

THE AMERICAN JOURNAL OF MANAGED CARE®

Evidence-Based Diabetes Management

SPECIAL ISSUE: SENIORS AND DIABETES

Medicare Measures

Quality Measure Improvement Strategies for Elderly Patients With Diabetes

JOHN J SHEEHAN, PHD, RPH; AND
JOANNA P MACEWAN, PHD

Possibly the first treatment guidelines and the precursors to quality metrics survive in one of the oldest known medical texts. In 1862, Edwin Smith discovered an ancient Egyptian papyrus with medical instruction predating Hippocrates by at least a millennia. The papyrus included sound medical advice. For example, after head trauma it instructed the physician to remove splinters from the brain before bandaging. It also included some questionable advice—the papyrus recommended the physician apply a crushed ostrich egg topically after skull fracture. Notably, prior to describing the recommended treatment for each of the 48 listed conditions, the papyrus instructed the physician to determine which of 3 prognoses best suited the patient. It advised that, depending on the condition, physicians should tell patients they will either: (1) treat the condition, (2) contend with the condition, or (3) not treat the condition. In the first case, the physician practically guarantees success, and in the second case, the physician offers his best effort. The third option, which appeared here for the first time, is the most foreign—why would a physician not treat a patient? Scholars believe the papyrus advises against the treatment of certain difficult conditions in an effort to protect the reputation of the physician.¹ After all, a physician who takes on many hopeless cases may struggle to build a successful track record.

Today, moral, legal, and geographic constraints forbid the denial of care to

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Payer Perspective

Florida Blue Program Focuses on Weight Loss—and Fun—to Prevent Type 2 Diabetes in Older Adults

CARMELLA SEBASTIAN, MD, MS, CPE; AND KARLA LOGSTON, RN, BS, CDE

At Florida Blue, we saw a trend. As Florida's largest health insurer, with more than 4 million members, we saw that the risk for diabetes was one of the top 4 risks found in the majority of our members who completed a personal health assessment. Furthermore, at Florida Blue, the average per member per month (PMPM) medical cost trend of someone with diabetes is approximately 3 times higher than for someone without diabetes.

According to the American Diabetes Association (ADA), more than half of Americans, age 65 or older, have prediabetes and are at risk of developing type 2 diabetes (T2D).¹ Prediabetes is a “yellow light,” warning individuals that blood sugars are higher than normal, but not yet high enough for a diabetes diagnosis. Nearly 12 million, or 26%, of Americans age 65 and older already have a diagnosis of diabetes, and that figure is climbing.² An analysis by the CDC, in 2010, estimated that 1 in 3 adults could have diabetes by 2050 if nothing is done to stop existing trends.³ The current national spending to treat diabetes, prediabetes, and related complications is staggering. In 2012, the United States spent \$322 billion on diabetes care, according to the ADA, with 1 out of 3 Medicare dollars spent treating diabetes or its complications.⁴

With Florida's large senior population, these numbers are particularly

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Scaling Prevention

History Lessons in Innovation: Digital Behavioral Medicine Can Address the Diabetes “Double Epidemic” Facing Medicare and America's Seniors

MIKE PAYNE, MBA, MSCI

In 1941, Australian pharmacologist and pathologist Howard Florey demonstrated—for the first time—an effective process for the mass production of penicillin, the antibiotic commonly referred to as the “first wonder drug.” Although Sir Alexander Fleming discovered penicillin in 1928, it was actually Florey's methods for large-scale production of the mold *P. chrysogenum* that fully unlocked the potential of the drug. His work, and the large-scale production by US companies, came just in time to address a widespread epidemic of bacterial disease proliferated by the carnage of World War II. In the 25 years following 1943, the prevalence and incidence of serious bacterial infection in the United States plummeted—a true inflection point in the epidemiology of infectious disease, largely brought about by Florey's scaling innovation (FIGURE).

Seventy-five years after Florey's ground-breaking discovery, society is facing a new epidemic. However, this time it is “metabolic” disease, characterized in affected patients by abnormal levels of sugar and certain hormones in the blood, leading to (and, in turn, perpetuated by) excess body weight. These conditions are most prominently affected by human behavior and consumption. Abnormal blood sugar and associated issues predispose people to obesity and type 2 diabetes (T2D), chronic conditions the CDC labeled “the public health challenge of the 21st century” in 2009.¹

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MEDICATION MANAGEMENT
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Authors from University of Minnesota School of Pharmacy discuss how the many choices for therapy create conditions for suboptimal medication management in diabetes.

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BIDDING PROGRAM UNDER FIRE.

CMS' bidding program for diabetes test strips has been found to cause disruption in the supply chain, resulting in increases in mortality, inpatient admissions, and higher costs, SP252.

FIGHTING FOR CGM. A Medicare beneficiary's account of what it takes to gain access to continuous glucose monitoring in the face of policies designed to prevent access, SP258.

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Clockwise from upper left: Moderator Peter Salgo, MD; and participants John W. Kitchens, MD; Rishi P. Singh, MD; and Steven Peskin, MD, MBA, FACP, discussed the growing diabetes burden and how to screen for patients with diabetic macular edema.

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From left, John W. Kitchens, MD; Steven Peskin, MD, MBA, FACP; Peter Salgo, MD; and Rishi P. Singh, MD; discuss the cost burden of diabetic macular edema and the need for screening in the first of 2 parts of an AJMC Peer Exchange.

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SCALING PREVENTION

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MIKE PAYNE, MBA, MSCI

Treating and Preventing Diabetes Among Our Seniors

The current issue of *Evidence-Based Diabetes Management* examines the topics of cost, treatment, and prevention of the disease among seniors. The share of the population over age 65 with diabetes, most of it type 2, is much too high—25.9%, or 11.8 million individuals, according to the American Diabetes Association. Slowing the march of the disease here would have a profound impact on the quality of life among retirees and on the nation’s healthcare tab, as diabetes accounts for \$1 of every

“Slowing the march of the disease would have a profound impact on the quality of life for retirees and on the nation’s healthcare tab, as diabetes accounts for \$1 of every \$3 spent in Medicare.”

\$3 spent in Medicare. As we planned this issue, news came that Medicare would soon pay for the National Diabetes Prevention Program (NDPP), an evidence-based initiative piloted with the Y, which we have previously featured in this publication. We are proud that this issue includes commentary from leaders in the world of technology, who will bring the NDPP to new audiences, using bold, proven electronic formats.

We are equally pleased to feature such an array of viewpoints. We hear from payers at Florida Blue, who confront the challenge of diabetes prevention in seniors as few do, as well as leaders in medication management from the University of Minnesota, who are coming up with novel ways to

improve adherence among those with diabetes. We learn about studies that are exploring the connections between insulin resistance and cognitive impairment, and whether some of the therapies used in diabetes care might have value for conditions like Alzheimer’s.



MIKE HENNESSY, SR

Finally, we feature 2 articles that discuss how the federal government is failing those with diabetes, despite its professed desire to follow principles of cost-effective, value-based care. First, Dr Jaime Davidson and Mr Christopher Parkin, who were part of the research team that recently reported results in *Diabetes Care*, discuss the failures of a CMS competitive bidding program for diabetes test strips—and how patients were harmed. Next, we hear firsthand from a patient with type 1 diabetes who has confronted one of the most vexing policy issues in diabetes care today: Medicare’s refusal to pay for continuous glucose monitoring systems, despite consensus opinions from leading endocrinology associations that this position is “imprudent.” Dan Patrick’s story is a must-read for anyone who has dealt with government bureaucracy at its worst.

There are many good things happening in diabetes care for seniors, but as you will learn from this issue, much work remains. As always, thank you for reading.

Sincerely,

Mike Hennessy, Sr
CHAIRMAN AND CEO

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Paying for Diabetes Prevention Is a Worthwhile Investment

ROBERT A. GABBAY, MD, PHD, FACP

All of us who care for those with diabetes know a simple truth: so many of the patients we see didn't need to get this sick, suffer so many complications, or be burdened with costly co-payments for medication.

How many of those with type 2 diabetes (T2D) could we have spared this result, if we could have stopped the disease from progressing?

For years, Medicare has asked this question but done little about it when it came to reimbursement. The results speak for themselves: according to the American Diabetes Association, 25.9% of those age 65 and older have diabetes, and 1 in 3 dollars Medicare spends is tied to the disease.¹

Virtually everyone with T2D has some other co-morbidity, whether it's hypertension, obesity, or conditions like kidney disease, that are both expensive to treat and devastating to one's quality of life.² This makes treatment a challenge for the primary care physicians who are on the front lines for much of today's diabetes care.

All this changed on March 23, 2016, when HHS Secretary, Sylvia Mathews Burwell, announced that by year's end, Medicare will pay for diabetes prevention. More precisely, CMS will update the physician fee schedule to include payment for the Diabetes Prevention Program (DPP), a CDC-certified model that is evidence-based, and has been tested for several years in partnership with the YMCA of the USA.

Joslin Diabetes Center has been a leader in studying the DPP, which is a lifestyle program that promotes increased exercise, dietary changes, and assistance in identifying barriers to healthy living. The program has been shown to decrease body weight by an average of 7%, and to reduce the development to diabetes by 58%.³ Long-term follow-up has found the DPP more effective than metformin in preventing the onset of T2D in high-risk adults.⁴

In making the announcement, the Office of the Actuary, at HHS, pointed to the bottom line: testing with the YMCA

showed that Medicare saved \$2650 for every person who enrolled in the program over 15 months. Those who attended at least 4 weekly sessions lost 4.73% of their body weight; those who took all 9 sessions lost 5.17%.⁵

To make it possible to bring the program to the millions in Medicare who are at risk of T2D (an estimated 86 million have prediabetes),¹ it should be possible to deliver the DPP in a digital format, and companies are lining up to deliver this option. CDC has created the Diabetes Prevention Recognition Program to certify those programs that meet evidence-based standards, and to serve as a signal to payers that they are worth funding.

For those of us who have spent years advocating for value-based care, this is a transformative moment. At last, the biggest payer of all—Medicare—is taking a giant step from rewarding “sick care” toward paying for keeping patients well. One can only hope that more change is coming, in diabetes care, and beyond. **EBDM**

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Joslin Diabetes Center

**ROBERT A. GABBAY,
MD, PHD, FACP**

Dr Gabbay is chief medical officer and senior vice president of Joslin Diabetes Center. He serves as editor in chief of *Evidence-Based Diabetes Management*.



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Comprehensive Medication Management Services: Benefits for Seniors With Diabetes

KYLEE A. FUNK, PHARMD, BCPS, AND TODD D. SORENSEN, PHARMD

ABOUT THE AUTHORS



**KYLEE A. FUNK,
PHARMD, BCPS**

Dr Funk is assistant professor in the Department of Pharmaceutical Care and Health Systems, College of Pharmacy, University of Minnesota. As a clinical faculty member, she splits her time among College of Pharmacy activities and her practice site where she provides CMM services.



**TODD D. SORENSEN,
PHARMD**

Dr Sorensen is professor and associate department head in the Department of Pharmaceutical Care and Health Systems, College of Pharmacy, University of Minnesota. He is also executive director of the Alliance for Integrated Medication Management, a nonprofit that supports health care organizations in quality improvement initiatives focused on medication use.

Comprehensive medication management calls for evaluating individual need and defining problems within a framework.

The spectrum of treatment strategies available, the importance of diligent patient self-management, frequent presentation of comorbidities, and the number of healthcare providers often engaged in the care of a patient, frequently make diabetes a complex chronic illness to manage. Unfortunately, the result of this complexity is that, despite good intentions, oversight of a patient's complete medication regimen may be incomplete and create opportunities for suboptimal management. This is illustrated in the following case.

CASE

Bob is a 68-year-old patient with diabetes referred for comprehensive medication management (CMM) services offered by one of the authors (KF). Bob's primary care physician (PCP) made the referral after noting he was not taking his insulin as directed and his glycated hemoglobin (A1C) was now 11.3%. The PCP was particularly concerned that Bob had developed gangrene in 1 foot. From the comprehensive medication review, it was learned that Bob was choosing to ration his insulin in order to save money, so he could afford medications for secondary stroke prevention and depression. During the assessment, Bob also noted that he did not feel the medication prescribed for depression was achieving the desired outcome. While this patient was referred specifically for support in taking his medication as prescribed, the result of a comprehensive evaluation of all of his medication-related needs revealed the following medication-related problems:

- Poor control of diabetes secondary to nonadherence (by choice) with the prescribed insulin regimen
- Lack of control of depression secondary to the wrong (ineffective) drug prescribed
- Risk for stroke secondary to a medication regimen deemed unaffordable by the patient.

As part of developing a care plan to address the 3 medication-related problems, the pharmacist collaborated with the 3 physicians involved in prescribing Bob's medications to,

1. Transition to a less-expensive medication for stroke prevention
2. Alter treatment for depression to a medication that was less expensive and expected to produce a better clinical outcome
3. Help Bob understand the implications of rationing insulin use.

As a result of these changes, Bob's A1C improved to 8.5% within 6 months, symptoms of depression improved and reached defined treatment goals, and Bob was able to maintain an antiplatelet regimen that provided appropriate stroke protection.

MEDICATION USE AND THE TRIPLE AIM

The Institute of Medicine has stated, "Pharmaceuticals are the most common medical intervention, and their potential for both help and harm is enormous. Ensuring that the American people get the most benefit from advances in pharmacology is a critical component of improving the national health care system."¹ Thus, the influence of medication use

on the ability to achieve the Triple Aim² is enormous. This is evident in the case presented above, where Bob's medication-related problems related to each component of the Triple Aim:

1. He was not achieving the clinical goals associated with his medical conditions
2. His healthcare experience was negatively influenced by his inability to afford his medications
3. The cost associated with his care was higher than necessary, secondary to preventable complications from his diabetes.

In cases like Bob's, fragmentation of healthcare often produces a scenario in which no medical provider is monitoring and assuming responsibility for all components of a patient's medication-related treatment plan. Unfortunately, thousands of patients across the United States encounter these situations every day. The frequency of suboptimal medication use may occur even more often in seniors with diabetes, because medication complexity increases in people with diabetes,³ and adverse drug events are more prevalent with increased age.⁴

COMPREHENSIVE MEDICATION MANAGEMENT

CMM services are emerging as a solution to this problem. This service involves application of a specific assessment process to ensure that all of a patient's medication-related needs are met and existing medications are appropriately indicated, their medications are achieving their intended clinical effects, they will not produce adverse effects (given other medications or comorbidities), and the medication-related treatment plan aligns with the lifestyle and needs of the individual patient.⁵

CMM services are typically provided by pharmacists collaborating with a primary care team. A defined care process is applied with each patient, which begins with an assessment, followed by identification of problems, development of a care plan, and follow-up.⁵ However, the manner in which the assessment is completed is distinct. When providing CMM services, a pharmacist will systematically assess medication needs in the context of the individual patient, categorizing medication-related problems using a defined framework (TABLE 1)⁵. To resolve medication-related problems, the pharmacist collaborates with the patient's medical providers to confirm and implement a revised care plan that addresses all of the patient's medication-related needs.

Application of this assessment process and problem categorization system reveals some interesting findings regarding the prevalence of what factors are driving sub-optimal outcomes from medication use. While a great deal of attention has recently been placed on ensuring patient adherence to medication regimens, the work of 3 large health systems in Minnesota, that have consistently integrated CMM programs in their primary and specialty care clinics, demonstrates that nonadherence is only the third most common medication-related problem (TABLE 2).⁶ More frequently, patients are not achieving therapeutic goals because,

1. Patients have not been prescribed a medication indicated for their medical situation
2. Medications are not prescribed at a dose high enough to achieve the desired goal.

TABLE 1. Categorization of Medication-Related Problems⁵

| PRIMARY CATEGORIES | SECONDARY CATEGORIES |
|---|--|
| Indication Appropriateness of the medication | Unnecessary drug therapy: Is each medication appropriate for the medical condition being treated? Needs additional drug therapy: Does the patient have an indication for a medication that has not been prescribed? |
| Effectiveness Effectiveness of the medication | Ineffective drug therapy: Is the most effective drug product being used for the medical condition? Dose too low: Is the dose appropriate and able to achieve the intended goals of therapy? |
| Safety Safety of the medication | Adverse drug reaction: Is the patient experiencing (or at risk of experiencing) an adverse event from the medication? Dose too high: Is the dose so high it could cause toxicity in the patient? |
| Convenience Adherence to the medication | Nonadherence: Is the patient able and willing to take the medication as intended? |

TABLE 2. Categorization of 108,402 Medication-Related Problems Derived From CMM Data Across 3 Large Health Systems⁶

| UNNECESSARY DRUG THERAPY | NEEDS ADDITIONAL DRUG THERAPY | INEFFECTIVE DRUG THERAPY | DOSE TOO LOW | ADVERSE DRUG REACTION | DOSE TOO HIGH | NONADHERENCE |
|--------------------------|-------------------------------|--------------------------|--------------|-----------------------|---------------|--------------|
| 7.8% | 20.1% | 6.7% | 26.2% | 12.0% | 11.0% | 16.1% |

CMM: BENEFITS FOR SENIORS WITH DIABETES

Clinical and financial outcomes associated with patients with diabetes receiving CMM have been positive. In one study, patients with diabetes referred for CMM services experienced A1C reductions of 1.3% to 2.7%.⁷ Furthermore, CMM services have been associated with a positive impact on cardiovascular risk factors, such as blood pressure (BP) and low-density lipoprotein (LDL) cholesterol in patients with diabetes.⁷ A trial that compared outcomes of patients enrolled in a pharmacist-managed diabetes service compared with those who were referred to this service, but never attended, found that not only were A1C reductions greater in the pharmacist-managed group, but more patients in this group achieved BP- and LDL-cholesterol goals, more frequently took aspirin as indicated, and had greater adherence to smoking-cessation measures. These outcomes occurred even though patients enrolled in the pharmacist service had a more complex medical history and medication regimens.⁸

Seniors represent a group likely to benefit from CMM services because medication regimens often become more complex as one ages. Although seniors comprise only 13% of the US population, they receive 30% of all prescriptions dispensed.⁹ They also tend to have more prescribers than younger patient groups and also more frequently use multiple pharmacies. Both of these factors put seniors at greater risk of adverse drug reactions.¹⁰

Cost savings associated with CMM services have also been reported. One health system analyzed costs associated with patients that experienced over 9000 CMM encounters and projected a 12:1 return on investment from CMM.¹¹ Other studies have also demonstrated cost savings from CMM services or similar programs.^{12,13}

OPPORTUNITIES FOR CMM

Although improved health outcomes and cost savings are associated with CMM, this service remains limited in its presence in healthcare settings. One reason is that typical fee-for-service programs, operated by payers, generally do not recognize services provided by pharmacists as a covered benefit. However, as our healthcare system continues to expand value-based payment principles, it is likely that the integration of CMM services will increase due to the positive impact on quality, cost, and experience metrics that will drive the design of care delivery models in the future.

While the negative aspects of Bob's healthcare are quite commonly observed in our healthcare system today, the positive experience derived from having CMM included in the spectrum of services provided by his primary care team could become the norm of the future. Bob personally saw the value in these services and expressed gratitude for the positive

influence CMM had on his health. Additionally, Bob's medical providers expressed appreciation for the team-based approach to care that enhanced the care they were providing and produced a more effective treatment regimen. While the complex nature of his medication regimen made Bob an ideal candidate for CMM services, the presence of this service in primary care remains limited. It is our hope that the positive data and patient stories produced by CMM services will quickly influence healthcare service design, making access to these services possible for all patients with complex medication-related needs. **EBDM**

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“It is our hope that the positive data and patient stories produced by CMM services will quickly influence healthcare design.”

Although seniors comprise only 13% of the population, they receive 30% of all prescriptions dispensed.



Pharmacist led diabetes care improves glycemic control. View at <http://bit.ly/24vVBVU>.

Technology, Seniors, and Sense Making

TRISHAN PANCH, MD, MPH, AND ELAINE GOODMAN, MD, MBA

ABOUT THE AUTHORS



TRISHAN PANCH, MD, MPH

Dr Panch is the co-founder, chief medical officer, and head of product at Wellframe, Boston, MA.



ELAINE GOODMAN, MD, MBA

Dr Goodman is assistant in medicine at Massachusetts General Hospital and medical director at Wellframe.

As primary care physicians and leaders of Wellframe—a mobile health company working with payers and physicians groups to extend care between visits for patients with complex comorbidities—Drs Panch and Goodman discuss their experiences building a mobile application used by elderly patients to communicate with clinicians and manage chronic disease.

Symbiotically, the medical delivery system has grown around us to not just treat our ailments, but to help us make sense of our experiences with illness. The clinical consultation is, therefore, not only the fundamental unit of information exchange between a patient and clinician; it also serves as the forum for a patient to recruit their doctor in helping them make sense of what is happening and to find an ally for their healthcare journey. If successful, a therapeutic bond forms that can bridge the temporal chasms between consultations and make each individual exchange more effective. In contrast, many health apps and patient-facing technology products have been designed to work in parallel with or in place of the patient-clinician relationship. However, we believe that it is the clinician's skills in empathy, sense making (forming and testing hypotheses from poorly structured and incomplete data), and communication that enable relationships, and that these uniquely human skills should be amplified, rather than replaced, by technology.

We have also become convinced that these supportive “between-visit” relationships are of particular importance to older patients. With aging, comes a longer list of medical problems that have a lower probability of cure. Therefore, this need for ongoing management, rather than definitive solutions, dramatically increases the demand by seniors for both healthcare resources and the continuing patient-physician relationship to make sense of their situation. With an aging population and rapidly rising levels of effectively incurable cardiometabolic diseases, the need for these sense-making relationships that underpin care rises exponentially. Thus, we are faced with a situation in which the demand for the human beings involved in care delivery is growing unsustainably in parallel with costs.

Enter stage left, technology: robots, telemedicine, mobile devices, and, more recently, artificial intelligence have each had their time in the limelight. But can these technologies meaningfully influence those patients that need them most? Understandably, many have raised concerns that the answer in elderly populations will be “No,” given the lack of access to or familiarity with enabling technologies—namely, mobile devices (smartphones and tablets) and the Internet—among the elderly. In many studies, data have borne out these concerns. But our experiences have shown that there are ways to design technology with seniors in mind that mitigate many of these challenges.

WELLFRAME'S EXPERIENCE BUILDING TECHNOLOGY FOR SENIORS

Although new technologies, such as smartphone apps, may be second nature to younger members of the population, seniors notoriously find these advances more difficult to use and they blame themselves for these difficulties. In multiple focus groups with seniors, in the early stages of designing the Wellframe app, we observed that older users underestimated their abilities (“I am just not good at these kind of things”) and blamed themselves for technology failures (“I must have done something wrong, but I just could not get it to open.”)

