SPECIAL ISSUE: **LIFESTYLE, THE EVIDENCE**

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Evidence-Based DIABETES MANAGEMENT™

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ABOUT THIS SPECIAL ISSUE

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PAYER PERSPECTIVE

New physical activity guidelines from the American Diabetes Association reflect growing evidence that employers should promote physical activity. A 2016 agreement between Aetna and Apple made the Apple Watch available to the payer's employees at a reduced cost, and the program may expand to select Aetna customers to promote movement during the work day, **SP131**.

PAYING FOR "NUDGES"

As digital health expands, healthcare must figure out how to pay for the ongoing support it provides. Bundled payments are a possibility, and so are models based on other industries, **SP132**.

PHOTO OF ACCU-CHEK 360 AVIVA EXPERT METER, COURTESY OF ROCHE DIAGNOSTICS.

IN THE TRENCHES

Results of a community-based diabetes management program in Mount Airy, North Carolina, show what comes from listening to patients and taking cultural cues, **SP134**.

YOGA, MINDFULNESS, AND MANAGED CARE

As the evidence accumulates that these practices reduce stress and improve health, can yoga and mindfulness adapt to healthcare payment models? Or should managed care adapt instead? **SP137**.

BEHAVIORAL EVIDENCE

Diabetes: An Opportunity to Have a Lasting Impact on Health Through Lifestyle Modification

Hena N. Patel, MD; Andrew M. Freeman, MD, FACC; and Kim A. Williams MD, FACC

TYPE 2 DIABETES (T2D) IS a costly chronic illness that is increasing in prevalence and associated with significant health problems, including cardiovascular disease (CVD).[1] In fact, CVD is listed as the cause of death in nearly 65% of individuals with diabetes.[2]

Historically, T2D was labeled a "coronary artery disease equivalent" in light of the 7-year risk of myocardial infarction (MI) equaling that of a person without diabetes who is post-MI[3] in the prestatin-treatment era and the marked improvement in adverse cardiac events with statin therapy.[4] Given this grave prognosis, and with longstanding work showing diabetes remission from lifestyle interventions as far back as the 1940s,[5] there is no better and more economical way to treat this epidemic.

EVIDENCE IS ACCUMULATING THAT DIETARY CONTENT AFFECTS THE DEVELOPMENT OF DIABETES. COMPARED WITH A STANDARD AMERICAN DIET THE PREVALENCE OF DIABETES WAS REDUCED 23% WITH A SEMI-VEGETARIAN DIET AND 75% WITH A VEGAN DIET. © JOLOPES /FOTOLIA

Diabetes and CVD share multiple modifiable lifestyle risk factors, such as obesity and physical inactivity, that tend to comingle for many adults, adding to the threat of severe adverse effects already present from a genetic predisposition and other acquired risk factors.[6-8] In the United States, diabetes affects at least 29.1 million individuals, the equivalent of 9.3% of the entire population and 12.3% of the adult population.[9] Depending on the cohort surveyed and the definition used, another 5.4 million are estimated to have undiagnosed diabetes.[9]

CONTINUED ON SP144

ORIGINAL RESEARCH

Differential Weight Loss Effects on Type 2 Diabetes Remission Among Adults

Virender Kumar, PhD; William Encinosa, PhD; Hena Thakur; and Kisha Thakur

Introduction

Generally, type 2 diabetes (T2D) has been viewed as a chronic, progressive, and controllable, but irreversible, disease.[1] Interventions that occur soon after diagnosis reduce the risk of macro- and microvascular disease and can slow disease progression.[2] However, plasma glucose continues to increase regardless of the intensity of diabetes control or treatment type.[3] Nevertheless, a number of clinical trials and case-control studies have, over time, reported a remission in T2D with bariatric weight loss surgery or with intensive lifestyle management.[4-11]

Recently, a retrospective study using a cohort of adults with T2D identified with administrative data from Kaiser Permanente, Northern California, suggested that T2D remissions do occur without bariatric surgery, but are rare.[12] The study found that the cumulative incidences of partial and prolonged diabetes remission over a period of 7 years were 1.5% and 0.007%, respectively.

CONTINUED ON SP147

DIGITAL HEALTH

Reaching Beyond the Exam Room: How Technology-backed Lifestyle Intervention Is Improving Health Outcomes for Diabetes and Hypertension Management

Andreas Michaelides, PhD, and Ed Pienkosz, MS

IN 2003, SUSAN L. NORRIS, MD, MPH, a researcher at McMaster University, Ohio State University, and the CDC Center for Diabetes Translation, and her colleagues sought an operational definition of chronic disease management. Based on their review

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FEATURES

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FROM THE CHAIRMAN

The Evidence on Lifestyle Management and the Role of Payers

MIKE HENNESSY, SR

THIS ISSUE OF *Evidence-Based Diabetes Management*™ reveals the quiet revolution happening in diabetes care: fed up with rising morbidity and the costs of diabetes and obesity, policy makers, public health leaders, and payers are seeking new ways to prevent diabetes or slow its progression.

As patient-centered, value-based payment models gain ground, US health systems are seeking new ways to help those at risk embrace healthier diets, exercise, and stress reduction strategies. We are learning more about the role of sleep in taming insulin resistance. The overview of evidence from Hena N. Patel, MD; Andrew M. Freeman, MD, FACC; and Kim A. Williams MD, FACC, reveals the measurable benefits of improved nutrition and activities such as yoga and meditation. As the article by Virender Kumar, PhD; William Encinosa, PhD; Hena Thakur; and Kisha Thakur shows, for a subset of patients, lifestyle management can even reverse diabetes.

The question for payers is: how can this knowledge be translated into cost-effective programs of care? If health insurers are inclined to pay for these activities, how can they decide which ones are worthy of reimbursement? Finally, as Virta Health's Mike Payne, MBA, MSci, discusses, how do we pay for ongoing support when our old models of care require a visit to the doctor or nurse? Aetna's Kenneth Snow, MD, MBA, shares how payers must rethink their definition of what constitutes "exercise" in light of new evidence that small steps matter, literally.

Throughout this issue, readers will appreciate the growing role of technology in giving patients the push they need to stick with a lifestyle management program. It remains to be seen how the repeal and replacement of the Affordable Care Act will affect Medicare's plans to implement the Diabetes Prevention Program in 2018, but as speakers at the American Enterprise Institute said early in 2017, the move toward value and prevention will continue. Policies should support the entrepreneurial spirit of new companies looking for ways to "meet patients where they are," such as Noom, Virta, and Omada Health. Each has its own approach, but the founders agree that the $245 billion annual cost of diabetes in the United States cannot be sustained.

There will always be a role for new therapies in caring for this disease, but the nation is crying out for ways to keep people healthy in the first place. ◆

Sincerely,
Mike Hennessy, Sr
CHAIRMAN AND CEO

FROM THE EDITOR-IN-CHIEF

Why WAIT Results Highlight the Value of Lifestyle Intervention

ROBERT A. GABBAY, MD, PHD, FACP

GABBAY

MORE CHANGE IS COMING TO the US healthcare system. Experts agree, however, that some things the Affordable Care Act set in motion should not change, including the focus on preventing chronic disease. In diabetes care, we are familiar with this statistic: the disease costs the United States $245 billion a year in medical costs and lost productivity.[1] Therefore, since it's been shown that it costs 2.3 times more to care for someone with diabetes than a person who stays free of disease, preventing diabetes, or stopping its progression, has the potential to save Medicare billions of dollars.[2]

While genetics certainly plays a role in who develops diabetes, improvements in lifestyle—through healthier diets, more (or different) exercise, getting enough sleep, and reducing stress—can go a long way toward preventing diabetes or slowing complications among those already diagnosed. For years, the secrets of helping people stick with healthier habits have proved elusive—but this is changing.

At Joslin Diabetes Center, we've spent years following the success of the Why WAIT study, led by Osama Hamdy, MD, PhD, FACE. Why WAIT (Weight Achievement and Intensive Management) is an initial 12-week multidisciplinary intervention for obese patients who have diabetes. It combines disease management, improved nutrition, and exercise, especially the maintenance of muscle mass through strength training. The program also focuses on medication adherence and includes team-based care from endocrinologists, dietitians, exercise physiologists, behavioral health providers, and diabetes educators. And it has produced fantastic results: an average weight loss of 23.8 pounds, or 9.7% of body weight, after 12 weeks, most of which has been maintained after a year.

WHILE GENETICS PLAYS A ROLE IN WHO DEVELOPS DIABETES, LIFESTYLE IMPROVEMENTS CAN GO A LONG WAY IN PREVENTING OR REDUCING COMPLICATIONS.

New results published in January show that the benefits of the Why WAIT intervention can last 5 years. On average, participants maintained a weight loss of 16 pounds, or 6.4% of body weight. This is significant because weight loss of this magnitude is considered "transformational," meaning it produces lasting health benefits.[3]

As Dr Hamdy and his colleagues found, at the 5-year mark, Why WAIT revealed something else: some patients who did not keep the weight off maintained certain benefits. There also was a sharp difference between those who lost 7% of their body weight during the initial intervention and those who did not: those who were less successful with weight loss had markedly higher glycated hemoglobin levels at the 5-year mark, even though they were taking a lot more medication than the high weight-loss group.

Dr Hamdy tells *Evidence-Based Diabetes Management*™ that these kinds of results don't happen by themselves—they require trained staff to support people working toward a weight loss goal. He is working to share the lessons of Why WAIT with our Joslin affiliates around the country so that more staff can be trained and more patients can benefit.

There are also discussions of piloting Why WAIT with the YMCA, not unlike the group's demonstration of the National Diabetes Prevention Program (DPP), which led to the decision for funding the program in Medicare starting next year.[4] This marked a historic step toward reversing long-term trends of type 2 diabetes in the United States, since more than half the population aged 65 or older is living with prediabetes.[5] Assuming the program launches next year »

FROM THE EDITOR-IN-CHIEF *(continued)*

WHY WAIT STUDY PARTICIPANTS. PHOTO COURTESY OF JOSLIN DIABETES CENTER.

on schedule, it will be the first time a diabetes preventive service becomes eligible for widespread coverage through Medicare.[6] Scaling a program that meets the needs of patients who already have diabetes could spare them complications such as eye problems, heart disease, or limb loss.

PAYER SUPPORT FOR LIFESTYLE INTERVENTION ISN'T UNIVERSAL. MEDICARE IS STILL WORKING ON REIMBURSEMENT FOR THE DIABETES PREVENTION PROGRAM.

Payer support for lifestyle intervention isn't universal, however. Medicare is still working out the reimbursement details for DPP, and it's struggling with how to add digital providers[4] despite their increased popularity among commercial payers and employers. As the cost of diabetes care rises, the case for funding prevention will be more compelling and more payers may ask, "Why wait?" ◆

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EDITORIAL MISSION

To present policy makers, payers, and providers with the clinical, pharmacoeconomic, and regulatory information they need to improve efficiency and outcomes in diabetes.

PAYER PERSPECTIVE

Payer-Provided Fitness Rewards: Employers Will Look At Evidence

Kenneth Snow, MD, MBA

TYPE 2 DIABETES (T2D) IS A DISEASE that is profoundly influenced by lifestyle. The value of exercise in helping prevent or control T2D is well recognized. As such, suggestions to add exercise to treatment have been a standard part of diabetes care. These often translate into recommendations for formal exercise programs only, which means the contributions from daily activities can be easily overlooked.

Over the past several decades, the amount of activity performed as part of daily living has decreased. Shifts in transportation from walking to driving, shopping over the internet rather than at the mall, and home entertainment opportunities have contributed significantly to this drop in activity. The nature of the workplace also has changed for many people, with greater amounts of time spent in front of a computer screen. In addition, people who have not been participating in an exercise program for decades are often not willing to add one, such as attending a gym, on a regular basis. Those who do may not continue with it long term. As such, while exercise may be an effective therapy, the recommendation to participate in an exercise program can have limited efficacy.

