and use of beta blockers, ACE inhibitors, and ARBs in patients with hypertension.

Blood pressure control is the most important recommendation in patients with HFrEF. The guidelines recommend aggressive treatment — often with several drugs with complementary mechanisms of action. ACE inhibitors and/or ARBs are often considered as first-line agents.

Increasing hospitalizations are another challenge for HFrEF patients. Among 6,076 consecutive acute heart failure admissions at Mayo Clinic Hospitals from 1987 to 2001, the prevalence of HFrEF increased from 38% in the first five years to 54% in the final five years, according to a recent study in *Current Heart Failure Reports*.

In addition, the survival of hospitalized HFrEF patients improved over the study period, but there was no improvement in acute heart failure patients with HFrEF.

“We need new medicines for patients with HFrEF, given that 50% of all hospital admissions are for patients with preserved ejection fraction,” says Jessup. “This is a poorly understood syndrome, and there are no evidence based therapies that modify its overall course.”

The need for new medical therapies is widely recognized. In June, the FDA granted breakthrough status for Novartis’s serelaxin, which produced a 37% reduction in death at six months for hospitalized acute heart failure patients.

“Serelaxin may be an important advance, but we have been excited about other drugs in the past and they have been disappointing in larger studies,” says Jessup. Serelaxin missed at least one endpoint in its phase 3 trial.

**Complex nature**

“Heart failure is a common, high-profile condition because of its complex nature, with many comorbidities and frequent hospitalizations,” says Solow. “Disease management programs don’t work as well as we would like them to. People end up with dyspnea or fluid buildup, or in the worse case are back in the hospital for many different reasons that are hard to control.”

Many CHF readmissions are related to inadequate medication therapy.
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*Based on a Phase 3, double-blind, randomized-withdrawal maintenance trial in patients with schizophrenia; Abilify Maintena (n=269) vs placebo (n=134).

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INDICATION

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IMPORTANT SAFETY INFORMATION

Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk (1.6 to 1.7 times) of death compared to placebo (4.5% vs 2.6%, respectively). Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Abilify Maintena is not approved for the treatment of patients with dementia-related psychosis.

Contraindication: Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

Cerebrovascular Adverse Events, Including Stroke:

Increased incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, have been reported in clinical trials of elderly patients with dementia-related psychosis.

Contraindication: Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

Neuroleptic Malignant Syndrome (NMS):

A potentially fatal symptom complex sometimes referred to as NMS may occur with administration of antipsychotic drugs, including Abilify Maintena. Rare cases of NMS occurred during aripiprazole treatment. Signs and symptoms of NMS include hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (e.g., irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available.

Tardive Dyskinesia (TD):

The risk of developing TD (a syndrome of abnormal, involuntary movements) and the potential for it to become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. Prescribing should be consistent with the need to minimize TD. There is no known treatment for established TD, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn.

Continued on next page.

Please see IMPORTANT SAFETY INFORMATION continued, and BRIEF SUMMARY of FULL PRESCRIBING INFORMATION, including Boxed WARNING, on the following pages.
FOR THE TREATMENT OF SCHIZOPHRENIA

An option to help protect your members from relapse

Once-monthly Abilify Maintena has demonstrated it can significantly delay the time to relapse vs placebo for up to 1 year* (P<0.0001).

Visit AbilifyMaintena.com for product information and Formkit.com for formulary information.

*Based on a Phase 3, double-blind, randomized-withdrawal maintenance trial in patients with schizophrenia, Abilify Maintena (n=269) vs placebo (n=134).

INDICATION and IMPORTANT SAFETY INFORMATION for Abilify Maintena™ (aripiprazole) for extended-release injectable suspension

INDICATION
Abilify Maintena is an atypical antipsychotic indicated for the treatment of schizophrenia.

 Efﬁcacy was demonstrated in a placebo-controlled, randomized-withdrawal maintenance trial in patients with schizophrenia and additional support for efﬁcacy was derived from oral aripiprazole trials.

IMPORTANT SAFETY INFORMATION

Increased Mortality in Elderly Patients with Dementia-Related Psychosis
Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk (1.6 to 1.7 times) of death compared to placebo (4.5% vs 2.6%, respectively). Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Abilify Maintena is not approved for the treatment of patients with dementia-related psychosis.

Contraindication: Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

Cerebrovascular Adverse Events, Including Stroke: Increased incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, have been reported in clinical trials of elderly patients with dementia-related psychosis treated with oral aripiprazole.

IMPORTANT SAFETY INFORMATION (continued)

Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as NMS may occur with administration of antipsychotic drugs, including Abilify Maintena. Rare cases of NMS occurred during aripiprazole treatment. Signs and symptoms of NMS include hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (e.g., irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available.

Tardive Dyskinesia (TD): The risk of developing TD (a syndrome of abnormal, involuntary movements) and the potential for it to become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. Prescribing should be consistent with the need to minimize TD. There is no known treatment for established TD, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn.

Continued on next page.

Please see IMPORTANT SAFETY INFORMATION continued, and BRIEF SUMMARY of FULL PRESCRIBING INFORMATION, including Boxed WARNING, on the following pages.
**ABILIFY MAINTENA**<sup>™</sup> (aripiprazole) for extended-release injectable suspension (continued)

**Metabolic Changes:** Atypical antipsychotics have been associated with metabolic changes that include:

1. **Hyperglycemia/Diabetes Mellitus:** Hyperglycemia, in some cases extreme and associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics including aripiprazole. Patients with diabetes should be monitored for worsening of glucose control those with risk factors for diabetes and should undergo baseline and periodic fasting blood glucose testing. Any patient with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continued monitoring for the duration of the treatment.

2. **Dyslipidemia:** Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics. There were no significant differences between aripiprazole- and placebo-treated patients in the proportion of change from normal to clinically significant levels for fasting/nonfasting total cholesterol, fasting triglycerides, fasting low-density lipoproteins (LDLs), and fasting/nonfasting high-density lipoproteins (HDLs).

3. **Weight Gain:** Weight gain has been observed. Clinical monitoring of weight is recommended.

**Orthostatic Hypotension:** Aripiprazole may cause orthostatic hypotension. Abilify Maintena should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, or conditions which would predispose them to hypotension.

**Leukopenia, Neutropenia, and Agranulocytosis:** Leukopenia, neutropenia, and agranulocytosis have been reported. Patients with a history of clinically significant low white cell blood (WBC) count or drug-induced leukopenia/neutropenia should have their complete blood count monitored frequently during the first few days of therapy while receiving Abilify Maintena. In such patients, consider discontinuation of the drug at the first sign of a clinically significant decline in WBC count or the appearance of fever.

**Seizures/Convulsions:** Abilify Maintena should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

**Potential for Cognitive and Motor Impairment:** Abilify Maintena may impair judgment, thinking, or motor skills. Instruct patients to avoid operating hazardous machinery including automobiles until they are certain Abilify Maintena does not affect them adversely.

**Body Temperature Regulation:** Disruption of the body’s ability to reduce core body temperature has been attributed to antipsychotics. Due to the potential for inappropriate temperature regulation, appropriate care is advised for patients who may exercise strenuously, may be exposed to extreme heat, receive concomitant medication with anticholinergic activity, or are subject to dehydration.

**Dysphagia:** Esophageal dysmotility and aspiration have been associated with Abilify Maintena. Use caution in patients at risk for aspiration pneumonia.

**Alcohol:** Advise patients to avoid alcohol while taking Abilify Maintena.

**Concomitant Medication:** Dosage adjustments are recommended in patients who are CYP2D6 poor metabolizers and in patients taking concomitant CYP3A4 inhibitors or CYP2D6 inhibitors for greater than 14 days. If the CYP3A4 inhibitor or CYP2D6 inhibitor is withdrawn, the Abilify Maintena dosage may need to be increased. Avoid the concomitant use of CYP3A4 inhibitors or CYP2D6 inhibitors for greater than 14 days. If the CYP3A4 inhibitor or CYP2D6 inhibitor is withdrawn, the Abilify Maintena dosage may need to be increased. Avoid the concomitant use of CYP3A4 inhibitors, CYP2D6 inhibitors or CYP3A4 inducers for less than 14 days. For patients taking concomitant CYP3A4 inhibitors, the findings pertain to patients receiving ABILIFY MAINTENA as well.

**Pregnancy/Nursing:** Atypical antipsychotics are not available. Patients with an established diagnosis of diabetes mellitus who discontinue antipsychotics are not available. Patients with an established diagnosis of diabetes mellitus who discontinue antipsychotics may require continued diabetes management. Patients with a history of diabetes mellitus should be monitored for worsening of glucose control; those with risk factors for diabetes and symptoms suggestive of hyperglycemia should be tested for diabetes. Over 10 years of exposure to placebo-controlled trials (median exposure 40 to 42 days), there were no significant differences between aripiprazole- and placebo-treated patients in the proportion of patients with any injection site-related adverse reaction (15.0% vs 13.4%, respectively), but there were trends toward increased injection site reactions with aripiprazole. In patients treated with ABILIFY MAINTENA, injection site reactions were uncommon and did not significantly differ between aripiprazole-treated and placebo-treated patients (2.3% vs 1.9% for injection site reaction, respectively). In patients treated with atypical antipsychotics for greater than 14 days, if the CYP3A4 inhibitor or CYP2D6 inhibitor is withdrawn, the Abilify Maintena dosage may need to be increased. Avoid the concomitant use of CYP3A4 inhibitors or CYP2D6 inhibitors for greater than 14 days. If the CYP3A4 inhibitor or CYP2D6 inhibitor is withdrawn, the Abilify Maintena dosage may need to be increased. Avoid the concomitant use of CYP3A4 inhibitors, CYP2D6 inhibitors or CYP3A4 inducers for less than 14 days.

**Dyslipidemia:** Distinguishable alterations in lipids have been observed in patients treated with atypical antipsychotics.

**Weight Gain:** Weight gain has been observed. Clinical monitoring of weight is recommended.

**Dyskinesia:** The term dyskinesia is used to describe a spectrum of movements that are abnormal, involuntary, and may interfere with patient function. It includes a wide range of phenomena that are associated with the use of antipsychotics, including extrapyramidal symptoms (EPS) and tardive dyskinesia (TD). Extrapyramidal symptoms, also known as EPS, are of sudden onset and have been described in association with the use of all antipsychotic drugs. The term TD refers to movements partially or completely, if antipsychotic treatment is withdrawn. Antipsychotic treatment, itself, may possibly mask the underlying process. The effect of symptomatic suppression on the long-term course of the syndrome is unknown.

**Dyslipidemia:** Atypical antipsychotics have been associated with metabolic changes that include:

- **Total Cholesterol:** Mean changes from baseline for patients treated with atypical antipsychotics for at least 4 weeks and treated within 14 days of enrollment were based on pooled data from 13 placebo-controlled monotherapy trials (all atypical antipsychotic drugs). Mean change in total cholesterol (fasting/nonfasting) was not significantly different than in placebo-treated patients (+2.2 mg/dL (n=42) and +9.6 mg/dL (n=1057) in the fasted groups). A pooled analysis from 17 trials (median exposure 21 to 25 days), fasting triglycerides (treated from eight trials, median exposure 21 to 25 days), and HDL cholesterol (treated from four trials, median exposure 21 to 25 days), revealed that aripiprazole treatment was not associated with any specific changes in lipids.

- **Triglycerides:** A pooled analysis from eight trials (median exposure 25 days; N=1057) was not significantly different than in placebo-treated patients (+4.4 mg/dL; median exposure 25 days; N=1057) was not significantly different than in placebo-treated patients (+4.4 mg/dL; median exposure 25 days; N=1057). There were no significant differences between aripiprazole- and placebo-treated patients in the proportion with changes from baseline to unusually low fasting total cholesterol (less than 50 mg/dL). Over 10 years of exposure to placebo-controlled trials (median exposure 40 to 42 days), there were no significant differences between aripiprazole- and placebo-treated patients in the proportion of patients with any injection site-related adverse reaction (15.0% vs 13.4%, respectively), but there were trends toward increased injection site reactions with aripiprazole. In patients treated with ABILIFY MAINTENA, injection site reactions were uncommon and did not significantly differ between aripiprazole-treated and placebo-treated patients (2.3% vs 1.9% for injection site reaction, respectively). Over 10 years of exposure to placebo-controlled trials (median exposure 40 to 42 days), there were no significant differences between aripiprazole- and placebo-treated patients in the proportion of patients with any injection site-related adverse reaction (15.0% vs 13.4%, respectively), but there were trends toward increased injection site reactions with aripiprazole. In patients treated with ABILIFY MAINTENA, injection site reactions were uncommon and did not significantly differ between aripiprazole-treated and placebo-treated patients (2.3% vs 1.9% for injection site reaction, respectively). Over 10 years of exposure to placebo-controlled trials (median exposure 40 to 42 days), there were no significant differences between aripiprazole- and placebo-treated patients in the proportion of patients with any injection site-related adverse reaction (15.0% vs 13.4%, respectively), but there were trends toward increased injection site reactions with aripiprazole. In patients treated with ABILIFY MAINTENA, injection site reactions were uncommon and did not significantly differ between aripiprazole-treated and placebo-treated patients (2.3% vs 1.9% for injection site reaction, respectively).
ABILIFY MAINTENA™ (aripiprazole) for extended-release intramuscular injection for schizophrenia

DOSAGE AND ADMINISTRATION
ABILIFY MAINTENA is contraindicated for the treatment of patients with a history of seizures or with a history of significant seizure disorders. Aripiprazole is metabolized by the cytochrome P450 (CYP) 2D6 isoenzyme (in part as arottenb, pentoxylic acid, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of the atypical antipsychotic.

Seizures/Convulsions: Abilify Maintena should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Potential for Cognitive and Motor Impairment: Abilify Maintena may impair judgment, thinking, or motor skills. Instruct patients to avoid operating hazardous machinery including automobiles until they are certain Abilify Maintena does not affect them adversely.

Body Temperature Regulation: Disruption of the body’s ability to reduce core body temperature has been attributed to the administration of antipsychotic drugs, including antipsychotics with neuroleptic activity. Hyperthermia, frank (e.g., heat stroke, intracranial hypertension) or subclinical (e.g., fever, elevated body temperature) events, have occurred in patients receiving Abilify Maintena. In some cases, hyperthermia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of the atypical antipsychotic.

Metabolic Changes: Aripiprazole is metabolized by the cytochrome P450 (CYP) 2D6 isoenzyme (in part as arottenb, pentoxylic acid, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of the atypical antipsychotic.
Reactions that occurred in 2% or more of patients treated with oral aripiprazole (doses ≥2 mg/day) therapy (up to 6 weeks in schizophrenia and up to 3 weeks in bipolar mania), including only those pooled incidence, rounded to the nearest percent, of adverse reactions that occurred during acute treatment. Many patients maintained with clinically significant reactions for fewer or other symptoms or signs of oral aripiprazole therapy and were then randomized to receive ABILIFY MAINTENA. A total of 832 patients were treated with ABILIFY MAINTENA for at least 180 days (at least 7 consecutive injections) and 630 patients treated with ABILIFY MAINTENA had 1 year of treatment (at least 13 consecutive injections). Adverse reactions associated with the use of oral aripiprazole in patients with schizophrenia were generally consistent with those reported in the short-term, placebo-controlled trials. In a randomized, double-blind, placebo-controlled study of 784 schizophrenia patients (262 patients assigned to receive aripiprazole 15 mg/day, 20 mg/day, and 30 mg/day) to placebo. This analysis, stratified by study, indicated that the only adverse reaction to have a possible dose response relationship, and then most prominent adverse reaction associated with the use of oral aripiprazole in patients with schizophrenia was weight gain. Adverse reactions are usually expected during the initiation of treatment with oral aripiprazole and are considered more likely due to an increase in the metabolic rate than to a direct effect of the drug. Adverse reactions occurring in 2% or more of patients treated with oral aripiprazole in a manner that cannot be attributed to the conditions being treated. Conditions that lower the seizure threshold include drugs such as phenothiazines, disulfiram, and carbamazepine. Conditions that lower the seizure threshold may require consideration. Aripiprazole is a benzamide. However, the reactions reported occurred during treatment with aripiprazole, they were not considered to be related to the drug. In addition, in a long-term, active-controlled study, the incidence of tremor was 5% (40/859) in patients treated with oral aripiprazole compared with 2% (20/906) in patients treated with placebo. Adverse reactions reported by at least 2% of patients treated with oral aripiprazole, except psychiatric disorders, are shown in Table 4. The largest known case of acute ingestion with a known course of aripiprazole overdose (alone or in combination with other substances) include vomiting, abdominal pain, rhabdomyolysis, severe hypotension, and prolonged QT interval. Several weeks of treatment with oral aripiprazole may be required to achieve peak effects, and the mean time to peak effects was approximately 100 days. In short-term, placebo-controlled trials in adults with schizophrenia treated with oral aripiprazole 10 mg/day, 20 mg/day, 30 mg/day, and 30 mg/kg/day (1 times, 3 times, and 10 times the oral MRD) on a mg/m² basis of aripiprazole perinatally and postnatally (from day 17 of gestation through day 21 postpartum), slight to moderate structural and functional abnormalities were observed in pups. Aripiprazole is excreted in human breast milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Some newborn and infant animals exposed to aripiprazole perinatally and postnatally exhibited an increased incidence of tremor, extrapyramidal or withdrawal symptoms. Some neonates recovered within hours or days without sequelae. German Center admissions. Aripiprazole is a benzamide. However, the reactions reported occurred during treatment with aripiprazole, they were not considered to be related to the drug.
Oral Temperature Regulation:

Body Temperature Regulation: Disruption of the body’s ability to reduce core body temperature may occur with antipsychotic drugs and/or with fever. Appropriate care is advised when prescribing ABILIFY MAINTENA for patients who are experiencing conditions which may contribute to the body’s inability to regulate temperature (e.g., stroke, hypothyroidism, exposure to heat, severe infections, central nervous system depression, hypothyroidism, sepsis, heat stroke), and refrigerating reconstituted medication with anticholinergic activity, or being subject to dehydration.

