FEE-FOR-SERVICE IS DEAD
LONG LIVE FEE-FOR-SERVICE?

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IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS DEHYDRATION IN PEDIATRIC PATIENTS
Trulance™ is contraindicated in patients less than 6 years of age; in nonclinical studies in young juvenile mice administration of a single oral dose of plecanatide caused deaths due to dehydration. Use of Trulance should be avoided in patients 6 years to less than 18 years of age. The safety and efficacy of Trulance have not been established in pediatric patients less than 18 years of age.

Contraindications
- Trulance is contraindicated in patients less than 6 years of age due to the risk of serious dehydration.
- Trulance is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.

Warnings and Precautions
Risk of Serious Dehydration in Pediatric Patients
- Trulance is contraindicated in patients less than 6 years of age. The safety and effectiveness of Trulance in patients less than 18 years of age have not been established. In young juvenile mice (human age equivalent of approximately 1 month to less than 2 years), plecanatide increased fluid secretion as a consequence of stimulation of guanylate cyclase-C (GC-C), resulting in mortality in some mice within the first 24 hours, apparently due to dehydration. Due to increased intestinal expression of GC-C, patients less than 6 years of age may be more likely than older patients to develop severe diarrhea and its potentially serious consequences.
- Use of Trulance should be avoided in patients 6 years to less than 18 years of age. Although there were no deaths in older juvenile mice, given the deaths in young mice and the lack of clinical safety and efficacy data in pediatric patients, use of Trulance should be avoided in patients 6 years to less than 18 years of age.

Diarrhea
- Diarrhea was the most common adverse reaction in the two placebo-controlled clinical trials. Severe diarrhea was reported in 0.6% of patients.
- If severe diarrhea occurs, the health care provider should suspend dosing and rehydrate the patient.

Adverse Reactions
- In the two combined CIC clinical trials, the most common adverse reaction in Trulance-treated patients (incidence ≥2% and greater than in the placebo group) was diarrhea (5% vs 1% placebo).
Diarrhea is not efficacy—it’s time to address the age-old tradeoff in CIC.1,2

Trulance is structurally identical to naturally occurring uroguanylin with the exception of one amino acid.3-6

Trulance provided more regular, well-formed bowel movements.3*

Efficacy, true to form.

TrulanceTM offers convenient once-daily dosing, with or without food.3 For more information about Trulance, please contact your account manager with NDC #70194-003-30. Learn more at TrulanceHCP.com

*Results over 12 weeks were statistically significant vs placebo, as shown in two Phase 3 clinical studies.3

Indication

• Trulance (plecanatide) 3 mg tablets is indicated in adults for the treatment of chronic idiopathic constipation (CIC).


Please see Brief Summary of full Prescribing Information, including Box Warning, on the following page.
Trulance™ (plecanatide) tablets, for oral use

Rx only

Brief Summary — Consult the package insert for complete prescribing information.

**INDICATIONS AND USAGE:** Trulance is indicated in adults for the treatment of chronic idiopathic constipation (CIC).

- **Contraindications:** Trulance is contraindicated in patients 6 years to less than 18 years of age, in non-clinical studies in young juvenile mice, administration of a single oral dose of plecanatide caused death due to dehydration [see Contraindications, Use in Specific Populations].

- **Warnings and Precautions:** Risk of Serious Dehydration in Pediatric Patients — Trulance is contraindicated in patients less than 6 years of age. The safety and effectiveness of Trulance in patients less than 18 years of age have not been established. In young juvenile mice (human age equivalent of approximately 1 month to less than 2 years), plecanatide increased fluid-secretion into the intestines as a consequence of stimulation of guanylate cyclase-C (GC-C), resulting in mortality in some mice within the first 24 hours, apparently due to dehydration. Due to increased intestinal expression of GC-C, patients less than 6 years of age may be more likely than patients 6 years of age and older to develop severe diarrhea and its potentially serious consequences.

- **Adverse Reactions:** In nonclinical studies, deaths occurred within 24 hours in young juvenile mice, with the deaths in younger mice and the lack of clinical safety and efficacy data in pediatric patients, avoidance of use of Trulance in patients 5 years to less than 18 years of age [see Contraindications, Warnings and Precautions, Use in Specific Populations].

- **Diarrhea:** Diarrhea was the most common adverse reaction in two placebo-controlled clinical trials. Severe diarrhea was reported in 0.6% of patients [see Adverse Reactions]. If severe diarrhea occurs, suspend dosing and rehydrate the patient.

- **Adverse Reactions:** Clinical Trials Experience — Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

- **Safety Data:** The safety data described below reflect data from 1733 adult patients with CIC randomized in two double-blind, placebo-controlled clinical trials (Study 1 and Study 2) to receive placebo or 3 mg of Trulance once daily for 12 weeks. Demographic characteristics were comparable between the Trulance and placebo groups [see Clinical Studies in the full prescribing information].

- **Most Common Adverse Reactions:**

  | Table 1: Most Common Adverse Reactions* in Two Placebo-Controlled Trials of Trulance (Study 1 and Study 2) in Patients with CIC |
  | Trulance | Placebo |
  | 3 mg | Placebo |
  | (N = 863) | (N = 870) |
  | **Adverse Reaction** | **%** | **%** |
  | Diarrhea | 5 | 1 |

*reported in at least 2% of Trulance-treated patients and at an incidence greater than placebo.

- **Diarrhea:** The majority of reported cases of diarrhea occurred within 4 weeks of treatment initiation. Severe diarrhea was reported in 0.6% of Trulance-treated patients compared to 0.3% of placebo-treated patients. Severe diarrhea was reported to occur within the first 3 days of treatment [see Warnings and Precautions].

- **Adverse Reactions Leading to Discontinuation:** Discontinuations due to adverse reactions occurred in 4% of Trulance-treated patients and 2% of placebo-treated patients. The most common adverse reaction leading to discontinuation was diarrhea: 2% of Trulance-treated patients and 0.5% of placebo-treated patients withdrew due to diarrhea.

- **Less Common Adverse Reactions:** Adverse reactions reported in less than 2% of Trulance-treated patients and at an incidence greater than placebo were:

  - sinusitis, upper abdominal pain, upper respiratory tract infection, abdominal bloating, abdominal tenderness, and increased liver biochemical tests (2 patients with alanine aminotransferase (ALT) greater than 5 to 15 times the upper limit of normal and 5 patients with aspartate aminotransferase (AST) greater than 5 times the upper limit of normal).

- **Use in Specific Populations:** Pregnancy — Risk Summary

  *Plecanatide and its active metabolite are negligibly absorbed systemically following oral administration [see Clinical Pharmacology in the full prescribing information] and maternal use is not expected to result in fetal exposure to the drug.

  The available data on Trulance use in pregnant women are not sufficient to inform any drug-associated risks for major birth defects and miscarriage. In animal developmental studies, no effects on embryofetal development were observed with oral administration of plecanatide in mice and rabbits during organogenesis at doses much higher than the recommended human dosage.

  The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defects, loss, or other adverse outcomes. In the United States general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

- **Data:**

  - **Animal Data:**

    - Pregnant mice and rabbits were administered plecanatide during the period of organogenesis. There was no evidence of harm to embryo-fetal development at oral doses up to 800 mg/kg/day in mice and 250 mg/kg/day in rabbits. Oral administration of up to 600 mg/kg/day in mice during organogenesis through lactation produced no developmental abnormalities or effects on growth, learning and memory, or fertility in the offspring through maturation.

    - The maximum recommended human dose is approximately 0.05 mg/kg/day, based on a 60-kg body weight. Limited systemic exposure to plecanatide was achieved in animals during organogenesis (area under the plasma concentration-time curve (AUC) = 449 ng•h/mL in rabbits given 250 mg/kg/day). Plecanatide and its active metabolite are not measurable in human plasma following administration of the recommended clinical dosage. Therefore, animal and human doses should not be compared directly for evaluating relative exposure.

    - **Lactation:**

      - There is no information regarding the presence of plecanatide in human milk, or its effects on milk production or the breastfed infant. No lactation studies in animals have been conducted. Plecanatide and its active metabolite are negligibly absorbed systemically following oral administration [see Clinical Pharmacology in the full prescribing information].

      - It is unknown whether the negligible systemic absorption of plecanatide by adults will result in a clinically relevant exposure to breastfed infants. Exposure to plecanatide in breastfed infants has the potential for serious adverse effects [see Use in Special Populations]. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for Trulance and any potential adverse effects on the breastfed infant from Trulance or from the underlying maternal condition.

    - **Pediatric Use:**

      - Trulance is contraindicated in pediatric patients less than 6 years of age. Avoid use of Trulance in patients 6 years to less than 18 years of age [see Contraindications, Warnings and Precautions].

      - In nonclinical studies, deaths occurred within 24 hours in young juvenile mice (human age equivalent of approximately 1 month to less than 2 years) following oral administration of plecanatide, as described below in Juvenile Animal Toxicity Data. Because of increased intestinal expression of GC-C, patients less than 6 years of age may be more likely than patients 6 years of age and older to develop diarrhea and its potentially serious consequences. Trulance is contraindicated in patients less than 6 years of age. Given the deaths in young juvenile mice and the lack of clinical safety and efficacy data in pediatric patients, avoid the use of Trulance in patients 6 years to less than 18 years of age.

    - **Juvenile Animal Toxicity Data:**

      - Single oral doses of plecanatide at 0.5 mg/kg and 10 mg/kg caused mortality in young juvenile mice on postnatal days 7 and 14, respectively (human age equivalent of approximately 1 month to less than 2 years). Treatment-related increases in the weight of intestinal contents were observed in juvenile mice following single doses of plecanatide on postnatal day 14 (human age equivalent of approximately less than 2 years), consistent with increased fluid in the intestinal lumen. Although the recommended human dose is approximately 0.05 mg/kg/day, based on a 60-kg body weight, plecanatide and its active metabolite are not measurable in adult human plasma, whereas systemic absorption was demonstrated in the juvenile animal toxicity studies. Animal and human doses should not be compared directly for evaluating relative exposure.

    - **Geriatric Use:**

      - Clinical studies of Trulance did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from patients 18 years to less than 65 years of age. Of 2071 subjects in clinical trials of Trulance, 273 (10%) were 65 years of age and over, and 47 (2%) were 75 years and over. In general, dose selection for an elderly patient should be cautious, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

    - **Dosage and Administration:** Recommended Dosage — The recommended adult dosage of Trulance is 3 mg taken orally once daily, with or without food. [See Preparation and Administration Instructions in the full prescribing information].

      - **Trulance** is a trademark of Synergy Pharmaceuticals Inc. Copyright 2017© Synergy Pharmaceuticals Inc.
Donald Berwick’s Triple Aim has been the go-to metaphor of health care reform and attempts to manage care for well over a decade.

In an essay published in JAMA earlier this year, Berwick proposed a new three-infused trope for American health care, organized by eras.

In Era 1, which he dates back to Hippocrates, physicians were autonomous. Era 2 is the welter of data, measurement, and incentives that now dominates. It has become a distressing time, in Berwick’s view. Physicians and other clinicians are feeling angry, misunderstood, and overcontrolled. Payers, government officials, and consumer groups feel suspicious, resisted, and often helpless. Our cover story this month about physician payment echoes some of these sentiments.

So it’s time to usher in Era 3, a “moral era,” argues Berwick, who was briefly head of CMS in the Obama administration during the early days of the ACA. Berwick would bring Era 3 about by, among other things, sweeping away the multitude of process measures and replacing them with a much smaller set of outcomes. He thinks there should be a moratorium on complex incentive programs and that his former agency should limit its value-based payment models to large groups.

Other Era 3 ingredients: heavy doses of improvement science in health care curriculums and job descriptions; easier access to the troves of data at CMS and commercial payers; and a halt to the current “tolerance for greed” in health care.

The Triple Aim suffers from an aspiration–actuality gap. Taking aim is one thing, hitting the target, another. Berwick’s Era 3 seems like it could be a golden age in health care. Will it ever come to pass? We have our doubts.

Berwick: Time for a New ‘Era 3’
In American Health Care
By Peter Wehrwein

Donald Berwick

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Fresh Faces: Anthem’s Geoffrey B. Crawford

The 35-year-old medical director of the plan’s office of medical policy and technology assessment has broad interests, but he’s particularly keen on wellness. His take: Rely less on active patient participation.  
By Frank Diamond

Cover Story

Fee for Service Still Follows the Money

Value-based payment is supposed to end the incentives that can wind up paying doctors for delivering unnecessary services. But fee for service is still with us. Will the way doctors are paid ever change?  
By Jan Greene

Direct Primary Care: Working Stiff’s Concierge

Qliance has closed and direct primary care still occupies a small niche. But proponents say federal legislation that would allow people to pay the monthly fee with HSA dollars would help direct primary care take off.  
By Charlotte Huff

Upstart Helps Cleveland Clinic With Insurance

Oscar Health, a small insurer with big ambitions, has been enlisted to assist the famous health care provider launch its own insurance plan. The thinking goes like this: Why develop a health plan from scratch?  
By Susan Ladika

Original Research

Proteomic Testing Improves Lung Cancer Care

Accurate prognostic estimates can predict and document expected response to treatment, avoid ineffective and costly overtreatment, and facilitate meaningful discussions with lung cancer patients.

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Insurers, PBMs Asked To Help Stanch Nation’s Raging Opioid Epidemic

FDA chief Scott Gottlieb hopes to be able to stem the flood of opioids fueling the worst drug crisis in U.S. history by blocking them at some of their sources: health plans and PBMs.

Bloomberg reported that Gottlieb wants to meet with leaders of those industries this month to discuss ways to better regulate opioid prescriptions.

“The way to reduce the rate of new addiction is to reduce the rate of exposure, and the way to reduce the rate of exposure is to make sure people are receiving prescriptions when it’s only medically appropriate,” Gottlieb told Bloomberg.

Gottlieb will need to use his powers of persuasion on insurers, who are not regulated by the FDA but rather by HHS and state insurance commissions.

He thinks insurers and PBMs can help by changing instructions on drug labels, or perhaps requiring doctors to educate patients about the risks of taking prescriptions for longer periods of time.

“There shouldn’t be 30-day prescriptions for a tooth extraction, or 30-day prescriptions for a hernia repair,” Gottlieb told Bloomberg.

Gottlieb also wants to experiment with making sure that prescribing conforms more to clinical guidelines. “They’re not in there right now,” Gottlieb said. “There’s no information in the drug label about what the appropriate dispensing should be.”

Better adherence to guidelines could possibly make prescribing less burdensome, he added.

The interview also touched on Endo International’s pulling its opioid Opana ER from the market in June because of the FDAs concerns that the drug became a favorite of people abusing opioids.

“This represented a shift in that the FDA considered not just how a drug is used by the appropriate patients, but also how it is being abused by addicts. “We’re constantly looking retrospectively to what’s on the market and making sure that it still makes sense relative to today’s marketplace and what’s available,” Gottlieb said.

Regarding the FDA’s approval process, Gottlieb reiterated what other experts have noted: That process is already one of the quickest in the world. It’s the clinical trials that need to be streamlined, Gottlieb said.

Number of Docs Jumps 12%

A bit of good news for those worrying about the coming physician shortage: the Federation of State Medical Boards (FSMB) says that the number of doctors increased 12% from 2010 to 2016. There were 953,695 actively licensed physicians in the United States in 2016, up from 850,085 in 2010. “United States first-year medical school enrollment has increased by 28% since 2002,” according to an FSMB census. “In 2016, 88,304 medical students were enrolled, compared with 81,934 medical students in 2012.”

Demand will surely grow; the organization points not just to baby boomers but also to millennials, those born between 1982 and 2000. “With the inclusion of immigration, millennials are expected to grow in number, reaching their peak population around 2036,” the FSMB states. “Future planning needs to take into account the health care needs of all generations.”

Predictions from about 10 years ago pegged the doctor shortage to be about 160,000 by 2025, but the number has gone down from between 40,800 to 104,900 by 2030, which the FSMB calls a “still-alarming” shortage.

The FSMB relied on data from state medical and osteopathic boards that are responsible for the licensing and disciplining of doctors in the United States. The database contains more than 2 million doctor records and includes information about doctors who are currently licensed, are no longer licensed, or who are dead.

“As the aging physician population remains a concern in terms of health care supply, some of the fastest growing segments of the physician population in the United States— including females, DOs, and Caribbean medical graduates—tend to be younger compared [with] the overall physician population,” according to the FEMB. In 2010, 30% of doctors were females; in 2016, that proportion rose to 34%.

“The increase in the number of female physicians coincides with the steady rise of first-time medical licenses issued to female physicians in past decades, as well as a greater percentage of female physicians graduating from U.S. medical schools,” the FSMB census states.

Design Thinking Applied to Problems

It happens too often in too many American cities: Someone is admitted to a hospital emergency department with a gunshot wound. Doctors, nurses, and technicians work frantically to save the patient’s life. But this swarm of health care providers too often functions like a swarm: with no clear leader.

