HOSPITAL-ACQUIRED INFECTIONS
Rates are far too high, and health plans are the biggest losers. Is it time for financial penalties?

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**Hospital-Acquired Infections Should Not be Tolerated**

By Frank Diamond

It’s not just the daunting challenges that occasionally defeat us. Sometimes plain old-fashioned inertia makes us hit the snooze button once too often. Our cover story on page 22 leads with a challenge: “Almost immediately, hospitals could cut in half the number of infections that patients contract each year in health care facilities, but we lack the will or have failed to install the proper financial incentives to do so, experts say.”

Contributing editor Joseph Burns presents an in-depth package that looks at the problem of hospital-acquired infections (HAIs) and what can be done about it. Something’s already being done about it in some hospitals that have made ending HAIs such a priority that they are now near zero incidents. Other hospitals, though, not so good. Isn’t that the way it has always been in health care? There’s a wide disparity in quality.

Lives are at stake and no one shrugs, least of all clinic executives at health insurance companies. Their beneficiaries suffer, as well as their bottom lines. “Insurance companies could and should prioritize safety in hospitals more than they are doing,” says John Santa, MD, medical director of Consumer Reports.

There are success stories when it comes to developing systems. Thomas A. Scully, who ran CMS under President George W. Bush, tells us in our Q&A (page 31) that two of the things he’s most proud of from his tenure are Medicare Advantage and Medicare Part D. Either because of politics or simply from honest evaluation, some may argue that these do not count as accomplishments. Fair enough, as even Scully would admit. He liked trying to get bipartisan approval and appreciates rational discussion and disagreement.

But that’s a debate for another venue. Suffice it to say here, though, that he did get things done. Take heart.
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Submissions will be in any Microsoft Word format. Tables with more than two columns should be on spreadsheets, and all graphics should be in separate graphics files, not embedded in the Word document.

Further details about the peer review process, as well as conflict-of-interest forms, are at http://www.managedcaremag.com/callforpapers.
Patients at Health Centers Say They Like PCMH Care

Aspects of the patient-centered medical home (PCMH) model won over a tough audience — those who get care from federally funded health centers — in a recent study in *Annals of Family Medicine (AFM)*.

About 1,100 such centers serve more than 20 million people, 62% of whom are racial or ethnic minorities. “These high patient ratings among health centers are especially remarkable given that low-income and uninsured patients across the United States generally rate their care much lower,” says the study, “Effects of Patient-Centered Medical Home Attributes on Patients’ Perceptions of Quality in Federally Supported Health Centers,” in the November/December issue of *AFM*.

The study says that 84% of about 4,500 patients surveyed think that PCMHs provide excellent or very good overall quality, while 81% say that clinician care at PCMHs is excellent or very good.

In contrast, the Commonwealth Fund’s 2010 Biennial Health Insurance Survey found that only 35% of low-income adults and 27% of uninsured adults report excellent or very good care.

Patient perception counts for a lot. “Measuring patients’ perspectives of quality is important because these subjective measures of satisfaction relate to objective measures of quality,” the study says.

“For instance, patients who view their care positively are more likely to cooperate with their clinicians, and follow recommendations, leading to better outcomes. Patient satisfaction is also associated with greater clinician adherence to clinical practice guidelines, better recovery from symptoms, improved emotional health, and fewer diagnostic tests and referrals.”

The respondents were asked to evaluate seven PCMH attributes:

- Getting to the center
- Getting care once they got there
- Communicating with clinicians
- Communicating with staff
- Getting support to self-manage chronic conditions
- Getting support to self-manage behavioral risks
- Getting comprehensive preventive care

The data were gathered in face-to-face interviews conducted between September and December 2009.

The authors admit, though, that patient satisfaction might not always be an indication of how well a PCMH performs.

“Indeed, our study found that patients’ reports of certain PCMH attributes (i.e., self-management support for chronic diseases and behavioral risks, comprehensive preventive services) were generally not associated with patients’ ratings of quality.”

**Med School in 3? Let Debate Begin**

“Young doctor” could be considered a contradictory term because by the time physicians-to-be finish med school, residency, and a year of fellowship, they are not so young anymore. And they are saddled with debt.

To address those problems plus the physician shortage, some medical schools have eliminated the fourth year. Doing so will not only speed up the process but also, theoretically, increase the ranks of primary care physicians.

Those making this argument often cite an article in the March 21, 2012, issue of *JAMA* (http://tinyurl.com/JAMA-MED) by Ezekiel J. Emanuel, MD, PhD, and Victor R. Fuchs, PhD. Emanuel and Fuchs write, “[T]here is substantial waste in the education and training of U.S. physicians. Years of training have been added without evidence that they enhance clinical skills or the quality of care. This waste adds to the financial burden of young physicians and increases health care costs. The average length of medical training could be reduced by about 30% without compromising physician competence or quality of care.”

Paying off those enormous student loans might be one reason why aspiring doctors choose to be specialists, where they can make more money.

Not everybody likes this idea. Writing in the Sept. 19, 2013, issue of the *New England Journal of Medicine* (http://tinyurl.com/Goldfarb-piece), Stanley Goldfarb, MD, and Gail Morrison, MD, state that a similar effort was attempted in the 1970s for the same reasons: to reduce medical school costs and to increase the number of PCPs. It failed.

“The hope that students would opt for primary care careers was not consistently borne out,” they write. “Students enrolling in some accelerated BA–MD programs in community-based medical schools tended to enter careers in family medicine in higher numbers than did those from standard MD programs, but even those numbers were nowhere near the hoped-for 60% to 75%; and overall, these programs did not consistently boost the number of students choosing primary care careers.”
Briefly Noted

Many patients facing the prospect of having knees or hips replaced use the “I can’t live with this pain anymore” method of making the decision. That is, they put it off until they can’t put it off any longer. Thanks to work by researchers at Duke University, knee-replacement operations might become a thing of the past (http://tinyurl.com/knee-cart). They are trying to create artificial joint cartilage. Better for patients and, hopefully in time, better for cost management. Black women are much more likely to have high blood pressure than black men or white men and women, according to a study in the journal Circulation: Cardiovascular Quality and Outcomes. The study looks at about 70,000 people in the southeastern United States, a.k.a. the “stroke belt.” The overall rate of high blood pressure is 57%, but it’s 64% for black women. Patients at high risk for lung cancer will be able to get low-dose computed tomography (LDCT) screening without being charged a copayment or a deductible, thanks to a ruling by the U.S. Preventive Services Task Force. The task force gave LDCT a B recommendation. High-risk patients are people ages 55 to 80 who have smoked at least 30 packs of cigarettes a year, and former heavy smokers who have not smoked for 15 years. Researchers tracking about 6,500 women ages 65 to 79 in the United States find that those who have a history of heart disease had nearly a 30% increase in developing cognitive difficulties than women without heart problems, according to a study in the Journal of the American Heart Association (http://tinyurl.com/heart-dementia). Many types of heart disease and vascular disease are associated with declining brain function.

— Frank Diamond

NEWS & COMMENTARY

ACOs’ pharm management not up to snuff

Not everybody believes that accountable care organizations (ACOs), a bulwark of the Affordable Care Act, will ride to medicine’s rescue. In fact, in these pages, well-known policy experts such as Regina Herzlinger, PhD, of Harvard Business School, and David J. Brailer, MD, PhD, the health technology czar under President George W. Bush, have been downright dismissive (http://tinyurl.com/herzlinger-view and http://tinyurl.com/brailer-interview, respectively). In fact, Brailer told us, “Accountable care organizations are a publicity stunt created by Congress and the administration to make people feel like they were reforming care delivery when everyone knew they weren’t.” So, pressure’s on for those trying to make ACOs function. A study in the January issue of the Journal of Managed Care Pharmacy looks at how 46 ACOs handle pharmacy. They do a few things well, but some areas need improvement. For instance, only 9% are good at notifying a doctor when a prescription has been filled.

“Developing the capabilities to support, monitor, and ensure appropriate medication use will be critical to optimal patient outcomes and ACO success,” the authors say.

What are ACOs doing?

Percentage of 175 members of the American Medical Group Association that consider themselves highly ready to undertake each operation

<table>
<thead>
<tr>
<th>Activity</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Transmit prescriptions electronically</td>
<td>70%</td>
</tr>
<tr>
<td>View prescription and medical data in single system</td>
<td>54%</td>
</tr>
<tr>
<td>Encourage appropriate generic use with formularies</td>
<td>50%</td>
</tr>
<tr>
<td>Identify potential drug-drug, drug-disease, and/or polypharmacy concerns</td>
<td>43%</td>
</tr>
<tr>
<td>Use visit summaries to list allRx, potential adverse reactions, and clear directions for use</td>
<td>41%</td>
</tr>
<tr>
<td>Synchronize formularies across different care sites</td>
<td>35%</td>
</tr>
<tr>
<td>Alert providers of preventive care gaps</td>
<td>28%</td>
</tr>
<tr>
<td>Involve pharmacist in direct patient care</td>
<td>22%</td>
</tr>
<tr>
<td>Balance financial incentives with quality metrics for a diversity of conditions</td>
<td>22%</td>
</tr>
<tr>
<td>Notify care providers when Rx is prescribed</td>
<td>20%</td>
</tr>
<tr>
<td>Implement protocols to avoid duplicate medications/polypharmacy</td>
<td>17%</td>
</tr>
<tr>
<td>Capture patient-reported outcomes electronically</td>
<td>15%</td>
</tr>
<tr>
<td>Share potential drug-drug/drug-disease/polypharmacy concerns with care team</td>
<td>13%</td>
</tr>
<tr>
<td>Educate patients about alternatives/implications when determining the recommended medication care team</td>
<td>11%</td>
</tr>
<tr>
<td>Notify care providers when Rx is filled</td>
<td>9%</td>
</tr>
<tr>
<td>Quantify medication cost offsets</td>
<td>7%</td>
</tr>
</tbody>
</table>

Source: “Are ACOs Ready to be Accountable for Medication Use?” Journal of Managed Care Pharmacy, January 2014
Medicare, the Gorilla in the Room, Weighs in at More Than 800 Pounds

The system’s effect on the private sector has actually been underestimated. Medicare price changes often lead to amplified swings on the private side.

By John Carroll

Last summer, as physicians around the country were marshaling their forces in what has become an annual campaign to override the deep cuts to physician rates required by the Medicare budget, the president of the American Academy of Family Physicians voiced the added concern that whatever happened to Medicare’s payment rate, insurers would be sure to follow the feds’ marching orders on any cuts.

Snowball effect

“The impact, said Jeffrey Cain, MD, current board chairman of the AAFP, would “snowball as commercial insurers, who often base their payment on the Medicare rate, reduce their reimbursement to physicians as well.”

It’s no secret that providers are alert to even the smallest shift in what Medicare pays for a service. And not just because of the oversized role it plays as the nation’s largest single payer for health care services.

Professional physician societies have been acutely conscious of the lead role that Medicare plays among all payers, believing that a shift in the agency’s financial winds can be swiftly imitated among private payers as well.

Now a pair of economists with a longtime interest in health care say they can quantify the effect Medicare’s rates have on the private sector — concluding that a review of past changes in payment rates shows that price moves at Medicare lead to amplified swings on the private side.

For payers looking for a benchmark to cover thousands of coded services across a wide network of providers, the Medicare book of rates makes a logical template, the economists say, particularly when they’re setting rates for a large number of small doctor groups.

When insurers are negotiating with a host of independent practitioners, one way of managing the complexity involved is to use the Medicare rate sheet as a base menu of prices, possibly with an across-the-board hike and a “take-it-or-leave it” attitude.

That’s one reason why Medicare’s influence on benchmarking prices is strongest in areas with large numbers of providers who have not consolidated into large practices. When negotiating with hospitals or large physician groups, though, purchasers are more likely to hammer out rates for bundles of services. The bigger the market clout the providers have, says Gottlieb, the higher their rates are likely to be.

“We find that when there are more concentrated providers it is easier to negotiate away from the Medicare benchmark,” says Gottlieb. “In contrast, when providers are more dispersed, Medicare is used more strongly as a benchmark. The amplification is larger.

“If you’re an insurer negotiating with one or two groups, you can imagine them saying, ‘We’ll pay more for this, less for that,’” he adds. “But if there are 100 small groups, it’s more costly to negotiate with all of them, and then you’re more likely to take Medicare as a benchmark. It’s the same on both sides. Small physician groups with a couple of docs won’t invest in negotiations.”

Regular feature

Gottlieb’s study is consistent with what Greg Scott, MPA, has been seeing. As a principal in Deloitte Consulting, Scott’s been working directly with health plans around the country. The Medicare benchmark — along with a standard
INVOKANA™ (canagliflozin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

INVOKANA™ is not recommended in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS
- History of a serious hypersensitivity reaction to INVOKANA™.
- Severe renal impairment (eGFR <30 mL/min/1.73 m²), end stage renal disease, or patients on dialysis.

Please see additional Important Safety Information and brief summary of full Prescribing Information on the following pages.

ENVISION NEW POSSIBILITIES

INVOKANA is the #1 branded therapy prescribed by endocrinologists when adding or switching non-insulin type 2 diabetes medications*

*Data on file. Based on NBRx data sourced from IMS NPA Market Dynamics Database, weekly data through 9/20/13.

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Please see additional Important Safety Information and brief summary of full Prescribing Information on the following pages.

ENVISION NEW POSSIBILITIES
INVOKANATM (canagliflozin) 300 mg:

**Incidence of Hypoglycemia**

With metformin + a sulfonylurea over 52 weeks:
- INVOKANA™ (canagliflozin): 300 mg: 43.2%
- sitagliptin 100 mg: 40.7%

Insulin and insulin secretagogues are known to cause hypoglycemia when used alone or in combination with insulin or an insulin secretagogue.

**Convenient Once-Daily Oral Dosing**

Recommended starting dose: INVOKANA™ 100 mg
- Dose can be increased to 300 mg in patients tolerating 100 mg who have an eGFR 60 mL/min/1.73 m² and require additional glycemic control.

**IMPORTANT SAFETY INFORMATION (cont’d)**

**WARNINGS AND PRECAUTIONS**

**Hypoglycemia:** INVOKANA™ causes intravascular volume contraction. Symptomatic hypoglycemia can occur after initiating INVOKANA™, particularly in patients with impaired renal function (eGFR < 60 mL/min/1.73 m²), elderly patients, and patients on other diuretics or medications that interfere with the renin-angiotensin-aldosterone system (eg, angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs], or patients with low systolic blood pressure). Before initiating INVOKANA™ in patients with one or more of these characteristics, volume status should be assessed and corrected. Monitor for signs and symptoms after initiating therapy.

**Impairment in Renal Function:** INVOKANA™ increases serum creatinine and decreases eGFR. Patients with hyperkalemia may be more susceptible to these changes. Renal function abnormalities can occur after initiating INVOKANA™. More frequent monitoring for signs and symptoms after initiating INVOKANA™ in patients with impaired renal function and in patients predisposed to hyperkalemia due to medications or other medical conditions.

INVOKANA™ increases serum creatinine and decreases eGFR. Patients with hypovolemia may be more susceptible to these changes.

**Hypokalemia:** INVOKANA™ can lead to hyperkalemia. Patients with moderate renal impairment who are taking medications that interfere with potassium excretion, such as potassium-sparing diuretics, or medications that interfere with the renin-angiotensin-aldosterone system are more likely to develop hyperkalemia. Monitor serum potassium levels periodically after initiating INVOKANA™ in patients with impaired renal function and in patients predisposed to hyperkalemia due to medications or other medical conditions.

**Hypersensitivity Reactions:** Hypersensitivity reactions, some serious, were reported with INVOKANA™ treatment; these reactions generally occurred within hours to days after initiating INVOKANA™. If hypersensitivity reactions occur, discontinue use of INVOKANA™; treat per standard of care and monitor until signs and symptoms resolve.


**Macrosomia Outcomes:** There have been no clinical studies establishing conclusive evidence of macrosomia risk reduction with INVOKANA™ or any other antidiabetic drug.

**Please see additional Important Safety Information and brief summary of full Prescribing Information on the following pages.**

---

**Change in Body Weight**

Significant reductions in body weight at 52 weeks, each in combination with metformin + a sulfonylurea (P≤0.001)

**Difference from sitagliptin**
- 300 mg: −2.8%
- 100 mg: −1.0%

**Change in SBP**

Significant lowering of SBP at 52 weeks, each in combination with metformin + a sulfonylurea (P≤0.001)

**Difference from sitagliptin**
- 300 mg: −5.9 mm Hg
- 100 mg: −3.7 mm Hg

**INVOKANA™ is not indicated for weight loss or as antihypertensive treatment.**

**Prespecified secondary endpoint.**

**Adjusted mean.**

**References:**
4. GLT2: sodium glucose cotransporter 2.
5. Included 1 monotherapy and 3 add-on combination trials with metformin, metformin + sulfonylurea, or metformin + pioglitazone.
**INVOKANA™ 300 mg demonstrated greater reductions in A1C vs sitagliptin 100 mg at 52 weeks...**

**Adjusted Mean Change in A1C From Baseline (%): INVOKANA™ 300 mg vs Sitagliptin 100 mg, Each in Combination With Metformin + a Sulfonylurea**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>A1C Change at 52 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>INVOKANAtm 300 mg + metformin + a sulfonylurea</td>
<td>-2.8%</td>
</tr>
<tr>
<td>Sitagliptin 100 mg + metformin + a sulfonylurea</td>
<td>-2.1%</td>
</tr>
</tbody>
</table>

**DIFFERENCE FROM SITAGLIPTIN**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>INVOKANAtm 300 mg + metformin + a sulfonylurea</td>
<td>-0.37%</td>
</tr>
</tbody>
</table>

**POSSIBILITIES**

1. **INVOKANA™ provides SGLT2 inhibition, reducing renal glucose reabsorption and increasing urinary glucose excretion.**

2. **Significant reductions in body weight and systolic blood pressure (SBP)**

3. **Hypoglycemia With Concomitant Use With Insulin and Insulin Secretagogues:** Insulin and insulin secretagogues are known to cause hypoglycemia. INVOKANA™ can increase the risk of hypoglycemia when combined with insulin or an insulin secretagogue.

**WARNINGS AND PRECAUTIONS**

1. **Impairment in Renal Function:** INVOKANA™ increases serum creatinine and decreases eGFR. Patients with hypokalemia may be more susceptible to these changes. Renal function abnormalities can occur after initiating INVOKANA™. More frequent renal function monitoring is recommended in patients with an eGFR below 60 mL/min/1.73 m².