The recognition of the limits of adhering to an exercise program has led to a growing understanding that therapy may not necessarily be an exercise program, but rather that it should include an increase in the amount of aerobic activity in which someone participates each day. This activity might include walking, dancing, and even gardening. This activity should be added in throughout the day as part of activities of daily living. Walking to a store rather than driving, or driving to the mall but parking in a distant parking space, can add activity during the course of the day without the requirement to schedule formal activity. Less valuable is the type of activity; the degree of activity performed and the person's persistence or willingness to continue the activity in the long term are more important.

A recent study by Dempsey et al[1] demonstrated that brief periods of low-level activity, such as walking, can have a significant positive effect on improving insulin resistance compared with prolonged sitting. This information, combined with what is already known about the benefits of exercise,[2] has led the American Diabetes Association (ADA) to recommend that adults should interrupt prolonged periods of sitting every 30 minutes, as well as participate in a regular exercise program. The recommendation was featured for the first time in the *2017 Standards of Medical Care in Diabetes*.[3]

Paying to be Well. Aetna, like many other payers, has recognized that encouraging healthy behaviors will improve the health and wellness of our members, which should also decrease healthcare expenditures in the future. Wellness initiatives have been developed for employers to encourage their employees to participate in health programs and screenings that can improve their well-being. Subsidies for gym memberships help encourage physical activity. Rewards for participating in screenings for metabolic syndrome are common. In addition, by identifying health issues that can be modified—such as being overweight or having high blood pressure, elevated cholesterol, or impaired glucose tolerance—the hope is that members will make positive changes to improve their health. The early identification of these types of health problems can spur visits to primary care physicians to initiate treatment.

However, joining a gym does not necessarily translate into going to the gym, either intermittently or in any sustained fashion, and participating in a metabolic syndrome screening may uncover health issues, but there is no guarantee that the person will follow up with their healthcare provider, let alone make positive changes in their lives to address these issues. Exercise and activity levels have always been difficult to measure. Although dietary success can be assessed with weight, no simple measurement exists to assess participation in an exercise regimen. However, the advent of convenient activity tracking technology, such as the Apple Watch, Fitbit, and others, provides a way for people to track their level of activity and fitness, which was not possible in the past.

In 2016, Aetna entered into an agreement with Apple that makes the Apple Watch available to Aetna employees at a reduced cost. Financial rewards for Aetna employees participating in health-related activities, such as a metabolic screening, can be applied to the cost of the device. This program is also being offered to select Aetna customers, with plans to expand in the future. Not only does the new tracking technology provide an individual with the opportunity to better understand and track their own activity, it also enables a large employer, to understand the activity of its workforce.

The addition to the 2017 ADA guideline[3] recommending interrupting periods of prolonged sitting with activity every 30 minutes is one intervention that can now be assessed using this new technology. Data from fitness monitors can be retrieved and analyzed. At the simplest level, the information can be examined to see if certain behaviors, such as taking periodic breaks, occur. Even more exciting are the potential insights following data analysis. Behavioral activities that have been shown to be of benefit in controlled trials can be crowdsourced to see if the same benefits occur when scaled to large populations of people.

Naturally, lifestyle changes can only have an impact if they are actually implemented. The ability to reliably assess whether these changes actually occur allows employers to reward their employees for meeting activity-based metrics. These rewards for living a healthier life can be tied to ongoing and impactful health activities. They could be similar to those that are now provided for one-time health-related activities, such as contributions to health savings accounts, or they could occur for ongoing exercise participation, achieving certain levels of daily activity (such as meeting a weekly step target), or taking short breaks every 30 minutes to interrupt prolonged periods of sitting.

The likelihood of an employer adopting a fitness-based health rewards stystem depends on the ability to easily and reliably track the needed information, the impact on the health and well-being of their employees, and the strength of the evidence to support the activity. Although the level of evidence does not need to be as rigorous as what FDA requires for a new drug or medical device, more support from clinical studies and greater recognition of value from specialty societies means the recommendation is more likely to be adopted. The recent addition to the ADA guidelines of the need to avoid prolonged periods of inactivity is the type of support that helps these activities become commonplace. Adoption by other companies will require a growing level of comfort with the technology and a broader adoption—as Aetna has done. ◆

SNOW

Kenneth Snow, MD, MBA, is a medical director for Aetna. He has developed protocols for value-based reimbursement plans, including those in Medicare.

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FOR ADULTS WITH TYPE 2 DIABETES AND ESTABLISHED CV DISEASE*

Jardiance®
(empagliflozin) tablets
10 mg/25 mg

The only FDA-approved type 2 diabetes medication indicated to reduce the risk of CV death

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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 indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.

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 and symptomatic hypotension may occur. Before initiating JARDIANCE, assess and correct volume status in the elderly, in patients with renal impairment, low systolic blood pressure, or on diuretics. Monitor for hypotension.

Ketoacidosis

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 sodium glucose co transporter 2 (SGLT2) inhibitors, including JARDIANCE. Fatal cases of ketoacidosis have been reported in patients taking JARDIANCE. Patients who present with signs and 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 risk factors for ketoacidosis. Patients on JARDIANCE may require monitoring and temporary discontinuation in situations known to predispose to ketoacidosis.

Please see Important Safety Information and Brief Summary of Prescribing Information on adjacent pages.

*Patients with coronary artery disease, peripheral artery disease, or a history of myocardial infarction or stroke.
CV=cardiovascular.

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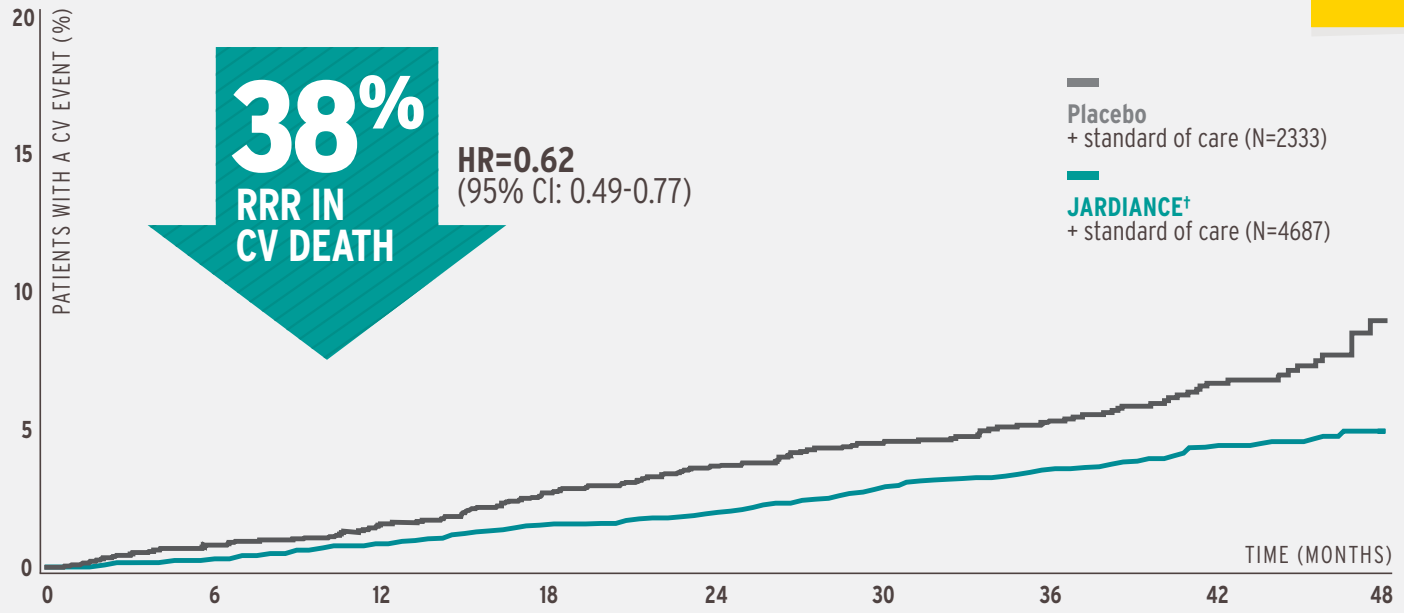
JARDIANCE powerfully reduced the risk of CV death on top of standard of care*

A consistent finding for the two JARDIANCE dosing strengths, 10 mg and 25 mg

REDUCED RISK OF CV DEATH



Absolute rates for CV death
3.7% JARDIANCE
VS 5.9% placebo

2.2%
ABSOLUTE RISK REDUCTION

EARLY AND SUSTAINED REDUCTIONS IN CV DEATH[1]

JARDIANCE DEMONSTRATED A 14% RRR FOR THE PRIMARY COMPOSITE ENDPOINT (p=0.04)

- **The absolute risk reduction for the composite endpoint was 1.6%**
- **There was no change in risk of nonfatal MI (HR=0.87 [95% CI: 0.70-1.09]) or nonfatal stroke (HR=1.24 [95% CI: 0.92-1.67]); the 14% RRR in CV events was due to a reduction in the risk of CV death (HR=0.62 [95% CI: 0.49-0.77])**

*Glucose-lowering and CV medications.

†Pooled data from JARDIANCE 10 mg and JARDIANCE 25 mg; similar magnitude of reduction was shown with both doses.

CI=confi dence interval; HR=hazard ratio; MI=myocardial infarction; RRR=relative risk reduction.

Study Design: A randomized, double-blind, parallel-group trial comparing the risk of experiencing a major adverse cardiovascular event between JARDIANCE and placebo when these were added to and used concomitantly with standard of care treatments for type 2 diabetes and cardiovascular disease. A total of 7020 patients were treated (JARDIANCE 10 mg [N=2345]; JARDIANCE 25 mg [N=2342]; placebo [N=2333]) and followed for a median of 3.1 years. All patients had established atherosclerotic cardiovascular disease at baseline, including one or more of the following: a documented history of coronary artery disease, stroke, or peripheral artery disease. The primary outcome was reduction in risk of cardiovascular events, defi ned by the composite of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Acute Kidney Injury and Impairment in Renal Function

JARDIANCE causes intravascular volume contraction and can cause renal impairment. Acute kidney injury requiring hospitalization and dialysis have been identified in patients taking SGLT2 inhibitors, including JARDIANCE; some reports involved patients younger than 65 years of age. Before initiating JARDIANCE, consider factors that may predispose patients to acute kidney injury including hypovolemia, chronic renal insufficiency, congestive heart failure and concomitant medications (diuretics, ACE inhibitors, ARBs, NSAIDs). Consider temporary discontinuation in settings of reduced oral intake or fluid losses. Monitor patients for signs and symptoms of acute kidney injury. If acute kidney injury occurs, discontinue JARDIANCE promptly and institute treatment.

JARDIANCE increases serum creatinine and decreases eGFR. Patients with hypovolemia may be more susceptible to these changes. Renal function should be evaluated prior to initiating JARDIANCE and periodically thereafter. More frequent monitoring is recommended in patients with eGFR <60 mL/min/1.73 m^2. JARDIANCE should be discontinued in patients with a persistent eGFR <45 mL/min/1.73 m^2.

Urosepsis and Pyelonephritis

Serious urinary tract infections including urosepsis and pyelonephritis requiring hospitalization have been identified 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.

Please see Important Safety Information and Brief Summary of Prescribing Information on adjacent pages.

FOR ADULTS WITH TYPE 2 DIABETES
AND ESTABLISHED CV DISEASE

Jardiance®
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JARDIANCE offers protection against the risk of CV death on top of standard of care

THE ONLY FDA-APPROVED
type 2 diabetes medication indicated to reduce the risk of CV death

38%
RRR IN CV DEATH
vs placebo on top of standard of care
2.2% absolute risk reduction
HR=0.62 (95% CI: 0.49-0.77)

CONVENIENT ORAL DOSING
taken once daily in the morning

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IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

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 when used in combination with JARDIANCE.

Genital Mycotic Infections
JARDIANCE increases the risk for genital mycotic infections, especially in patients with prior infections. Monitor and treat as appropriate.