Toronto-based physician and journalist Amitha Kalaichandran, MD, recently wrote in the New York Times that at many hospitals the team leader now wears an orange vest.
Another anecdote: Patients at Thomas Jefferson University Hospital in Philadelphia are asked to rate their pain on a scale of 1 to 10. However, that can sometimes be difficult for a child. So the hospital came up with CareCube, a six-sided square in which different faces are drawn to reflect different intensities of pain. “When asked about their pain levels, children in the hospital can simply take the cube and point to a face, which helps the nurse decide if their pain is being managed well,” Kalaichandran wrote.

These are examples of design thinking—ideas that spring from the people on the frontlines of health care—and they’re becoming more prevalent, wrote Kalaichandran. The approach is borrowed from the business world, where it was used to create innovative products. The solution should be simple and easy to implement. Kalaichandran continued, singing the praises of simplicity: “When I think of something as basic as a bright orange vest, it amazes me that such a simple and inexpensive idea from an experienced nurse could lead to improvements in how real trauma cases are handled.”

States Seek Medicaid Waivers

In an effort to reduce Medicaid spending, some states have requested waivers from the Trump administration that would place certain restrictions on who gets the aid. Those restrictions include making some recipients pay monthly premiums, submit to drug testing, and get jobs or, at least, higher paying jobs (with the states’ help). Most states spend more on Medicaid than on almost anything else, except education. Thanks to the expansion of the program under Obamacare, enrollment has soared by about 14 million people since 2014.

“‘To Medicaid’s staunchest supporters and most vocal critics alike, the waiver requests are a way to rein in the $500 billion program that has undergone unprecedented growth the past four years and now covers 75 million people,” Kaiser Health News reported.

The waivers, granted under the ACA, began to be made available on April 1. They can be used to bolster programs, as well as cut spending. For instance, Virginia used the money to make more residential drug treatment programs available for citizens. The number of such programs grew from four, in the beginning of the year, to over 70.

—Frank Diamond

Study: CareFirst’s patient-centered medical home didn’t save money for Medicare patients

CareFirst’s patient-centered medical home model, which provides financial incentives to primary care practices and care coordination for high-risk patients, did not reduce Medicare spending or hospitalizations, according to a study in JAMA Internal Medicine. Researchers with Mathematica Policy Research noted that if the program had proven successful, “CMS could expand it to other practices, potentially even nationwide.”

In 2012, CMS awarded CareFirst BlueCross BlueShield, the largest health plan in the Mid-Atlantic region, a $20 million Health Care Innovation Award to determine how cost-effective its model home program can be for Medicare. CareFirst selected 52 primary care practices in the commercial program to participate in the expansion in order to include about 35,000 Medicare beneficiaries, of whom 10% received intensive care coordination services. The program ran from August 2013 to December 2015. Using a difference-in-differences analysis, the program did not produce enough Medicare savings to pay for itself. (All-cause hospitalizations declined by 10% for both the intervention group and the comparison group, comprised of Medicare fee-for-service patients.)

Spending comparison of PCMH, non-PCMH groups by quarter
Medicare Parts A and B spending per patient per month

Source: Peterson GG et al., JAMA Internal Medicine, July 31, 2017
To Dent Soaring Drug Costs, States Turn to ‘Price-Gouging’ Laws

Maryland is the first state to enact legislation, but it must pass a court challenge.

By Richard Mark Kirkner, Contributing Editor

Maybe it was the smirk on now convicted felon Martin Shkreli’s face when the former Turing Pharmaceuticals CEO and founder went to Capitol Hill last year to defend the 5,400% price increase of the anti-parasitic drug Daraprim. Or the outrage over Mylan’s jacking up the price of its EpiPen for anaphylaxis 500% over seven years. The term “price gouging” has entered the public discourse on drug cost, and now state legislatures are picking up on the term in their efforts to rein in the costs of pharmaceuticals.

Maryland has already adopted a law (without Republican Gov. Larry Hogan’s signature) to thwart “unconscionable” price increases in generic drugs, and at least four other states are taking up legislation that mentions price gouging specifically.

It’s out of control

States are facing unsustainable health care costs, and prescription drugs for Medicaid beneficiaries and state employees are the reason. From 2009 to 2013, the consumer price index (CPI) for prescription drugs increased about 11% vs. 8% for the overall CPI. And the problem is getting worse; in 2014, the CPI for prescription drugs increased 6% while the overall CPI rose less than 1%.

That cost curve is only going to get steeper, explains Chuck Shih, PhD, a senior officer of the Pew Charitable Trusts Prescription Project. “Looking forward into future years, projections are that drug spending will increase at a faster rate than overall health care, and spending in health care is driven in large part by increases in drug spending.”

States have taken action on curbing drug costs before, but state-level laws and regulations have usually focused on Medicaid and prescription drug coverage for state employees. But now they are venturing into new territory with laws that require drug manufacturers and distributors to divulge what they charge. No fewer than 13 states have such laws pending. What’s new is the specific mention of price gouging in some of these laws.

Picking on generics

Maryland may soon find out the term price gouging may not mean much at all. Shortly after the law went into effect, the Association for Accessible Medicines (AAM), a trade group of generic-drug manufacturers, sued in federal court to block the law, which it claims is unconstitutional. The Maryland law only targets excessive price hikes of “essential” off-patent or generic drugs.

Essentially, the law empowers Maryland’s Medicaid program to notify the state’s attorney general of a “certain increase in the price” of a drug in a specific amount of time. The attorney general could then demand an explanation from the drug manufacturer and, if she or he determines a violation has occurred, order corrective action.

The Maryland law also defines price gouging: “an unconscionable increase in the price of a prescription drug.” It further defines “unconscionable” as “excessive” and not justified by the manufacturing or distributing costs and leaves consumers who need the drug with no other choice but to pay the higher price. The law targets the wholesale acquisition price.

Jeffrey Francer, the general counsel for the association, explains the constitutional basis for the challenge is that the law violates the Constitution’s commerce clause by giving the Maryland attorney general power to regulate business activity beyond the state’s borders and violates the due process clause by its vagueness. “The standards of the law are so vague,” Francer says. “When someone is driving on the highway, the speed limit is very clearly marked: You can’t go over 65 miles an hour. That’s definitely not the case with the Maryland law.”
Vinny DeMarco, CEO of the Maryland Citizens’ Health Initiative, a consumer group that pushed for the anti-gouging legislation, counters that the term “unconscionable” is well developed in law and that the courts are using it as a standard. What’s more, he says, the law provides guidelines the attorney general can use to determine an “unconscionable” price increase.

**Different approaches**

Pew is exploring different approaches states are taking to control drug costs. With regard to the Maryland law, Shih says, “This focus on price spikes of generic drugs may in fact have a more limited impact.”

Zeroing in on generic drugs has the AAM lawyers scratching their heads, too. “The Maryland law only applies to 26% of national prescription drug spending and ignores three quarters of it,” says Francer. “Why the legislature would want to harm the one sector in health care that’s actually deflationary is beyond me.”

AAM numbers from 2015 show generic drugs account for 89% of all prescriptions but 27% of drug costs. A 2017 Blue Cross Blue Shield Association analysis of member plans found pretty much the same thing: The share of prescribed drugs that are generic rose from 66% in 2010 to 82% in 2016, but the share of spending on generics actually dropped slightly, from 23% to 22%.

While the AAM is going all out in opposing the Maryland law, Pharmaceutical Research and Manufacturers of America, which represents the makers of brand-name products, registered only mild protest in a statement that mentioned concerns about the law giving the Maryland attorney general “broad and ambiguous powers.”

**Defining price**

States looking at price-gouging legislation—Massachusetts, New York, Rhode Island, and Tennessee—could learn from Maryland’s experience. But crafting such legislation is not easy, as Pew’s Shih explains, because the drug payment and supply chain is so complex. “It’s not the case that a manufacturer makes a drug and it’s put in the hand of a patient or even a pharmacy; there are different intermediaries involved.”

And trying to define drug “price”? Forget about it.

“It depends on what price you’re talking about and to whom,” Shih says. “If you’re thinking about it in the context of a list price, yes, certainly that is a price that’s set by the manufacturer. But we know that is not always the price that the patient pays. And it’s not always the price that various supply chain entities are paying either.”

While a price-gouging law is wending its way through New York State’s legislature, New York already has a model for controlling drug prices. If Medicaid spending surpasses a certain threshold, the state’s Medicaid program can enter into discussion with manufacturers to justify or lower the price. If that fails, the state can move to limit patient access to high-cost drugs and alter formularies so patients would be required to try generics before branded drugs. “That gives teeth to the state to lower spending on drugs,” Shih says.

AAM’s Francer notes that Vermont has also come up with another approach: The state health department is empowered to issue a report that includes the prices the state pays for prescription drugs.

**What’s justified?**

Massachusetts’ proposed price-gouging law mostly deals with greater price transparency. But like the Maryland statute, the Massachusetts law would give the attorney general the power to determine if a prescription price increase has been “excessively higher than justified.”

New York’s proposed law defers to the court to determine an “unconscionably excessive” drug price and sets up to $1 million in penalties. Rhode Island would forbid “unreasonably excessive” pricing during a market emergency—deferring to the governor or president to declare such shortages. Tennessee’s draft law would impose reporting requirements on the state to prevent price gouging of “essential” generic drugs.

Says Shih, “Everybody is trying to figure out what the right approach is to take.”

By targeting price gouging, they’re trying to wipe that smirk off Shkreli’s face, although it still seemed to be intact after his conviction last month for securities fraud.
Regimen Change: Gilead’s TAF Drugs Toppling TDFs in HIV Treatment
But for Truvada, there’s new life as a drug that people are taking to prevent HIV infection in the first place.

By Thomas Reinke, Contributing Editor

New variants of existing HIV treatment drugs are rapidly replacing their older ones, but one mainstay is moving on to an even more important role as the regimen that prevents infection with the virus.

Combination medicines that include tenofovir disoproxil fumarate (TDF), which was approved by the FDA in 2001, are among the leading antiretroviral agents in HIV treatment. They include:

- Atripla (tenofovir disoproxil fumarate, emtricitabine, efavirenz)
- Complera (tenofovir disoproxil fumarate, emtricitabine, rilpivirine)
- Striibild (tenofovir disoproxil fumarate, emtricitabine, elvitegravir, cobicistat)
- Truvada (tenofovir disoproxil fumarate, emtricitabine)

All have hit the blockbuster-level sales mark. All are marketed by Gilead, the heavyweight in the HIV drug market. A major reason for their popularity is that they have made HIV treatment so much simpler. What was once a complicated regimen is now a single pill.

But now Gilead has developed an improved formulation of tenofovir called tenofovir alafenamide (TAF). As a result, its TDF agents are slowly but surely ceding king-of-the-hill status to three new TAF products.

Genvoya (emtricitabine, elvitegravir, cobicistat, tenofovir alafenamide), the first regimen with TAF, was approved in November 2015. Last year, the FDA approved two additional TAF formulations, Odefsey (emtricitabine, rilpivirine, tenofovir alafenamide) and Descovy (emtricitabine, tenofovir alafenamide). Genvoya and Odefsey are considered complete therapy; Descovy is used in combination with other medications.

TAF is as effective as TDF but in much smaller quantities. The lower dose lessens the risk of kidney damage and bone mineral density problems, so new TAF combinations don’t need the TDF label warning about the risk of renal impairment and the need for creatinine clearance testing at the start of therapy.

But Gilead also has not-so-trivial business reasons for pushing the TAF drugs. The TDF patent for adult use expires in 2017 and in 2018 for pediatric use, so the new TAF drugs should help keep Gilead’s revenue from branded HIV drugs from petering out. HIV products account for about half of Gilead’s total annual revenue, and sales of its hepatitis C drugs—Sovaldi, Harvoni, and Epclusa—are slipping.

So far, Gilead seems to have played its cards well because sales of the TAF products are strong. First quarter 2017 sales for Genvoya were $769 million compared with first quarter 2016 sales of $158 million. Descovy’s first quarter 2017 sales were $251 million, putting it on track for blockbuster status this fiscal year. First quarter 2017 sales for Odefsey were in the same ballpark.

20% trend
Express Scripts’ 2016 Drug Trend Report highlights the impact of Gilead’s switch from TDF to TAF products. Express Scripts’ total expenditure increase (trend) for 2016 in the antiviral category was 21.7%, which includes a 5.5% increase in utilization and a 16.2% unit-cost increase. Only 5.3% of HIV prescriptions were for generic drugs, and the average cost per script was $1,556. Express Scripts anticipates the trend to continue at about 20%.

The top five drugs by market share in Express Scripts’ book of business were Truvada, Atripla, Viread, Norvir, and Genvoya. Norvir is an Abbvie product; the other four are Gilead’s.

Drug price information published on the NIH’s AIDSinfo website indicate that the average wholesale prices of Gilead’s new TAF combina-

Pre-exposure prophylaxis is practiced by about 80,000 people in the United States, says Erik Storholm, a Rand researcher.
tion drugs were comparable to its TDF-based products as of April 2016.

**Truvada’s second career**

Truvada, a TDF, was Gilead’s 2016 HIV sales leader, but this year the TAF drugs are cutting into its sales. But Truvada is getting a new lease on life as a preventive agent. It is the only drug approved to prevent HIV infections, and Truvada is the key pharmaceutical component of pre-exposure prophylaxis, which is aimed at preventing, rather than treating, HIV infection and transmission.

Truvada received approval for HIV prevention in 2012, eight years after its nod for HIV treatment. In two clinical trials, it demonstrated a 42% and 75% reduction in HIV infection and a 92% reduction in transmission in one of those studies. Those trials and others since have shown that adherence to Truvada as pre-exposure prophylaxis is the key to prevention. In fact, in one small study in which people were over 90% adherent, there were no infections.

Truvada for pre-exposure prophylaxis can be prescribed only to people who are HIV negative. Part of the reason for this approach is concern that if people who are HIV positive use Truvada for preventive purposes, they will unintentionally create HIV variants that are resistant to Truvada.

When the FDA approved Truvada for prevention in 2012, the FDA and Gilead took a cautious approach to its rollout, limiting use to high-risk individuals. The go-slow approach was understandable. Decades of funding for public education and promotion of safe sex practices were paying off. No one wanted to undo those public health achievements with an approach that might be misinterpreted as suggesting that a daily pill has replaced the need for other precautions.

Three years ago, the CDC’s HIV guidelines changed to include pre-exposure prophylaxis as an option. The CDC says pre-exposure prophylaxis is recommended as one prevention option for sexually active adult men who have sex with other men, heterosexually active men and women with HIV-positive partners, and adult injection drug users at substantial risk of HIV acquisition.

After the CDC guidelines came out, HIV clinics began telling the story of the potential of pre-exposure prophylaxis, and Gilead cranked up its marketing of pre-exposure prophylaxis. Truvada’s label now specifically mentions its use as part of pre-exposure prophylaxis for high-risk individuals.

Express Scripts provided MANAGED CARE with valuable insights into its experience with pre-exposure prophylaxis. A company spokesperson told us that Express Scripts spends more money on Truvada than any other HIV medication. Most (60%) of Truvada users take the drug for treatment purposes, but Express Scripts says the number of people taking the drug for pre-exposure prophylaxis has nearly doubled in the last year.

Erik Storholm, PhD, a Rand researcher, says pre-exposure prophylaxis is practiced by an estimated 80,000 individuals. The NIH reported that the April 2016 average wholesale price of Truvada was $1,760 for a monthly supply of the 300mg/200mg dose. Truvada is covered as a preferred drug in many Express Scripts formularies, and Storholm says coverage is common in the plans of other pharmacy benefit companies. In addition, it’s available through AIDS clinics and public health programs. Gilead also has various copay and patient assistance programs.

Overall, the HIV/AIDS epidemic is tapering off. The CDC says there were approximately 37,600 HIV infections in 2014, down from 45,700 in 2008. But the overall picture glosses over some of the glaring differences in population groups. For example, black men now account for 45% of new cases, even though they make up less than 7% of the total U.S. population.

The challenge facing pre-exposure prophylaxis and HIV diagnosis and treatment continues to be in achieving equity across all populations. In June, the FDA granted Teva Pharmaceuticals approval for a generic version of Truvada including the indication for pre-exposure prophylaxis. A generic version of Truvada would presumably be less expensive. But there’s uncertainty about exactly when the generic will be available—and its price.