Younger users, in contrast, were more likely to give feedback that the app was poorly designed if they struggled, rather than assuming that the issue was caused by a deficiency in their own ability or knowledge. These factors, alongside well-known limitations in vision and manual dexterity in the elderly, explain much of the reticence among some seniors to try new technologies and the propensity with others to stop using them quickly.

We also received qualitative feedback that the fact that the app was enabling more frequent interaction with a clinician, rather than only teaching self-management or tracking, was of huge value in the elderly population. Although we haven't formally studied the reasons that underpin this observation, we believe this likely has to do with the increased complexity of illness and the higher risk of social isolation/less robust social support systems that affect many of the elderly patients we work with.

THE WELLFRAME EXPERIENCE

- **Age distribution.** The median age of a Wellframe user is 54 years, with 22% over age 65. The average age for patients older than 65 is 70 years, with a median age of 69. The average age for users under age 65 is 47.5 years, with a median age of 51 (FIGURE 1).
- **Technology access.** As expected, the share of patients with smartphones declines with increasing age, going from 30% to 50% in those under age 65 (depending on the site) to between 5% and 30% in those over age 65, based on clinician reports at partner sites. We believe the differences in penetration between partner sites reflects varying socioeconomic circumstances and is consistent with published analyses¹.
- **Engagement.** Rates of engagement with our app (in terms of daily and weekly active patients) among those older than age 65 is equivalent to and, in some groups, greater than adults aged 25 to 65, but less than the very young (ages 16 to 25) (TABLE). Of note, all of the young people in the Wellframe sample are in community-based rehabilitation programs for the treatment of severe and persistent mental illness.

T A B L E. Difference in Daily Engagement With Wellframe by Age ($P < 0.001$)

| AGE (y) | DAILY ENGAGEMENT WITH THE WELLFRAME MOBILE APPLICATION | 95% CONFIDENCE INTERVAL |
|---------|--|-------------------------|
| 16-25 | 79.4% | 78.0% - 80.7% |
| 25-65 | 37.9% | 37.4 - 38.5% |
| 65+ | 45.8% | 44.6 - 47.0% |

- **Retention.** The share of patients who stay with Wellframe programs beyond 60 days are equivalent regardless of age, as seen in FIGURE 2, further illustrating that those over 65 who use our technology use it as avidly as those under age 65.

Qualitative analysis of users reveals that the principal driver of continuous adherence with the Wellframe technology-enabled programs is the knowledge that the app connects them to a person who they know and trust, and who is available to help them make sense of their journey.

In focus groups, older technology users underestimated their abilities while younger users would attribute difficulties to design flaws.

LESSONS LEARNED

In our experience rolling out our technology products with payers and providers, several big themes have emerged about how to successfully implement technology programs aimed at the elderly:

- **Making sense makes sense.** A therapeutic relationship not only helps in getting access to information and support in the tasks of diabetes self-care; it also helps patients, especially seniors, make sense of the deeper, more existential questions they face. We believe that a key design imperative for technology aimed at seniors is to help patients and clinicians build therapeutic relationships such that the software experience essentially melts away. The design of technology for seniors, from the feature set to the user interface to the user experience, should help these patients find meaning. A relationship with a clinician is a tried-and-tested way of doing this, and we believe that all technologies designed to be used by seniors in the clinical context should view themselves as communication technologies empowering patients to build therapeutic relationships with clinicians.

Experience has shown that innovations that are not connected to a clinician are only used in the short term. This is typical of most technology initiatives that treat patients as beacons of health data who are willing to take on self-management of their conditions. Such solutions in practice offer little value beyond self-tracking. Our payer and provider customers report that uptake of these tracking solutions is typically less than 10%, and 1-month retention rates less than 1%.

- **Change management matters.** Although the managed care context naturally serves to encourage alternative models of care delivery, the reality is that the consultation is still the fundamental unit of healthcare delivery and we are all primed to consider healthcare as what happens in consultations. Introducing digital tools, such as Wellframe, into the context of care delivery requires considerable investment in change management at the care-delivery level, enabled by a fundamental commitment to use such technologies to amplify clinical relationships by enabling participants to collaboratively create their positive effect at greater scale and with greater frequency.

We have consistently found that patient adoption follows clinician adoption. Although clinician adoption may be challenging at first, it takes off once the new technology demonstrates value and becomes the default. The initial “pilot mentality” that attracts the early-adopter patients and clinicians alike evolves into a more assured pattern in which clinicians see Wellframe as a default aspect of their care delivery model. This assuredness is implicitly and explicitly communicated to the patients and manifest as greater onboarding conversion rates and improved retention. As you might imagine, comfort and familiarity on the part of the clinicians is critical to being able to convince elderly patients that they will be successful in using a new technology product. As an older patient, if your (likely younger) care manager or doctor is intimidated by the technology, your own confidence will be understandably shaken as well.

- **Technology should be people-worthy.** It is sad that seniors blame themselves for the faults of technology creators. Muhammad Yunus, the Nobel Prize-winning economist who created a pioneering community-based model of microfinance for the poor, said, “It is not that people are not credit-worthy, but it is that banks are not people-worthy.”² The same could be said of the legacy of health technology

FIGURE 1. Age and Gender of All Wellframe Patients

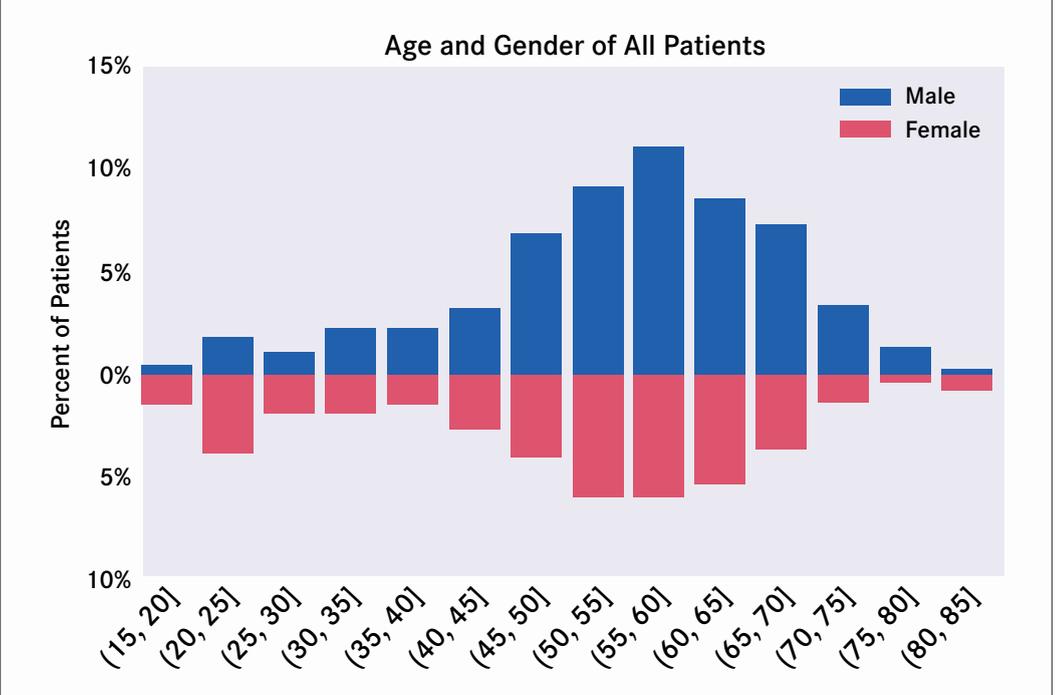
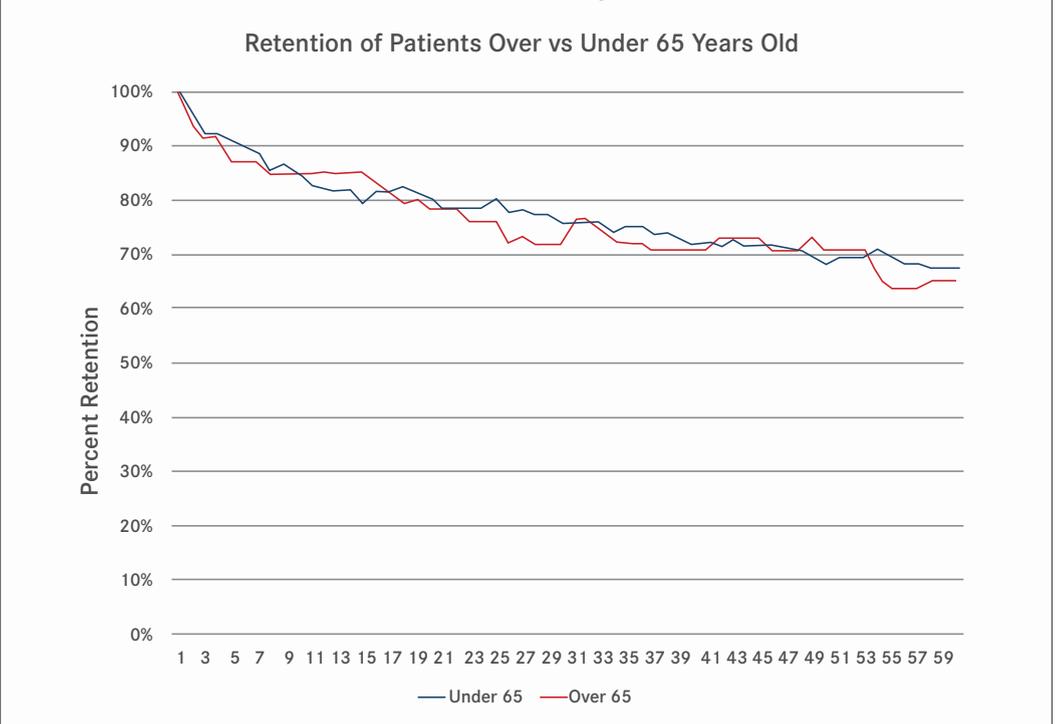


FIGURE 2. Retention of Patients Over vs Under Age 65



for seniors: it is not that seniors will not use technology, it is that the technology offered to them is often not “people-worthy.” Thinking about the essential questions that an elderly patient faces, and using technology to help them make sense of their experience, is what makes the difference between creating a solution that can be woven into the fabric of care instead of one that will alienate seniors and ultimately be discarded. **EBDM**

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Diabetes and Medicare Competitive Bidding: The “Perfect Storm” for Patient Harm

JAIME A. DAVIDSON, MD, FACP, FACE, AND CHRISTOPHER G. PARKIN, MS

ABOUT THE AUTHORS



**JAIME A. DAVIDSON,
MD, FACP, FACE**

Dr Davidson is clinical professor of internal medicine in the Division of Endocrinology, Touchstone Diabetes Center, The University of Texas Southwestern Medical Center in Dallas, Texas. He reports no conflicting interests.



**CHRISTOPHER G.
PARKIN, MS**

Mr Parkin is president of CGParkin Communications, Boulder City, Nevada. He reports consulting fees from Animas Corporation, CeQur SA, Dexcom, Inc, Insulet Corporation, Roche Diabetes Care, and Sanofi US.

INTRODUCTION

Given the growing epidemic and rising financial burden of diabetes in America, clinicians and payers are challenged to strike a balance between effectiveness and cost-efficiency in the allocation of healthcare resources. Achieving this balance is especially critical among patients with diabetes within the Medicare population. These patients now make up 29.9% (11.1 million) of the estimated 29.1 million Americans with diabetes.¹ The latest reports estimate that beneficiaries with diabetes consume approximately 30% of total Medicare expenditures.²

Clearly, there is a need to improve how we deliver the necessary medications, glucose monitoring products, and healthcare services to our older diabetes patients. However, the approach chosen by CMS, through its competitive bidding program (CBP), has created a perfect storm of increased costs and adverse health outcomes among Medicare beneficiaries.

IMPACT OF COMPETITIVE BIDDING ON ACQUISITION OF DIABETIC TESTING SUPPLIES

Background

In January 2011, CMS initiated its CBP in 9 test markets, which included approximately 444,000 fee-for-service Medicare Part D beneficiaries with insulin-treated diabetes. The goal of the program is to reduce beneficiary out-of-pocket expenses and save Medicare money while ensuring beneficiary access to quality items and services. In April 2012, CMS reported that there had been no disruption of access to diabetes testing supplies and that no negative healthcare consequences to beneficiaries were seen as a result of CBP.³

In March 2016, we reported findings from our own analysis of competitive bidding as it relates to beneficiaries with insulin-treated diabetes.⁴ Contrary to CMS's report of no disruption and no adverse health outcomes, we found that acquisition of supplies for self-monitoring of blood glucose (SMBG) was disrupted within the test markets, leading to increased percentages of beneficiaries who migrated from full SMBG acquisition in 2010 to partial/no SMBG acquisition in 2011. The populations most affected were females and African Americans. Migration to partial/no SMBG acquisition was significantly associated with increases in mortality, inpatient admissions, and costs.

Significance of Disruption

A key finding of our analysis was the relationship between SMBG acquisition and mortality. As presented in our report, survival was negatively associated with partial/no SMBG acquisition in both the test market and non-test-market populations ($P < .0001$).⁴ One possible explanation for this finding is the increased risk for hypoglycemia within the Medicare diabetes population or significant hyperglycemia by not knowing glucose levels and not taking the recommended insulin dose.

We know that elderly diabetes patients treated with insulin or insulinotropic agents are at significantly higher risk for severe or fatal hypoglycemia than younger patients.⁵⁻⁸ Although much of this is due to the increased prevalence of hypoglycemia unawareness within the elderly population,⁹ the risk of hypoglycemia-related mortality increases significantly among patients with cardiovascular disease.¹⁰ As reported, almost half of the beneficiaries included in our analysis had a diagnosis of heart failure at baseline.⁴ Because frequent use of SMBG enables patients to detect hypoglycemia in its early stages and take immediate action to prevent it from progressing,¹¹ it is understandable that when access to SMBG supplies

is disrupted, testing frequency decreases (or disappears altogether) and hypoglycemia increases. When hypoglycemia increases among patients with existing heart disease, we would expect to see increased mortality, increased hospitalizations, and increased costs.

THE LINK BETWEEN COMPETITIVE BIDDING AND ADVERSE HEALTH OUTCOMES

Inaccurate SMBG Systems

A factor that must be considered when exploring the link between competitive bidding and the increased mortality and hospitalizations observed in our study, is the questionable accuracy of many of the SMBG systems provided to beneficiaries. Because SMBG data are used in clinical decision making, obtaining accurate glucose data is critical. As reported by Breton and Kovatchev, inaccurate information on glucose levels can lead to severe, even deadly, consequences, either by failing to detect hypoglycemia or by prompting patients to overcorrect with insulin based on an erroneous high glucose result.¹²

Several recent studies have revealed significant inaccuracy and lot-to-lot variability in up to 45% of the SMBG systems currently marketed.¹³⁻¹⁶ Among these is the Prodigy Autocode system, which made up 26.9% of the Medicare claims for mail order test strips from October through December 2013.¹⁷

In our review of the FDA's MAUDE (Manufacturer and User Facility Device Experience) website, we found 202 event reports pertaining to the Prodigy Autocode, a vast majority of which describe events that involved the need for emergency medical assistance and/or hospitalization due to meter inaccuracies.¹⁸ Although it is troubling that the FDA allows the manufacturer to market its meters to beneficiaries, we are puzzled as to why 83 of these events, which date back to 2010, were not reported to the FDA until November 2013—almost 2 years after implementation of competitive bidding for test strips. This suggests a lack of oversight by the FDA in protecting Medicare beneficiaries, making the agency complicit in the increased mortality and hospitalizations reported in our study.

Interference With the Patient-Clinician Relationship

When competitive bidding was implemented, many beneficiaries were “switched” from their current SMBG system to a lower-cost system, according to a survey by the American Association of Diabetes Educators.¹⁹ This may explain why a significant percentage of beneficiaries discontinued their mail order acquisition and began purchasing their supplies from retail pharmacies.⁴ However, many beneficiaries continued with their new, lower-cost systems, and, in many cases, their physicians were unaware that switching of systems had occurred. This “disconnect” between clinicians and patients increased the potential for inadequate patient training and may have resulted in even greater and more frequent SMBG inaccuracies due to user error.

Because diabetes is a lifelong, self-managed disease, patients require ongoing support and encouragement from their healthcare team to stay actively engaged with their treatment regimens. If patients lack the confidence to properly use their SMBG meters and/or are discouraged (or have experienced harm) due to receiving inaccurate results, they will stop testing. Having proper monitoring technology is a right for patients with diabetes. Patients have significant problems, and we should do our best to make their lives easier, not more difficult. Government initiatives that interfere with the patient-clinician relationship are detrimental to patient outcomes and, ultimately, raise costs.

Inadequate Monitoring of Patient Safety

In December 2015, the National Minority Quality Forum (NMQF) published a 37-page report sharply criticizing the scientific methodology CMS used to monitor patient health and safety.²⁰ According to the report, findings of “no disruption of access” and “no adverse health outcomes” are not supported by the data and methodology descriptions presented in CMS’s reports. The report concluded that CMS’s approach to monitoring health status raises concerns about safety monitoring of the CBP and should be suspended until CMS can demonstrate that adequate safeguards have been adopted.

CMS’s apparent lack of “transparency” in reporting their findings is also troubling. According to the official statement from the American Diabetes Association (ADA), “The Association has met numerous times with CMS staff, including the Medicare Competitive Acquisition Ombudsman, to discuss issues involving beneficiaries with diabetes and to advocate that the beneficiary protections in the program be implemented in a meaningful way.”²¹

If the ADA has been working with CMS to resolve identified issues, why does CMS continue to report that there are no issues? This, alone, raises significant concerns about the trustworthiness of CMS.

Unsupported Claims of Cost Savings

In March 2014, the US Government Accountability Office (GAO) reported that “the number of beneficiaries furnished DME (durable medical equipment) items included in the CBP generally decreased more in the competitive bidding areas than in the comparator areas” during the first 2 years, and that, according to CMS, competitive bidding “may have reduced inappropriate usage of DME, and these decreases do not necessarily reflect beneficiary access issues.”²² The GAO report also states that competitive bidding achieved “cost savings of about \$400 million as estimated by CMS.”²²

How do we know this is true? As discussed earlier, CMS’s flawed methodology in monitoring beneficiary access makes it impossible to accurately assess the impact of competitive bidding on acquisition behaviors and costs. And, as reported in our study, hospitalizations and associated costs more than doubled.⁴ Given that the 9 test markets represented only 10% of Medicare beneficiaries, and that competitive bidding now includes SMBG supplies acquired through both mail order and retail channels, we find it highly unlikely that any cost savings have been achieved. Moreover, the impact of competitive bidding on other affected products (eg, oxygen, enteral) has yet to be studied. Although anecdotal reports suggest that significant harm has occurred among patients who use these products, we will never know the full extent to which competitive bidding has impacted patient lives and healthcare costs until studies similar to ours have been conducted.

SUMMARY

Our study demonstrated that the initial implementation of competitive bidding in the 9 test markets disrupted beneficiary access to needed SMBG supplies, resulting in increased mortality, hospitalizations, and costs.⁴ The NMQF report articulated numerous reasons why CMS’s claims of no disruption, no adverse outcomes, and cost savings are unsubstantiated and should be questioned.²⁰

As clinicians, we have an ethical obligation to our patients to, first, do no harm. Moreover, as with any clinical trial that involves human subjects, CMS has an ethical obligation to terminate competitive bidding now that harm has been detected. We do not know the full extent of the harm being done to beneficiaries by the national implementation of competitive bidding. However, we do have enough evidence to support suspension of competitive bidding until CMS can prove its ability to monitor patient safety. **EBDM**

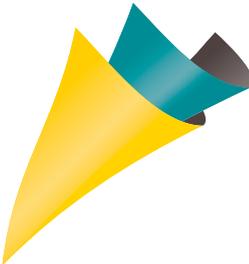
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“We do not know the full extent of the harm being done to beneficiaries by the national implementation of competitive bidding. However, we do have enough evidence to support suspension.”

—JAIME A. DAVIDSON, MD, FACP, FACE;
CHRISTOPHER G. PARKIN, MS

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(empagliflozin) tablets

10 mg/25 mg

JARDIANCE is an SGLT2 inhibitor for the treatment of adults with type 2 diabetes, in addition to diet and exercise

- Significant A1C reduction
- Once-daily oral dosing in the morning
- Significant weight loss demonstrated as a secondary endpoint*

* JARDIANCE is not indicated for weight loss.

INDICATION AND LIMITATION OF USE

JARDIANCE is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

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

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

JARDIANCE should not be used in patients with a history of serious hypersensitivity to JARDIANCE or in patients with severe renal impairment, end-stage renal disease, or dialysis.

WARNINGS AND PRECAUTIONS

Hypotension

JARDIANCE causes intravascular volume contraction. Symptomatic hypotension may occur after initiating JARDIANCE particularly in patients with renal impairment, the elderly, in patients with low systolic blood pressure, and in patients on diuretics. Before initiating JARDIANCE, assess for volume contraction and correct volume status if indicated. Monitor for signs and symptoms of hypotension after initiating therapy.

Ketoacidosis

Postmarketing reports of ketoacidosis, a serious life-threatening condition requiring urgent hospitalization, have been identified in patients with type 1 and type 2 diabetes mellitus receiving SGLT2 inhibitors, including JARDIANCE. Patients who present with symptoms of metabolic acidosis should be assessed for ketoacidosis, even if blood glucose levels are less than 250 mg/dL. If suspected, discontinue JARDIANCE, evaluate and treat promptly.

Before initiating JARDIANCE, consider patient risk factors for ketoacidosis including pancreatic insulin deficiency from any cause,

caloric restriction, and alcohol abuse. Patients on JARDIANCE may require monitoring and temporary discontinuation of therapy in clinical situations known to predispose to ketoacidosis.

Impairment in Renal Function

JARDIANCE increases serum creatinine and decreases eGFR. Renal function should be evaluated prior to initiating JARDIANCE and periodically thereafter. More frequent monitoring is recommended with eGFR below 60 mL/min/1.73 m². The risk of impaired renal function with JARDIANCE is increased in elderly patients and patients with moderate renal impairment. JARDIANCE should be discontinued in patients with a persistent eGFR less than 45 mL/min/1.73 m².

Urosepsis and Pyelonephritis

Serious urinary tract infections including urosepsis and pyelonephritis requiring hospitalization have been identified in postmarketing reports in patients receiving SGLT2 inhibitors, including JARDIANCE. Treatment with SGLT2 inhibitors increases the risk for urinary tract infections. Evaluate for signs and symptoms of urinary tract infections and treat promptly.

Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues

Insulin and insulin secretagogues are known to cause hypoglycemia. The use of JARDIANCE with these agents can increase the risk of hypoglycemia. A lower dose of insulin or the insulin secretagogue may be required to reduce the risk of hypoglycemia when used in combination with JARDIANCE.

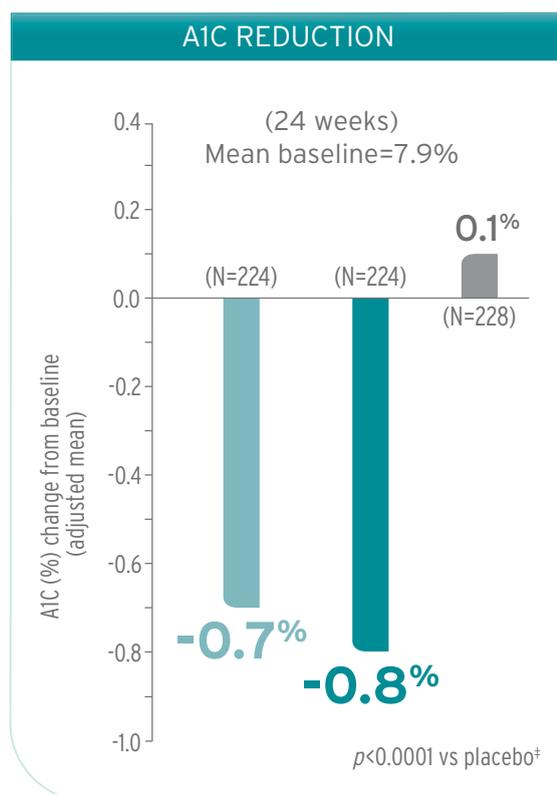
Genital Mycotic Infections

JARDIANCE increases the risk for genital mycotic infections. Patients with a history of chronic or recurrent genital mycotic infections were more likely to develop these infections. Monitor and treat as appropriate.

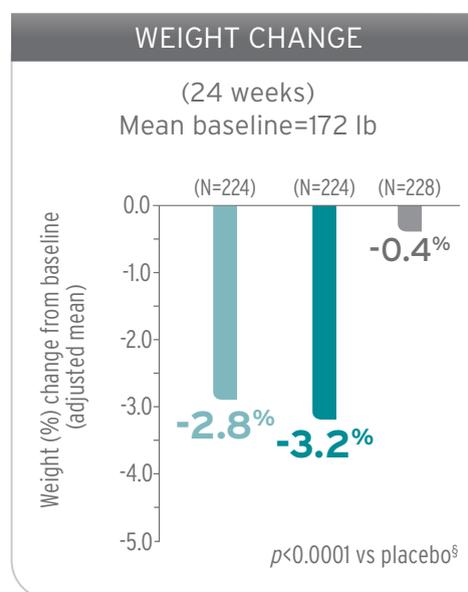
JARDIANCE is proven to significantly reduce A1C

In addition to lowering A1C, JARDIANCE significantly reduced weight[†]

JARDIANCE monotherapy vs placebo (24 weeks)



[†]JARDIANCE is not indicated for weight loss. Change from baseline in body weight was a secondary endpoint.¹



[‡]A1C reduction: Difference from placebo (adjusted mean) was -0.7% and -0.9% for JARDIANCE 10 mg and 25 mg, respectively.

[§]Weight change: Difference from placebo (adjusted mean) was -2.5% and -2.8% for JARDIANCE 10 mg and 25 mg, respectively.

Study design: In a 24-week, double-blind, placebo-controlled study of 676 patients with type 2 diabetes mellitus, the efficacy and safety of JARDIANCE 10 mg (N=224) and 25 mg (N=224) were evaluated vs placebo (N=228). The primary endpoint was A1C change from baseline.¹

JARDIANCE 10 mg and 25 mg significantly reduced systolic blood pressure (SBP)^{||} by -2.6 mm Hg (placebo-adjusted, p=0.0231) and -3.4 mm Hg (placebo-corrected, p=0.0028), respectively, at 24 weeks[¶]

^{||}JARDIANCE is not indicated as antihypertensive therapy. Change from baseline in SBP was a secondary endpoint.¹

[¶]SBP mean baseline: 133.0 mm Hg, 129.9 mm Hg, and 130.0 mm Hg for JARDIANCE 10 mg, 25 mg, and placebo, respectively.¹

■ JARDIANCE 10 mg ■ JARDIANCE 25 mg ■ Placebo

Reference: 1. Data on file. Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, CT; 2014.

IMPORTANT SAFETY INFORMATION (continued)

Increased Low-Density Lipoprotein Cholesterol (LDL-C)

Increases in LDL-C can occur with JARDIANCE. Monitor and treat as appropriate.

Macrovascular Outcomes

There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with JARDIANCE or any other antidiabetic drug.

ADVERSE REACTIONS

The most common adverse reactions (>5%) associated with placebo and JARDIANCE 10 mg and 25 mg were urinary tract infections (7.6%, 9.3%, 7.6%, respectively) and female genital mycotic infections (1.5%, 5.4%, 6.4%, respectively).

When JARDIANCE was administered with insulin or sulfonylurea, the incidence of hypoglycemic events was increased.

DRUG INTERACTIONS

Coadministration of JARDIANCE with diuretics resulted in increased urine volume and frequency of voids, which might enhance the potential for volume depletion.

USE IN SPECIAL POPULATIONS

Pregnancy

There are no adequate and well-controlled studies of JARDIANCE in pregnant women. JARDIANCE should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known if JARDIANCE is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from JARDIANCE, discontinue nursing or discontinue JARDIANCE.

Geriatric Use

JARDIANCE is expected to have diminished efficacy in elderly patients with renal impairment. The incidence of volume depletion-related adverse reactions and urinary tract infections increased in patients ≥75 years treated with JARDIANCE.

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Please see Brief Summary of full Prescribing Information on the adjacent pages.

JARDIANCE® (empagliflozin) tablets, for oral use

Rx only

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Please see package insert for full Prescribing Information.

INDICATIONS AND USAGE: JARDIANCE is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. **Limitation of Use:** JARDIANCE is not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

CONTRAINDICATIONS: History of serious hypersensitivity reaction to JARDIANCE; Severe renal impairment, end-stage renal disease, or dialysis [see Use in Specific Populations].

WARNINGS AND PRECAUTIONS: Hypotension: JARDIANCE causes intravascular volume contraction. Symptomatic hypotension may occur after initiating JARDIANCE [see Adverse Reactions] particularly in patients with renal impairment, the elderly, in patients with low systolic blood pressure, and in patients on diuretics. Before initiating JARDIANCE, assess for volume contraction and correct volume status if indicated. Monitor for signs and symptoms of hypotension after initiating therapy and increase monitoring in clinical situations where volume contraction is expected [see Use in Specific Populations]. **Ketoacidosis:** Reports of ketoacidosis, a serious life-threatening condition requiring urgent hospitalization have been identified in postmarketing surveillance in patients with type 1 and type 2 diabetes mellitus receiving sodium glucose co-transporter-2 (SGLT2) inhibitors, including JARDIANCE. JARDIANCE is not indicated for the treatment of patients with type 1 diabetes mellitus [see Indications and Usage]. Patients treated with JARDIANCE who present with signs and symptoms consistent with severe metabolic acidosis should be assessed for ketoacidosis regardless of presenting blood glucose levels, as ketoacidosis associated with JARDIANCE may be present even if blood glucose levels are less than 250 mg/dL. If ketoacidosis is suspected, JARDIANCE should be discontinued, patient should be evaluated, and prompt treatment should be instituted. Treatment of ketoacidosis may require insulin, fluid and carbohydrate replacement. In many of the postmarketing reports, and particularly in patients with type 1 diabetes, the presence of ketoacidosis was not immediately recognized and institution of treatment was delayed because presenting blood glucose levels were below those typically expected for diabetic ketoacidosis (often less than 250 mg/dL). Signs and symptoms at presentation were consistent with dehydration and severe metabolic acidosis and included nausea, vomiting, abdominal pain, generalized malaise, and shortness of breath. In some but not all cases, factors predisposing to ketoacidosis such as insulin dose reduction, acute febrile illness, reduced caloric intake due to illness or surgery, pancreatic disorders suggesting insulin deficiency (e.g., type 1 diabetes, history of pancreatitis or pancreatic surgery), and alcohol abuse were identified. Before initiating JARDIANCE, consider factors in the patient history that may predispose to ketoacidosis including pancreatic insulin deficiency from any cause, caloric restriction, and alcohol abuse. In patients treated with JARDIANCE consider monitoring for ketoacidosis and temporarily discontinuing JARDIANCE in clinical situations known to predispose to ketoacidosis (e.g., prolonged fasting due to acute illness or surgery). **Impairment in Renal Function:** JARDIANCE increases serum creatinine and decreases eGFR [see Adverse Reactions]. The risk of impaired renal function with JARDIANCE is increased in elderly patients and patients with moderate renal impairment. More frequent monitoring of renal function is recommended in these patients [see Use in Specific Populations]. Renal function should be evaluated prior to initiating JARDIANCE and periodically thereafter. **Urosepsis and Pyelonephritis:** There have been postmarketing reports of serious urinary tract infections including urosepsis and pyelonephritis requiring hospitalization in patients receiving SGLT2 inhibitors, including JARDIANCE. Treatment with SGLT2 inhibitors increases the risk for urinary tract infections. Evaluate patients for signs and symptoms of urinary tract infections and treat promptly, if indicated [see Adverse Reactions]. **Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues:** Insulin and insulin secretagogues are known to cause hypoglycemia. The risk of hypoglycemia is increased when JARDIANCE is used in combination with insulin secretagogues (e.g., sulfonylurea) or insulin [see Adverse Reactions]. Therefore, a lower dose of the insulin secretagogue or insulin may be required to reduce the risk of hypoglycemia when used in combination with JARDIANCE. **Genital Mycotic Infections:** JARDIANCE increases the risk for genital mycotic infections [see Adverse Reactions]. Patients with a history of chronic or recurrent genital mycotic infections were more likely to develop mycotic genital infections. Monitor and treat as appropriate. **Increased Low-Density Lipoprotein Cholesterol (LDL-C):** Increases in LDL-C can occur with JARDIANCE [see Adverse Reactions]. Monitor and treat as appropriate. **Macrovascular Outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with JARDIANCE or any other antidiabetic drug.

ADVERSE REACTIONS: The following important adverse reactions are described below and elsewhere in the labeling: Hypotension [see Warnings and Precautions]; Ketoacidosis [see Warnings and Precautions]; Impairment in Renal Function [see Warnings and Precautions]; Urosepsis and Pyelonephritis [see Warnings and Precautions]; Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues [see Warnings and Precautions]; Genital Mycotic Infections [see Warnings and Precautions]; Increased Low-Density Lipoprotein Cholesterol (LDL-C) [see Warnings and Precautions].

Clinical Trials Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. **Pool of Placebo-Controlled Trials evaluating JARDIANCE 10 and 25 mg:** The data in Table 1 are derived from a pool of four 24-week placebo-controlled trials and 18-week data from a placebo-controlled trial with insulin. JARDIANCE was used as monotherapy in one trial and as add-on therapy in four trials. These data reflect exposure of 1976 patients to JARDIANCE with a mean exposure duration of approximately 23 weeks. Patients received placebo (N=995), JARDIANCE 10 mg (N=999), or JARDIANCE 25 mg (N=977) once daily. The mean age of the

population was 56 years and 3% were older than 75 years of age. More than half (55%) of the population was male; 46% were White, 50% were Asian, and 3% were Black or African American. At baseline, 57% of the population had diabetes more than 5 years and had a mean hemoglobin A1c (HbA1c) of 8%. Established microvascular complications of diabetes at baseline included diabetic nephropathy (7%), retinopathy (8%), or neuropathy (16%). Baseline renal function was normal or mildly impaired in 91% of patients and moderately impaired in 9% of patients (mean eGFR 86.8 mL/min/1.73 m²). Table 1 shows common adverse reactions (excluding hypoglycemia) associated with the use of JARDIANCE. The adverse reactions were not present at baseline, occurred more commonly on JARDIANCE than on placebo and occurred in greater than or equal to 2% of patients treated with JARDIANCE 10 mg or JARDIANCE 25 mg.

Table 1: Adverse Reactions Reported in ≥2% of Patients Treated with JARDIANCE and Greater than Placebo in Pooled Placebo-Controlled Clinical Studies of JARDIANCE Monotherapy or Combination Therapy

| | Number (%) of Patients | | |
|--|------------------------|--------------------------|--------------------------|
| | Placebo N=995 | JARDIANCE 10 mg N=999 | JARDIANCE 25 mg N=977 |
| Urinary tract infection ^a | 7.6% | 9.3% | 7.6% |
| Female genital mycotic infections ^b | 1.5% | 5.4% | 6.4% |
| Upper respiratory tract infection | 3.8% | 3.1% | 4.0% |
| Increased urination ^c | 1.0% | 3.4% | 3.2% |
| Dyslipidemia | 3.4% | 3.9% | 2.9% |
| Arthralgia | 2.2% | 2.4% | 2.3% |
| Male genital mycotic infections ^d | 0.4% | 3.1% | 1.6% |
| Nausea | 1.4% | 2.3% | 1.1% |

^aPredefined adverse event grouping, including, but not limited to, urinary tract infection, asymptomatic bacteriuria, cystitis

^bFemale genital mycotic infections include the following adverse reactions: vulvovaginal mycotic infection, vaginal infection, vulvitis, vulvovaginal candidiasis, genital infection, genital candidiasis, genital infection fungal, genitourinary tract infection, vulvovaginitis, cervicitis, urogenital infection fungal, vaginitis bacterial. Percentages calculated with the number of female subjects in each group as denominator: placebo (N=481), JARDIANCE 10 mg (N=443), JARDIANCE 25 mg (N=420).

^cPredefined adverse event grouping, including, but not limited to, polyuria, pollakiuria, and nocturia

^dMale genital mycotic infections include the following adverse reactions: balanoposthitis, balanitis, genital infections fungal, genitourinary tract infection, balanitis candida, scrotal abscess, penile infection. Percentages calculated with the number of male subjects in each group as denominator: placebo (N=514), JARDIANCE 10 mg (N=556), JARDIANCE 25 mg (N=557).

Thirst (including polydipsia) was reported in 0%, 1.7%, and 1.5% for placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg, respectively. **Volume Depletion:** JARDIANCE causes an osmotic diuresis, which may lead to intravascular volume contraction and adverse reactions related to volume depletion. In the pool of five placebo-controlled clinical trials, adverse reactions related to volume depletion (e.g., blood pressure (ambulatory) decreased, blood pressure systolic decreased, dehydration, hypotension, hypovolemia, orthostatic hypotension, and syncope) were reported by 0.3%, 0.5%, and 0.3% of patients treated with placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg respectively. JARDIANCE may increase the risk of hypotension in patients at risk for volume contraction [see Warnings and Precautions and Use in Specific Populations]. **Increased Urination:** In the pool five placebo-controlled clinical trials, adverse reactions of increased urination (e.g., polyuria, pollakiuria, and nocturia) occurred more frequently on JARDIANCE than on placebo (see Table 1). Specifically, nocturia was reported by 0.4%, 0.3%, and 0.8% of patients treated with placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg, respectively. **Impairment in Renal Function:** Use of JARDIANCE was associated with increases in serum creatinine and decreases in eGFR (see Table 2). Patients with moderate renal impairment at baseline had larger mean changes. [see Warnings and Precautions and Use in Specific Populations].

Table 2: Changes from Baseline in Serum Creatinine and eGFR in the Pool of Four 24-week Placebo-Controlled Studies and Renal Impairment Study

| | | Pool of 24-Week Placebo-Controlled Studies | | |
|----------------|------------------------------------|--|-----------------|-----------------|
| | | Placebo | JARDIANCE 10 mg | JARDIANCE 25 mg |
| Baseline Mean | N | 825 | 830 | 822 |
| | Creatinine (mg/dL) | 0.84 | 0.85 | 0.85 |
| | eGFR (mL/min/1.73 m ²) | 87.3 | 87.1 | 87.8 |
| Week 12 Change | N | 771 | 797 | 783 |
| | Creatinine (mg/dL) | 0.00 | 0.02 | 0.01 |
| | eGFR (mL/min/1.73 m ²) | -0.3 | -1.3 | -1.4 |
| Week 24 Change | N | 708 | 769 | 754 |
| | Creatinine (mg/dL) | 0.00 | 0.01 | 0.01 |
| | eGFR (mL/min/1.73 m ²) | -0.3 | -0.6 | -1.4 |
| | | Moderate Renal Impairment ^a | | |
| | | Placebo | | JARDIANCE 25 mg |
| Baseline | N | 187 | – | 187 |
| | Creatinine (mg/dL) | 1.49 | – | 1.46 |
| | eGFR (mL/min/1.73 m ²) | 44.3 | – | 45.4 |

| Table 2 (Cont'd) | | Placebo | | JARDIANCE 25 mg |
|------------------|------------------------------------|---------|---|-----------------|
| Week 12 Change | N | 176 | – | 179 |
| | Creatinine (mg/dL) | 0.01 | – | 0.12 |
| | eGFR (mL/min/1.73 m ²) | 0.1 | – | -3.8 |
| Week 24 Change | N | 170 | – | 171 |
| | Creatinine (mg/dL) | 0.01 | – | 0.10 |
| | eGFR (mL/min/1.73 m ²) | 0.2 | – | -3.2 |
| Week 52 Change | N | 164 | – | 162 |
| | Creatinine (mg/dL) | 0.02 | – | 0.11 |
| | eGFR (mL/min/1.73 m ²) | -0.3 | – | -2.8 |

^aSubset of patients from renal impairment study with eGFR 30 to less than 60 mL/min/1.73 m²

Hypoglycemia: The incidence of hypoglycemia by study is shown in Table 3. The incidence of hypoglycemia increased when JARDIANCE was administered with insulin or sulfonylurea [see Warnings and Precautions].

Table 3: Incidence of Overall^a and Severe^b Hypoglycemic Events in Placebo-Controlled Clinical Studies

| Monotherapy (24 weeks) | Placebo (n=229) | JARDIANCE 10 mg (n=224) | JARDIANCE 25 mg (n=223) |
|--|-----------------------------|--|--|
| Overall (%) | 0.4% | 0.4% | 0.4% |
| Severe (%) | 0% | 0% | 0% |
| In Combination with Metformin (24 weeks) | Placebo + Metformin (n=206) | JARDIANCE 10 mg + Metformin (n=217) | JARDIANCE 25 mg + Metformin (n=214) |
| Overall (%) | 0.5% | 1.8% | 1.4% |
| Severe (%) | 0% | 0% | 0% |
| In Combination with Metformin + Sulfonylurea (24 weeks) | Placebo (n=225) | JARDIANCE 10 mg + Metformin + Sulfonylurea (n=224) | JARDIANCE 25 mg + Metformin + Sulfonylurea (n=217) |
| Overall (%) | 8.4% | 16.1% | 11.5% |
| Severe (%) | 0% | 0% | 0% |
| In Combination with Pioglitazone +/- Metformin (24 weeks) | Placebo (n=165) | JARDIANCE 10 mg + Pioglitazone +/- Metformin (n=165) | JARDIANCE 25 mg + Pioglitazone +/- Metformin (n=168) |
| Overall (%) | 1.8% | 1.2% | 2.4% |
| Severe (%) | 0% | 0% | 0% |
| In Combination with Basal Insulin (18 weeks ^c) | Placebo (n=170) | JARDIANCE 10 mg (n=169) | JARDIANCE 25 mg (n=155) |
| Overall (%) | 20.6% | 19.5% | 28.4% |
| Severe (%) | 0% | 0% | 1.3% |
| In Combination with MDI Insulin +/- Metformin (18 weeks ^c) | Placebo (n=188) | JARDIANCE 10 mg (n=186) | JARDIANCE 25 mg (n=189) |
| Overall (%) | 37.2% | 39.8% | 41.3% |
| Severe (%) | 0.5% | 0.5% | 0.5% |

^aOverall hypoglycemic events: plasma or capillary glucose of less than or equal to 70 mg/dL

^bSevere hypoglycemic events: requiring assistance regardless of blood glucose

^cInsulin dose could not be adjusted during the initial 18 week treatment period

Genital Mycotic Infections: In the pool five placebo-controlled clinical trials, the incidence of genital mycotic infections (e.g., vaginal mycotic infection, vaginal infection, genital infection fungal, vulvovaginal candidiasis, and vulvitis) was increased in patients treated with JARDIANCE compared to placebo, occurring in 0.9%, 4.1%, and 3.7% of patients randomized to placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg, respectively. Discontinuation from study due to genital infection occurred in 0% of placebo-treated patients and 0.2% of patients treated with either JARDIANCE 10 or 25 mg. Genital mycotic infections occurred more frequently in female than male patients (see Table 1). Phimosi occurred more frequently in male patients treated with JARDIANCE 10 mg (less than 0.1%) and JARDIANCE 25 mg (0.1%) than placebo (0%).

Urinary Tract Infections: In the pool five placebo-controlled clinical trials, the incidence of urinary tract infections (e.g., urinary tract infection, asymptomatic bacteriuria, and cystitis) was increased in patients treated with JARDIANCE compared to placebo (see Table 1). Patients with a history of chronic or recurrent urinary tract infections were more likely to experience a urinary tract infection. The rate of treatment discontinuation due to urinary tract infections was 0.1%, 0.2%, and 0.1% for placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg, respectively. Urinary tract infections occurred more frequently in female patients. The incidence of urinary tract infections in female patients randomized to placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg was 16.6%, 18.4%, and 17.0%, respectively. The incidence of urinary tract infections in male patients ran-

domized to placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg was 3.2%, 3.6%, and 4.1%, respectively [see Warnings and Precautions and Use in Specific Populations].

Laboratory Tests: Increase in Low-Density Lipoprotein Cholesterol (LDL-C): Dose-related increases in low-density lipoprotein cholesterol (LDL-C) were observed in patients treated with JARDIANCE. LDL-C increased by 2.3%, 4.6%, and 6.5% in patients treated with placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg, respectively [see Warnings and Precautions]. The range of mean baseline LDL-C levels was 90.3 to 90.6 mg/dL across treatment groups.

Increase in Hematocrit: In a pool of four placebo-controlled studies, median hematocrit decreased by 1.3% in placebo and increased by 2.8% in JARDIANCE 10 mg and 2.8% in JARDIANCE 25 mg treated patients. At the end of treatment, 0.6%, 2.7%, and 3.5% of patients with hematocrits initially within the reference range had values above the upper limit of the reference range with placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg, respectively.