Increased Low-Density Lipoprotein Cholesterol (LDL-C)
Monitor and treat as appropriate.

ADVERSE REACTIONS
The most common adverse reactions (>5%) associated with placebo and JARDIANCE 10 mg and 25 mg were urinary tract infections and female genital mycotic infections.

DRUG INTERACTIONS
Diuretics may enhance the potential for volume depletion when administered with JARDIANCE.

USE IN SPECIAL POPULATIONS

Pregnancy
JARDIANCE is not recommended during the second and third trimesters of pregnancy based on animal data showing adverse renal effects.

Lactation
JARDIANCE is not recommended while breastfeeding because of the potential for serious adverse reactions in breastfed infants.

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

JAR PROF ISI 12.3.16

Please see Important Safety Information and Brief Summary of Prescribing Information on adjacent pages.

Boehringer Ingelheim

Lilly

JARDIANCE® (empagliflozin) tablets, for oral use

BRIEF SUMMARY OF PRESCRIBING INFORMATION

℞ only

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; to reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and established cardiovascular disease. Limitations 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. Fatal cases of ketoacidosis have been reported in patients taking 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). **Acute Kidney Injury and Impairment in Renal Function:** JARDIANCE causes intravascular volume contraction *[see Warnings and Precautions]* and can cause renal impairment *[see Adverse Reactions]*. There have been postmarketing reports of acute kidney injury, some requiring hospitalization and dialysis, in patients receiving SGLT2 inhibitors, including JARDIANCE; some reports involved patients younger than 65 years of age. Before initiating JARDIANCE, consider factors that may predispose patients to acute kidney injury including hypovolemia, chronic renal insufficiency, congestive heart failure and concomitant medications (diuretics, ACE inhibitors, ARBs, NSAIDs). Consider temporarily discontinuing JARDIANCE in any setting of reduced oral intake (such as acute illness or fasting) or fluid losses (such as gastrointestinal illness or excessive heat exposure); monitor patients for signs and symptoms of acute kidney injury. If acute kidney injury occurs, discontinue JARDIANCE promptly and institute treatment. JARDIANCE increases serum creatinine and decreases eGFR. Patients with hypovolemia may be more susceptible to these changes. Renal function abnormalities can occur after initiating JARDIANCE *[see Adverse Reactions]*. Renal function should be evaluated prior to initiation of JARDIANCE and monitored periodically thereafter. More frequent renal function monitoring is recommended in patients with an eGFR below 60 mL/min/1.73 m^2. Use of JARDIANCE is not recommended when eGFR is persistently less than 45 mL/min/1.73 m^2 and is contraindicated in patients with an eGFR less than 30 mL/min/1.73 m^2 *[see Contraindications, Use in Specific Populations]*. **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.

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]*; Acute Kidney Injury and 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 m^2). 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%

[a]Predefined adverse event grouping, including, but not limited to, urinary tract infection, asymptomatic bacteriuria, cystitis

[b]Female 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).

[c]Predefined adverse event grouping, including, but not limited to, polyuria, pollakiuria, and nocturia

[d]Male 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 of 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. *Acute Impairment in Renal Function:* Treatment with 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]*. In a long-term cardiovascular outcome trial, the acute impairment in renal function was observed to reverse after treatment discontinuation suggesting acute hemodynamic changes play a role in the renal function changes observed with empagliflozin.

Table 2: Changes from Baseline in Serum Creatinine and eGFR[a] 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[b]		
		Placebo		**JARDIANCE 25 mg**
Baseline Mean	N	187	–	187
	Creatinine (mg/dL)	1.49	–	1.46
	eGFR (mL/min/1.73 m^2)	44.3	–	45.4
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
Post-treatment Change[c]	N	98	–	103
	Creatinine (mg/dL)	0.03	–	0.02
	eGFR (mL/min/1.73 m^2)	0.16	–	1.48

[a]Observed cases on treatment.
[b]Subset of patients from renal impairment study with eGFR 30 to less than 60 mL/min/1.73 m^2
[c]Approximately 3 weeks after end of treatment.

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[c]

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 +/- Metformin (18 weeks[d])	**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[d])	**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%

[a]Overall hypoglycemic events: plasma or capillary glucose of less than or equal to 70 mg/dL
[b]Severe hypoglycemic events: requiring assistance regardless of blood glucose
[c]Treated set (patients who had received at least one dose of study drug)
[d]Insulin dose could not be adjusted during the initial 18 week treatment period

Genital Mycotic Infections: In the pool of 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). Phimosis 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 of 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 randomized 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: *Risk Summary:* Based on animal data showing adverse renal effects, JARDIANCE is not recommended during the second and third trimesters of pregnancy. Limited data available with JARDIANCE in pregnant women are not sufficient to determine a drug-associated risk for major birth defects and miscarriage. There are risks to the mother and fetus associated with poorly controlled diabetes in pregnancy *[see Clinical Considerations]*. In animal studies, adverse renal changes were observed in rats when empagliflozin was administered during a period of renal development corresponding to the late second and third trimesters of human pregnancy. Doses approximately 13-times the maximum clinical dose caused renal pelvic and tubule dilatations that were reversible. Empagliflozin was not teratogenic in rats and rabbits up to 300 mg/kg/day, which approximates 48-times and 128-times, respectively, the maximum clinical dose of 25 mg when administered during organogenesis *[see Data]*. The estimated background risk of major birth defects is 6-10% in women with pre-gestational diabetes with a HbA1c >7 and has been reported to be as high as 20-25% in women with HbA1c >10. The estimated background risk of miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively. Clinical Considerations: *Disease-associated maternal and/or embryo/fetal risk:* Poorly controlled diabetes in pregnancy increases the maternal risk for diabetic ketoacidosis, pre-eclampsia, spontaneous abortions, preterm delivery, stillbirth, and delivery complications. Poorly controlled diabetes increases the fetal risk for major birth defects, still birth, and macrosomia related morbidity. *Data:* Animal Data: Empagliflozin dosed directly to juvenile rats from postnatal day (PND) 21 until PND 90 at doses of 1, 10, 30 and 100 mg/kg/day caused increased kidney

weights and renal tubular and pelvic dilatation at 100 mg/kg/day, which approximates 13-times the maximum clinical dose of 25 mg, based on AUC. These findings were not observed after a 13 week drug-free recovery period. These outcomes occurred with drug exposure during periods of renal development in rats that correspond to the late second and third trimester of human renal development. In embryo-fetal development studies in rats and rabbits, empagliflozin was administered for intervals coinciding with the first trimester period of organogenesis in humans. Doses up to 300 mg/kg/day, which approximates 48-times (rats) and 128-times (rabbits) the maximum clinical dose of 25 mg (based on AUC), did not result in adverse developmental effects. In rats, at higher doses of empagliflozin causing maternal toxicity, malformations of limb bones increased in fetuses at 700 mg/kg/day or 154-times the 25 mg maximum clinical dose. In the rabbit, higher doses of empagliflozin resulted in maternal and fetal toxicity at 700 mg/kg/day, or 139-times the 25 mg maximum clinical dose. In pre- and postnatal development studies in pregnant rats, empagliflozin was administered from gestation day 6 through to lactation day 20 (weaning) at up to 100 mg/kg/day (approximately 16 times the 25 mg maximum clinical dose) without maternal toxicity. Reduced body weight was observed in the offspring at greater than or equal to 30 mg/kg/day (approximately 4 times the 25 mg maximum clinical dose). **Lactation:** *Risk Summary:* There is no information regarding the presence of JARDIANCE in human milk, the effects of JARDIANCE on the breastfed infant or the effects on milk production. Empagliflozin is present in the milk of lactating rats *[see Data]*. 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 of the potential for serious adverse reactions in a breastfed infant, advise women that use of JARDIANCE is not recommended while breastfeeding. *Data:* Empagliflozin was present at a low level in rat fetal tissues after a single oral dose to the dams at gestation day 18. In rat milk, the mean milk to plasma ratio ranged from 0.634 -5, and was greater than one from 2 to 24 hours post-dose. The mean maximal milk to plasma ratio of 5 occurred at 8 hours post-dose, suggesting accumulation of empagliflozin in the milk. Juvenile rats directly exposed to empagliflozin showed a risk to the developing kidney (renal pelvic and tubular dilatations) during maturation. **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. In studies assessing the efficacy of empagliflozin in improving glycemic control in patients with type 2 diabetes, 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 glycemic 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 m^2, 91 patients exposed to JARDIANCE had an eGFR between 45 and 60 mL/min/1.73 m^2 and 97 patients exposed to JARDIANCE had an eGFR between 30 and 45 mL/min/1.73 m^2. 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. In a large cardiovascular outcomes study, there were 1819 patients with eGFR below 60 mL/min/1.73 m^2. The cardiovascular death findings in this subgroup were consistent with the overall findings. 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 Bundle of Nudges: Healthcare Payment in an Era of Behavioral Science

Mike Payne, MBA, MSci

PAYNE

Mike Payne, MBA, MSci, is currently head of commercial and policy at Virta Health. He last served as chief commercial officer and head of medical affairs at Omada Health. Previously, he worked at Gilead Sciences, Accenture, and McKinsey & Company.

ACCORDING TO THE CDC, the majority of deaths in the United States are due to diseases that are largely preventable. [1] Chronic diseases, such as diabetes, certainly have genetic components, but their etiology is also profoundly behavioral—driven by choices that individual patients make on a day-by-day, minute-by-minute basis.

A great deal of research has been done on maladaptive behaviors that people exhibit in the near term, even when they know that a different choice is best for the long term.[2] This phenomenon is accentuated among people facing alternatives that involve an addictive choice like alcohol[3] or sugar.[4] These choices often are informed by cognitive biases, notably attentional bias[5] and evaluative bias.[6]

Richard Thaler and Cass Sunstein's behavioral economics book *Nudge* is a broad romp through social policies that can influence a wide range of human behaviors to help people overcome cognitive biases.[7] The general point of the book—that behavioral science can and should be used to guide the libertarian free choices of people to better outcomes in the face of cognitive biases—has profound implications for healthcare in a world in which an increasing proportion of health gains are being pursued through behaviorial change and maintenance.

Progressive thinkers in healthcare are certainly on the case. Health and medical services that provide continuous, on-demand care, or "nudges" to behaviors associated with chronic disease, are proliferating, often facilitated by information technology and accompanied by published clinical results. There are simple care process improvement nudges to remind patients of immunizations, like Voxiva's text service, which was shown to produce a 30% improvement in influenza vaccination rates among women.[8]

In another example, more focused on direct delivery of "care nudges," Virta Health's Diabetes Reversal Clinic provides consistent personalized, electronically delivered nudges—the frequency of which vary—to individuals with type 2 diabetes (T2D) from Virta physicians and health coaches. Virta also provides personalized education to patients on a daily basis. Recent data show that the clinic achieved a 54% reversal of diabetes among its patients with T2D in just 70 days.[9]

MANY RIGOROUS HEALTH SERVICES FOR CHRONIC CONDITIONS NOW INVOLVE CONTACTING PATIENTS THROUGH INTELLIGENT TECHNOLOGY RATHER THAN HAVING A CLINICIAN MANUALLY EXECUTE ALL EFFORTS.

Most people believe that technology-enabled nudges make up the care model they need to address chronic disease. But traditional payment schemes for healthcare are ill-equipped to properly reimburse for nudge-based care, as recognized by many, including a recent, high-profile panel at the J.P. Morgan Healthcare Conference.[10] Traditional fee-for-service (FFS) models provide reimbursement for relatively long and in-person—or, as of late, telemedicine—visits. For example, in a model in which a Virta health coach contacts a patient 3 times a day with small nudges, it is administratively burdensome and overly costly to submit 3 insurance claims because of the $8-per-claim cost for such expenses as software/hardware, processing, and back-end collections.[11] On average, Virta and its patients interact 13 times per week; under a FFS model, submitting claims at this rate would not be practical in this case.