Dyskinesia: Exophthalmos, diplopia, and other ocular abnormalities have been associated with antipsychotic drug use, including ABILIFY MAINTENA. ABILIFY MAINTENA and other antipsychotic drugs should be used cautiously in patients at risk for retinal toxicity.

ADVERSE REACTIONS: The following adverse reactions are discussed in more detail in other relevant sections of the prescribing information:

- Increased Mortality in Elderly Patients with Dementia-Related Psychiatric Disorders (3.2)  
- Carcinogenesis, Mutagenesis, Impairment of Fertility (16)
- Metabolic/Endocrine Disorders (5.7)
- Leukopenia, Neutropenia, and Agranulocytosis (5.8)
- Body Temperature Regulation (5.9)
- Clinical Trials Experience: Pediatric Use (14.1)
- Nervous System Disorders (5.10)
- Psychiatric Disorders (5.10)
- Psychiatric Disorders: Treatment-Emergent Movement Disorders (5.10)
- Pyrexia (5.10)
- Delirium (5.11)
- Somnolence (5.11)
- Somnolence: Effects of Antipsychotic Drugs (5.11)
- Benign Prostatic Hypertrophy (5.12)
- Cataracts (5.12)
- Nerve Conduction Studies (5.13)
- Adverse Drug Reactions in Long-Term, Double-Blind, Placebo-Controlled Trials of Oral Aripiprazole:

Adverse Reactions of ABILIFY MAINTENA and Oral Aripiprazole: Aripiprazole’s effects on the body, as reflected in vital signs, ophthalmic examinations, or laboratory tests, were not statistically different from placebo in normal elderly subjects and in patients with schizophrenia treated with oral aripiprazole. A total of 1,270 patients were treated with ABILIFY MAINTENA for at least 180 days, and 1,503 patients completing oral aripiprazole treatment for at least 180 days. In the clinical trials, only adverse reactions that were considered treatment-related and occurred at an incidence of greater than or equal to 3% in either ABILIFY MAINTENA or oral aripiprazole are presented. A total of 122 patients were treated with ABILIFY MAINTENA for at least 180 days, and 309 patients completing oral aripiprazole treatment for at least 180 days. 

Adverse Reactions of ABILIFY MAINTENA and Oral Aripiprazole: Abnormal involuntary movements, extrapyramidal symptoms, dystonia, akathisia, and the Abnormal Involuntary Movement Scale (for dyskinesias) did not show a statistically significant difference from placebo in any trial. Adverse reactions reported in a 26-week, double-blind, placebo-controlled trial comparing oral aripiprazole and placebo included:

- 100=unbearably painful) was minimal and improved in subjects receiving ABILIFY MAINTENA from baseline to last injection.

- The largest known case of acute ingestion with a known

- The following adverse reactions were reported by at least 1% of patients treated with ABILIFY MAINTENA.

- The following adverse reactions were reported by at least 1% of patients treated with placebo.

- Other Adverse Reactions Occurring During the Postmarketing Evaluation of Oral Aripiprazole Following is a list of MedDRA terms that reflect adverse reactions reported by patients treated with oral aripiprazole and placebo in the flexible-dose (See Table 2) or fixed-dose (15 mg/day) studies. Adverse reactions, particularly those that are likely to be useful in the prescribing or that have interesting clinical significance, are included. Adverse reactions other than those occurring at equal or higher rates in the placebo group, or those occurring in at least 10% of oral aripiprazole patients, for which the relationship to drug is not necessarily caused by it.

- The following adverse reactions to have a possible dose response relationship, and then most prominent (the only adverse reaction to have a possible dose response relationship, and then most prominent

- The following adverse reactions rates observed in the clinical trials of a drug cannot be directly compared to rates in

- Approximately 8% of Caucasians and 3–8% of Black/African

- Postmarketing Experience: The following adverse reactions have been identified during postmarketing use of ABILIFY MAINTENA. These reactions are ordered by decreasing frequency of reporting. A single event may be listed as contributing to more than one adverse reaction and is counted once for each adverse reaction listed.

- The largest known case of acute ingestion with a known

- Disruptions of temperature regulation (e.g., stroke, hypothyroidism, exposure to heat, ventricular tachycardia

- Somnolence: Effects of Antipsychotic Drugs (5.11)

- Delirium (5.11)

- Somnolence (5.11)

- Somnolence: Effects of Antipsychotic Drugs (5.11)

- Benign Prostatic Hypertrophy (5.12)

- Cataracts (5.12)

- Nerve Conduction Studies (5.13)

- Adverse Drug Reactions in Long-Term, Double-Blind, Placebo-Controlled Trials of Oral Aripiprazole:

- Adverse Reactions of ABILIFY MAINTENA and Oral Aripiprazole: Abnormal involuntary movements, extrapyramidal symptoms, dystonia, akathisia, and the Abnormal Involuntary Movement Scale (for dyskinesias) did not show a statistically significant difference from placebo in any trial. Adverse reactions reported in a 26-week, double-blind, placebo-controlled trial comparing oral aripiprazole and placebo included:

- 100=unbearably painful) was minimal and improved in subjects receiving ABILIFY MAINTENA from baseline to last injection.

- The largest known case of acute ingestion with a known

- Other Adverse Reactions Occurring During the Postmarketing Evaluation of Oral Aripiprazole Following is a list of MedDRA terms that reflect adverse reactions reported by patients treated with oral aripiprazole and placebo in the flexible-dose (See Table 2) or fixed-dose (15 mg/day) studies. Adverse reactions, particularly those that are likely to be useful in the prescribing or that have interesting clinical significance, are included. Adverse reactions other than those occurring at equal or higher rates in the placebo group, or those occurring in at least 10% of oral aripiprazole patients, for which the relationship to drug is not necessarily caused by it.

- The following adverse reactions to have a possible dose response relationship, and then most prominent (the only adverse reaction to have a possible dose response relationship, and then most prominent

- The following adverse reactions rates observed in the clinical trials of a drug cannot be directly compared to rates in

- Approximately 8% of Caucasians and 3–8% of Black/African
Will More Transparency Finally Force Physicians and Hospitals To Compete for Patients?

Health plans have more incentives than ever to foster competition, but efforts in the past have failed

By Joseph Burns
Contributing Editor

The theory is simple. Give consumers information on the costs and quality of health care and they will make physicians and hospitals compete. Competition will drive down prices. And we'll all live happily ever after.

Well, not exactly, because price transparency is largely missing in health care. And there is even less information on the quality of physician and hospital care than on prices.

In May the federal Centers for Medicare & Medicaid Services (CMS) launched a database showing what 3,000 hospitals charge and some information on how they perform, judged by standard hospital quality metrics. The result may be that consumers are more bewildered, not less, according to an analysis published in the Journal of the American Medical Association (JAMA), "Release of Data on What Hospitals Charge Appears More Likely to Confuse Rather Than Enlighten Consumers." The site provides a great volume of data but is cumbersome (http://go.cms.gov/18qgrKU).

Compared with the amount and quality of data available to consumers seeking to buy a car, a household appliance, or any electronic device today, the site is woefully inadequate.

The data that CMS released barely tell the story of actual charges and payments that consumers can expect. What hospitals charge Medicare is not related to what consumers would pay a hospital because insurers negotiate rates that are usually between what hospitals bill Medicare and what Medicare pays, as JAMA points out. The only group of consumers likely to benefit from the CMS data is the uninsured, because they are most likely to be charged the highest rate for care in hospitals and physicians’ offices, JAMA reports.

Shocked!

Uwe E. Reinhardt, PhD, an economics professor at Princeton University, wrote about this problem earlier this year in an article in the New York Times titled appropriately, "Shocked, Shocked Over Hospital Bills" (http://nyti.ms/1dez7AY). (And see our Q&A with Reinhardt on page 21 and on video at http://www.managedcaremag.com/blog/managed-cares-prospects-health-reform-era or at http://bit.ly/1hnGqq9.)

Americans shouldn’t be shocked by hospital bills, Reinhardt wrote, because national publications have covered the issue extensively. The best recent example of how hospitals obfuscate pricing for consumers came in a cover story in Time magazine on March 4, “Bitter Pill: Why Medical Bills Are Killing Us,” by Steven Brill. (Subscription required at http://ti.me/18qhASC.)

The Affordable Care Act was supposed to address this issue. In fact, the ACA is why CMS issued its report on what it pays hospitals. But as JAMA reports, there is not much useful information on the site. For a typical consumer seeking prices from a local hospital, CMS provides estimated hospital-specific charges, collected in 2011, for outpatient services.

Indeed, price transparency tools are in their infancy, says Katherine Hempstead, a senior program officer at the Robert Wood Johnson Foundation. RWJF asked information technologists to build apps to help consumers use the CMS hospital price data more efficiently, and more generally to
create models that could incorporate other data sources.

“Consumers need price, quality, and mapping information to help them make choices,” she says. “The CMS price information is fantastic but limited because it’s not necessarily useful for consumers shopping on price. We need more quality information too. We need tools that are available when we shop for other products and services.”

In fact, some of the best tools are provided by health plans, Hempstead adds. For years, insurers have been developing tools to make it easier for members to compare hospital and physician prices and quality.

Harvard Pilgrim Health Care (HPHC), UnitedHealthcare, Aetna, and other health plans have all been in the news this year for introducing tools that let members evaluate providers on price and quality standards.

Health plans recognize that by fostering competition they may be able to get physicians and hospitals to compete on price and quality. Whether they do actually compete remains to be seen. Some critics predict that once low-rate doctors and hospitals see what others charge, they will raise their prices.

But health plans also recognize that because so many consumers are enrolled in high-deductible health plans (HDHPs), consumers will be more cost-conscious than in the past.

Consumers using public and private exchanges will seek low-cost options and thus choose high-deductible health plans over standard health plans because their premiums are lower. A recent survey found that many large companies are now offering only an HDHP linked to a savings account for medical expenses.

That survey, by Towers Watson and the National Business Group on Health, reports that this year, 66% of companies with 1,000 or more employees offered at least one HDHP linked to a savings account. Next year, 79% of these employers will offer such plans. In addition, about 15% offer only an HDHP linked to a savings account, almost double the rate in 2010.

“If we can drive more volume to lower-cost providers, then, in theory, we should be able to save on health insurance premiums,” says Rick Weisblatt, PhD, senior vice president for provider

Consultant: CDHPs have one last shot at success

Relatively low enrollment in consumer-directed health plans (CDHPs) reflects failure to promote these plans successfully, says John Young, CEO of Consumerdriven, a consulting company in Minneapolis.

The percentage of enrollees in CDHPs is far too low, given the advantages these plans provide to consumers, health insurers, and the health system itself, Young says. In August, the Kaiser Family Foundation/Health Research & Educational Trust (HRET) 2013 Employer Health Benefits Survey showed that 20% of employees are in these plans. Critics of these plans have suggested that to keep spending low, consumers in CDHPs will not get recommended care.

“The data has been out for 13 years showing that these plans work to reduce cost and improve health,” Young says. He cited the case of Textron, a company in Providence, R.I., that has had a CDHP since 2002 and reported that medical utilization declined and preventive care visits rose after the program was introduced, according to an article in HR Magazine (http://bit.ly/1hnMH5d).

“Members in these plans are not avoiding care;” Young says. “They are getting healthier, they are saving money, and they are slowing the growth of health care costs. Yet not enough consumers are enrolled in these plans, and that’s a failure of leadership. It will take all stakeholders — employers, brokers, and insurers — to push these plans as a front-line system.”

A study by the Employee Benefit Research Institute earlier this year found that consumers enrolled in CDHPs typically seem to be in better health and have higher education and higher income levels than those with traditional coverage, says Paul Fronstin, PhD, the author of the report and director of EBRI’s Health Research and Education Program. But cause and effect have not been studied, he adds.

In other words, there is no proof that being in a CDHP leads to better health.

Studies by Cigna show that consumers in complete replacement plans get healthier each year, Young says, citing the Seventh Annual Cigna Choice Fund Experience Study released earlier this year. The report provides empirical evidence that properly designed consumer-directed plans have a beneficial effect on total medical cost without compromising care or shifting costs from the employer to employees, Cigna says.
networks and product development at Harvard Pilgrim Health Care. “If the market becomes more competitive and providers are forced to be more efficient and then improve their cost structure and lower their prices, that should mean we could lower the cost of insurance. If a consumer can pay $800 for a service instead of the current $2,000, that saves the system $1,200. And if the consumer is getting the same quality service that would have been obtained from a higher-cost provider, then the consumer gets better value. The more that happens, the more it will affect insurance premiums.”

Three initiatives
Harvard Pilgrim is introducing three initiatives to help members understand the cost and quality of the physicians, hospitals, and other providers that contract with the plan, which has 1.2 million members in Maine, Massachusetts, and New Hampshire. First, Castlight Health, a company that provides members with pricing and quality information on health care providers, will help Harvard Pilgrim members make more informed purchasing decisions. Second, the SavOn program gives Harvard Pilgrim members financial incentives to choose lower-cost providers. And in September, Harvard Pilgrim started offering price and quality information on the web and on smartphones in a program called Now iKnow.

Insurers’ cost and quality transparency tools have been inadequate to the task, says John Young, CEO of Consumerdriven, a consulting company.

These three programs are needed to address the problem stated succinctly in this recent headline from the Washington Post: “How much does an MRI cost? In D.C., anywhere from $400 to $1,861.”

Knowing that similar price disparities are common in every market nationwide, including New Hampshire and Massachusetts, Weisblatt says that HPHC needs to offer accurate cost and quality information to members.

“Unlike other markets, where information is available, in health care it’s very hard for consumers to get information on the value of the products or services they’re buying,” he adds, explaining that high value is a combination of high quality and low cost. “We are trying to expose the value of these services to members by showing them that there are differences in quality and price. We want them to understand that there are many prices for the tests and procedures that they will get and that prices tend to be much higher in some hospitals than they might be in a clinic or freestanding facilities, for example.”

This information needs to be available at the point of purchase so that plan members can see how a particular service will affect their deductibles, Weisblatt adds. That’s why HPHC and other insurers are linking their cost and quality transparency efforts to each member’s plan and updating that information continually. That way a member can see that a high-cost provider could affect the member’s deductible more than a lower-cost provider. The transparency tools also allow members to see what many providers in an area — defined by a member’s home ZIP code — charge, so that the member can compare them.

All of these efforts are designed to foster competition, of course, and perhaps they will. But none of these efforts would be needed if the Affordable Care Act had required full price and quality transparency, says Regina E. Herzlinger, PhD, the Nancy R. McPherson professor of business administration at Harvard Business School. She is the author of the 2007 book Who Killed Health Care? When drafting the ACA in 2010, President Obama and Congress should have added requirements like those in the Securities Act of 1933, which called for the formation of the Securities and Exchange Commission, Herzlinger says. The SEC helps educate investors by requiring public companies to disclose the risks of investing in the companies. Today, the SEC publishes a wide variety of information on every public company on its web site.

Fearing the truth
A similar system is needed in health care so that consumers may see what every procedure costs and how the various providers, including physicians and hospitals, are rated in terms of the quality they provide, Herzlinger says. “True transparency will never happen if the status quo providers and plans are in charge. Like the businesses pre-SEC, they fear that the truth will harm them.”

HPHC and other health plans are racing to introduce tools to allow consumers to make more
informed choices based on price and quality.

“What’s different today is the specificity we’re offering and the link to the members’ own benefits plans,” Weisblatt says. In the past, health plans would have a symbol for what a doctor or hospital might charge. One dollar sign designated low-cost providers and three dollar signs meant high-cost providers.

“Now we’re showing the actual contractual rates for each service from each doctor and each facility. That means you can look up a surgeon in our network and see what he or she would charge for a knee arthroscopy, for instance. Or you could look up the hospital to see what the actual cost would be to have your knee surgery done there.” The tool allows members to see what their deductible and copayment would be for a surgical procedure.

Having this information before the surgery is done provides a better picture than any cost tools used in the past. “You will clearly see what you would pay and what would be left to pay on your deductible after this procedure,” Weisblatt adds.

Evaluating physicians on quality is much more difficult because the systems used to evaluate physician and hospital quality have limited utility, Weisblatt says. “Right now it’s HEDIS measures and we are working to see what other quality measures we could add. Physicians sometimes complain about how we evaluate them for our tiered products or how we use quality measures, and my answer is that we use the quality tools available to us in the market. As specialty societies introduce more quality measures, we will use them.”

Aetna’s approach

Aetna has a price-estimation tool similar to the one HPHC uses. It is called the Member Payment Estimator, and it provides up-to-date out-of-pocket cost estimates based on a member’s benefit plan, says Chris Riedl, head of product strategy for national accounts at Aetna. Like the HPHC Now iKnow initiative, the estimator provides cost estimates and cost comparisons for more than 650 commonly used, non-emergency, in-network health services. The Member Payment Estimator also provides estimates for out-of-network physician services. Using the estimator, members who obtained cost estimates on commonly selected health care services chose the provider whose out-of-pocket cost estimate was, on average, $170 lower than the average of the estimates they received.