Postmarketing Experience: Additional adverse reactions have been identified during postapproval use of JARDIANCE. Because these reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure: Ketoacidosis [see Warnings and Precautions]; Urosepsis and pyelonephritis [see Warnings and Precautions].

DRUG INTERACTIONS: Diuretics: Coadministration of empagliflozin with diuretics resulted in increased urine volume and frequency of voids, which might enhance the potential for volume depletion [see Warnings and Precautions].

Insulin or Insulin Secretagogues: Coadministration of empagliflozin with insulin or insulin secretagogues increases the risk for hypoglycemia [see Warnings and Precautions].

Positive Urine Glucose Test: Monitoring glycemic control with urine glucose tests is not recommended in patients taking SGLT2 inhibitors as SGLT2 inhibitors increase urinary glucose excretion and will lead to positive urine glucose tests. Use alternative methods to monitor glycemic control.

Interference with 1,5-anhydroglucitol (1,5-AG) Assay: Monitoring glycemic control with 1,5-AG assay is not recommended as measurements of 1,5-AG are unreliable in assessing glycemic control in patients taking SGLT2 inhibitors. Use alternative methods to monitor glycemic control.

USE IN SPECIFIC POPULATIONS: Pregnancy: Pregnancy Category C: There are no adequate and well-controlled studies of JARDIANCE in pregnant women. JARDIANCE should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Based on results from animal studies, empagliflozin may affect renal development and maturation. In studies conducted in rats, empagliflozin crosses the placenta and reaches fetal tissues. During pregnancy, consider appropriate alternative therapies, especially during the second and third trimesters.

Nursing Mothers: It is not known if JARDIANCE is excreted in human milk. Empagliflozin is secreted in the milk of lactating rats reaching levels up to 5 times higher than that in maternal plasma. Since human kidney maturation occurs *in utero* and during the first 2 years of life when lactational exposure may occur, there may be risk to the developing human kidney. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from JARDIANCE, a decision should be made whether to discontinue nursing or to discontinue JARDIANCE, taking into account the importance of the drug to the mother.

Pediatric Use: The safety and effectiveness of JARDIANCE in pediatric patients under 18 years of age have not been established.

Geriatric Use: No JARDIANCE dosage change is recommended based on age. A total of 2721 (32%) patients treated with empagliflozin were 65 years of age and older, and 491 (6%) were 75 years of age and older. JARDIANCE is expected to have diminished efficacy in elderly patients with renal impairment [see Use in Specific Populations]. The risk of volume depletion-related adverse reactions increased in patients who were 75 years of age and older to 2.1%, 2.3%, and 4.4% for placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg. The risk of urinary tract infections increased in patients who were 75 years of age and older to 10.5%, 15.7%, and 15.1% in patients randomized to placebo, JARDIANCE 10 mg, and JARDIANCE 25 mg, respectively [see Warnings and Precautions and Adverse Reactions].

Renal Impairment: The efficacy and safety of JARDIANCE were evaluated in a study of patients with mild and moderate renal impairment. In this study, 195 patients exposed to JARDIANCE had an eGFR between 60 and 90 mL/min/1.73 m², 91 patients exposed to JARDIANCE had an eGFR between 45 and 60 mL/min/1.73 m² and 97 patients exposed to JARDIANCE had an eGFR between 30 and 45 mL/min/1.73 m². The glucose lowering benefit of JARDIANCE 25 mg decreased in patients with worsening renal function. The risks of renal impairment [see Warnings and Precautions], volume depletion adverse reactions and urinary tract infection-related adverse reactions increased with worsening renal function. The efficacy and safety of JARDIANCE have not been established in patients with severe renal impairment, with ESRD, or receiving dialysis. JARDIANCE is not expected to be effective in these patient populations [see Contraindications and Warnings and Precautions].

Hepatic Impairment: JARDIANCE may be used in patients with hepatic impairment.

OVERDOSAGE: In the event of an overdose with JARDIANCE, contact the Poison Control Center. Employ the usual supportive measures (e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive treatment) as dictated by the patient's clinical status. Removal of empagliflozin by hemodialysis has not been studied.

Additional information can be found at www.hcp.jardiance.com

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A Medicare Appeal for CGM Coverage: *One Patient's Never-Ending Story*

DAN PATRICK

ABOUT THE AUTHOR



DAN PATRICK

Mr Patrick has lived with type 1 diabetes for 50 years.

Although most commercial insurers now cover continuous glucose monitoring (CGM) devices, payment for this technology is routinely denied for an important and growing group with diabetes: Medicare beneficiaries.^{1,2} This occurs despite the May 2015 statement from leading professional societies of endocrinologists that such denials are “imprudent” for patients on intensive insulin regimens with a history of hypoglycemic events or frequent hospitalization.³ While appealing for CGM coverage is not easy, some persons with type 1 diabetes (T1D) do try. Evidence-Based Diabetes Management asked Dan Patrick, an Ohio Medicare beneficiary, who this spring, became a 50-year Joslin Medalist,⁴ to share his story.

CMS has taken a profound, deeply troubling, and dangerous, clinically unsupported therapeutic direction³ through a local policy which effectively blocks the reimbursement for a CGM under a Medicare rule. Through an arduous appeal process, I managed to win coverage for my CGM. Here is my story.

This spring, I reached the 50-year mark of living with T1D. For most of that time, I lived without CGM, but that changed more than 3 years ago. In 1999, our family adopted a puppy named Maggie, and for 10 years, she served as my sleeping service dog. Maggie would lick my face to wake me in advance of a dangerous hypoglycemic event, and the necessary corrections were made. In the fall of 2009, Maggie was diagnosed with T1D, which is relatively common in female dogs as they age.⁵ For the next 3.5 years, I became her caregiver and never really slept to be prepared for hypo events. After Maggie passed, it was time for a different CGM model. Starting in January 2013, I began using a CGM system. I had not yet turned 65 when I started using CGM, so it was covered by commercial insurance.

In 2014, when I reached 48 years as a patient with T1D, I had become unable to discern the onset of hypoglycemic events and was diagnosed with a condition called hypoglycemia unawareness.⁶ That same year, I turned 65 on May 4, 2014, and became eligible for Medicare effective May 1, 2014. At the time of my appeal, CMS’ policy for CGM coverage was spelled out in the Local Coverage Article: Glucose Monitors—Policy Article—January 2014 (A47238). (This article has since been removed from the CMS website, but a copy is available as an electronic appendix.⁷) In 2014, and in compliance with Medicare rules, I enrolled. There are clearly defined parameters for enrollment, with financial penalties the patient for noncompliance.⁸

My Medicare enrollment was also required by my personal healthcare coverage, which changed from a private non-Medicare plan to a Medicare Advantage PPO plan (MAP). At this point, all medical information had to be refiled, even though I was still with the same insurance company and had the same identification number. At first it seemed that I would receive CGM under Medicare without any problems: this particular insurance company went so far as to suggest choices of medical pharmacies to supply the 3 required CGM components, and I chose an in-network pharmacy to reduce costs. A box of 4 CGM sensors arrived every 28 days, starting in May 2014.

The bottom fell out, in August 2014, with the reorder of a CGM transmitter. The reason given when Medicare refused to pay was that the transmitter was not covered under my MAP insurance plan, in compliance with Medicare rule (A47238).⁷ It’s worth noting that I had no trouble receiving approval from the same insurer for use of a CGM in December 2012, when I began using it in January 2013. The approval process, under my private non-Medicare plan, had only involved processing by my endocrinologist. The necessary CGM components were

all covered outside Medicare. What changed, before and after enrolling in Medicare, that a lifesaving medical piece of equipment was not necessary to manage my T1D condition? The answer was, and still is, nothing.

I have been an active viewer of discussions and information regarding various denials by Medicare via the Diabetes Online Community (DOC). Denials for Medicare CGM reimbursement are increasing, creating serious negative impacts on families of persons with T1D. These continued actions have prompted introduction of federal legislation to overrule prior individual CGM Medicare denials.^{1,2} Members of the DOC have come together, and a Diabetes Patient Advocacy Coalition (DPAC) has been initiated, making it easy to keep policy makers’ attention on people with diabetes.⁹ While federal legislation was introduced to overrule prior CGM Medicare denials in 2013, there was no action in the 113th Congress (2013-2014).¹⁰ The 114th Congress (2015-2016) reintroduced the legislation; the current bills are S.804 in the Senate and H.R. 1427 in the House, with 273 co-sponsors. No action had been taken at press time.¹¹

Given the lack of Congressional action, this became a personal fight for my life. In 2014, after living with T1D for 48 years, I realized that it would be imperative to prepare objective documentation to support an appeal to CMS. At the start of my appeal, there was no real guidance on how to proceed for approval of a CGM.

Denial of coverage for the transmitter came in a letter, which arrived in October 2014 and clearly referenced the specific Local Policy (A47238). It is interesting that the MAP made no reference to any communications with my endocrinologist and considered my initial appeal to be from the patient only. How is it that the endocrinologist was removed from the discussion regarding my life with T1D? The blatant disregard of my medical condition, without consulting the specialist who handles my care, made no sense. I decided to assemble the documentation for review and consult with my endocrinologist for this appeal. This action continued through the first level of appeal with the MAP, and the second level would be with the independent reviewer of Medicare claims, Maximus Federal Services.

Maximus’ mission is very specific: they are appeals experts. Medicare retains Maximus to review files and decide on the accuracy of a Medicare Advantage health plan’s decision—Maximus works for Medicare, not the plan.¹² What was frustrating at this stage was that Maximus’ charge was not to look at the facts—which is what my physician and I assembled—but to look at the narrow question of what constituted Medicare policy, and whether the health plan had applied it.

To me, and to all persons with T1D, facts matter. My professional and personal life has a clear focus on measured data, to document my progress in striving to obtain a goal at hand. How can I clearly and conclusively document how CGM achieve a personal outcome of near normal glucose levels with minimized hypoglycemic events? The challenge for all T1Ds is to reduce hypoglycemic events, especially at night. Needless to say, Maximus ruled against allowing coverage, and the next step—Level 3—would be before an administrative law judge.

Interestingly, to address the fears of parents of children with diabetes, a new tool has been introduced by Dexcom: Dexcom G5, which has been approved by the FDA for children as young as age 2.¹³ Thus, young children have an approved tool to manage their diabetes, but those over age 65 are denied Medicare coverage for CGMs. How absurd. My CGM had already proved to be an assistance in dealing with nighttime hypoglycemic events. The need for evidence to overturn a policy requires a

“What changed, before and after enrolling in Medicare, that a lifesaving medical piece of equipment was not necessary to manage my T1D condition?”

—DAN PATRICK

The challenge for all T1Ds is to reduce hypoglycemic events, especially at night.

review of the policy to present cogent points against it.

I obtained a printout of Local Policy (A47238). The article reads:

Local Coverage Article: Glucose Monitors – Policy Article – January 2014 (A47238). Under the section, Non-Medical Necessary Coverage and Payment Rules, the following line has been added:

Continuous glucose monitors (A9276-A9278) are considered precautionary and therefore non-covered under the DME benefit.⁷

A9276-A9278 are the billing codes for sensors, the transmitter, and the receiver. DME stands for Durable Medical Equipment. The Local Coverage Article applies to 7 states: Illinois, Indiana, Kentucky, Michigan, Minnesota, Ohio, and Wisconsin.

The actions taken by MAP raise serious questions regarding the use of age and geographical factors. The most thought-provoking and compelling question becomes: on what basis is the Local Coverage Article an absolute, offering no ability for a successful appeal for this lifesaving monitoring system? Failed appeals, thus far, outnumber permanent successes.

It is important in an appeal process to clearly define the terms. Medicare did not define or describe CGMs. My choice for a CGM was a Dexcom product. The Dexcom G4 Platinum Continuous Glucose Monitoring System was approved by FDA's Medical Devices section on October 5, 2012. The FDA wrote the following under: What will it (Dexcom G4 Platinum) accomplish:¹⁴

“People with diabetes can use the tracking and trending glucose information to help understand patterns in their glucose levels, and be alerted when glucose values are approaching potentially dangerous high (hyperglycemic) and/or dangerous low (hypoglycemic) levels. When used along with a blood glucose meter to obtain a more accurate reading of actual blood glucose levels, the Dexcom G4 PLATINUM can also help people with diabetes make long-term adjustments to their treatment plan to keep blood glucose levels in a safe range.”

What would the receiver screen of a CGM look like for a nondiabetic? A contributor to the leading diabetes blog DiabetesMine.com provided a humorous look at what persons without this disease take for granted (FIGURE 1).

For those of us with T1D, a CGM presents a real time view of trending interstitial glucose. As part of my filing with the Medicare Administrative Law Judge, I included a link to the video “What is Continuous Glucose Monitoring?”¹⁵

The most troubling word in this short Local Article is “precautionary,” which is the basis for Medicare denying CGM coverage as a DME. This is a statutory term, and CMS bases its interpretation on FDA labeling that calls for a self-monitoring blood glucose test with CGM before an insulin dose. But this narrow reading flies in face of evidence and expert opinion. While the term “precautionary” draws a blank via an internet search under medical definitions, it takes on a totally different meaning with requirements when defined as a precautionary principle. This is a precautionary approach, and the objective is to set policy that is not harmful; the burden of proof rests with Medicare.

Can Medicare supply sound evidence with clinical consensus that removing reimbursement coverage for T1D using CGM will not cause any harm to the individual, their family, the community, and the public? CMS cannot. The website Children With Diabetes, offers an excellent product discussion on CGMs that includes a list of more than 40 links that offer support for the importance of CGM, including clinical studies.¹⁶

The journal *Endocrine Practice* reported a study, in December 2014, which found that patients older than 65 years achieve a significant and durable improvement in glycemic control when using CGM, comparable with younger patients. In fact, the reduction in severe hypoglycemia may be of particular benefit to older patients.¹⁷

FIGURE 1. CGM for Someone Without Diabetes



And in May 2015, after a review of the evidence, the American Association of Clinical Endocrinologists and the American College of Endocrinology issued a joint statement calling it “imprudent” for payers to deny coverage for high-risk patients with intense insulin regimens, a history of hypoglycemia or hospitalizations, or other risk factors.³

The Local Policy declared that a CGM is a non-durable equipment (DME). However, the definition for DME has been, and is defined by Social Security, as “equipment which can withstand repeated use” and is used primarily for a medical purpose.¹⁸ How does one reconcile the Social Security rule with this attempt by CMS to totally change the definition of DME? What other historical facts are available that could assist in my appeal?

The Diabetes Control and Complications Trial (DCCT) is the seminal clinical trial that began in 1983. This study settled the question that keeping glucose levels as close to normal as possible with intensive insulin therapy, with glycated hemoglobin (A1C) equal to or less than 7%, would stave off complications when compared with conventional insulin therapy that maintains A1C at or greater than 9%. However, the DCCT found a 2- to 3-fold increase in hypoglycemic events for individuals utilizing an intensive insulin therapy due to a lack of tools.¹⁹

Edward Damiano, PhD, professor of biomedical engineering at Boston University, has a succinct discussion on the challenges to manage T1D with insulin in the first-half of a YouTube presentation.²⁰ Insulin is a miraculous substance; while it regulates glucose levels in the blood, it also has a high toxicity index and a narrow therapeutic range. A slight overdose of insulin can prove lethal. For a person with T1D, the greatest fear is having severe hypos at night—this keeps us awake at night. Insulin allows those diagnosed with T1D the ability to survive, but we suffer long-term complications, armed with the knowledge gained in the DCCT study.²¹

Since CGMs did not exist during the DCCT study, the case can be made that a CGM is a new technical tool for T1Ds to manage our condition. My personal opinion is that I have been successful in decreasing severe hypoglycemia during the night, which is the deadliest period of the day for a T1D. The fear of severe hypoglycemia is documented in the multiple surveys by Children with Diabetes.²² A CGM brings a visual representation of glucose trending levels.

One particular finding of the DCCT was that it took up to 3 years to substantiate the success of intensive insulin therapy. Using Dexcom Studio software, I pulled data from my first months of using a Dexcom G4 Platinum CGM, in January 2013. Next, I assembled data from the same period 2 years later, in January 2015, making a comparison guided by the standard set in the DCCT study.

FIGURE 2. A Summary Report from Daily Trends Graphs via Studio Member Utilized a Dexcom G4 Platinum for the Period Friday, January 25, 2013, to Wednesday, April 24, 2013.

| GLUCOSE TARGET | | TIME RANGE | | PERCENTAGE |
|---|---|---|---|--------------------------------------|
| RANGE IN MG/DL | TOTALS 12:00 AM THRU 11:59 AM IN MG/DL | TOTALS 12:00 PM THRU 11:59 PM IN MG/DL | GRAND TOTAL (ALL READINGS) IN MG/DL | PERCENT COMPARED TO ALL LEVELS |
| Total All Levels | 21785 | 21785 | 43570 | 100.000% |
| Hyper > 240 | 1225 | 1225 | 2450 | 5.623% |
| High 131-240 | 11399 | 11399 | 22798 | 52.325% |
| Normal 80-130 | 7466 | 7466 | 14932 | 34.271% |
| Low 55 - 70 | 1487 | 1487 | 2974 | 6.826% |
| Hypoglycemia <55 | 208 | 208 | 416 | 0.955% |
| Non-normal <55 & 55-79 131-240 & >240 | 14319 | 14319 | 28638 | 65.729% |

The above data can be found in the Daily Trends (1/25/2013 to 4/24/2013) on page 2/2 for each graphic report for DMP. DMP indicates Daily Medical Plan. Designer, Dan Patrick.

FIGURE 3. A Summary Report from Daily Trends Graphs via Studio Member Utilized a Dexcom G4 Platinum for the Period Sunday, January 11, 2015 to Friday, April 10, 2015

| GLUCOSE TARGET | | TIME RANGE | | PERCENTAGE |
|---|---|---|---|--------------------------------------|
| RANGE IN MG/DL | TOTALS 12:00 AM THRU 11:59 AM IN MG/DL | TOTALS 12:00 PM THRU 11:59 PM IN MG/DL | GRAND TOTAL (ALL READINGS) IN MG/DL | PERCENT COMPARED TO ALL LEVELS |
| Total All Levels | 24936 | 24936 | 49872 | 100.000% |
| Hyper > 240 | 838 | 838 | 1676 | 3.361% |
| High 131-240 | 10875 | 10875 | 21750 | 43.612% |
| Normal 80-130 | 10342 | 10342 | 20684 | 41.474% |
| Low 55 - 70 | 2676 | 2676 | 5352 | 10.731% |
| Hypoglycemia <55 | 205 | 205 | 410 | 0.822% |
| Non-normal <55 and 55-79 131-240 and >240 | 14594 | 14594 | 29188 | 58.526% |

The above data can be found in the Daily Trends (1/11/2015 to 4/10/2015) on page 2/2 for each graphic report for DMP. DMP indicates Daily Medical Plan. Designer, Dan Patrick.

The 4 figures (FIGURES 2-5) below present compelling data to support my appeal for approval for CGM coverage by Medicare.

FIGURE 2 shows data from the first months of my use of a Dexcom G4 Platinum CGM. The time frame is for a 90-day period. The patient was only able to obtain a normal glycemic level for 34.2% of the given time period. Non-normal glycemic time was 65.7%.

FIGURE 3 covers a 90-day period 24 months later, beginning in January 2015. I obtained a normal glycemic level for 41.5% of the time period. Non-normal glycemic time was 58.5%. During the time frame presented in **FIGURE 3**, my A1C was 7.0%. It is interesting to note that a grade of 41.5% is not a passing grade and does not indicate exemplary success in the given outcome.

FIGURE 4 displays an average time in minutes at various glucose levels for a 24-hour day. A given 24-hour day has 1440 minutes. A Dexcom G4 CGM can record a total of 288 reading every 5 minutes in a 24-hour day. The denial of the usage of a CGM would mean total reliance upon blood glucose meter

readings of 10 per day. The increase in measured data points by a CGM facilitates a greater ability to initiate micro adjustments to avoid either hyper- or hypoglycemic events.

FIGURE 5 compares the Dexcom glucose readings for 90-day periods at the start of 2013 and 2015. The most telling point is the fact that I obtained a reduction in the percentage of time in hypoglycemic events. The denial of coverage for a CGM by Medicare could lead to a 2- to 3-fold increase in hypoglycemic events as documented in the DCCT, without the use of a CGM.

As my case progressed, another working its way through the system had a direct impact on mine. On May 26, 2015, the United States District Court, Eastern District, Wisconsin, in the case *Whitcomb v. Burwell*, Case No. 13-cv-990, ruled in favor of Jill A. Whitcomb to have coverage for a CGM. Her appeal began in 2012. She was represented by Debra Parrish and Robert Theine. Even though UnitedHealth continued to fight the ruling and deny Whitcomb payment, her successful resolution at the 5th appeal level was responsible for favorable rulings in many other cases—including my appeal, which ended with a successful resolution at the Medicare Administrative Law Judge, Level 3 appeal.^{23,24}

On July 29, 2015, a Medicare Administrative Law Judge (ALJ) ruled that my CGM is medically reasonable and necessary as part of my diabetic care. Contained within the ruling was precedential information, listed below, which were cornerstone determinations to my successful appeal at Level 3. The ALJ made the ruling retroactive to July 2014.

What is the outlook for Medicare coverage in the wake of the Whitcomb case, and mine? Unfortunately, it's not good. According to Mike Hoskins, a journalist with T1D who writes for *DiabetesMine*, the outlook for coverage is getting worse, not better.²⁵ Hoskins has encouraged the DOC to be vocal about the situation with Medicare.

Here are 3 key points I have learned about Medicare and CGM coverage since my appeal:

1. The Local Article should not have been used as a reason to deny coverage for CGM. This was a key finding of *Whitcomb*.²⁴
2. CMS, and lawmakers, must start to take into account the cost of hypoglycemic events among those with T1D in making coverage decisions. A groundbreaking study in *The American Journal of Managed Care*, found that following an hypoglycemic event the average cost of an inpatient admission was \$17,564, the average cost of an emergency department visit was \$1387, and the average cost of an outpatient visit was \$394.²⁶ Now that measurement of hospital readmission is a cornerstone of value-based reimbursement, Medicare payment for CGM seems, not only clinically necessary, but also imperative.
3. Finally, HHS Secretary, Sylvia Mathews Burwell, did not file an appeal within the statutory deadline with the US District Court in *Whitcomb*. According to information from her caregiver, Dan Kraft, the federal court's ruling recognizes that government's refusal to cover a CGM for the management of Whitcomb's diabetes was not supported in law or fact. Simply put, the local article is not singular reason for denial for CGM coverage by the MAP and Medicare. The doctor-patient relationship was brought back into the equation.