Furthermore, many rigorous health services for chronic conditions now involve contacting patients through intelligent technology rather than having a clinician manually execute all efforts involved in the interaction. For example, ginger.io, an online care service to combat depression and anxiety, uses machine learning to evaluate device sensor data and patient survey responses to support the provision of more personalized care.[12] The sensor and survey data are often supplied many times per day. In a FFS world in which there are only codes for medical devices and human–clinician visits, there are few, if any, codes that exist for these frequent high-value patient touchpoints driven by technology rather than humans.

Like ginger.io, the Virta model is a particularly challenging one for a FFS environment, since it involves a broad variety of touchpoints with patients: clinician interaction, technology-personalized educational curriculum delivered via text and video, and measurement and tracking of patient biometrics. Virta touchpoints with patients also happen both real-time as well as asynchronously in an online chat-style interface, allowing the patient to engage whenever it is convenient for them. Applying a FFS claims approach to this care setting would lead to drastic underappreciation of the value provided by the Virta Diabetes Reversal Clinic.

These are just 2 examples, of many. Rock Health, a venture fund dedicated to digital health, notes that of 300 digital health funding deals executed in 2016, 15% were investments into nudge-based care companies.[13]

There are 2 potential solutions here:

- **Per nudge:** reformulate coding rules to allow the creation of codes for nudges as outlined above and to reduce claims transaction costs to pennies. To use a music payment analogy, this is the "pay per song" model espoused for a decade by Apple.
- **Bundle of Nudges:** providers get no reimbursement for individual nudges; they are paid a per-patient amount for a bundle of services to be provided, preferably with payment based on agreed-upon clinical outcomes achieved by the nudges, rather than just payment for the bundle of nudges itself. In effect, this is a value-based bundled payment model similar to the Comprehensive Care for Joint Replacement model tested by Medicare for knee and hip-replacement surgery—but applied to treatment for chronic care.

The Bundle of Nudges approach is a clearly preferable model. It does not require massive overhaul of claims systems or FFS coding rules and it allows for further innovation and application of technology to the achievement of desired behavioral change and mod-

ification. So what is standing in the way of a Bundle of Nudges payment from catching on? Three key hurdles must be overcome.

First, health insurance carrier leaders must embrace the idea that technology-enabled remote healthcare services can be as good as, or better than, in-person versions of similar programs, especially in disease states for which nudge-based approaches are considered standard-of-care. A recent example of a large payer ignoring such an undeniable trend can be seen in CMS' decision not to reimburse for digitally delivered Diabetes Prevention Programs (DPPs) during year 1 of coverage under the new Medicare Diabetes Prevention Program (MDPP)[14] despite the existence of quality data from DPP providers, such as Omada Health.[15] This regrettable decision by CMS is a setback, but should not deter the proliferation of technology-enabled, nudge-based healthcare services. Insurers in private markets are leading the way by agreeing to work with such companies, [16] and digital providers have organized under the Council for Diabetes Prevention[17] to press Medicare to include them when MDPP reimbursement rules are finalized later this year.

Second, we must agree on the clinical outcome that the nudges are intended to achieve and for which providers of nudge-based care models—like Virta—will be reimbursed. In the area of diabetes, Virta's model is to get paid if, and only if, specific HbA1c targets are achieved and/or maintained. Although this may seem like common sense, agreement on value-based clinical metrics is hard to achieve in healthcare, so visionary health plan leaders need to "put a stake in the ground" on what good management of chronic disease looks like from an outcomes perspective.

Third, health insurance carriers must pave the way for speedy signing of contracts using Bundle of Nudges schemes. Currently, most health plans have a provider network contracting group that is responsible for signing FFS network contracts and a medical management group that is responsible for evaluating more innovative models, like bundled-payment models. The problem is, the medical management groups are often not empowered or incentivized to sign these bundled-payment contracts quickly since they are new and untested. However, most health plan senior executives still say that bundled and value-based payment models, like the Bundle of Nudges concept, are the wave of the future.[18]

This is a particular challenge since many nudge-based treatment approaches are being pioneered by small companies, like Virta Health, that do not have the financial luxury of waiting 5 years to be evaluated and go through the tedious process of securing a bundled payment contract from large health plans. This shorter-term view should not make insurance carriers skittish, however. In general, there are surrogate endpoints for chronic healthcare services, measured at 6-12 months, that can act as reliable statistical proxies for longer-term outcomes. For example, reduction in HbA1c in Virta's clinic has been shown to be highly correlated to 12-month HbA1c and diabetes reversal outcomes and is thus a valid proxy.[19] Insurance carriers need to make it easier for the best of these innovators to secure bundled contracts quickly.

If we are to truly address chronic diseases that have become the largest medical scourge of today's society, we need technology-enabled, nudge-based care to become prevalent. That, in turn, requires health insurance carriers to develop models beyond classic FFS schemes to reimburse bundles of nudges and to make the new bundled-payment schemes quickly available to the clinical innovators, like Virta, that are demonstrating the immense value and potential of nudge-based approaches. ◆

DISCLOSURES

Mike Payne, MBA, MSci, is currently head of commercial and policy at Virta Health. He last served as chief commercial officer and head of medical affairs at Omada Health. Previously, he worked at Gilead Sciences, Accenture, and McKinsey & Company.

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COMMUNITY HEALTH

Making Diabetes Self-Management Education Patient-Centered: Results From a North Carolina Program

Paige Johnson Cartledge, RN, BSN

CARTLEDGE

Paige Johnson Cartledge RN, BSN is the program coordinator of the Diabetic Center of Excellence, Northern Family Medicine, Mount Airy, North Carolina.

AT PRESENT IN THE UNITED STATES, 29 million individuals have diabetes[1] and 86 million have prediabetes, and the CDC estimates that 9 of every 10 persons with prediabetes are unaware of the condition.[2] The annual financial toll of the disease is $245 billion in healthcare and lost productivity costs, according to the American Diabetes Association (ADA).[3]

How can we change these statistics? Based on my experiences as a nurse and diabetes educator, we will not be effective in fighting the nation's diabetes epidemic without more foot soldiers in the trenches alongside our patients. It's during this day-to-day work that we, as diabetes educators, spend time with our patients—evaluating them and encouraging them. Once we understand the daily barriers to success, we can make adjustments for when life happens.

In October 2014, Northwest Medical Partners of Mount Airy, North Carolina, created a Diabetic Center of Excellence. (The practice has since joined Northern Family Medicine of Surry County.[4]) From inception, this center was designed to produce measurable and reportable patient outcomes and, when possible, to reduce the amount of medication patients needed while improving glycated hemoglobin (A1C) levels.[5] The overall goal of this program is to equip each patient with the resources, tools, and empowerment to achieve a quality of life that comes with effective management of diabetes. In the short term, the primary aim of this program is to help patients achieve A1C levels at or below 7.0%, in line with recommended ADA targets.[6]

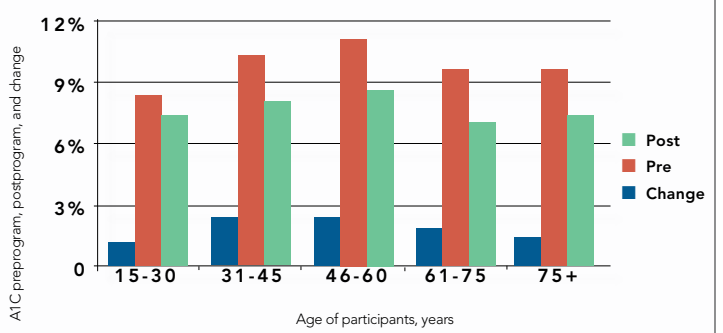
Background of Northwest Medical Partners

D. Nelson Gardner, MD, founded Northwest Medical Partners in 2000 (now part of Northern Family Medicine) to provide care consistent with the principles of the Cooper Institute in Texas. The Cooper Institute's mission is built around preventive health and the value of exercise. With that front-and-center, the institute works with leading academic institutions on scientific research in these areas.[7] Gardner built a 30,000-square-foot facility that included a primary care practice, a pharmacy, and a medically directed weight loss program. The facility also featured a fully equipped fitness center featuring an indoor/outdoor pool, a basketball court, and an exercise room. This early vision positioned Northwest Medical Partners for the shift that came in 2010, when the Affordable Care Act (ACA) promoted the transition from fee-for-service to value-based medicine.[8] By the time the ACA became law, the weight loss and smoking cessation initiatives were already designed as outcomes-based programs.

Our experience with patients enrolled in the weight loss program revealed that a subset of this group would benefit from a different education program, one that focused on diabetes management. A pilot program was proposed for 30 patients with A1C levels of at least 8.0%; the average A1C for this initial group was greater than 9.0%. The new program would allow evaluation of a patient-centered approach, while offering the opportunity to test value-based principles that would affect the private practice as it transitioned to risk-based reimbursement.

The program design promotes highly individualized disease management. Our unpublished data show that this intense interaction produces results, which cannot be achieved without support. We enrolled our first 30 patients in October 2014 and have since expanded to 116 patients—this includes patients with baseline A1C levels below 8.0%. Here, we report data through June 2015 for 58 patients for whom we had a baseline A1C and who successfully complied with the program (see Compliance below). These patients saw an average A1C reduction of 2.4%. The majority of the patients enrolled in the program have type 2 diabetes (T2D). The greatest A1C reductions, both numerically and on a percentage basis, have occurred in patients who are between 31 and 60 years of age (**Figure 1**)

FIGURE 1. A1C Change by Age Group



Change in glycated hemoglobin (A1C) for first 58 patients as of June 2015.
Source: Northern Family Medicine.

and who have had diabetes for anywhere between 5 and 10 years.

Program Design

A vital component of the program is an evidence-based, 4-step pattern management approach that allows our Diabetes Center of Excellence to optimize therapy and engage patients in order to improve program outcomes.

This approach includes simple, easy-to-use healthcare provider implementation and patient engagement tools to integrate and teach these concepts in a practice setting. This was particularly appealing since our plan was to duplicate the program.

The 4 steps are:

Step 1. Identify the patient's chief glycemic abnormality. The patient learns about 3 priorities: reducing hypoglycemic events, reducing fasting hyperglycemia, and reducing postprandial hyperglycemia.

Step 2. Determine the frequency and timing of priority events for each patient.

Step 3. Investigate potential causes for these events.

Step 4. Develop an action plan to reduce events.

Participants in our program engaged with blood glucose meters in the Accu-Chek 360° Diabetes Management System, made by Roche.[9] Patients used either the Accu-Chek 360° Aviva model (Aviva; 17.5%); the Aviva Expert model, which includes a bolus advisor for patients using multiple daily injections (61.3%); or the

Accu-Chek Aviva Combo (Combo) insulin pump (19.2%).

As education is crucial to patient success, we designed classes that met both corporate needs and the individual needs of our patients. Classes have 10 to 12 attendees to ensure adequate attention to personal needs. A small group medical visit is led by a physician's assistant, who serves as program director, and a class on medication is taught by a pharmacist. Other units are presented by the program coordinator, who is a registered nurse. A series of 6 sessions, given once a month, involves the following:

Class 1. Patients are introduced to diabetes terms and the "diabetes triangle" of care, which calls for improved glucose levels, limited glucose variability, and avoidance of hypoglycemia through diet, exercise, and medication adherence.[10] Patients are asked to complete the Roche Accu-Chek 360˚ View Tool, which offers a snapshot of blood glucose patterns over 3 days.[11] This tool empowers patients to take ownership of their diabetes diagnosis; it places them on common ground, helps them recognize behavior patterns, and aids them in understanding the effects of diabetes and the consequences of noncompliance with a treatment regimen.

Class 2. The program director conducts a small group medical visit using a shared appointment model that includes 1-on-1 medical consultations that focus on individual care plans, which are derived from the Accu-Chek 360˚ View Tool.

Classes 3 through 5. These classes focus on carbohydrate counting, reading food labels, and meal planning. Classes are highly interactive and give patients a sense of normalcy. Many have commented that these classes "make them feel they are not alone in this crazy world of diabetes."