A report of the FDA’s approval on POZ.com, an HIV/AIDS news site, reports that the uncertainty may be tied to a patent dispute. Other drug manufacturers—Lupin, Cipla, and Amneal Pharmaceutical—are developing their own generic versions of Truvada.
In COMFORT-I* and COMFORT-II†, Jakafi® (ruxolitinib) significantly reduced spleen volume compared with patients receiving placebo or best available therapy, respectively.1-3

The primary end point was the proportion of patients achieving a ≥35% reduction in spleen volume from baseline at week 48 as measured by CT or MRI.1,3

* COMFORT-I (COntrolled MyeloFibrosis study with ORal JAK inhibitor Treatment-I) was a randomized, double-blind, placebo-controlled phase 3 study with 309 patients with intermediate-2–risk or high-risk myelofibrosis.1,2

† COMFORT-II (COntrolled MyeloFibrosis study with ORal JAK inhibitor Treatment-II) was a randomized, open-label phase 3 study with 219 patients with intermediate-2–risk or high-risk myelofibrosis.1,3

‡ Best available therapy in COMFORT-II included hydroxyurea (46.6%) and glucocorticoids (16.4%), as well as no medication, anagrelide, epoetin alfa, thalidomide, lenalidomide, mercaptopurine, thioguanine, danazol, peginterferon alfa-2a, interferon-α, melphalan, acetylsalicylic acid, cytarabine, and colchicine.4

The primary end point was the proportion of patients achieving a ≥35% reduction in spleen volume from baseline at week 24 as measured by CT or MRI.1,2

Important Safety Information

- Treatment with Jakafi can cause thrombocytopenia, anemia and neutropenia, which are each dose-related effects. Perform a pre-treatment complete blood count (CBC) and monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated
- Manage thrombocytopenia by reducing the dose or temporarily interrupting Jakafi. Platelet transfusions may be necessary
- Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi
- Severe neutropenia (ANC <0.5 × 10⁹/L) was generally reversible by withholding Jakafi until recovery
- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting Jakafi until active serious infections have resolved. Observe patients receiving Jakafi for signs and symptoms of infection and manage promptly
- Tuberculosis (TB) infection has been reported. Observe patients taking Jakafi for signs and symptoms of active TB and manage promptly. Prior to initiating Jakafi, evaluate patients for TB risk factors and test those at higher risk for latent infection. Consult a physician with expertise in the treatment of TB before starting Jakafi in patients with evidence of active or latent TB. Continuation of Jakafi during treatment of active TB should be based on the overall risk-benefit determination
- Progressive multifocal leukoencephalopathy (PML) has occurred with ruxolitinib treatment for myelofibrosis. If PML is suspected, stop Jakafi and evaluate
- Advise patients about early signs and symptoms of herpes zoster and to seek early treatment
- Increases in hepatitis B viral load with or without associated elevations in alanine aminotransferase and aspartate aminotransferase have been reported in patients with chronic hepatitis B virus (HBV) infections. Monitor and treat patients with chronic HBV infection according to clinical guidelines
Indications and Usage
Jakafi is indicated for treatment of patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis.

Overall survival was a prespecified secondary end point in COMFORT-I and COMFORT-II.

- **COMFORT-I**: At 3 years, survival probability was 70% for patients originally randomized to Jakafi and 61% for those originally randomized to placebo.
- **COMFORT-II**: At 3 years, survival probability was 76% for patients originally randomized to Jakafi and 59% for those originally randomized to best available therapy.

Because of progression-driven events or at the physician's discretion, patients randomized to placebo (COMFORT-I) or best available therapy (COMFORT-II) who crossed over to receive Jakafi continued to be grouped within their original randomized assignment for analysis purposes.

All patients in the placebo group either crossed over or discontinued.

- When discontinuing Jakafi, myeloproliferative neoplasm-related symptoms may return within one week. After discontinuation, some patients with myelofibrosis have experienced fever, respiratory distress, hypotension, DIC, or multi-organ failure. If any of these occur after discontinuation or while tapering Jakafi, evaluate and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi without consulting their physician. When discontinuing or interrupting Jakafi for reasons other than thrombocytopenia or neutropenia, consider gradual tapering rather than abrupt discontinuation.
- Non-melanoma skin cancers including basal cell, squamous cell, and Merkel cell carcinoma have occurred. Perform periodic skin examinations.
- Treatment with Jakafi has been associated with increases in total cholesterol, low-density lipoprotein cholesterol, and triglycerides. Assess lipid parameters 8-12 weeks after initiating Jakafi. Monitor and treat according to clinical guidelines for the management of hyperlipidemia.
- The three most frequent non-hematologic adverse reactions (incidence >10%) were bruising, dizziness, and headache.
- A dose modification is recommended when administering Jakafi with strong CYP3A4 inhibitors or fluconazole or in patients with renal or hepatic impairment. Patients should be closely monitored and the dose titrated based on safety and efficacy.
- Use of Jakafi during pregnancy is not recommended and should only be used if the potential benefit justifies the potential risk to the fetus. Women taking Jakafi should not breast-feed.

Please see Brief Summary of Full Prescribing Information for Jakafi on the following pages.

To learn more about Jakafi, visit Jakafi.com/HCP.

WARNINGs and PRECAUTIONS

Thrombocytopenia, Anemia and Neutropenia
Treatment with Jakafi can cause thrombocytopenia, anemia and neutropenia. [see Dosage and Administration (2.1) in Full Prescribing Information]. Manage thrombocytopenia by reducing the dose or temporarily interrupting Jakafi. Platelet transfusions may be necessary [see Dosage and Administration (2.1.1) and Adverse Reactions (6.1) in Full Prescribing Information]. Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi. Severe neutropenia (ANC less than 0.5 X 10^9/L) was generally reversible by withholding Jakafi until recovery [see Adverse Reactions (6.1) in Full Prescribing Information]. Perform a pre-treatment complete blood count (CBC) and monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated. [see Dosage and Administration (2.1.1) and Adverse Reactions (6.1) in Full Prescribing Information].

Risk of Infection
Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting therapy with Jakafi until clinical parameters support clinical stability and bacterial and/ or fungal infections are resolved. Patients with myelofibrosis have experienced one or more of the following adverse events after discontinuing Jakafi: fever, respiratory distress, hypotension, DIC, or multi-organ failure. If one or more of these occur after discontinuation of, or while tapering the dose of Jakafi, evaluate for and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi therapy without consulting their physician. When discontinuing or interrupting therapy with Jakafi for reasons other than thrombocytopenia or neutropenia [see Dosage and Administration (2.2) in Full Prescribing Information], complete a course of prophylactic therapy. Jakafi should not be used in patients with active or latent tuberculosis until a complete course of prophylactic therapy has been administered. Treat patients with active or latent tuberculosis as defined by standard clinical practice. A complete course of prophylactic therapy is defined as 6 to 12 months of isoniazid. Consult a physician with expertise in the treatment of tuberculosis before starting treatment with Jakafi. The decision to continue Jakafi during treatment of active tuberculosis should be based on the overall risk-benefit determination. N Engl J Med 2010;363:1090-1101. Patients with chronic HBV infection should be treated and monitored according to current clinical guidelines. Symptom Exacerbation Following Interruption or Discontinuation of Treatment with Jakafi Following discontinuation of Jakafi, symptoms from myeloproliferative neoplasms may return to pre-treatment levels over a period of approximately one week. Some patients with myelofibrosis have experienced one or more of the following adverse events after discontinuation of Jakafi: fever, respiratory distress, hypotension, DIC, or multi-organ failure. If one or more of these occur after discontinuation of, or while tapering the dose of Jakafi, evaluate for and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi therapy without consulting their physician. When discontinuing or interrupting therapy with Jakafi for reasons other than thrombocytopenia or neutropenia [see Dosage and Administration (2.2) in Full Prescribing Information], complete a course of prophylactic therapy. Jakafi should not be used in patients with active or latent tuberculosis until a complete course of prophylactic therapy has been administered. Treat patients with active or latent tuberculosis as defined by standard clinical practice. A complete course of prophylactic therapy is defined as 6 to 12 months of isoniazid. Consult a physician with expertise in the treatment of tuberculosis before starting treatment with Jakafi. The decision to continue Jakafi during treatment of active tuberculosis should be based on the overall risk-benefit determination. N Engl J Med 2010;363:1090-1101. Patients with chronic HBV infection should be treated and monitored according to current clinical guidelines. Symptom Exacerbation Following Interruption or Discontinuation of Treatment with Jakafi Following discontinuation of Jakafi, symptoms from myeloproliferative neoplasms may return to pre-treatment levels over a period of approximately one week. Some patients with myelofibrosis have experienced one or more of the following adverse events after discontinuation of Jakafi: fever, respiratory distress, hypotension, DIC, or multi-organ failure. If one or more of these occur after discontinuation of, or while tapering the dose of Jakafi, evaluate for and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi therapy without consulting their physician. When discontinuing or interrupting therapy with Jakafi for reasons other than thrombocytopenia or neutropenia [see Dosage and Administration (2.2) in Full Prescribing Information], complete a course of prophylactic therapy. Jakafi should not be used in patients with active or latent tuberculosis until a complete course of prophylactic therapy has been administered. Treat patients with active or latent tuberculosis as defined by standard clinical practice. A complete course of prophylactic therapy is defined as 6 to 12 months of isoniazid. Consult a physician with expertise in the treatment of tuberculosis before starting treatment with Jakafi. The decision to continue Jakafi during treatment of active tuberculosis should be based on the overall risk-benefit determination. N Engl J Med 2010;363:1090-1101. Patients with chronic HBV infection should be treated and monitored according to current clinical guidelines.

ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of the labeling: • Thrombocytopenia, Anemia and Neutropenia [see Warnings and Precautions (5.1) in Full Prescribing Information] • Risk of Infection [see Warnings and Precautions (5.2) in Full Prescribing Information] • Symptom Exacerbation Following Interruption or Discontinuation of Treatment with Jakafi [see Warnings and Precautions (5.3) in Full Prescribing Information] • Non-Melanoma Skin Cancer [see Warnings and Precautions (5.4) in Full Prescribing Information]. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. Clinical Trials Experience in Myelofibrosis The safety of Jakafi was assessed in 617 patients in 6 clinical studies with a median duration of follow-up of 13.9 months, including 301 patients with myelofibrosis in two Phase 3 studies. In these two Phase 3 studies, patients had a median duration of exposure to Jakafi of 5.6 months (range 0.5 to 79 months), with 80% of patients treated for more than 6 months and 25% treated for more than 12 months. One hundred and eleven (111) patients started treatment at 15 mg twice daily and 190 patients started at 20 mg twice daily. In patients starting treatment with 15 mg twice daily (pretreatment platelet counts of 100 to 200 X 10^9/L) and 20 mg twice daily (pretreatment platelet counts greater than 200 X 10^9/L), 65% and 25% of patients, respectively, required a dose reduction below the starting dose within the first 8 weeks of therapy. In a double-blind, randomized, placebo-controlled trial of Jakafi, among the 155 patients treated with Jakafi, the most frequent adverse drug reactions were thrombocytopenia and anemia [see Table 2]. Thrombocytopenia, anemia and neutropenia are dose related effects. The three most frequent non-hematologic adverse drug reactions were bruising, dizziness and headache [see Table 1]. Discontinuation for adverse events, regardless of causality, was observed in 11% of patients treated with Jakafi and 11% of patients treated with placebo. Table 1 presents the most common adverse reactions occurring in patients who received Jakafi in the double-blind, placebo-controlled study during randomized treatment.

Table 1: Myelofibrosis: Adverse Reactions Occurring in Patients on Jakafi in the Double-blind, Placebo-controlled Study During Randomized Treatment

<table>
<thead>
<tr>
<th></th>
<th>Jakafi (N=155)</th>
<th>Placebo (N=151)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades (%)</td>
<td>Grade 3 (%)</td>
</tr>
<tr>
<td>Bruising</td>
<td>23</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Dizziness</td>
<td>18</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Headache</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Urinary Tract Infections</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Weight Gain</td>
<td>7</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Flatulence</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Herpes Zoster</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2: Myelofibrosis: Adverse Reactions Occurring in Patients on Jakafi in the Double-blind, Placebo-controlled Study

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>All Grades (%)</th>
<th>Grade 3 (%)</th>
<th>Grade 4 (%)</th>
<th>All Grades (%)</th>
<th>Grade 3 (%)</th>
<th>Grade 4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>70</td>
<td>9</td>
<td>4</td>
<td>31</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Anemia</td>
<td>96</td>
<td>34</td>
<td>11</td>
<td>87</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>19</td>
<td>5</td>
<td>2</td>
<td>4</td>
<td>&lt;1</td>
<td>1</td>
</tr>
</tbody>
</table>

Additional Data from the Placebo-controlled Study 25% of patients treated with Jakafi and 7% of patients treated with placebo developed newly occurring or worsening Grade 1 abnormalities in alanine transaminase (ALT). The incidence of greater than or equal to Grade 2 elevations was 2% for Jakafi with 1% Grade 3 and no Grade 4 ALT elevations. 17% of patients treated with Jakafi and 8% of patients treated with placebo developed newly occurring or worsening Grade 1 abnormalities in aspartate transaminase (AST). The incidence of Grade 2 AST elevations was <1% for Jakafi with no Grade 3 or 4 AST elevations. 17% of patients treated with Jakafi and <1% of patients treated with placebo developed newly occurring or worsening Grade 1 elevations in cholesterol. The incidence of Grade 2 cholesterol elevations was <1% for Jakafi with no Grade 3 or 4 cholesterol elevations. Clinical Trial Experience in Polycythemia Vera In a randomized, open-label, active-control study, 110 patients with polycythemia vera resistant to hydroxyurea received Jakafi and 111 patients received best available therapy [see Clinical Studies (14.2) in Full Prescribing Information]. The most frequent adverse drug reaction was anemia. Table 3 presents the most frequent non-hematologic treatment emergent adverse events occurring up to Week 22. Discontinuation for adverse events, regardless of causality, was observed in 4% of patients treated with Jakafi.
Jakafi includes dyspnea and dyspnea exertional
c includes dizziness and vertigo
a National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0
Table 3: Polycythemia Vera: Treatment Emergent Adverse Events Occurring in ≥ 6% of Patients on

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>All Grades (%)</th>
<th>Grade 3-4 (%)</th>
<th>All Grades (%)</th>
<th>Grade 3-4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>16 (&lt;1)</td>
<td>19 (&lt;1)</td>
<td>15 (&lt;1)</td>
<td>15 (&lt;1)</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>15 (&lt;1)</td>
<td>15 (&lt;1)</td>
<td>15 (&lt;1)</td>
<td>15 (&lt;1)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>15 (&gt;7)</td>
<td>13 (0)</td>
<td>15 (3)</td>
<td>15 (3)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>15 (&lt;1)</td>
<td>23 (4)</td>
<td>13 (0)</td>
<td>13 (0)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>15 (0)</td>
<td>4 (0)</td>
<td>15 (3)</td>
<td>15 (3)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>14 (&lt;1)</td>
<td>23 (4)</td>
<td>23 (4)</td>
<td>23 (4)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>13 (&lt;1)</td>
<td>4 (0)</td>
<td>13 (&lt;1)</td>
<td>13 (&lt;1)</td>
</tr>
<tr>
<td>Muscle Spasms</td>
<td>12 (&lt;1)</td>
<td>5 (0)</td>
<td>12 (&lt;1)</td>
<td>12 (&lt;1)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>9 (0)</td>
<td>8 (0)</td>
<td>8 (0)</td>
<td>8 (0)</td>
</tr>
<tr>
<td>Constipation</td>
<td>8 (0)</td>
<td>3 (0)</td>
<td>8 (0)</td>
<td>8 (0)</td>
</tr>
<tr>
<td>Cough</td>
<td>8 (0)</td>
<td>5 (0)</td>
<td>8 (0)</td>
<td>8 (0)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>7 (0)</td>
<td>6 (0)</td>
<td>6 (0)</td>
<td>6 (0)</td>
</tr>
<tr>
<td>Asthma</td>
<td>7 (0)</td>
<td>11 (2)</td>
<td>7 (0)</td>
<td>11 (2)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>6 (0)</td>
<td>3 (0)</td>
<td>6 (0)</td>
<td>3 (0)</td>
</tr>
<tr>
<td>Herpes Zoster</td>
<td>6 (&lt;1)</td>
<td>0 (0)</td>
<td>6 (&lt;1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Nausea</td>
<td>6 (0)</td>
<td>4 (0)</td>
<td>6 (0)</td>
<td>4 (0)</td>
</tr>
</tbody>
</table>

Table 3: Polycythemia Vera: Treatment Emergent Adverse Events Occurring in ≥ 6% of Patients on

a National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0

Table 4: Polycythemia Vera: Selected Laboratory Abnormalities in the Open-Label, Active-controlled Study up to Week 32 of Randomized Treatment

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>All Grades (%)</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>72 (&lt;1)</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>58</td>
<td>0</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>27 (5)</td>
<td>&lt;1</td>
<td>24</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>3 (0)</td>
<td>&lt;1</td>
<td>10</td>
<td>&lt;1</td>
<td>0</td>
</tr>
<tr>
<td>Chemistry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>35 (0)</td>
<td>0</td>
<td>8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Elevated ALT</td>
<td>25 (0)</td>
<td>&lt;1</td>
<td>16</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Elevated AST</td>
<td>23 (0)</td>
<td>0</td>
<td>23</td>
<td>&lt;1</td>
<td>0</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>15 (0)</td>
<td>0</td>
<td>13</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 4: Polycythemia Vera: Selected Laboratory Abnormalities in the Open-Label, Active-controlled Study up to Week 32 of Randomized Treatment

a Presented values are worst Grade values regardless of baseline
b National Cancer Institute Common Terminology Criteria for Adverse Events, version 3.0

DRUG INTERACTIONS Drugs That Inhibit or Induce Cytochrome P450 Enzymes Ruxolitinib

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Revised: March 2016 RUX-1779
Seemingly everyone in health care is on board with the notion that dollars should reward value rather than volume or intensity of care. There is far less agreement about what value-based care should actually be. Today’s versions have been shaped by a hodgepodge of quality measures, re-engineered delivery systems, and alternative reimbursement schemes. Each embodies value for someone—but not necessarily for all of those who deliver, pay for, and use health care services.