2. **Hyperkalemia:** INVOKANA™ can lead to hyperkalemia. Patients with moderate renal impairment who are taking medications that interfere with potassium excretion, such as potassium-sparing diuretics, or medications that interfere with the renin-angiotensin-aldosterone system are more likely to develop hyperkalemia. Monitor serum potassium levels periodically after initiating INVOKANA™ in patients with impaired renal function and in patients predisposed to hyperkalemia due to medications or other medical conditions.

**Adverse Reactions**

- **Hypoglycemia With Concomitant Use With Insulin and Insulin Secretagogues:** Insulin and insulin secretagogues are known to cause hypoglycemia. INVOKANA™ can increase the risk of hypoglycemia when combined with insulin or an insulin secretagogue. Therefore, a lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with INVOKANA™.

- **Genital Mycotic Infections:** INVOKANA™ increases the risk of genital mycotic infections. Patients with a history of genital mycotic infections and uncircumcised males were more likely to develop genital mycotic infections. Monitor and treat appropriately.

- **Hypersensitivity Reactions:** Hypersensitivity reactions (eg, generalized urticaria), some serious, were reported with INVOKANA™ treatment; these reactions generally occurred within hours to days after initiating INVOKANA™. If hypersensitivity reactions occur, discontinue use of INVOKANA™; treat per standard of care and monitor until signs and symptoms resolve.

- **Increases in Low-Density Lipoprotein (LDL-C):** Dose-related increases in LDL-C occur with INVOKANA™. Monitor LDL-C and treat per standard of care after initiating INVOKANA™.

- **Macrovascular Outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with INVOKANA™ or any other antidiabetic drug.

**Please see additional Important Safety Information and brief summary of full Prescribing Information on the following pages.**
**INDICATIONS AND USAGE**

INVOKANA™ (canagliflozin) is indicated as an adjunct to diet and exercise to reduce blood glucose in adults with type 2 diabetes mellitus (see Clinical Studies). INVOKANA™ is not recommended as initial treatment for patients with type 1 diabetes mellitus.

**CONTRAINDICATIONS**

History of a serious hypersensitivity reaction to INVOKANA (see Warnings and Precautions)

Severe renal impairment (eGFR less than 30 mL/min/1.73 m²) and stage 4 renal disease or patients on dialysis (see Warnings and Precautions and Use in Specific Populations).

**WARNINGS AND PRECAUTIONS**

Hypoglycemia: Hypoglycemia is more commonly reported in patients with type 1 diabetes mellitus or in patients taking insulin or an insulin secretagogue. Hypoglycemia may occur in patients treated with INVOKANA if concomitant insulin or insulin secretagogue therapy is initiated or modified. Therefore, a lower dose of INVOKANA or insulin may be required (see Warnings and Precautions).

Hypertension: Hypertension may occur, requiring dose adjustment or discontinuation of INVOKANA if necessary (see Warnings and Precautions)

**ADVERSE REACTIONS**

The most common (≥25%) adverse reactions were female genital mycotic infections, urinary tract infections, and increased urination. Adverse reactions in ≥2% of patients were male genital mycotic infections, vulvovaginal pruritus, thirst, nausea, and constipation

Please see brief summary of full Prescribing Information on the following pages.

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**INVOKANA™ (canagliflozin) tablets, for oral use**

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**INDICATIONS AND USAGE**

INVOKANA™ (canagliflozin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (see Clinical Studies). (For full Prescribing Information) See Warnings and Precautions and Use in Specific Populations.

**CONTRAINDICATIONS**

History of a serious hypersensitivity reaction to INVOKANA (see Warnings and Precautions)

Severe renal impairment (eGFR less than 30 mL/min/1.73 m²) and stage 4 renal disease or patients on dialysis (see Warnings and Precautions and Use in Specific Populations)

**WARNINGS AND PRECAUTIONS**

Hypoglycemia: Hypoglycemia increases serum creatinine and decreases HbA1C. Patients with hypoglycemia may be more susceptible to hemodynamic effects of hypoglycemia when combined with INVOKANA. Therefore, a lower dose of INVOKANA or insulin may be required (see Warnings and Precautions).

Hypertension: Hypertension may occur requiring dose adjustment or discontinuation of INVOKANA if necessary (see Warnings and Precautions)

**ADVERSE REACTIONS**

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Severe renal impairment (eGFR less than 30 mL/min/1.73 m²) and stage 4 renal disease or patients on dialysis (see Warnings and Precautions and Use in Specific Populations)

**WARNINGS AND PRECAUTIONS**

Hypoglycemia: Hypoglycemia increases serum creatinine and decreases HbA1C. Patients with hypoglycemia may be more susceptible to hemodynamic effects of hypoglycemia when combined with INVOKANA. Therefore, a lower dose of INVOKANA or insulin may be required (see Warnings and Precautions).

Hypertension: Hypertension may occur requiring dose adjustment or discontinuation of INVOKANA if necessary (see Warnings and Precautions)

**ADVERSE REACTIONS**

The most common (≥25%) adverse reactions were female genital mycotic infections, urinary tract infections, and increased urination. Adverse reactions in ≥2% of patients were male genital mycotic infections, vulvovaginal pruritus, thirst, nausea, and constipation.

Please see brief summary of full Prescribing Information on the following pages.
USE IN SPECIFIC POPULATIONS

Pregnancy Category C: There are no adequate and well-controlled studies of INVOKANA™ in pregnant women. Based on results from rat studies, canagliflozin may affect fetal development and maturation. In a juvenile rat study, increased kidney weights and renal pelvic and tubular dilatation were evident at 30.5 times clinical exposure from a 300-mg dose. These outcomes occurred with drug exposure during the second and third trimester of human development. During pregnancy, consider alternative, appropriate therapeutic options, especially during the second- and third-trimester. INVOKANA™ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

• Nursing Mothers: It is not known if INVOKANA™ is excreted in human milk. INVOKANA™ is secreted in the milk of lactating rats, reaching levels 1.4 times higher than that in maternal plasma. Data in juvenile rats directly exposed to INVOKANA™ showed risk to the developing kidney (renal pelvis and tubular dilatations) during maturation. Since human kidney maturation occurs in utero and during the first 2 years of life when lactalional exposure may occur, there may be risk to the developing human kidney, because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from INVOKANA™, a decision should be made whether to discontinue nursing or to discontinue the drug or to discontinue INVOKANA™ taking into account the importance of the drug to the mother.

• Pediatric Use: Safety and effectiveness of INVOKANA™ in pediatric patients under 18 years of age have not been established.

• Geriatric Use: Two thousand thirty-four (2014) patients 65 years and older, and 345 patients 75 years and older were exposed to INVOKANA™ in new clinical studies of INVOKANA™. Patients 65 years and older had a higher incidence of adverse reactions related to reduced intravascular volume with INVOKANA (such as hypotension, postural dizziness, orthostatic hypotension, syncope, and dehydration), particularly with the 300-mg daily dose, compared to younger patients; more prominent increases in the incidence was seen in patients who were 75 years of age. Smaller reductions in HbA1C with INVOKANA™ relative to placebo were seen in older (56 years and older; -0.6% with INVOKANA™ 100 mg and -0.8% with INVOKANA™ 300 mg relative to placebo) compared to younger patients (0.72% with INVOKANA™ 100 mg and -0.8% with INVOKANA™ 300 mg relative to placebo).

• Renal Impairment: The efficacy and safety of INVOKANA™ have been evaluated in a study that included patients with moderate renal impairment (eGFR 30 to less than 60 mL/min/1.73 m²), elderly patients (eGFR greater than 60 mL/min/1.73 m², with end-stage renal disease or patients on dialysis. INVOKANA™ is not expected to be effective in these patient populations.

• Impairment in Renal Function: INVOKANA™ has not been studied in patients with severe hepatic impairment and it is therefore not recommended.

• Hepatic Impairment: No dosage adjustment is necessary in patients with mild or moderate hepatic impairment. The use of INVOKANA™ has not been studied in patients with severe hepatic impairment and it is therefore not recommended.

OVERDOSE

There were no reports of overdose during the clinical development program of INVOKANA™ (canagliflozin).

In the event of an overdose, contact the Poison Control Center. It is also reasonable to employ the usual supportive measures, eg, remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive treatment as dictated by the patient’s clinical status. Canagliflozin was negligibly removed during a 4 hour hemodialysis session. Canagliflozin is not expected to be dialyzable by peritoneal dialysis.

ADVERSE REACTIONS

The most common (25%) adverse reactions were female genital mycotic infections, urinary tract infections, and increased urination. Adverse reactions in ≥2% of patients were male genital mycotic infections, subungual pustulosis, thirst, nausea, and constipation.

Please see brief summary of full Prescribing Information on the following pages.
**Table 1: Adverse Events From Pool of Four 26-Week Placebo-Controlled Trials Reported Per 1% of INVOKANA-Treated Patients**

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Placebo</th>
<th>INVOKANA 100 mg</th>
<th>INVOKANA 300 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobinuria</td>
<td>0.6%</td>
<td>0.9%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Urosepsis</td>
<td>0.0%</td>
<td>0.1%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>1.7%</td>
<td>3.9%</td>
<td>5.3%</td>
</tr>
<tr>
<td>Infections</td>
<td>5.0%</td>
<td>6.4%</td>
<td>6.9%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.5%</td>
<td>2.2%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Insomnia</td>
<td>0.5%</td>
<td>0.7%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Metabolism</td>
<td>3.4%</td>
<td>3.8%</td>
<td>4.1%</td>
</tr>
<tr>
<td>Oral Cavity</td>
<td>0.1%</td>
<td>0.2%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Urinary Tract</td>
<td>0.2%</td>
<td>0.4%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Nausea</td>
<td>1.4%</td>
<td>1.8%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1.0%</td>
<td>1.2%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Weight Gain</td>
<td>0.7%</td>
<td>1.0%</td>
<td>1.3%</td>
</tr>
<tr>
<td>Weight Loss</td>
<td>0.8%</td>
<td>1.0%</td>
<td>1.2%</td>
</tr>
</tbody>
</table>

**Table 2: Population With at Least One Volume-Derived Adverse Reaction (Percent of Patients From 3 Clinical Trials)**

<table>
<thead>
<tr>
<th>Volume Characteristic</th>
<th>Compositional Factors</th>
<th>urine output increased</th>
<th>micturition urgency</th>
<th>nocturia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (+/-SD)</td>
<td>1.7% (+/-2.6%)</td>
<td>2.6% (+/-3.7%)</td>
<td>3.5% (+/-5.0%)</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3: Changes in Serum Creatinine and aFPR Associated With INVOKANA Treatment**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Baseline</th>
<th>Placebo</th>
<th>INVOKANA 100 mg</th>
<th>INVOKANA 300 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.43</td>
<td>0.43</td>
<td>0.43</td>
<td>0.39</td>
</tr>
<tr>
<td>aFPR (mg/dL)</td>
<td>2.5</td>
<td>2.2</td>
<td>2.0</td>
<td>1.8</td>
</tr>
</tbody>
</table>

**Table 4: Incidence of Hypoglycemia* in Controlled Clinical Studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Placebo</th>
<th>INVOKANA 100 mg</th>
<th>INVOKANA 300 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>4 (5.8%)</td>
<td>3 (4.1%)</td>
<td>9 (12.5%)</td>
</tr>
</tbody>
</table>

* Number of patients experiencing at least one event of hypoglycemia.
INVOKANA™ (canagliflozin) tablets

<table>
<thead>
<tr>
<th>Placebo</th>
<th>INVOKANA 100 mg</th>
<th>INVOKANA 300 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male genital mycotic infections</td>
<td>0%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Female genital mycotic infections</td>
<td>0.0%</td>
<td>1.6%</td>
</tr>
</tbody>
</table>

Table 1: Adverse Reactions From Pool of Four 26-Week Placebo-Controlled Studies Reporting on ≥ 2% of INVOKANA Treated Patients

INVOKANA™ (canagliflozin) tablets

<table>
<thead>
<tr>
<th>Placebo</th>
<th>INVOKANA 100 mg</th>
<th>INVOKANA 300 mg</th>
<th>INVOKANA 100 mg + Sulfonylurea</th>
<th>INVOKANA 300 mg + Sulfonylurea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male genital mycotic infections</td>
<td>0%</td>
<td>1.9%</td>
<td>1.8%</td>
<td>0%</td>
</tr>
<tr>
<td>Female genital mycotic infections</td>
<td>2.7%</td>
<td>0.4%</td>
<td>1.5%</td>
<td>3.8%</td>
</tr>
</tbody>
</table>

Table 2: Population of Patients With at Least One Volume-Derived Adverse Reaction (Post-Established Clinical Trials)

INVOKANA™ (canagliflozin) tablets

<table>
<thead>
<tr>
<th>Placebo</th>
<th>INVOKANA 100 mg</th>
<th>INVOKANA 300 mg</th>
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<td>3.0%</td>
<td>0.4%</td>
<td>1.5%</td>
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</tr>
</tbody>
</table>

Table 3: Changes in Serum Creatinine and eGFR Associated with Changes in Systolic Blood Pressure

INVOKANA™ (canagliflozin) tablets

<table>
<thead>
<tr>
<th>Placebo</th>
<th>INVOKANA 100 mg</th>
<th>INVOKANA 300 mg</th>
<th>INVOKANA 100 mg + Sulfonylurea</th>
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<td>3.0%</td>
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</table>
INVOKANA™ (canagliflozin) tablets

OVERDOSAGE

There were no reports of overdose during the clinical development program of INVOKANA (canagliflozin).

In the event of an overdose, contact the Poison Control Center. It is also reasonable to employ the usual supportive measures, e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive treatment as dictated by the patient's clinical status. Canagliflozin is negligibly removed during a 4-hour hemodialysis session. Canagliflozin is not expected to be dialyzable by peritoneal dialysis.

PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Medication Guide).

Instructions: Instruct patients to read the Medication Guide before starting INVOKANA™ (canagliflozin) therapy and to reread it each time the prescription is renewed.

Inform patients of the potential risks and benefits of INVOKANA and of alternative modes of therapy. Also inform patients about the importance of adherence to dietary instructions, regular physical activity, periodic blood glucose monitoring and HbA1C testing, recognition and management of diabetes complications. Advise patients to seek medical advice promptly during periods of stress such as fever, trauma, infection, or surgery, as medication requirements may change.

Instruct patients to take INVOKANA only as prescribed. If a dose is missed, advise patients to take it as soon as it is remembered unless it is almost time for the next dose, in which case patients should skip the missed dose and take the medicine at the next regularly scheduled time. Advise patients not to take two doses of INVOKANA at the same time. Inform patients that the most common adverse reactions associated with INVOKANA are genital mycotic infection, urinary tract infection, and increased urination.

Inform female patients of child bearing age that the use of INVOKANA during pregnancy has not been studied in humans, and that INVOKANA should only be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Inform patients to report pregnancies to their physicians as soon as possible.

Inform nursing mothers to discontinue INVOKANA or nursing, taking into account the importance of drug to the mother. Inform them to discontinue nursing or to discontinue INVOKANA, taking into account the importance of the drug to the mother.

Laboratory Tests: Due to its mechanism of action, patients taking INVOKANA may have increased levels of glucose in their urine.

Hypoglycemia: Inform patients that symptomatic hypoglycemia may occur with INVOKANA and advise them to contact their doctor if they experience any symptoms (see Warnings and Precautions). Inform patients that hypoglycemia may increase the risk for hypoglycemia, and to have adequate fluid intake.

Genital Mycotic Infections in Females (e.g., Vulvovaginitis): Inform female patients that vaginal yeast infection may occur and provide them with information on the signs and symptoms of vaginal yeast infection. Advise them of treatment options and when to seek medical advice (see Warnings and Precautions).

Genital Mycotic Infections in Males (e.g., Balanitis or Balanoposthitis): Inform male patients that yeast infection of penis (e.g., balanitis or balanoposthitis) may occur, especially if uncircumcised males and patients with prior history. Provide them with information on the signs and symptoms of balanitis and balanoposthitis (itch or redness in the glans or foreskin of the penis). Advise them of treatment options and when to seek medical advice (see Warnings and Precautions).

Hypersensitivity Reactions: Inform patients that serious hypersensitivity reactions such as anaphylaxis and rash have been reported with INVOKANA. Advise patients to report immediately any signs or symptoms suggesting allergic reaction or angioedema, and to take no more drug until they have consulted prescribing physicians.

Urinary Tract Infections: Inform patients of the potential for urinary tract infections. Provide them with information on the signs and symptoms of urinary tract infections. Advise them to seek medical advice if such symptoms occur.

Active ingredient made in Belgium

Finished product manufactured by:
Janssen Ortho, LLC
Swartho, PA 08081
Manufactured for:
Janssen Pharmaceuticals, Inc.
Touwville, NJ 08960
Licensed from Mitsubishi Tanabe Pharma Corporation
© 2013 Janssen Pharmaceuticals, Inc.
premium from insurers — has been a regular feature for insurers looking to establish a rate sheet with their network of providers.

One important development, he adds, has been the rapid consolidation of physicians into ever-larger groups. Those groups may be likely to accept thousands of Medicare’s benchmarks, but they’re increasingly likely to pick out dozens of codes or bundles of codes that have the biggest impact on their bottom line — and negotiate over those on a case-by-case basis.

“When large plans and systems come together, each has done its homework. Each understands which subset of services will make or break its financial performance, which is even bigger than the 80–20 rule, where 20% of the codes drive 80% of the fees.” The core of the negotiation often comes down to 10% of the total — and that’s where the dickering can become intense.

Cost-based formulas

Medicare’s dominant role in health care may be dragging down efforts to switch the entire system over to more of a value-based approach to paying for care. That’s because in Medicare, the bulk of the pricing formula is based on cost.

Medicare’s rates are set on what the agency calls relative value units, or RVUs, which are based on three factors: Primarily the amount of work that goes into a procedure, the practice expense involved, and a smaller percentage assigned for malpractice expenses. That rate is then multiplied by a special geographic formula assigned to the area doctors work in.

An RVU is assigned a value (in 2013 the value was $34.02) and each procedure is assigned a certain number of RVUs, or points. And the basic formula involved has endured for more than 20 years.

But Bruce Vladeck, who ran Medicare and Medicaid under President Bill Clinton, says that Medicare has generally been leading the private sector in payment reform, not blocking it.

“There’s nothing in the Old or New Testament that says once you have RVUs you can’t fiddle with them,” says Vladeck. “But if the question is what is your starting point for a system of payments, you don’t have a lot of choices.”

As the Washington Post pointed out last year, those RVUs are updated using figures from an advisory group of medical societies led by the American Medical Association.

Charges

They survey doctors on the work involved in each procedure, including the amount of time it takes to complete a procedure. And the relationship has spurred charges that physicians have been routinely inflating their time to inflate payment rates — which are in turn used to determine what insurers pay.

The economists are careful to point out that they weren’t assessing whether the Medicare benchmark encourages overpayments or underpayments.