It’s been used since 2010, and Aetna has been giving cost and quality information to members for more than 10 years, Riedl says.

“We started with a hospital comparison tool that allows members to compare quality metrics of hospitals and then added geographic average prices for services both in and out of the Aetna network a few years later,” she says. “After that we added the physician- and facility-specific cost information for members. But then in 2010, we introduced the Member Payment Estimator, which combines the negotiated rate information from providers with each member’s benefit design.”

Since the program started, Aetna has provided more than 2.9 million cost estimates to members, and averages about 106,000 such requests per month. In July, it had 118,667 requests, the most for any one month since the program started. Aetna has been giving cost and quality information to members for more than 10 years, Riedl says.

Aetna says the program estimates the member’s out-of-pocket costs based on Aetna’s negotiated rate with the health care provider and the member’s benefits plan. Aetna does not release information related to the accuracy of estimates compared with the rates that members actually pay.

Members enrolled in Aetna’s consumer-directed health plans (CDHPs) use this program about twice as much as members in traditional plans. Also, members in CDHPs are more engaged in making health care decisions than members of traditional plans, according to the ninth annual Aetna HealthFund study, which Aetna says is the longest-running review of CDHPs in the health insurance industry.

Members in CDHPs use generic drugs at about the same rate as members in PPO plans, but they are 30% more likely to participate in disease management programs, the study found.

Aetna also has a companion to the price-estimator that lets physicians or other providers prepare an estimate in the office for the member to consider. “That opens up very different discussions from what patients had with doctors in the past,” Riedl says.
Cigna launched Find a Doctor a year and a half ago and gets more than 1 million visits per month. About 20% are seeking information on costs and quality, says Cigna spokesman Joe Mondy. The Cigna initiative is similar to Aetna’s cost estimator in that it allows members to assess the cost of 200 common procedures, which account for 80% of all claims for primary care visits, visits to specialist physicians, and hospital visits. Before choosing a physician or hospital, members get up-to-date information on their plan deductibles, co-insurance, and health account funds, he adds.

Like the Aetna and HPHC programs, the Cigna initiative is more robust than what’s been offered in the past.

Promises, promises

For years, health plans have promised to deliver meaningful cost information to consumers, but what they delivered did not represent what the member would pay specifically, Mondy says. Instead, health plans gave members average payments or broad ranges of payments.

Just as Aetna found that its members in CDHPs were more engaged in making decisions about their care than were non-CDHP members, so too did Cigna. Its members in CDHPs were 59% more likely to use Cigna’s physician directory to get cost and procedure information to help them review potential medical costs, they were twice as likely to complete a health risk assessment, and those with chronic illnesses were 25% more likely to participate in disease management programs than those enrolled in traditional plans.

CDHP members were more likely to choose generic medications than those in traditional plans and they used the emergency room at a 6% lower rate than people enrolled in HMO and PPO plans, Cigna reports.

Anemic enrollment

Despite the success that Aetna and Cigna have seen with their CDHPs, enrollment in these plans should be much more robust. That it is not is partly because so far, yesterday’s industry cost and quality transparency tools were inadequate to the task, says John Young, CEO of Consumerdriven, a CDHP consulting company. Before starting this company earlier this year, Young was a senior vice president at Cigna Healthcare.

Consumers in account-based plans naturally demand more information on the costs of care and the quality of all providers, he says. “The most important job we can do today is to create more of a demand for the information that people need to make care decisions. We need to support them because they have the right to information on price and quality,” he claims.

“They also have the right to know all the alternatives to the medications or procedures that they are being prescribed or recommended. They need to know which alternatives might be cheaper or better than what their doctors recommend. I’m encouraged by today’s tools and what the industry is developing. The more we can do to empower the customer to move into a stronger position in this equation, the more we will influence the costs of care so that we can start to bring those costs down to a reasonable level and thus create a truly consumer-driven system.”

“You know when kids are good or bad? Are you part of government surveillance?”
A Conversation With Uwe E. Reinhardt, PhD

Health Care Deserves More Respect
The internationally known health care economist says we have been heading in the right direction all along — we just have to tackle problems in the right order

Health care economist Uwe E. Reinhardt, PhD, is bullish on health care. The decline in the growth of health care costs looks as if it is permanent, and the innovations being developed in information technology are exciting, says Reinhardt, the James Madison Professor of Political Economy and professor of economics and public affairs at Princeton University. He suggests, however, that the industry tackle prices and administrative costs before putting any more pressure on hardworking doctors and nurses, and that insurers take over wellness programming. It’s a safe bet that people are listening. A member of the Institute of Medicine and the National Academy of Sciences, Reinhardt has advised organizations such as the World Bank, the Physician Payment Review Commission, the Veterans Administration, and the United States Department of Health and Human Services. He is a member of the Kaiser Family Foundation’s Commission on Medicaid and the Uninsured. Reinhardt contributes to the New York Times Economix blog and is on the editorial board of Health Affairs. He previously served on the editorial boards of the New England Journal of Medicine and the Journal of the American Medical Association, among others. This publication, in fact, is one of those others. Reinhardt is on the board of Boston Scientific, a medical device company, and is a director at two mutual funds: the Hambrecht & Quist Life Sciences Fund and the Health Care Fund. He received a bachelor of commerce degree from the University of Saskatchewan and earned a PhD in economics at Yale University. He spoke recently with MANAGED CARE Managing Editor Frank Diamond on the campus of Princeton University (see the unabridged version on video at http://www.managedcaremag.com/blog/managed-cares-prospects-health-reform-era).

MANAGED CARE: Professor, everybody knew something had to be done to fix the health care system, and everybody knew one of the main problems with the system was costs. Does the Affordable Care Act address the problem of costs?

UWE E. REINHARDT, Ph.D.: The Affordable Care Act doesn’t really address directly the issue of costs. In fact, it would add expenditures. Other things being equal, it raises annual health spending by 5 percent — for the extra insured. But it developed a lot of instruments that could be used for cost containment. It actually happens to be true that starting in 2002, the rate of growth of health care spending in America started falling. So when you draw a graph, you see a steep decline in the annual growth rate of health spending per capita. Economists have looked at it; the bulk of it is recession-driven. There is a fairly close relationship between health spending per capita and GDP per capita, but with a lag. It doesn’t hit all at once. Some of it hits in the first year, but it has about a four-year lag effect.
The Altarum Institute and Kaiser Family Foundation did some research, and it tracks quite closely. And then there are some additional things like increased cost-sharing by patients through higher deductibles, and so on. A variety of things started to lower the growth in health spending. It used to be that health spending annually grew 2 percentage points faster than GDP grows. That’s down below 1, sort of .5, so — GDP plus a half percent. It might go to .8 when the economy recovers fully. So something happened long before the Affordable Care Act was passed. But the Affordable Care Act offers, for example, comparative-effectiveness analysis. Unfortunately, not cost-effectiveness — that was ruled out by Congress — but at least you could say which drug works better than another. There are attempts at payment reform — bundled payments rather than fee for service or capitation. The accountable care organization, that’s a more iffy bag. The idea there is essentially to build something like Kaiser Permanente but without going all the way that Kaiser did. It could be just contractual with hospitals and doctors. But notice what already happened. Only about half of the physicians in America are still self-employed. There has already been this movement, and it predates the Affordable Care Act, of buying doctors and building larger systems where you can have integrated care. But the Affordable Care Act accelerates that and gives incentives for that. There’s a lot in the bill that could help cost containment, but for President Obama to claim that it was an instrument of cost containment, or that what we have seen is because of the Affordable Care Act — I don’t buy that.

MC: The managed care industry has lobbied to allow health insurers to sell insurance across state lines, basically become national health care insurers. Is there any credence to that?

Reinhardt: What is it actually that is being sold? What is being sold is in states with very lax regulation of the insurance industry. If you go to New Jersey or New York, they really tightly regulate the insurance companies. You go to other parts of the country — Iowa, maybe, or Texas, where there is not that much regulation — there is not all of this mandated coverage of wigs and this and that. So what you are selling is insurance with less regulatory protection. That’s what is being marketed. Because when an Iowa or a Texas insurer insures a New Yorker, they have to buy the health care in New York at New York prices, which are high. They are not like Iowa prices. So therefore an Iowa company selling insurance to an Iowa person can quote a much lower rate than an Iowa company could selling insurance to a New York person, because they would have to pay Mount Sinai and Columbia-Presbyterian prices. So the only reason they can be cheaper than a New York-based company is the less burdensome regulation of the state. If you look internationally and ask why do we spend twice as much as most European countries or Canada per capita, the answer is almost all prices. Name anything, and our price is twice as what it would be in Germany or in Canada. Even for the same drug or the same procedure, and so on. It’s prices. We wrote a paper, Gerard Anderson and I and some others — it’s quite famous now — called, “It’s the Prices, Stupid.” It’s in Health Affairs. Because we realized, if you actually look, we have far fewer hospital days per capita than Germans or Canadians, we have fewer doctor visits, we eat fewer pills. The only thing where we consume a little more is some high-tech procedures like imaging, and in some heart surgery and cancer care, we are more aggressive. But in most other stuff, the kind you shoot at with cost sharing, we are already very dainty consumers. Americans don’t flock to the doctor. We have the lowest physician visit rate per capita in the world.

MC: Does that perplex you? Is it one of those problems that seem insolvable?

Reinhardt: Have you ever seen a perplexed economist? We have an answer for everything! Here’s my answer: In all of these countries — Canada, Germany, etc. — the demand side, the payment side, has a lot of power. In Canada, it has what we economists call monopsony power — single payer.
There’s only one payer. And so the doctors and the hospitals, they negotiate with one payer. The power of the market is all on the payment side. The supply side is splintered. With us, it’s exactly the other way around. Particularly as the hospitals increasingly consolidate. The insurance companies are splintered. You could say that Aetna is big, WellPoint is big. They are big nationally, but in any given market, they don’t dominate. They may be relatively big, but something like Partners in Boston or Mount Sinai in New York, you couldn’t write insurance without them in it. And Mount Sinai knows that. And therefore they have market power over even a big company like United. I wrote a paper called “Divide et Impera” — divide and rule. And I said, what we have done, we splintered the payer side into thousands of little payers, against the increasingly consolidated supply side, particularly in the hospital area, that has market moxy, and that is what drives these prices so high.

MC: It seems that insurance companies have made stupid decisions in the past, and you just mentioned that their power is waning. Have they learned lessons on management and how to get people not to view them as the bad guy anymore?

Reinhardt: I don’t view them as the bad guy or as stupid. I’ve never thought they were stupid. No, it’s just simply that they were weak because they were splintered. Even their administrative costs are caused in good part by this pluralism. We have so many thousands of different insurance policies, each with their own rules. It’s an attempt to please the customer, but the more choice you have — choice is expensive. And that is why — I have seen papers — our hospitals spend twice as much on administration as any hospital anywhere in the world because of all of this complexity. Stupidity cannot explain very much at all in our health system. Mind you, a Martian who would land here would say, “Why the hell did they set it up this way?” But everyone within it is quite clever, etcetera. It’s just that when you are splintered, like the insurance industry is, each guy sitting on the other side of the table of a consolidated hospital system is weak. Even in Boston, Partners just owns that town. They are willing to negotiate. They will give you a little bit, but not a lot. Their prices are high.

MC: Do you see an evolution toward a single-payer health care system?

Reinhardt: No. That’s what some people claim; I see it go the other way. If anything, we would go to a three-tiered system, where it might be that our kids — the ones I teach now — they might say, you don’t have to be 100 percent equalitarian in health care. You give everyone a guarantee to something. And so we’ll have public clinics and public hospitals, and we’ll budget them, and if you’re poor, instead of being in Medicaid, you’ll go to that hospital. Then for the middle class, you and me, you would have what is called reference pricing. Insurers negotiate prices with different hospitals, and tell their insured, “If you go to this hospital or this hospital and have your baby there, we’ll pay 90 percent. If you go to another hospital that is more expensive, you pay the whole difference between this reference price and what they charge you.” WellPoint has just introduced that for CalPERS personnel, the state employees in California, only for two procedures — hips and knees — but it lowered the prices by something like 20 percent. And everyone else came down. And then boutique medicine for the elite, which they already have. I personally never begrudge them that. I mean, why should a corporate CEO, when he gets sick, be in a ward when they never mix with humanity as you and I know it? They have their limos, their jets. They have mansions and presidential suites in the Ritz when they go to Washington. It would be almost cruel to say, “When you get sick, we stick you in a ward.” I don’t mind that they have a little suite — every hospital in America has that.

MC: Or a Hollywood wing?

Reinhardt: Who cares, as long as they pay for it? It shouldn’t be tax funded. I don’t think people would begrudge people to have boutique medicine, other than if it really noticeably affected survival. I mean, if boutique people got the hearts before anyone else in transplant, that would bug people. But if they had butlers, I don’t think anyone would care.

MC: Where do you see all of this going from here? The health care costs, the ACA? Where do you think that we’re going to be in five years?

Reinhardt: I am actually quite optimistic about health care. First of all, it never was that bad a sec-

Prices negotiated between hospitals and doctors are trade secrets. So if you don’t know prices, competition can’t work.
tor. People always say it’s the most inefficient sector in the world. It’s just all bullshine. If you compare health care to education, health care towers over education in terms of concern about quality, concern about cost effectiveness, et cetera. Compare it to jurisprudence. Have judges ever worried how much time of the jury they pulverize? So I think the health care system actually is a lot better than people claim it to be. We keep beating up on doctors and nurses, and they work very hard. But actually where we should start — there was an Institute of Medicine study out that said we spend $190 billion more per year on administration than we should. It seems to me that should be attacked before I keep hounding more doctors and nurses. There is unnecessary stuff, and people always claim that. But you know I always joke about the vertical and horizontal economists. When we are vertical, we talk a tough game. “Don’t do marginally beneficial things.” When you are horizontal, even when you are an economist, on an operating table....

MC: You want all of the tests.

Reinhardt: Do the low-hanging fruit, the thing that demonstrably couldn’t hurt the patients if you went there. One hundred and ninety billion dollars a year would be much more than we need to cover all the uninsured — 100 percent universal coverage. So that’s what we should go after. For some reason, we talk about evidence-based clinical practice, but not ever about evidence-based administration. What we really need is evidence-based administration. Say, how could you run an insurance system more cheaply than we do? How much should we save? Whatever we are spending, cut it in half. It’s achievable with some ingenuity. On the other hand, there is going to be a lot of innovation coming, made possible for two reasons. One, computational capacity has enormously increased. We now increasingly know how to measure quality. Ten years ago, we really didn’t. And the labor market, tragic or not, is sluggish now. In the ’90s, the labor market was tight. Employers couldn’t do anything. Remember the managed care backlash? Managed care was a good idea. Now, labor is kind of on the run, and it is much easier for employers to impose networks on patients or cost sharing. It’s easier to innovate. I go to these venture capitalist meetings. Healthspottr, I was recently at, and you hear the energy of these young people dreaming up innovations — IT-based — in claims processing, in wellness — computerized wellness where you have some gizmo that speaks to your iPhone and in your iPhone you get a graph that tells you how your weight’s gone this month. Stuff that people need. Make a game out of wellness. There is going to be a lot of innovation coming down the pike. And even within biomedical research, I think you will have a lot of labor-saving innovation. For example, home care that you can do electronically. You don’t need a daily visit to these people if the metrics that get radioed to some center look OK. So I think first of all of the bending of the cost curve, and I am persuaded it’s actually more permanent. We always thought it would go up again when the economy improves. I don’t think so. It is still very expensive, but more under control than before. And there will be a lot of innovation. I love the kids I teach, I really do. The energy I see there. When I look at those 30- to 40-year-old entrepreneurs, and they are up at 6, running, making deals, I think they will change things. We are coming into a different era. These people are more open to change. Don’t forget, until now, the health system has been a cozy cartel. Everyone knew each other, we’re all in this together, and somebody pays the bill. I think those days are over. And you know, it’s always been said that necessity is the mother of invention. But for 40 years, invention was the mother of necessity in health care. Somebody invented a machine that went, “beep, beep, beep,” rather than just, “beep, beep,” and every doctor had to have the “beep, beep, beep” machine. No more. The way device companies and drug companies sell to hospitals isn’t anymore to the individual doctor and his or her desires, it’s to committees. Things are changing. I am actually far more optimistic than I would have been 10 years ago.

MC: Thank you. MC
Employers Show New Interest
In Private Insurance Exchanges

Employees won’t be abandoned by their companies,
whose contributions will continue to rise — somewhat

By John Carroll

There’s nothing new about private health insurance exchanges. They’ve been a regular part of the insurance scene for years, with a well-developed market among retirees. But this year the private exchange marketplace for active workers has grabbed headlines as some big employers shifted employees out of standard self-insured plans.

The prospect of a tidal shift as more employers follow the path cut by the corporate trailblazers has big implications for insurers looking to grab — or keep — market share.