It’s fair to say, however, that value-based care as we know it today is still in beta. A National Academy of Medicine paper earlier this year acknowledged that there is still scant evidence about what works among today’s payment-reform models and which skills physicians and patients need to be effective players within them. As it evolves, value-based care’s flaws will be exposed and, ideally, addressed. “We have to build this plane while we fly it,” remarks Alan Balch, CEO of the Virginia-based Patient Advocate Foundation.

Many of today’s value-based care models trace their roots to the Institute for Healthcare Improvement’s Triple Aim. Arguably, their sustainability may hinge on how true they stay to that trinity of improving population health, the patient experience, and per capita costs.

Population health

Some incarnations of value-based care, such as ACOs and episode-based payments, have strong population-based components. David J. Bailey, MD, president and CEO of Nemours, a pediatric health system spanning six East Coast states, says provider groups struggle to understand what population health means.

“You see the term used to talk about a sophisticated form of chronic disease management. That’s not population health, as far as I’m concerned,” says Bailey. To him, improving population health compels health care systems to form partnerships with community-level agencies to address social determinants of health.

Three decades’ worth of research has proven that education, income, housing, employment, racism, and violence are potent influences on health. In some localities where the need is great, Medicaid ACOs and special needs health plans—the Trenton Health Team in New Jersey and Amida Care in New York City come to mind—have developed relationships with community-based groups outside of health care to address these influences, but on a national level movement has been slow. A dozen years ago, Nemours got ahead of the curve, establishing a division dedicated to addressing social determinants of health in collaboration with community organizations.

In 2012, Nemours took what it learned from
Improving population health entails health plans forming partnerships with community organizations, says David J. Bailey, MD, CEO of Nemours.

**What's best for the patient?**

All this activity comes down to what’s best for the patient, or as IHI frames it in the Triple Aim, the patient experience. In the eyes of Balch, at the Patient Advocate Foundation, which helps patients with arbitration, mediation, and negotiation for care- and expense-related issues, the patient focus is a crucial ingredient missing from many of today’s forms of value-based care.

“One of the challenges with [quality] measurement is that we don’t really have good ways to measure outcomes that matter to patients,” he says, noting that patient-reported outcomes and the technology for measuring and reporting them are limited. “We really need a moonshot, if you will, to come up with innovative ways to measure outcomes that matter to patients.”

In a *Health Affairs* blog in May, Balch and Darius Lakdawalla of Precision Health Economics, a health economics research firm with ties to academia and big pharma, argued that patients are willing to make tradeoffs, depending on what they want out of their care: fewer side effects in exchange for an acceptable degree of efficacy; avoidance of work life disruptions; access to an oral medication in place of an infusion that might leave them wasted for three days. If we are moving toward a system that places more cost on the patients, they wrote, it is reasonable that their preferences be reflected in formularies and coverage policies.

It may be easy for a payer to dismiss this as the stuff of quality of life. But Balch says listening to the patient might reveal variables affecting outcomes that the payer can grasp, such as willingness to adhere to a regimen, recovery time, or the ability to stay out of the hospital.

“Payers and clinicians struggle with this. They say, ‘The outcome we’re going to measure is survivorship. Or patient satisfaction.’ I understand the need to measure outcomes in a clinically defined way that may be appropriate for a population of patients or the average patient, but there needs to be a way to augment that with outcomes that are more specific to the patient in front of you because they may be very different from the average patient.”

Balch thinks of it as having a menu of options that reflect outcomes the patient identifies as important. As described in the foundation’s recent report, “The Roadmap to Consumer Clarity in Health Care Decision Making,” those options could supplement standardized outcomes measures that a payer or health system wants to use.

Integrating patient-reported outcomes into clinical value assessments means patients and clinicians will have to learn to communicate in meaningful ways. As a means to that end, Balch holds up as an example the work of the Life Raft Group, whose super-registry for patients with gastrointestinal stromal tumors (GIST) fosters collective learning. It also has led to identification of research gaps. For instance, researchers...
used patient-reported and clinical data to gain clarity on the effects of different drugs as third- and fourth-line therapies for GIST that helped inform the sequencing of therapies.

Now that CMS is collecting patient-reported outcomes, assessments of their use are gaining steam. Writing in *Value in Health* in June, Lee Squitieri, MD, of the David Geffen School of Medicine at the University of California–Los Angeles, outlined a consensus panel’s recommendations for the role of patient-reported outcomes in value-based payment reform: a clear rationale for the measurement and the intended context of its use; use of measures appropriate for the indication; and some level of standardization.

Balch believes that the best patient-reported outcomes are windows into a patient’s actual or potential clinical outcomes, adherence to treatment, and the financial consequences for the patient. “To the extent we’re defining patient value and satisfaction as the ‘hospitality suite’ I think we are doing a disservice to patients and the role they should play in measuring and paying for value.”

**Cost of mixed reimbursement models**

Lowering per capita cost is the final dimension of the Triple Aim, but that leaves some important unanswered questions in today’s value-based care models. “When folks talk about reducing costs, a pertinent question is ‘Reduce costs for whom?’” says Bailey at Nemours. “Is it for the patient? For the health system? For the payer?” In Nemours’s asthma-care model, savings benefit the payer—a situation that Bailey says “still has not been corrected.”

Like Nemours, many health systems have one foot planted in a fee-for-service environment and the other in a value-based world. On this, Bailey offers a cautionary tale.

The asthma pilot reduced ER visits and hospital stays—exactly the goal—but it meant a loss of revenue to Nemours. The hitch is that this sort of value-based model of care adds administrative costs that has kept Nemours from expanding it to other chronic diseases as rapidly as Bailey would like.

“An issue that isn’t spoken much about is the increased cost of maintaining multiple care models and reimbursement models,” says Bailey. “The administrative work to produce the data needed to support the outcomes in a simple pay-for-performance plan is remarkable … it will drive costs up for health systems in a mixed reimbursement environment.”

Now, pile on the complexity of value-based care: It may mean pay for performance, bundled payments, shared risk, or full risk. Bailey observes, “When you say ‘value-based,’ you are indicating one of a whole host of different reimbursement mechanisms that require their own administration and skill set.”

One way to confront this reality is through internal efficiencies. Nemours did this through the adoption of Lean principles, which encourage employees to identify and eliminate wasteful processes. Applying Lean allowed Nemours to maintain its asthma-care model—with its higher administrative costs—even after the grant for the pilot ended.

Lean and value-based care are compatible, says Bailey. “You want to strive for outcomes that are important to patients, and whether you are in a value-based or fee-based environment, the object is to drive waste out of the system.”

**Three-part harmony**

The dimensions of the Triple Aim are intended to work in concert, making value-based care an ongoing lesson in systems theory. Overreliance on any one dimension skews the application of value. Yes, fee for service has perverse incentives, but so may value-based care, points out Bailey—pointing to incentives not to provide care, the danger that has shadowed every venture into managing care.

“The reimbursement models are morally equivalent—it’s what you are able to do within a reimbursement system that makes one better than the other. Regardless of reimbursement system, we need to do what is best for the patient—and the rest will take care of itself.”
He’s successful, handsome, and seems like a genuinely nice guy. Even his dog is cute. (He sent pictures.) So, as much as the Green Monster, (we’re talking jealousy here, not Fenway Park), might want to nudge you toward disliking Geoffrey B. Crawford, a medical director in Anthem’s office of medical policy and technology assessment, it just can’t be done.

Crawford, who has dual U.S./Canadian citizenship, lived in Jakarta, Indonesia, from ages 4 to 14 and a lot of other places growing up. They included Scotland and Calgary, Canada. His family moved around so much because his father worked in the oil and gas industry while his mother taught at international schools. The years in Indonesia were a major influence: They sparked an interest in medicine and population health “given my inevitable exposure to the gross health inequalities of a nonfunctioning health care system.” (Another young man who got there in a hurry also spent part of his childhood in Indonesia: former President Barack Obama.)

Crawford crushed it in school, graduating with distinction from McGill University, earning an MD magnum cum laude from Albany Medical College, and then topping it off with a master’s degree in epidemiology from the University of Maryland. He completed his internship in internal medicine at Stanford and residency at the University of Maryland.

So make no mistake: He’s ambitious. He also knows his limitations. “For something as complicated as health care, I don’t believe that any one person understands the system in its entirety,” Crawford says. “You have to try to see as much of that as you can while focusing on the one expertise that you’re trained in.”

He’s also capable of the pithy and insightful quote like: “Engineers have saved more lives in medicine than physicians.” When Crawford praises the work of engineers, he’s talking specifically about chlorination of the water supply, which indeed has saved millions. He is board certified in public health and general preventive medicine (population medicine), which reflects his interest in the overall health care system.

Less is more
He thinks wellness proponents should make that an example—the best wellness programs would be those in which active patient participation is least.

“If you want to keep people healthy, if you can do it in a way to engineer health, you are more likely to be successful,” Crawford says. “Growing up and later,
in medical school, I discovered how complicated the health care system is and I wanted to be involved in a way that’s meaningful to me.”

Crawford became increasingly concerned about the entire health care system. “As meaningful as it is to impact patients’ lives on a daily basis working in a clinic or daily practice, I wanted to have influence on hundreds, thousands, even millions of people and can do that through the work we do at Anthem,” says Crawford. “I get satisfaction from impacting health processes at the system level.”

That may have a lot to do with why he is now a medical policy director for Anthem, which creates medical policy for all the company’s affiliated commercial, Medicaid, and Medicare medical plans nationwide. Crawford has been at Anthem for more than six years, first in clinical analytics, where he worked to bolster member engagement in evidence-based care, and now in the office of medical policy, where he works on clinical coverage policies used to determine utilization management and formulary decision making.

Crawford thinks that creating a team atmosphere is one of the more important aspects of being a physician manager. “Clinicians are particular types of personalities, so they’re going to try to solve the problem that’s in front of them,” he says. “And many of the problems in health care, if not all of them, are impossible to solve as one person.”

**Boost from technology**

Wellness is a topic very much on Crawford’s mind. It “ties into the evidentiary component of my position—evaluating the scientific literature to support evidence-based medicine; as well, I provide clinical leadership for evaluation and implementation of preventive health service recommendations.” He appreciates the common criticism of wellness programs: They haven’t really been shown to improve health, let alone save money. “There haven’t been a lot of great studies that have shown that wellness intervention will ultimately lead to the type of health outcomes that we are looking for,” Crawford says. “Part of the problem is human nature. People think they’re healthy when they’re not feeling unwell.”

In wellness, as in the rest of health care, technology is not always the answer, in Crawford’s opinion. The person who could most benefit from IT-based solutions is probably the least plugged in. “I think those are solutions that make a lot of sense, but they’re really something that’s probably only going to be utilized by the young and healthy, or the curious.”

Still, technology could give wellness programs a boost. As an example, Crawford mentions a conceptual app that would use data about demographics, health care records, and consumer purchases to match behavior against evidence-based care. Digital reminders would tell people when they need health screenings and follow-up visits.

Wellness may be a somewhat nebulous term, but traditional medicine is always about the numbers. “We’ve developed a process at Anthem,” says Crawford. “All coverage decisions are based on evidence made by our medical policy and technology assessment committee, a majority of whom are external physicians from various specialties, practice environments, and geographic areas.”

That doesn’t necessarily lead to easy solutions. “It gets more challenging with the gene therapies that are on the horizon,” Crawford says, citing a study by the Institute for Clinical and Economic Review this year that states that the cost of gene therapies will equal the approximately $3 trillion a year that we currently spend on all health care. “There has to be a balance between affordability and care,” says Crawford. “Start with evidence and you’re in a good position to think about various solutions and strategies.”

Crawford also sees another shift on the way. “Everybody before the 20th century used to be cared for in the home,” he says. We now get care in the hospital because hospitals house the technology. But what if homes housed the technology? “We can go back to providing care in a way that makes sense, and that people enjoy, and that may end up being less costly, and utilizing technology to sort of bring back care to a human level,” Crawford says.

ACOs? While eyes in other heads may glaze over, ACOs are what excites Crawford most these days. Some details still need to be hammered out, he says, such as exactly how reimbursement should work in a pay-for-performance system. But he sees them as the nearest big chance of ushering in a new way of providing and paying for health care: “The ACO is where the data are being freely shared, where impediments are minimized, and where, as a clinician, you can hopefully see all of your hard work manifest itself in patients getting better.”

And, yes, Crawford is not spared the ubiquitous: Where do you see yourself in five years? He laughs, then responds: “In five or 10 years, I hope I’m doing exactly what I’m doing now, with more experience and more knowledge. Because there is so much to be learned.”

**Wellness “ties into the evidentiary component of my position—evaluating the scientific literature to support evidence-based medicine.”**
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With all the talk about value-based payment models taking over health care, it would seem the system has already flipped over from its traditional à la carte payment to a prix fixe menu, with providers taking on financial risk for groups of patients.

But the reality appears to be a much slower transition.

The market was still 95% fee for service as of just a few years ago, and the latest surveys show alternative payment models still making up just a small fraction of doctors’ income. Alternative payment models meant to shift doctor pay toward shared savings or capitation—to incentivize higher quality, more efficient care—are still limited to relatively small-scale models.

The ultimate goal of payment reform is to fix a system that is wasteful and loaded with perverse incentives that pay big money for all the wrong things. In a better system, there would be fewer pointless arthroscopic knee surgeries that fix nothing but ring up $3 billion a year, and more dollars available for services that patients want and need, like a quick email consult or a conversation about an elderly parent’s end-of-life wishes.

The question is, how to get there? CMS, Congress, and many private payers are going all-in for value-based payment models, which tend to be paperwork-heavy, carrot-and-stick approaches to motivating physicians.

So why not just do it the easy way—rejigger the Medicare fee schedule so they are paid more for the things that work and less for those that don’t?

Urban Institute fellow Bob Berenson argues for that approach. Medicare’s fee schedule, which measures physician labor by relative value units (RVUs) was for many years the main vehicle for deciding which medical services are valuable. The schedule has some flaws that have produced some unintended consequences. Critics have long complained about the secretive committee of specialty society representatives convened by the American Medical Association (AMA) to establish the relative values of physician

Value-based payment arrangements represent a relatively small source of physician compensation, although 3 in 10 physicians now receive some compensation from value-based arrangements

Do you currently receive compensation from any of the following sources of payment? (More than one answer permitted)

<table>
<thead>
<tr>
<th>Source of Payment</th>
<th>2014</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional (salary or fee for service)</td>
<td>86%</td>
<td>84%</td>
</tr>
<tr>
<td>Value-based payment models</td>
<td>30%</td>
<td>25%</td>
</tr>
<tr>
<td>Episode-based payments</td>
<td>16%</td>
<td>15%</td>
</tr>
<tr>
<td>Bundled payments</td>
<td>13%</td>
<td>12%</td>
</tr>
<tr>
<td>Shared-savings arrangements</td>
<td>10%</td>
<td>7%</td>
</tr>
<tr>
<td>Capitation payments</td>
<td>10%</td>
<td>6%</td>
</tr>
<tr>
<td>Shared-risk arrangements</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Global capitation, including outpatient, inpatient, Rx</td>
<td>4%</td>
<td>N/A</td>
</tr>
</tbody>
</table>

services. New procedures and technology get added to the list but never adjusted downward even after doctors perfect techniques and use less effort to carry them out. The result is overpayment for some services—and the overvaluing of specialty care in general to the detriment of primary care.

But there's not much political interest in fixing the fee schedule now that Congress has gone all-in on MACRA, which will soon be paying doctors based on federally determined quality scores. “The fee schedule has largely dropped off the radar screens for policymakers,” complains Berenson, who is trying to revive interest in using the schedule as the lever to achieve good outcomes.