Class 6. A pharmacist introduces terms in pharmacology and questions patients on the pertinent points in the program. Patients are instructed on how to use a maintenance guideline tool to closely track A1C levels. An informal, verbal knowledge test is given at the conclusion.

Program Advancement. The program began in October 2014 without additional dedicated funds. In March 2015, bonus payments received through the CMS Physician Quality Reporting System/Meaningful Use program were directed to support the initiative.[12] Because the practice is aligned with a local hospital through a nonprofit partnership, the program has applied for and received a $148,500 grant from the Kate B. Reynolds Charitable Trust.[13] With this step, the program is transitioning to a full diabetes self-management and support program.

Compliance. Patients who are receiving insulin attend monthly evaluations; however, A1C is measured quarterly. Those receiving oral medications also are evaluated quarterly. For the initial group of patients, 6 classes were required. Only the shared appointment with the physician assistant required a co-payment; the rest of the classes were free. Today, the program has been revised to 5 classes, which the participants must take to be in compliance.

Support. In addition to scheduled evaluations, all participants have ongoing access to the program coordinator, who is available for individual phone consultations. The program coordinator has advised individual patients on diet, activity, and medication adjustments during glycemic events, which has prevented trips to the emergency department and/or hospitalizations.

Input From Patients Is Key

As an integral part of the program, we have created a Patient Advisory Committee to further the goals of population health management within our personalized program model. We strive to provide a holistic preventive approach to patient care, so patients can be successful and bring about behavioral changes that improve their quality of life. Recommendations from the Patient Advisory Committee resulted in combining 2 of the original 6 classes into a single session.

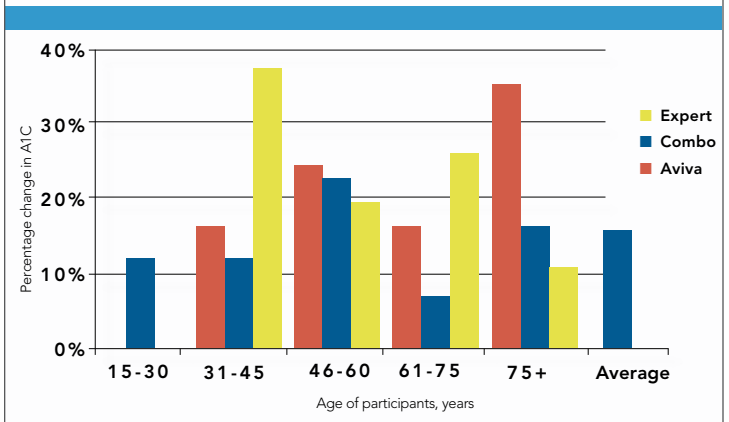
The curriculum reflects years of input from patients, starting with those in the practice's weight loss clinic. Ours is an "in the trenches" approach that identifies individual patient needs and daily struggles. The program has a "home grown" character that reflects the values, socioeconomic status, and cultural realities for the patients we serve. For example, we address practical topics such as how to avoid sugary sweets when babysitting grandchildren. Meetings with the Patient Advisory Committee also led to the publication of a cookbook for people with diabetes,[14] as well as 2 instructional videos on how to shop at the grocery store and how to prepare a healthy meal.

Results

To obtain baseline A1C, we used either the most recent A1C result from the patient's health records or the initial result after starting the program. The first 58 patients were evaluated in June 2015 and showed an average A1C reduction of 2.4% (**Figure 1**). Reductions were seen across all age groups (15 to 30 years, 31 to 45 years, 46 to 60 years, 61 to 75 years, and 75 years and older), and 13 of the 53 participants who started with an A1C above 7% were able to attain A1C goal. The largest reductions were seen among patients with the highest A1C levels: of the 20 patients who began with an A1C ≥11%, 4 achieved the ADA recommended goal of <7% and 8 achieved an A1C between 7% and 8%.

The study showed a difference in results from patients using the Accu-Chek Aviva Expert meter relative to those who used the standard Aviva meter. This was especially true among patients 31 to 45 years and 61 to 75 years (**Figure 2**).

FIGURE 2. Percentage in A1C Change by Age Group Across Products



A1C indicates glycated hemoglobin; Aviva, Roche Accu-Chek 360 Aviva model; Combo, Accu-Chek Aviva Combo; Expert, Aviva Expert with bolus advisor.
Source: Northern Family Medicine.

Discussion

Patients using the Aviva Expert meter have been able to optimize their insulin doses; this allows them to use less insulin overall, resulting in weight loss and decreased glucose variability. Patients are encouraged by A1C reductions and the more accurate carb ratios produced by the 360˚ View tool, which allows them to see a relationship between behavioral change and improved results. By eliminating the effect of constantly "chasing a sugar," as well as expected weight gain from insulin, patients show greater ability to maintain a healthy diet and exercise regimen.

Limitations

Data from the following patients were not included:

1. Those who did not meet program compliance requirements of taking all class sessions
2. Those whose baseline A1C was not measured
3. Those who had not completed the 6-session program at the time of data collection. »

Conclusion

The Diabetic Center of Excellence in Mount Airy, North Carolina, now part of Northern Family Medicine, has demonstrated that measurable reductions in A1C are achievable for patients with diabetes. The program director's grandmother was a participant, having been diagnosed with T2D at the age of 71. By fully embracing the program, she began to exercise, make smarter food choices, and lose weight. She continued to drive herself to the facility's gym for walks on a padded track until age 92. When she died at age 94, her A1C was 5.8%. This is the experience the program seeks to offer all participants: the opportunity for a high quality of life well into old age and a chance to spend time with loved ones. ◆

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Correspondence: Paige Johnson Cartledge, RN, BSN
564 Indian Grove Church Road,
Mount Airy, NC, 27030

Email: paigejohnson2899@gmail.com.

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SIDEBAR

High Deductibles Cause Low-Income Patients With Diabetes to Forego Medical Care

MARY CAFFREY

A STUDY IN *DIABETES CARE*, the journal of the American Diabetes Association (ADA), has confirmed the stories physicians have shared in recent years at major medical conferences: the rise of high-deductible plans is changing the behavior of those with diabetes and limited means, causing them to cut corners with some care.

The past 2 meetings of the ADA Scientific Sessions have been marked by stories of patients deferring care, struggling to pay for insulin, and having to endure interruptions in the Medicare supply chain for diabetes test strips, which CMS denied in a September 2016 report to the Government Accountability Office.[1-2]

In a March 2016 study, Diabetes Care found that complaints about the test strip availability had validity, and the recent study finds evidence to support other complaints.[3-4]

Led by David L. Rabin, MD, MPH, the study used data from the 2011-2013 Medical Expenditure Panel Survey to evaluate demographic status, medical service use, and health status among all privately insured adults with diabetes aged 18 to 64 years.[4] They were grouped according to those who were below 200% of the federal poverty level and those above that level and by whether they had no deductible, a low deductible (less than $1000 for an individual or $2400 for a family), or a high deductible (above $1000 for an individual or above $2400 for a family).

Compared with those with no deductible, privately insured persons with diabetes and a low deductible reported decreases in services: 27% fewer primary care visits, 39% fewer checkups, and 77% fewer specialty care visits. For those with a high deductible, the decline was even greater: the decreases were 42%, 65%, and 86%, respectively. Among those with higher incomes, the decreases were highest for specialty care (28%) and emergency department visits (37%).

Diabetes care measures were similar by income and by insurance type; however, deferred service was twice as high for those who had medical debt and lower income. "These patients are more likely to report forgoing needed medical services," the authors wrote.

The phenomenon of patients who end up in high-deductible plans that may not be appropriate for their medical needs is much discussed among those who care for patients with diabetes. During a session at the 2016 annual meeting of the American Association of Diabetes Educators, an attendee shared that her health system was requiring educators to bring up "bad debt" with patients during clinic visits, something that this professional felt was inappropriate.[5] What was needed, she said, was help for patients with diabetes to select benefit designs that were more appropriate for people who use a lot of medical care.

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ALTERNATIVE TREATMENTS

Can Yoga, Mindfulness Fit With Managed Care?

Mary Caffrey

IF AN INSURER FOUND AN ACTIVITY with growing evidence of health benefits,[1-3] the chance to help seniors stay active,[4] and a following that had grown by 16 million people in 4 years,[5] would it make sense to pay for it?

That's a question being asked about yoga, and the related practice of mindful meditation, as health systems seek low-cost ways to prevent and treat diabetes, obesity, and metabolic syndrome.

Over the past decade, and especially in the past 3 years, evidence has accumulated about the benefits of yoga and mindfulness, which are rooted in Eastern spiritual practices but have soared in popularity in the West.[5] Studies show that yoga can help people reduce waist circumference[6,7] and body mass index (BMI),[2,3,5,8] improve cognitive functioning[9] and sleep,[10,11] and reduce depression.[3,9,11] There is some evidence that yoga can improve blood glucose levels,[12] although results vary.[2]

Related to yoga is mindfulness, with a focus on meditation instead of gentle movement. A recent clinical trial that added mindfulness to 1 arm of a weight-loss intervention found that the group with mindfulness training lost a bit more weight, but showed significant improvements in fasting blood glucose.[13] A proof-of-concept study recently found that an intervention combining exercise, yoga, and mindfulness meditation greatly reduced anxiety, depression, and stress.[11]

With all this evidence, why don't more health plans pay for yoga and mindfulness? While there is interest—especially from the national health insurer Aetna—the very nature of these practices may make them a tough fit for payer reimbursement. Managed care seeks standardization, while the practice of yoga or mindfulness can vary widely by teacher or tradition. As influential teacher Bo Forbes, PsyD, asked in a 2010 commentary: Can yoga be part of managed care and still be yoga?[14]

Frederick Hecht, MD, research director for the Osher Center for Integrative Medicine at the University of California San Francisco, told *Evidence-Based Diabetes Management™ (EBDM™)* in an interview that while evidence of the health benefits of yoga and mindfulness is growing, more work is needed before managed care plans will consider reimbursement.

"I think it could be on the horizon," Hecht said, but first, more randomized controlled trials are needed to show how the practices contribute to weight loss and glucose control. Hecht was the senior author on a recent study in *Obesity* that showed patients with mindfulness training achieved greater glycemic control than those without training, but variation among teachers made a difference. One instructor did poorly on student ratings compared with the other 2, and this instructor's students lost less weight than those in the other 2 groups.[13] "We're trying approaches with our new work to see if we can get more consistent results," he said in an interview. Before managed care would fund mindfulness, he said, "We have to ask, 'How do we get the optimal results, consistently and reasonably?'"

In the short term, the best bet for healthcare dollars to cover yoga and mindfulness training may be through health savings accounts (HSAs). Both President Donald Trump and House Speaker Paul Ryan advocate support for HSAs in whatever legislation replaces the Affordable Care Act (ACA).[15] Legislation will soon be reintroduced[16] to allow HSAs to pay for physical activity, including yoga, according to Dani Mackey of Yoga Alliance, a nonprofit professional association.

Mindfulness and Blood Glucose Levels

Scientific literature increasingly references "mindfulness-based stress reduction," or MBSR. Rebecca S. Crane, PhD, MA, director of the Centre for Mindfulness Research and Practice at Bangor University, Wales, United Kingdom, and her co-authors describe MSBR as "underpinned by a model of human experience, which addresses the causes of human distress and the pathways to relieving it." MBSR seeks a "present-moment focus," and engages participants in a "sustained, intensive training in mindfulness meditation practice, in an experiential, inquiry-based learning process and in exercises to develop understanding."[17]

In 2016, researchers from Brown University in Providence, Rhode Island, found an association between mindfulness, glucose regulation, and diabetes. They measured dispositional or "everyday" mindfulness, which is a keen awareness of one's thoughts, using the Mindful Attention Awareness Scale (MAAS) on 382 participants taking part in a broader health study. Those with high MAAS scores had 83% greater prevalence of good cardiovascular health, and were especially superior in BMI, physical activity, fasting glucose, and rates of smoking.[18]

Mindfulness doesn't come naturally for many, so the next question is: Can it be taught? And if so, do health outcomes improve? Hecht's work suggests the answer to both is "yes." In the *Obesity* study, 194 adults with BMI ≥30 were randomized to participate in a 5.5-month diet and exercise program, with or without mindfulness training. Assessments were at baseline and at intervals of 3, 6, 12, and 18 months. While researchers did not find a significant difference in weight loss between the 2 groups, the fasting glucose levels in the mindfulness group were 3.1 mg/dL lower at 12 months, a difference that increased to 4.1 mg/dL at 18 months. At 12 months, the mindfulness arm also had lower triglycerides.[13]

Can New Payment Models Help?