Aon Hewitt, Buck Consultants, Mercer, and Towers Watson are all among the benefit consultants operating private exchanges. Walgreens turned heads just weeks ago when it announced plans to move its 160,000 employees into a private exchange run by Aon Hewitt, where 18 employers will participate and 20 insurers will offer plans. The move was cheered on by Helen Darling, president of the National Business Group on Health, who endorsed the switch as an effort to provide workers with “competitive, cost-effective, flexible benefit choices.”

These private exchanges are a much different breed from the public exchanges being rolled out under Obamacare for individuals and small businesses. They raise related questions about which system will offer the best coverage options and eventually may provide contrasting options for employers that would like to stop being self-insured. The private exchanges also are raising concerns among consumer advocates who fear that this latest shift is another big step on the long road from defined benefits to defined contribution, shifting the bulk of the cost of health insurance, and the risk, to individuals.

Private exchanges “are independent of what is going on with reform,” says Mike Christie, the eloquent marketing chief for Aon Hewitt’s exchange. “But we have concepts in common, trying to do things to drive sustainability and the affordability of health insurance.”

Christie has a persuasive pitch. Large employers that sign up for these national private exchanges can offer workers a subsidy and a place to shop for a plan that the employee decides best suits his or her family. Christie says that the health plans can take every innovation they like to the table, from newly adopted narrow — or high-performing — networks to accountable care organizations, without having to design each offering for a self-insured company’s likes and dislikes. “In our model there’s more control and accountability for the carrier,” says Christie.

Mike Thompson is a top consultant at PwC (PricewaterhouseCooper’s preferred name now), which is sticking with its traditional business of advising companies and staying out of the private exchange business. “In its purest form, this is a predefined marketplace of plans arranged by the private exchange,” says Thompson. “What we’re seeing is that more and more flexibility is being built into the predefined marketplace. The presumption is that the private exchanges will bring economies of scale and sophistication in terms of negotiations with vendors.”

Getting advice

One of the added roles that a private exchange can offer, adds Thompson, is as a gateway to the public exchanges. While employees cannot take company subsidies into a public exchange, they can get advice on how they would fare on a public exchange with the government subsidies that are available. And a

There must be transparency to understand the long-term value of these arrangements,” says Mike Thompson, a consultant at PwC. He’s talking about private health exchanges.

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subset of employees could find it to their advantage to go with a public exchange.

Critics say that if the private exchange offering sounds too good to be true, that’s because it is. Where Aon and the companies are offering a multitude of plans and benefits, consumer advocates see a simple step forward in the switch from defined benefits to defined contributions, with thorny problems awaiting people with the highest medical expenses.

Choice isn’t always good

“The concept is to give workers lots of choices,” says Kathleen Stoll, director of health policy at Families U.S.A. “That’s good, but choice isn’t always good in the world of health insurance.

“If young, healthy employees opt for less expensive and less costly plans on a private exchange, it wouldn’t be surprising to see older, less healthy employees choosing more comprehensive, more expensive plans. That kind of cherry picking is likely to lead to a bad case of cost acceleration for more costly plans.” And real problems arise when you have a “death spiral in rising premiums for more comprehensive plans.”

“The second concern, and one we share, is about moving to a defined contribution instead of a defined benefit,” Stoll adds. “It allows employers to delink the inflation that’s underlying health care costs and reflected in premium inflation.

“It’s really just another way that some employers can shift more costs to workers,” she adds. “Not because they’re bad guys. When premiums rise at a double-digit rate, they’re more likely to say we can’t offer that plan, but here’s a thinner plan that shifts costs to workers.”

That position reflects what Christie sees as a fundamental misunderstanding about the market dynamics involved. If employers wanted to move to a defined contribution, capping their exposure, they could do it today without changing anything else.

“Most employers are not assuming their contribution will stay the same,” says Christie, adding that most are looking for ways to rein in the growth. “They are assuming it will adjust according to rising costs. This is a solution with a better promise of reducing the trend curve over time.”

Thompson agrees, up to a point. The private exchange changes are a step in the direction of defined contributions, he offers, but they are not just about limiting a company’s financial exposure. Companies have a vested interest in making sure that active employees have good benefits, with health insurance often figuring prominently in a company’s plan to recruit and retain the best staff. Also, there’s no easy way for any company to wash its hands of the plans being offered.

“Because the coverage continues to be offered on a group basis for active employees, it’s hard to disassociate the company from the benefit offering,” says Thompson. “It’s not pure defined contribution. They still have skin in the game on how these costs are managed.”

What just about everyone agrees on is that this is one sector of the health insurance market poised for fast growth.

“We’re in the early days of what we think will be a very significant marketplace over the next four to five years,” says Rich Birhanzel, managing director of Accenture’s health administration services.

“There’s a million, maybe more, members on private exchanges, enrolling this fall, and we think that number will expand significantly over the next few years to 40 million by 2018.

“We found that 83% of U.S. customers surveyed don’t know what a private exchange is, but over half are attracted by the idea once it is explained,” adds Birhanzel. And that’s not too surprising, if you consider that people are growing increasingly comfortable with online shopping exchanges for auto insurance and other products.

All options

“We know from our surveys that 40% of employers will be considering private exchanges in the next few years,” adds Thompson. “Employers are keeping all options on the table, but many employers don’t believe they’re in the health care business.”

Whatever you do, Thompson advises businesses, don’t lose sight of the small print about who’s paying what. Some private exchanges rely on commissions from insurers. Some are paid fees. And some get side deals that no one reports.

Adds Thompson: “There must be transparency to understand the long-term value of these arrangements.”

A million members have enrolled on private exchanges this fall “and we think that number will expand to 40 million by 2018,” says Rich Birhanzel of Accenture.
Choosing the Right Oral Antiplatelet Medication

Which of three drugs is best for a given patient? The answer remains clouded by clinical uncertainty—and the sun isn’t going to break through soon.

By Jack McCain

Today physicians managing patients with an acute coronary syndrome (ACS) have a choice among three oral products intended to reduce the risk of thrombotic events by decreasing platelet aggregation. These drugs are clopidogrel (Plavix, approved by the FDA in 1997), prasugrel (Effient, approved in 2009), and ticagrelor (Brilinta, approved in 2011). Prasugrel and ticagrelor are available only as branded products, but generic clopidogrel is on the market. At a retail price of about $0.40 per day, generic clopidogrel enjoys a substantial price advantage, as prasugrel and ticagrelor cost at least 20 times as much. Price alone would seem to make generic clopidogrel the obvious choice in managed care, but these P2Y12 inhibitors aren’t sufficiently similar to make the choice easy.

First, a substantial percentage of patients are poor responders to clopidogrel, often owing to gene polymorphisms, notably the following (Campo 2011):

- **ABCB1*2,** associated with increased expression of an intestinal glycoprotein that ushers environmental toxins and drugs out of cells, leading to decreased absorption of clopidogrel. Carriers are at increased risk of death, MI, and stroke when they receive clopidogrel.
- **CYP2C19*2,** which encodes a nonfunctional cytochrome P450 enzyme resulting in decreased conversion of clopidogrel, a prodrug, into its active metabolite. Found in about 25% of Caucasians, this polymorphism is associated with an increased risk of death, MI, and stent thrombosis when carriers receive clopidogrel at the usual dose.
- **CYP2C19*17,** a mutation associated with increased transcription of the gene, causing clopidogrel to be metabolized more rapidly.

Unfortunately, the clinical utility of genetic screening tests aimed at personalizing clopidogrel therapy (or prasugrel therapy, for that matter, in which the 2C19 alleles also may come into play [Cuisset 2012]) hasn’t been adequately demonstrated yet, no doubt because genetic factors affecting metabolism are only a portion of the many factors that influence a patient’s response to clopidogrel (Steinhubl 2010).

Second, in the clinical trials that led to their FDA approval, both prasugrel and ticagrelor were com-

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**Acute coronary syndromes: distinguishing unstable angina from NSTEMI and STEMI**

About 1.4 million people in the United States are diagnosed every year with acute coronary syndrome (ACS) (Go 2013).

ACS includes unstable angina (UA), usually caused when a thrombus temporarily blocks a coronary artery, resulting in chest pain or discomfort from ischemia; non-ST segment elevation myocardial infarction (NSTEMI), caused by a thrombus that partially occludes a coronary artery, resulting in death of part of the heart muscle it supplies; and the more serious form of MI, ST segment elevated MI (STEMI), in which a thrombus completely occludes a coronary artery, causing death of all the heart muscle supplied by the artery. UA and NSTEMI account for about 70% of ACS diagnoses.

Unlike stable angina, which is characterized by chest or arm discomfort that occurs with physical exertion or stress and which resolves with rest, UA often is identified by severe pain that occurs at rest or with minimal exertion. Such pain can last 10 minutes or more. Subsequent episodes of UA occur with greater frequency, increasingly intense pain, and increasing duration.

Tests for elevated cardiac biomarkers indicative of myocardial necrosis (eg, troponins) distinguish UA from MI, and ECGs distinguish STEMI from NSTEMI. These findings guide medical and interventional treatment decisions.
pared with clopidogrel, and each outperformed clopidogrel in many respects. Third, ticagrelor brings with it some adverse effects, notably dyspnea, that aren’t seen with clopidogrel or prasugrel and that could affect patients’ adherence to therapy.

**Decision-making process**

Fourth, oral antiplatelets are used in conjunction with aspirin, and in the complicated setting of ACS they may be used concurrently with or instead of many other drugs, including intravenous glycoprotein IIb/IIIa inhibitors, intravenous or subcutaneous anticoagulants, oral anticoagulants, and proton pump inhibitors, further complicating the decision-making process.

In the absence of definitive head-to-head trials of prasugrel and ticagrelor, researchers have turned to pharmacodynamic analyses and meta-analyses in an attempt to determine whether or not one drug has an edge over another. Several such studies have been published recently and will be discussed below, along with some ongoing studies aimed at clarifying the role of oral antiplatelets.

During the decades-long evolution of oral antiplatelet medications for reducing the risk of thrombotic events in patients with ACS, the challenge has been to achieve an acceptable balance between preventing thrombosis and avoiding hemorrhage — navigating between Scylla and Charybdis, as one commenter put it (Bhatt 2007). After oral agents that block glycoprotein IIb/IIIa receptors were found to be counterproductive — they increased the risk of major bleeding but failed to reduce the risk of ischemic events — attention turned to the oral antiplatelets that work, at the molecular level, by inhibiting the P2Y12 adenosine diphosphate (ADP) platelet receptor. Blocking this receptor reduces platelet reactivity, thereby lowering the risk of thrombosis. One such drug, ticlopidine, was used together with aspirin to reduce the risk of stent thrombosis in patients receiving coronary stents, helping to make this intervention common. But when clopidogrel was found to have similar efficacy and a better safety profile than ticlopidine, ticlopidine fell by the wayside as the combination of clopidogrel and aspirin came to be used to treat patients with all forms of ACS. Clopidogrel has its flaws, as previously noted. That left room for prasugrel and ticagrelor to enter the fray.

Apparenty reflecting the absence of a clearly superior product, the three largest commercial PBMs (Medco, Express Scripts National Preferred Formulary, and Caremark) all designate Brilinta, Effient, and generic clopidogrel as preferred products, excluding only branded Plavix. In addition, the most recent guidelines issued jointly by the American College of Cardiology and the American Heart Association for UA/NSTEMI (unstable angina and non-ST-segment-elevation myocardial infarction, Jneid 2012), STEMI (ST-segment-elevation myocardial infarction, Kushner 2009), and percutaneous coronary intervention (PCI) (Levine 2011) don’t make much of a distinction among clopidogrel, prasugrel, and ticagrelor, but that doesn’t mean the drugs are interchangeable in all cases.

Clopidogrel and prasugrel are prodrugs that require oxidation via cytochrome P-450 isoenzymes to become active metabolites. The active compounds bind irreversibly to the P2Y12 platelet receptor for the life of the platelet (7 to 10 days), preventing platelet activation and aggregation. This characteristic is of great concern whenever patients need bypass surgery immediately, but of less importance when surgery isn’t being considered or when it’s elective.

In contrast, ticagrelor needs no metabolic action to become active, and its metabolite also is active. In theory, this could enable ticagrelor to inhibit platelet activation more rapidly than prasugrel. A team of Greek cardiologists recently conducted a head-to-head pharmacodynamics study, in STEMI patients undergoing PCI, with the expectation that it would confirm this hypothesis. To the cardiologists’ surprise, they found no statistically significant difference in platelet reactivity at 1 hour (the primary endpoint) between patients randomized to ticagrelor vs. prasugrel or at 2, 6, or 24 hours (Alexopoulos 2012). By day 5, platelet reactivity was statistically significantly lower in the ticagrelor group than in the prasugrel group, but any clinical significance of this difference remains unknown.

**Platelet reactivity**

In both arms of the study, however, rates of high on-treatment platelet reactivity (HTPR) were high initially, ranging from 45% to 67% in the prasugrel group and 52% to 74% in the ticagrelor group at hour 1, and from 32% to 46% in the ticagrelor group.

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2. In PLATO, the phase 3 trial of ticagrelor, discontinuation rates owing to dyspnea were 0.9% and 0.1% among patients receiving ticagrelor and clopidogrel, respectively.
and 20% to 35% in the prasugrel group at hour 2; none of the between-group differences were statistically significant at any time point.

**Improvement necessary**

The authors say that in the setting of STEMI and PCI, where rapid and robust platelet inhibition is important, further improvement is necessary, perhaps in the form of higher loading doses of P2Y12 inhibitors, administration of P2Y12 inhibitors before hospitalization, or concurrent use of a fast-acting intravenous platelet inhibitor to address the initial lack of antiplatelet action seen with both drugs.

Other researchers have tried to use meta-analysis to delineate clinical differences among clopidogrel, prasugrel, and ticagrelor in ACS. One recent meta-analysis (Aradi 2012) included four randomized controlled trials (RCTs) in which clopidogrel was compared with placebo (n=64,027) and five RCTs in which prasugrel or ticagrelor was compared with clopidogrel (n=43,446), including a prasugrel study published in late 2012 (Roe 2012). The researchers excluded RCTs enrolling fewer than 500 subjects to reduce the effect of small-study bias on their primary endpoint, the risk of stroke. In the placebo-controlled RCTs, clopidogrel was associated with modest statistically significant reductions in the rates of MI, total stroke, and a composite endpoint (CV death, MI, and stroke) and a slight but still statistically significant reduction in the rate of CV death (Table 1). However, there was no statistically significant difference between rates of hemorrhagic stroke in the clopidogrel and placebo groups. When clopidogrel served as the active comparator in the RCTs of prasugrel or ticagrelor, prasugrel or ticagrelor was associated with statistically significant reductions in rates of MI, CV death, and the composite endpoint but not in rates of total stroke or hemorrhagic stroke.

**A head-to-head contest, sort of**

In an effort to identify clinical differences between prasugrel and ticagrelor in lieu of head-to-head studies, a group of Italian researchers conducted an indirect meta-analysis in patients with ACS, using two RCTs in which ticagrelor was compared with clopidogrel (PLATO and DISPERSE-2) and TRITON TIMI 38, which compared prasugrel with

---

**TABLE 1**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Clopidogrel (events/patients)</th>
<th>Placebo (events/patients)</th>
<th>ARD, clopidogrel vs placebo</th>
<th>Odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>945 / 32,025 (2.95%)</td>
<td>1165 / 31,996 (3.64%)</td>
<td>-0.69%</td>
<td>0.80 (0.74–0.88)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CV death</td>
<td>2039 / 32,025 (6.37%)</td>
<td>2181 / 31,996 (6.82%)</td>
<td>-0.45%</td>
<td>0.93 (0.87–0.99)</td>
<td>.02</td>
</tr>
<tr>
<td>Total stroke</td>
<td>317 / 32,025 (0.99%)</td>
<td>379 / 31,996 (1.18%)</td>
<td>-0.19%</td>
<td>0.84 (0.72–0.97)</td>
<td>.02</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>70 / 30,953 (0.23%)</td>
<td>73 / 30,913 (0.24%)</td>
<td>-0.01%</td>
<td>0.96 (0.69–1.33)</td>
<td>.79</td>
</tr>
<tr>
<td>Composite: CV death, MI, stroke</td>
<td>9.21%</td>
<td>10.44%</td>
<td>-1.24%</td>
<td>0.84 (0.76–0.93)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**Prasugrel / ticagrelor vs clopidogrel**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Clopidogrel (events/patients)</th>
<th>Prasugrel / ticagrelor (events/patients)</th>
<th>ARD, prasugrel or ticagrelor vs clopidogrel</th>
<th>Odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>1624 / 21,330 (7.61%)</td>
<td>1397 / 22,122 (6.32%)</td>
<td>-1.29%</td>
<td>0.83 (0.74–0.93)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CV death</td>
<td>926 / 21,330 (4.34%)</td>
<td>809 / 22,122 (3.66%)</td>
<td>-0.68%</td>
<td>0.86 (0.78–0.94)</td>
<td>.002</td>
</tr>
<tr>
<td>Total stroke</td>
<td>236 / 21,330 (1.11%)</td>
<td>253 / 22,122 (1.14%)</td>
<td>+0.03%</td>
<td>1.06 (0.88–1.26)</td>
<td>.55</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>50 / 20,878 (0.24%)</td>
<td>60 / 21,347 (0.28%)</td>
<td>+0.04%</td>
<td>1.16 (0.75–1.81)</td>
<td>.49</td>
</tr>
<tr>
<td>Composite: CV death, MI, stroke</td>
<td>11.65%</td>
<td>9.97%</td>
<td>-1.68%</td>
<td>0.85 (0.79–0.92)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

ARD=absolute risk difference, CI= confidence interval; CV=cardiovascular, MI=myocardial infarction

Source: Aradi 2012
clopidogrel (Biondi-Zoccai 2010). (For a discussion of the validity of this approach, see Song 2003.) These RCTs were among the five studies of prasugrel/ticagrelor vs. clopidogrel used in the meta-analysis mentioned above; of the two studies that weren’t used, one enrolled patients undergoing urgent or elective PCI (Wiviott 2005), some of whom (the elective patients) didn’t have ACS and thus had a much lower risk of stent thrombosis, and the other (Roe 2012) hadn’t been published.