Suzanne Delbanco, executive director of Catalyst for Payment Reform, supports movement toward value-based payment but also believes the fee schedule could provide straightforward methods for incentivizing quality care. “If we started to pay less for C-sections and more for vaginal births, you wouldn't have to do quality measurement,” she says. “It would change overnight.”

Changing the underlying fee schedule might be more direct, Berenson says, but that's actually the problem. What orthopedic surgeon or anesthesiologist wants to share the wealth with lesser-paid specialties as the AMA's relative value committee debates how to divvy up a limited resource, the Medicare physician payment budget? The painful political reality of taking money out of one pocket to put it into another has kept the fee schedule intact.

“People don't want to touch it with a 10-foot pole,” says Delbanco. “Nobody wants to think about the winners and the losers, but it's really going to be critical to think about that stuff and not just get caught up in new bells and whistles.”

Skeptics like Berenson don't hate all value-based payment concepts—in fact, he thinks the system should move more toward the deep end of that pool, into capitation. It's just that he doesn't want the fee schedule to be ignored, as Congress does with the twice-yearly pleas for reforms lobbed over from the nearby offices of the Medicare Payment Advisory Commission (MedPAC). There is some movement toward tweaking the fee schedule to reward conversation-based (rather than procedure-based) care.

“A lot of the value-based payment stuff is purely aspirational at this point,” says Robert Berenson of the Urban Institute. “Most doctors are still paid on fee schedules.” Even managed care is dependent on fee schedules.

“CMS has done one thing very well: They've tried to define new codes,” he says, noting the rollout of new coverage in 2017 for behavioral health management and diagnosing dementia. Still, he complains, “they've done nothing to revalue codes to deal with mismeasurement” of the physician time and effort it takes for various tasks in the RVU process. His favorite example is paying dermatologists for 23 minutes of their time to freeze a skin lesion with liquid nitrogen that actually takes one minute to perform.

Headed to capitation?

MACRA is now the highly influential law of the land that will require about 550,000 physicians in medium-to-large independent practices to start reporting on at least one performance measure by the end of 2017, and more in 2018; the resulting score will determine whether a doctor gets a 4% bonus or 4% penalty in 2019, with higher stakes in later years. Alternatively, they can skip the reporting and gain a 5% bonus by joining an approved alternative payment model.

### Distribution of physicians by ownership status

<table>
<thead>
<tr>
<th>Owner</th>
<th>Employee</th>
<th>Independent contractor</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>10%</td>
<td>20%</td>
</tr>
<tr>
<td>30%</td>
<td>40%</td>
<td>50%</td>
</tr>
</tbody>
</table>

Value-based payment comes in a wide variety of flavors: ACOs, bundled payments, innumerable variations on pay for performance. CMS has been playing in this sandbox for several years with models and experiments it expects will involve more than 200,000 physicians in 2018. Private insurers are trying out alternative payment models as well. Still, the vast majority of payment remains fee for service, or a variation on pay for productivity.

“A lot of the value-based payment stuff is purely aspirational at this point,” Berenson says. “Most doctors are still paid on fee schedules. And medical groups, even if they receive payments in other ways, end up using work RVUs to compensate their physicians. Even in managed care, even in ACOs, even in risk-bearing ACOs, they are still heavily dependent on the fee schedule.” Berenson guesses that just 10% to 20% of doctors are early adopters of new approaches that at least put them on the road to taking financial risk. Enthusiasts of provider payment reform don’t disagree about the glacial progress, but they see it as early days—not an indication that it can’t or won’t work. “The momentum is building, but it’s not like a deafening roar,” says Randolph Gordon, MD, a managing director for Deloitte consulting.

Of course, physician payment models exist along a spectrum, with varying amounts of evidence to support each.

The evidence on pay for performance, for instance, is still coming in, but Congress has bought into the concept and built MACRA around it. Berenson is a skeptic, pointing to a 15-country study that found hospital pay for performance had no positive impact. He dislikes the concept, and MACRA along with it, enough to wish that Congress would just kill it.

But pay for performance has plenty of supporters. When asked for evidence, they usually point to one of the leaders in the field, the Integrated Healthcare Association in California, whose extensive pay-for-performance initiative involves about 200 medical practices. Lindsay Erickson, director of pay for performance for IHA, says its work has found traction because it has gone beyond simple payments for hitting a quality goal and moved into shared savings, an arrangement that makes physicians partners in the work and often reinvests savings in improving care.

IHA participants are also ahead of the curve because they already have a set of quality measures agreed upon by IHA’s members. “That’s half the battle with meaningful incentives, a huge piece of the work,” Erickson says.

Sadly for MACRA, the new payment program is saddled with an unwieldy, bewildering array of quality measures participating practices can choose to report on. CMS recently said it would pare down its massive list of measures but it remains too long for a typical physician practice to make sense of, physician advocates complain.

The fact that MACRA is now drawing so much fire from doctors is ironic given that provider groups helped to draft the law. A long list of quality measures was added on purpose, notes Mark Jamilkowski, managing director of health care actuarial services for KPMG. “The idea was to have a lot of quality metrics to provide a lot of flexibility” so doctors could choose to report on the measures likely to make them look good.

**Physicians strongly prefer the fee-for-service model**

Share of physicians who prefer these payment models

<table>
<thead>
<tr>
<th>Payment Model</th>
<th>Share of Physicians Preference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fee for service</td>
<td>73%</td>
</tr>
<tr>
<td>Pay for performance</td>
<td>15%</td>
</tr>
<tr>
<td>Capitation</td>
<td>8%</td>
</tr>
<tr>
<td>Other</td>
<td>4%</td>
</tr>
</tbody>
</table>

And it pays to remember what MACRA replaced—a yearly charade in which Congress deflected a required 20% across-the-board cut. Congress kicked the can up the road for 15 years (the annual sustainable growth rate fix) until finally taking a stand behind value-based payment in 2015.

**But does it work?**

Deciding whether these new models will produce better efficiency and quality than fee for service remains an open question, even as researchers crunch data furiously to figure it out.

IHA's Erickson argues the evidence base may be lacking because it’s so hard to tease out what’s actually happening when a practice participates in an experimental payment model, particularly if it represents just a small portion of its income. "Providers are influenced by so many competing demands and requirements that isolating the impact of one initiative by itself is really hard," she says.

It would be nice if there turned out to be one answer to the question “what works best to pay doctors," but the experts who spend a lot of time with the data all seem to say “it depends.” It depends on the local marketplace and its competitiveness, it depends on the region of the country and the comfort level with taking risk, it depends on the sophistication and size and ownership and culture of the physician practice. “We believe strongly it will vary by market and players and level of capability, so it’s really about experimenting and evaluating” payment models, says Delbanco. But she’s willing to hazard a guess as to which models will get traction. "The shared-risk concept is one that appeals very much to employers, and there are still things we should be doing to fix fee for service on the relative amounts we pay for things.”

There's other innovation on pricing too. CalPERS, California’s giant state employee retirement system, has used its clout as payer for 1.4 million retirees' health care to push down prices for both hospital and physician care. It has put in place a growing assortment of reference-pricing schemes that encourage patients to use less-expensive hospitals and surgeons for common procedures. "Health plan and provider competition, as well as price transparency, have been very effective in reshaping the medical delivery system in the direction of value over volume for CalPERS," says Kathy Donneson, MD, chief of CalPERS’ health policy and administration division.

Survey after survey suggests that physicians hate—or perhaps worse—don't even know what MACRA is. They resent the idea that some of the economy's most highly educated people can be manipulated to do what some bureaucracy wants for a few dollars. The ever-quotable health economist Uwe Reinhardt noted, “The idea that everyone’s professionalism and everyone’s good will has to be bought with tips is bizarre.”

Which suggests that a more sophisticated approach that appeals to physicians' motivations for being in medicine will work better than simplistic carrot-and-stick schemes. Influential physician Don Berwick has argued for a new "moral era" in reimbursement, putting most clinicians on salary and ending all of the measurement and financial incentives except for the largest medical groups. Still, pay for performance seems to be gaining ground, albeit with some adjustments. For instance, IHA has learned that pay for performance is most successful when the organization works closely with its physician clients to learn what motivates them. There is no single approach to compensating physicians, Erickson says, and working with a practice’s specific culture and preferences engages doctors so they are more open to quality improvement projects and receiving feedback on their own performance.

Physicians who feel they are engaged in decision making in their organizations, whether it’s a large medical practice or a health system, are more likely to participate in value-based payment models, according to a 2017 survey by Bain and Co. But that engagement may be lacking in some health systems that have been part of the recent buying spree of physician practices and have not had time to focus on the care and feeding of their new physicians, says Bain partner Josh Weisbrod. "You have physicians saying, 'Hey, I
Physicians also want to know they are making change that matters, not just ticking a box for a bureaucrat. Jeffrey LeBenger, MD, runs a large and growing multispecialty practice in northern and central New Jersey that has embraced the elements of modern care; it was an early adopter of an electronic health record and carefully tracks physician performance, manages its patients in all settings with a broad-based, integrated model, and works with payers to take on risk with a shared savings model. Just reporting on a few measures is not as meaningful, LeBenger says, as truly managing patients’ care in a comprehensive way. “It’s ingrained in our group,” he says of the now 750-member Summit Medical Group. “We all want to perform at high standards and with high quality.”

Summit works closely with an insurer partner to move into capitation; health plans are increasingly reaching out to medical practices to try out alternative payment models. To work best, the partners have to share data on patient status to track performance, requiring at least an amiable relationship. The trend raises interesting questions about the traditional friction between doctors and health plans. From an employer point of view, Delbanco says, she’s not sure she wants to see the two adversaries play too nicely together because that friction is what keeps prices under control.

That kind of talk irks KPMG’s Jamilkowski, who believes employers benefit when all the players work together to improve quality and efficiency. “When you get to the negotiating table you can have effective collaboration between the insurance company and provider that results in zero increase if it’s done correctly. That’s better cost savings than if they are trying to beat each other up.”

Shifting practice ownership
The success of financial incentives to adjust physician behavior will also be affected by the trend toward hospitals and health systems buying doctors’ practices. The AMA in May reported an important milestone: fewer than half of U.S. physicians (47%) now own a stake in their own practices; still, the trend appears to be a slow and gradual one. A little more than half (55.8%) of physicians work in a practice owned by physicians and just 7.4% of physicians are hospital employees (although that is up from 5.6% in 2012). The trend is expected to accelerate as practices face up to the reporting realities of MACRA; surveys indicate a significant proportion of doctors still don’t fully understand their obligations under the law midway through its first year of implementation. Practices that are overwhelmed with the cost and complexity of complying may just sell out to a nearby hospital system.

Staying independent is going out of style and is largely a concern of older doctors, says Steve Look, head of recruiting for the Medicus Firm in Texas. Eight of 10 young physicians working with the recruiter take employment contracts with hospitals that offer security and regular hours.

Once doctors are employed, their contracts are usually the traditional salary plus bonus, with the bonus largely based on volume. Quality performance is starting to become a factor in employment contracts, Look says, but still makes up just 10% or 20% of the bonus. Once employed, physicians are largely obligated to follow the approach the hospital takes, which could be a traditional volume-based approach or something more integrated and progressive.

Meanwhile, independent physician practices are still grappling with how to take performance-based bonuses and risk-based arrangements and distribute the carrots or the sticks among the physicians. They run into problems with figuring out which physician is responsible for which patient—particularly hard for patients with multiple chronic illnesses—and who is assigned to which alternative payment model when the practice has dozens of payer contracts all with different methods of payment and incentivizing.

The pay-for-value movement is also slowed by the rural nature of large parts of the U.S., where more practices are small and can’t spread the risk of expensive patients. Fee for service may never die in sparsely populated rural America, experts say. And in the rest of the country, alternatives are likely to take many years to take root. “Physician contracts—you don’t change those on a dime,” notes Deloitte’s Gordon.

Jan Greene, an experienced health care journalist based in northern California, is a regular contributor to Managed Care. A former daily newspaper reporter, she now writes about health policy for a number of national publications.
Direct Primary Care
Is About To Take Off—or Maybe Not

Some call it concierge care for the masses. Born out of physician frustration with insurers, ‘DPC’ could become more popular if Congress passes legislation that allows people to use HSA funds to pay the monthly fee.

By Charlotte Huff

Direct primary care, sometimes described as concierge care for the masses, is still a relative newcomer to the health system. But despite its currently small footprint and the recent closure of one of the larger providers of direct primary care, several political and insurance trends appear to be shifting to the model’s advantage.

Direct primary care, which enthusiasts like to shorten to DPC, is not insurance. Instead patients pay participating doctors a monthly fee—typically less than $100—for a range of primary care services. As of 2017, nearly 3% of family physicians operated DPC practices, according to survey data from the American Academy of Family Physicians (AAFP). This summer’s closure of Seattle-based Qliance—one of the earliest providers with a chain of DPC clinics—reignited the debate over whether DPC is the coming thing or just a boutique item with a rather uncertain future.

Some trends are playing to DPC’s strengths, most notably high-deductible insurance and health savings accounts (HSAs). An increasing number of people who have insurance through their employers are covered by high-deductible plans. According to the 2016 survey by the Kaiser Family Foundation and the Health Research & Educational Trust, 29% of American employees have high-deductible plans. High-deductible plans also figure prominently among the policies sold on the shaky ACA exchanges.

“There’s no stopping DPC,” says John Bender, MD, a Colorado family physician and AAFP board member whose practice has started converting to the model. “High-deductible health plans are not going away regardless of whether the ACA is repealed.”

The future of the DPC model, in terms of its ability to capture the interest of employers and other large payers, will likely depend upon whether it clears a few hurdles. Can DPC providers build a convincing case for employers that a monthly DPC fee on top of their share of an insurance premium will save them money overall by increasing utilization of primary care, thereby decreasing hospitalizations and episodes of pricey specialty care?

DPC proponents are closely monitoring legislation in Congress that could eliminate the prohibition against individuals using HSA funds to pay the DPC monthly fees. They believe that the legislation, which has bipartisan backing, could be the secret sauce that makes the economics for individuals more attractive and popularizes the model.

The data are still not there to convince employers of DPC’s cost-efficiency, says Carolyn Engelhard of the University of Virginia School of Medicine. More studies, please.

Origin story
DPCs started to emerge more than a decade ago when a handful of doctors saw them as a way to rid themselves of the overhead and innumerable hassles involved with dealing with multiple insurers. By reducing the number of patients they needed to treat to
earn a living, the doctors argued that the DPC model would allow them to spend more time with patients and improve the quality of care overall. The model gained some traction several years ago when the AAFP issued a supportive policy statement.

DPC practices share some similarities with concierge care, but the monthly fees are typically lower. (The patient is encouraged to carry some type of catastrophic policy for cancer or other nonprimary care medical crises.) The monthly fee costs vary, with a median of $75, according to an analysis of cost data from 116 practices published in 2015 in the *Journal of the American Board of Family Medicine*. Typically, the monthly fee is paid by the patient, although in some cases it’s picked up by the employer.

Large DPC players include Colorado-based Paladina Health and Boston-based Iora Health, although Iora recently closed down Turntable Health, its first membership-based primary care practice based in Las Vegas, citing a slowdown in that local economy.

Solid supporting data for the model’s impact on health costs and treatment outcomes—particularly in peer-reviewed journals—have been scarce, hobbling the ability of these practices to convince larger employers to enroll their workers, says Carolyn Engelhard, who directs the health policy program at the University of Virginia School of Medicine. “Employers don’t want to put out $50 more a month per employee when they are already paying for their health insurance, unless they feel like it’s worth the investment,” she says.

Cost and quality data are in the process of being collected, says Brian Forrest, MD, a North Carolina family physician and one of the model’s early pioneers, who is participating in a federal quality improvement initiative involving DPC. In the meantime, he maintains that accelerating high-deductible trends, which have the political winds at their backs, will likely further propel interest and uptake.

If ACA’s individual mandate goes away, either by law or lack of enforcement by the Trump administration, then more Americans will probably purchase some kind of catastrophic coverage with a high deductible, Forrest says. If things play out that way, some Americans will prefer to cap the cost of their basic care with a monthly fee rather than paying per-visit out of pocket, he says. “Especially for patients with chronic disease like diabetes and hypertension, if the mandate gets repealed, I think that is going to drive more patients to direct primary care.”

**Growth challenges**

Some case studies and white papers have attempted to make the cost-savings case to larger payers, including a frequently cited analysis involving an employer released late last year by Nextera Healthcare, a direct primary care provider near Denver.

Nextera studied seven months of DPC enrollment for 205 employees and dependents seen by Nextera physicians. In the DPC group, monthly claims declined by 25.4%, from $284 to $212 per enrollee. In the comparison group, claims costs declined by 4.1%, from $408 to $388, according to the case study analysis by a third-party vendor.

Clint Flanagan, MD, Nextera’s CEO, says that the bulk of the provider’s business already involves contracting with employees, which he views as a growth market. “Not only do I think that—we are doing that,” he says, regarding scalability. As of mid-summer, Nextera was operating 15 medical clinics in two states and the Washington, D.C., area and was in the process of opening additional locations, according to Flanagan.