The ACA's focus on preventive care and wellness raised yoga's profile with payers. But Forbes, a leading integrative yoga therapist, wasn't convinced. Writing in the *International Journal of Yoga Therapy* (*IJYT*), she wrote that yoga's benefits flow not from the instructor but from the practitioners' embrace of it. Yoga and managed care, Forbes wrote, had fundamentally different ways of measuring success. Drawing on frustration from her days as a clinical psychologist, she said of managed care, "Is the breadth and depth of yoga therapy better served—and protected—by practicing outside its confines? Is there a middle ground between working with and working outside managed care that gives us the opportunity to do what we do best without compromising our values?"[14]

In that same issue of *IJYT*, author Scott Laurence, PhD, asked whether outcomes-based standards—which focus on results and not process—could help yoga find a place in health systems. »

EVIDENCE IS ACCUMULATING ON THE HEALTH BENEFITS OF YOGA AND MINDFULNESS MEDITATION.

New payment models, "are efficient, effective, and conform to both modern medical practices and to third-party reimbursement requirements," he wrote. "Outcome-based approaches maintain the spirit and identity of the yogic approach to change and are, thus, superior to strictly evidence-based therapies."

"Outcome-based therapy," Laurence wrote, "is a middle way between a reductionist, allopathic medical model approach and a free-wheeling, forever spontaneous philosophy that eschews research and evidence."[19]

Last year, authors led by Alyson Ross, PhD, RN, suggested that a large-scale, longitudinal study using the National Institutes of Health PROMIS (Patient Reported Outcome System) measures, which were created to standardize the collection of patient-reported outcomes, could help the field "compare yoga therapy to traditional Western medicine." If enough yoga therapists embraced this tool, the authors wrote, "the data collected could be used to assess comparable effectiveness."[20]

"IF YOGA WAS MADE MORE AFFORDABLE AND ACCESSIBLE THROUGH HEALTH INSURERS, IT'S LIKELY MANY PEOPLE WILL ACTUALLY USE THIS INSURANCE BENEFIT."

—Marlynn Wei, MD, JD

The Aetna Experience

Pain medication brought Aetna CEO Mark T. Bertolini no relief after he suffered a devastating ski injury in 2004. More pills were not the answer, but yoga was. After studying with Gary Kraftsow of the American Viniyoga Institute (AVI), Bertolini brought the lessons to the workplace, launching a collaboration with AVI and Duke Integrative Medicine.[21] Using its own employees, Aetna studied the effects of 2 programs: Mindfulness at Work and Viniyoga for Stress Reduction. Employees who took part saw health improvements across the board—they lowered triglycerides, blood glucose levels, low-density lipoprotein or "bad" cholesterol, blood pressure, and waist circumference.[22]

Since publishing the results in 2012, Aetna has expanded the Mindfulness at Work meditation program to all its employees. Aetna spokesman Ethan Slavin told *EBDM*™ that the payer has found:

- Participants are regaining 62 minutes per week of productivity
- A per-employee dollar return, just on productivity, of more than $3000.

Slavin said more than 13,000 employees have, so far, participated in the program. In 2014, participants who completed the program, and took a survey before and after participation, reported a 28% reduction in perceived stress level, 20% improvement in sleep quality, and a 19% reduction in pain level.

Calls for Healthcare to Change

Some experts reject the idea that yoga or meditation should change to fit healthcare—it's the payers who should adapt, for the simple reason that the practices save money. Findings from an intervention called 3RP—for relaxation, response, and resiliency—found a 43% reduction in healthcare use among participants who took stress-reduction training at the Benson-Henry Institute for Mind Body Medicine at Massachusetts General Hospital (MGH) in Boston.[23] The authors emphasize that stress management skills *can* be taught, and at a much lower cost than treating what stress does to the body.

Marlynn Wei, MD, JD, a psychiatrist and author of the forthcoming book, *The Harvard Medical School Guide to Yoga*,[24] argues that yoga has the evidence, the cost-effectiveness, and the growing popularity to make it an effective part of preventive care.[25]

A 2016 study commissioned by *Yoga Journal* and the Yoga Alliance found that while $16 billion was spent each year on classes, clothing, and other costs, most prefer to practice at home (65%).[5] Seasoned practitioners can practice effectively by themselves, but it takes time to learn yoga—and cost was the biggest concern in selecting a studio or gym to take classes for half the respondents.[5]

"Yoga is the most popular form of mind-body practice in America today," Wei wrote in a blog post. "That means if yoga was made more affordable and accessible through health insurers, it's likely many people will actually use this insurance benefit."[25] ◆

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Jardiance Gains First Approval for CV Indication for Patients With Type 2 Diabetes

Mary Caffrey

ON DECEMBER 2, 2016, the FDA approved a new indication for empagliflozin (Jardiance) to reduce the risk of cardiovascular (CV) death for adults with type 2 diabetes (T2D). This marked the first time a diabetes drug has received this indication.[1]

The new indication sets Jardiance apart from its competitors among sodium glucose cotransporter-2 (SGLT2) inhibitors more than a year after the CV benefits of the drug were found in the EMPA-REG OUTCOME study and presented in Stockholm, Sweden. In that trial, which involved 7000 patients, Jardiance was found to reduce the risk of CV death, compared with a placebo, when added to standard-of-care therapies for diabetes and atherosclerotic CV disease.[2]

Thus, Jardiance was the first diabetes drug to show a CV benefit in high-risk patients, which researchers considered a "holy grail."[3] The safety trial that uncovered the benefit was the result of findings from a decade prior in which an earlier blockbuster class of diabetes drugs was found to have potential risks, which caused the FDA to change its approval process to require postmarketing cardiovascular outcomes trials.[4]

"AVAILABILITY OF ANTIDIABETES THERAPIES THAT CAN HELP PEOPLE LIVE LONGER BY REDUCING THE RISK OF CARDIOVASCULAR DEATH IS AN IMPORTANT ADVANCE FOR ADULTS WITH TYPE 2 DIABETES."

—Jean-Marc Guettier, MD

"Cardiovascular disease is a leading cause of death in adults with type 2 diabetes," said Jean-Marc Guettier, MD, CM, director of the Division of Metabolism and Endocrinology Products in the FDA's Center for Drug Evaluation and Research. "Availability of antidiabetes therapies that can help people live longer by reducing the risk of cardiovascular death is an important advance for adults with type 2 diabetes."[1]

The CDC reports that death from CV disease is 70% higher among those with diabetes than those without,[5] and just this week, a journal of the American College of Cardiology reported that among the 3 main risk factors—the other 2 being hypertension and obesity—those who have diabetes by age 45 face the greatest increase in risk of dying from heart failure.[6]

SGLT2 inhibitors work through a distinct mechanism of action: excess glucose is expelled from the body through the urinary tract. The drug class is known to have positive effects on hypertension and may produce modest weight loss. SGLT2 inhibitors are only approved for use in T2D, but they are being studied in patients with type 1 diabetes. ◆[7,8]

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FDA Approves Tresiba for Pediatric Use

AJMC® Staff

NOVO NORDISK HAS GAINED FDA approval for children and adolescents to use Tresiba (insulin degludec), the long-acting, once-a-day basal insulin that is the successor to Lantus.

Tresiba, first approved by the FDA in September 2015, was approved on December 19, 2016, to improve glycemic control in patients with type 1 and type 2 diabetes from the age of 1 year through adulthood, making it the only insulin approved in both types of diabetes for patients that young.[1] A key advantage of Tresiba, its 25-hour half-life, would give young patients and their parents the flexibility of dosing just once a day.

"We are seeing a rise in the number of children and adolescents in the United States, especially those with type 2, and are proud to support these patients by offering new and effective treatment options," said Todd Hobbs, MD, US chief medical officer for Novo Nordisk, in a statement. "It can be challenging for children with type 1 diabetes and their parents to manage blood sugar levels and keep up with multiple injections throughout an already busy day." [1]

The FDA's action was based on results of the BEGIN Young trial, a 26-week, phase 3b, randomized controlled trial that compared Tresiba's results with those of Levemir (insulin detemir, rDNA origin), a long-acting insulin analogue from Novo Nordisk approved in 2005.[2] The results showed that Tresiba improved glycemic control in patients aged 1 to 17 years in combination with insulin aspart, a mealtime insulin. ◆

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MANAGED CARE UPDATES

CMS Takes Step Toward Medicare Coverage of CGM for Seniors With Diabetes

Mary Caffrey

CMS HAS UPDATED ITS DEFINITION of durable medical equipment to include continuous glucose monitors (CGMs) that are approved for dosing, a step that advocacy groups hailed as the first toward getting the devices covered by Medicare.[1]

The policy change was announced January 12, 2017, by JDRF, formerly known as the Juvenile Diabetes Research Foundation, which has led the drive for CGM coverage in Medicare. In a statement, JDRF said the new definition created a "pathway toward the extension of coverage for the devices that will bring the nation's largest insurer in line with the vast majority of the country's private payers."[2]

"JDRF is encouraged by this decision, which will bring us one step closer to Medicare coverage for continuous glucose monitors," said Aaron Kowalski, PhD, chief mission officer. The group thanked leaders in Congress who had pressed for this change, including Senators Susan M. Collins (R-ME) and Jeanne Shaheen (D-NH).[2] Collins previously authored a commentary in support of CGM coverage in *Evidence-Based Diabetes Management*™, stating that Medicare's blanket denial of CGM reimbursement was at odds with the positions of the FDA and the National Institutes of Health.[3] »

CGMs, which give patients real-time data on their blood glucose levels—and where they are headed—has been shown to help patients reduce glycated hemoglobin and greatly limit glucose variability, the highs and lows in blood glucose levels that have harmful health effects. Because the original FDA approval required patients to take a separate finger-stick test each time they decided how much insulin to use, Medicare had labeled the devices "adjunctive" and thus not eligible for reimbursement.[4] Thursday's decision reclassifies devices with proper FDA labeling as "therapeutic," which should open the door to payer coverage.[1]

CMS spelled out 5 specific criteria for a device to meet the definition of DME:[1]

- It can withstand repeated use
- It has an expected life span of at least 3 years
- It serves a medical purpose
- It is generally not useful in the absence of a disease or injury
- It is appropriate for home use

Right now, the Dexcom G5, which gained FDA approval in December 2016 for use in deciding insulin doses,[5] is the only device that meets the new CMS standard for reimbursement, but it is expected that other manufacturers will soon seek approval. Dexcom hailed the decision. "This landmark CMS ruling will make available the most important technology in diabetes management to the Medicare population," said Kevin Sayer, president and CEO.[6]

Sayer vowed last July to work for Medicare coverage of CGMs, the day after an FDA panel voted to amend approval of Dexcom's mobile G5 to allow patients to make dosing decisions without a separate finger stick.[7]

Lack of coverage for CGMs has been a growing concern among patients, especially those with type 1 disease (T1D). As CGM use gained wider acceptance among patients with T1D, frustration mounted that patients over 65 had to pay for CGMs out-of-pocket or go without, even though they might benefit the most from the technology. As individuals with T1D age and live with diabetes for longer periods, they become "hypo-unaware," which means they stop experiencing symptoms that signal they are heading into hypoglycemia. A CGM warns patients their blood glucose is plummeting and gives them time to take action, thereby avoiding a trip to the emergency department.