“We don’t say overpayment or underpayment,” notes Gottlieb. “This is the payment level. It’s much tougher to say it’s too high or too low; that depends on your point of view. But it does suggest that the reaction is based in sound economics; if you view Medicare as overpaying, you would expect the private sector to make the same mistake. That would be the same for lower payments.”

When Clemens and Gottlieb’s study appeared, the Post pounced, noting in their story that the new study underscored that “the government may be spending billions of dollars more than necessary for some products and services. Moreover, the influence of Medicare prices means that those faults may be replicated throughout U.S. health care.”

Medicare’s influence is so pervasive, say the study authors, that it could also defeat the move toward more value-based payments. Medicare’s accountable care organizations are paid according to the old RVU-unit formula, along with added bonuses, says Gottlieb.

“The big thing we see is the relative pricing across services,” adds Gottlieb. “It encourages private insurers to pay in a cost-based manner rather than value-based because that’s how Medicare is set up, with a higher payment for higher input costs, or a lower payment for lower input costs.”

Cost shifting

Their conclusions also raise questions about another theory: that throttling down Medicare payments puts pressure on providers to increase what they charge private insurers to make up for the shortfall.
"It makes a lot of economic sense," says Gottleib about his and Clemens's conclusions on Medicare's influence, "but that said, much of the existing literature on hospitals has tended to find cost shifting, to find that lower Medicare rates increase private rates."

There are a variety of ways that health plans can do the math around RVUs, says Douglas E. Henley, MD, the executive vice president and CEO of the AAFP. While Medicare operates with one conversion rate, the conversion rate on the private insurance side can vary.

"Primary care physicians may have one conversion factor," he says, while an ear, nose and throat group that could be harder to find — and badly needed for the insurer's network — could negotiate a higher conversion rate. While Medicare changes its conversion rate every year, private insurers could stick with an older, less expensive formula.

"If you are small or medium-sized, either you take it or you leave it," says Henley about the insurer's rate sheet. "And it may take saying 'no' to get their attention." It could also persuade physicians to improve their clout by consolidating.

"I think one of the most fascinating things is this issue of provider consolidation," says Gottleib. "There's this tradeoff. When they consolidate, they can charge more, but it also means that negotiating away from the Medicare schedule is cheaper, so you can have benefits in getting away from it and coming up with your own pricing."

Moving to a new model

The pricing issue has been a central theme with the unveiling of state insurance exchanges called for under Obamacare. Kaiser Health News (KHN) recently noted that while insurers and physicians often steer clear of a blunt assessment of payment rates, it's been clear that quite a few insurers have set exchange rates well below the Medicare benchmark.

They concluded that a $90 Medicare rate for a relatively complex visit to the doctor's office which would earn $100 from a private plan is sometimes priced at $60 to $70 on some of the exchange plans. And in many cases, doctors are finding out the hard way.

"I've participated with Oxford since 1985. They don't send me a contract every year to sign. They don't send me the rates. You don't know the rates," Paul Orloff, MD, the president of the New York County Medical Society, told KHN. "It's the only game in town, so you sign. They have a right to unilaterally change the rates at any time during the contract."

Ultimately, payers and providers may want to move toward more of a blended payment model, combining a fee for service along with capitation — a monthly fee for a set of services for a group of patients, weighted by risk factors, says Henley.

"If you do it well, that should work out very nicely," he adds, "especially in the context of the patient-centered medical home."

Medicare's leadership

But Medicare's lead role will probably be a key factor in any lasting change. Scott, for one, doesn't expect Medicare to abandon its role as the 800-pound gorilla in health care pricing anytime soon.

"Medicare's impact is going to remain consequential," says Scott, "but there may be some shift over time as private models become more creative."

"Inevitably," notes Henley, "a new model will certainly have more stickiness if Medicare is moving in that direction."

"This is not a great model that we have," says Scott. "I think all across the spectrum, in Medicare and private insurance, there are various embryonic approaches to at least try and introduce a value perspective, to integrate pricing and quality using clinical process and outcome measures."

But for any major changes to occur, he adds, Medicare will need to make some major adjustments in the way it pays for services. [MC]
The Enigma That Is Swiss Health Care
Compulsory medical insurance with a twist: Plans play a crucial role
By Robert Royce, PhD

LONDON — Where can you find a health system with universal coverage via compulsory insurance purchased through individual insurers, not from governmental agencies, that delivers world-class services yet has a relatively low level of health care directly funded by taxation and high levels of patient satisfaction despite a high level of copayments?

The answer is Switzerland, a country whose health system can paradoxically delight both free marketers and socialists — providing they ignore the features of that system that do not fit into their conventional notions of what a consumer-directed or a social-solidarity-based health system should look like. Swiss health care defies such easy characterization.

Mandatory insurance is a highly contentious subject in America, which sets it apart from much of Europe, where essentially a social consensus exists that all citizens should be provided with at least basic coverage. What that coverage consists of, and how it is delivered, does of course vary between states. Switzerland fits into the European mainstream on this issue, but it has a distinct way of delivering such coverage, and it is likely to appeal to many Americans.

There is no government-run health insurance plan, although both the national government and the cantons do provide premium subsidies for low-income citizens. Switzerland, with a population of about 7.8 million, is a federation of 26 cantons, which have a level of autonomy somewhat akin to U.S. states.

Everyone is required to have health insurance. Parents also have to buy coverage for their children, although the premiums for children are much lower than those for adults.

Subsidies are available — up to 100% for the poorest citizens. You can choose a basic package with different deductibles and premiums from products offered by the 80+ private health insurers that operate in Switzerland.

Those insurers must offer the basic package and they must charge all customers the same premium for that policy, regardless of age and health status. Insurers cannot earn profit on the basic benefit package but can do so by selling supplementary insurance policies, which are risk-adjusted. They also look to take advantage of the inadequacy of the current risk equalization mechanism that tries to ensure that those who end up with higher-risk patients on the basic package aren’t penalized.

Somewhat surprisingly, as the basic package is very generous by most countries’ standards, about 70% of the population has some form of supplementary insurance. This consists mainly of items such as private hospital rooms, dental coverage, and ensuring coverage for drugs and services (rehabilitation, for example) that are excluded under the basic package.

On pharmaceuticals there is a "positive" list (a formulary) of drugs that are covered within the basic package. Every item on this list is covered by every health insurer for anywhere in Switzerland. Drugs are also subject to copayments. Choosing a brand-name drug for which a generic substitute is available can result in a coinsurance payment of 20% of the cost of the more expensive drug unless the physician has expressly prescribed the brand name.

Switzerland has a higher level of out-of-pocket (OOP) expenditure than most countries — about 28% of Swiss health spending — and lower direct government funding. Insurance premiums cover about one third of Swiss health care costs, with taxes and OOP each contributing a third.

Minimum deductible

Everyone must have a minimum deductible of 300 Swiss francs (about $330) with a maximum deductible of 2,500 Swiss francs (about $2,350). Once the deductible for the policy the individual has chosen is met, there is 10% coinsurance for services up to a maximum of 700 Francs ($770) a year. Finally there

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is a copayment of just 10 francs ($11) a day for most inpatient care.

Macro level

There is not much evidence that these levels of coinsurance curb demand for health care in Switzerland at a macro level, given that the country’s health care expenditure was 11.3% of GDP in 2012, set against an OECD (Organization for Economic Co-operation and Development) average of 9.3%, and it has one of the highest average lengths of stay (ALOS) and numbers of doctors, beds and high-technology equipment such as MRIs in Europe (Health at a Glance 2013 OECD Indicators (http://bit.ly/oecd-glance)).

Of course, 11.3% looks very reasonable compared with the United States’ 17.6%, whilst a study by Felder and Werblow (Swiss Social Health Insurance: Copayments Work; http://bit.ly/dice-03) concluded that the roughly 40% of the population that chooses high-deductible plans have a markedly lower rate of health care usage than the 60% who choose the minimum. So, as with so much else in the Swiss health care system, there are features to encourage whatever is your preferred mechanism for health reform.

If you favor the use of the private sector to deliver insurance, you can point to the free choice among a large number of insurers, the high quality of care available to all, and the lack of government-set payments for providers. However, one would also have to acknowledge that of the 80+ insurers, six account for 80% of the market, that insurers are basically just the payers of bills, and that there is little health outcome or quality information available on the Swiss health system.

In that sense, it is not acting like the American consumer-directed health system because consumers have little information on the quality of care that is being provided and no opportunity to choose providers based on price/quality. Moreover, despite sizeable differences in premium costs between insurance products, few people switch insurers.

The premiums vary considerably among the cantons. Each canton is effectively a discrete market. People are not allowed to shop between cantons for insurance, and this appears to reflect both the desirability of the canton as a place of residence and work and also the relative density of health care providers. In 2000, the Geneva canton had an average premium that was 2.5 times that of Appenzell Innerrhoden canton.

These differences remain essentially undisturbed over time, as do the premium price differentials within cantons. Price setting in Switzerland has been described by Uwe Reinhardt, PhD (“The Swiss Health System: Regulated Competition Without Managed Care”; JAMA. 2004;292(10):1227–1231. doi:10.1001/jama.292.10.1227) as “… a de facto cartel of insurers and health care practitioners who transact with one another in a tight web of government regulations.” This method of working is quite common in Europe, but it hardly appeals to market purists.

What accounts for this apparent apathy? Innate conservatism as a national characteristic? The fact that subsidies for the poorer section of the population and the indifference to cost of the richest mean only a minority truly have an incentive to switch? The fact that there are so many plans to choose from and the confusion this can cause?

No easy label

So this is a system that defies an easy label and has a number of notable flaws. It is a complicated regulatory environment and will not win any competitions for efficiency. However, there are few citizens of any developed country who wouldn’t be delighted to receive the range and standard of services available to Switzerland’s poorest citizens.

As this is delivered by a country that many consider the epitome of capitalism, this should give ideologues of all persuasions pause for thought. MC

Feedback please! Send your letters and comments to editors@managedcaremag.com
About 9.6 million adults age 18 or older suffered from a significant mental illness in 2012, according to the Substance Abuse and Mental Health Services Administration. About 6 million of these received treatment. They could be treated as an outpatient or inpatient and, in each category, with or without medication. Only 7.2% percent received all three types of care (outpatient counseling, inpatient counseling, and medication); the majority received two types.

Those who did not get mental health care gave a variety of reasons, and inability to afford treatment topped the list (46%). It should be noted, however, that “health insurance did not cover any treatment” comes in dead last (6%) and just a couple of spaces up is “health insurance did not cover enough treatment” (8%). The top of the list includes those who thought they could handle the problem without treatment (28%), and those who didn’t know where to get care (23%).

### Why mental health services were not sought

- **Could not afford care**: 46%
- **Could handle the problem without treatment**: 28%
- **Did not know where to go for services**: 23%
- **Did not have time**: 14%
- **Did not feel the need for treatment**: 10%
- **Concerned about confidentiality**: 10%
- **Might cause neighbors/community to have negative opinion**: 10%
- **Fear of being committed or having to take medicine**: 10%
- **Did not want others to find out**: 8%
- **Might have a negative effect on job**: 8%
- **Health insurance did not cover enough treatment**: 8%
- **Treatment would not help**: 7%
- **Health insurance did not cover any treatment**: 6%

Source: “Results From the 2012 National Survey on Drug Use and Health: Mental Health Detailed Tables,” Center for Behavioral Health Statistics and Quality, December 2013
Almost immediately, hospitals could cut in half the number of infections that patients contract each year in health care facilities, but we lack the will or have failed to install the proper financial incentives to do so, experts say.

Instead of using payment penalties to drive down infection rates, health plans and government payers actually pay hospitals more to care for patients with hospital-acquired infections (HAIs), according to researchers at the Johns Hopkins Armstrong Institute for Patient Safety and Quality.

A recent study in *JAMA Internal Medicine* by researchers at the Center for Patient Safety Research and Practice at Brigham and Women’s Hospital and at Harvard Medical School found that almost 441,000 patients contract one of five HAIs each year, and about 50% of these infections are avoidable. The five most common, costly, preventable, and well-tracked infections in hospitals are surgical site infection (SSI), central-line-associated blood-stream infection (CLABSI), catheter-associated urinary tract infection (CAUTI), ventilator-associated pneumonia (VAP), and *Clostridium difficile* infection (CDI). They added methicillin-resistant *Staphylococcus aureus* (MRSA) as a sub-category under SSIs and CLABSIs.

In effect, hospitals are infecting a population the size of Atlanta every year, says Leah Binder, president and CEO of the Leapfrog Group, an organization that issues a twice-a-year hospital safety score that grades efforts to address errors, accidents, injuries, and infections that harm or kill patients.

“A number of hospitals have improved by one or even two grades, indicating they’re taking steps toward safer practices,” she says. “But these efforts aren’t enough.”

Indeed, the hard part begins now, because some hospitals have been innovative early adopters of methods to limit HAIs, leaving behind stragglers that have yet to make infection control a priority, says John Santa, MD, medical director of *Consumer Reports*. The laggards may not have the desire or the necessary funding, or they may assume incorrectly...
that infections can happen to anyone, he adds.

“Four years ago, the School of Public Health at the University of California–Berkeley predicted what we see happening,” says Santa. “It said 200 to 300 hospitals would be getting to zero on multiple infections. But it also found that hundreds of hospitals were doing poorly financially, had serious leadership problems, and were not reducing the rate of hospital-acquired infections.”

Today, some hospitals are approaching zero central-line and surgical-site infection rates, Santa reports, adding pointedly: “When it comes to patient safety — including infection rates, wrong-site surgery, and other common forms of patient harm — the only acceptable goal is zero.”

Nationally, according to the study published in September in *JAMA Internal Medicine*, we are not close to that goal.

In the 13 years since the Institute of Medicine published its famous report on patient harm, *To Err is Human: Building a Safer Health System*, U.S. hospitals are still far less safe than they should be. HAIs still account for a “large proportion of the harms caused by health care and high rates of morbidity, mortality, and costs,” the researchers wrote in *JAMA Internal Medicine*, “Health Care–Associated Infections. A Meta-Analysis of Costs and Financial Impact on the U.S. Health Care System.” They estimate that each year, there are 441,000 of those five common HAIs and the annual cost of treating patients with these infections is $9.8 billion annually. (See “5 Costliest Hospital-Acquired Infections” on opposite page.)

So if these infections are costly and harmful to patients, why do they remain so common? One reason is that for consumers, patient safety is unrelated to cost, says Binder of the Leapfrog Group.

“We need consumers and purchasers saying that safety matters,” says Leah Binder, president and CEO of the Leapfrog Group. “That’s the only way that patient safety will get to the top of the hospital CEO’s agenda.”

Clearly, health insurers have an opportunity to control these costs while also improving patient care. “Insurance companies could and should prioritize safety in hospitals more than they are doing,” says Santa.

Ten years ago, Santa was on Oregon’s Public Employees Benefits Board, the largest health care purchaser in the state. “We tried to get our insurers to penalize hospitals that had high rates of never events. They would not do it, arguing instead that their priorities for contracting with hospitals were based on rates. They wanted the best rates, and any time they asked for any improvements in outcomes, we had to be prepared to pay for it in terms of higher rates.”

Even today, HAIs aren’t considered never events, but they should be, Santa says. “Hospitals don’t even have to report all infections publicly, so the public has no idea how serious and prevalent they are,” he says. “And most health plans do not have explicit penalties for hospitals based on their HAI rates. But they should!”

**‘It’s the incentives, stupid’**

François de Brantes, executive director of the Health Care Incentives Improvement Institute, makes a similar point. “The methods of payment in use today actually provide an incentive for complications, which is crazy. Private sector plans would rather pay for complications than upset their provider networks by spending time discussing what’s avoidable and what’s not,” says de Brantes, author of *The Incentive Cure: The Real Relief for Health Care.*

“Clearly moving to bundled payments solves that
problem, but because some infections materialize after discharge, you need to bundle the cost of the inpatient stay with the associated professional and post-acute costs to capture all costs associated with HAIs,” he says. “In Medicare payment, if the post-op infection requires a readmission, it gets tagged under the all-cause readmission rule and the facility gets penalized, but if the care is outpatient based, then Medicare just pays more for something that it shouldn’t pay for. Hence the importance of bundling.”

Blunt instrument

“But private sector payers continue to struggle with operationalizing bundled payments and use that as an excuse — among other reasons — to avoid taking any action,” de Brantes adds. “Certainly global capitation would help as well, but capitation is a blunt instrument that few organizations are willing or capable of implementing well.”

Health plans also should consider financial penalties. “Knocking a percentage off the hospital bill based on the occurrence of HAIs would be a simple payment incentive,” de Brantes suggests. “Health plans could calculate average HAI rates for a region, and then, for a specific hospital, subtract a percentage of fees based on the excess over average.

“All of these ideas are simple enough to implement, but the continued shift in the balance of negotiating power toward providers has led health plans to shy away from any payment policy that would institute penalties,” de Brantes says. “There’s also a failure by state governments to publicly shame hospitals into reducing HAIs. If states published every hospital’s HAI rate, they might force these facilities into improving.”

At the least, HAIs should be listed as never events, a step that would force U.S. hospitals to aim for zero infections, suggests Patrick R. Murray, PhD, the worldwide director of scientific affairs for BD Diagnostics. Murray cites statistics for methicillin-resistant Staphylococcus aureus (MRSA), which causes life-threatening bloodstream infections, pneumonia, and surgical site infections.

“When you look at the international data for infection rates from MRSA, the average in the United States is about 6.5% for all hospitalized patients,” says Murray. “In the best ICUs, it varies dramatically from 5% to 17%.” However, he adds, in some other countries — notably the Netherlands — that percentage is being driven down to zero.

“In Dutch hospitals, infections from multi-drug-resistant gram-negative organisms have been virtually eliminated,” he adds. “That’s because these institutions have established programs of rapid screening diagnostics for these organisms combined with very aggressive infection-control practices.”

Some hospitals in the United Kingdom are as bad as or worse than their counterparts in the United States in this regard, yet other U.K. hospitals’ experience mimics that of hospitals in the Netherlands. “This suggests that you can control these diseases,” Murray says.

As Santa theorizes, better results come from making the elimination of HAIs a goal. Kaiser Permanente consistently ranks among the best in the nation in Consumer Reports’ scoring of hospitals because the health plan makes it a priority to reduce HAIs, he says. (Kaiser’s hospitals all earned A’s on Leapfrog’s last hospital safety score rankings, as well.)

Kaiser Permanente has an advantage over other health plans because it owns most of the hospitals in its networks, “but that doesn’t mean employers and health plans shouldn’t expect the same thing,” he says. “Employers should not say, ‘It’s OK for more of our employees to die in your facilities because you can’t manage as well as Kaiser does.’”