The DPC model intrigues employers because it could provide some long-sought influence over the costlier end of employee treatment—specialty care and hospitalizations, says Michael Thompson, CEO of the National Alliance of Healthcare Purchaser Coalitions. By contracting with direct primary care practices, “they become your carve-in,” he says, “to support the health of your employees and help to manage in terms of how referral patterns happen within that [medical] community.”

But lack of data remains a significant hurdle to scaling the concept beyond the small independent practices that have shown that DPC can work, says Philip Eskew, DO, a DPC physician in Wyoming who follows the industry trends and an author of the 2015 analysis of the 116 practices.

The dearth of data is a catch-22, Eskew notes. Doctors are drawn to DPC, in part, because they want to spend more time on patient care by shedding a lot of the measurements and related documentation required by insurers. Persuading doctors to justify DPC with a lot of reporting on costs and patient metrics is challenging, he says.

For Engelhard at the University of Virginia, the absence of external oversight that is a selling point for doctors considering DPC is something to worry about. “There are no additional quality-control eyes that look at physicians to see: Are you practicing evidence-
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based medicine? Are you overtreating? Is there overdiagnosis?” she says.

Moreover, while Engelhard agrees that overworked primary care doctors should be better compensated, she worries that DPC’s expansion could exacerbate the nation’s primary care shortage. In direct primary care, a physician’s panel of patients is typically 600 to 800 vs. 2,000 to 2,500 for a traditional family medicine practice, according to the AAFP.

And doctors might be tempted to cherry pick patients, given that they’re paid the same monthly fee regarding how many appointments the patient makes, Engelhard points out. Why not pick the healthiest individuals, she asks, to fill those membership slots?

Buy-in
What is emerging with DPCs is a mixed bag of practice approaches—varied both in design and scale. While some practices avoid insurance from the beginning, others continue with a mix of insured patients either temporarily or longer as they build their direct primary care clientele.

Forrest is a bit of a purist, arguing that the goal for DPC physicians should be to shed any interaction with insurance companies in order to reduce costly administrative overhead, although the model assumes that patients will carry insurance for health care outside of their primary care needs. In recent years, Forrest has launched Access Healthcare Direct, which has provided consulting and other services, including pooling resources for purchasing, to a national network of DPC practices.

Not surprisingly, he argues that building physician networks is the optimal way to expand DPC to reach more patients—and thus entice the interest of larger employers—while still enabling physician autonomy. Access Healthcare Direct also participates in, and is collecting data on, direct primary care as part of one of the quality improvement projects through the CMS’ Transforming Clinical Practice Initiative.

In Texas, Austin-based Healthcare2U has adopted a hybrid approach to more quickly offer multiple DPC locations for employers in a given region, according to CEO Andy Bonner. The strategy is to partner with doctors in existing practices, who designate some slots on each day’s schedule for direct primary care patients, he says. “Going down the highway, you’re not going to see a Healthcare2U sign anywhere.”

By early summer, Healthcare2U was operating more than 100 clinics total in at least a dozen states, including Connecticut, Florida, and New Jersey, according to Bonner.

Healthcare2U, which places a lot of emphasis on chronic disease management, markets to both businesses and individuals. Like others interviewed, Bonner is closely watching movement on the congressional level, specifically with the Primary Care Enhancement Act of 2017.

The bill, which would enable individuals to pay the monthly DPC fees with HSA dollars, was first introduced on the House side by Rep. Erik Paulsen, whose district includes the outer ring of the Minneapolis suburbs and, in June, in the Senate by Bill Cassidy of Louisiana.

If Congress passes the legislation, Bonner predicts, “the floodgates will open up for [DPC] practices.”

More data are in the works, in part due to heightened interest by public employers. Late last year, the health benefits programs for state and school employees in New Jersey launched a three-year pilot program that will give employees there the option to use a DPC practice for primary care.

Paladina Health and R-Health were selected as the providers. Each physician practice is limited to no more than 1,000 patients. An outside vendor will analyze quality metrics and total costs per DPC enrollee, says Mason Reiner, CEO of R-Health in suburban Philadelphia.

But Reiner maintains that the potential for averting costlier specialty care is already self-evident to employers. “There’s that old adage, right? ‘An ounce of prevention is worth a pound of cure.’

“Nobody is running around and saying that health care costs are out of control because people have too much primary care,” he adds.

Charlotte Huff is a freelance health and business journalist in Fort Worth, Texas. She has written for Health Affairs, Stat, and Slate among many other publications.
And the Oscar (Health) Goes to Cleveland (Clinic)
The insurance upstart, Oscar Health, is joining forces with Cleveland Clinic as more large health care systems are becoming insurers.

By Susan Ladika

Cleveland Clinic, the storied health care giant in the country’s midsection, is teaming up with Oscar Health, the upstart insurer in New York City cofounded by Jared Kushner’s brother, to become the latest provider to launch its own health insurance plan. The plan is for individual policies to be available in five northeastern Ohio counties both on and off the state’s health insurance exchange.

With this move, Cleveland Clinic joins more than 100 other providers that have their own health insurance plans, but the arrangement is a first for Oscar and cofounder Josh Kushner.

Each member of the new plan will be matched with a Cleveland Clinic care team made up of a primary care provider, physician assistants, and other health care professionals, as well as an Oscar Health concierge team made up of a nurse and care guides.

The concierge team will help each member navigate such things as understanding the details of their health insurance benefits and choosing a primary care physician. The goal is to “create a much better member experience and help each member get the right care,” says Thorsten Wirkes, Oscar’s vice president of strategic partnership operations. And with Oscar, all telehealth visits are free of charge.

Meanwhile, the care team will focus on members’ clinical care and help them manage chronic conditions, says Kevin Sears, the clinic’s executive director of market and network services. “Good clinical management with the right insurance benefits really can lead to differentiated outcomes relative to the Triple Aim,” says Sears.

Despite the cloud of uncertainty enveloping the ACA and health insurance in general, “the individual insurance segment is not going to disappear,” notes Sears. “Cleveland Clinic is committed to serving our entire community. The individual marketplace is an important and growing segment,” and the clinic wants to offer another option for coverage.

Cleveland Clinic is, course, one of American health care’s crown jewels. Last year, it had operating revenue of $8 billion, up from $7.25 billion in 2015. However, earnings from operations fell to $243 million in 2016, down from $480 million in 2015. Meanwhile, Oscar is puny in comparison and still proving itself. The company lost $25.8 million in the first quarter of this year, an improvement over the $48.5 million it lost in the first quarter of 2016. Oscar currently operates in the individual and small group markets and has almost 100,000 members in New York, California, and Texas.

By joining forces, Cleveland Clinic and Oscar Health will each focus on their strengths, Sears says, and the clinic doesn’t have to develop a health insurance plan from scratch. But their partnership isn’t as common as providers having their own health insurance plan. California-based Kaiser Permanente is, of course, the prime example, and it has more than 11 million members across eight states and Washington, D.C.

A 2015 McKinsey report found that 13% of all health systems offered their own health insurance plans and covered about 18 million members, as of 2014. Between 2010 and 2014, the number of provider-led plans inched up from 94 to 107, according to the report, and its lead author, Gunjan Khanna, estimates that there are between 110 and 120 such plans today. From a cost perspective, “it can be more effective if the provider and the payer are more tightly aligned,” Khanna says. However, Khanna advises a careful look before the leap: “Entities have to be very thoughtful before moving into it [setting up their own health plans],” he says. “Insurance is much more regulated than provider entities may realize.”

The initial focus of these provider-led plans typically was the Medicaid market, but it has gradually expanded. As of 2014, about half of those enrolled in provider-led insurance were in Medicaid plans, while about 7 million had commercial insurance, according to the McKinsey report. 

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Imagine being handed a newborn baby who appears to be entirely healthy, but shortly after birth drools excessively and coughs and suddenly turns blue as its first feeding returns back to you through the nose and mouth. This is what happens when the esophagus does not connect to the stomach but instead dead ends into a pouch or connects to the trachea. The child cannot eat until this problem is corrected because any attempts to swallow will be followed by the liquid being regurgitated or aspirated into the lungs, where pneumonia is a sure result.

The condition is called esophageal atresia (EA) and is described as “a developmental defect of the upper gastrointestinal tract in which the continuity between the upper and lower esophagus is lost.” EA has been associated with numerous environmental and heritable conditions, including trisomy 21, 18, and 13. In most cases, it is impossible to pinpoint the specific cause. EA can occur with or without a fistula, or connection, between the trachea and the esophagus. A tracheoesophageal fistula (TEF), as it is called, occurs in about 1 of 3,000 to 5,000 newborns.

The anatomical abnormalities of EA are varied, but the most common is distal TEF, which accounts for more than 80% of cases. Isolated EA, when the esophagus ends in a pouch, accounts for about 8% of all cases.

**Surgery fraught with danger**

Initial emergent treatment is to place a tube into the stomach through the abdominal skin to feed the infant. Open-chest surgery has long been the main option for these infants, although thoracoscopic repair is also used by some physicians. Surgery aims to correct the fistulas—there may be more than one—between the esophagus and the trachea and to reconnect the esophagus so food goes into the stomach.

Surgical procedures (and sometimes many are needed) are fraught with danger because they involve opening and entering the chest either with incisions or with a thoracoscope. Short term, there is a risk of infection. Long term, the adverse events include shoulder weakness, winged scapula, and thoracic scoliosis.

**Using magnets**

If there is a long gap between the esophageal ends, the Foker technique, named for John Foker, MD, at Boston Children’s Hospital, allows sur-
geons to place “traction sutures” in the esophageal ends, where tension on the sutures is increased daily until the two parts stretch and grow long enough to connect. Then a second surgical procedure is done to reconnect the tubes.

Although the Foker technique leads to significantly shorter time to definitive anastomosis and lower risk of complication compared with traditional surgery, it is controversial, partly because outcomes at some centers have not been good.

But the traction sutures gave scientists an idea: What if you could create “tension” between the two ends of the esophagus so the two ends of the esophagus would stretch to meet without a surgical procedure? You would still need to “open” the pouch on each end and reconnect them surgically—or would you? How could this be done? How about using magnetic force!

Over the past four decades, numerous iterations have used magnets, but no commercially sold device was available in this country until this year. Recently a small company named Wilson-Cook Medical, located in Winston-Salem, N.C., finally received FDA approval for a device that does all of the work.

**Anastomosis confirmed**

The Flourish Pediatric Esophageal Atresia Device is indicated for lengthening atretic esophageal ends and creating an anastomosis with a nonsurgical procedure. It was approved for use in patients up to one year old with esophageal atresia without tracheoesophageal fistula (TEF) or patients for whom a concurrent TEF has been closed as a result of a prior procedure. The device is indicated for atretic segments less than four centimeters apart.

Basically, the device consists of a magnet that goes into the top pouch and another into the lower pouch. It is a complex device because of the need to perform imaging and suctioning of secretions. It has two parts, an oral-esophageal catheter and a gastric catheter, both with two openings. The oral-esophageal catheter has an attached magnet and uses one opening for suction of saliva and the other for injection of contrast to confirm anastomosis. The gastric catheter uses one opening for balloon inflation and deflation and the second for placement of the magnet and for flushing as well as feeding.

After assessing suitability for use of the Flourish device, the top catheter is inserted through the mouth and the lower one by an incision through the abdominal wall into the stomach. The oral-esophageal catheter is inserted orally and advanced until the magnet is located at the distal end of the upper pouch. The gastric catheter is inserted over a wire guide with fluoroscopy through a gastric stoma (which is typically created for tube feedings) until the magnet is at the distal end of the lower pouch. Both catheters are secured and the waiting begins.

During the clinical trial, after 3 to 13 days, the traction caused by the magnets pulled the ends of the esophagus together. Eventually, surrounding tissues grew together and the tissue between the magnets started to die.

Once the anastomosis is confirmed with fluoroscopy, the upper catheter is cut, leaving the magnet behind. Then both magnets and the lower catheter are removed via the gastrostomy lumen. A new orogastric tube or nasogastric tube is placed for a few days to promote healing.

No procedure or device is free of adverse events, and the Flourish device is no exception. But the results are pretty impressive. The clinical trial leading to approval was limited to 16 patients, but all experienced successful anastomosis. No patient experienced an anastomotic leak. Most (81%) needed endoscopic dilation, which is about double the rate seen with standard surgical care. Many also had residual issues with gastroesophageal reflux disease, tracheomalacia, dysmotility of the esophagus requiring treatment, asthma, and recurrent pulmonary infections, problems that also can occur in patients treated with traditional surgical techniques.

The device is contraindicated for patients with teeth (which could damage the oral catheter), those with existing (uncorrected) TEF, for creating an anastomosis other than in the esophagus, for patients without an appropriately sized tract, and for patients with signs of significant infection at the gastrostomy site.

As a condition of approval, the FDA required a postapproval study consisting of a prospective, single-arm, new observational study with a minimum of 20 subjects followed for two years.

EA, although uncommon, is a complex and dangerous newborn birth defect with, until now, only chest surgical approaches. The Flourish Pediatric Esophageal Atresia Device is a remarkable alternative to traditional chest surgical procedures.
In a world of new access models and price-conscious consumers, the traditional route of patients making appointments to see doctors is being squeezed. These days, consumers are really only interested in schlepping to see a physician when faced with more complex needs. From the physician perspective, this creates a dilemma: While the mix of patients coming in the door is—on average—more complex, the physician compensation model continues to be one that rewards volume and throughput. Complex patients require more time to be properly cared for: more time for their face-to-face interaction with the doctor, more time for clinical documentation, more time for referral management, more time for appropriate follow-up, and so on down the line. When it comes to physician compensation, the dialogue is only beginning to catch up to the new reality.

This isn’t to say the industry hasn’t noticed. In a fact sheet released earlier this summer with the proposed 2018 rule on the Medicare Physician Fee Schedule, CMS stated that it wants “to start a national conversation about … how Medicare can contribute to making the delivery system less bureaucratic and complex.” In essence, they are seeking to re-evaluate prior regulations to simplify and ease clinician burden. This is a step in the right direction toward helping physicians function at top-of-license efficiency.

But what about the more transformative economic shift necessary to reward value over volume?

MACRA and collaboration
The introduction of MACRA establishes new and greater incentives for physicians to embrace performance risk, making models such as MSSP Track 1 more attractive than ever before. This appears to address some of the concern surrounding the greater time investment for more complex patients. However, in true accountable, outcomes-driven models, there is an implicit expectation that physicians, payers, and other caregivers will be working together in new and collaborative ways. This introduces entire new layers of time and effort as new processes must be forged and evaluated, supported by investments in training, technology, and staff. And all of this takes away from the time physicians have available to see patients.

Further consolidation
These issues are making it increasingly challenging for independent physicians and small group practices to keep up. On the administrative side, increased complexity and cost come right from the practice’s pocket. On the clinical side, participation on integrated care teams and performance committees is incredibly time consuming. On the economic side, the uncertainty surrounding value-based payment makes it unfeasible to change the business model in hopes of future shared savings. Not to mention the data collection and analysis necessary to monitor and track performance. Collectively, these factors are driving large numbers of independent physicians and small group practices to join large multispecialty groups, often organized by a health system. Such groups have the resources and infrastructure to support and enable value-based care constructs.

The path forward
This continues to be a tumultuous time in health care. Physician compensation is only just beginning to be pulled into the fray.

With so much focus today on reducing costs, integrating information, and building connectivity to consumers, we mustn’t forget that the point of all of this is to achieve better outcomes for the patient. Fundamentally, physicians need compensation incentives and supporting infrastructure to efficiently deliver the best possible care while bringing their “A” game, including the right focus, attitude, and motivation.

Zachary Hafner leads the Advisory Board’s strategy consulting practice.

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Health Plans Start To Focus More On Social Needs of Beneficiaries

By Gerard A. Vitti

Your health is strongly influenced by dozens of factors, but we commonly chalk it up to our genes, a few behaviors like smoking or eating poorly, and access to good medical and dental care. But your ZIP code may be just as important. If you are fortunate enough to live in a clean, safe neighborhood, you stand a better chance of enjoying good health than someone who doesn't.

Distance between neighborhoods isn't necessarily a big factor. My home in Milton, a leafy, affluent suburb of Boston, is less than a mile from the city's Mattapan neighborhood, yet these two communities have dramatically different rates of chronic disease. For example, emergency room visits for asthma and diabetes are more than two times higher in Mattapan than in Milton.

Why does where we live—and the resources we have available to us—affect our health in such a significant way? Because those resources give us the wherewithal to get access to the type of care and services we need. In Milton, orthodontia is a right of passage for teens; in Mattapan, there are children who have gone years without visiting a dentist.