In the meta-analysis by Biondi-Zoccai et al, the pooled data for prasugrel and ticagrelor show that, compared with clopidogrel, these drugs reduced the risk of the composite endpoint and overall death by 17%, nonfatal MI by 21%, and stent thrombosis by 39% (Table 2). Clopidogrel performed statistically significantly better than prasugrel and ticagrelor, however, with respect to major bleeding unrelated to bypass, major or minor bleeding, and drug discontinuation.

In the head-to-head comparison of prasugrel and ticagrelor, there were no statistically significant differences in the composite endpoint, overall death, nonfatal MI, and nonfatal stroke (Table 3). The risk of stent thrombosis, however, was 36% lower with prasugrel, but prasugrel also was associated with a statistically significant increase in the risk of major bleeding, major bleeding associated with bypass surgery, and major or minor bleeding.

The authors believe their study could help guide treatment decisions for individual patients, as follows:

- Either prasugrel or ticagrelor could be considered instead of clopidogrel in ACS patients who aren’t at high risk of bleeding.
- Because prasugrel appears to be more effective than ticagrelor in preventing stent thrombosis, in ACS patients who are undergoing PCI with drug-eluting stents and who aren’t at high risk of bleeding, prasugrel could be started at the time of PCI.
- Ticagrelor could be best for ACS patients with-

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**TABLE 2**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Prasugrel / ticagrelor (events / patients [rate])</th>
<th>Clopidogrel (events / patients [rate])</th>
<th>ARD, prasugrel &amp; ticagrelor vs. clopidogrel</th>
<th>Odds ratio* (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite: overall death, nonfatal MI, nonfatal stroke</td>
<td>1613 / 16,480 (9.79%)</td>
<td>1904 / 16,413 (11.60%)</td>
<td>−1.81%</td>
<td>0.83 (0.77–0.89)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Overall death</td>
<td>594 / 16,480 (3.60%)</td>
<td>707 / 16,413 (4.31%)</td>
<td>−0.70%</td>
<td>0.83 (0.74–0.93)</td>
<td>.001</td>
</tr>
<tr>
<td>Nonfatal MI</td>
<td>991 / 16,480 (6.01%)</td>
<td>1228 / 16,413 (7.48%)</td>
<td>−1.47%</td>
<td>0.79 (0.73–0.86)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Nonfatal stroke</td>
<td>198 / 16,480 (1.20%)</td>
<td>167 / 16,413 (1.02%)</td>
<td>+0.18%</td>
<td>1.12 (0.91–1.38)</td>
<td>.28</td>
</tr>
<tr>
<td>Stent thrombosis, definite or probable</td>
<td>188 / 12,062 (1.56%)</td>
<td>300 / 12,071 (2.49%)</td>
<td>−0.93%</td>
<td>0.61 (0.51–0.74)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**Ticagrelor and prasugrel vs clopidogrel — safety analysis**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Prasugrel / ticagrelor (events / patients [rate])</th>
<th>Clopidogrel (events / patients [rate])</th>
<th>ARD, prasugrel &amp; ticagrelor vs. clopidogrel</th>
<th>Odds ratio* (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major bleeding</td>
<td>953 / 16,310 (5.23%)</td>
<td>781 / 16,229 (4.81%)</td>
<td>+0.42%</td>
<td>1.09 (0.99–1.21)</td>
<td>.08</td>
</tr>
<tr>
<td>Major bleeding unrelated to bypass</td>
<td>367 / 15,976 (2.30%)</td>
<td>288 / 15,902 (1.81%)</td>
<td>+0.49%</td>
<td>1.27 (1.09–1.49)</td>
<td>.002</td>
</tr>
<tr>
<td>Major bleeding related to bypass</td>
<td>470 / 15,976 (2.94%)</td>
<td>482 / 15,902 (3.03)</td>
<td>−0.09%</td>
<td>0.97 (0.85–1.10)</td>
<td>.63</td>
</tr>
<tr>
<td>Bleeding, major or minor</td>
<td>1249 / 15,976 (7.82%)</td>
<td>1137 / 15,902 (7.15%)</td>
<td>+0.67%</td>
<td>1.10 (1.01–1.20)</td>
<td>.02</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>431 / 16,310 (2.64%)</td>
<td>386 / 16,229 (2.38%)</td>
<td>+0.26%</td>
<td>1.11 (0.97–1.28)</td>
<td>.13</td>
</tr>
<tr>
<td>Drug discontinuation</td>
<td>2695 / 16,480 (16.35%)</td>
<td>2453 / 16,413 (14.95%)</td>
<td>+1.41%</td>
<td>1.12 (1.05–1.19)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*Odds ratio <1.0 favors prasugrel and ticagrelor; odds ratio >1.0 favors clopidogrel
ARD=absolute risk difference, CI= confidence interval; MI= myocardial infarction
Source: Biondi-Zoccai 2010
out severe bleeding risk who are to be managed by an initial conservative strategy.

- Ticagrelor may be a better choice than prasugrel if urgent CABG is likely.
- Clopidogrel may remain the best choice for patients with high risk of bleeding (e.g., history of stroke, advanced age, severe renal impairment).
- Owing to its low cost, clopidogrel may be more attractive than prasugrel or ticagrelor in patients with low risk of ischemia or high risk of bleeding.

**Next steps**

As appealing as genetic assays are, a genetic profile of a patient usually is insufficient in itself to guide treatment decisions. That’s because interactions among genes are complex, and because genes interact with many factors in the environment in which the genes exist (”environment” meaning the person’s body and the world in which that body lives). Given these circumstances, some experts think that combining genotypic information with phenotypic information will provide a practical way to match patients with antiplatelet medications. For example, genetic screening showing an absence of loss-of-function genes such as CYP2C19*2 might suggest that a patient is likely to achieve acceptable platelet reactivity values if clopidogrel is used, but if the patient has diabetes, which is associated with high platelet reactivity values when the treatment is clopidogrel, prasugrel or ticagrelor might be a better choice (Campo 2011).

To test the idea of using genotypic and phenotypic information to help clinicians select the most appropriate antiplatelet medication for a given patient, the Italian Society of Invasive Cardiology launched a 4,000-patient study, GENE-MATRIX (NCT01477775), in January 2012. The investigators are comparing standard practice (i.e., physician’s exercise of clinical judgment to choose clopidogrel, prasugrel, or ticagrelor) with an algorithm incorporating phenotypic and genotypic information to determine drug choice for patients who underwent coronary angioplasty with stent emplacement.

Their hope is that the algorithm will increase the percentage of patients who achieve the therapeutic range for P2Y12 activity after 30 days to 70% (compared with 50% of patients receiving standard care), and that this improvement will translate into improved outcomes after one year.

This study is expected to be completed by December 2015, with all data for the primary outcome (time to first occurrence of cardiovascular death, MI, stroke, or type 2, 3, or 5 bleeding as defined by the Bleeding Academic Research Consortium) in hand by December 2014.

Meanwhile, the Agency for Healthcare Research and Quality (AHRQ) is underwriting a comparative effectiveness review of the medical literature in an attempt to answer important unresolved questions (Table 4) surrounding the use of P2Y12 blockers and related drugs in the setting of UA/NSTEMI (AHRQ 2012). But when the final report is posted on the

**TABLE 3**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Odds ratio* (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite: death, MI, or stroke</td>
<td>0.99 (0.86–1.33)</td>
<td>.86</td>
</tr>
<tr>
<td>Death</td>
<td>1.22 (0.96–1.55)</td>
<td>.11</td>
</tr>
<tr>
<td>MI</td>
<td>0.89 (0.75–1.06)</td>
<td>.20</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.86 (0.55–1.33)</td>
<td>.49</td>
</tr>
<tr>
<td>Stent thrombosis, definite or probable</td>
<td>0.64 (0.43–0.93)</td>
<td>.02</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.43 (1.10–1.86)</td>
<td>.007</td>
</tr>
<tr>
<td>Major bleeding not related to bypass</td>
<td>1.06 (0.77–1.45)</td>
<td>.74</td>
</tr>
<tr>
<td>Major bleeding related to bypass</td>
<td>4.30 (1.74–10.64)</td>
<td>.002</td>
</tr>
<tr>
<td>Major or minor bleeding</td>
<td>1.27 (1.04–1.55)</td>
<td>.02</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>1.07 (0.79–1.45)</td>
<td>.65</td>
</tr>
<tr>
<td>Drug discontinuation</td>
<td>1.03 (0.88–1.20)</td>
<td>.73</td>
</tr>
</tbody>
</table>

*Odds ratio <1.0 favors prasugrel; odds ratio >1.0 favors ticagrelor
CI= confidence interval, MI= myocardial infarction
Source: Biondi-Zoccai 2010

**Clinical uncertainty**

“Current clinical practice regarding the dose and timing of oral P2Y12 treatment varies dramatically. Given the recent… approval of prasugrel and ticagrelor and the absence of direct comparisons of these agents, clinical uncertainty also remains about which agent is ideal for individual patients.”

—Evidence-based Practice Center, Agency for Healthcare Research and Quality, December 2012
**TABLE 4**

Key questions surrounding the use of oral antiplatelets and related drugs in UA/NSTEMI

<table>
<thead>
<tr>
<th>Key questions</th>
<th>Interventions</th>
<th>Comparators</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. In patients undergoing an early invasive approach (before cardiac catheterization or during PCI) for treating UA/NSTEMI:</td>
<td>Aspirin IV glycoprotein IIb/IIIa inhibitors</td>
<td>a. Before catheterization — dose and timing of intravenous or oral antiplatelets with anticoagulants plus aspirin</td>
</tr>
<tr>
<td>a. What are the comparative effectiveness (dose and timing) and comparative safety of an intravenous glycoprotein IIb/IIIa inhibitor versus oral antiplatelet agent as initial therapy before going to the catheterization laboratory?</td>
<td>Abciximab, Eptifibatide, Tirofiban</td>
<td>b. During PCI — dosing and timing of IV or oral antiplatelet with anticoagulants, plus aspirin</td>
</tr>
<tr>
<td>b. What are the comparative effectiveness (dose and timing) and comparative safety of coadministration of intravenous or oral antiplatelet agents in patients undergoing PCI for improving cardiovascular outcomes? Do the effectiveness and safety vary based on which initial anticoagulant is used or the combination of anticoagulant and antiplatelet agents?</td>
<td>Clopidogrel, Prasugrel, Ticagrelor Anticoagulants Bivalirudin, Enoxaparin Fondaparinux, Unfractionated heparin</td>
<td></td>
</tr>
<tr>
<td>c. Based on demographic and other clinical characteristics, are there subgroups of patients for whom the effectiveness and safety differ?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. In patients undergoing an initial conservative approach for treating UA/NSTEMI:</td>
<td>Aspirin Oral antiplatelets</td>
<td>a. Dosing and timing of anticoagulant plus aspirin</td>
</tr>
<tr>
<td>a. What are the comparative effectiveness (dose and timing) and comparative safety of different anticoagulants on improving cardiovascular outcomes?</td>
<td>Clopidogrel, Prasugrel, Ticagrelor Anticoagulants Enoxaparin, Fondaparinux, Unfractionated heparin</td>
<td>b. Dosing and timing of oral antiplatelets plus aspirin</td>
</tr>
<tr>
<td>b. What are the comparative effectiveness (dose and timing) and comparative safety of different antiplatelet agents on improving cardiovascular outcomes?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Based on demographic and other characteristics, are there subgroups of patients for whom the effectiveness and safety differ?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. In patients treated for UA/NSTEMI post discharge:</td>
<td>Aspirin Oral antiplatelets</td>
<td>a. Dose and duration of oral antiplatelets in combination with aspirin at different doses</td>
</tr>
<tr>
<td>a. What are the comparative effectiveness (dose and duration) and comparative safety of the oral antiplatelet agents given in combination with aspirin? Do the effectiveness and safety vary based on the dose of aspirin used?</td>
<td>Clopidogrel, Prasugrel, Ticagrelor Anticoagulants Apixaban, Dabigatran, Rivaroxaban, Warfarin</td>
<td>b. PPIs vs no PPIs</td>
</tr>
<tr>
<td>b. What are the comparative effectiveness and comparative safety of PPIs for reducing bleeding events in patients receiving dual antiplatelet therapy after UA/NSTEMI? Do the effectiveness and safety vary by oral antiplatelet therapy and PPI?</td>
<td>Proton pump inhibitors Esomeprazole, Lansoprazole, Omeprazole, Pantoprazole, Rabeprazole</td>
<td>c. Dual antiplatelet therapy (aspirin with oral antiplatelet) vs triple therapy (oral anticoagulant, aspirin, and oral antiplatelet)</td>
</tr>
<tr>
<td>c. In patients with an indication for long-term anticoagulant therapy, what are the comparative effectiveness and comparative safety of adding an oral anticoagulant to aspirin and another antiplatelet agent for improving cardiovascular outcomes?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Based on demographic and other characteristics, are there subgroups of patients for whom the effectiveness and safety differ?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: AHRQ 2012
For more information, ask your Synagis Account Manager about Cradle with Care today.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

**INDICATION**

Synagis is indicated for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in children with bronchopulmonary dysplasia (BPD), infants with a history of premature birth (≤35 weeks gestational age), and children with hemodynamically significant congenital heart disease (CHD).

**SELECT SAFETY INFORMATION**

The recommended dose of Synagis is 15 mg/kg of body weight given monthly by intramuscular injection. The first dose of Synagis should be administered prior to commencement of the RSV season and the remaining doses should be administered monthly throughout the RSV season. Children who develop an RSV infection should continue to receive monthly doses throughout the RSV season.

Synagis is contraindicated in children who have had a previous significant hypersensitivity reaction to Synagis. Cases of anaphylaxis and anaphylactic shock, including fatal cases, have been reported following initial exposure or re-exposure to Synagis. Other acute hypersensitivity reactions, which may be severe, have also been reported on initial exposure or re-exposure to Synagis. The relationship between these reactions and the development of antibodies to Synagis is unknown. If a significant hypersensitivity reaction occurs with Synagis, its use should be permanently discontinued. If a mild hypersensitivity reaction occurs, clinical judgment should be used regarding cautious readministration of Synagis. As with any intramuscular injection, Synagis should be given with caution to children with thrombocytopenia or any coagulation disorder. Palivizumab may interfere with immunological-based RSV diagnostic tests, such as some antigen detection-based assays.

Please see accompanying Brief Summary of Prescribing Information for Synagis on the next page.
Synagis® (PALIVIZUMAB)

Intramuscular Administration

For Intramuscular Administration Rx only

INDICATIONS AND USE

Synagis is indicated for the prevention of serious lower respiratory tract disease caused by respiratory syncytial virus (RSV) in children at high risk of RSV disease. Safety and efficacy were established in children with bronchopulmonary dysplasia (BPD), infants with a history of premature birth (less than or equal to 35 weeks gestational age), and children with hemodynamically significant congenital heart disease (CHD).

The following point should be considered when prescribing Synagis:
- The safety and efficacy of Synagis have not been established for treatment of RSV disease.

DOSEAGE AND ADMINISTRATION

Dosing Information

The recommended dose of Synagis is 15 mg per kg of body weight given monthly by intramuscular injection. The first dose of Synagis should be administered prior to commencement of the RSV season and the remaining doses should be administered monthly throughout the RSV season. Children who develop an RSV infection should continue to receive monthly doses throughout the RSV season. In the northern hemisphere, the RSV season typically commences in November and lasts through April, but it may begin earlier or persist later in certain communities. Synagis serum levels are decreased after cardio-pulmonary bypass. Children undergoing cardio-pulmonary bypass should receive an additional dose of Synagis as soon as possible after the cardio-pulmonary bypass procedure (even if sooner than a month from the previous dose). Thereafter, doses should be administered monthly as scheduled.

The efficacy of Synagis at doses less than 15 mg per kg, or of dosing less frequently than monthly throughout the RSV season, has not been established.

CONTRAINDICATIONS

Synagis is contraindicated in children who have had a previous significant hypersensitivity reaction to Synagis.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Cases of anaphylaxis and anaphylactic shock, including fatal cases, have been reported following initial exposure or re-exposure to Synagis. Other acute hypersensitivity reactions, which may be severe, have also been reported on initial exposure or re-exposure to Synagis. Synagis may cause immediate or delayed systemic hypersensitivity reactions that may be related to the development of antibodies to Synagis. The relationship between these reactions and the development of antibodies to Synagis is unknown. If a significant hypersensitivity reaction occurs with Synagis, its use should be permanently discontinued. If anaphylaxis or other significant hypersensitivity reaction occurs, administer appropriate medications (e.g., epinephrine) and provide supportive care as required. If a mild hypersensitivity reaction occurs, clinical judgment should be used regarding cautious readministration of Synagis.