The T1D community owes a debt of gratitude to Jill Whitcomb, her caregiver, Kraft, and her legal team. She traversed a complete 5-step Medicare appeal and won. The length of time for her appeal is obscene, and such delays in the process need to be examined and changed as quickly as possible. On the question of payment, Medicare is a secondary payer. This Local Policy can be viewed as an attempt to prevent appeals, and it complicates the process by not reim-

FIGURE 4. Time in Minutes at Various Glucose Levels, for an Average 24-hour Day (1440 minutes), for the Period 1-11-15 to 4-10-15

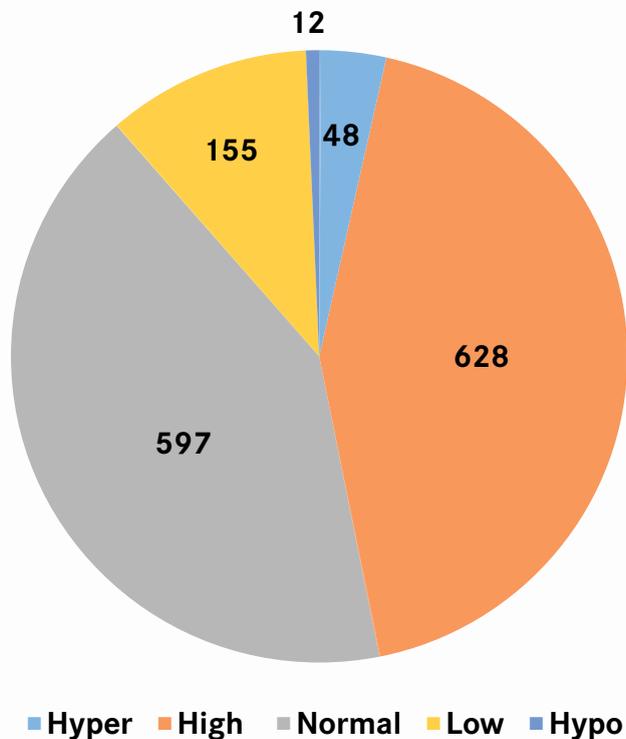
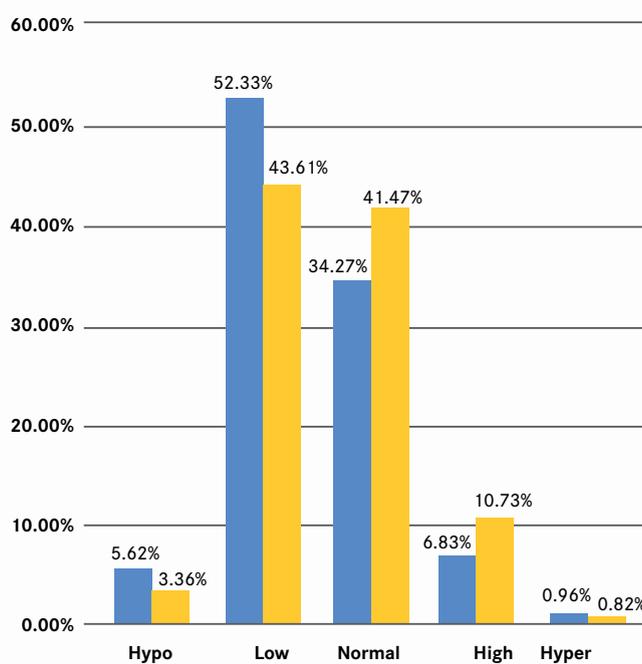


FIGURE 5. Dexcom Glucose Readings, 90-day Periods 2013 versus 2015 for DMP



bursing the MAP for the coverage of a CGM for any T1Ds. If the MAP knows it will not be paid, it will not want to cover an individual's claim for CGM coverage. However, there is a serious challenge which plagues T1Ds. We need help to overcome the long-term complications, which is a plague to our morbidity and dramatically shortens our lifespans. Medicare's attempt to reduce short-term costs will further exasperate the issue. The real cost factors with diabetes are the necessary services and taking care of complications resulting from a lack of knowledge or tools. A CGM is another step in responding to the challenges for a T1D to manage our condition and live a healthier complete life with near-normal glucose levels, and striving to minimize hypoglycemic events and no severe hypoglycemia.

Was my appeal the end of the story? Sadly, no. In March of 2016, I received a notice that once again, the MAP is denying payment for a replacement transmitter. I've sent a letter asking how this can happen when I have a ruling from Medicare Administrative Law Judge: my story highlights the need for Congress to act—and act now—to compel CMS to give T1D persons in Medicare access to CGM technology that makes sense clinically and is cost-effective. Our lives depend on it. **EBDM**

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The T1D community owes a debt of gratitude to Jill Whitcomb, her caregiver, Dan Kraft, and her legal team.

Widespread Adoption of Evidence-Based Practices Is Essential for a Growing Medicare Population

BERNADETTE MELNYK, PHD, RN, CPNP/PMHNP, FNAP, FAAN

ABOUT THE AUTHOR



BERNADETTE MELNYK, PHD, RN, CPNP/PMHNP, FNAP, FAAN

Dr Melnyk is associate vice president for Health Promotion, chief wellness officer, and professor and dean of the College of Nursing at The Ohio State University. She also is a professor of pediatrics and psychiatry at the university's College of Medicine.

“For older Americans, the difference in traditional ‘we’ve always done it that way’ practice versus evidence-based practice is magnified.”

—BERNADETTE MELNYK, PHD, RN, CPNP/PMHNP, FNAP, FAAN

Studies show that baccalaureate-prepared nurses are more likely to espouse evidence-based practices and achieve better outcomes.

When providers move from employing traditional practices to new methods that are steeped in evidence, this benefits patient health. The result is higher-quality, more affordable care, often stemming from lower rates of hospital infections, readmissions, and, in general, improved outcomes. This is probably a song that most healthcare leaders have heard before.

It’s a tune that bears repeating, though, until evidence-based practices are being performed in all healthcare settings in America. Quite certainly, to raise our nation’s standard of care, particularly as the older segment of our population increases in size, providers need to embrace methods that combine scientific research, clinician expertise, and patient preferences, which directly improve quality and safety measures.

While addressing these basic tenets of evidence-based practice is said to be a high priority area for hospital leadership, our recent study in *Worldviews on Evidence-Based Nursing*¹ shows that adoption of evidence-based practices is alarmingly low. This fact jeopardizes both the Institute of Medicine’s goal to have all healthcare decisions based in evidence by 2020,² as well as the health of all Americans, particularly the over-65 demographic that accounts for approximately 35% of hospitalizations. Because Medicare, which generally covers adults 65 years or older and the disabled, is the primary payer for 40% of total hospital stays, change here would not only benefit this population, but would have ripple effects across healthcare.³

For many older Americans, the difference in traditional “we’ve always done it that way” practice versus evidence-based practice is magnified. Studies show that older patients are at greater risk for functional decline⁴ and are more susceptible to experiencing falls and delirium, and developing infections, pressure ulcers, and adverse drug reactions during hospitalization.⁵ Knowing these facts, and the fact that the care of adults 80 years and older is the largest expense for Medicare,⁶ it’s imperative that payers like Medicare incentivize evidence-based practices in hospitals and primary care settings for all providers, including physicians, physician assistants, nurse practitioners, and others, rather than continuing with age-old, traditional methods.

Imagine the following:

- What if the standards of care outlined by the American Diabetes Association, which include evidence-based practices for treating and diagnosing diabetes, were being adhered to in healthcare settings? These practices include, among others, regular foot, eye, and dental examinations and annual screening for microalbuminuria.⁷
- What if catheters were removed based on nurse-driven protocol, which is proven to be more efficient and leads to fewer infections than physician orders?⁸
- What if we ensure that intravenous catheters are not being replaced more frequently than every 72 to 86 hours? It is often an unpleasant experience for patients and is deemed unnecessary if the catheter is deemed functional and there is no inflammation present.⁹
- What if stable patients were encouraged to sleep, rather than woken up every 4 hours to have vital signs checked, impeding critical recovery time¹⁰
- What if, to prevent pressure ulcers, we were turning pa-

tients every 2 hours, as studies indicate is best practice¹¹

- What if depression screening was routinely conducted in primary care settings and cognitive-behavior therapy was provided first, instead of antidepressants, to older adults with mild to moderate depression as indicated by best practice guidelines?¹² We would detect depression earlier and probably see fewer recurring episodes of depression as well as improvements in chronic conditions.
- Why isn’t delirium screening on patients in the intensive care unit (ICU) the norm? Approximately 80% of patients in the ICU are affected by delirium. Not performing the screening costs between \$4 billion and \$16 billion annually.¹³

These and many other examples of evidence-based practices will help shape a more sustainable and functional course for Medicare and provide better care for patients.

WHAT ARE THE BARRIERS TO IMPLEMENTING EVIDENCE-BASED PRACTICE?

Recent studies have shown that the adoption of evidence-based practices in hospitals and healthcare settings is lacking, even though leaders and executives believe in it. According to the *Worldviews* survey data of 276 chief nurse executives, more than 50% of the respondents said that evidence-based practices are utilized in their setting either “somewhat” or “not at all.”¹⁴ In addition, even more respondents reported that money wasn’t being allocated for resources to support the growth of an evidence-based practice culture in their healthcare environments, despite the fact that many hospitals are currently falling short of performance benchmarks for National Database of Nursing Quality Indicators measures.¹

Lastly, the study illuminated a striking disconnect among nurse executives, most of whom say quality and safety are their top priorities, despite the fact that they may not be using evidence-based practices.¹ In healthcare settings that may see a surge in the numbers of older adults, coupled with rising healthcare costs,¹⁴ barriers to implementing evidence-based practices must be addressed.

A good place to start is by improving the level of education of nurses and investing funds in continuing education programs and evidence-based practice mentors to equip them with the skills needed to consistently deliver evidence-based care. Studies show that baccalaureate-prepared nurses are more likely to espouse evidence-based practices and achieve better outcomes.¹⁵ Relatedly, hospitals with magnet recognition report better quality and workplace environments than nonmagnet hospitals.¹⁶ In order for healthcare systems to deliver the highest quality of care, they must devote a portion of their budgets to developing and sustaining a culture and environment that supports the delivery of evidence-based care by all nurses and other health professionals.

WHY SHOULD MEDICARE CARE ABOUT EVIDENCE-BASED PRACTICE?

A recent study by the Kaiser Family Foundation, citing US Census data, projects that the United States population over the age of 65 will nearly double between 2010 and 2050,⁶ and enrollment in Medicare will increase. The implications will be higher spending and a heftier burden on healthcare personnel and resources. According to National Health Expenditure pro-

jections by CMS, increased enrollment from the baby boomer generation, increased utilization of care, and an improved economy will drive up payment rates, factoring into a yearly spending growth of 7.3%.¹⁴

The US Department of Health and Human Services, in partnership with the private sector, is looking to transition from volume-based, fee-for-service (FFS) payment models to models that are population-based and reward value. The following chart breaks down payment models across 4 different categories, with the goal of having 90% of Medicare FFS payments transition to value-based purchasing models (categories 2 through 4) by 2018 (see **TABLE**).¹⁷

According to CMS, the transition to value-based payment models will be accelerated if we “collaborate to generate evidence, share approaches, and remove barriers.” By making evidence-based practice a priority within their organizations and institutions, hospital executives can help expedite the shift from category 1 to category 4. In addition, it’s important that patients are empowered to ask the right questions about their care and demand that they are treated according to the soundest knowledge available.

Last year, Medicare reached the 50-year mark, and for it to remain viable for future generations, payment models need to be remedied and providers must evolve to create an environment that offers best practices for patients. To that end, it’s time all providers and patients add their voices to the evidence-based practice chorus. **EBDM**

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T A B L E. Models for Moving from Fee-for-Service to Value-Based Purchasing

| CATEGORY 1 | CATEGORY 2 | CATEGORY 3 | CATEGORY 4 |
|---|--|---|--|
| Fee-for-service with no link of payment to quality | Fee-for-service with a link of payment to quality | Alternative payment models built on fee-for-service architecture | Population-based payment |
| Payments are based on volume of services and not linked to quality. | At least a portion of payments may vary based on the quality of efficiency or healthcare delivery. | Some payment is linked to effective management of a population or an episode of care. Payments are still triggered by delivery of services. | Payment is not directly triggered by service delivery so volume is not linked to payment. Clinicians and organizations are paid and responsible for the care of a beneficiary for a long period. |

Source: CMS fact sheet. CMS website. <https://www.cms.gov/Newsroom/MediaReleaseDatabase/Fact-sheets/2015-Fact-sheets-items/2015-01-26-3.html>. Published January 26, 2015. Accessed April 19, 2016.

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The transition to value-based payment models would be accelerated if we collaborate to generate evidence, share approaches, and remove barriers.

Research Emerging That Links Insulin Resistance to Cognitive Decline

Earliest Studies Involving Diabetes Therapy for Alzheimer's Are Recruiting Patients

ANDREW SMITH

ABOUT THE EXPERT



**GEERT JAN BIESSELS,
MD, PHD**

Dr Biessels is professor of Neurology, Rudolph Magnus Institute.

“It is possible to look at the autopsy studies and conclude that a lot of diabetics with vascular dementia are being diagnosed with Alzheimer's.”

—GEERT JAN BIESSELS, MD, PHD
RUDOLPH MAGNUS INSTITUTE

Retrospective analyses^{1,2} of patient records have long tended to find an increased risk of incidence of Alzheimer's disease among patients with type 2 diabetes (T2D). In more recent years, as rates of T2D have soared, rates of Alzheimer's disease—although far lower, overall—have risen at a similar rate, and a number of studies^{3,4} have found evidence that suggests Alzheimer's disease can be slowed or even reversed by increasing either the amount of insulin in the brain or the brain's ability to respond to existing insulin.

This evidence has convinced many that diabetes can trigger Alzheimer's disease in many patients who would otherwise have escaped it, or that Alzheimer's disease is essentially a type of diabetes that affects the brain, sometimes in conjunction with T2D, sometimes on its own. Other observers believe the evidence linking diabetes and Alzheimer's disease, to date, is interesting, but inconclusive—particularly when one considers study results that find no connection between the 2 conditions.

The symptoms of Alzheimer's disease can be nearly identical to the symptoms of vascular dementia, a form of cognitive decline, that certainly can result directly from T2D's effects on the circulatory system or indirectly from T2D-related strokes.⁵ Indeed, the only sure way to diagnose Alzheimer's disease is via autopsy, and studies that have looked for T2D after confirming Alzheimer's disease via autopsy, have not found it nearly as frequently as population-based studies would predict.^{6,7} According to Geert Jan Biessels, MD, PhD, a professor of Neurology at the Rudolph Magnus Institute, who spoke with *Evidence-Based Diabetes Management (EBDM)*, studies, that have used positron emission tomography (PET) scans to compare amyloid protein levels in patients with and without T2D, have not found diabetic patients to have the sort of protein buildup that would indicate elevated risk of Alzheimer's disease.⁸

Many investigators are working to solve the apparent contradictions by focusing their research on the pathways that could connect the 2 diseases, and on the effort to see whether any existing treatment for T2D can also treat Alzheimer's disease.⁹ There is hope, looking forward, that such treatments could be a breakthrough in Alzheimer's care.

That said, researchers have been investigating possible links between T2D and Alzheimer's disease for many years. A review, published by *Diabetes Care* nearly 2 decades ago,¹⁰ gathered evidence from 19 controlled studies on patients with T2D, and noted that 13 of those studies reported that diabetics performed worse than controls on at least 1 aspect of cognitive function. All the remaining studies, the review authors noted, lacked the statistical power to find a relatively strong gap in cognitive abilities.

That review did not find enough evidence to distinguish among vascular dementia, Alzheimer's disease, or other types of cognitive impairment, but another review,¹¹ published, just 2 years later by *Diabetic Medicine*, went further. “There is also evidence for an elevated risk of both vascular dementia and Alzheimer's disease in Type 2 DM albeit with strong interaction of other factors such as hypertension, dyslipidemia and apolipoprotein E phenotype,” the authors wrote. “Both vascular and nonvascular factors are likely to play a role in dementia in diabetes.”

Such conclusions soon led other researchers to look at

health record databases in search of further evidence, and their findings varied significantly. *International Psychogeriatrics*, for example, published a 2002 analysis¹² of records from 702 people aged 80 years or more. Among the 187 patients to receive a dementia diagnosis at some point during the study period, 31 began the study with T2D. After adjusting for age, gender, education, smoking habits, and circulatory diseases, the investigators calculated that diabetics were more than twice as likely as other people to develop vascular dementia, but no more likely than others to develop Alzheimer's disease. On the other hand, a 2004 study that appeared in *Archives of Neurology*¹³, followed 824 Catholic nuns, priests, and monks who received thorough clinical evaluations each year, and found that preexisting T2D did predict elevated risk of Alzheimer's disease. The 127 patients who began the study with T2D had a 65% greater risk of incidence of Alzheimer's disease than nondiabetic counterparts (95% CI, 1.10-2.47), even after adjusting for age, sex, and education.

Several newer analyses have pulled their data from far larger datasets in hopes of drawing stronger and more accurate conclusions. A 2014 paper that appeared in *PLoS One*¹⁴ used information on 1 million randomly sampled people to compare the 71,433 diabetics in the group with 71,311 nondiabetics matched by age, sex, hypertension, hyperlipidemia and previous stroke history. Incidence of Alzheimer's disease was rare in both groups (0.48% vs 0.37%, $P < .001$). Still, over a follow-up period of up to 11 years, T2D patients were far more likely than controls to develop Alzheimer's disease (hazard ratio [HR], 1.76; 95% CI, 1.50-2.07; $P < .001$).

Another large study, published by *Diabetes Care* in 2015,⁶ concluded that although dementia risk is most elevated in patients with longstanding cases of T2D, that risk begins to go up as soon as patients start demonstrating resistance to insulin. Investigators from Canada used records from Ontario's health administration databases to match 225,045 seniors with newly-diagnosed T2D and 668,070 controls, and followed them up to 17 years. A fully-adjusted Cox model found the risk of dementia to be significantly higher among diabetic patients (HR, 1.16; 95% CI, 1.15-1.18). Risk of Alzheimer's disease increased within a month of T2D diagnosis, and it kept rising over time.

“When testing the proportional hazards assumption, we did detect a significant interaction between diabetes status and time,” the study authors wrote. “The HR associated with diabetes status was 1.19 (HR; 95% CI, 1.16-1.22), and this effect increased by about 1% per year (HR for diabetes \times year interaction: 1.009; 95% CI, 1.004-1.014). Thus, after 10 years of duration, diabetes was associated with a nearly 30% higher incidence of dementia.”

Collectively, the evidence from the individual population studies has convinced the authors of several meta-studies that T2D patients do face significantly elevated risk of Alzheimer's disease. A review that appeared in *The Lancet Neurology* in 2006, found that 8 of 13 included studies linked T2D with Alzheimer's, while 6 of 9 included studies linked T2D with vascular dementia.¹ A 2012 meta-analysis that appeared in *Internal Medicine Journal*,² pooled the relative risks found in 19 studies with nearly 45,000 subjects and found that T2D patients, compared to other patients, faced a higher risk of Alzheimer's disease (relative risk [RR], 1.46; 95% CI, 1.20-1.77),

vascular dementia (RR, 2.48; 95% CI, 2.0-2.96), any dementia (RR, 1.51; 95% CI, 1.31-1.74) and mild cognitive impairment (RR, 1.21; 95% CI, 1.02-1.45).

Further evidence that T2D is linked to Alzheimer's disease comes from research that finds evidence of insulin resistance in the brains of Alzheimer's patients. A 2012 study, published in *The Journal of Clinical Investigation*,¹⁵ found that markers of insulin resistance increased "commonly and progressively from normal cases to mild cognitively impaired cases to Alzheimer's disease cases, regardless of diabetes." Researchers from the University of Pennsylvania tested tissue samples collected by 2 cohort studies that also measured cognitive decline and found that, "Brain insulin resistance thus appears to be an early and common feature of Alzheimer's disease, a phenomenon accompanied by IGF-1 resistance and closely associated with IRS-1 dysfunction, potentially triggered by A β oligomers and yet promoting cognitive decline independent of classic Alzheimer's disease pathology."

Other studies have found that intranasal insulin can improve memory in older adults with Alzheimer's disease. A 2006 study, published in *Neurobiology of Aging*,³ which gave insulin or placebo to 35 controls and 26 memory-impaired subjects (13 with early Alzheimer's disease; 13 with mild cognitive impairment), reported that insulin facilitated significantly improved recall among Alzheimer's patients in 2 measures of verbal memory. The *Journal of Alzheimer's Disease* reported, 2 years later, how insulin affected another group of 59 controls and 33 memory-impaired adults. Again, insulin produced significant gains only in memory-impaired subjects without the apolipoprotein E epsilon4 allele.⁴

"There's a growing body of evidence that Alzheimer's disease is, at its core, a condition defined by insulin resistance in the brain. The brain is the target of a particular kind of diabetes that some people call, type 3 diabetes. This form of diabetes can obviously occur independently of type 2 diabetes, as many people with Alzheimer's disease do not have type 2 diabetes, but it also looks very likely that the 2 diseases can arise from the same causes, or that type 2 diabetes can either trigger or worsen Alzheimer's disease in people who are otherwise prone to it," said Suzanne de la Monte, MD, MPH, a professor of pathology, laboratory medicine and neurosurgery, at Brown University, in an interview with EBDM.

"It appears, at this point, like there may be some parallels between Alzheimer's disease and other conditions characterized by localized insulin resistance. Metabolic syndrome is a disease of localized insulin resistance, as is nonalcoholic fatty liver disease. Both of them can exist independent of diabetes, but it's certainly wise for people who treat diabetic patients to test regularly for them in hopes of spotting them early and treating them before they progress," de la Monte added.

Despite the evidence that Alzheimer's disease is associated with insulin resistance in the brain, and that insulin can temporarily improve the memory for some patients with the disease, some observers think it's too early to conclude that T2D can trigger or worsen Alzheimer's disease, and that it's way too early to begin thinking of Alzheimer's disease as a specialized type of diabetes. This resistance stems both from the belief that too little is known about Alzheimer's disease for so sweeping a statement about its fundamental nature, and by the observation that some types of research tend to find little, if any, connection between T2D and Alzheimer's disease.