Kaiser’s role

Sue Barnes, RN, Kaiser’s national leader for infection prevention and control, says that one of the primary responsibilities for all staff members in all of Kaiser’s facilities is prevention and control of HAIs. KP has 9 million members, 37 hospitals, and 588 medical office buildings in seven states and the District of Columbia and performs 149,000 inpatient surgeries annually. Kaiser and Sentara were among the hospital systems that achieved straight-A grades on Leapfrog’s recently released national report — 100% of Kaiser and Sentara hospitals received the highest grade the group gives.
“Preventing HAIs takes the form of performance-improvement projects focused on all the different types of infection, and in all the different settings and for all patients,” says Barnes. “Infection prevention and control departments work to lead and train physicians, nurses, administrators, and other staff in the prevention of infections and how to control the infrequent occurrence of outbreaks of infectious disease. We also team up with employee health professionals to follow up on communicable disease exposures, to ensure proper testing and treatment as needed.

How hospitals profit from their own mistakes

Last May, researchers at the Johns Hopkins Armstrong Institute for Patient Safety and Quality showed that hospitals benefit financially when patients’ hospital stays are complicated by preventable bloodstream infections. The researchers also reported that insurers rather than hospitals would reap the most savings by supporting programs to prevent hospital-acquired infections (HAIs). The study was published online in the American Journal of Medical Quality (http://bit.ly/well-good).

“Hospitals should be financially rewarded for preventing harm rather than for treating the resulting illness,” says study leader Eugene Hsu, MD, an anesthesiology resident at Johns Hopkins. “Instead, hospitals have a perverse financial incentive to keep patients longer and provide more interventions.”

The cost to care for any ICU patient who develops an avoidable central-line-associated bloodstream infection (CLABSI) is nearly three times what it would be for a similar patient without such an infection, the researchers found.

These patients spend an average of 23 extra days in the hospital, and hospitals receive eight times as much margin per patient, they reported. Yet Hsu asserts that most physicians and hospitals are not driven by the potential financial gains, but rather by a desire to deliver the best quality care possible for patients.

“We have known that hospitals often profit from complications, even ones of their own making,” says Peter J. Pronovost, MD, PhD, senior vice president for patient safety at Johns Hopkins Medicine and one of the authors of the research. “What we did not know was by how much, and that private insurers are largely footing the bill.”

For the study, researchers reviewed hospital records at Queens Medical Center in Honolulu. The hospital participated in the statewide Comprehensive Unit Based Safety (CUSP) program to reduce central line infections from 2009 through 2011. The program determined costs, payment, and profit margin for 16 HAI patients and compared them with 64 ICU patients who did not have line infections. For treating an infected patient, the hospital’s average margin per patient was $54,906, but for treating a similar but uninfected patient, the hospital lost $6,506.

For 10 government-insured ICU patients with CLABSIs, the mean payment to the hospital was $154,832, and for 39 ICU patients who did not have a CLABSI, the mean payment was $58,327, for a difference of $96,594. The figure did not achieve statistical significance.

For five commercially insured ICU patients who had a CLABSI, the mean hospital payment was $495,000, and for 23 ICU patients who did not have a CLABSI, it was $100,000, a difference of $395,000.

Private insurers pay more for outliers than government insurers do, even when the triggering event is preventable, says Peter Pronovost, MD, PhD, senior VP for patient safety for Johns Hopkins Medicine.

The diagnosis-related group (DRG) payment system that most health insurers use to pay hospitals provides a perverse incentive by paying more for more complicated care, Pronovost explains.

DRGs pay by the episode, which should provide an incentive for hospitals to keep costs low, but hospitals can receive more for complex care under provisions for outliers. With outlier payments, a hospital is paid a percentage of charges, meaning the more it charges, the more it receives, Pronovost adds. Most of the CLABSIs in the study were considered outliers and thus generated a large payout.

And for outliers, private insurers pay more than government insurers, even when the triggering event is preventable, adds Pronovost.

Pronovost, the author of Safe Patients, Smart Hospitals: How One Doctor’s Checklist Can Help Us Change Health Care from the Inside Out, suggests that insurers could realize significant returns by investing the money used to pay for just one preventable infection in quality-improvement programs.

When hospitals in Michigan and Rhode Island adopted a checklist and other interventions that Pronovost developed and tested at Johns Hopkins Hospital in Baltimore, they nearly eliminated catheter infections.

— Joseph Burns
“We in prevention and control departments also spend a lot of time making sure that best practices are shared throughout the facility, the region, and the organization so that patients benefit throughout our organization,” Barnes continues. “Equally important is that we share the bad stuff — the opportunity areas — so that we can improve care and prevent errors from recurring.”

A toolkit developed by Kaiser’s national infection prevention department is posted on the web (http://bit.ly/infect-kit) for easy access by any health care professional interested in infection control.

Other health plans may want to follow insurers that are revising how they pay for care. Michael S. Sherman, MD, senior vice president and chief medical officer at Harvard Pilgrim Health Care (HPHC), explains that under some payment models, the federal Centers for Medicare & Medicaid Services (CMS) and health plans say they will not pay for treatment of avoidable complications such as HAIs. “But that also leads to lots of negotiation about what is avoidable and what isn’t,” he says. “Fixed-revenue models such as global payments address that issue.”

It’s unlikely that any hospital would seek to boost revenue by intentionally infecting patients, Sherman adds. “But I would say that hospitals, like other businesses, go where the money is, and if reducing readmissions, infections and complications threatens to hurt them financially, then switching to a system of fixed payments for episodes of care can be a win-win-win for health plans, patients, and purchasers.”

Although HPHC does not intentionally pay for such complications, it still expects hospitals to reduce HAIs, Sherman adds. “We have not gathered enough data to demonstrate this type of reduction explicitly.”

The company rewards low rates of HAIs by including them as process and outcomes measures in its pay-for-performance program and by including them among the key measures that determine which hospitals qualify for the HPHC honor roll. Among the outcome measures that HPHC collects on hospitals are the number of CLABSIs, catheter–associated urinary tract infections (CAUTIs), and SSIs from colon surgery.

Seeking to minimize infection risk, the Harvard Pilgrim Health Care Institute participated in a study published in May on a protocol designed to cut bloodstream infections. Researchers showed that when hospitals use antimicrobial soap and ointment on all intensive-care patients, they can make a big difference. In the study of 75,000 patients in 43 community hospitals in 16 states, daily bathing

To cut HAIs, hospital system will use antimicrobial copper

Sentara Healthcare in Norfolk, Va., will be among the first hospitals in the United States to use antimicrobial copper surfaces on countertops, over-the-bed tables, and bed rails when it opens a 129-bed patient tower at Sentara Leigh Hospital.

Early this year, Sentara will add antimicrobial copper textiles, ranging from bed linens to patient gowns, throughout the building. Sentara announced in November. The 11-hospital health system will study the effects of using copper surfaces and textiles to determine whether they decrease rates of hospital-acquired infections.

In April, a study published in the Journal of Infection Control and Hospital Epidemiology reported that using antimicrobial copper surfaces in hospital rooms can reduce HAIs by 58%.

Patients in ICU rooms with copper alloy surfaces had a significantly lower rate of incident HAIs than those patients who had standard rooms, the researchers reported.

Funded by the Department of Defense, the study was done at Medical University of South Carolina, Memorial Sloan-Kettering Cancer Center in New York, and the Ralph H. Johnson Veterans Affairs Medical Center in Charleston, S.C. Researchers evaluated 650 patients and 16 rooms (half of them standard rooms, and half with copper-alloy surfaces) between July 2010 and June 2011. The study is significant because the use of copper as an antimicrobial is outside of the normal way of thinking about infection control, says Archelle Georgiou, MD, a health care consultant.

“Antimicrobial copper is not normally used in health care, but perhaps a disruptive innovation like this is what’s needed to begin to control hospital-acquired infections,” she says.

— Joseph Burns
How the Leapfrog Group grades hospitals

The Leapfrog Group Hospital Safety Score function (www.hospitalsafetyscore.org) assigns general hospitals a grade of A to F for how safe they are for patients. The upshot is that many hospitals still aren't doing enough to prevent hospital-acquired infections.

For this year’s survey, Leapfrog added measures on catheter-associated urinary tract infections (CAUTIs) and surgical-site infections: colon (SSI: Colon). While CAUTIs and SSI: Colon have not received as much public attention as other measures, they are among the most common hospital infections and take a combined 18,000 lives each year. With data from the Center for Medicare & Medicaid Services “Hospital Compare” web site and the Leapfrog Hospital Survey, Leapfrog now has the publicly available data needed to include these critical measures in the score.

― Joseph Burns

Inappropriate antibiotic use in ED contributes to HAI problem

For children, rate of inappropriate use has fallen

Reviews of the misuse of antibiotics generally focus on inpatient or outpatient settings and ignore emergency departments, say the authors of one of the first studies that tracks the problem in EDs.

About 126 million people were treated in EDs for acute respiratory tract infections (ARTIs) from 2001 to 2010 and 61% of these were treated with antibiotics, says the study “Antibiotic Utilization for Acute Respiratory Tract Infections in U.S. Emergency Departments” in the journal Antimicrobial Agents and Chemotherapy.

“This is likely multifactorial and may result from lack of insurance, lack of primary care access, or patient preference to seek care in the ED setting,” say the authors. “Our results support the hypothesis that many U.S. EDs are functioning as ‘safety-net’ care centers, with the majority of ARTI patients being uninsured or insured by Medicaid.”

The authors’ list of antibiotics includes penicillins, cephalosporins, macrolides, sulfonamides and lincomycin derivatives, quinolones, carbapenems, aminoglycosides, glycyllcyclines, glycopeptides, and leprostatins.

The rates of antibiotic utilization in the ED when the drugs weren't needed decreased overall from 621 (in 2001–2002) to 577 (in 2009–2010) per 1,000 ED visits. For patients 5 and younger, they decreased from 261 per 1,000 visits to 203. Patients ages 5 to 19 saw the greatest decrease: 444 to 275.

Unnecessary antibiotic use for patients ages 20 to 64 remained about stable: 535 per 1,000 visits in 2001–2002 and 500 in 2009–2010. Rates rose about 10% for people 65 and older, from 595 per 1,000 visits in 2001–2002 to 666 in 2009–2010.

“The observed lack of change in antibiotic utilization for adult ARTI patients, especially those ARTIs for which antibiotics are not indicated, is concerning,” the study states.

Antimicrobial stewardship programs (ASPs) have met with success, the authors note, but have focused mainly on inpatients. The ED, says the report, “has unique challenges that may not be amenable to standard ASPs. For example, emergency physicians may not be willing to stop and consult antimicrobial guidelines, given the high-volume, high-acuity nature of the ED. Doctor-patient relationships in the ED are episodic, and thus ED patients may be less willing to accept emergency physician advice on antibiotic use.”

Appropriate antibiotic use in the ED might “involve a combination of patient education, rapid diagnostic testing, ED-specific guidelines and treatment pathways, antibiotic order forms, or postprescription reviews.”

― Frank Diamond

For Santa, this study and other research suggest that hospitals must introduce protocols and follow them. “Strategies for limiting the spread of HAIs have been shown to decrease them dramatically,” he says. “It’s possible to introduce protocols for all infections whether they are SSIs, CLABSIs, MRSA infections, or cases of Clostridium difficile,” he says.

“Peter Pronovost, MD, of Johns Hopkins Medicine and others have made the checklist approach popular, and that’s important. We just need to introduce these strategies and follow them.”

When that is done, he says, the straggler hospitals will enter the mainstream — and do less inadvertent harm to patients.
New rules governing treatment of patients with mental health and substance abuse disorders raise more questions than they answer. In November, three federal departments, including Health and Human Services, issued rules under the Mental Health Parity Act that do not allow health insurers to discriminate against members seeking treatment for mental health and substance use disorders. Essentially, the rules say insurers must cover mental and physical health equally — or at parity.

Questions abound
But will these new rules cause all costs to rise? Will insurers then need to raise their premiums because they are operating under the medical loss ratio rules under the Affordable Care Act? Will health plans limit care by arguing that some mental health treatments are not medically necessary? These are questions that advocates for mental health patients are asking and they are one side of the story. Another side comes from a psychologist who serves as a health plan executive. He believes the parity rules give health plans an opportunity to improve care for all patients.

For now, however, it’s impossible to predict how health insurers will comply with the new rules, says Rebecca Farley, MPH, director of policy and advocacy for the National Council for Behavioral Health, an organization representing providers. The rules become effective for all plan years beginning after July 1, 2014. For most plans, that means Jan. 1, 2015.

“The rules say plans cannot have any restrictions that apply to any mental health or addiction treatment benefit that does not also exist for predominantly all benefits for medical-surgical patients,” Farley explains. “That means that if you apply a $20 copayment for outpatient mental health therapy, the plan also must apply a $20 copayment to most of the medical-surgical services that are similar, such as outpatient medical visits. Under the rules, insurers would not be allowed to impose limits on mental health and additional benefits that are more stringent than those typically applied for medical-surgical patients.”

In addition, treatments for some mental health or substance abuse problems are unquantifiable, she says. How would medical necessity be defined? Would it be more restrictive for mental health patients than others? How can you tell?

“Here’s another question: Do you require a patient to fail first on two generic drugs before getting access to a brand-name drug?” Farley continues. “Do you require preauthorization on mental health and additional treatment and is that preauthorization different from what’s required for a medical or surgical patient?”

The law, enacted in 2008, and the rules issued last year are needed because insurers had low annual limits on how much mental health care they would pay for while having much higher limits on medical-surgical care, she says. Also, health insurers have had higher copayment, deductible, and out-of-pocket limits for mental health care than they had for medical-surgical care, she adds.

Working within the rules
“The rules are designed to ensure that mental health and addiction treatment benefits are considered equitably when it comes to utilization management,” Farley says. Before the passage of the Affordable Care Act, plans were allowed to have annual and lifetime limits. Given that the parity act was enacted before the ACA, HHS then had to...
find a way to make the parity act work within the guidelines of the ACA, she says.

If insurers may not impose annual or lifetime limits and they have to work within the parity rules, what other means of cost control will they have?

**Medical necessity**

Lisa Kantor, a partner in Kantor & Kantor, a law firm in Northridge, Calif., says that one means of cost control is the question of medical necessity. A specialist in helping patients pursue denied claims, Kantor says mental health care is one of the most challenging and costly conditions insurers face.

“People talk about cancer and what a terrible and costly illness it is, and many people say cancer could be licked in a number of years. But no one is talking about solving the mental health problem,” she says.

Among the most costly benefits for patients needing mental health or substance abuse care is residential treatment. “Everyone is concerned about the cost of residential care because some behavioral health patients may need 100 days in a mental health treatment facility,” she says. “But what insurer would pay for a patient on the medical side to have 100 days in a skilled nursing facility? In a SNF, 100 days would be very expensive and would be a new cost for insurers.

“In the past, insurers could exclude residential coverage for mental health care but under the new parity rules, they can’t have a residential exclusion and still provide the same benefit on the medical-surgical side.”

Very few medical-surgical patients are hospitalized for 100 days, yet many mental health and substance abuse patients may need 100 days, she says. “Does that mean health plans will seek to limit length of stay for behavioral health problems?” she asks.

**Long-term care**

What about health plan members who have major accidents and need many days or weeks of rehabilitation treatment? What about patients with brain trauma? For these patients, health insurers

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**New mental health parity rules at a glance**

Achieving true mental health parity has been a struggle that stretches back more than two decades. Regulations issued in November mean care is likely to improve for patients needing behavioral health care, but the fight is far from over to ensure that patients requiring mental health treatment will not face discrimination from managed care insurers, say advocates for patients with behavioral health and substance abuse disorders.

On November 8, the federal departments of Treasury, Labor, and Health and Human Services issued a final rule governing the implementation of the Mental Health Parity and Addiction Equity Act. At the time, the Parity Implementation Coalition, a group that represents patients and providers of addiction and mental health treatment, offered muted praise for the new rules that apply to managed care plans, the Children’s Health Insurance Program (CHIP), or to alternative benefit plans, such as the new Medicaid expansion plans that some states are implementing under the Affordable Care Act.

The coalition is pushing the federal agencies to issue the rules for these entities by May 8.

**Complex history**

Long a goal of advocates of equity in the treatment of patients with mental health and substance abuse disorders, the mental health parity rules were complicated by history. Congress passed the mental health parity act in 2008 and President Bush signed the act into law in October 2008.

The Affordable Care Act was passed and signed into law in March 2010 and the ACA removed all annual and lifetime spending limits and eliminated the rules that allowed health plans to reject applicants with pre-existing conditions.

By eliminating these rules, the ACA complicated federal efforts to write new rules governing mental health parity.

Essentially, the parity law and the rules issued in November seek to end discrimination against those seeking treatment for mental health and substance use disorders by requiring insurers to cover mental and physical health equally, according to the American Psychological Association (APA). Under the law, insurers may no longer arbitrarily limit the number of hospital days or outpatient treatment sessions, or assign higher copayments, deductibles, or out-of-pocket spending limits for those patients needing services of a psychologist or other mental health provider, the APA said. The rules also ensure mental health coverage for in-network and out-of-network services.

Ideally, the law will lead the health system to treat the whole person, both mind and body, the APA says.
may suggest long-term care insurance, Kantor says. “But while long-term care insurance covers treatment for brain injuries, it doesn’t cover mental health care. Therefore, long-term care insurance is appropriate for many people, but there is not a corresponding product for people who are mentally ill.”

**Medical necessity**

That’s why the medical necessity argument is crucial for the insurance industry. “That’s the fight I have every day,” Kantor says. “When the facility or the people treating the patient say a patient needs another 10 to 15 more days of inpatient care, but insurers won’t pay, that’s a shortsighted care decision. If a mental health or substance abuse patient is sent home too early, you have the revolving door problem. Patients want to get well and get on with life. But insurers just want to contain costs.”

For Andrew Kolbasovsky, PsyD, the director of provider group clinical management for Emblem Health, the mental health parity rules are an opportunity for health plans to provide more and better behavioral health services to all members. Based in New York City, Emblem Health has 2.8 million members in New York state.

“The rules are a very good thing,” says Kolbasovsky, a psychologist and author of *A Therapist’s Guide to Understanding Common Medical Problems: Addressing a Client’s Mental and Physical Health*, published by Norton Professional Books in 2008. “There is so much more health plans can do to enhance behavioral health care. These patients need case management to help them better manage their mental health and physical health outside of the doctors’ office and away from the hospital.”

**Cooperation is key**

One way health plans can deliver better care to patients needing mental health and substance abuse care is to put behavioral health providers in offices with primary care physicians.

with primary care physicians, he recommends. Doing so allows primary care and mental health providers to identify patients in need of mental health care and collaborate on treatment.