Coagulation Disorders

Synagis is for intramuscular use only. As with any intramuscular injection, Synagis should be given with caution to children with thrombocytopenia or any coagulation disorders.

RSV Diagnostic Test Interference

Palivizumab may interfere with immunological-based RSV diagnostic tests such as some antigen detection-based assays. In addition, palivizumab inhibits virus replication in cell culture, and therefore may also interfere with viral culture assays. Palivizumab does not interfere with reverse transcriptase-polymerase chain reaction based assays. Assay interference could result in false-negative RSV diagnostic test results. Therefore, diagnostic test results, when obtained, should be used in conjunction with clinical findings to guide medical decisions.

Treatment of RSV Disease

The safety and efficacy of Synagis have not been established for treatment of RSV disease.

Proper Administration

The single-dose vial of Synagis does not contain a preservative. Administration of Synagis should occur immediately after dose withdrawal from the vial. The vial should not be re-entered. Discard any unused portion.

ADVERSE REACTIONS

The most serious adverse reactions occurring with Synagis are anaphylaxis and other acute hypersensitivity reactions.

Clinical Studies Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to Synagis (n=1639) compared with placebo (n=1143) in children 3 days to 24.1 months of age at high risk of RSV-related hospitalization in two clinical trials. Trial 1 was conducted during a single RSV season and studied a total of 1502 children less than or equal to 24 months of age with bronchopulmonary dysplasia (BPD) or less than or equal to 35 weeks gestational age who were less than or equal to 6 months of age at study entry. Trial 2 was conducted over four consecutive seasons among a total of 1287 children less than or equal to 24 months of age with hemodynamically significant congenital heart disease.

In Trials 1 and 2 combined, fever and rash were each reported more frequently among Synagis than placebo recipients, 27% versus 25%, and 12% versus 10%, respectively. Adverse reactions observed in the 153-patient crossover study comparing the liquid and lyophilized formulations were comparable for the two formulations, and were similar to those observed with Synagis in Trials 1 and 2.

Immunogenicity

In Trial 1, the incidence of anti-palivizumab antibody following the fourth injection was 1.1% in the placebo group and 0.7% in the Synagis group. In children receiving Synagis for a second season, one of the fifty-six children had transient, low titer reactivity. This reactivity was not associated with adverse events or alteration in serum concentrations. Immunogenicity was not assessed in Trial 2.

A trial of high-risk preterm children less than or equal to 24 months of age was conducted to evaluate the immunogenicity of the lyophilized formulation of Synagis (used in Trials 1 and 2 above) and the liquid formulation of Synagis. Three hundred seventy-nine children contributed to the 4 to 6 months post-final dose analysis. The rate of anti-palivizumab antibodies at this time point was low in both formulation groups (anti-palivizumab antibodies were not detected in any subject in the liquid formulation group and were detected in one subject in the lyophilized group (0.5%), with an overall rate of 0.3% for both treatment groups combined).

These data reflect the percentage of children whose test results were considered positive for antibodies to palivizumab in an enzyme-linked immunosorbent assay (ELISA) and are highly dependent on the sensitivity and specificity of the assay. The ELISA has substantial limitations in detecting anti-palivizumab antibodies in the presence of palivizumab. Immunogenicity samples tested with the ELISA assay likely contained palivizumab at levels that may interfere with the detection of anti-palivizumab antibodies.

An electrochemical luminescence (ECL) based immunogenicity assay, with a higher tolerance for palivizumab presence compared to the ELISA, was used to evaluate the presence of anti-palivizumab antibodies in subject samples from two additional clinical trials. The rates of anti-palivizumab antibody positive results in these trials were 1.1% and 1.5%.

Postmarketing Experience

The following adverse reactions have been identified during post approval use of Synagis. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Blood and Lymphatic System Disorders: severe thrombocytopenia (platelet count less than 50,000 per microliter)

General Disorders and Administration Site Conditions: injection site reactions

Limited information from post-marketing reports suggests that, within a single RSV season, adverse events after a sixth or greater dose of Synagis are similar in character and frequency to those after the initial five doses.

DRUG INTERACTIONS

No formal drug-drug interaction studies were conducted. In Trial 1, the proportions of children in the placebo and Synagis groups who received routine childhood vaccines, influenza vaccine, bronchodilators, or corticosteroids were similar and no incremental increase in adverse reactions was observed among children receiving these agents.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C: Synagis is not indicated for adult usage. It is not known whether Synagis can cause fetal harm or could affect reproductive capacity when administered to a pregnant woman.

Animal Data

Animal reproduction studies have not been conducted.

Pediatric Use

The safety and effectiveness of Synagis in children greater than 24 months of age at the start of dosing have not been established.

OVERDOSAGE

Overdoses with doses up to 70 mg per kg have been reported in clinical studies and post-marketing experience with Synagis, and in some cases, adverse reactions were reported. In case of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment instituted.

PATIENT COUNSELING INFORMATION

The healthcare provider should discuss the potential benefits and risks of Synagis with the parents or guardians of Synagis recipients. Parents or guardians should be informed of the possible side effects of Synagis and of the signs and symptoms of potential allergic reactions and should be advised of the appropriate actions. Parents or guardians should understand the dosing schedule and the importance of compliance with the full course of therapy.

Synagis® is a registered trademark of MedImmune, LLC.

Manufactured by: MedImmune, LLC Gaithersburg, MD 20878 U.S. License No. 1799 1-877-633-4411

Revision Date: April 2013 RAL-SYNV16 Component No.: 10423A

MedImmune, LLC
AHRQ web site, many of these questions are likely to remain unresolved, owing to the lack of head-to-head studies of the new oral antiplatelet agents. In the draft being circulated for peer review prior to posting of the final report, 17 outcomes of interest are listed involving comparisons among clopidogrel, ticagrelor, and prasugrel.

For eight outcomes, including all-cause mortality at 30 days and cardiovascular mortality at 30 days, the strength of the evidence is rated as insufficient, and for seven others the strength of evidence is rated as low. For only two composite outcomes (CV mortality, nonfatal MI, or nonfatal stroke at 30 days and one year) is the strength of evidence deemed moderate.

In sum, the question of which oral antiplatelet is best for a given patient remains clouded by clinical uncertainty, and the sun isn’t going to break through any time soon. As the indirect meta-analysis by Aradi et al suggests, it seems likely that each P2Y12 blocker has an important role to play in the diverse ACS population, but much of the evidence for more clearly defining those roles has yet to emerge. 

REFERENCES


How Does Management of Echocardiography Affect Use Across Risk Groups?

UM for outpatient discretionary echocardiography appeared to reduce testing rates significantly

Andrea DeVries, PhD; Gosia Sylwestrzak, MA; Abiy Agiro, PhD, all at HealthCore Inc., Wilmington, Del.; and Thomas Power, MD, AIM Specialty Health, Deerfield, Ill.

ABSTRACT
Purpose: This study evaluated the impact of an outpatient echocardiography utilization management (UM) program relative to a matched control (non-UM) group by measuring changes in utilization rates overall and within specific cardiac-risk subgroups.

Methodology: Administrative claims data for enrollees from five states were queried from the HealthCore Integrated Research Database (HIRD). Inclusion required continuous eligibility from Oct. 1, 2008, through Sept. 30, 2009, for pre-UM implementation and from Oct. 1, 2010, through Sept. 30, 2011, for post-UM implementation. Members were followed for one year before and one year after the implementation period; propensity-score matched; categorized as low, medium or high-risk for a cardiac event; and stratified into UM and non-UM cohorts. Changes in utilization rates were compared among the matched cohorts using the difference-in-difference approach; generalized estimating equations were used to adjust for relevant factors including age, gender and cardiac risk score.

Results: Members (N=2.5 million) were propensity-score matched (1:1) into UM and non-UM cohorts. Post vs. pre-UM implementation, unadjusted utilization rates (echocardiography tests per 1,000 members) decreased for both the UM (16.9 percent) and non-UM (1.51 percent) cohorts, a difference of –15.42 points; the low risk subgroup had the greatest difference between UM and non-UM trends (–20.14 points) followed by the medium (–17.32 points) and high risk (–12.5 points) subgroups. Post implementation, 4.46 tests were avoided per 1,000 members in the UM cohort. After adjusting for relevant factors, the reduction in the UM group was estimated at –15.7% or 3.05 avoided tests per 1,000 members. In the low risk subgroup, 2,102 (49 percent of total) echocardiograms were avoided, followed by 1,302 (30%) in the medium and 917 (21%) in the high risk subgroups.

Conclusion: UM for outpatient discretionary echocardiography appeared to reduce testing rates significantly after controlling for factors including age, gender, and risk score. Utilization avoidance was greatest in the low and medium risk groups. These findings add new insights in a field where there is a lack of knowledge regarding appropriate utilization by risk category.

INTRODUCTION
Increasing utilization and high geographic variability drive concerns about the clinically inappropriate use of echocardiography and have resulted in the implementation of utilization management (UM) programs for many commercial health plans (Duszak 2012, Levin 2005). UM incorporates clinical review methods and tools to assess the appropriateness of health care services for specific patients and is designed to produce the best outcomes and optimized resource utilization (Duszak 2012, Hendel 2008, Otero 2006, Wickizer 2002). UM is used to guard against overutilization (Otero 2006, Handel 2008). Also, UM may avoid additional unnecessary follow-up testing when results are inconclusive. UM programs often are required for pre-certification and prior authorization (Weiner 2005, Wickizer 1995, Wickizer 2002).

Common UM models for medical imaging services include radiology benefits managers (RMBs) and real-time decision support (DS) tools. (Duszak 2012) These UM models can be mandatory, enforced through reimbursement consequences, or voluntary. Prospective clinical review employing clinical guidelines based
on appropriate-use criteria developed by the American College of Cardiology Foundation and other relevant literature are used increasingly to manage echocardiography (Bhatia 2012, Mansour 2012, Parikh 2012).

Health care expenditures have been growing rapidly toward 20 percent of the United States gross domestic product (CBO 2012). Spending on diagnostic imaging outpaced all other medical services over the last two decades (Iglehart 2009). The Medicare Payment Advisory Commission (MedPAC) reported that expenditures doubled for imaging services, from $6.6 billion to $13.7 billion from 2000 to 2005, and the utilization rate of advanced diagnostic imaging by Medicare outpatients increased 72.7% (Levin 2011). Estimates of the total spent on imaging among commercial insurers were not readily available.

Recently, the growth rate for imaging services has slowed substantially (Duszak 2012, Levin 2012, Levin 2010, Levin 2011). The compound annual growth rate (CAGR) for non-invasive diagnostic imaging grew by just 1.4% from 2005 to 2008 (Levin 2011). Medicare data indicate that the volume of imaging services decreased by 2.5 percent from 2009 to 2010 (Med Pac 2012).

The current peer-reviewed literature demonstrating the effectiveness of UM programs for outpatient imaging is limited, especially on whether avoided utilization occurs among particular risk groups or across all categories of patients.

This large-scale population analysis of a mandatory UM program attempted to address this knowledge gap. The design included one-to-one propensity score matching based on claims-derived cardiac risk status, which increased the comparability of the case and control cohorts. Members were categorized according to their cardiac risk levels, and clinical elements were used to validate claims-based cardiac risk assessment.

The objective of this study was to evaluate changes in echocardiography utilization rates between managed (UM) and unmanaged (non-UM) members during the post-implementation (follow-up) period compared with the pre-implementation (baseline) period for the entire study population and for the low, medium and high cardiac risk subgroups.

Methods
Data sources and study design
UM Program
This echocardiography clinical review program was implemented with an educational focus (without claims compliance enforcement) by AIM Specialty Health (AIM) in 2008 with the goal of managing discretionary diagnostic cardiac imaging. By the fourth quarter of 2010, the program was used for claims compliance and incorporated pre-authorization requirements for outpatient echocardiography services. The clinical review criteria developed for the program were based on American College of Cardiology Foundation’s appropriate-use criteria and other relevant literature (AIM 2012, Bonow 2012, Douglas 2011, Fleisher 2007, Mieres 2005, Warnes 2008).

Study population and design
Administrative medical claims data were queried from the HealthCore Integrated Research Database (HRID), a repository of fully adjudicated medical, pharmacy and laboratory claims data for approximately 43 million Medicare outpatients increased 72.7% (Levin 2011). Estimates of the total spent on imaging among commercial individuals were not readily available.

The objective of this study was to evaluate changes in echocardiography utilization rates between managed (UM) and unmanaged (non-UM) members during the post-implementation (follow-up) period compared with the pre-implementation (baseline) period for the entire study population and for the low, medium and high cardiac risk subgroups.

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Study population and design
Administrative medical claims data were queried from the HealthCore Integrated Research Database (HRID), a repository of fully adjudicated medical, pharmacy and laboratory claims data for 43 million Medicare outpatients.

Exclusion criteria
Health plan members from the five target states were included in the UM group if they were fully insured and were continuously eligible during the baseline period (Oct. 1, 2008, through Sept. 30, 2009) and during the follow-up period (Oct. 1, 2010, through Sept. 30, 2011). In addition, members were required to belong to specific employer groups that were subject to the AIM echocardiography UM program during the post-implementation period.

The non-UM cohort was required to meet all the eligibility requirements except for the fully insured requirement during the study time frame and did not belong to any of the employer groups that were subject to AIM echocardiography UM program in the post-implementation period.

Members with missing age and gender information were excluded, as were those with Medicare Supplemental, Medicare Advantage, or Medicaid coverage.
Propensity score matching

To minimize group bias and approximate the robustness of a randomized trial in an observational study setting, UM members were matched based on their propensity score to the nearest non-UM members using claims-derived cardiac risk scores. These scores reflected the probability of cardiovascular hospitalizations in the post-implementation period for each member and were estimated using predictive variables from the pre-implementation period.

The list of ICD–9 diagnoses codes for cardiovascular conditions was adapted from the SCORE project (Conroy 2003) and defined as International Classification of Diseases, Ninth Revision (ICD–9) diagnoses codes 401 through 414 and 426 through 443 but did not include the following ICD–9 diagnoses codes for definitely non-atherosclerotic causes of hospitalization: 426.7, 429.0, 430.0, 432.1, 437.3, 437.4, and 437.5. Logistic regression was used to calculate the probability of cardiovascular hospitalization; a p-value of 0.05 was used to retain variables considered good predictors of such hospitalizations. The final model included gender, age, history of cardiovascular hospitalization, number of distinct medications, and history of cardiac imaging use as the top five claims-derived predictors with the highest discriminatory power. Using estimated propensity scores for cardiovascular hospitalization, the UM cohort members were matched with the non-UM cohort members who had similarly predicted probability using Greedy nearest neighbor 1:1 ratio matching techniques (Parsons 2012).

Risk group stratification

Recognizing that the need for diagnostic imaging varies with cardiac risk status, AIM gathers clinical data for each health plan member for whom a cardiac imaging test was requested to calculate a cardiac risk score and categorizes members into low, medium, or high-risk groups. These data serve as critical inputs into the clinical review process. Included in AIM’s stratification model are clinical data such as age, diagnosis of diabetes, gender, smoking status, systolic blood pressure, and total cholesterol levels. The availability of such clinically based risk categorization data presented an opportunity to compare our claims-derived risk scores against clinical data on the subset of the UM population that requested cardiac imaging through AIM. To evaluate the performance of the claims-based risk model, average claims-based risk scores (reflecting the probability of cardiac hospitalization) were calculated for patients in each AIM-defined risk group (low, medium, and high) for the subset of members in our study for whom AIM provided clinically based risk group identification. The results of this check showed that the average claims-based risk score (probability of cardiac hospitalization) was 0.0131, 0.0255, and 0.0366 (or 1.31%, 2.55%, and 3.66%) for low, medium, and high AIM-defined risk subgroups, respectively. The claims-derived risk scores reflected consistently higher risk from low- to high-risk cohorts in AIM’s clinically determined categorization. For the purpose of examining differences in utilization rate changes across the three claims-derived risk groups, members with a greater than 5% percent chance of cardiac hospitalization were classified as high risk (5% being about five times higher than the population average), medium risk was represented by 2% to 5% probability, and low risk was less than 2% probability.

Outcome measure

The outcome measured in this study was the difference between the change in echocardiography utilization rate in the matched study population with that of each of the low, medium, and high cardiac risk member subgroups.

Statistical analysis

Descriptive statistics include the mean, standard deviation (SD), and relative frequencies reported for continuous and categorical data, respectively. Differences in descriptive characteristics between the UM and non-UM groups during the baseline and follow up periods were assessed using Pearson’s chi-square tests for categorical data; Student’s t-tests or non-parametric analysis were used for numeric data whenever appropriate. A difference-in-difference (DID) approach was used to test the difference in echocardiography utilization changes net of pre-UM differences and other covariates. DID was assessed with generalized estimating equations (GEE). Poisson distribution with log link was used to model changes in cardiac imaging utilization. Exponentiated coefficients and corresponding confidence intervals (CI) are presented and are interpreted as incident rate ratios (RR) among groups. In addition, the predicted values from the generalized estimating equations model were used to calculate covariate adjusted mean difference values (expressed as echocardiography tests avoided per 1,000 members) to simplify interpretation of the results. All statistical analyses were conducted with SAS 9.2 version software. Alpha was set at 0.05 for each test.