Unlike the retrospective analyses of large health record databases, which have typically found T2D patients far more likely than others to develop Alzheimer's disease, studies that diagnose Alzheimer's disease via autopsy rather than medical claims, often find little or no connection. A 1997 study, which appeared in *Neurology*,¹⁶ compared the amount of Alzheimer-type pathology in the postmortem brains of diabetics and age-matched control subjects. "There was no significant difference between diabetics and control subjects with respect to severity of Alzheimer-type pathology, on average, or with respect to age," the study authors wrote. "This finding was true for

diabetics with and without insulin dependence." These conclusions were echoed in a 2004 study published in *The Journal of Gerontology*.¹⁷ Investigators traced 385 consecutive autopsies of residents from a single nursing home (15.8% of whom were diabetic) and found that diabetes was negatively correlated with Alzheimer's disease neuropathology. "Diabetics had significantly fewer neuritic plaques ($P = .008$) and NFTs ($P = .047$) in the cerebral cortex than did nondiabetics. In the hippocampus, diabetics had significantly lower plaque ratings than did nondiabetics ($P = .019$)." (They are based, in part, on autopsies that have positively associated T2D with Alzheimer's disease,¹⁸ but they are in the minority.)

"The results of the autopsy studies are a significant counterweight to the belief that diabetes greatly increases the risk of Alzheimer's disease because autopsy is the only definitive way to distinguish Alzheimer's from the vascular dementia that diabetes certainly causes. It is possible to look at the autopsy studies and conclude that a lot of diabetics with vascular dementia are being diagnosed with Alzheimer's. The other evidence that this may be the case is when we look at levels of amyloid proteins. If diabetes triggered or worsened Alzheimer's in some significant percentage of patients, we'd expect diabetic patients to have unusually high levels of the amyloid proteins that are so closely associated with Alzheimer's, but we don't tend to see that in PET scans or in cerebrospinal fluid," said Biessels.

"This is not to say that diabetes cannot cause or accelerate Alzheimer's disease, but if it does, we're a long way from understanding which pathways connect diabetes and Alzheimer's—and there probably will be multiple pathways, just as there are multiple pathways that we now know to lead from diabetes to vascular dementia," he said.

Researchers are also a long way from understanding which diabetes medications, if any, can provide any value in treating Alzheimer's disease. A number of studies have found individual diabetes medications that can treat Alzheimer's disease in mice. The 2 most cited of those are a 2012 study, published in *The Journal of Clinical Investigation*,¹⁵ which found that exendin-4 (exenatide) protected mice from defective insulin signaling associated with Alzheimer's, and a *NeuroMolecular Medicine* article that reported that liraglutide had a number of anti-Alzheimer's effects.¹⁹

Researchers began recruiting humans with Alzheimer's disease for a liraglutide trial more than a year ago,²⁰ but results from that and other trials on other diabetes medications are still years away. There is some evidence from other types of studies—such as a 2008 postmortem study, published in *Neurology*²¹—that diabetes medications may reduce Alzheimer's neuropathy, but other studies have found no comparable effect. Large population studies from Canada and Taiwan, for example, found no connection between diabetes medication and Alzheimer's progression among diabetic patients. **EBDM**

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“There’s a growing body of evidence that Alzheimer’s disease is, at its core, a condition defined by insulin resistance in the brain. The brain is the target of a particular kind of diabetes that some people call type 3 diabetes.”

—SUZANNE DE LA MONTE, MD, MPH
BROWN UNIVERSITY

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DIABETES SELF-MANAGEMENT

Seniors, Diabetes, and the Art of Self-Management

MARY CAFFREY

ABOUT THE EXPERT



SAINT PETER'S
UNIVERSITY HOSPITAL
A MEMBER OF SAINT PETER'S HEALTHCARE SYSTEM

MEENA MURTHY, MD, FACE

Dr Murthy is chief of the Division of Endocrinology, Nutrition, and Metabolism at Saint Peter's Healthcare System, New Brunswick, NJ.

Long before terms like “care coordination” or “patient-centered medical home” became common, the principles that govern the movement to value-based care were second nature to Meena Murthy, MD, FACE, when she set up the diabetes care unit in 2000 at Saint Peter's University Hospital in New Brunswick, New Jersey.

Murthy, an endocrinologist with advanced training in geriatrics, who is Saint Peter's chief of the Division of Endocrinology, Nutrition, and Metabolism, convinced the hospital to embrace a team-based approach to diabetes care, years before it became the thing to do—and before insurers understood that it makes sense for certified diabetes educators (CDEs), nutritionists, and social workers to collaborate with physicians on patient care.

Even with more help than was customary at the time, Murthy also knew that managing diabetes requires more hands than any hospital could ever afford. The most important “hands” needed to manage a chronic disease belong not to the provider, but to the patient—with plenty of support, of course.

As she described Saint Peter's program in interviews with *Evidence-Based Diabetes Management*, she said, building a patient's abilities was always part of the approach. Said Murthy, “It's in our DNA.” Thinking that a patient can be handed a few prescriptions and a list of instructions to manage their disease is unrealistic, she said. “With diabetes, that will never happen.”

What's true in diabetes, generally, is especially true among the senior population. Many have built up poor lifestyle habits over decades, but at the same time, Murthy said, they often resist accepting help. She's seen it over and over—a person retires, the metabolism slows, and there's more access to food with less activity—and soon a person has gained 10 pounds. It's little wonder, then, that according to the American Diabetes Association (ADA), the disease affects 25.9% of the population over age 65, mostly type 2 diabetes.¹

Murthy is passionate about her mission—not just improv-

ing the numbers, which is important—but also in treating the whole patient. For her, diabetes care is both art and science; it's unacceptable to declare success if the glycated hemoglobin (A1C) looks good on the electronic health record (EHR), but the patient is gaining weight or struggling with side effects. She has a clever description: “The e-patient is doing well,” but the real one, not so much.

Especially for seniors, she said, “if a regimen is beyond their self-management capacity, they'll be miserable and they won't stick with it.”

More and more, the experts agree. The ADA's 2016 Standards of Medical Care in Diabetes, published in January, featured a lengthy update on care for persons over age 65, including a call for individual goals based on each patient's medical, functional, and cognitive status, as well as social capacity. The update states: “Glycemic goals for some older adults might be reasonably relaxed, using individual criteria, but hyperglycemia leading to symptoms or risk of acute hyperglycemic complications should be avoided in all patients.”²

Translating this into better care for older adults means teaching them to work healthy habits into everyday life. Today, Murthy, and her team, work not only with seniors who have diabetes, but they also work to prevent disease among those at risk, which will be a greater focus of Medicare going forward.³

Over time, Murthy has trained a powerful army in her cause—the seniors themselves. Her face lights up as she describes the stories of people with diabetes who came for education, and later became peer leaders and finally “master trainers,” a certification of the Stanford Diabetes Self-Management Program⁴ used at Saint Peter's.

THE STANFORD PROGRAM

Around the time that Murthy founded the diabetes unit, research going on at Stanford University School of Medicine, led

MD
MAGAZINE

New findings on how aflibercept may target galectin-1, a factor associated with proliferative diabetic retinopathy. View at <http://bit.ly/1SLInhj>.

by Katie Lorig, DrPH, laid the groundwork for the program used at Saint Peter's today.⁵

At that time, Lorig's work in chronic disease self-management did not involve persons with diabetes per se, but those with a range of conditions—patients who had suffered strokes, heart disease, lung disease, or had arthritis. Results, of a 2001 study, showed that after 2 years, patients trained in self-management experienced fewer than expected visits to the emergency department, fewer hospitalizations, had less health distress and perceived themselves as more capable of managing their condition.⁵

The same principles—that patients educated to work with their doctors will fare better—informed the development of the Diabetes Self-Management Program. Based on a 2.5-hour session offered over 6 weeks, the Stanford program trains those with diabetes to be active partners with their doctors, nurses, and other providers.

Topics include techniques to deal with the symptoms of the disease, such as fatigue, pain, or hypoglycemia; how to handle the stress of managing diabetes every day; how to exercise to maintain strength and endurance; and what kind of foods to eat.⁴ Results from a clinical trial, published in 2009, found that participants had fewer symptoms of hypoglycemia, reduced depression, and better communication with physicians. Even after a year, patients were eating better and reading food labels more closely. Because the program was peer-led, it cost less to implement than alternatives.⁶

Murthy said Saint Peter's works hard to understand to gain the “common cultural intelligence” needed to help the many ethnic groups, in central New Jersey, adapt their native diets to their health needs. Understanding the disease—why diet matters, and especially what each pill is for—is critical for adherence and long-term success, she explains. For providers, it's a new way of thinking toward educating, and not just prescribing. “The patient needs to learn as much as you!” she said.

The core of the program is the weekly action plan, which lets each person with diabetes set goals and specific ways to achieve them. Patients discuss the roadblocks they encounter while trying to fulfil their action plan and gain problem-solving skills.

“Action plans have to be very specific,” Murthy said. Patients can't simply state a goal; they must spell out *how* they are going to achieve it, such as on which days they will exercise. Involvement from family members is critical, so there is support at home for dietary changes.

FROM TREATMENT TO PREVENTION

A follow-up visit to Saint Peter's happened on a big day for those in diabetes care: that morning, HHS Secretary, Sylvia Mathews Burwell, announced that Medicare would start paying for the National Diabetes Prevention Program (NDPP),³ the evidence-based initiative piloted at the YMCA that had been shown to reduce care costs for persons over age 65.

About 20 members of the Saint Peter's team from multiple sites—from endocrinologists and nurses to CDEs to social workers to dietitians—have gathered for a meeting to share data and ideas. They discuss strategies for getting seniors to show up for all 6 sessions of the self-management program, not just the nutrition classes. One team member reports progress in getting more patients to eye exams. Much of the talk involves breaking down barriers for populations struggling just to access programs, must less control diabetes.

Saint Peter's team approach received a boost in 2013, when the health system received a \$20.5 million, 5-year grant from New Jersey's Delivery System Reform Initiative. The award was part of the state's Medicaid waiver with CMS, and it called for Saint Peter's to create a patient-centered medical home to deliver better diabetes education and preventive care for at-risk adults. The award followed a needs assessment that found that 56.2% of the adults on the region Saint Peter's serves had at least 1 chronic condition, with diabetes and hypertension being most common.⁷⁻⁸

As much as overeating gets attention for the nation's diabetes crisis, the team meeting in March 2016 discussed how lack of food causes just as many problems, especially for patients on insulin. Saint Peter's commitment to serving the poor in and around New Brunswick—including some who are undocumented—calls for creativity and partnerships with many agencies beyond its walls, from food pantries to the school system.

When the group hears the news about NDPP, there's applause—and lots of questions. Like other safety net hospitals, Murthy said, Saint Peter's could substantially reduce readmissions if it could do more to prevent diabetes. Reducing the barriers to prevention is just as important as reducing the barriers to good care; because there has been no tradition of teaching people self-management or prevention, “we have very low standards,” Murthy said.

But that also means the potential for improvement is enormous.

FACTS ABOUT SAINT PETER'S UNIVERSITY HOSPITAL

BASICS. Founded in 1907, the 478-bed teaching hospital is located in New Brunswick, NJ.^a

ORGANIZATION. Centerpiece of Saint Peter's Healthcare System, created in 2007 to organize the hospital, its foundation, and care at other sites, including St. Peter's Adult Day Care, Monroe, NJ.^a

SIZE. Saint Peter's University Hospital serves 30,000 inpatients and 235,000 outpatients, per year. Approximately, 1050 physicians and dentists have privileges at the hospital.^a

CHARITY CARE. Of its \$428 million budget in 2014, the healthcare system provided \$39.7 million in charity care and community benefits.^b

AWARDS AND RECOGNITION. Leapfrog Score “A” renewed Spring 2016.^c Silver Beacon for ICU Nurses.^a

DIABETES CARE. Saint Peter's Thyroid and Diabetes Center provides self-management education that is certified by the American Diabetes Association. The center also offers care for obesity, hypertension, and lipid orders, and care for a variety of hormonal and metabolic disorders, as well as calcium and Vitamin D disorders. Services for seniors are also offered at Saint Peter's facility in Monroe.^d

A patient-centered medical home, for treatment and prevention of diabetes and hypertension, received a \$20.5 million, 5-year grant through 2017 from the NJ Delivery System Reform Incentive Payment program.^e

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So much of teaching people to eat properly and care for themselves is simple. “If it has a label, it is already suspicious,” Murthy says with a laugh. “A banana doesn't have a label.”

The big challenge in diabetes is that on any given day, the obstacles change. There's a birthday party, or food at the office. There's a thunderstorm that makes walking outside impossible. The person with diabetes must constantly adjust, because on most days, there are no symptoms, only temptations.

Says Murthy, “The day is full of negotiation.” **EBDM**

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Reaching Patients Who Should Be Screened, Treated for Diabetic Macular Edema

PART 1: SEE PART 2 IN THE SEPTEMBER ISSUE

MARY CAFFREY

ABOUT THE PANEL



PETER SALGO, MD

Dr Salgo is associate director of Surgical Intensive Care, New York-Presbyterian Hospital.



JOHN W. KITCHENS, MD

Dr Kitchens is a vitreoretinal surgeon at Retina Associates of Kentucky.

With the population of Americans who have either type 1 diabetes (T1D) or type 2 diabetes (T2D) now having exceeded 29.1 million,¹ the need to reach those at risk for complications is great. The American Diabetes Association (ADA) estimated in 2013 that the disease costs the United States \$245 billion each year² in healthcare spending and lost productivity—and that second part occurs when adults below retirement age develop conditions that make it impossible for them to work.

Eye complications are common among those with diabetes,³ yet with proper care, these complications are preventable and, if they occur, more treatable than ever. In recent years, a new class of therapy called VEGF inhibitors, which target the vascular endothelial growth factor, has emerged to treat ocular conditions associated with diabetes, including diabetic macular edema (DME).

The American Journal of Managed Care recently convened an expert panel for a Peer Exchange, “Diabetes-Related Complications: a Focus on Diabetic Macular Edema.” Experts discussed new therapeutic options in DME, the importance of screening persons with diabetes for eye complications, and the factors that payers consider when evaluating the value of new therapy.

Taking part in the discussion were John W. Kitchens, MD, a vitreoretinal surgeon at Retina Associates of Kentucky; Rishi P. Singh, MD, staff physician at the Cleveland Clinic and assistant professor of ophthalmology at Case Western Reserve University; and Steven Peskin, MD, MBA, FACP, executive medical director of Population Health for Horizon Healthcare In-

novations in New Jersey. Peter Salgo, MD, associate director of Surgical Intensive Care at New York-Presbyterian Hospital moderated the discussion. This is the first of 2 parts on the discussion; the second part will appear in the September issue of *Evidence-Based Diabetes Management*.

OCULAR CONDITIONS AND THE COST BURDEN

Singh explained that whereas almost everyone can develop cataracts if they live long enough, about 25% of those with diabetes have retinopathy, which can go unnoticed at first. Kitchens explained that although symptoms are mild at first, the condition can get worse over time.

“It can progress to proliferative diabetic retinopathy, where abnormal blood vessels grow in the back of the eye, and those blood vessels can bleed and leak,” he said. This, Kitchens explained, is the leading cause of blindness for patients with diabetes.

DME specifically occurs when this leakage causes the retina to swell, after which blurring develops in the central field of vision. As diabetes complications go, Salgo asked if this was among the worst.

“Yes, I’d say that’s a pretty profound complication,” Peskin said.

Kitchens said the cost burden of eye complications is substantial—\$3 billion a year.⁵ Singh said a recent study found that the average person with diabetes required \$9000 in annual healthcare spending, but a person with diabetic retinopathy required \$29,000.⁶

“That comes from a lot of different things,” Singh said.

Imaging, surgery, and lost productivity all contribute to the cost burden. Patients who lose vision become more depressed as well, he said.

"It's a downward spiral," Kitchens said. "If you can't see, how are you going to dose your insulin? How are you going to know what pills you're taking? How are you going to make it to your doctors visits? So now, you're increasing the burden on your family, and those are all the indirect costs that add up."

GETTING PATIENTS SCREENED FOR EYE COMPLICATIONS

Kitchens said both the American Academy of Ophthalmology and the ADA call for those with T2D to have a baseline eye screening at diagnosis and for those with T1D, within 5 years of diagnosis. (A recent survey found young adults with diabetes are less likely to get screening at recommended intervals.⁴)

According to Peskin, payers focus on the annual exam. "Within the health plan, the Health Effectiveness Data and Information Set and the annual dilate exam can be done by an optometrist or an ophthalmologist." When he teaches residents, Peskin said, he emphasizes the need for the annual retinal exam, as well as the monofilament foot test and the microalbumin screening for early signs of kidney damage.

But getting patients with diabetes an annual eye exam is easier said than done, especially if the burden of checking falls on a primary care physician. Singh said that Cleveland Clinic did a study and found that 75% to 80% of endocrinologists always asked about eye-related issues during exams, but only 15% to 20% of internists did, even with patients who have diabetes. "The internists failed to ask, probably because they are so inundated with everything else, that they failed to get to that point," Singh said. The result, Kitchens said, is that only about 50% of those at risk for eye complications are being screened on schedule.

WHAT KEEPS PATIENTS FROM GETTING EYE EXAMS?

Salgo asked, "What are the barriers for patients who want to get eye exams but cannot get them?" Kitchens mentioned insurance, cost, and transportation.

Singh said it's more complicated than that—sometimes it's not clear whether the exam is covered by a patient's medical benefit or a vision plan. Since the Affordable Care Act took effect, he said, "People are looking at deductibles and not understanding necessarily where this falls in their deductible range. These are all medical examinations covered by insurance."

Peskin said payers are trying to make things less complicated. Besides sending reminders to patients who need annual retinal exams, for Medicaid patients, his company is eliminating co-payments to encourage this group to get the screening.

Salgo asked how health plans keep track of who is getting screened and who isn't. Peskin said Horizon is tracking longitudinal data and making it available to clinical partners, and the results can be "a bit humbling." Most physicians, he said, think they are keeping glycated hemoglobin (A1C) for the vast majority of their patients at 8% or below, and they find out that's not the case. "Making that information available, not in a punitive way, but in a collaborative way, is a big part of what we do," he said.

Singh and Kitchens contrasted the differences between an academic medical center like Cleveland Clinic—where the eye exam and the rest of care might be under one roof—and private practice, where Kitchens says he deals with a variety of hospital systems and tracking patient care is more challenging.

"Ergo, the 50% who aren't getting followed," Salgo said.

Kitchens credits insurers, and the rise of quality metrics, with reinforcing the idea among physicians that those with

diabetes need eye screening. Peskin agreed that having claims data is a start and that his insurer is making strides with "harmonizing" that information with the electronic health record.

WHAT IS THE LEVEL OF AWARENESS?

Salgo asked if, in the age of the Internet, those with diabetes had greater awareness that vision was at risk. Kitchens said not really. Socioeconomic factors play a bigger role, and so does age, with Medicare patients more likely to follow up on eye exams than young adults.

Peskin agreed—to a point. While it's true that people become more engaged in their health as they age and gain education, it's not perfect. "We know from research that we've done that there are people who are Master's prepared that are also not health-literate or health-numerate," he said. "So, we've got plenty of challenges in front of us to engage those persons."

He's less concerned that patients know words like "retinopathy" than getting across the message that annual eye exams are a must. Horizon, Peskin said, is trying to reach out not only to clinical partners to engage them to take annual measures, but also to employers. "Ultimately, they are the ones who are paying the bills, right?"

Singh said the challenge with raising awareness about screening—or anything with diabetes—is that it's a very time-consuming disease. He cited a study that found patients made 20 doctors' visits a year. That amount of time off, he said, would consume all his vacation.

Kitchens said engaging patients is very difficult. "It's hard to expect patients to understand their retinopathy when sometimes they come in and they don't even know their A1C. And that's a scary thing. I'd say probably 25% of our patients don't know what their A1C is." **EBDM**

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ABOUT THE PANEL



**STEVEN PESKIN, MD,
MBA, FACP**

Dr Peskin is executive director of Population Health, Horizon Healthcare Innovations.



RISHI P. SINGH, MD

Dr Singh is staff physician, Cleveland Clinic, and assistant professor of ophthalmology, Case Western Reserve University.

“If you can't see, how are you going to dose your insulin? How are you going to know what pills you're taking?”

—JOHN W. KITCHENS, MD

AARP Finds Seniors Hit Hard as Drug Price Hikes Outstrip Inflation

MARY CAFFREY

Price hikes for the drugs used most often by Medicare beneficiaries outstripped those for other consumer goods between 2006 and 2013, according to a recent report from the AARP Public Policy Institute.¹ (AARP is formerly known as the American Association of Retired Persons.)

Over the period covered, 2013 was a high-water mark for rising drug costs affecting seniors, the report found. AARP's combined market basket—a roster that includes 622 brand name and generic drugs commonly prescribed to those in Medicare—rose 9.4%, while general inflation rose only 1.5% in the same period.

“Increases in the retail price of prescription drugs have a corresponding impact on the cost of drug therapy for the individual and all other payers,” wrote the authors, Stephen W. Schondelmeyer, PharmD, PhD, of the PRIME Institute at the University of Minnesota, and Leigh Purvis, MPA, of AARP. The average annual cost of therapy, which includes specialty drugs, was \$11,341 per year, coming close to the average Social Security benefit of \$15,526 per year.

The specialty therapy tier, which includes drugs for cancer, hepatitis C, or HIV, drove up costs in 2013, as many expensive cancer drugs dominated the specialty pharmacy market. The worst was yet to come, however, as overall therapy prices spiked again in 2014 when the hepatitis C drug Sovaldi hit the market at a cost of \$1000/day.²

Although specialty pharmacy drugs were the primary driver of rising prescription costs, generic drugs were not immune to the trend. Many health plans created nonpreferred generic tiers that appeared to have no other purpose than to charge consumers higher out-of-pocket costs, according to an editorial that appeared in *The American Journal of Managed Care*.³

Seniors have been hit hard by drug pricing trends, because as gas prices and other consumer goods have remained stable, inflation has remained flat. In

2016, this meant there was no cost-of-living increase in Social Security benefits. Policy experts say this combination has been difficult for seniors to manage.⁴

Generic drug prices remain comparatively low, accounting for 18.3% of all drug expenditures, compared with 69.4% of all prescriptions written. Brand name drugs, by contrast, account for only 29.3% of the prescriptions, but 64.1% of the expenditures, according to the report. And specialty drugs account for 17.6% of expenditures even though the category covers only 1.2% of all prescriptions. Thus, drops in generic drug prices are more than offset by the increases in brand name and especially specialty drug prices, the authors found.