“In our patient-centered medical homes, we have behavioral health providers working closely with primary care physicians where they can provide screening and treatment services when they are needed,” he says.

He often hears from medical groups that Emblem contracts with that more needs to be done to manage patients with behavioral health problems. “Maybe these patients have psychiatric problems or are substance abusers, or they might need help finding appropriate housing or struggle financially,” says Kolbasovsky. “All of these issues are barriers to care that get in the way of a doctor’s ability to manage the medical conditions of these patients.”

**Navigating the system**

Patients with mental health conditions or who are abusing drugs or alcohol also may not understand their health care benefits and so may use the health system inappropriately by visiting the emergency room frequently instead of seeking care from a primary care physician, he adds.

“We have to help these patients navigate the health system, especially those who have chronic psychiatric or medical conditions,” Kolbasovsky says. In fact, many patients who are diagnosed with schizophrenia or bipolar disorder also have diabetes, asthma, and heart conditions, all of which drive up health costs, he adds.

When behavioral health providers are located in offices with primary care physicians, they can help these patients manage their behavior by helping them get more exercise, eat a more nutritious diet, and lose weight if necessary, he says.

“Mental health providers have a background in helping people change behavior, which is important when managing patients with chronic medical conditions. The more these providers work in primary care settings, the more influence they can have on patient outcomes,” he says.

Once health plans implement the mental health parity rules, they will begin to see that providing more care to patients with mental health and substance abuse disorders is likely to improve patient outcomes and may help plans control medical-surgical costs as well, Kolbasovsky says.
As administrator of the Centers for Medicare & Medicaid Services from 2001 to 2004, Thomas A. Scully oversaw a long list of reforms. He led charges to change the name of the agency, overhaul Medicare Advantage, launch Medicare Part D, and introduce a series of quality reporting requirements for hospitals, nursing homes, home health agencies and dialysis centers.

He didn’t, however, create a bundled payment system for post-acute care — a move he would now like to see.

Known for his transitions between government and the private sector, Scully today sees managing the money spent on post-acute care as a huge business opportunity. He has helped found a company that promotes a model in which third-party, PBM-like companies would manage a patient’s move from the hospital to a nursing home or other post-acute setting.

CMS launched pilot projects on bundled payments for post-acute care in January, and Scully’s NaviHealth is participating. But CMS could have done a better job of structuring the payments, he says, and he predicts that the road to change may be long. Convincing health plans may be easier for now, he believes. “There is no bureaucracy involved in going to a health plan and saying, ‘Hey, we guarantee we are going to lower your post-acute care costs by 2%, and we think we’ll lower them by 15%, with better outcomes,’” he says.

Scully is chairman of NaviHealth, which he founded in 2011; senior counsel at the law firm Alston & Bird; and a general partner at Welsh Carson Anderson & Stowe, the private equity company that backed NaviHealth. In addition to running CMS for George W. Bush’s administration, Scully served as deputy assistant to George H. W. Bush and as an associate director of the Office of Management and Budget during that administration. Scully worked for five years with Slade Gorton, a Republican senator from Washington.

He also has served as president and CEO of the Federation of American Hospitals, was a partner at Patton Boggs, and worked with the law firm Akin Gump Strauss Hauer & Feld. Scully received his bachelor’s degree from the University of Virginia and his law degree from Catholic University of America. He spoke recently with Managed Care contributing editor MargaretAnn Cross.

**MANAGED CARE:** The New York Times Magazine ran a pretty comprehensive article about you and NaviHealth in October (“The President Wants You to Get Rich on Obamacare,” Oct. 31, 2013). What was the response?

**Thomas A. Scully:** You have heart failure, obviously, when the New York Times calls, but it turned out OK. The reporter was very thorough and fair. The reaction has been positive.

**MC:** You explained that as you explored business openings created by health care reform, the post-acute care market stood out to you as the biggest opportunity.

**Scully:** The post-acute world is very understructured and very undermanaged. The focus of managed care plans has been much more on the pre-acute and acute sides than on the post-acute side. Plans are trying to create incentives that lower hospitalizations and the overall net cost of care. When you talk about post-acute care, you get a...
blank stare. Some plans have done a very good job, but most of them acknowledge that it’s not a big area for them. If somebody comes out of the hospital after a stroke, they can go to rehab or a nursing home or home health. There’s no incentive to look at the overall quality of care or the cost. Inevitably CMS is going to have to go to a bundled payment for post-acute care, much as it did for hospitals with DRGs. That’s what’s coming.

**MC:** And that’s why you started the company?

**Scully:** Yes. But it’s going to take CMS longer than I had hoped to get there. It’s going to take three or four or maybe five years as opposed to what I thought when I got started, which was two. So we have focused on developing the product and selling it to managed care plans as a subcapitation, post-acute care product where we can say we will lower your costs for managed care.

**MC:** What was the initial concept?

**Scully:** I thought that if the time had come for CMS to do a post-acute bundled payment for services, let’s try to get ahead of that trend. I really started thinking about the opportunity. Seventy percent of the population in Medicare is still fee for service, and there are a lot of reasons for Medicare to operate a lot more efficiently than it does. That was the original idea, and I found this small IT company in Nashville that had a great tool to build it on. It was called SeniorMetrix, and had been doing the infrastructure for Kaiser’s post-acute management for years, and for Scripps Health and a couple of other small health plans, too. As I got into trying to build out SeniorMetrix into a broader company, I discovered that the reality was that it was going to take CMS years to restructure its payment system and go through all of the necessary demonstration programs and processes.

**MC:** So managed care plans became your first customers, rather than hospitals or Medicare?

**Scully:** We are doing a bunch of Medicare demonstrations with acute-care hospitals, but that is going to take a while to develop. We are working with hospitals, too, in the short term. But health plans don’t have to follow the rules that fee-for-service Medicare does; they can just become more efficient. Working through a fee-for-service model at CMS is much more difficult, unfortunately. So we are adjusting to reality.

**MC:** What do the bundled payments look like in the pilot projects?

**Scully:** We are involved in five demonstrations that started January 1. My frustration is that we spent a lot of time with CMS people when they were developing it, and they should have designed it a little differently. In the demonstration program, the hospital has to take the entire bundle — from the day the patient walks into the hospital to the day he gets out of post-acute care. That scares a lot of hospitals. They don’t want to do it. CMS should have broken out the post-acute part into a separate bundle. They did a bundled payment for nursing homes and home health agencies, but it doesn’t start until the patient gets to that setting. So if you are a home health agency or a nursing home, you can take all the risk once the person gets to you. But if a patient walks out of a hospital, determining from the get-go which is the most efficient place to go is step one. Should he be in home health, a nursing home, rehab? That initial decision drives a lot of behavior. CMS could have done the bundles differently, but we are doing everything we can to make them work. A more rational way to do it is to come up with a post-acute bundled payment that looks more like a Part D Medicare payment, where you have kind of a PBM function, a convener for risk for the post-acute side.

**MC:** Would you explain a little more?

**Scully:** The right thing to do is to come up with 55 or 60 post-acute DRGs, like on the inpatient side, and say, “If a patient comes out of a hospital with the following diagnosis, then we are going to use the post-acute convener, like PBMs. The post-acute bundle should be just like what Medicare does for drugs. We give a third-party convener the money and say, “You manage this.” Years ago, I was the president of the Federation of American Hospitals, the for-profit hospital trade association. I knew from that point that while there are some exceptions, most hospitals do not manage post-acute care. They just don’t see managing nursing homes and home health as their core function. Some hospitals may want to do it, but most don’t. The missing ingredient is somebody who is basically a care manager to take continued on page 38
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the risk and manage this, to drive efficient services across the different settings — which are basically home health, nursing homes, and long-term acute care hospitals. The goal is to have the right patient in the right place to get the best outcomes.

**MC:** NaviHealth starts working with patients when they are in the hospital?

**Scully:** In our best models with managed care plans, we have a nurse practitioner or a nurse in the hospital talking to the patient on the second day of a hospitalization, saying, “Mrs. Jones, you’ve had a stroke, and here’s our plan for the next 60 days. You need to go to a rehab hospital for X number of days and you can go home after that, or you can go to a nursing home for Y days and get Y therapy.” We have a very detailed data-driven methodology that tells us based on the treatment histories of 800,000 prior clients where a patient should go and for how long.

**MC:** Are Medicare Advantage plans your biggest market?

**Scully:** Commercial plans have post-acute spending on nursing homes, but our business is heavily focused on Medicare Advantage because the senior population uses post-acute services so much more than the commercial population. They are the ones who are getting hip replacements and having strokes. It happens in commercial populations, but it’s a much smaller spend for the client.

**MC:** What is your pitch to managed care executives?

**Scully:** You are not as aware of what’s going on with your rehab hospitals, your nursing homes, your long-term-care hospitals, and your home-health utilization as you probably could be. For example, health plans may have 1,800 nursing home days per thousand per year in their Medicare population. Our long-term clients have 600 to 1,000 days per thousand. We have been working with Kaiser — as SeniorMetrix — for 12 years. I think we can go in and manage post-acute care better. Most nursing home patients who are on fee-for-service Medicare go to a nursing home for 20 days because that is what is covered in full. The same thing happens with managed care plans. But frequently a patient who has a minor stroke can be in a nursing home for 12 days and then go home, where they get better care and better outcomes and they are happier patients. So our pitch is: “Tell us what you are spending on your post-acute care and your Medicare managed care plan today, and we are very comfortable that we can come in and improve your star ratings, improve your performance, and raise your patient satisfaction. We’ll guarantee you that we’ll lower your costs by 2%, and if we save more, we’ll do a gain share and split it with you.” We believe that we can lower costs as much as 20%.

**MC:** That’s the agreement?

**Scully:** Every contract is different. When we take full risk, it would be with a small plan with 15,000 or 20,000 members. For a bigger plan, it’s usually some kind of hybrid risk share. So every model is different, but we always look at the percentage that we save. There’s generally not an upfront fee.

**MC:** The range of savings has been from 2% to 20%?

**Scully:** It depends on what you are measuring. If you look at Kaiser, we have helped reduce their nursing home utilization significantly over the past 12 years. One very large national health plan gave us a state a year ago. We really focused on nursing homes and mental health and lowered their spending by over 15%. Various plans have different levels of how much they are willing to give up the reins, but we have yet to find a plan where we couldn’t reduce spending by close to 10%.

**MC:** When you were at CMS, you encouraged people in the private sector to consider public service. Why?

**Scully:** I spent 16 years in the government, and I enjoyed every minute of it. I’m not sure how my family felt about it — the reimbursement’s not as good. But I loved my time at CMS, and I liked my time in the White House. I think it’s great that people do public service. But I also think that people in public service would like to work in the private sector. If you are regulating hospitals, it’s important to spend some time working in a hospital so you understand the impact of the regulations. It doesn’t mean that you are going to agree with them, but it’s important to understand the lives of the people you are regulating.

**MC:** How did having industry experience inform your perspective when you were at CMS?

**Scully:** I happened to like the Tenet guys, but I had a huge regulatory fight with Tenet when I was at CMS. I wasn’t easy on my former federation members; some of them are still mad at me about it. But the ones that are good actors, I treated fairly, and the ones who were not treating the public programs well, I didn’t go easy on. That’s the way it should
be. When I ran the for-profit hospital association, hospital companies could go to Capitol Hill and say, "We're starving, we're doing terribly," and then would fly to New York and tell investors how great things were — "so buy our bonds and stocks." If people are underpaid, the government should understand and pay them more. If they are overpaid, they should also understand that and pay them less.

Measuring quality differences and paying people differently is a good thing.

MC: You brought others from industry into CMS. Can you give us some examples?

Scully: I thought it was very important to get Wall Street information and CMS's point of view and give it to the agency, so I hired a guy who was a Wall Street analyst. He stayed long after I was gone. He came in basically just to consolidate the Wall Street investor reports on the health care industry for the people at CMS. Whether they are nonprofit or for-profit, companies can't mislead their bondholders or shareholders. They have to tell the truth. Consolidating that information so that regulators could tell whether a nursing home or a hospital or a health plan was underpaid or overpaid is important. Also, when I got there, nobody understood kidney dialysis very well. I had been on the board of a dialysis company, so I hired a guy from a dialysis company and it improved the understanding of the dialysis sector. It didn't mean we were nice to them or mean to them, it just meant that we had a much better understanding of what they were doing.

MC: That sounds like something you are proud of. You were brought in as a reformer.

Scully: I am very proud of it. I changed the name the first week I was there to CMS, the Centers for Medicare & Medicaid Services. The Health Care Financing Administration was perceived to be bureaucratic. I spent a lot of time coming up with patient satisfaction surveys and hospital quality measures. I used to say that the chairman of the surgery department at Harvard gets paid the same for surgery as the worst doctor in Boston. That's not a rational setup, so measuring quality differences and paying people differently is a good thing. CMS is doing a lot more of that now, but we started that back in 2003. When I first got there, there was no such thing as the Hospital Consumer Assessment of Healthcare Providers and Systems, there were no patient satisfaction surveys. We standardized those, and they are now part of how providers get paid.

MC: What else are you proud of?

Scully: I am very proud of Medicare Advantage, which used to be called Medicare+Choice. When I got there in 2001, we had 3% of people in the Medicare risk program, and now we've got over 30%. A lot of that is because of the redesigning we did in 2003. The fundamental problem with fee-for-service Medicare is that it fixes prices. When every hospital gets paid the same, it just doesn't work. So I was committed to trying to get people out of single-payer, fixed-price health care and into capitated health care. And I went back into the government in 2001 mainly to get a drug benefit passed. We spent a lot of time designing Medicare Part D and getting that passed. I am very proud of both of those.

MC: Why was the drug benefit so important to you?

Scully: Reagan passed the Medicare Catastrophic Coverage Act with a drug benefit in '88, with a Democratic Congress. It was a bipartisan bill, and it was repealed before it started in the summer of '89. When I was in the White House in 1989, my first job with President Bush was trying to keep that law from being repealed, and we failed. I always thought it was crazy to have an insurance benefit with no drug benefit, especially for low-income seniors, so I spent a lot of my time outside of the government thinking about that. I worked for Bush senior for many years. I didn't really know President Bush 43, but when he won and came in, he asked me to run CMS. When I agreed to do that, I told him my primary goal was to design a drug benefit and get it through Congress. Unfinished business, I guess. A lot of people thought we'd never do that. They thought we weren't serious about it. But seniors needed a drug benefit, especially poor seniors. Medicare Part D was a compromise. I personally would never have subsidized wealthy seniors, but to get the bill through, we had to do that.

MC: What do you wish you had done differently at CMS?

Scully: It would take forever to answer that question. But when I look back, there are some things that you spend a lot of time on, so you lose sight of other things. Post-acute bundles are a perfect example. If only I had thought about it at the time.

MC: Thank you.
Biotechnology’s Reach Extends Author’s Grasp

Can an injectable biologic really replace a delicate surgery for treatment of Dupuytren’s disease?

By Jack McCain

Editor’s note: In health care, we deal in numbers so often that unless you are the treating physician, you sometimes cannot appreciate the quality of the personal experience that a successful or failed treatment might have. Here, an exceptionally articulate and knowledgeable patient describes how Xiaflex made a world of difference in treating hand-disabling Dupuytren’s disease. A professional writer, Jack McCain is a regular contributor to Managed Care. His fingers are important to us.

Some time in the late 1990s, my right hand began looking rather gnarly. I attributed its rugged appearance to various leisure-time activities: tennis, gardening, retrieving stones from the woods and fields and stacking them into rough walls. Then my ring finger began to bend down, and it couldn’t be straightened without applying painful pressure. My primary care physician said the palm and finger certainly looked interesting but he had no idea why. A short time later, during vacation, I showed my hand to a semiretired physiatrist.

As a physiatrist, he dealt with a considerably older patient population, mostly elderly male veterans. It took him just a few seconds to identify the problem. First, he ruled out rheumatoid arthritis. Then he asked me to try to flatten my hand on the picnic table. Seeing that I couldn’t satisfactorily perform the “tabletop test,” he said I had Dupuytren’s disease (see “Fast Facts About Dupuytren’s” on page 42) and told me that it probably would get worse and that I’d need surgical repairs.

Eventually it became difficult or impossible to

Jack McCain is a freelance medical writer and editor in Durham, Connecticut.

Author’s left hand, with (A) zigzag scar from open palmar fasciectomy performed in 2004 to correct contracture of the ring finger; (B) site of Dupuytren’s cord into which Jennifer Wolf, MD, injected Xiaflex in 2012, resulting in cord rupture and release of little finger contracture; (C) pit and ridge from diseased tissue not injected; (D) a Dupuytren’s nodule not injected owing to risk of tendon rupture; nodule causes slight bend in finger but does not impair function.
perform ordinary activities, such as inserting my hand in a pocket, grasping objects, and washing my face. Washing entailed the risk of poking the bent finger in my eye, which I did more than once. So in 2003, I consulted a hand specialist at the University of Connecticut Health Center, and soon she performed a delicate surgery — open palmar fasciectomy. It took her about 90 minutes to remove the collagenous cord that prevented the finger from being straightened.

Hand in a splint

By design, the procedure resulted in an open surgical wound that required daily care. At night, I slept with my hand in a splint to keep it straight. During the day, I did various exercises to restore function and strength, which were complemented by a long and tedious series of visits to a physical therapist. I experienced little postoperative pain, though my fingertips tingled unpleasantly for months, but while waiting for my PT appointments, I saw some patients in considerable pain. The next year, I went through the same routine with the ring finger on my left hand. At my last visit, my surgeon told me my disease was so active she expected me to need additional treatment eventually.

Her prediction was accurate: About two years ago, new collagen buildup became evident on my left palm, and my little finger began bending. Eventually normal function was impaired — I couldn't type well, couldn't apply shaving cream easily, couldn't play the piano more than a few minutes without discomfort. So I returned to the health center for evaluation to determine if I was a candidate for a new biologic, XIAFLEX, instead of surgery. Although I was pleased with the results of the surgeries, I wanted to avoid a third one if at all possible.

XIAFLEX (collagenase Clostridium histolyticum; Auxilium Pharmaceuticals) had been in clinical trials when I had my surgeries, but in early 2010 it was approved by the FDA for treatment of adults with Dupuytren's contracture, provided they have a palpable cord; it's a recombinant enzyme intended to break up the collagenous deposits. By this time, my original surgeon was no longer with the institution, but her successor, Associate Professor of Orthopedic Surgery Jennifer Wolf, MD, a hand specialist, said XIAFLEX would indeed be appropriate.