The resource gap is particularly pronounced when it comes to an individual with a disability. Raising a child with a disability is an immense undertaking. It is a full-time job just ensuring that your child gets the care and support that he or she needs. I know, because I have a daughter with a rare physical, intellectual, and psychiatric disability. My wife, Erin, and I have resources, and we don't have to think twice about how my daughter will get to a medical appointment or how we can get some support so that we don't burn out as caregivers.

But for low-income families struggling to get by—including those living just a mile from us in Mattapan—all of these things that pose no problem to us become major barriers. Nothing is easy. For families without a car, rides need to be carefully coordinated. Appointments are missed, so care becomes disjointed, fraying the doctor-patient relationship and undermining people's understanding of their health problems.

Lack of government spending on health is not the main reason we have these health challenges. Rather, it's a question of not spending money in the right way—and at the right time. Prevention is key. We need to invest in helping people stay healthy rather than treating them after they get sick.

Address social needs

Health plans have known for years that there are many nonhealth factors that play a role in a person's health and well being. That's why many plans have gone to such lengths to invest in prevention by promoting fitness and creating member newsletters that address issues like healthful eating.

Now a coterie of health plans is starting to tackle factors that were seen as being completely outside the purview of anyone in the health care system, let alone a health plan.

A project undertaken by the UPMC Health Plan in Pittsburgh showed that providing housing and other social supports to individuals on its Medicaid health plan led to a 23% decrease in total costs.

A similar pilot project in Massachusetts that provided case management and other social supports to a chronically homeless population generated a return of between $1.61 and $2.43 for every dollar invested in the program, according to a study recently conducted by the Boston University School of Social Work.

New strategies are needed to address health disparities. Investing in community services, not just clinical ones, should become the rule rather than the exception for Medicaid agencies and others serving low-income populations.

Managed care organizations that serve people covered by Medicaid and served by other public insurance programs are best suited to devise strategies that can narrow the health gap. They know this population, and they know what works. Operating outside the bounds of government, they can tap into an entrepreneurial spirit and data-driven tolerance for risk to devise strategies that have never been tried before.

John F. Kennedy famously said, “Life is unfair.” And indeed it is. But we can take steps by freeing up government to innovate and let our managed care plans help lead the way, so health outcomes are less unfair.

Gerard A. Vitti is the founder and CEO of Healthcare Financial, a company based in Quincy, Mass., that helps individuals get health coverage.
By Jack Plotkin

CTO, Virtual Health

Population-health management (PHM) is one of the most important directions in modern health care and a key driver behind the promise of value-based care. Unfortunately, many PHM programs treat populations as a homogeneous whole rather than a collection of heterogeneous individuals. It is important to remember that even when people have the same diagnosis or suffer from the same comorbidities, they are dealing with vastly different socioeconomic, cognitive, and environmental factors that influence how, when, and where they get health care.

Health care organizations are making strides with PHM by improving risk stratification and fine-tuning quality measures. Those are important first steps. But many PHM strategies fall short because they fail to address three critical components that relate to patient-centeredness.

1) Patient-centered education

PHM strategies that succeed assess and account for cognitive factors that affect patients’ ability to understand their health needs, care goals, and recommended interventions. Does a patient have the cognitive ability to support his or her care plan? Does she or he have the knowledge necessary to understand not only what constitutes a care plan but also why and how it can be followed? Gaining this level of insight requires structured and timely interaction with the patient. Both must be embedded in the care management fabric of the PHM program.

Only after there is a clear picture of a patient’s cognitive skills and knowledge base is it possible to provide the patient with the appropriate level of educational information and outreach. If people truly understand their care plans, adherence improves and better outcomes are more likely.

2) Patient-centered social indicators

Imagine two 60-year-old male patients who have recently been diagnosed with type 2 diabetes. One has a strong family support network, lives within walking distance of his primary care physician and pharmacy, and has a computer and high-speed internet access. The other lives alone, doesn’t have a convenient way to get to his physician or pharmacy, and does not own a computer.

Many PHM programs would put these patients in the same category based on claims data. But clearly the level of support required by the man who lives alone is far, far greater than the other man. PHM shouldn’t be used as an excuse for fudging over important differences like this.

Meanwhile, the boundaries of what’s considered health care are expanding. By incorporating social and environmental indicators into the PHM strategy, health care organizations can identify the supports individuals need. One-size-fits-all never was and never will be. Instead, the goal should be for everyone to have a size that fits.

3) Patient-centered technology

Many Medicaid managed care organizations have member portals—and nearly all of them have members who rarely, if ever, use the portals. The reason is remarkably basic: Most people in Medicaid plans use smartphones rather than home computers to connect to the Internet. Smartphone apps, not web-based member portals, is the way to serve Medicaid plans and their members.

By identifying how patients are willing to engage, PHM programs can procure and configure technology that optimally support these preferred engagement channels. In turn, these expanded lines of communication between care teams and patients can ensure the timely flow of information and education.

Each of these three components is absolutely essential for population health strategies to work. If there’s an overall lesson here, it’s that health care organizations can’t just measure a few quality metrics, tinker with them, and call that population health.

The population is the patient in population health. But improving that patient’s health means working at the individual level to change the behavior of individuals.

Jack Plotkin is CTO of VirtualHealth, a health technology company in New York City that specializes in population health and value-based care.
Targeted Literature Review

The Role of Proteomic Testing in Improving Prognosis And Care Planning Quality Measures for Lung Cancer

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INTRODUCTION
Non–small-cell lung cancer (NSCLC) provides a critically relevant example of the importance and difficult nature of planning for cancer care as defined within recent value-based payment programs and care delivery models adopted by the Centers for Medicare and Medicaid Services (CMS). The Medicare Access and CHIP Reauthorization Act of 2015 (MACRA), the Oncology Care Model (OCM), and accountable care organizations (ACOs) all reflect the national movement to steer the health care system away from traditional fee-for-service and toward programs that provide incentives for high-quality care, using the leverage of Medicare reimbursement policies (CMMI 2015). With the dual aim of improving quality of care and lowering costs, these systems are designed to incorporate quality performance metrics as a partial determinant of Medicare reimbursement.

NSCLC is a terminal disease. Although recent and continuing therapeutic advancements for NSCLC offer better care and hope for life extension, none are curative. Furthermore, a high proportion (>79%) of patients are diagnosed with lung and bronchus cancer at an advanced, metastatic, and highly aggressive stage (Howlader 2017), with five-year survival rates of only 15% for men and 21% for women (ACS 2017).

Biomarker tests are now available to help guide treatment decisions, but few tools are available for accurate prognosis of NSCLC. As a result, oncologists are often forced to make imprecise estimates of prognosis based on patient-performance status or population statistics—indicators that may not always be reliable (Christakis 2000, Glare 2003, Gripp 2007, Llobera 2000, Taniyama 2014, Viganò 1999).

The VeriStrat test, a serum-based...
Proteomic Testing in Lung Cancer

Proteomic test, is a promising tool offering direction in achieving more accurate NSCLC prognoses. VeriStrat is a sole-source test offered by Biodesix, in Boulder, Colo. The test uses a single blood draw that is sent to the Biodesix laboratory for processing, and it renders results for physicians within 72 hours of receipt of the sample. VeriStrat uses matrix-assisted laser desorption ionization time-of-flight (MALDI-ToF) mass spectrometry to measure the presence of circulating immune-related proteins associated with the aggressive disease (Taguchi 2007).


The availability of high-quality, actionable prognostic information when managing complex diseases like NSCLC under OCM may contribute to attaining performance payments. The OCM quality measures were selected from the National Quality Strategy and align with the quality measures used in other CMS quality payment programs. Such programs emphasize quality over quantity of care (CMS 2017).

BOX 1

Information in a cancer care plan

Utilizing patient-centered communication and shared decision making, the cancer care team collaborates with patients to develop a cancer care plan. Here are some examples of the components in a patient-specific cancer care plan:

- Patient information (e.g., name, date of birth, medication list, allergies)
- Diagnosis, including specific tissue information, relevant biomarkers, and stage
- Prognosis
- Treatment goals (curative, life-prolonging, symptom control, palliative care)
- Initial plan for treatment and proposed duration, including specific chemotherapy drug names, doses, and schedule as well as surgery and radiation therapy (if applicable)
- Expected response to treatment
- Treatment benefits and harms, including common and rare toxicities and how to manage these toxicities, as well as short-term and late effects of treatment
- Information on quality of life and a patient’s likely experience with treatment
- Who will take responsibility for specific aspects of a patient’s care (e.g., the cancer care team, the primary care/geriatrics care team, other care teams)
- Advance care plans, including advanced directives and other legal documents
- Estimated total and out-of-pocket costs of cancer treatment
- A plan for addressing a patient’s psychosocial health needs, including psychological, vocational, disability, legal, or financial concerns and their management
- Survivorship plan, including a summary of treatment and information on recommended follow-up activities and surveillance and risk reduction and health promotion activities

Sources: CMMI 2015, IOM 2013

ABBREVIATIONS

ACO – accountable care organization
APM – alternative payment model
BSC – best supportive care
CMS – Centers for Medicare and Medicaid Services
NAM – National Academy of Medicine, formerly the Institute of Medicine of the National Academies
MACRA – Medicare Access and CHIP Reauthorization Act of 2015
MIPS – Merit-based Incentive Payment System
NSCLC – non–small-cell lung cancer
OCM – Oncology Care Model
OS – overall survival
PFS – progression-free survival
QALY – quality-adjusted life-years
CMS implemented the OCM to address challenges specific to advanced cancers: namely, the difficult tradeoffs between aggressive treatment, life extension, and quality of life that patients and physicians must grapple with when faced with these often-incurable forms of cancer. The OCM includes financial and accountability for episodes of care surrounding therapy administration to cancer patients. OCM and MIPS quality measures place strong emphasis on patient-centered communication and shared decision making.

The OCM itself is complicated, requiring six enhanced services to be provided to improve patient outcomes, as well as a multitude of quality measures, largely focusing on processes, that each practice must report. However, it is clear from enhanced services requirements that participating practices must prepare for every patient a comprehensive, documented cancer care plan that includes 13 components recommended in a 2013 report prepared by the Institute of Medicine of the National Academies, which is now called the National Academy of Medicine (NAM) (CMMI 2015, IOM 2013). The NAM care plan (Box 1) represents some of the most important clinically focused quality measures in the OCM, and it includes determination of disease prognosis and its effective communication to the patient (IOM 2013). Accurate disease prognosis is essential to developing a high-quality care plan because it informs all the treatment and other decisions that follow.

The following report provides a targeted literature review supplemented with real-world clinical experience from physicians utilizing the VeriStrat test in clinical practice. The goal is to consolidate the current base of knowledge and guidelines regarding the value of prognosis in planning for NSCLC care, within the framework of the OCM and the NAM 13-point cancer care plan, and to illustrate how VeriStrat is used to help meet the specific requirements in these frameworks.

**METHODS**

**Objective**

The objective of this study was to review current evidence and standards of care relating to the establishment and communication of prognosis and care planning for patients with NSCLC, including the use of VeriStrat testing in participating OCM locations. Specific focus was placed on three topics relevant to the OCM and how the VeriStrat test relates to:

1. Current prognostication techniques and the value of the VeriStrat test for improving the accuracy of prognosis and the quality of treatment decision making.
2. The impact of an accurate prognosis on cancer care planning.
3. How VeriStrat prognostic results can be used to meet MIPS and OCM quality metrics and OCM treatment planning requirements from the NAM 13-point care plan.

**Identification and screening of the literature**

Using the NCBI PubMed database, this study reviewed available MEDLINE-indexed literature (January 1997–January 2017) on the topic of lung cancer prognosis and cancer care planning. The following terms were used either singly or in combination: actionable, biomarker, cancer, communication, cost, end of life, hospice, lung cancer, outcomes, palliative, prognosis, prognostic tools, quality of life, treatment preferences (Table 1).

English-language literature describing U.S. based clinical trials, survey-based studies, clinical practice guidelines, and organizational reports and commentaries were included. Studies that did not discuss prognosis or that focused on diagnostic procedures or the outcomes of medical procedures, or that were unrelated to lung cancer, were excluded.

Finally, the authors included comments regarding their own experiences with prognosis, the utility of VeriStrat in the clinic, and/or involvement in OCM-participating practices to illustrate how the VeriStrat test has been used in real-world clinical practice to make meaningful treatment decisions about prognosis and to assist in meeting OCM requirements.

**RESULTS**

The initial search using the terms in Table 1 yielded 356 articles, of which 67 were duplicates and another 175 were determined to be irrelevant. An additional 24 articles identified in the reference lists but not found during the original search were also reviewed. The final number of references reviewed was 138. Because of space limitations, only the most informative and relevant of those were cited in this review.

For OCM applicants and participating organizations, quality measures and requirements related to prognosis and cancer care planning are defined (Table 2). Metrics include establishment of treatment goals and expected response, avoidance of hospital admissions and overtreatment at the end of life, and timely referral to hospice. Meanwhile, requirements for participating OCM organizations—specifically, the NAM’s 13 components of cancer care planning—emphasize the importance of establishing and communicating prognosis, selecting optimal treatment for each patient, and discussing specific treatment goals, expected response to and cost of treatments, and expected quality of life (Box 1). Together, these measures underscore the importance of establishing and communicating prognosis to the patient.
Proteomic Testing in Lung Cancer

Current prognostication techniques and the value of the VeriStrat test

Even in the face of observable declines in patient health, it can be difficult for physicians to make precise estimates about survival (Detterbeck 2013). Standard cancer prognostication is based on performance status, general survival statistics, and standard laboratory tests, which do not always inform personalized survival prediction (Christakis 2000, Gissler 2003, Gripp 2007, Taniyama 2014, Wolf 2013). Predictive models using prognostic factors such as cancer site, metastases, performance score, and patient characteristics have also proven incomplete (Chiu 2015). Therefore, new validated diagnostic tools are needed for precise prognosis.

The VeriStrat test is a noninvasive tool that assists physicians with prognostic discussions. Within 72 hours of blood sample collection, the VeriStrat test provides information regarding expected response to treatment as well as overall prognosis, independent of treatment.

In addition to patient-specific predictions about the efficacy of systemic and EGFR-TKI therapies, the test provides a binary prognostic answer (“VSGood” or “VSPoor”) that, when combined with clinical information, has been shown to provide the basis of a highly accurate estimate of survival duration (Table 3) (Akerley 2013b, Akerley 2017, Amann 2010, Carbone 2012, Gadgeel 2017, Gregoric 2014, Grossi 2017, Vansteenkiste 2012).

The VeriStrat test’s ability to predict which patients will experience longer progression-free survival (PFS) and/or overall survival (OS) in response to treatment has been demonstrated across a multitude of therapies, including first-line standard chemotherapy (Grossi 2017, Vansteenkiste 2012, Amann 2010), second-line erlotinib (Carbone 2012), second-line sorafenib (Dingemans 2013), first-line gemcitabine, erlotinib, and a combination of the two (Stinchcombe 2013), EGFR-TKIs (Sun 2014), erlotinib plus carboplatin/paclitaxel (Lara 2016), and second-line afatinib or erlotinib (Gadgeel 2017). Furthermore, in a multivariate analysis of 76 first-line patients, VeriStrat was found to be the only statistically significant predictor of OS (Grossi 2017). Grossi and colleagues showed that VeriStrat classification (VSGood versus VSPoor) was the only statistically significant predictor of OS (HR, 0.23; P<.001) while ECOG performance score, EGFR, KRAS, ALK mutation status, chemotherapy type, gender, prior radiotherapy, and prior surgery were nonstatistically significant predictors of OS in a multivariate analysis.

Based on the literature review as well as real-world feedback from the authors, the prognostic information provided by the VeriStrat test guides optimal treatment decisions effectively. A 2017 study by Akerley et al analyzed treatment plans of 989 physicians. Treatment considerations were analyzed before and after VeriStrat results for 2,494 patients with NSCLC. The test classified 1,950 patients as VSGood and 544 patients as VSPoor. Prior to receiving test results, active treatments were under consideration for 99% of patients. After testing, physicians changed their recommendations such that BSC was recommended to 25% of patients with a VSPoor result (n=136) and active treatments for 75% (n=408). Overall, 98% of physicians’ treatment recommendations were made in accordance with VeriStrat test results, and these changes in treatment recommenda-
Proteomic Testing in Lung Cancer

Cost savings was $10,414 per patient, with a net 24% shift from active treatment to BSC. The shift in therapies, to less expensive and more effective therapies based on test results, creates cost savings that more than offset the cost of testing (Page 2017).