Rising drug costs don't just affect taxpayer funded programs such as Medicare and Medicaid, the authors found. “Spending increases driven by high, and growing drug prices will eventually affect all Americans in some way,” they wrote. “Those with private health insurance will pay higher premiums and cost sharing for their health coverage, and, over time, higher drug

prices could lead to higher taxes and/or cuts to public programs to accommodate increased government spending.”

The average annual cost of a therapy in the AARP basket in 2013 was more than double the cost in 2006, when the average was \$5571 per year, the report found. (This was the first year of Medicare Part D.) Of course, the average annual cost varied widely by category:

- Brand name drugs: \$2960
- Generic drugs: \$283
- Specialty therapy: \$53,384

The cost of prescription drugs is one of the few issues that resonates with voters across the political spectrum, based on polling by the Kaiser Family Foundation and on behalf of the Campaign for Sustainable Drug Pricing (CSRXP).^{5,6}

The AARP report “provides new evidence that drug companies are raising prescription drug prices on patients indiscriminately,” said CSRXP Executive Director John Rother in a statement. “Specialty and branded drugs alike are going up 6 times faster than inflation. The exorbitant increases make health care more expensive for families, taxpayers, and job creators, and put a major strain on federal and state governments. It's going to take market-based policy solutions to deal with this unsustainable trend.”⁷

Former Secretary of State Hillary Clinton⁸ and Republican frontrunner Donald Trump⁹ are on record criticizing pharmaceutical companies for high prices and calling for reforms that would allow Medicare to negotiate drug prices. **EBDM**

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“Increases in the retail price of prescription drugs have a corresponding impact on the cost of drug therapy for the individual and all other payers.”

—STEPHEN W. SCHONDELMAYER, PHARM.D, PH.D; AND LEIGH PURVIS, MPA

Scientists Find Accidental Cure for Type 2 Diabetes: *Imatinib*

MARY CAFFREY

The cancer drug imatinib—marketed as Gleevec—known as a game-changer for conditions like chronic myeloid leukemia may prove the same in type 2 diabetes (T2D), according to a study published recently in *Diabetes*.¹

Researchers in the United States and in South Korea found that imatinib controls peroxisome proliferator activated receptor γ (PPAR γ), which lowers the level of insulin resistance, thus reducing a patient's risk of hyperglycemia and obesity. PPAR γ affects how the body metabolizes glucose and stores fat, as well as immune and inflammatory responses.

This same mechanism of action was at work with the class of drugs known as the thiazolidinediones (TZDs), the most famous of which was rosiglitazone (Avandia). Risks reported in the *New England Journal of Medicine* forced Avandia off the market and others in the class followed, although a follow-up trial exonerated the drug.²

The mechanism of action seen in Gleevec was previously seen in a class of anti-diabetic therapy known as TZDs, which have fallen out of favor.

The study team noted that the phosphorylation of PPAR γ is related to developing T2D taking away the phosphoric acid from PPAR γ , which has an anti-diabetic effect. In the laboratory, the team found that imatinib had the same “blocking” effect on PPAR γ phosphorylation but without some of the effects seen from the TZDs.

Researchers can see the “what” but don't understand the “why” just yet. “Although studies have

shown that Gleevec (imatinib) treatment may show improved insulin sensitivity and decreased blood glucose in patients with known diabetes, the exact cause hasn't been proven yet,” said Jang Hyun Choi, PhD, assistant professor, Ulsan National Institute of Science and Technology in South Korea. The team tested imatinib in mice that had been fed a high-fat diet. The drug improved insulin sensitivity without causing severe side effects that had been observed with the TZDs. **EBDM**

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SENIORS WITHOUT CGM ACCESS REPORT MORE TRIPS TO ED, SURVEY FINDS

MARY CAFFREY

In recent years, the JDRF (formerly the Juvenile Diabetes Research Foundation) has cited a 2011 study in *The American Journal of Managed Care* while making the case that Medicare beneficiaries should have access to continuous glucose monitoring (CGM): the study found that the average cost of an inpatient admission for hypoglycemia in 2008 was \$17,564 and the average cost of an emergency department (ED) visit was \$1387.^{1,2}

Now, a new survey that comparing insulin-dependent diabetic adults age 65 or older with and without access to CGM finds that having access makes a patient less likely to experience a hypoglycemic event and less likely to end up at the ED. Those with CGM access also report better quality of life.³ Study authors were William H. Polonsky, PhD, CDE, of the University of California San Diego; Anne L. Peters, MD, of the University of Southern California; and Danielle Hessler, PhD, of the University of California San Francisco. Dexcom funded the study.

Although the study's authors acknowledge that the 2 groups were not entirely balanced—those with CGM had higher levels of education and income—these implications are noteworthy: they suggest that wealthier Medicare beneficiaries who can pay for CGM on their own will continue to have access after they retire, while poorer beneficiaries will do without, absent a policy change from CMS. Noting that even those using CGM face a higher risk of hypoglycemic events as they age, the authors wrote: “Given the potential vulnerability of this older population and the resulting costs associated with these events, it is unfortunate that [CGM] is not, at this time, covered as a benefit under Medicare, thereby often making it all but unaffordable to those in the elderly population at lower or fixed income levels.”

Researchers evaluated survey results from 296 adults age 65 or older who either had type 1 diabetes (T1D) or were using insulin to treat type 2 diabetes. The mean age of the respondents was 70.7 years and 48.1% were female. Of the group, 210 were using CGM, 75 hoped to obtain CGM access, and 11 had previously used CGM. The last group was too small to be separately analyzed.

INCOME AND EDUCATION. Those using CGM were less likely to have low incomes: only 14.4% made less than \$50,000/year compared with 42.7% of the group who desired CGM but did not have access. The group using CGM also had more education: only 26.7% had not completed college compared with 45.3% of the group hoping to gain CGM access.

PATIENT-REPORTED HEALTH RESULTS. Those hoping for CGM access were more likely to report at least 1 moderate hypoglycemic episode in the past 6 months than those who were using CGM (90.7% vs 78.1%). Those without access also reported more ED visits for hypoglycemia during the previous 6 months (18.7% vs 6.7%). The group hoping for CGM was also more likely to report an incident in the previous 6 months that required another person's help (80.0% vs 57.6%), which the authors found important since the chances of living alone increase with age.

QUALITY OF LIFE. Those hoping for CGM access reported poorer overall well-being, greater hypoglycemic fear, and more overall diabetes distress. This was especially true among those with T1D who were not using CGM.

In the past year, scientific societies have weighed in on the value of CGM, calling on CMS to change its policy, while legislation that would require coverage has accumulated co-sponsors but no action so far (see **SP258**). In May 2015, the American Association of Clinical Endocrinologists and the American College of Endocrinology called it “imprudent” for payers to deny coverage for high-risk patients with intense insulin regimens.⁴ The American Diabetes Association called for CGM coverage in Medicare in its 2016 guidelines update, which included a lengthy overhaul of treatment recommendations for seniors.⁵

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Quality Measure Improvement Strategies for Elderly Patients With Diabetes

(CONTINUED FROM COVER)

needy patients, and assessment of care quality has evolved from informal provider reputations to a rigorously-quantified system. Medicare quality measures are arguably the most important quality measure systems among elderly patients, in the United States. These measures assess quality using a 5-star rating system based on prior years' performance. The program applies material incentives to improve performance: reputational incentives around the actual star rating, financial incentives around bonus payments, and recruitment incentives around expanded enrollment windows.^{2,3} Diabetes ranks among—if not the most—important conditions in the assessment of quality performance. The Medicare Shared Savings Program (MSSP) for accountable care organizations includes diabetes on a short list of chronic conditions, particularly important to the Medicare population. When simply counting the number of measures for various conditions, diabetes ties for first with ischemic heart disease for most measures in the MSSP.⁴ Moreover, when *Consumer Reports* ranked health insurance plans nationwide, the authors used how well the plan managed patients with diabetes as the sole measure of plan performance, based on the assumption that diabetes management served as a valid proxy for overall plan performance.⁵

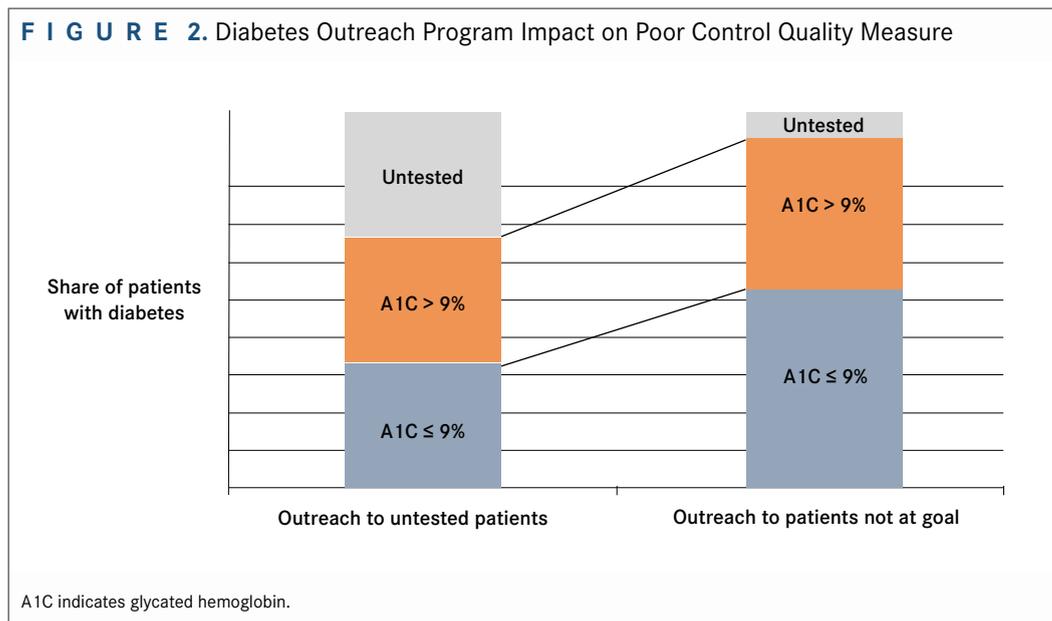
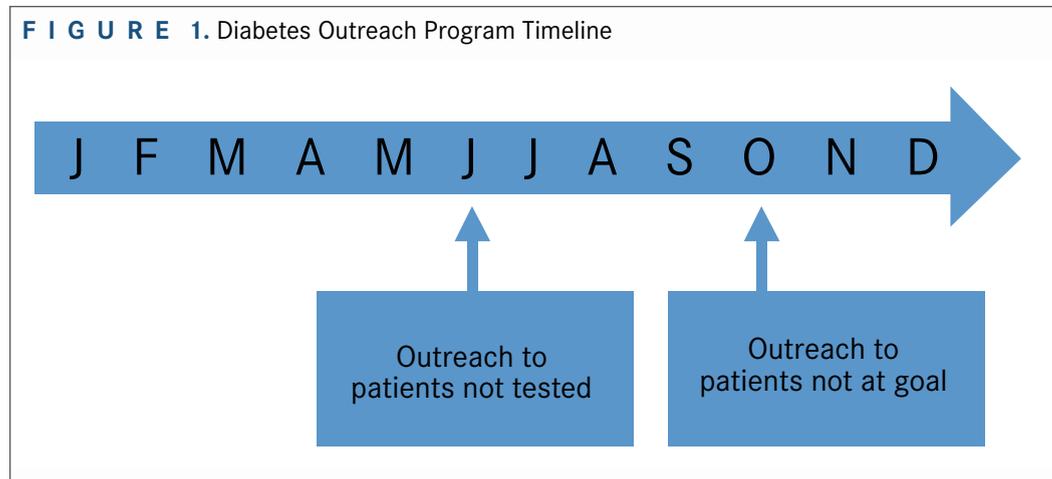
Diabetes likely ranks high because of the prevalence of the condition, the cost of treatment, and the holistic treatment approach to the disease that quality measure creators seek to encourage. Additionally, the HHS considers good performance measures relevant, measurable, accurate, and feasible; the treatment of diabetes lends itself to measures that meet these 4 criteria. The quality measures themselves are drawn from treatment guidelines and are components of the transition toward value-based care and alternative payment models.

As part of a comprehensive approach to minimize the risk of complications of diabetes, treatment guidelines feature glucose control as a major focus in diabetes management. The joint American Diabetes Association/European Association for the Study of Diabetes recommend a glycemic target of glycated hemoglobin (A1C) 7% for most patients.⁶ However, the guidelines recommend flexibility around this target depending on patient and disease features including disease duration, life expectancy, and risks associated with hypoglycemia. Therefore, an older patient with long-standing diabetes may pursue a less-stringent target. The American Association of Clinical Endocrinologists and American College of Endocrinology also recommend individualization of targets, but list an A1C level of less than or equal to 6.5% as the typical target.⁷

Specific to A1C, CMS translates these guideline-based targets into the quality measure: Diabetes HbA1c {Poor Control}.⁸ This measure scores a plan on the number of patients whose most recent HbA1c level during the year was greater than 9% among the total number of patients with diabetes between 18 and 75 years old. The lower the share of patients who measure above 9%, the better. As an outcome measure, the HbA1c Poor Control score contributes triple weight compared with a process measure, such as Adult Body Mass Index Assessment. The selection of this modest A1C goal by CMS likely reflects a do-no-harm perspective, considering the vulnerability of the Medicare population and the recommendation to set less stringent glycemic targets for these patients. However, given the growing number of classes of medication available to treat diabetes with a low intrinsic risk of hypoglycemia, and that every 1 percentage point reduction in A1C reduces the risk of developing eye, kidney, and nerve disease by 40%, it is not clear that setting a more stringent population-level goal for Medicare patients would not ultimately generate net benefit.⁹ We also note that other programs (eg, HEDIS) include more stringent A1C targets of 7% and 8%. How, for example, should a plan approach benefit design if it seeks to improve performance on the quality measure HbA1c Poor Control?

Shortly after launch of a new medication, pharmacy decision makers rely on clinical trial data and cost-effectiveness models. These economic models extrapolate clinical trial results and include outcomes of interest to decision makers: the predicted health and economic outcomes of different treatment pathways.¹⁰ However, these models do not completely capture the short- to mid-term needs of a US pharmacy director seeking to put together a competitive benefit package at a competitive price, in a marketplace where patients may change insurers. Predicted quality measure achievement of different pharmacotherapy treatment pathways, over a shorter time-horizon, may also be relevant to US decision makers. This methodology was used to compare canagliflozin and sitagliptin in a “cost-efficiency” model.¹¹ Importantly, current, or likely future, quality measures for patients with diabetes go beyond A1C and include medication adherence, blood pressure, hypoglycemia, body weight, and blood lipids. In general, quality measure creators should consider tailoring diabetes quality measures and measures of holistic care to provide appropriate overall incentives in the management of patients. The pharmacologic effects of different classes of diabetes medications on these additional outcomes vary. Fortunately, cost-effectiveness models already account for these additional outcomes allowing smooth incorporation of these quality measure-based outcomes into cost-efficiency models.

As a simple stylized example, how might an insurer institute a program to improve performance on the quality measure HbA1c Poor Control? Start with the low-hanging fruit: patients who do not test A1C by definition do not meet the treatment goal. Reaching out to untested patients with diabe-



tes at mid-year to encourage A1C testing is a simple strategy that could prove hugely effective (FIGURES 1 AND 2). By waiting until mid-year, the plan avoids the cost of the intervention among patients who would otherwise receive a test and reach target on their own, but the intervention remains early enough so that improvement is possible. Ideally, an outreach program would be designed to enhance shared decision making and target those patients who otherwise would not seek testing. The importance of targeting the program appropriately increases as the cost of the intervention increases (eg, a pharmacist phone call compared with an automated email). If things go well, patients above goal receive an intervention (diet, exercise, and/or pharmacotherapy) to improve A1C. If the clinician selects pharmacotherapy, the patient's benefit design steers the patient to the treatment most likely to improve overall quality measure performance. Finally, the same outreach program could target those patients above goal at mid-year to return for a second test 3 months later, so that those patients, who were above goal initially, receive a documented final A1C that, ideally, meets goal. The significant improvements in A1C in the Mobile Diabetes Intervention Study, among others, suggest that outreach programs that enable shared decision making, patient education/coaching, and provider communication have real potential to improve performance on quality measures and patient health outcomes.^{12,13}

This strategy would improve quality measure performance while benefiting patients. We concede the program described above certainly does not constitute all that could be done to help patients with diabetes, and falls short of guideline-recommended monitoring. However, in the absence of any program from the insurer, this intervention will likely improve quality measure performance and benefit patients. Moreover, the plan could expand the program further to include other quality measures among patients with diabetes.

Overall, quality measures derive from ever-evolving treatment guidelines and seek to assure quality healthcare and improved health outcomes. Quality measures and incentives are increasingly important. The management of patients with diabetes constitutes a particularly important component of overall quality measure performance. To maximize performance on diabetes-related quality measures, plans should factor quality measure performance when implementing outreach programs and planning formulary design. **EBDM**

DISCLOSURES

The contents of this paper do not necessarily represent the views of AstraZeneca Pharmaceuticals or Precision Health Economics.

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ABOUT THE AUTHORS



JOHN J. SHEEHAN, PHD, RPH

John J. Sheehan, PhD, RPH, is a senior director, Health Economics and Outcomes Research at AstraZeneca, Fort Washington, PA.



JOANNA P. MACEWAN, PHD

Joanna P. MacEwan, PhD, is a research economist at Precision Health Economists, LLC, Los Angeles, CA.

PAYER PERSPECTIVE

Florida Blue Program Focuses on Weight Loss—and Fun—to Prevent Type 2 Diabetes in Older Adults

(CONTINUED FROM COVER)

worrisome. However, they present an opportunity to improve the health of people in our communities.

The good news is that we know how to prevent or delay T2D. The National Diabetes Prevention Program (NDPP) was started by the CDC after gathering information from a successful clinical trial carried out by the National Institutes of Health.⁵ Outcomes from the trial demonstrated that individuals can reduce their risk of developing T2D by 58% through changes in lifestyle such as better nutrition, increased physical activity, and weight loss of as little as 5% to 7%.⁶

Another key finding from the study was that weight loss is the most important factor in reducing the overall risk. While exercise is an important component, its effect on reducing risk for T2D is only moderate without weight loss.⁶ More recent studies have shown that even limited periods of these lifestyle changes have long-lasting effects on diabetes occurrence.^{7,8}

An even more exciting fact is that participants in the clinical trial who were over the age of 60 reduced their risk for T2D by 71%.⁹ As adults experience age-related health changes,

ABOUT THE AUTHORS



**CARMELLA SEBASTIAN,
MD, MS**

Dr Sebastian is vice president of medical affairs for Florida Blue.



**KARLA LOGSTON,
RN, BS, CDE**

Ms Logston is senior manager for the Florida Blue health promotion department, Better You.

they gain a strong desire to change their health behaviors. Results from a study focusing on older adults and which factors encourage them to participate in group exercise classes, demonstrated that 84% like the socialization factor.¹⁰ Respondents also stated they gained encouragement from peers and the instructors, and enjoyed being able to ask instructors health- and fitness-related questions. The classes during the initial diabetes prevention clinical trials and those provided as part of the NDPP are offered in small group settings, providing socialization as well as peer support, and information that allows senior participants to improve their health and avoid further decline that may result from aging.

Data released in 2015 show that, for the first time in a generation, fewer Americans are being diagnosed with diabetes. New cases in the United States fell from 1.7 million in 2008 to 1.4 million in 2014.¹¹ Much of this progress may be a result of NDPP programs, which have been launched across the country. The NDPP has partnered with multiple organizations to offer classes in community settings across the United States, including government agencies such as health departments, private insurers, churches, and community organizations such as the YMCA.¹²

Florida Blue reviewed the program knowing our members' high risk for diabetes and the subsequent increased costs of their medical care. We also evaluated the clinical efficacy, cost effectiveness, and sustainability of the NDPP and determined it was the right type of program to offer to our members, as it works to prevent disease and can improve their quality of life.

Florida Blue applied for, and was awarded, a grant to provide a diabetes preventative program through America's Health Insurance Plans and the CDC, in 2012. Our program, called My Healthy Turnaround, consists of 16 weekly sessions with a lifestyle coach in a group setting. Participants learn lifestyle changes that can positively affect the onset or delay the effects of diabetes, including:

- How to lose weight through healthy meal planning
- Understanding food and nutrition labels
- Nutrition, exercise, and healthy lifestyle changes
- Group support and encouragement

To help individuals stay on track after the program ends, 8 monthly maintenance sessions are also held.

Florida Blue began providing classes under the grant in late 2012. To date, more than 1500 individuals have enrolled in our classes, with more than 76% completing the program. In 2013, more than 13% of participants achieved weight loss goals—34% in 2014 and more than 45% in 2015. In addition, members completing the entire program had a \$166 PMPM lower medical cost compared with individuals who enrolled but did not complete the program. Those participants who had any weight loss greater than 5% also saw a reversed medical cost trend of approximately 20%.

We have seen great results in the diabetes prevention program over the past 4 years. Preventing this devastating disease has a profound impact on quality of life for our members and our community. We are excited about the prospect of offering this program more widely through a health insurance plan benefit.

On March 23, 2016, the Obama administration announced plans that proposed Medicare coverage of programs to prevent diabetes for those at risk of developing T2D. Sylvia Burwell, HHS secretary, announced the proposal at a YMCA in Washington, DC. The YMCA of the USA has provided the NDPP under a federal grant since 2012. After evaluation of the results, Burwell said, "This program has been shown to reduce healthcare costs and help prevent diabetes."¹³

Federal officials have reported a savings to Medicare of \$2650 after 15 months for each participant enrolled in the prevention program, compared with similar beneficiaries not in the program. This is more than sufficient to cover costs, as

the average cost per participant is approximately \$425. In addition, officials said Medicare beneficiaries in the program lost about 5% of their body weight, which was enough to reduce their risk of developing T2D.

Under the Affordable Care Act, the health secretary can, by regulation, expand projects such as the NDPP nationwide if they are found to reduce Medicare spending without reducing the quality of care, and if the Medicare actuary agrees. This proposal will go through a public comment period, but it is expected that regulators will have the program in place before President Obama leaves office in January 2017.