A few weeks later, after my health insurer had issued prior authorization and a specialty pharmacy had collected my copayment, she made three shallow injections in my palm, directly into the cord, with a very fine needle. It took about 10 seconds for all three, and the discomfort was minimal. I say this as a person with an extreme dislike of needles. She didn't inject any collagenase into or near the diseased area along the proximal phalanx because of the risk of tendon rupture at that site. She told me my hand would swell as the collagenase acted, and she wrapped my hand in gauze to protect the area that might become tender. She asked me to return the following morning so she could manipulate the injected area and break the weakened cord.

I drove home by myself, in contrast to being driven home after the outpatient surgeries with my arm in a sling and my head in the asteroid belt, and I attended to some income-generating work — in contrast to sprawling on a bed for the rest of the day while oxycodone dulled the postsurgical pain. In 2003, as the time for the first surgery neared, not knowing what I'd be able to do afterward, I declined a freelance project that might have generated $3,000 or $4,000 in badly needed income — and that decision turned out to be a "good" one.

By the time I went to bed, I had discarded the gauze. I slept well but awoke around 2 a.m. and, without thinking, stretched the fingers of my left hand. As I did, I heard a rather loud pop emanate from my hand — the sound of the cord breaking! Now very alert, I realized I had straightened all my fingers.

An octave and a third

In the morning, before leaving for my follow-up appointment, I sat down at the piano and discovered I once again could span an octave and a third (10 white keys) — an impossibility on the previous day, and for many months before that — and that I could play without experiencing the discomfort previously induced by only a few minutes of playing. I thought I was an outlier with respect to my ex-
perience with collagenase injections. When I described my experience to a former regional sales director for Auxilium at the time of Xiaflex’s launch, he told me my case sounded fairly typical. The sales director works for another pharmaceutical company now, but he says that in his 36 years in drug sales, Xiaflex stands out as the “funnest” drug he’s ever sold. That’s because positive results often are seen very quickly, to the delight of patient and physician alike.

**Dramatic results**

“Very seldom do you see such dramatic results 24 hours after a person receives a drug,” he says. “I saw hundreds of patients injected with Xiaflex. About 85% had a hand that was close to or nearly flat after the first set of injections, and another 10% needed a second set of injections.” In a small percentage, he says, the injection didn’t work the first time, possibly because the physician prepared the syringe improperly or failed to inject the drug properly, or both.

The former sales director managed a team of seven specialty sales managers in the Pacific Northwest, augmented by a group of three support personnel (reimbursement specialist, medical scientific liaison, market access director). Initially, the sales team encountered healthy skepticism about Xiaflex when calling on hand specialists, whether at teaching institutions

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**Fast facts about Dupuytren’s**

- Benign connective tissue disorder of the palmar fascia that may lead to disabling contracture of one or more fingers, owing to formation of collagenous cords along fascia
- Joints commonly affected: metacarpophalangeal (MCP), proximal interphalangeal (PIP)
- Most commonly affects people of northern European descent; about 3% to 6% of white adults will develop Dupuytren’s in their lifetime
- Other risk factors: tobacco use, diabetes, alcohol use, HIV
- Usually emerges in middle age, affecting both hands in many patients
- Diagnoses per year, U.S.: 300,000
- Surgeries per year, U.S.: 70,000
- Most common physician-reported complications in patients with **primary** disease: wound-healing complications and pain
- Most common physician-reported complications in patients with **recurrent** disease: injuries to digital nerve or artery (about 20%, vs. 2% in primary disease)
- All interventions are corrective, not curative
  - Open palmar fasciectomy — the leading surgical approach
  - Percutaneous needle aponeurotomy — office-based procedure more common in Europe than U.S.A.
  - Xiaflex — recombinant collagenase injected into cord in office-based procedure
- Famous people who’ve had Dupuytren’s: President Ronald Reagan, U.K. Prime Minister Margaret Thatcher, Scottish actor David McCallum (Man From U.N.C.L.E., NCIS), English actor Bill Nighy, Irish playwright Samuel Beckett, Scottish author and playwright James Barrie (Peter Pan), classical pianist Misha Dichter (of Polish-Jewish descent), who feared Dupuytren’s had ended his career but eventually regained virtually all his skills after surgery in 2007

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**Ranking Xiaflex, percutaneous needle aponeurotomy, and palmar fasciectomy**

<table>
<thead>
<tr>
<th>safest</th>
<th>longest-lasting</th>
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<tr>
<td><strong>1. Xiaflex</strong></td>
<td><strong>1. Fasciectomy</strong> — excises diseased tissue</td>
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<tr>
<td>1/1000 risk of tendon rupture</td>
<td><strong>2. Xiaflex</strong> — lyses some diseased tissue</td>
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<tr>
<td>Very slight risk of nerve damage</td>
<td><strong>3. Needle aponeurotomy</strong> — disrupts cord without removing any diseased tissue</td>
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<td>Bruising, skin tearing more common</td>
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| **2. Needle aponeurotomy** | **2. Fasciectomy** — a day or two |
| 1/200 risk of infection | **3. Needle aponeurotomy** — a week or so, sometimes less |
| 1/200 risk of permanent nerve damage | **3. Fasciectomy** — several months |

| **3. Fasciectomy** | **Fastest recovery** |
| 23/100 risk of wound-healing complication | **1. Needle aponeurotomy** |
| 7/200 risk of permanent nerve damage | **2. Xiaflex** — a week or so, sometimes less |
| 2/100 risk of infection | **3. Fasciectomy** — several months |
| 2/100 risk of bleeding | |
| 1/100 risk of finger amputation, owing to loss of circulation | |

Source: Keith Denkler, MD
or in private practice. We’re surgeons, we’re trained to cut — that was their general reaction. Once they saw how well and rapidly the drug worked, however, their skepticism vanished, he says.

High patient appeal reported

I wondered whether some physicians initially shied away from Xiaflex, consciously or unconsciously, because injecting collagenase is a quick office-based procedure generating less revenue in comparison with palmar fasciectomy. The sales director says that wasn’t the case, because physicians soon realized they could spend more time with other patients if they treated their Dupuytren’s patients with Xiaflex, and because patients who received Xiaflex tended to be very happy.

Further, he says, in contrast to the manufacturer’s expectation that many patients would need two or three separate sets of injections about four weeks apart, most required only one set. Making just one copayment (mine was about $700, but copayments may be considerably higher or lower, depending on the patient’s health plan) instead of three presumably enhances the drug’s appeal to patients.

My surgeon, Wolf, says that’s been her experience, too. At UConn, where her patients are drawn from the general population, she sees about 30 or 60 Dupuytren’s patients annually, compared with 150 in a previous position serving veterans. The majority of her patients receiving Xiaflex have needed only one set of injections, and she has yet to provide any patient with three sets.

“I haven’t done a Dupuytren’s surgery in a while,” she said when I recently visited her in my role as freelance writer, noting that one was scheduled for the following week. The few fasciectomies she per-

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**Dupuytren’s disease timeline**

- c 1000 BC — An Egyptian dies with Dupuytren’s contracture in the left hand, as determined by examination of the mummified remains in 2010.
- 1500s — “Curse of the MacCrimmons” is said to afflict the little finger on the right hand of renowned bagpipers on the Isle of Skye, causing their fingers to bend so deeply into their palms that they can’t play their instruments.
- 1614 — A Swiss doctor, Felix Plater, describes a stonemason whose left ring finger and little finger were contracted into his palm, but he incorrectly ascribes the condition to a problem with the tendons.
- 1777 — The eminent English surgeon and anatomist Henry Cline Sr. describes finger contractures caused by the fascia (as opposed to tendons); he later proposes a surgical approach — palmar fasciectomy.
- 1822 — Astley Cooper, a student of Cline’s, describes a surgical treatment for the condition now known as Dupuytren’s contracture (which just as easily could have been named Cline-Cooper’s contraction).
- 1831 — The famous French anatomist and surgeon Baron Guillaume Dupuytren presents a lecture, in which he, like Cline, reports that the fascia is the cause of the contractures. During his lecture he performs an open fasciectomy on a 40-year-old coachman.
- 1971 — “Enzyme fasciomy” using trypsin and hyaluronidase is employed during surgery to treat Dupuytren’s but without producing satisfactory long-term results.
- 1972 — A specialized fibroblast, the myofibroblast, is implicated in the pathogenesis of Dupuytren’s disease.
- 1980s — At Stony Brook University Medical Center, Lawrence Hurst, MD, and Marie Badalamente, PhD, begin investigating novel noninvasive treatments for Dupuytren’s contracture.
- 1996 — In vitro study by Hurst, Badalamente, et al. suggests the possibility of using collagenase injections to treat Dupuytren’s.
- 2007 — Start of CORD I (NCT00528606), a phase 3 trial comparing collagenase injections vs. placebo in 308 patients with Dupuytren’s contracture (Hurst 2009).
- 2009 — Hurst, Badalamente, and Edward Wang, MD, receive the Orthopaedic Research & Education Foundation Clinical Award for two decades of research suggesting that collagenase injections could be used to treat Dupuytren’s contracture.
- 2010 — FDA approves Xiaflex (collagenase Clostridium histolyticum) for treatment of Dupuytren’s contracture in patients with a palpable cord.
- 2013 — Final data collection for CORDLESS (NCT00954746), a long-term assessment of the durability of the response to collagenase injections in patients who received at least one injection of collagenase in trials sponsored by the manufacturer, Auxilium Pharmaceuticals.
- 2013 — University of Alberta begins recruiting 300 patients for a trial (NCT01776892) comparing collagenase injections with needle aponeurotomy; study also will compare the combination of aponeurotomy and collagenase injections with each individual treatment; it is expected to be continued until 2020 to allow long-term evaluation.
forms today are for patients with recurrent disease or those whose contracture is caused by a retrovascular cord (on the dorsal side of the fascia and hence not palpable on the palm). On occasion, she performs a fasciectomy for the rare patient who insists on the surgery out of a desire to have all the diseased tissue excised to reduce the risk of recurrence. For the moment, Wolf thinks recurrence rates after fasciectomy or collagenase injections are similar, but she’s eager to see long-term recurrence data published for XIAFLEX to support her perception.

On the other hand

As an academician, Wolf says the chief drawback to using injectable collagenase is that it denies her the marvelous opportunity afforded by open fasciectomies to teach students and residents about the intricacies of hand anatomy. Conversely, she says, administering XIAFLEX enables her to teach others about an “amazing new technology.”

Wolf says patients who want to make sure they receive XIAFLEX if it’s appropriate should consult surgeons with a thorough understanding of hand anatomy and ask them about their familiarity and experience with XIAFLEX and whether or not they have completed the training program required under the FDA’s Risk Evaluation and Management Strategy for XIAFLEX.

Some physicians may not yet be familiar with XIAFLEX because it got off to a slow start.

The former market access director who worked in the Northwest said XIAFLEX had to overcome a unique set of challenges when the product was launched. Before the availability of a product-specific J-code for XIAFLEX, physicians had to submit lots of documentation to support commercial prior-authorization requests and eventual claim to payment. Even Medicare required billing specification to support reimbursement for a product-unlisted J-code and an unlisted procedural CPT code. In addition, there was the question of how to bill for the post-injection manipulation — a lot of hassle.

Another hurdle that physicians faced was determining how to acquire the drug. Did they want to emulate oncologists and engage in “buy-and-bill,” laying out a lot of their own money up front, or did they want to have their patients go through specialty pharmacies? As orthopedic and plastic surgeons, the physicians lacked familiarity with buy-and-bill and prior authorization, and so did their staffs.

Yet another formidable barrier was that Auxilium was trying to introduce a foreign concept to surgeons: “We were telling surgeons to put down their scalpels and pick up a syringe,” the former market access director says. “It wasn’t easy to change their approach.”

Moreover, although there’s a substantial population in the U.S. with Dupuytren’s, initially far fewer patients sought treatment with XIAFLEX than the company expected, he says. So Auxilium turned to direct-to-consumer advertising in places with an older population that includes a substantial percentage of people of northern European descent, good payer coverage, and a solid “injector base,” chiefly hand specialists.

Greater Pittsburgh, where I was born and raised, is a good example of a community meeting these criteria, and Auxilium sometimes runs full-page ads in the Pittsburgh Post-Gazette to alert readers to the availability of XIAFLEX. The ads feature a large photograph of a hand with a crooked ring finger and a discernible cord, presumably to catch the attention of people who recognize the condition but don’t know its name.

Best approach

Keith Denkler, MD, a clinical professor of plastic surgery at the University of California – San Francisco with a private practice in Larkspur, Calif., was one of the first physicians in the U.S. to use XIAFLEX after its FDA approval, and to date he’s used 400 vials to treat patients with Dupuytren’s. He also was the first physician on the West Coast to perform percutaneous needle aponeurotomy, having performed over 3,500 since learning the procedure in 2005 through a training program in Paris. Although he’s a paid speaker for Auxilium, he doesn’t steer patients toward XIAFLEX. Instead, he says, he helps patients determine the best therapeutic approach by asking them which factor they regard as most important (see “Ranking XIAFLEX, Percutaneous Needle Aponeurotomy, and Palmar Fasciectomy” on page...
Today he treats about half of his Dupuytren’s patients with needle aponeurotomy and half with collagenase injections, sometimes using aponeurotomy and Xiaflex in combination (an approach that isn’t an FDA-approved application for Xiaflex).

**Unorthodox approach**

Only a small percentage of Denkler’s Dupuytren’s patients undergo fasciectomy — in his office, under local anesthesia (Denkler 2005) — and only for primary disease. If a patient previously treated with fasciectomy presents with recurrent disease, Denkler uses Xiaflex the second time because he likes the way the enzyme breaks up scar tissue. He said he shuns fasciectomy for recurrent Dupuytren’s because the risk of serious complications (digital artery and nerve injuries) is about 10 times as high in patients with recurrent disease as in primary disease, roughly 20% vs. 2% (Denkler 2010).

When Denkler uses Xiaflex, he uses the whole vial instead of discarding unused collagenase. Since this involves five or six injection sites and sometimes more, instead of the usual three injection sites, he numbs the area prior to injection. Although this is not an FDA-approved application for Xiaflex, he’s confident in his unorthodox approach: “So far I’ve used 400 vials without hitting the nerve and without tendon rupture or infection,” he says.

“Spreading out the injections makes it less likely to dissolve deep in any one area and cause tendon injury,” he explains. It is his first choice for patients who have already had surgery since, he says, it dissolves scar tissue and Dupuytren’s without injuring neurovascular structures containing a different type of collagen that Xiaflex does not affect. He also recommends Xiaflex as an excellent first step for severe proximal interphalangeal (PIP) contractures (Denkler 2012).

**Radiation therapy**

Denkler expects Xiaflex to gain favor among managed care organizations for treatment of Dupuytren’s because of its diminished complication rate, which he says should result in savings. He also says MCOs should be alert to increased use of radiation therapy to treat Dupuytren’s. Some patients with early disease but no impairment are so anxious about experiencing any loss of function that he refers them to a therapeutic radiologist; the expensive treatment seems to quiet the disease process in about 1/3 of patients. The former managed care director says that from a payer’s perspective, the cost of collagenase injections is approximately equal to that of fasciectomy plus physical therapy, but from the patient’s perspective, taking quality of life and lost income into consideration, Xiaflex often is the clear winner. Overall, Wolf and Denkler both agree that Xiaflex is a welcome addition for treating Dupuytren’s contracture and will lessen the need for invasive hand surgery with its long rehab and increased complication risk.

**Sources cited**


Compliance Critical Factor In Heart Treatment’s Future

A bigger portion of the population is expected to have cardiac disease but live longer, and researchers argue for stopping it before it shows

By Frank Diamond
Managing Editor

The costs of heart disease will go up substantially in the next decades. Using data from the National Health and Nutrition Examination Surveys to make the forecast, a recent study in *Health Affairs* (http://tinyurl.com/heart-data) predicts that the average 10-year risk of heart disease will rise about 15% for men and 9% for women by 2030, from a baseline of 12.7% and 6.8% in 1991.

Compliance, or lack of it, will play a huge role. The study says, “Pessimistic assumptions of 50% compliance with treatment resulted in 3 million additional cases of cardiovascular disease in 2030, compared to base-case assumption of 75% compliance.”

That’s a spread made big by the somewhat unpredictable factor of compliance with prevention methods. Take, for instance, cholesterol.

Data from the Centers for Disease Control and Prevention (http://tinyurl.com/CDC-data-brief) show that after improving in the last decade, total cholesterol levels remained constant over the last few years. The CDC would also like to see about 86% of Americans screened every five years. That number has remained stubbornly at about 70% since 1999.

There is some good news in the CDC data. Fewer Americans had low levels of HDL in 2010-2011 than in 2009–2010. Still, not quite what health officials want to see. “Although the percentage of adults aged 20 and over with high total cholesterol declined substantially from 1999 to 2010, there was no change between 2009–2010 and 2011–2012. There was also no change in the percentage of adults screened for cholesterol.”

Cholesterol screening rates, percentages, 2011-2012

<table>
<thead>
<tr>
<th></th>
<th>Both sexes</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic white</td>
<td>71.8%</td>
<td>70.6%</td>
<td>72.9%</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>71.9%</td>
<td>66.8%</td>
<td>75.9%</td>
</tr>
<tr>
<td>Non-Hispanic Asian</td>
<td>70.8%</td>
<td>70.6%</td>
<td>70.9%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>59.3%</td>
<td>54.6%</td>
<td>64.2%</td>
</tr>
</tbody>
</table>

NOTE: Screened for cholesterol is having cholesterol checked within the past 5 years.

Percent who had low HDL cholesterol, 2011–2012

<table>
<thead>
<tr>
<th></th>
<th>Both sexes</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Hispanic white</td>
<td>17.1%</td>
<td>9.3%</td>
<td>12.7%</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>19.1%</td>
<td>7.8%</td>
<td>14.3%</td>
</tr>
<tr>
<td>Non-Hispanic Asian</td>
<td>24.5%</td>
<td>5.1%</td>
<td>21.8%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>32.6%</td>
<td>11.3%</td>
<td>17.1%</td>
</tr>
</tbody>
</table>

NOTE: HDL is high-density lipoprotein. Low HDL is <40 mg/dL.
Give credit to anybody willing to make a prediction about health care these days, even to companies in the prediction-making business. Moody's, the bond rating corporation, says that medical utilization could increase this year, but does so with plenty of qualifications. Stephen Zaharuk, a senior vice president, notes that the Affordable Care Act complicates everything.

"First, there are many more individuals who had previously been without insurance coverage who may require substantial medical care," says Zaharuk. "The Obama administration released data indicating that the population enrolled in exchanges’ insurance plans is older than anticipated, which will also likely lead to increased utilization."

The insurance companies may have anticipated higher costs as a result of expanded coverage as required by the law. However, as more people use the system, there will be more volume, and with that, more challenges to manage care effectively.”