Results

Study population

A total of 2.5 million members were identified in the HIRD; approximately 1.2 million in the non-UM and 1.3 million UM cohorts. After propensity-score matching and selecting preferred provider organization (PPO) enrollees, 0.9 million members were assigned to the UM cohort and
1.1 million to the non-UM cohort. These members were stratified by risk group, as shown in Figure 1.

Demographic and clinical characteristics at baseline

Overall
The mean age for the UM and non-UM cohorts was approximately 34.5 years, and slightly fewer than half of each group was female, as shown in Table 1. Mean Deyo-Charlson Comorbidity Index (DCI) scores (Deyo 1992) were roughly similar in the UM and non-UM groups, ranging from 0.19–0.21, indicating a low comorbidity burden in the relatively young population. The most common comorbidities were dyslipidemia and hypertension, both of which were just below 15% across all the groups. Coronary heart disease (CHD) was reported at a rate of 2.79% in the overall study population, 2.82% in the non-UM cohort and 2.75% in the UM cohort. The proportion of members who received cardiac procedures such as coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI) or coronary angioplasty, and cardiac catheterization, among other procedures during the baseline period did not exceed 0.2% in any cohort.

Low risk
A total of 1.8 million members were classified as having low risk for a cardiac event; 976,546 in the non-UM group and 778,693 in the UM cohort. The mean age was approximately 31 years across the cohorts and females constituted about 50% of each group. The mean DCI score was 0.09 across cohorts reflecting the low comorbidity burden and reflecting the risk status of the group. The most common comorbidities were dyslipidemia, ranging from 7.8 percent to 9.0 percent, and hypertension, ranging from 4.3 percent to 5.2 percent, as shown in Table 2.

Medium risk
This risk category had a total of 183,128 members with 107,872 in the non-UM and 75,256 in the UM categories. The mean age was approximately 55 years and women constituted about 45% of each cohort. The mean DCI score was 0.6 across cohorts reflecting both the medium risk status and low comorbidity burden of the study population. More than 70% of the members had a diagnosis of hypertension, greater than 50% in each group had a dyslipidemia diagnosis, and more than 10% in each group had CHD (Table 2).

High risk
A total of 68,006 members were classified as high risk, 41,656 non-UM and 26,350 UM. Members had a mean age of approximately 60 years, and women were approximately 40% of each cohort. The mean DCI scores were higher in this risk category, reflecting a comparatively elevated comorbidity burden: 1.79 for the UM and 1.85 for the non-UM cohorts (Table 2). In excess of 80% of the members were diagnosed with hypertension, while more than 60% and 40% had dyslipidemia and diabetes mellitus, respectively. In addition, CHD was reported for approximately 40% of the members in this cohort. During the baseline period, approximately 5% of the cohort received heart procedures.

Changes in echocardiography utilization rates
Changes in Overall Population
Within the overall study population, the UM group had 29 echocardiography procedures per 1,000 members in the pre-UM period versus 24 per 1,000 members post-UM, a utilization reduction rate of 16.9%.
For the non-UM cohort, there were 28.5 procedures per 1,000 members in the pre-management period compared with 28 per 1,000 in the post-management period, a reduction rate of 1.51%, as shown in Table 3. Comparing the post and pre-UM implementation periods, the percentage point difference in unadjusted utilization rates changes between the UM and non-UM cohorts overall was –15.42%. This trend differential resulted in 4.46 avoided tests per 1,000 members for the UM cohort.

Changes by risk group

The largest trend differential (percentage point difference) was observed in the low risk group (–20.14%) followed by the medium (–17.32%) and high risk (–12.5%) groups. A total of 2,102 (49% of all avoided tests) echocardiography tests in the low risk group, 1,302 (30% of all avoided tests) in the medium risk group, and 917 (21% of all avoided tests) in the high risk group were avoided (Table 3).

This means that of the 4.46 tests avoided per 1,000 members of the UM population, 2.19 tests were avoided by the low risk group, 1.34 were avoided by medium risk, and 0.94 were avoided by high risk members.

Adjusted results

Results from the DID regression estimating the effect of UM program implementation on echocardiography utilization across UM-group and non-UM groups are shown in Table 1.

The primary coefficient of interest in the model was an interaction term (post period X UM group), which estimated the effect of implementing the UM program, while controlling for baseline differences and other model covariates.

The UM-group experienced a significant 15.7% (RR = 0.843, [CI: 0.823, 0.865]) reduction in echocardiography utilization during the post-implementation period when compared with the non-UM group and baseline utilization.

### TABLE 1
Member demographics and clinical characteristics at baseline (10/01/2008 and 09/30/2009)

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>UM</th>
<th>Non-UM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of members</td>
<td>2,006,373</td>
<td>1,126,074</td>
<td>880,299</td>
</tr>
<tr>
<td>Age</td>
<td></td>
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<tr>
<td>Mean</td>
<td>34.53</td>
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<tr>
<td>Female</td>
<td>986,101</td>
<td>561,869</td>
<td>424,232</td>
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<td>Type of health plan</td>
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<tr>
<td>PPO</td>
<td>2,006,373</td>
<td>1,126,074</td>
<td>880,299</td>
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<tr>
<td>Deyo-Charlson comorbidity index (DCI) Score</td>
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<tr>
<td>Mean score</td>
<td>0.20</td>
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<td>Heart procedures (HP)</td>
<td>3,795</td>
<td>2,000</td>
<td>1,795</td>
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<td>Coronary heart disease (CHD)</td>
<td>56,007</td>
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<td>Congestive heart failure (CHF)</td>
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<td>Myocardial infarction (MI)</td>
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<td>Cardiac valve disease (CVD)</td>
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<td>Renal disease</td>
<td>19,836</td>
<td>12,061</td>
<td>7,775</td>
</tr>
<tr>
<td>Renal failure</td>
<td>10,388</td>
<td>6,426</td>
<td>3,962</td>
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</table>
## TABLE 2
Member demographics and clinical characteristics at baseline by risk category

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Non-UM group</th>
<th>UM group</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N/Mean</td>
<td>%/SD</td>
<td>N/Mean</td>
<td>%/SD</td>
</tr>
<tr>
<td><strong>Low risk</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Number of members</td>
<td>1,755,239</td>
<td>976,546</td>
<td>778,693</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
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<tr>
<td>Mean</td>
<td>31.33</td>
<td>17.49</td>
<td>30.78</td>
<td>17.69</td>
</tr>
<tr>
<td>Female</td>
<td>878,372</td>
<td>50.04</td>
<td>496,089</td>
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<td>Deyo-Charlson Comorbidity Index (DCI) Score</td>
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<tr>
<td>Mean</td>
<td>0.09</td>
<td>0.39</td>
<td>0.09</td>
<td>0.39</td>
</tr>
<tr>
<td>Heart Procedures</td>
<td>39</td>
<td>0.00</td>
<td>23</td>
<td>0.00</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>6,254</td>
<td>0.36</td>
<td>3,255</td>
<td>0.33</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>525</td>
<td>0.03</td>
<td>345</td>
<td>0.04</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>211</td>
<td>0.01</td>
<td>108</td>
<td>0.01</td>
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<tr>
<td>Cardiac valve disease</td>
<td>7,982</td>
<td>0.45</td>
<td>4,208</td>
<td>0.43</td>
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<tr>
<td>Carotid artery disease</td>
<td>218</td>
<td>0.01</td>
<td>104</td>
<td>0.01</td>
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<tr>
<td>Hypertension</td>
<td>83,386</td>
<td>4.75</td>
<td>42,558</td>
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<tr>
<td>Diabetes mellitus</td>
<td>25,058</td>
<td>1.43</td>
<td>14,294</td>
<td>1.46</td>
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<tr>
<td>Dyslipidemia</td>
<td>146,764</td>
<td>8.36</td>
<td>76,589</td>
<td>7.84</td>
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<tr>
<td><strong>Medium risk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of members</td>
<td>183,128</td>
<td>107,872</td>
<td>75,256</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>55.30</td>
<td>7.79</td>
<td>55.74</td>
<td>8.56</td>
</tr>
<tr>
<td>Female</td>
<td>81,740</td>
<td>44.64</td>
<td>49,166</td>
<td>45.58</td>
</tr>
<tr>
<td>DCI Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>0.62</td>
<td>1.02</td>
<td>0.62</td>
<td>1.03</td>
</tr>
<tr>
<td>Heart Procedures</td>
<td>550</td>
<td>0.30</td>
<td>323</td>
<td>0.30</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>21,765</td>
<td>11.89</td>
<td>11,897</td>
<td>11.03</td>
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<tr>
<td>Congestive heart failure</td>
<td>1,744</td>
<td>0.95</td>
<td>1,065</td>
<td>0.99</td>
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<tr>
<td>Myocardial infarction</td>
<td>1,536</td>
<td>0.84</td>
<td>864</td>
<td>0.80</td>
</tr>
<tr>
<td>Carotid artery disease</td>
<td>1,888</td>
<td>1.03</td>
<td>990</td>
<td>0.92</td>
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<tr>
<td>Hypertension</td>
<td>134,416</td>
<td>73.40</td>
<td>75,920</td>
<td>70.38</td>
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<tr>
<td>Diabetes mellitus</td>
<td>37,017</td>
<td>20.21</td>
<td>21,544</td>
<td>19.97</td>
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<tr>
<td>Dyslipidemia</td>
<td>97,612</td>
<td>53.30</td>
<td>54,739</td>
<td>50.74</td>
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<tr>
<td><strong>High risk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of members</td>
<td>68,006</td>
<td>41,656</td>
<td>26,350</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>61.20</td>
<td>9.07</td>
<td>62.48</td>
<td>9.70</td>
</tr>
<tr>
<td>Female</td>
<td>25,989</td>
<td>38.22</td>
<td>16,614</td>
<td>39.88</td>
</tr>
<tr>
<td>DCI Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>1.82</td>
<td>1.70</td>
<td>1.85</td>
<td>1.72</td>
</tr>
<tr>
<td>Heart Procedures</td>
<td>3,206</td>
<td>4.71</td>
<td>1,654</td>
<td>4.71</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>27,988</td>
<td>41.16</td>
<td>16,658</td>
<td>39.99</td>
</tr>
</tbody>
</table>

*table continues*
modeling (the adjusted reduction estimate and predicted values for utilization in non-UM group) were used to demonstrate that –3.05 [CI: –3.46, –2.64] tests were avoided per 1,000 members in the UM-group, which represents covariate adjusted mean difference between the two cohorts.

Claims-derived cardiac risk has a significant relationship to echocardiography utilization. Compared with the high-risk group, the low risk group had 88.8% (RR = 0.112, [CI: 0.109, 0.116]) lower utilization, and the medium-risk group had 50.9% (RR = 0.491, [CI: 0.480, 0.502]) lower utilization. As expected, age and co-morbidity burden (expressed by both DCI score and the number of distinct medications) increased echocardiography utilization. Being female also was associated with slightly increased use of imaging.

**Discussion**
Significant decreases were observed in the rate of echocardiography utilization in the UM cohort relative to the non-UM group overall and across the cardiac-risk subgroups. As might be

---

### TABLE 2
**Member demographics and clinical characteristics at baseline by risk category**

<table>
<thead>
<tr>
<th>Overall</th>
<th>Non-UM group</th>
<th>UM group</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/Mean</td>
<td>%/SD</td>
<td>N/Mean</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>5,769</td>
<td>8.48</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>4,534</td>
<td>6.67</td>
</tr>
<tr>
<td>Cardiac valve disease</td>
<td>9,500</td>
<td>13.97</td>
</tr>
<tr>
<td>Carotid artery disease</td>
<td>4,126</td>
<td>6.07</td>
</tr>
<tr>
<td>Hypertension</td>
<td>57,731</td>
<td>84.89</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>30,251</td>
<td>44.48</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>43,803</td>
<td>64.41</td>
</tr>
</tbody>
</table>

---

### TABLE 3
**Annual echocardiography utilization rate per 1,000 for all members**

<table>
<thead>
<tr>
<th>UM minus</th>
<th>UM minus</th>
<th>Total number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-UM</td>
<td>expected</td>
<td>of tests</td>
</tr>
<tr>
<td>UM</td>
<td>UM</td>
<td>avoided in UM</td>
</tr>
<tr>
<td>Percentage point difference</td>
<td>Number of tests avoided per 1000</td>
<td>Total number of tests avoided in UM population</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall</th>
<th>Non-UM</th>
<th>UM minus Non-UM</th>
<th>UM minus expected UM</th>
<th>Percentage point difference</th>
<th>Number of tests avoided per 1000</th>
<th>Total number of tests avoided in UM population</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRE</td>
<td>POST</td>
<td>%Change*</td>
<td>PRE</td>
<td>POST</td>
<td>%Change*</td>
<td>Percentage point difference</td>
</tr>
<tr>
<td>n=880,299</td>
<td>880,299</td>
<td>1,126,074</td>
<td>1,126,074</td>
<td>28.92</td>
<td>24.03</td>
<td>–16.93%</td>
</tr>
<tr>
<td>High risk</td>
<td>n=26,350</td>
<td>26,350</td>
<td>41,656</td>
<td>41,656</td>
<td>288.425</td>
<td>143.947</td>
</tr>
<tr>
<td>Medium risk</td>
<td>n=75,256</td>
<td>75,256</td>
<td>107,872</td>
<td>107,872</td>
<td>99.886</td>
<td>67.33</td>
</tr>
<tr>
<td>Low risk</td>
<td>n=778,693</td>
<td>778,693</td>
<td>976,546</td>
<td>976,546</td>
<td>13.281</td>
<td>15.783</td>
</tr>
</tbody>
</table>

---

*Percent change = %Change = (Post — Pre) / Pre

*Percentage point difference = (%Change UM — %Change non-UM)

*Number of tests avoided per 1,000 = Number of imaging tests avoided by UM group = (Post of UM — expected Post of UM given non-UM %change)
expected, the low and medium risk subgroups contributed the greatest proportion of avoided echocardiography tests. This finding reinforced the hypothesis that while UM programs may result in reductions in overall service volume, they are guided by the principle that health care services should be necessary and appropriate. (Duszak 2012, Otero 2006)

The adjusted rate reduction (15.7 percent) observed overall in this study was witnessed during a two-year period; there was a one-year implementation (silent) period between the pre- and post-UM periods. This reduction was statistically significant, and it was substantive because it meant that 1 in every 6 echocardiography tests was avoided.

Our findings are consistent with an overall pattern that suggested a flattening in the growth rate of diagnostic imaging utilization in the United States. (Duszak 2012, Lessler 2000, Levin 1996, Levin 2010, Levin 2012). With respect to echocardiography, such a drop in the growth rate not only reduces proximate costs but also reduces inappropriate procedures which could lead to false positives or inconclusive test results, resulting in additional potentially invasive diagnostic procedures. It is noteworthy that both the UM and non-UM groups experienced service decreases during the study period. This result might be a reflection of the lower trend increase in overall health care spending in the United States between 2009 and 2011. Nonetheless, it is possible that a program spillover effect caused some of the utilization decrease in the non-UM group, as many of the members of the non-UM cohort lived in geographic areas where the AIM program was implemented and used the same provider networks. It is possible that providers have not always differentiated among members who needed prior authorization and those who did not. This possibility may reflect a level of bias; however, its effect would have created favorable results in the non-UM population.

The slowing of growth in utilization of diagnostic imaging marked an important departure from the escalating trends in the last two decades. The fact that a portion of the reductions seen in this study was attributable to UM would suggest its effectiveness and might represent a shift toward appropriate utilization rather than the imposition of unit cost pressures on providers. If true, this result has important implications for managed care companies because targeting high volume procedures is an important focus of cost containment strategies.

The findings in this study are a timely addition to a growing research direction in which population databases are queried for patients with defined characteristics in an effort to quantify usage levels and ascertain the patterns and appropriateness of key aspects of health care utilization. Although the prior authorization requirement for certain imaging procedures has been well established

<table>
<thead>
<tr>
<th>TABLE 4</th>
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</thead>
<tbody>
<tr>
<td>Echocardiography utilization rates per 1,000 members — adjusted results*</td>
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</table>

<table>
<thead>
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<th>Parameter estimate</th>
<th>LCL</th>
<th>UCL</th>
<th>P-value</th>
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</thead>
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<tr>
<td>Post period</td>
<td>0.831</td>
<td>0.815</td>
<td>0.847</td>
</tr>
<tr>
<td>UM group</td>
<td>0.975</td>
<td>0.993</td>
<td>0.956</td>
</tr>
<tr>
<td>Post period x UM group†</td>
<td>0.843</td>
<td>0.865</td>
<td>0.823</td>
</tr>
<tr>
<td>Age</td>
<td>1.006</td>
<td>1.005</td>
<td>1.006</td>
</tr>
<tr>
<td>Female</td>
<td>1.167</td>
<td>1.151</td>
<td>1.184</td>
</tr>
<tr>
<td>Deyo-Charlson Index comorbidity score</td>
<td>1.063</td>
<td>1.057</td>
<td>1.070</td>
</tr>
<tr>
<td>Low-risk group (claims-derived)‡</td>
<td>0.112</td>
<td>0.109</td>
<td>0.116</td>
</tr>
<tr>
<td>Medium risk group (claims-derived)‡</td>
<td>0.491</td>
<td>0.480</td>
<td>0.502</td>
</tr>
<tr>
<td>Medication count</td>
<td>1.028</td>
<td>1.027</td>
<td>1.030</td>
</tr>
<tr>
<td>Covariate adjusted mean difference§</td>
<td>–3.05</td>
<td>–2.64</td>
<td>–3.46</td>
</tr>
</tbody>
</table>

*Analysis conducted with Generalized Estimating Equations using Poisson distribution and log link function. All coefficients are presented in exponentiated form and are interpreted as incident rate ratios.
†Post period x UM group: difference-in-difference coefficient indicates the change in UM group after UM program implementation in comparison to non-UM group and pre-program period.
‡Compared to the high risk group, low and medium risk variables were defined as 1 for presence of low/medium risk and 0 otherwise.
§Covariate-adjusted mean difference is obtained from the results of difference-in-difference modeling. Mean difference indicates the change in echocardiography tests per 1,000 members in UM group after program implementation in comparison to the non-UM group and pre-implementation period.
within the commercial insurance industry, the results of this study are timely. Echocardiography, the specific imaging modality evaluated in this study, has not, until recently, been included in prior authorization programs; therefore, the effect of these programs on echocardiography utilization has not been evaluated. A relatively inexpensive and non-invasive procedure, echocardiography has not traditionally been a focus for utilization management. This test, however, can serve as a gateway to additional costlier diagnostics, and the benefits of appropriate management would extend beyond this initial test. This study highlights that significant utilization reductions can be accomplished as more health plans move to manage the use of this procedure.