CMS' policy change comes after 40 patients with T1D successfully navigated a lengthy, multistep appeals process to gain coverage. Debra M. Parrish, the attorney who handled the first successful appeal, *Whitcomb v. Burrell*,[8] in which a federal judge vacated CMS' position that CGM use was "precautionary," explained the significance of the policy change in an e-mail:

"Last summer, when a Medicare beneficiary challenged the Medicare policy that held CGMs are 'precautionary' and did not serve a medical purpose, CMS tried to argue that even if a CGM did not require a confirmatory finger-stick before making an insulin adjustment (many Medicare beneficiaries testified they made insulin adjustments based on CGM readings without performing a confirmatory test), because CGM sensors did not last 3 years, a CGM would not meet the durability requirements to be considered durable medical equipment and covered by Medicare. CMS has abandoned that logic and now holds that the receiver performs the medically necessary function of a CGM by informing a user of his or her glucose level," Parrish wrote.

Allowing CGM coverage for Medicare patients would potentially help more hospitals and health systems avoid 30-day readmissions, which is a key quality indicator as the nation's health system moves to a value-based payment system. JDRF has frequently cited a 2011 study in *The American Journal of Managed Care®* that found each inpatient admission from hypoglycemia costs $17,564.[9] ◆

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Council for Diabetes Prevention Selects Board, Focuses on Medicare Launch of DPP

Mary Caffrey

THE COUNCIL FOR DIABETES PREVENTION, created 4 months ago to promote the success of the National Diabetes Prevention Program (DPP), has elected its first board of directors. The council, a nonprofit group consistently mostly of providers, was formed to promote access, program quality, and sustainability of the DPP, which will be covered by Medicare, for the first time, in January 2018.

"We need all stakeholders to come together to solve the diabetes epidemic in America," Anne Woodbury, executive director of the Council for Diabetes Prevention, said in a statement. "I'm looking forward to working with the diverse members of our board, who each bring their unique expertise, leadership, and vision to help realize the mission of making the National DPP accessible to all Americans who need it."[1]

The council's agenda shifted with the election of President Donald Trump, whose vow to repeal the Affordable Care Act (ACA) could upend Medicare's plans to pay for NDPP. Educating members of Congress about this "unintended consequence" is on the council's immediate agenda, Woodbury said in an interview with *Evidence-Based Diabetes Management™ (EBDM™)*.

Directors, who will serve an initial term of 1 year, are:

- Marlayna Bollinger, founder and executive director of the Skinny Gene Project
- Julia Hu, MBA, CEO of Lark Technologies
- Neal Kaufman, MD, founder and chief medical officer of Canary Health
- Brenda Schmidt, MBA, MS, founder and CEO of Solera Health; acting president of the council; and a contributor to AJMC.com.
- Lisa Shaffer, senior vice president of industry relations and business development for the Blood Centers of America.[1]

When it formed in September 2016, council members voiced the need to work together to ensure the long-term viability of the DPP, which has more than 1400 providers with CDC recognition. At the time, Schmidt said it was clear that providers needed an entity through which they could share information and best practices. In the group's first statement, Schmidt described the council as a "big-tent forum" that would allow members to stay current on government policy.[2]

At the time, CMS was taking comments on the rules that will govern Medicare's launch of the DPP. The agency has since set eligibility criteria, but is still working on rules for reimbursement, including how to work with digital providers like Canary Health and Omada Health.[3] In the interview, Woodbury explained that, until recently, digital providers were barred from obtaining CDC recognition, which can take several years.

"IT IS GOING TO BE PIVOTAL TO HAVE DIGITAL PROVIDERS IN THE MIX TO SCALE THIS PROGRAM."

—Anne Woodbury, Council for Diabetes Prevention

As it stands, Medicare wants to require CDC recognition for reimbursement, but that could exclude digital providers who have not had time to achieve recognition. Without them, she said, "You're going to have a lot of frustrated seniors—and, more importantly, seniors who should get the benefit."

Said Woodbury, "It is going to be pivotal to have digital providers in the mix to scale this program." The importance of scalability was explained by an Omada Health executive last spring in *EBDM™*.[4]

A new challenge is ensuring that Medicare can still pay for the DPP, even if the ACA is repealed. HHS secretary Sylvia Mathews Burwell authorized reimbursement through a provision that allowed Medicare to fund programs after a successful pilot within the Center for Medicare & Medicaid Innovation. If that path to reimbursement goes away, Congress must allow a new one, Woodbury said.

The National DPP is based on research funded by the National Institutes of Health; the initial study showed that participants with prediabetes reduced their risk of developing type 2 disease by 58%.[5] A 10-year follow-up study published in *The American Journal of Managed Care®* found that long-term risk reduction among adherence participants was nearly 50%, and these individuals incurred fewer medical costs than those who took metformin to prevent diabetes.[6] ◆

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Omada Health Taps Former Sanofi Executive as Chief Medical Officer

Mary Caffrey


CHEW


SCHOENHERR

DIGITAL PROVIDER OMADA HEALTH announced 2 key additions to its leadership team on January 6, 2017, including one that may be a sign of the times: the former global chief medical officer for Sanofi, a leading manufacturer of diabetes and cardiovascular drugs, will now join a company whose mission is to reduce the need for such therapies.[1]

Paul Chew, MD, formerly of Sanofi, will be Omada's new chief medical officer, and Omada's new chief commercial officer will be Tom Schoenherr, who held the same post with Counsyl, Inc, the DNA-testing company.

Omada works with both insurers, including Humana and Kaiser Permanente, and employers to deliver digital behavioral health counseling, supplemented by in-person coaching.

"For the last 5 years, we've worked to establish Omada Health as a leader in digital health, publishing clinically validated results and operating on an outcomes-based revenue structure since day one," Omada co-founder and CEO Sean Duffy said. "Bringing on Paul and Tom, experts in their fields with proven track records for clinical development and scaling healthcare businesses, is the next step in Omada's evolution. Employers, payers, and health systems know digital health is here to stay, »

and the companies that will succeed are those that deliver outcomes and scale effectively. We've built a team to do exactly that."[1]

Chew and Schoenherr arrive at Omada as the company makes Medicare reimbursement of the National Diabetes Prevention Program (DPP) a centerpiece of its strategy. Chew's transition from a major pharmaceutical manufacturer to a company focused on prevention comes as payers are pushing back against the cost of diabetes and cardiovascular therapies; in recent weeks, both Sanofi and rival insulin maker Novo Nordisk have made significant job cuts.[2]

Omada, by contrast, is poised to scale up its ability to deliver DPPs. Barring a course change from the Trump administration, CMS will spend 2017 working on rules to let digital providers bring DPPs through Medicare starting in January 2018. Schoenherr will play a key role in that process, as the first rule CMS issued on Medicare DPP did not say how digital providers would participate.[3]

Diabetes is a leading cost driver in healthcare. A recent *JAMA* study[4] found that the annual rate of spending growth from the disease was 6.1% between 1996 and 2013. In its announcement of the appointments of Chew and Schoenherr, Omada said that at that pace, diabetes spending could reach the entire current Medicare budget by 2029.

"Diabetes and cardiovascular diseases drove some of the most widespread, most expensive, and most preventable healthcare costs," Chew said in the company's statement. "Omada's approach to scaling a proven intervention, and personalizing that intervention through data science, while publishing peer-reviewed evidence, has set an example across the digital health industry. I look forward to continuing to help the company build the medical case for covering the Omada program."

During his tenure at Counsyl, Schoenherr increased revenues from $1 million to $100 million. He has also worked as a regional vice president at Quest Diagnostics and at Siemens Healthcare. "I've been in healthcare for more than 2 decades, working with companies ranging from start-ups to industry leaders," Schoenherr said in the statement. "Sean and his senior team have spent the last 5 years making smart decisions about how to grow this business and have developed a revenue structure that truly puts their money where their mouths are. My expectation is that we can replicate, or even exceed, the success our team delivered at Counsyl." ◆

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CVS Health Creates "Transform Diabetes Care"

Mary Caffrey

Clients of CVS Health can now benefit from Transform Diabetes Care, a new program that seeks to deploy analytics to improve population health management for those with diabetes under the umbrella of the pharmacy benefit manager (PBM). The program seeks to cut pharmacy costs by tracking glycated hemoglobin (A1C) and behavioral change, all through "trend management" that will take what's learned during face-to-face encounters at pharmacies and MinuteClinics to identify opportunities for outreach or treatment improvements, according to the company.[1]

Transform Diabetes Care started early this year and will involve CVS' 9600 retail pharmacies and 1100 MinuteClinics, according to a company statement.

"Enrolled members will receive personalized support and coaching, designed to help improve medication adherence, better track and control A1C levels, and support healthy lifestyle behaviors through CVS Health consumer touch points," the company said in a statement.

CVS Health predicts that its PBM clients could save $3000 to $5000 per year for each member who successfully improves control of his or her diabetes. The company notes that antidiabetic drugs were the "leading driver" of gross costs for its clients in 2016. Transform Diabetes Care is designed to "help our clients manage the unsustainable increases in the cost of diabetes care by maximizing the value and effectiveness of our engagement with patients to improve clinical outcomes, while also employing strategic approaches to actively manage and control costs."

"ENROLLED MEMBERS WILL RECEIVE PERSONALIZED SUPPORT AND COACHING, DESIGNED TO HELP IMPROVE MEDICATION ADHERENCE, BETTER TRACK AND CONTROL A1C LEVELS, AND SUPPORT HEALTHY LIFESTYLE BEHAVIORS THROUGH CVS HEALTH CONSUMER TOUCH POINTS."

—CVS Health statement

Although CVS' announcement did not mention rising insulin costs, this has been a hot topic since the American Diabetes Association asked Congress to investigate why prices tripled between 2002 and 2013.[2] As the US population ages—and more Americans struggle with obesity and diabetes—the number of patients who need insulin to manage diabetes is expected to increase. Approximately 1.25 million Americans have type 1 diabetes and all use insulin; while it's not known precisely how many with type 2 diabetes would benefit from insulin, experts say patients who live with type 2 diabetes to old age will likely need it.

CVS Health has pushed back hard against rising insulin prices. The PBM stunned Sanofi in August 2016 when it dropped its longtime mainstay insulin, Lantus, from its formulary and said it would cover a biosimilar, Basaglar, in 2017.[3] ◆

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CDC Reports Mixed Progress in Fighting Obesity

Mary Caffrey

WHEN THEN-CDC DIRECTOR Tom Frieden, MD, MPH, set a series of public health goals early in his tenure, he aimed high. Calling them "Winnable Battles," Frieden set aggressive benchmarks for fighting food poisoning, infections, and obesity that he wanted to achieve before the end of 2015.

As he took stock in late 2016, Frieden was candid: when it comes to obesity, including obesity among the youngest children, America might not be losing, but it's not winning, either. "The Winnable Battles approach is all about accountability, setting ambitious goals, working with a broad group of partners, and holding ourselves to the high standard of rapid health improvement," Frieden said. "The past 6 years show that with focus and commitment, we can win battles against the most important health problems Americans face every day."

Frieden launched Winnable Battles when long-term gains in areas like reducing the number of Americans who were smoking had stalled. Some areas improved—adult cigarette smoking dropped 27% from 2009 to 2015 and youth cigarette smoking plummeted 45% over that same period—but other areas showed less progress. The battle against obesity remains a stubborn one.

A CDC report shows, in the areas of nutrition, physical activity, and obesity, the uneven nature of progress, which came amid the historic passage of the Affordable Care Act (ACA)—a law that took aim against chronic disease and its fallout on the healthcare system. With President Donald Trump promising to wipe away the ACA, it is unclear what will come of the limited progress made in reversing generations of neglect in some populations that suffer outsized rates of obesity, diabetes, and heart disease and the associated complications.