Zaharuk points out that setting insurance premiums requires forecasting. "Most policies run on a calendar year basis. The health insurance companies made their assumptions for utilization and medical costs for 2014 several months ago and now have to manage toward them.”

Beyond the ACA, there are other reasons we may see increased medical utilization. "The trend for the last four years has been lower than in previous years," Zaharuk notes. "While the administration credits the ACA for this trend, many economists say the lower cost results from a combination of a struggling economy and changes in the benefits...

Expanding Medicaid rolls might not mean higher utilization

The rickety launch of the Affordable Care Act includes at least one positive development for poor Americans. There has been a huge surge in Medicaid rolls, with about 6.3 million more people deemed eligible as of mid-January. Adults at or below 138% of the federal poverty level (FPL) can now sign up; before the ACA’s passage, it was 106%.

Having more Medicaid enrollees will increase medical utilization somewhat because there are people who have forgone needed care in the past, says Ann O’Malley, MD, a senior fellow at Mathematica Policy Research. How much use increases will vary by state, as some states have decided to expand Medicaid eligibility while others have not.

The eligibility for parents and other adults in 21 of the nonparticipating states “will remain below 100% of the [federal poverty level, FPL], with eligibility levels below half of poverty in 14 states,” according to a study by the Kaiser Family Foundation (http://tinyurl.com/Medicaid-surge). “Overall, the medium eligibility level for parents in these states will be just 47% of the FPL...”

Median Medicaid income eligibility limits for adults as a percentage of the FPL, January 2013 and January 2014

<table>
<thead>
<tr>
<th>States:</th>
<th>Expanding Medicaid</th>
<th>Not expanding Medicaid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parents</td>
<td>106%</td>
<td>48%</td>
</tr>
<tr>
<td>Other adults</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Parents</td>
<td>138%</td>
<td>138%</td>
</tr>
<tr>
<td>Other adults</td>
<td>47%</td>
<td>0%</td>
</tr>
</tbody>
</table>

FPL: Federal poverty level
structure, mostly in the employment sector. In particular, employees are seeing lower benefits in the form of higher deductibles and higher copayments.”

**Reinhardt’s take**

One of the economists watching medical utilization is Uwe E. Reinhardt, PhD, professor of economics and public affairs at Princeton University. He thinks utilization will remain flat.

“There could be a short-lived blip for some elective procedures — it was reported to have occurred in December; but I would not make anything of it,” says Reinhardt. “Some people on Wall Street argue that faster economic growth will drive up utilization again this year. I would doubt it. First, the growth won’t be that much faster. Second, other forces (e.g., high cost sharing) may continue to depress utilization. I think that utilization has not only been flat, but that in some sectors it has been down — even in Medicare.”

Zaharuk agrees that a lot hinges on how the economy does, but if it grows, “there is pent-up demand for medical services from people who have put off elective surgeries and who have put off starting families. Now, with a general sense that the economy is improving, they may feel a little more comfortable in changing their medical spending pattern.”

Ann O’Malley, MD, a senior fellow at Mathematica Policy Research, says that any uptick in utilization will come from the roughly 5% of the population in the individual market. “There’s a whole lot of transition in the individual market and there always has been.” She adds that “People in the individual market tend to be a younger, healthier population, or to be between jobs.”

They are not the sort of people, in other words, who would get a hip replaced now because they’re worried about what it might cost a year from now. In addition, she cites the uncertainty about just what insurers need to include in plans to meet federal standards for coverage. “Given all these moving parts, I think it’s premature to say that all of a sudden utilization is going up because people are worried about not getting coverage for certain things.”

Expansion of Medicaid under the ACA might increase utilization as people gain coverage and start to seek care. (See “Expanding Medicaid Rolls Might Not Mean Higher Utilization” on page 47.) But such use will vary a lot by state.

“So you’ve got states like Texas that has decided not to increase the income threshold for Medicaid eligibility to 138% of the federal poverty level that is allowed under the ACA,” says O’Malley. Texans who continue to lack insurance will probably postpone care until they can’t postpone it anymore.

“If they have a chronic condition like congestive heart failure, or diabetes, or obstructive lung disease, they tend to put off care until they have a horrible exacerbation and then they end up in the emergency room or they end up in the hospital. The literature strongly supports that if people are uncovered, and continue to be uncovered in states that don’t expand Medicaid, they’re just going to enter the system in a sicker state. The disease will be more advanced.”

Like Reinhardt, she wouldn’t be surprised to see utilization in Medicare fall rather than rise. “The acceleration of spending has leveled off in the last couple of years. There’s a lot more pressure on hospitals to make sure they do a really good job at the time of patient discharge to transition people back into the outpatient setting so that patient doesn’t wind up being readmitted. Providers are getting these types of signals and that partly accounts for the decline in Medicare spending.”

**Outlook for Medicare**

Zaharuk isn’t totally convinced. “The media have stoked up fears about more people coming into the system leading to a shortage of doctors,” he says. “That may get people who would normally put off an appointment to get an appointment now. In addition, the employer mandate starts in 2015, and people are hearing stories about the potential of losing their coverage.”

Even so, Zaharuk does not think there will be a sudden major shift in the utilization pattern. Noting that behavioral changes take time, he says, “Utilization will trend up gradually, but there will be pressure on insurers to manage this increase within reasonable limits to match their initial financial assumptions.”

Expect Medicare utilization to stay flat, says Ann O’Malley, MD, of Mathematica Policy Research. “There’s a lot more pressure on hospitals to make sure they do a really good job at the time of patient discharge to ensure that the patient isn’t readmitted.”

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One of the most rapidly evolving areas of genetic testing is for germline mutations — changes in the DNA of egg or sperm cells that are passed on to offspring, potentially popping up in a person’s life as a heritable condition.

The test for breast cancer susceptibility in the **BRCA1** and **BRCA2** genes is probably the most widely recognized germline mutation test. Angelina Jolie’s recent prophylactic double mastectomy as a result of this test gave a real boost to hereditary breast cancer testing.

**More testing**

“There has been an increase in **BRCA** testing since the Angelina Jolie news article” last April, says David Finley, MD, Cigna’s national medical officer for enterprise affordability and policy. “We did not anticipate that the interest would be sustained. I thought it would have peaked two or three months after the news, but it has continued,”

The most visible development in germline testing is for hereditary cancers. Tests involving individual genes have grown to panel tests incorporating multiple genes, in some cases more than 25. Some of these tests provide one-stop shopping, covering multiple hereditary cancers.

The banner on the home page of Myriad Genetics, the commercial lab with the original **BRCA** test that was the subject of the Supreme Court case on the patentability of genes (decision: no patents), blares “hereditary cancer — know your history, know your risks,” touting its 25-gene test. Other commercial laboratories, such GeneDX and Ambry Genetics, offer similar tests.

The developments with hereditary cancers are one example of the expansion of genetic testing on all fronts as costs fall, new biomarkers are discovered, and the power to accurately detect alterations increases.

While these advances offer hope in personalized medicine, they far outstrip the ability of clinicians to effectively integrate genetics into their practices, posing numerous problems for health plans.

**Three challenges**

In September 2013 Cigna initiated a clinical management program for genetic testing that addresses three very important challenges: improving consumers’ understanding of genetic testing, ensuring appropriate utilization, and helping physicians incorporate genetics into their practices. Cigna has become the first national health plan to use genetic counseling as an integral part of genetic testing.

Pretest counseling by a certified genetic counselor is required before test precertification for breast, ovarian, and colon cancers and a cardiac condition known as long QT syndrome. Cigna has contracted with Informed DNA to provide genetic counselors to referring physicians and patients, locally or by phone.

The program is a first step in responding to widespread challenges in genetic testing. “About 80% of the tests that go through our review program do not require genetic counseling,” says Finley. “There are many genetic tests that can be done, but most have very limited clinical impact because we do not know what to do with the results. The three cancers that we link to genetic counseling are a minority of our volume, but the biomarkers and tests for them are well established, and there are clear patient management approaches based on the results.”

**Commonly misused**

“The goal of the program is to provide an opportunity for doctors and patients to become more fully informed about these complex genetic tests,” says Finley. “The reason we focus on those tests is that they are commonly misunderstood and misused, and the volume is high. “There is no question that the **BRCA1** and **2** tests
have clinical value if used according to the criteria that would establish a man or woman as having high risk.

“The problem is that the tests and risk criteria are misunderstood by both doctors and patients, and the tests are frequently ordered for people who are not at high risk for the alteration.”

**Variability in training**

Misuse of the testing partly stems from variability in training and knowledge of genetic testing among the wide range of doctors who order the tests — oncologists, internists and family physicians, obstetricians/gynecologists, breast surgeons, cancer surgeons, and cardiologists.

“Our program is designed to get very accurate information through the use of genetic counselors in collecting and analyzing customers’ personal

and family history information,” says Finley. “Based on their risk assessment, the counselors make a positive or negative recommendation for testing.

**Cigna has become the first national health plan to use genetic counseling as an integral part of genetic testing.**

“Another important part of the counselors’ job is to explain the entire testing process to patients and their doctors, including such things as what to expect from the test results and how that information may affect services after the test. Patients should have a clear understanding of why they are or are not having the test as well as the basis for that

**What to do about incidental findings?**

The genetic tests for some hereditary conditions are rapidly expanding from tests of individual genes into tests of panels of genes, driven by the power of next-generation sequencing and rapidly decreasing costs.

Development of multigene tests is a trend that experts say in many cases will lead to even broader tests — exome and genome sequencing. Genome sequencing analyzes all of the genes in an individual’s complete DNA of 23 pairs of chromosomes.

Exome sequencing is an analysis of all exons, which constitute about 1% of the genome. Exons are components of DNA that cause gene mutations by altering the function of essential proteins in tissues and organs. Exome sequencing is much more efficient and thorough than genome sequencing, with a faster turnaround time.

The American College of Medical Genetics and Genomics (ACMG) says exome and genome sequencing play a key role in several clinical areas: understanding rare diseases, personalized cancer treatment, pharmacogenomics, and pre-conception screening. Currently exome and genome sequencing are used in limited clinical situations, such as in children who have been through a diagnostic odyssey for a rare condition.

Because of their very broad analytical approach, exome and genome sequencing are likely to identify clinically significant alterations which are not directly related to the primary reason or indication for the test. These incidental findings pose many problems in terms of what should be reported to patients.

Reporting incidental findings is of growing concern as exome and genome sequencing become more common. In response, the ACMG working group on incidental findings has developed a policy statement to serve as a guide in reporting these results.

Opinions about what should be reported range from including all disease-associated alterations that could be medically useful to reporting only results where there is strong evidence of benefit. In response to the varied opinions, the working group developed three categories of results that determine what is to be reported: known pathogenic results, expected pathogenic results, and genetic variants of unknown significance. Known and expected pathogenic results are to be included in test results and genetic alterations of unknown significance are not.

The statement recommends that labs sequence a set of 57 genes that may indicate the presence of 24 disorders for which early intervention is likely to reduce or prevent morbidity or mortality.

Including expected pathogenic results creates a gray area for clinicians and patients. Test results will become part of a patient’s medical record, and the idea of an expected pathogenic result sitting in a patient record creates an obligation for future follow-up by the lab performing the test and the patient’s physician.

The ACMG policy covers other aspects of results reporting: respecting patient preferences about receiving test results and handling of test results in children or informing their family members about inherited traits.
recommendation.” The genetic counselors’ services also help physicians understand genetic testing.

**Recommendation**

If the doctor wants to order a test, the patient must first see a board-certified counselor who will decide whether the patient meets the criteria. Cigna reviews the counselor’s recommendation before certifying the test.

Accurately determining risk is important because of the relative low incidence of confirmatory results from genetic tests for hereditary diseases. The NCI says the BRCA1 and BRCA2 mutations account for about 20%–25% of hereditary breast cancers and about 5%–10% of all breast cancers. Mutations in these genes account for about 15% of ovarian cancers.

Genetic tests like the BRCA1 and 2 test commonly also identify alterations in these genes that are separate from variants that are directly associated with the disease. These additional alterations can cause confusion and concern among patients and thus they reinforce the need for a thorough risk assessment and referral of only appropriate high-risk patients for testing.

“The chances of having a mutation of unknown significance are as high as or even higher than the chances of getting a positive result for the primary indication,” says Finley.

“By using the test for people who are not truly high-risk, you open a can of worms by subjecting them to a test where you get a result that you do not know what do with.”

**IOM report**

As an example, a 2011 Institute of Medicine report on incorporating genetic information into...
clinical practice said that at that time, more than 150,000 patients had been tested for \textit{BRCA1} variants and tests detected 10 to 20 new missense variants each week.

\textbf{New alterations}

This reflects the current state of the art in genetic testing: While genes like \textit{BRCA1} and 2 are associated with a particular disease, new alterations pop up as more people are tested, and geneticists have not identified the cause or causes of disease-producing mutations.

Since testing within specific genes produces a steady stream of new alterations, the recent development of multigene breast cancer tests and gene-panel tests for multiple hereditary cancers increases the possibility of identifying more alterations of unknown significance.

Cigna's program lays out procedures to ensure that the first steps of genetic testing are properly handled — in this case by conducting thorough risk assessments and ensuring appropriate access to testing by truly high-risk patients. From there, Cigna plans to move ahead carefully.

“This is a new program and it’s complicated,” says Finley. “Because there are many moving pieces and constant developments in genetics, we decided to start with a small number of tests and get the wrinkles ironed out. The two major pieces of this program are very different from other clinical management programs and we want to make sure that we are doing it absolutely correctly and that our customers are satisfied.” (The two major pieces are using counselors to obtain a detailed and complete family history and then allowing people who might have questions to meet with counselors.)

\textbf{Growing recognition}

Use of genetic counselors to conduct better risk assessments and provide a recommendation for tests ordered by physicians is a novel approach to precertification. It reflects the growing recognition of the role that genetic counselors can play in this very complex area of medicine, and it helps physicians integrate genetics into their practices. But it also injects a new precertification procedure that some physicians may object to. \textit{MC}

\textit{Thomas Reinke writes on pharmaceuticals and other topics for Managed Care.}

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David M. Cutler, PhD
Mary Barton, MD, MPP
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Lucian Leape, MD
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Cancer-Fighting Immunotherapies Flex Muscles

Viruses. You don’t want one — unless it’s one that attacks disease instead of promoting it. And yes, such a thing exists.

In a trial involving patients with stage 3 or 4 melanoma, talimogene laherparepvec, or T-vec, Amgen’s cancer-fighting virus, came out swinging against granulocyte-macrophage colony-stimulating factor (GM-CSF). In an open-label study, median overall survival (OS) in patients receiving T-vec was 23.3 months, 4.3 months more than patients given GM-CSF. T-vec is injected into cancer tissue, where it replicates and releases antitumor antigens.

The irony in T-vec’s development is that it was shepherded at Amgen by Roger Perlmutter, MD, PhD, who is now Merck’s R&D chief. Perlmutter is pushing hard for quick FDA approval of Merck’s own immunotherapy, MK-3475. Merck is wrapping up a phase 3, head-to-head melanoma trial of the PD-1 inhibitor against ipilimumab (Yervoy), and in late 2013, MK-3475 demonstrated an 81% 1-year OS in a phase 18 trial involving more than 1,000 patients with advanced metastatic skin and lung cancers.

T-vec and MK-3475 are just two immunotherapies on the forefront of development; two more are also nearing the R&D finish line. Further back, there’s CTL019, an interesting entry that might remind you of Provenge. The personalized regimen draws T cells from a patient’s blood, engineers them to hunt for cancer cells that express certain proteins, then re-injects them into the body. In an early-stage trial, CTL019 induced complete remission in 19 of 22 children and 7 of 32 adults with leukemia. Five children relapsed.

Novartis has licensed CTL019 from the University of Pennsylvania.

Ponatinib is back

With a new indication and a black box warning about heart failure and the risk of vascular events, ponatinib (Iclusig) is back on the market. The Food and Drug Administration asked Ariad Pharmaceuticals to stop sales and marketing last October after real-world experience with the kinase inhibitor resulted in greater incidence of blood clots than what the drug’s label showed. As part of its new agreement with the FDA, Ariad will engage in postmarketing pharmacovigilance activities.

Committee OKs vedolizumab

An FDA review prepared in advance of an advisory committee vote on vedolizumab, Takeda’s

Specialty/specialty combinations take stage at ASH

As biologics and oral specialty drugs to treat cancer proliferated during the previous decade, the custom in clinical trials was to combine them with chemotherapies and measure the effects against chemotherapy alone. Now, we’re hearing more and more about specialty/specialty drug combinations. Two such cocktails made headlines at December’s American Society of Hematology meeting in New Orleans.

In a phase 3 trial of previously treated patients with chronic lymphocytic leukemia, 220 people were randomized to receive either idelalisib in combination with rituximab (Rituxan) or rituximab alone. Idelalisib is Gilead’s first-in-class, oral drug that inhibits the activity of PI3K-δ, a driver of malignant cell growth. Among those getting idelalisib, progression-free survival (PFS) at 24 weeks was 93%, compared with 46% in the rituximab-only arm. The difference in overall response was even greater — 81% vs. 13% respectively.

Novartis, meanwhile, was touting results from two studies of panobinostat in patients with relapsed or refractory multiple myeloma. Panobinostat inhibits deacetylase enzymes, a sort of on-off switch for processes that enable cell growth. In both, oral panobinostat was paired with a combination of bortezomib (Velcade) and dexamethasone. Data from a randomized phase 3 trial are still being crunched, but a topline analysis indicated that the addition of panobinostat significantly extended PFS compared with the bortezomib/chemo combination alone. Novartis released full data from an open-label phase 2 study showing strong PFS and overall survival (OS) gains in heavily treated patients whose disease was resistant to bortezomib.

The buzz these studies generated was not unlike that at the American Society for Clinical Oncology’s 2012 meeting, where biologic combinations for metastatic melanoma made news. But as whispered at ASCO, the cost of specialty/specialty combinations may push society and policymakers closer for metastatic melanoma made news. But as whispered at ASCO, the cost of specialty/specialty combinations may push society and policymakers closer
leukocyte-targeting antibody for people with ulcerative colitis (UC) and Crohn's disease, raised concern about the drug's potential to cause progressive multi focal leukoencephalopathy (PML). Nobody in vedolizumab clinical trials developed PML, but that was also true when natalizumab (Tysabri) hit the market in 2004. Since then, 343 people taking natalizumab have developed PML. Natalizumab was later re-launched with a diagnostic test to detect the JC virus, which causes the demyelinating condition.