This summer, Florida Blue will start a pilot program for members of our Medicare Preferred HMO plan in collaboration with our partner, Alignment Health. **EBDM**

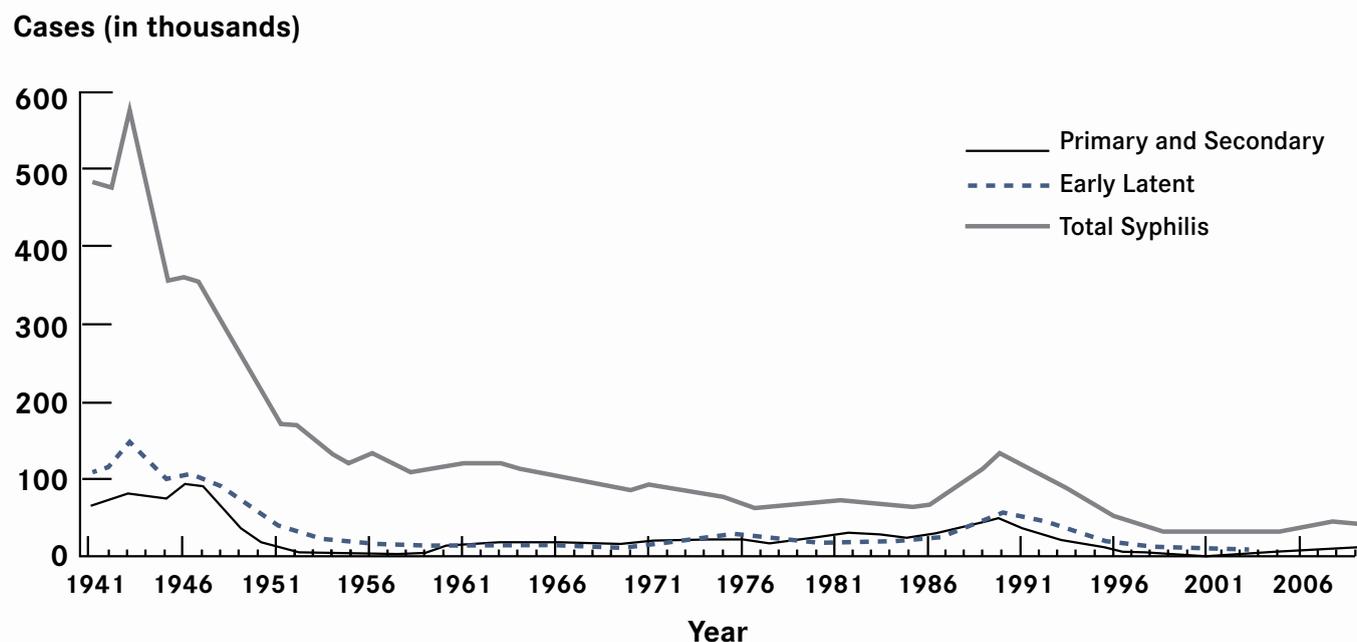
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History Lessons in Innovation: Digital Behavioral Medicine Can Address the Diabetes “Double Epidemic” Facing Medicare and America’s Seniors

(CONTINUED FROM COVER)

FIGURE. Decline in US Syphilis Cases Following Large-Scale Production of Penicillin



SOURCE: Syphilis—reported cases by stage of infection, United States, 1941-2009. CDC website. <http://www.cdc.gov/std/stats09/figures/33.htm>.

ABOUT THE AUTHOR



MIKE PAYNE, MBA MSCI

Mike Payne, MBA, MSci, is chief healthcare development officer at Omada Health.

In the context of this new epidemic, March 23, 2016, may well be remembered as a day that the largest healthcare payer in the United States took a critical step toward, driving an inflection point similar to that seen in the early 1940s with infectious disease.

On that date, HHS Secretary Sylvia Mathews Burwell declared that the delivery of the Diabetes Prevention Program (DPP) has been certified as both clinically effective and cost saving when delivered to Medicare beneficiaries. She further suggested that CMS would soon provide reimbursement for administration of DPP to Medicare beneficiaries.²

To understand the potential impact of Secretary Burwell’s landmark announcement, we must first understand the true scope of the epidemic, as well as the critical role that a new innovation called “digital behavioral medicine” can play in scaling these interventions.²

Since 2011, baby boomers have aged into Medicare at the rate of about 10,000 per day.³ Today, there are almost 45 million individuals aged 65 and older in the United States. By 2030, the US Census Bureau projects that number will be nearly 73 million.⁴ Given these projections, Medicare enrollment in that year will be equal to a quarter of the entire US population today.

Coupled with this demographic mega-trend are clinical dynamics that make the situation even more frightening: more than half of those over 65—a population of more than 22 million—already have prediabetes,⁵ and every year, up to 10% of this population will progress to T2D. The CDC estimates that 1 in 3 American adults will have T2D by 2050.⁶ More than one-third of those older than age 65 also have some form of heart disease⁷ a condition closely correlated to prediabetes.

In 2014, Medicare spent more than \$15,700 managing the health of each beneficiary with diabetes, which included 991 annual emergency department (ED) visits for every 1000 beneficiaries with the condition and a 30-day readmission rate of 20%.⁸ The numbers related to heart failure—often closely correlated with T2D profiles—were even worse: Medicare annually spends more than \$41,000 on those beneficiaries, who

average 1657 ED admissions per 1000 beneficiaries, with a 30-day readmission rate of 24%. The Diabetes Care Project already estimates that 1 in every 3 Medicare dollars is spent treating beneficiaries with diabetes.⁹

The parallels between cardiometabolic chronic disease in the 21st century and infectious disease at the dawn of the 20th century are evident—this time, with a medical expense epidemic accompanying the clinical one. How can today’s healthcare leaders address both?

The answer lies in prevention, to mitigate both medical impact and the bulk of expense. Fortunately, appropriate clinical interventions have been shown to significantly lower the risk of T2D for those at risk. In 2002, the National Institutes of Health (NIH) published results of a clinical trial that demonstrated the effectiveness of the DPP, a behavioral intervention, in helping patients lose clinically meaningful amounts of body weight, reduce their blood sugar levels, and lower the risk for diabetes by 58%.¹⁰

Secretary Burwell’s DPP announcement implies that the NIH’s clinical work, along with recent efforts by CMS to show the medical expense impact of DPP, provide the evidence base that DPP may play a key role in addressing the diabetes “double epidemic” of disease and cost.^{11,12}

For the past 3 years, the Center for Medicare & Medicaid Innovation (CMMI) has operated a demonstration project at 17 YMCA sites in 8 states. In the project, the Y administered the DPP to more than 77,000 seniors who had been diagnosed with prediabetes.¹² Payments to the YMCA were dependent on how many sessions beneficiaries attended and what percentage of body weight—a recognized indicator of downstream diabetes risk reduction—those participants lost. In the final evaluation, the CMS Office of the Actuary estimated that the intervention ultimately saved Medicare \$2650 per beneficiary in just 15 months.¹³

However, Secretary Burwell’s announcement of the CMMI/YMCA project’s excellent results does not alone guarantee victory in the battle against diabetes and its associated costs. The combination of the original NIH trial and the CMMI/

“The parallels between cardiometabolic chronic disease in the 21st century and infectious disease at the dawn of the 20th century are evident.”

—MIKE PAYNE, MBA, MSci

Broadly defined, digital behavioral medicine refers to the digitally-enabled delivery and continuous improvement of proven effective lifestyle interventions like the DPP, while maintaining a high level of clinical fidelity to the original research.

YMCA project included approximately 9000 individuals with prediabetes, just 0.01% of the total US population with prediabetes. DPP delivered face-to-face to YMCAs, churches, clinics, and other community settings will be difficult to scale to 22 million Americans seniors—let alone the additional 65 million Americans who also have prediabetes.

Digital behavioral medicine may hold the answer to this problem of clinical impact and cost-effectiveness at scale. In fact, it may be the equivalent of Florey's scaling methods that supported the production of 646 billion penicillin doses annually by 1945, up from fewer than 10 doses in 1942.

Broadly defined, digital behavioral medicine refers to the digitally-enabled delivery and continuous improvement of proven effective lifestyle interventions like the DPP, while maintaining a high level of clinical fidelity to the original research. For the past 5 years, Omada Health has done just that, developing a version of the DPP, which it delivered remotely, and leveraging insights about behavioral design, user experience, and data science to layer an already effective program with predictive analytics and personalization. Today, we are the largest CDC-recognized¹⁴ provider of the DPP in the country, in-person or remote, with an enrollment of more than 55,000 participants across all 50 states.

Most relevantly, Omada Health's results with seniors indicate that digital delivery of the DPP can and should be an essential part of Medicare's DPP expansion. Administering the DPP digitally can scale the program to the scope of the problem, by lowering barriers to access and success, and by ensuring that this program reaches the populations which need it the most.

To date, Omada Health has enrolled more than 2000 participants over the age of 65. Overall, 84% of these participants, with an average age of 69, have remained active in the program after 6 months. More impressively, they've lost an average of 7.8% of their body weight, reducing their 3-year risk of developing T2D by more than 58%. Every day, our data science, product, and engineering teams are refining the program to adapt it for seniors' lifestyles, stimulate even more engagement, and generate better clinical outcomes. Digital behavioral medicine has far-ranging implications for seniors with prediabetes, as well as all those at elevated risk of an entire suite of obesity-related chronic diseases.

For the first time in history, demographic trends are forcing a fundamental rethinking of how we orient care in our public payer programs like Medicare. The current administration—and hopefully the next—has shown a willingness to embrace prevention strategies, as well as nontraditional online providers of DPP that can demonstrate excellent clinical outcomes and program integrity at scale.

At Omada Health, it is not lost upon us that Florey's penicillin-based innovations are credited with saving over 82 million lives. This number is tantalizingly close to the 87 million Americans currently living with prediabetes. We are invigorated by the vision that in 30 years, we will look at an epidemiological graph showing a drastic drop in US T2D incidence starting in 2018 and know that, like those penicillin pioneers, our innovative approach to delivery of a proven health intervention had a truly historic impact of the health of this country. **EBDM**

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CONTEMPORARY
Clinic

Waist shape may predict heart disease. View at <http://bit.ly/1X6RayH>.



BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION

For complete details, see Full Prescribing Information.

1 INDICATIONS AND USAGE

EYLEA® (afibercept) Injection is indicated for the treatment of patients with Neovascular (Wet) Age-Related Macular Degeneration (AMD), Macular Edema following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR) in Patients with DME.

2 DOSAGE AND ADMINISTRATION

2.1 Important Injection Instructions. For ophthalmic intravitreal injection. EYLEA must only be administered by a qualified physician.

2.2 Neovascular (Wet) Age-Related Macular Degeneration (AMD). The recommended dose for EYLEA is 2 mg (0.05 mL or 50 microliters) administered by intravitreal injection every 4 weeks (monthly) for the first 12 weeks (3 months), followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months). Although EYLEA may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated when EYLEA was dosed every 4 weeks compared to every 8 weeks.

2.3 Macular Edema Following Retinal Vein Occlusion (RVO). The recommended dose for EYLEA is (0.05 mL or 50 microliters) administered by intravitreal injection once every 4 weeks (monthly).

2.4 Diabetic Macular Edema (DME). The recommended dose for EYLEA is (0.05 mL or 50 microliters) administered by intravitreal injection every 4 weeks (monthly) for the first 5 injections followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months). Although EYLEA may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated when EYLEA was dosed every 4 weeks compared to every 8 weeks.

2.5 Diabetic Retinopathy (DR) in Patients with DME. The recommended dose for EYLEA is 2 mg (0.05 mL or 50 microliters) administered by intravitreal injection every 4 weeks (monthly) for the first 5 injections, followed by 2 mg (0.05 mL) via intravitreal injection once every 8 weeks (2 months). Although EYLEA may be dosed as frequently as 2 mg every 4 weeks (monthly), additional efficacy was not demonstrated when EYLEA was dosed every 4 weeks compared to every 8 weeks.

2.6 Preparation for Administration. EYLEA should be inspected visually prior to administration. If particulates, cloudiness, or discoloration are visible, the vial must not be used. Using aseptic technique, the intravitreal injection should be performed with a 30-gauge x 1/2-inch injection needle. For complete preparation for administration instructions, see full prescribing information.

2.7 Injection Procedure. The intravitreal injection procedure should be carried out under controlled aseptic conditions, which include surgical hand disinfection and the use of sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a topical broad-spectrum microbicide should be given prior to the injection.

Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry. If required, a sterile paracentesis needle should be available.

Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment (e.g., eye pain, redness of the eye, photophobia, blurring of vision) without delay (see Patient Counseling Information).

Each vial should only be used for the treatment of a single eye. If the contralateral eye requires treatment, a new vial should be used and the sterile field, syringe, gloves, drapes, eyelid speculum, filter, and injection needles should be changed before EYLEA is administered to the other eye. After injection, any unused product must be discarded.

3 DOSAGE FORMS AND STRENGTHS

Single-use, glass vial designed to provide 0.05 mL of 40 mg/mL solution (2 mg) for intravitreal injection.

4 CONTRAINDICATIONS

EYLEA is contraindicated in patients with

- Ocular or periocular infections
 - Active intraocular inflammation
 - Known hypersensitivity to afibercept or any of the excipients in EYLEA.
- Hypersensitivity reactions may manifest as severe intraocular inflammation

5 WARNINGS AND PRECAUTIONS

5.1 Endophthalmitis and Retinal Detachments. Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments (see Adverse Reactions). Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately (see Dosage and Administration and Patient Counseling Information).

5.2 Increase in Intraocular Pressure. Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA (see Adverse Reactions). Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with vascular endothelial growth factor (VEGF) inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately (see Dosage and Administration).

5.3 Thromboembolic Events. There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The

incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in the Warnings and Precautions section of the labeling:

- Endophthalmitis and retinal detachments
- Increased intraocular pressure
- Thromboembolic events

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

A total of 2711 patients treated with EYLEA constituted the safety population in seven phase 3 studies. Among those, 2110 patients were treated with the recommended dose of 2 mg. Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment. The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous floaters, intraocular pressure increased, and vitreous detachment.

Neovascular (Wet) Age-Related Macular Degeneration (AMD). The data described below reflect exposure to EYLEA in 1824 patients with wet AMD, including 1223 patients treated with the 2-mg dose, in 2 double-masked, active-controlled clinical studies (VIEW1 and VIEW2) for 12 months.

Table 1: Most Common Adverse Reactions (≥1%) in Wet AMD Studies

| Adverse Reactions | EYLEA (N=1824) | Active Control (ranibizumab) (N=595) |
|--|----------------|--------------------------------------|
| Conjunctival hemorrhage | 25% | 28% |
| Eye pain | 9% | 9% |
| Cataract | 7% | 7% |
| Vitreous detachment | 6% | 6% |
| Vitreous floaters | 6% | 7% |
| Intraocular pressure increased | 5% | 7% |
| Ocular hyperemia | 4% | 8% |
| Corneal epithelium defect | 4% | 5% |
| Detachment of the retinal pigment epithelium | 3% | 3% |
| Injection site pain | 3% | 3% |
| Foreign body sensation in eyes | 3% | 4% |
| Lacrimation increased | 3% | 1% |
| Vision blurred | 2% | 2% |
| Intraocular inflammation | 2% | 3% |
| Retinal pigment epithelium tear | 2% | 1% |
| Injection site hemorrhage | 1% | 2% |
| Eyelid edema | 1% | 2% |
| Corneal edema | 1% | 1% |

Less common serious adverse reactions reported in <1% of the patients treated with EYLEA were hypersensitivity, retinal detachment, retinal tear, and endophthalmitis.

Macular Edema Following Retinal Vein Occlusion (RVO). The data described below reflect 6 months exposure to EYLEA with a monthly 2 mg dose in 218 patients following CRVO in 2 clinical studies (COPERNICUS and GALILEO) and 91 patients following BRVO in one clinical study (VIBRANT).

Table 2: Most Common Adverse Reactions (≥1%) in RVO Studies

| Adverse Reactions | CRVO | | BRVO | |
|--------------------------------|---------------|-----------------|--------------|----------------|
| | EYLEA (N=218) | Control (N=142) | EYLEA (N=91) | Control (N=92) |
| Eye pain | 13% | 5% | 4% | 5% |
| Conjunctival hemorrhage | 12% | 11% | 20% | 4% |
| Intraocular pressure increased | 8% | 6% | 2% | 0% |
| Corneal epithelium defect | 5% | 4% | 2% | 0% |
| Vitreous floaters | 5% | 1% | 1% | 0% |
| Ocular hyperemia | 5% | 3% | 2% | 2% |
| Foreign body sensation in eyes | 3% | 5% | 3% | 0% |
| Vitreous detachment | 3% | 4% | 2% | 0% |
| Lacrimation increased | 3% | 4% | 3% | 0% |
| Injection site pain | 3% | 1% | 1% | 0% |
| Vision blurred | 1% | <1% | 1% | 1% |
| Intraocular inflammation | 1% | 1% | 0% | 0% |
| Cataract | <1% | 1% | 5% | 0% |
| Eyelid edema | <1% | 1% | 1% | 0% |

Less common adverse reactions reported in <1% of the patients treated with EYLEA in the CRVO studies were corneal edema, retinal tear, hypersensitivity, and endophthalmitis.

Diabetic Macular Edema (DME). The data described below reflect exposure to EYLEA in 578 patients with DME treated with the 2-mg dose in 2 double-masked, controlled clinical studies (VIVID and VISTA) from baseline to week 52 and from baseline to week 100.

Table 3: Most Common Adverse Reactions (≥1%) in DME Studies

| Adverse Reactions | Baseline to Week 52 | | Baseline to Week 100 | |
|--------------------------------|---------------------|-----------------|----------------------|-----------------|
| | EYLEA (N=578) | Control (N=287) | EYLEA (N=578) | Control (N=287) |
| Conjunctival hemorrhage | 28% | 17% | 31% | 21% |
| Eye pain | 9% | 6% | 11% | 9% |
| Cataract | 8% | 9% | 19% | 17% |
| Vitreous floaters | 6% | 3% | 8% | 6% |
| Corneal epithelium defect | 5% | 3% | 7% | 5% |
| Intraocular pressure increased | 5% | 3% | 9% | 5% |
| Ocular hyperemia | 5% | 6% | 5% | 6% |
| Vitreous detachment | 3% | 3% | 8% | 6% |
| Foreign body sensation in eyes | 3% | 3% | 3% | 3% |
| Lacrimation increased | 3% | 2% | 4% | 2% |
| Vision blurred | 2% | 2% | 3% | 4% |
| Intraocular inflammation | 2% | <1% | 3% | 1% |
| Injection site pain | 2% | <1% | 2% | <1% |
| Eyelid edema | <1% | 1% | 2% | 1% |

Less common adverse reactions reported in <1% of the patients treated with EYLEA were hypersensitivity, retinal detachment, retinal tear, corneal edema, and injection site hemorrhage.

6.2 Immunogenicity. As with all therapeutic proteins, there is a potential for an immune response in patients treated with EYLEA. The immunogenicity of EYLEA was evaluated in serum samples. The immunogenicity data reflect the percentage of patients whose test results were considered positive for antibodies to EYLEA in immunoassays. The detection of an immune response is highly dependent on the sensitivity and specificity of the assays used, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to EYLEA with the incidence of antibodies to other products may be misleading.

In the wet AMD, RVO, and DME studies, the pre-treatment incidence of immunoreactivity to EYLEA was approximately 1% to 3% across treatment groups. After dosing with EYLEA for 24-100 weeks, antibodies to EYLEA were detected in a similar percentage range of patients. There were no differences in efficacy or safety between patients with or without immunoreactivity.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy. Pregnancy Category C. Afibercept produced embryofetal toxicity when administered every three days during organogenesis to pregnant rabbits at intravenous doses ≥3 mg per kg, or every six days at subcutaneous doses ≥0.1 mg per kg. Adverse embryo-fetal effects included increased incidences of postimplantation loss and fetal malformations, including anasarca, umbilical hernia, diaphragmatic hernia, gastroschisis, cleft palate, ectrodactyly, intestinal atresia, spina bifida, encephalomeningocele, heart and major vessel defects, and skeletal malformations (fused vertebrae, sternabrae, and ribs; supernumerary vertebral arches and ribs; and incomplete ossification). The maternal No Observed Adverse Effect Level (NOAEL) in these studies was 3 mg per kg. Afibercept produced fetal malformations at all doses assessed in rabbits and the fetal NOAEL was less than 0.1 mg per kg. Administration of the lowest dose assessed in rabbits (0.1 mg per kg) resulted in systemic exposure (AUC) that was approximately 10 times the systemic exposure observed in humans after an intravitreal dose of 2 mg. There are no adequate and well-controlled studies in pregnant women. EYLEA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers. It is unknown whether afibercept is excreted in human milk. Because many drugs are excreted in human milk, a risk to the breastfed child cannot be excluded. EYLEA is not recommended during breastfeeding. A decision must be made whether to discontinue nursing or to discontinue treatment with EYLEA, taking into account the importance of the drug to the mother.

8.4 Pediatric Use. The safety and effectiveness of EYLEA in pediatric patients have not been established.

8.5 Geriatric Use. In the clinical studies, approximately 76% (2049/2701) of patients randomized to treatment with EYLEA were ≥65 years of age and approximately 46% (1250/2701) were ≥75 years of age. No significant differences in efficacy or safety were seen with increasing age in these studies.

17 PATIENT COUNSELING INFORMATION

In the days following EYLEA administration, patients are at risk of developing endophthalmitis or retinal detachment. If the eye becomes red, sensitive to light, painful, or develops a change in vision, advise patients to seek immediate care from an ophthalmologist (see Warnings and Precautions). Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations (see Adverse Reactions). Advise patients not to drive or use machinery until visual function has recovered sufficiently.

REGENERON

Manufactured by:
Regeneron Pharmaceuticals, Inc.
777 Old Saw Mill River Road
Tarrytown, NY 10591-6707

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Regeneron U.S. Patents 7,070,959;
7,303,746; 7,303,747; 7,306,799;
7,374,757; 7,374,758; 7,531,173;
7,608,261; 7,972,598; 8,029,791;
8,092,803; 8,647,842; and other
pending patents. LEA-0721



Discover Strength in efficacy

As demonstrated in phase 3 clinical trials in patients with Wet AMD, Macular Edema following RVO, DME, and DR in patients with DME

Choose EYLEA® (aflibercept) Injection from the start

Learn about EYLEA at EYLEA.us/op

INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

- EYLEA® (aflibercept) Injection is indicated for the treatment of patients with Neovascular (Wet) Age-related Macular Degeneration (AMD), Macular Edema following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR) in Patients with DME.

CONTRAINDICATIONS

- EYLEA® (aflibercept) Injection is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA.

WARNINGS AND PRECAUTIONS

- Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. Intraocular inflammation has been reported with the use of EYLEA.
- Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.

- There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

ADVERSE REACTIONS

- Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment.
- The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous floaters, intraocular pressure increased, and vitreous detachment.

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

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EYLEA®
(aflibercept) Injection
For Intravitreal Injection
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