Limitations

The population used in this study provided important research advantages, but was subject to the limitations associated with employing administrative claims data for research purposes. Disease severity and other potential confounders that could influence outcomes are generally not observable with claims data and are not typically included in claims-based analyses. While a claims-based risk score was assigned to the population, we did not have clinical information available for the comparison group. Lacking such information means that using clinical elements to compare appropriateness of the tests avoided was out of the scope of this study and could be an area for further work. Because the study sample was from a large managed care database and included continuously enrolled patients, it might not be possible to replicate or generalize these findings across other demographic groups.

The study design, using a DID estimator, assumes that underlying trends in the outcome variables would be similar for both groups, in the absence of a UM program. Unmeasured factors such as changing economic conditions are assumed to affect both groups in similar ways. This assumption is not testable but our careful selection of covariates included in the cardiac risk scoring model and rigorous approach to matching members from both groups makes this a reasonable assumption.

Finally, this study focused on outpatient services and excluded emergency room (ER) procedures. Some members who received denials in the outpatient setting could have been redirected to the ER, however this care pathway was out of the scope of this analysis.

Conclusions

This study demonstrated that UM programs targeting outpatient echocardiography reduced testing rates significantly overall and across the different cardiac risk categories. The fact that utilization avoidance was greatest in the low-risk group suggested that UM could have an important effect on promoting service appropriateness. In addition, UM-derived benefits from avoiding unnecessary additional follow-up procedures may include lower costs and reduced exposure to radiation from follow up testing. It is often difficult to measure the effect of UM programs given the challenges of identifying appropriate comparison groups. This pre-post design with cohorts matched by cardiac risk status demonstrated that there can be a significant effect from claims-compliant UM programs.

References


Diagnostic Imaging Utilization Management 2012 Program Guidelines V.8.0 Effective Date: November 1, 2012. AIM Specialty Health, Chicago, IL.


Levin DC, McArdle GH, Lockard CD. Capi
tated contracting in radiology: negotiating


Rates of chicken pox drop dramatically when patients receive two doses of the varicella vaccine, according to a study in the journal *JAMA Pediatrics*. Researchers looked at two locations: Antelope Valley, Calif., and West Philadelphia to see what happened when the two-dose regimen was introduced in 2006. Antelope Valley saw a 76% decline in varicella between 2006 and 2010; West Philadelphia saw a 67% drop.

“Declines in varicella incidence were seen across all age groups….Varicella-related hospitalizations in the active surveillance areas declined nearly 50% during the first five years of the two-dose varicella vaccination program. With full implementation of the two-dose varicella vaccination program, it may be possible to eliminate the most severe outcomes of varicella.”

West Philadelphia, a Philadelphia neighborhood, had about 272,000 residents as of 2010; Antelope Valley had about 373,000. The data for West Philadelphia were gathered by the Philadelphia Department of Public Health’s Kids Immunization Database. In Antelope Valley, Kaiser Permanente Southern California gathered the data through its Kaiser Immunization Tracking System.

Metabolic Syndrome Program Aims for Competitive Advantage
Aetna hopes that an experiment with its employees turns into a product that it can put on the market next year
By Frank Diamond

The idea, says Adam Scott, is to develop approaches to improving outcomes that, if successful, Aetna hopes to bring to market at least three years ahead of competitors. That’s what led the insurer to create Aetna Innovation Labs at the end of 2011, says Scott, the labs’ managing director.

Daunting problems
The program is headquartered in Hartford, Conn., and though the plural is correct (more than one laboratory) the “lab” part is loosely defined. We’re not talking test tubes and burners here, although some of the professionals involved — including doctors and nurses — have access to such things if desired. This is more a collection of a business innovation centers. The labs take aim at some of the more daunting and costly health care problems.

For instance, one third of U.S. adults have metabolic syndrome; 79% have at least one risk factor. “Someone with metabolic syndrome costs 1.6 times as much as someone without metabolic syndrome,” says Scott.

Last month, Aetna launched a pilot program with the disease management vendor Newtopia aimed at reducing the risk for metabolic syndrome. A saliva-based genetic test screens people for three genes associated with body fat, appetite, and eating behavior — specifically with how the body expresses dopamine receptivity or, in other words, at what point cravings are satisfied.

Aetna wants to study metabolic syndrome which leads to the development of serious chronic conditions like cardiovascular disease, diabetes, or stroke. Metabolic syndrome means that someone is out of the normal range — as defined by the National Heart, Blood and Lung Institute — for three or more of these five risk factors: abdominal girth or waist circumference, blood pressure, triglyceride levels, HDL cholesterol, and blood glucose.

Example: a man with a blood pressure reading of more than 130/85 mmHg, a level of triglycerides greater than 150 mg/dL, and a waist circumference of more than 40 inches.

“That suggests that that individual is two times more likely than someone without metabolic syndrome to develop cardiovascular disease, and five times more likely to develop diabetes,” says Scott.

Five hundred Aetna employees enrolled. They are given tools to log their eating habits and physical activity. They also have access to a personal coach who will be guided by the participant’s motivational and personality profiles — to look at the underlying psychological causes of overeating.

The idea is to catch those most vulnerable before a certain disease or condition strikes, says Scott. As with any wellness program, patient engagement is crucial. That will be measured in how long patients stick with the program, or track their eating habits using the Newtopia website. They’ll also be supplied with pedometers, and Newtopia will watch how carefully patients track those data, as well.

The 500 Aetna employees volunteered after it had been pointed out that they are at risk. “One of our primary outcomes will be measuring the reduction of metabolic risk by how these individuals improve their numbers in each of these five categories,” says Scott.

Relative weight loss
Next October the participants will be compared to other Aetna workers. “We’ll be looking at clinically relevant weight loss,” says Scott. “That is, people who lose 7 percent or more of their body weight. We’ll hopefully have our answers and be able to roll it out at that point.”
More employers want to offer consumer-directed health plans, according to the Aon Hewitt 2013 Health Care Survey. It’s one way to shift more costs to workers and some employers will use the Affordable Care Act to help with this. The insurance exchanges will give adult dependents — spouses and older children — another means to obtain coverage. “Further, we expect to see continued design-based cost sharing. In doing so, employers will increasingly embrace CDHP approaches, including full-replacement models [offering no other plan options]. We believe CDHP approaches are most successful when simultaneously aligned with programs and incentives aimed at improving health.”

Employers who are considering CDHPs are interested in both health reimbursement accounts (HRAs) and health savings accounts (HSAs). “More than one-third of employers (40%) offer an HSA with an employer contribution to the HSA today; another 42% are considering it for the next three years. Fourteen percent of employers offer an HSA-eligible plan, but do not fund the account. Twenty-three percent offer an HRA with employer funds in the HRA, another 33% are considering it for the future.”

The data were collected in interviews conducted in December 2012 and January 2013 with more than 800 employers. More than half of the respondents have operations outside of the United States.

How do consumers feel about CDHPs? Aon Hewitt asks this in another study, “The Consumer Health Mindset: Turn Good Intentions Into Great Outcomes,” and sees that enthusiasm waned somewhat last year, though one shouldn’t read too much into that. “Even though CDHP satisfaction has slipped, 89% of consumers who are currently in a CDHP and have a choice of plans expect to re-enroll in this type of plan. This expectation is especially true for those who have been in a CDHP for more than two years. Ninety-seven percent of this group plan to re-enroll in a CDHP.”

### Shift to Consumer-Directed Health Plans Continues

<table>
<thead>
<tr>
<th>Plan Type</th>
<th>Currently Offer</th>
<th>May Offer in 3–6 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-deductible plan with health savings account</td>
<td>40%</td>
<td>42%</td>
</tr>
<tr>
<td>High-deductible plan with health reimbursement arrangement</td>
<td>23%</td>
<td>33%</td>
</tr>
<tr>
<td>High-deductible plan with no account funding</td>
<td>14%</td>
<td>32%</td>
</tr>
</tbody>
</table>

Source: “Aon Hewitt 2013 Health Care Survey”

### How Satisfied Are You with Your CDHP?

<table>
<thead>
<tr>
<th>Satisfactory Level</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completely satisfied</td>
<td>15%</td>
<td>12%</td>
</tr>
<tr>
<td>Satisfied</td>
<td>44%</td>
<td>44%</td>
</tr>
<tr>
<td>Slightly satisfied</td>
<td>17%</td>
<td>22%</td>
</tr>
<tr>
<td>Slightly dissatisfied</td>
<td>6%</td>
<td>10%</td>
</tr>
<tr>
<td>Dissatisfied</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Completely dissatisfied</td>
<td>3%</td>
<td>5%</td>
</tr>
</tbody>
</table>

Source: “The Consumer Health Mindset: Turn Good Intentions Into Great Outcomes”
Tuberculosis (TB) is not something people take much time to think about, many very wrongly assuming that it is a defeated disease in the United States. TB has been around for a long time, and although it is significantly reduced in developed countries, still poses a considerable threat to this country.

Long time
Evidence of TB in humans has been found in 6,000-year-old skeletal remains, and Egyptian mummies from 3,000 to 2,400 B.C. demonstrated the damage of spinal TB. Hippocrates described TB as the most widespread disease during his lifetime. In the Americas, evidence has been found dating from the time of Jesus. Tubercles, fibrous infected masses of active TB bacillus and white cells found in lungs in the pulmonary form of the disease, were described by Dr. Richard Morton in 1689, eventually leading to the name tuberculosis. Robert Koch, a German doctor, discovered the bacillus Mycobacterium tuberculosis (MTB) in 1882, which led to a Nobel Prize two decades later. During his lifetime in Europe, TB accounted for one in four deaths!

The primary means of transmission of TB is through the inhalation of airborne organisms: As few as 10 bacteria can cause an infection. A single sneeze from an infected person can expel 40,000 droplets, each droplet capable of containing enough active bacteria to cause an infection.

Fortunately, most people with TB develop a latent form of the infection that is not typically contagious to others. But about 10% of those with latent TB will eventually progress to the infectious active form of TB, typically when their immune system deteriorates because of age, other diseases, immunosuppressive medications.

Classic symptoms of TB include fever and chronic cough, often associated with blood-tinged sputum and night sweats. If the bacillus infects other organs, a number of other symptoms can exist, which can confuse the diagnosis. In days past, TB was often called “consumption” because of the weight loss associated with untreated, advanced infection.

Although only about 5% to 10% of people in the United States test positive for having had contact with the disease, in some places, such as parts of Asia and Africa, upward of 80% of the population test positive. Immigrants from these areas are a major source of TB in the United States.

In active cases, a specific stain (the acid-fast smear) can enable trained clinicians to see the TB bacterium under the microscope. Although this test is rather simple, it depends on having a sufficient number of bacteria in the sputum sample to see the organism.

The microscopic exam thus misses many infections; therefore it is followed by culture, a process that takes weeks. If a sputum sample is found not to contain TB under microscopic examination, but later the culture is found to grow the TB bacillus, it is termed smear-negative. Microscopy also cannot tell whether the organism is resistant to the traditional drugs.

Sanatoriums
Early TB intervention included separation of infected people from the masses and the creation of TB sanatoriums. A crude vaccine, the BCG vaccine, is used worldwide but is only partially effective.

Thomas Morrow, MD

New DNA Test Quickly Identifies Multidrug-Resistant Tuberculosis
Physicians will be able to order the correct therapy in as little as two hours after taking a sample for testing
Thomas Morrow, MD

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Thomas Morrow, MD, is the immediate past president of the National Association of Managed Care Physicians. He has 24 years of managed care experience at the payer or health plan level. Contact him at TMorrow@ManagedCareMag.com.
The first antibiotic used to treat TB, streptomycin, was developed in 1946. Numerous others have been developed, including isoniazide, rifampin, pyrazinamide, ethambutol, amikacin, ethionamide, moxifloxin, and para-aminosalicylic acid. These drugs have been the mainstay of therapy for some time.

New threat

But a new threat is becoming a public health nightmare, the development of multidrug-resistant TB (MDRTB). This form of the disease, although not as common, is much more dangerous. One of the major concerns related to MDRTB is the rather long time it takes to actually diagnose the presence of TB and, in particular, the resistant form. Until now, there was not an easy-to-use, reliable, accurate, and fast way of positively identifying TB and, especially, MDRTB.

The other two major human lethal infections, malaria and HIV, both have rather simple and rapid tests capable of being done in primary care settings.

Recently, the FDA approved Xpert MTB/RIF, created by Cephid, a Sunnyvale, Calif., company. It is the first test that can rapidly and simultaneously detect *M. tuberculosis* and rifampin resistance. Rifampin resistance is associated with a specific gene, the rpoB gene, and is a marker for multidrug resistance.

The test works by using a now common process of amplifying the DNA of the organism with polymerase chain reaction (PCR) technology and detecting whether the genetic markers specific for MTB and/or rifampin resistance are present. The test is also very fast — two hours as opposed to nearly six weeks for culture and sensitivity testing.

The controlled clinical trials leading to approval compared test results from the Xpert MTB/RIF assay to traditional culture and sensitivity testing, the gold standard. In these trials, Xpert MTB/RIF rapidly detected more than 92% of pulmonary TB with a sensitivity of over 97% and a specificity of 99.5%, meaning it detected specifically the form of MTB it was intended to detect. It was also able to detect 72.5% of those forms that are smear-negative.

A subsequent “real-world” study was done in numerous less developed countries (Peru, Azerbaijan, South Africa, Uganda, India, and the Philippines), performed by technicians with little or no computer or laboratory experience — with almost identical results.

The FDA stated that the Xpert MTB/RIF assay “is intended for use with specimens from patients in whom there is clinical suspicion of TB and who have received no anti-TB therapy or less than three days of therapy.” The specimen can be raw sputum or concentrated sediments prepared from induced or expectorated sputum. The specimen is loaded into the Xpert MTB/RIF assay cartridge that is then loaded onto the GeneXpert Instrument System platform that performs the automated sample processing and real-time PCR for detection of DNA.

Since it is detecting the presence or absence of specific genetic material, it uses an algorithm to report these easy-to-understand results:

<table>
<thead>
<tr>
<th>Presence of <em>Mycobacterium tuberculosis</em></th>
<th>Rifampin resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detected</td>
<td>Detected</td>
</tr>
<tr>
<td>Not detected</td>
<td>Not detected</td>
</tr>
<tr>
<td>Indeterminate</td>
<td></td>
</tr>
</tbody>
</table>

According to the FDA decision summary, the test “must be used in conjunction with mycobacterium culture to address the risk of false negative results and to recover the organism for further characterization and drug susceptibility testing.”

$300,000 per case

The treatment of drug-resistant TB differs considerably from normal treatment in a number of ways and according to one report (http://bit.ly/19Gl01Y) can cost $300,000 per case! Knowing that the infection is present and whether it is resistant can facilitate accurate and rapid treatment, significantly reducing the chance of spread.

The approval and rollout of the Xpert MTB/RIF test again proves that advances in genetic testing will be a foundation of Tomorrow’s Medicine.

The author is a director in the value-based health department at Genentech. He has had no other industry affiliations in the past three years. The views expressed in Tomorrow’s Medicine are the author’s alone.
Slowdown in prescription drug spending won’t last

Spending on prescription drugs will rise more steeply in a couple of years, with researchers predicting an average annual 6.5% increase between 2015 and 2022, according to a study in the October issue of Health Affairs.

The study, from the Centers for Medicare & Medicaid Services, notes that this is a significant change from what’s been going on lately. “In 2012 prescription drug spending is estimated to have accounted for $260.8 billion in health spending — a decline of 0.8% and down from 2.9% growth in 2011.”

The authors attribute the slowdown in part to brand-name drugs losing patent protection and in part to increased use of generics.

“In 2014, prescription drug spending growth is projected to accelerate to 5.2%, driven by increases in the use of prescription drugs by people who are newly insured and those who move to more generous insurance plans.” The spending is expected to rise “as the economy improves and the impact of patent expirations continues to diminish.”

Those growth in the newly insured is a result of the Affordable Care Act, whose effect the authors also measure, though they admit that much remains uncertain.

“The supply-side effects of the Affordable Care Act, such as changes in providers’ behavior in reaction to an influx of newly insured patients, remain highly speculative and are not included in these estimates.”