Days after the release of the FDA review on vedolizumab, the advisory panel played down the danger, convinced that Takeda adequately warns prescribers and patients about it in product labeling. But the committee split on when treatment with the drug should be initiated. The group voted 20–0 that the drug was effective as maintenance therapy, but 12–9 that the drug was appropriate for induction therapy. The FDA will decide by February 18 on a UC indication and by June on Takeda's Crohn's disease application.

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**BIOLOGICS IN DEVELOPMENT**

### SELECTED FDA APPROVALS OF BIOLOGIC AND SPECIALTY DRUGS, NOV. 15, 2013–JAN. 15, 2014

<table>
<thead>
<tr>
<th>Date (type)</th>
<th>Manufacturer</th>
<th>Drug (trade name); administration</th>
<th>Indication</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nov. 22, 2013 (NDA)</td>
<td>Janssen</td>
<td>simprevir (Olysio); oral</td>
<td>In combination with peg-interferon alfa and ribavirin, in patients with genotype 1 chronic HCV infection</td>
<td>Protease inhibitor cut the amount of interferon that hepatitis C patients require, compared with two other drugs in its class, telaprevir (Incivek) and boceprevir (Victrelis). Sofosbuvir approval days later, however, eliminated need in most patients for an interferon regimen.</td>
</tr>
<tr>
<td>Dec. 6, 2013 (NDA)</td>
<td>Gilead</td>
<td>sofosbuvir (Sovaldi); oral</td>
<td>Chronic HCV as part of a combination regimen with ribavirin in all 4 genotypes. Addition of interferon alfa is recommended in patients with genotypes 1 and 4 except in patients ineligible for interferon.</td>
<td>First all-oral treatment for hepatitis C without a need for co-administration of interferon. AWP of a 24-week supply is $84,000.</td>
</tr>
<tr>
<td>Dec. 20, 2013 (BLA)</td>
<td>Novo Nordisk</td>
<td>coagulation factor XIII A-subunit (recombinant), (Tretten); IV injection</td>
<td>Prophylaxis of bleeding in patients with congenital factor XIII A-subunit deficiency</td>
<td>Orphan drug is the first treatment for patients with this rare genetic disorder, seen in about 1 in 5 million births. The FDA approved Tretten on the basis of a 77-person trial.</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Drug (trade name)</th>
<th>Type of drug</th>
<th>Proposed use</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanofi</td>
<td>alemtuzumab (Lemtrada)</td>
<td>recombinant DNA-derived humanized monoclonal antibody</td>
<td>Relapse-remitting multiple sclerosis</td>
<td>Dec. 30 CRL described the FDA's concern about “serious adverse effects,” primarily the risk of autoimmune disorders. The FDA required new clinical trials with different designs; Sanofi is appealing. Alemtuzumab was approved in Canada Dec. 13.</td>
</tr>
</tbody>
</table>

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**Did you hear?**

The FDA told 23andMe to stop selling its personal genome service until it gets marketing clearance. By sending 23andMe a saliva sample, consumers can get information on BRCA-related genetic risk or warfarin sensitivity, among other things. The company will comply but still offers raw genetic data without interpretation.

— Michael D. Dalzell

*All clinical trials described in this column are phase 3, randomized, controlled studies unless otherwise specified.*
Thirteen of the 27 drugs receiving Food and Drug Administration approval in 2013 were biologics and other specialty pharmaceuticals. It’s the first time since 2009 that more than half of FDA approvals were for conventional drugs.

That the number of specialty drugs and biologics making it to market slipped from 25 in 2012 to 13 last year doesn’t mean that small molecules are back in vogue. On the contrary, a report released late last year by the Tufts Center for Drug Development noted that big pharma has made a dramatic shift in its R&D focus from small-molecule drugs to biotechnology.

Cancer continues to be a hotbed of specialty drug development. Of the 13 specialty drugs and biologics approved last year, 9 carry oncology indications and hefty price tags. None were chemotherapies. —Michael D. Dalzell

### 2013 DRUG-APPROVAL TIMELINE

<table>
<thead>
<tr>
<th>Trade name</th>
<th>Use</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kynamro</td>
<td>Homozygous familial hypercholesterolemia</td>
<td>$176,000(^a)</td>
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<tr>
<td>Pomalyst</td>
<td>Multiple myeloma</td>
<td>$10,500</td>
</tr>
<tr>
<td>Kadryla</td>
<td>Breast cancer</td>
<td>$9,800</td>
</tr>
<tr>
<td>Tecfidera</td>
<td>Multiple sclerosis</td>
<td>$55,000(^a)</td>
</tr>
<tr>
<td>Xofgo</td>
<td>Prostate cancer</td>
<td>$69,000(^a)</td>
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<td>Mekinist</td>
<td>Melanoma</td>
<td>$8,700</td>
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<tr>
<td>Taflinar</td>
<td>Melanoma</td>
<td>$7,600</td>
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<tr>
<td>Gilotruf</td>
<td>Lung cancer</td>
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<td>Tivicay</td>
<td>HIV</td>
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<tr>
<td>Gazyva</td>
<td>Chronic lymphocytic leukemia</td>
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<td>Imbruvica</td>
<td>Mantle cell lymphoma</td>
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<tr>
<td>Olysio</td>
<td>Hepatitis C</td>
<td>$66,360(^d)</td>
</tr>
<tr>
<td>Solvaldi</td>
<td>Hepatitis C</td>
<td>$28,000(^f)</td>
</tr>
</tbody>
</table>

\(^a\)Cost per month, unless otherwise noted.
\(^b\)Per year.
\(^d\)6-injection course of therapy.
\(^e\)3-month course of therapy.
\(^f\)6-month course of therapy.

Wellness Debate Irrelevant For Insurers Eyeing the Market

Despite last year’s fiasco at Penn State and growing concern about the effectiveness of such programs, employers are still believers

By Frank Diamond

Reports about wellness programs have occupied this space many times. Why shouldn’t they? Employers demand, insurers supply.

Jaan Sidorov, MD, a consultant, former health plan medical director, and member of our editorial advisory board, says, “It’s a no-brainer.” He adds, “Employers and their employees want them. Laypersons believe that wellness programs, thanks to prevention and health promotion, should translate into lower premiums.”

Yet thanks in part to last year’s fiasco at Penn State, the benefits of wellness have been questioned. Writing in the Los Angeles Times (http://tinyurl.com/op-ed-wellness), Rahul K. Parikh, MD, asked, “Do such programs have the intended effect of healthier employees and lower health-care costs? As more businesses embrace health incentives, these questions are becoming more urgent.”

Does it work?

There’s no doubt where Al Lewis stands. Lewis, the founder of the Disease Management Purchasing Consortium, says that if wellness programs were so popular with employees, then the penalties and incentives would not have doubled in the last four years.

“People have to be paid to do wellness,” says Lewis. “If something is valuable, people will pay you to do it. For example, I’m talking to you on an iPhone. Apple did not pay me to take the iPhone off their hands; I paid Apple. Wellness programs are so worthless that employers basically have to force their employees to lose money if they don’t participate.”

Further, Lewis contends, there’s no evidence that wellness programs work — that they actually improve outcomes. He cites a study in 2009 in Health Affairs co-written by Katherine Baicker, PhD, a professor of health economics in the department of health policy and management at the Harvard School of Public Health (http://tinyurl.com/sBaicker-article).

“In the top-tier journals, there’s been only one. Ever. One ever. That supported wellness,” Lewis says. Baicker’s article says that wellness can generate an ROI of 3.27:1. Lewis, who says he has a lot of respect for Baicker, also mentions that she “walked it back” on the NPR show Marketplace last year.

“She goes on Marketplace and says, ‘It’s too early to tell; we have to keep experimenting.’”

Baicker basically corroborates this, telling Managed Care that the “Health Affairs article includes many caveats, but of course such academic nuances are rarely reported in the popular press. Whenever I am interviewed, I try to reintroduce those cautions alongside the main results of the paper — so my comments on Marketplace mirror what we said in the paper itself.”

What she said: First, there are clearly limitations in the broader generalization of these findings. Second, the companies implementing these programs are probably those with the highest expected returns. Third, it is difficult to gauge the extent of publication bias, with programs seeing high return on investment most likely to be written about and studies with significant findings of positive returns most likely to be published. Fourth, almost all of the studies were implemented by large employers, which are more likely than others to have the resources and economies of scale necessary both to implement and to achieve broad savings through employee wellness programs.

Lewis argues that the only ones who believe in wellness programs are those who get to sell them. “There’s wellness that’s done to employees, and there’s wellness that’s done for em-
employees. The Penn State program was clearly done to employees. Is it something that people like intuitively, or is it something people have to be forced into? They were definitely forced into it.”

No one objects to someone losing weight, stopping smoking, or exercising more. But Lewis believes that you can’t pay people to do those things.

It is especially difficult to lose weight. He calls the connection between weight and health a loose correlation.

“Most of those comorbidities don’t happen until you’re over 65,” says Lewis. “Even if they do happen when you’re under 65 — like diabetes — the actual complications and the facts that are going to cause the money to go up are over 65. So as an employer, if you’re seeking out cases of very early stage pre-diabetes, you’re simply going to create costs for yourself.”

**Difficult to gauge**

Parikh, in his *Los Angeles Times* article, said, “A number of recent studies have cast doubt on both the cost savings and the sustainability of some employee wellness programs.”

One such study, Parikh wrote, showed that fewer employees were hospitalized. Money saved, right? Well, no. Those savings were offset by more visits to the doctor and use of prescription drugs.

For health insurers, though, this debate is academic. Randel K. Johnson, the senior vice president for labor, immigration, and employee benefits at the U.S. Chamber of Commerce, wrote an op-ed last April in *The Hill* with the telling headline, “The Truth About Workplace Programs: Everybody Wins” (http://tinyurl.com/Johnson-article).

“In identifying impending and current chronic disease and illnesses, these programs offer another way to advance our country’s health care evolving approach beyond simply treating diseases and caring for the sick to improving health and maintaining wellness. These wellness programs give people tools to identify their risk factors, improve their health, modify unhealthy behavior, and stay well both in the workplace and at home.”

We circle back to Sidorov’s point: Employers want wellness programs. He also argues that they are not as ineffectual as Lewis and others think.

“I think insurers have internal numbers that have not been made public that do show a beneficial impact on utilization,” says Sidorov. “What’s more, even if there isn’t that much of a return on investment, it’s what the market wants, and that alone qualifies as a classic loss-leader.

**Wellness programs are so worthless that employers basically have to force their employees to lose money if they don’t participate,” says Al Lewis, founder of the Disease Management Purchasing Consortium.**

“In addition, health plans with a reputation for strong wellness programs may benefit from stickiness with consumers who are baseline healthy and dilute the risk pool. Last but not least, health plans are, whether they like it or not, in the public spotlight and, from a brand as well as public policy perspective, need to be perceived as part of the solution.”

It comes down to execution, Sidorov believes. Penn State shows how things can go wrong, but is not an indictment of wellness programs. “I have some opinions about Penn State — charging more for nonparticipation, a school in turmoil, ultimately meritless but hot-button concerns over privacy, suspicious faculty, effective communications from a few alarmed professors, a rather ham-fisted administrative response, and the distractions that come from a national spotlight. These have more to do with execution than merit.”

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COPD inhalers – hold your breath

With the approval of Breo Ellipta in May 2013 and Anoro Ellipta in December 2013, formulary decision makers are faced with more treatment options for chronic obstructive pulmonary disease (COPD) than ever before. There are now three inhalers that are combination products of a long-acting beta agonist and a glucocorticoid that can potentially help patients with moderate to severe COPD. Research comparing these available therapeutic options is limited, making differentiation difficult. Despite that, let’s take a look at several notable differences among these drugs.

— Krishna R. Patel, PharmD, RPh

<table>
<thead>
<tr>
<th></th>
<th>Administration once daily</th>
<th>Administration twice daily</th>
<th>Black box warning</th>
<th>Approved for COPD</th>
<th>Approved for asthma</th>
<th>Recommended in GOLD guidelines for moderate–severe COPD</th>
</tr>
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<tbody>
<tr>
<td>Advair</td>
<td></td>
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<tr>
<td>Breo Ellipta</td>
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<td>Symbicort</td>
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Source: GOLD (Global Initiative for Chronic Obstructive Lung Disease)
In 1974 a Thomas Jefferson Medical College professor asked my medical school class: “Who would like to admit to having a genetic disorder?” Of course, none of this group of over 200 of the best and brightest would ever chance to raise a hand. The professor went on to order every one of us to raise a hand. For even in the mid 1970s he knew that every human genome on the planet had the basis of some medical condition, even if no technology available at that time could hope to find it.

President Reagan’s 1987 budget included a funding request for the Human Genome Project (HGP) that led the way to the official start of this massive endeavor in 1990. Compared to the United States’ goal of putting a man on the moon, the decade-long HGP will most assuredly exceed that historic accomplishment in helping mankind.

Directly as a result of the knowledge gained through the HGP, a relatively silent revolution is taking place in oncology offices around the country. Many cancer patients will be faced with the opportunity to know exactly what genes are the actual “deviant” genes that have led to this dreaded and once mysterious diagnosis.

As eloquently described in the landmark article by Douglas Hanahan from the University of California – San Francisco and Robert Weinberg from the Massachusetts Institute of Technology, “The Hallmarks of Cancer,” in the Jan. 7, 2000 issue of Cell, cancer is largely an acquired genetic disease. Their single statement, “Cancer cells have defects in regulatory circuits that govern normal cell proliferation and homeostasis,” has done more for the typical physician’s understanding of the etiology of cancer than virtually any other sentence. Hanahan and Weinberg went on to define “six essential alterations in cell physiology that collectively dictate malignant growth.”

Although other experts have suggested adding to these six, they remain the foundational hallmarks of cancer. The six are:

- Self-sufficiency in growth signals
- Insensitivity to growth-inhibitory (antigrowth) signals
- Evasion of programmed cell death (apoptosis)
- Limitless replicative potential
- Sustained angiogenesis
- Tissue invasion and metastasis

Most current oncology drug development is focused on these “targets” leading to revolutionary changes in the hope for those with a diagnosis of cancers containing “targets” for existing or research drugs.

Although not yet the norm, a corollary to the development of targeted drugs is the development of “companion diagnostics”; a biomarker test associated with tumors that reflect the presence of a genomic change of the cancer cell that is also the target for the associated drug.

But testing for genetic changes in tumors is not isolated to trying to prove the presence of the handful of tumor markers that have associated targeted treatments. Oncologists around the country are now able to identify virtually all tumor-derived genetic alterations. And these tests can be done serially.

**Tumors reproduce sloppily**

It seems that the genetic make-up of tumors is dynamic. Tumors basically reproduce sloppily, and in fact accumulate genetic change over time and partly in response to treatment. This trait makes it desirable to test tumors chronologically.

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.
In addition, the genetic content of tumor cells can often be found in free circulating plasma allowing oncologists to identify tumor-derived genetic alterations with a “simple” blood test, and thereby gain a better understanding of a patient’s tumor characteristics not dependent on ability to obtain a biopsy. The testing is designed to detect alterations in actual chromosomal copies, rearrangements of chromosomes, and amplification of the actual cancer driver genes with an alphabet soup list of names such as: HER2, EGFR, BRAF, ERBB2, CDK6, KRAS, PIK, PTEN, NOTCH 1–4 and others.

Treasure trove
A few of the 100+ genetic deviants have associated drugs that target the defect, but most currently do not. The actual testing result becomes a treasure trove to those researching treatment for cancer.

This approach to better understanding tumor biology is the result of large scale DNA sequencing termed “Next Generation” or “Next Gen” sequencing that allows for extremely rapid analysis of DNA to actually sequence the genetic code of more than 20,000 human genes in a matter of days, not decades.

Only a relatively small percentage of all genetic material has to be analyzed, significantly simplifying the task. Thus, companies involved in genome cancer screening are not attempting to actually create the library of the entire genome for a given patient. They are only identifying the actual gene coding sequences of the cancer DNA that are called exomes (although this is still an enormous feat!).

There are basically two approaches; whole exome assay which captures all 20,000 plus genes, or a more selective approach that looks at those 100+ genes that reflect the Hallmarks of Cancer” approach. These genes reflect those cellular activities that have deviated from normal and are the actual trigger for malignancy in most tumors. Reports back to the physician include the actual base substitutions, insertions, deletions, rearrangements, and copy number alterations.

With this information, physicians can search for relevant clinical trials focusing on studying drugs for the specific mutations if no drug currently exists. Although numerous academic institutions are offering these services, the leading commercial companies involved in this service are Personal Genome Diagnostics, a company created by the researchers from Johns Hopkins University who were the first to sequence the entire cancer genome, and Foundation Medicine, a collaborative effort of MIT, Harvard Medical School, and Google Ventures among others. (Of note, Google’s interest is not random; these efforts require enormous computing power!)

But, as exciting as this approach is to oncologists and patients, health plans have a far different opinion on the utility of this approach. Health plans are clear in their policies that they do not pay for this “shotgun” testing in the absence of clinical evidence supporting not only the test but any resultant treatment. Because there are only a literal handful of genetic changes associated with FDA approved therapies, health plans see Next Gen testing as potentially leading physicians to approach cancer from a biomarker perspective instead of a clinical trial proven, tissue-based approach.

For instance in the clinical trial approach, a drug approval for a given mutation is based on improved outcome for a specific type and stage of cancer based on site of origin (e.g., lung or breast or skin) along with the proven presence of the receptor. But Next Gen testing opens up a totally different list of questions. What if the same mutation is found on a far different tumor where no FDA approval (or even completed research) is available? Health plans fear physicians will attempt to “throw in the kitchen sink” to treat a genetic marker with a targeted therapy that has not been studied in that particular type or stage of tumor. They are also concerned that patients will demand access to these speculative drugs to gain hope.

Does it work?
Despite the conflict, the likes of Foundation Medicine, Personal Genome Diagnostics and others will continue to push Tomorrow’s Medicine to the limits, testing not only the tissue and plasma samples, but also the technology committees of health plans in the process!  

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.
Improving economic conditions and some success in fighting heart disease and HIV mean that more people live longer lives — a good thing, but also a driver of global dementia rates, according to a study by Alzheimer’s Disease International, a consortium of research and advocacy organizations. “Population aging is the main driver of projected increases,” says “The Global Impact of Dementia 2013–2050” (http://tinyurl.com/study-dementia).

About 135 million people worldwide will suffer from dementia in 2050, a substantial increase from a projection in 2009 of 115 million. The updated projection results partly from more sources of data. “Since 2009, the global estimate base has expanded, most particularly with a new systemic review of the prevalence of dementia in China comprising 75 studies, most published in Chinese language journals, and with seven studies from five sub-Saharan African countries, where previously only one study from Nigeria had been available.”

**People with dementia worldwide (2010–2050)**

![Graph showing the increase in people with dementia worldwide from 2010 to 2050](image)


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