Collectively, the literature shows that the VeriStrat test helps establish prognosis in NSCLC, guide optimal treatment decisions, predict expected response to treatment, avoid costly and ineffective treatment, and identify patients for whom BSC may be most appropriate (Akerley 2013b, Akerley 2017, Amann 2010, Carbone 2012, Gregorc 2014, Grossi 2017, Vansteen-

<p>| TABLE 2 | Oncology Care Model and Merit-based Incentive Payment System quality measures related to prognosis and cancer care planning for cancer patients |</p>
<table>
<thead>
<tr>
<th>Category</th>
<th>Measure/number</th>
<th>Requirement or measure description (CMMI 2015)</th>
<th>Impact of prognosis and VeriStrat testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer care plan</td>
<td>OCM Documented care plan MIPS 47,130,374</td>
<td>The documented cancer care plan must include conversations about prognosis, goals of treatment, and expected response to treatment</td>
<td>Planning and communicating cancer care relies on accurate prognosis. VeriStrat is prognostic and predictive of outcomes across multiple treatments, allowing physicians to have a precise tool to have prognostic conversations with patients with NSCLC when planning care (Gregorc 2014, Stinchcombe 2013, Taguchi 2007).</td>
</tr>
<tr>
<td>Hospital/ICU/ER admissions</td>
<td>OCM-1 OCM-2 MIPS 454,455</td>
<td>Proportion of patients with all-cause hospital admissions, all-cause ED visits or observation stays, all-cause ICU admissions</td>
<td>Prognosis and expected treatment response allows physicians to balance precise treatment benefit with toxicity and to avoid toxic ineffective therapies (Akerley 2017, Grossi 2017). Tissue biopsy for lung cancer patients often results in medical complications, including hemorrhaging of the lungs or infection, at times leading to ED visits (Dale 2012). VeriStrat is a serum-based test that provides prognostic information and does not require tissue biopsy.</td>
</tr>
<tr>
<td>Over-treatment</td>
<td>MIPS 453</td>
<td>Proportion of patients who died from cancer while receiving chemotherapy in the last 14 days of life</td>
<td>Precise prognosis using VeriStrat allows physicians to optimize treatment and decrease over-treatment when appropriate (Akerley 2017).</td>
</tr>
<tr>
<td>Timing and referral to hospice</td>
<td>OCM-3 MIPS 456</td>
<td>Proportion of patients who died from cancer but were never admitted to hospice</td>
<td>Appropriate timing of referral to hospice requires precise prognosis. VeriStrat acts as a tool to facilitate conversations about timing of palliative or best supportive care when appropriate (Akerley 2017, Page 2017).</td>
</tr>
</tbody>
</table>
Proteomic Testing in Lung Cancer

Impact of an accurate prognosis on planning cancer treatment

With these results as a framework, we reviewed clinical practice guidelines and literature about the importance of communicating a clear prognosis with patients across the continuum of care (Table 4). All nationally recognized clinical practice guidelines supported the importance of early and regular communication regarding prognosis (Detterbeck 2013, Ferrell 2017, Ford 2013, Masters 2015, NCCN 2017a, NCCN 2017b, Pallis 2014).

The OCM advanced care plan requirements specifically call for establishing goals of treatment (CMMI 2015, IOM 2013), including the associated benefits, risks, costs, and outcomes. Patients can develop realistic personal goals and preferences for care only if they and their care team have accurate prognostic information available at the time when those treatment decisions are being discussed (Ford 2013, Gwilliam 2011). Patients were found to want an accurate prognosis from their physicians as a matter of trust (Kirk 2004), and, indeed, a number of studies reported that as many as 95% of patients wanted to know their prognosis even if it was poor (Hagerty 2004, Hagerty 2005, Kirk 2004, Yun 2004).

The literature review found that prognosis has a definitive impact on treatment preferences (Gwilliam 2011). Patients who believed they were going to live for at least six months were more likely (OR=2.6, 95% CI (1.8–3.7) to favor life-extending therapy over comfort care compared to patients who thought there was at least a 10% chance they would not live six months (Weeks 1998).

In a study by Mack and colleagues, patients with advanced cancer who understood that their chemotherapy was “not at all” likely to cure their cancer were no less likely to receive chemotherapy, but they were more likely than other patients to enroll in hospice (N= 722, OR=1.97, 95% CI=1.26–2.66) (Mack 2015).

How VeriStrat prognostic results can be used to meet MIPS quality metrics and OCM treatment planning requirements from the NAM 13-point care plan

Lung cancer is the second most commonly diagnosed cancer in the United States and the leading cause of death from cancer (ACS 2016). As such, the OCM, NAM cancer care planning framework, and MIPS quality measures highlight conversations around prognosis, expected response to treatment, palliative care through-

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>6-month survival, %</th>
<th>Median OS, months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VSGood</td>
<td>VSPoor</td>
<td>VSGood</td>
</tr>
<tr>
<td>Treatment-naïve</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grossi 2017 (N=76)</td>
<td>platinum doublet (carboplatin/pemetrexed)</td>
<td>70</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>platinum doublet (cisplatin/pemetrexed)</td>
<td>90</td>
<td>43</td>
</tr>
<tr>
<td>Vansteenkiste 2012 (N=202)</td>
<td>platinum doublet (cisplatin/gemcitabine)</td>
<td>86</td>
<td>56</td>
</tr>
<tr>
<td>Amann 2010 (N=102)</td>
<td>erlotinib</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>erlotinib (n=252)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>placebo (n=144)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gregorc 2014 (N=287)</td>
<td>erlotinib (n=143)</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>chemotherapy (n=142)</td>
<td></td>
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<tr>
<td>Gadgeel 2017 (N=675)</td>
<td>afatinib (n=336)</td>
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<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>Patient overall survival by VeriStrat test result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study</td>
<td>Treatment</td>
</tr>
<tr>
<td>---------</td>
<td>------------------------------------</td>
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<tr>
<td></td>
<td>VSGood</td>
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</table>
out treatment, avoidance of hospital admission, avoidance of ICU admissions, avoidance of excessive ER visits, avoidance of overtreatment at the end of life (CMS 2017), and timely referral to BSC and hospice when appropriate (CMMI 2017). All these measures are directly affected by the decision to undergo active treatment versus inactive treatment options such as patient monitoring, BSC, or hospice—a decision that may be facilitated when the VeriStrat test is included as part of the diagnostic workup prior to initiation of treatment.

**Physician-patient communication**

Many patients do not currently receive precise prognostic estimates or understand the implications with respect to curative versus palliative therapy. In a large observational trial of patient expectations about chemotherapy, 69% of the 710 stage IV lung cancer patients did not understand that chemotherapy, while life-prolonging, was not at all likely to cure their cancer (Weeks 2012). While some of this gap is likely due to patient-related factors, physicians often find it difficult to have candid conversations with patients and their families or caregivers out of the fear of extinguishing hope (Steinhauser 2001). However, realistic information about prognosis can decrease patient anxiety stemming from fears of the unknown when it is delivered with empathy and honesty (Hagerty 2005).

**TABLE 4**

Guidelines supporting physician-patient communication about prognosis and the planning of cancer treatment

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Position or statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCO guidelines, palliative care (Ferrell 2017)</td>
<td>Emphasizes early integration of prognostic conversations into goal setting, continual assessment of patient understanding and awareness about prognosis and treatment goals, and early discussion of hospice.</td>
</tr>
<tr>
<td>ASCO guidelines, systemic therapy for stage IV non–small-cell lung cancer (Masters 2015)</td>
<td>Recommends initiating conversations about prognosis at time of diagnosis, with new conversations about risks, benefits, and prognosis before each line of therapy.</td>
</tr>
<tr>
<td>CHEST guidelines, diagnosis and management of lung cancer (Detterbeck 2013)</td>
<td>Notes the complexity of prognostic classification, which depends not only on stage classification but also on comorbidities, performance status, and treatment given.</td>
</tr>
<tr>
<td>CHEST guidelines, palliative and end-of-life care in lung cancer (Ford 2013)</td>
<td>Recommends that clear, consistent conversations about prognosis and goals of care begin at diagnosis and continue throughout the course of the illness to alleviate emotional distress and facilitate informed, timely decision making about end-of-life care.</td>
</tr>
<tr>
<td>EORTC Elderly Task Force, Lung Cancer Group and International Society for Geriatric Oncology (Pallis 2014)</td>
<td>Notes that treatment decisions require adequate information and participation of the patient and family and clear information regarding prognosis, treatment options, benefits and risks, and potential negative effects of over- and undertreatment.</td>
</tr>
<tr>
<td>NCCN guidelines, NSCLC, v7.2017 (NCCN 2017b)</td>
<td>Notes that good prognostic factors include early-stage disease at diagnosis, good performance status (PS: ECOG 0,1, or 2), no significant weight loss (no more than 5%), and female gender.</td>
</tr>
<tr>
<td>NCCN guidelines, palliative care (NCCN 2017a)</td>
<td>Emphasizes clear, consistent, and empathetic communication with the patient and family about the natural history of the patient’s cancer, the prognosis, potential response to treatments, and setting therapeutic and palliative care goals that are consistent with estimated life expectancy.</td>
</tr>
</tbody>
</table>

It can also allow patients adequate time to prepare emotionally, spiritually, and practically for their passing (Steinhauser 2001, Temel 2010). Because of its reliable, predictive, and prognostic results, the VeriStrat test has been shown to be an excellent tool for facilitating these difficult but necessary discussions between physicians and patients (Akerley 2017).

Real-world case reports from the authors exemplify the clinical utility of VeriStrat testing to support, facilitate, and document physician-patient communication and monitoring in the OCM.

In one case, a 61-year-old female was diagnosed with stage IV adenocarcinoma but was unable to tolerate palliative chemotherapy. The physician ordered first-line testing including VeriStrat to evaluate treatment options. A VSPoor result and presence of metastatic disease were major factors in the author’s decision to shorten the follow-up schedule from the standard...
6 months to every 3 months. Based on physician-patient discussions and consideration of all clinical factors (metastatic disease, negative for programmed death ligand 1 [PD-L1] expression, positive for KRAS mutation), the patient enrolled in a clinical trial evaluating nivolumab + ipilimumab; however, the patient progressed quickly on therapy. In this case, a VSPoor result assisted the physician in discussing clinical trial options with the patient and determining appropriate monitoring.

**Expected response to treatment**

As noted above, VeriStrat has been shown to predict which patients are likely to respond to first-line, standard-of-care platinum doublet therapy (Grossi et al., Vansteenkiste 2012) and to EGFR-TKIs in multiple lines (Carbone et al., Gregorc et al. 2014). Grossi et al demonstrated that in non-squamous patients treated with standard chemotherapy in the first-line setting, patients classified as VSGood had longer PFS and OS than those classified as VSPoor: 6.5 vs. 1.6 months (P<.001) and 10.8 vs. 3.4 months (P<.001), respectively. Additionally, VeriStrat testing identifies which patients will not benefit from EGFR-TKI therapies. Carbone et al demonstrated that for patients with tests results of VSPoor, treatment with an EGFR-TKI (erlotinib) was not statistically better than treatment with placebo (P=.11). Additionally, Gregorc et al reported that in a prospective randomized phase 3 trial, patients classified as VSPoor had better median survival on chemotherapy compared with treatment with erlotinib (6.4 vs. 3.0 months, P=.002). Numerous others studies have confirmed that VeriStrat test results are predictive of response (OS and PFS) to a variety of front- and second-line, as well as targeted, therapies (Table 3) (Akerley 2013a, Dingemans 2013, Gadgeel 2017, Grossi 2017, Lara 2016, Schwartzberg 2012, Stinchcombe 2013, Sun 2014, Vansteenkiste 2012).

Another case report by the authors describes the use of VeriStrat to understand expected response to therapies and how it was used to discuss treatment options with the patient. The patient, a 71-year-old male, was diagnosed with stage IV metastatic adenocarcinoma of the lung, with poor performance status. Carboplatin with pemetrexed was administered as the first-line treatment with no response. Testing for PD-L1 expression and genetic mutations yielded negative results for driver mutations and positive PD-L1 results at >50%. Targeted therapies were therefore not a viable option, but immunotherapies could be considered. For information regarding prognosis, the physician ordered VeriStrat, and results were VSPoor. Without this information, the physician would typically administer standard chemotherapy. Instead, he had an informed, shared decision making discussion to consider other options based on patient preference. Based on the VSPoor result, the author explained to the patient that he would not do well on chemotherapy and had a median expected survival of about four months. The potential risks and benefits of discontinuing active therapy, considering hospice care, and pursuing immunotherapy were discussed. In the end, the patient chose to receive immunotherapy (pembrolizumab) based on the patient-physician communication around limited expected response to chemotherapy. The patient remains on active treatment and is routinely restaged to assess response.

The results of the literature review showing the prognostic utility of VeriStrat are further confirmed in the experience of the practicing authors (Page, Argento, Schaefer). The VeriStrat test has proven useful during the treatment planning process and to facilitate conversations about treatment options and expected responses. For patients classified as VSPoor, the test results and supporting studies indicate patients are less likely to respond to treatment. The results can help inform a number of crucial treatment decisions, including the duration of first-line therapy, how long to wait for indications of possible effectiveness, the advisability of enrollment in a clinical trial and, overall, the formulation of realistic expectations about outcomes.

**Palliative care, BSC, hospice, and avoidance of overtreatment**

Availability of an accurate prognosis has been shown to affect planning for palliative care. Without such care, patients near the end of their lives can suffer from severe uncontrolled pain, functional decline, and confusion (McCarthy 2000). These effects are often related to timing; physicians may refer patients to palliative care too late. In a survey of 2,515 Medicare beneficiaries, patients generally preferred treatment focused on palliation rather than life extension, with 83.9% of patients indicating that they did not want potentially life-prolonging drugs that made them feel worse all the time (Barnato 2007). Consistent with these wishes, adequate palliative care has been shown to have positive impacts on patient quality of life (Akerley 2017, Bakitas 2009, Howie 2013), rates of depression (Hui 2014), hospitalization and associated costs (Hui 2014, Smith 2010, Zhang 2009), in-hospital deaths (Hagerty 2005, Zhang 2009), and aggressive overtreatment at the end of life (Ferrell 2017, Jang 2015, Lambden 2016).

Hospice care is not used enough. While the Medicare program provides hospice care benefits for patients with a prognosis of six months or fewer, the median duration of hospice use is less than a month, with more than a third of patients referred to hospice within the last week of life (NHPCO 2015).
Hospice-associated quality metrics within OCM are meant to ensure that patients receive the benefits of hospice care: dying with dignity, dying at home, reduced pain, and reduced burden on caregivers.

VeriStrat test results were used in another author case to support, facilitate, and document shared decision making discussions related to hospice care. A 67-year-old female diagnosed with stage IIIB metastatic lung cancer with an ECOG performance status of 2–3 was treated with carboplatin plus taxol and radiation in the front line. Within three months, the patient had locoregional progression and metastatic invasion into the esophagus. At this point, the physician changed treatment to immunotherapy with pembrolizumab, but the patient had poor tolerance and response. The patient was restaged (stage IV), and a VeriStrat test resulted in VSPoor. Ultimately, the patient and physician discussed the options available using VeriStrat results, and together determined that enrolling the patient in hospice care was a better option than pursuing more chemotherapy. This discussion was important to the patient, showing her that quality of life at the end of life could be optimized, while physical and financial burden that would come with additional lines of potentially ineffective therapy could be minimized.

These experiences are consistent with the findings from the 2017 study by Akerley and colleagues. Results discussed prior suggest that the VeriStrat test helped patients avoid ineffective overtreatment in favor of the quality-of-life gains afforded by BSC and hospice. Real-world experiences find that it usually changes the timing of the discussion, but depending on other patient and disease characteristics, it may be just as likely to prompt a shift toward newer oncology drugs or clinical trials.

Limitations

This report has a number of limitations. We made our best effort to be systematic in our literature search; however, given the short time frame since the implementation of the OCM and 13 steps of cancer planning, we found little to no quantitative data available with which to evaluate the effects of specific approaches, tools, and interventions on providers’ ability to comply with OCM and the 13 steps of cancer care planning. Furthermore, while there are a reasonable number of published studies about the utility of the VeriStrat test, none have yet been designed to specifically address this question. The arguments presented here have been extrapolated from multiple, separate pieces of evidence, combined with personal experience and opinion. Rigorous, prospective, studies would be useful to determine the real-world influence of more accurate lung cancer prognoses on cancer care planning, quality scores, and costs.

Conclusion

In conclusion, knowledge and communication of prognosis, expected response to treatment, and quality of life are central to quality management of patients with cancer, especially within models like OCM and MIPS. While these payment models are complex, the 13 components of cancer care planning establish steps to better cancer management. Tools to help meet those components are important and at times lacking, but they are important for meeting documented care plan requirements and quality metrics. By combining the predictive and prognostic value of VeriStrat testing with clinical factors, physicians and practices participating in the OCM are better able to predict and document expected response to treatment, avoid ineffective and costly overtreatment, and have meaningful conversations with patients about the timing of BSC or hospice care when appropriate. By providing independent prognostic information, the VeriStrat test is a validated, commercially available tool that physicians can use to improve cancer care planning and composite performance scores associated with quality payment models.

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