The CDC report stated the following:

- The CDC set a goal for childhood obesity (rates among those aged 2 to 19 years) to not exceed 15.4% by 2015. The prevalence of obesity remains around 17% and affects about 12.7 million individuals. One sign of progress: the rate among children aged 2 to 5 years decreased from 13.9% in 2003-2004 to 8.4% in 2013-2014.
- A major public health goal was increasing the share of children who were breastfed, as this is associated with lower rates of childhood obesity. Although rates increased, they did not reach the target of 58.9% by 2015; however, rates exceeded the original target of 50% by 3.6%.
- More adults have met the aerobic "Physical Activity Guidelines for Americans." The share of adults meeting these guidelines increased from 43.5% in 2008 to 49.8% in 2015. The US Surgeon General promoted a campaign to get all Americans to walk about 22 minutes per day in 2015.
- Between 2010 and 2015, 26 states updated their physical activity requirements for children in child care settings.
- Healthy eating was a major focus of the Obama administration. Between 2010 and 2015, 26 states made 455 specific improvements to nutrition standards and state licensing regulations for settings that provide child care to children aged 0 to 5 years.
- As of July 2016, more than 19,800 early childhood education providers pledged to follow best practices in providing healthy food and drinks to kids and in providing support services for breast-feeding mothers. ◆

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Lexicon Reports Positive Results for Sotagliflozin in Type 1 Diabetes

Mary Caffrey

LEXICON PHARMACEUTICALS HAS REPORTED THAT its pivotal phase 3 trial of sotagliflozin, a first-in-class treatment for type 1 diabetes (T1D), met its primary endpoint of statistically significant reductions in glycated hemoglobin (A1C) for these patients at 24 weeks.[1]

Top-line results from the trial, inTandem,[2] show that patients had mean A1C reductions of 0.39% from baseline while taking 200 mg of sotagliflozin and 0.37% on 400 mg of the drug compared with a mean reduction of 0.03% on placebo. According to a statement from Lexicon, the results were achieved "with a favorable overall safety profile, including rates of severe hypoglycemia similar to placebo and low overall rates of diabetic ketoacidosis."

Sotagliflozin is an oral dual inhibitor, which means it targets 2 proteins that affect glucose regulation in patients with diabetes: the sodium glucose co-transporter-2 (SGLT2) protein, which is involved in glucose reabsorption in the kidney, and the SGLT1 protein, which affects glucose absorption in the gastrointestinal tract.

"THE POTENTIAL TO SIGNIFICANTLY LOWER A1C LEVELS WITHOUT AN INCREASE IN HYPOGLYCEMIA WOULD REPRESENT A MAJOR SHIFT IN THE TREATMENT PARADIGM FOR TYPE 1 DIABETES."

—Thomas Danne, MD

There are several SGLT2 inhibitors already approved that allow excess sugar to be expelled through the urinary tract. SGLT2 inhibitors are approved to treat patients with type 2 diabetes and are being studied in patients with T1D who have taken it alongside insulin.[2-3] Patients in the inTandem2 study were all on optimized insulin therapy.[1]

There is an additional ongoing study, inTandem3, involving 1400 patients treated with sotagliflozin (400 mg/daily) or placebo on a background of insulin therapy, but without insulin optimization prior to randomization. Sanofi is responsible for this trial, according to the statement. Lexicon has a collaborative agreement with Sanofi to license and develop sotagliflozin.

"The inTandem2 study demonstrated a compelling safety and efficacy profile for sotagliflozin in adults living with type 1 diabetes," said Thomas Danne, MD, head of the Center for Children Endocrinology and Diabetes, at the Children's Hospital on the Bult in Hannover, Germany. "The potential to significantly lower A1C levels without an increase in hypoglycemia would represent a major shift in the treatment paradigm for type 1 diabetes." ◆

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BEHAVIORAL EVIDENCE

Diabetes: An Opportunity to Have a Lasting Impact on Health Through Lifestyle Modification

Hena N. Patel, MD; Andrew M. Freeman, MD, FACC; and Kim A. Williams MD, FACC

PATEL

FREEMAN

WILLIAMS

Hena N. Patel, MD, and Kim A. Williams, MD, FACC, are with the Rush University Medical Center, Division of Cardiology, Chicago.

Andrew M. Freeman, MD, FACC, is with the Department of Medicine, Division of Cardiology, National Jewish Health, Denver.

Kim A. Williams, MD, served as the 2015-2016 president of the American College of Cardiology.

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Diabetes-related care accounts for more than $1 of every $5 spent on healthcare in the United States, equating to $245 billion in total costs in 2012.[10] Not surprisingly, average medical expenses are more than twice as high for a person with diabetes as they are for a person without diabetes.[10]

Although drug therapy may be required to control metabolic risk factors, particularly when they arise from genetic aberration and aging, modification of life habits remains at the heart of the public health strategy for prevention of CVD and diabetes. Research has repeatedly demonstrated the benefits of lifestyle interventions,[11] including engaging in physical activity, adopting healthier eating practices, managing stress, and using social-environmental support to initiate and sustain health-related behaviors.

Several advances in diabetes management over the past few decades have improved the health of many patients and should not be understated. However, these advances are beneficial only to the extent that patients use them appropriately. To do so requires knowledge, problem-solving skills, motivation, environmental support and effective coping skills for life's many stressors. Additionally, due to these behavioral challenges of daily diabetes self-management and despite the technological advances in diabetes care, patients have limited resources, perhaps even limited free will, in their management decisions. Despite this, research still shows that individual behavior can be shaped and behavioral interventions can help patients make better choices for their own diabetes self-management, even in the context of difficult circumstances.

Diabetes self-management is central to diabetes care overall, and much of this entails individual behavior change, particularly around dietary patterns and physical activity. Published recommendations for the treatment of people with diabetes assert the importance of diet, exercise, and education to diabetes treatment.[12,13] Nutrition is key in the management of diabetes and CVD risk prevention. Current recommendations for patients with diabetes center around a dietary pattern that emphasizes fruits, vegetables, reduced saturated fat, and low-fat dairy products, as well as modification of macronutrient intake to accommodate individual needs for the distribution of calories and carbohydrates throughout the day. The Dietary Approaches to Stop Hypertension, Mediterranean, low-fat, and monitored carbohydrate diets are effective for controlling hyperglycemia and lowering CVD risk factors.[12] The Prevención con Dieta Mediterránea (PREDIMED) trial was a randomized trial that found a 30% reduced risk of CVD events in diabetic patients randomized to the Mediterranean diet, suggesting that this diet may promote CVD risk reduction in this population.[14]

Dietary content heavily impacts the development of diabetes. In the Adventist Health Studies, the prevalence of diabetes was lower in vegetarians than in nonvegetarians,[15] an effect likely mediated by the lower body weights of the vegetarians. And when compared with a standard American diet, the prevalence of diabetes was reduced by 23% with a semi-vegetarian diet, 38% by consuming a pesco-vegetarian diet, 55% with a lacto-ovo-vegetarian diet, and 75% with a vegan diet. Dietary interventions with a whole foods plant-based nutrition (vegan diet) have even been shown, through a small randomized trial, to reduce the pain levels in diabetic neuropathy.[18] Similarly, foods with a lower glycemic index have been associated with a lower risk of diabetes development in the Nurses Health Studies.[17] In contrast, the Health Professionals Follow-up Study indicated that eating processed meats increases the risk of developing diabetes.[16]

More recently, several trials have shown surprising outcomes for a commonly consumed food: eggs. One of the larger of these analyses of 14 studies found that for those who consumed the most eggs, there were 19% and 68% increased risks for developing CVD and diabetes, respectively, compared with those who ate the fewest eggs. Further, for those who already had diabetes, the risk for developing heart disease from eating the most eggs jumped to 83%. The authors concluded, "There is a dose-response positive association between egg consumption and the risk of CVD and diabetes."[19]

Research has also demonstrated the benefits of meditation, both mindfulness and transcendental, for diabetes management. A randomized trial published in *JAMA* found that meditation reduced blood pressure, increased insulin resistance, and significantly reduced the rates of CVD events.[20]

Multiple epidemiological studies suggest that both obesity and physical inactivity are independent risk factors for diabetes, and the reduction or elimination of such factors appears to be related to prevention and management of this disease.[21] Further, physical activity and weight loss improve blood pressure and lipid levels, thereby positively affecting other CVD risk factors. This robust and consistent observational evidence has given rise to large-scale randomized controlled trials that have used lifestyle intervention (including behavioral strategies for reinforcement of prescribed changes in nutritional intake, physical activity, or both) in populations at high risk of developing diabetes. The aim of these trials was to reduce the rate of incident diabetes and ameliorate risk factor profiles associated with both diabetes and cardiovascular morbidity and mortality.[21,22] For instance, the Diabetes Prevention Study and the Diabetes Prevention Program demonstrated that dietary improvement and increased physical activity reduced the incidence of diabetes by nearly 60% in 4 years.[23,24] The Da Qing study later compared diet, exercise, and diet plus exercise with a no-treatment control group and found that all 3 lifestyle approaches reduced the risk of developing diabetes by 31% to 46%.[25] Later, the Finnish Diabetes Prevention Study demonstrated similar results in over 500 overweight subjects with impaired glucose tolerance—lifestyle intervention designed to produce weight loss improved dietary intake and physical activity and reduced the risk of diabetes by 58%.[6,7]

More recently, the Look AHEAD (Action for Health in Diabetes) study, conducted from 2001 to 2012, provided extensive longitudinal data on the effect of an intensive lifestyle intervention—targeting weight reduction through caloric restriction and increased physical activity—on CVD rates and risk factors among adults with diabetes.[26] Published in 2013, the primary results of Look AHEAD showed that greater weight loss was observed in the

TABLE. Lifestyle Management and Diabetes: Evidence

NUTRITION		
PREDIMED[14]	Mediterranean diet offers best protection against CVD	2014
Adventist Health Studies[15]	Diabetes less prevalent among vegetarians	2009
Health Professionals Follow-up Study[16]	Total and saturated fat linked to increased T2D	2002
Nurses Health Study[17]	Carbs with low glycemic index linked to reduced diabetes risk	1997
MEDITATION		
Paul-Laborador et al. [20]	Meditation lowers risk of BP, reduces CVD events	2006
PHYSICAL ACTIVITY		
Da Qing Study [25]	Exercise reduces diabetes incidence in those with IGT	1997
LIFESTYLE PROGRAMS		
Diabetes Prevention Program [23]	Lifestyle change better than metformin to reduce T2D risk	2002
Finnish Diabetes Prevention Study [24]	Improved diet, exercise reduces risk of T2D	2005
Look AHEAD [26]	Intensive intervention boosts weight loss; lowers A1C	2013
IDES [27]	Exercise intervention improves A1C, CV profile	2010

A1C indicates glycated hemoglobin; BP, blood pressure; CV, cardiovascular; CVD, cardiovascular disease; IGT, increased glucose tolerance; T2D, type 2 diabetes.

intervention arm (8.6%) compared with the usual care arm (0.7%). Additionally, patients in the intervention group had improved physical fitness and high-density lipoprotein (HDL) cholesterol levels, greater reductions in glycated hemoglobin (A1C) and waist circumference, and required less pharmacotherapy for glucose, blood pressure, and lipid control. Although the trial was stopped early due to futility (possibly from discontinuation of cardioprotective drugs, such as statins), the results inform clinicians that increased physical activity and improvements in diet can safely lead to weight loss and a reduced requirement for medications to control CVD risk factors without a concomitant increase in the risk of cardiovascular events.

The Italian Diabetes and Exercise Study (IDES) was another randomized trial designed to examine the effects of an intensive exercise intervention strategy on modifiable CVD risk factors in diabetics. The subjects were randomized to an exercise group or control group (structured individualized counseling alone) for 12 months. Compared with the control group, supervised exercise produced significant improvements in physical fitness, A1C, systolic and diastolic blood pressures, HDL- and low-density lipoprotein cholesterol levels, waist circumference, body mass index, insulin resistance, inflammation, and coronary heart disease (CHD) risk scores.[27]

Ensuring a Sustained Impact

These important lines of research, while demonstrating the benefits of behavioral interventions, also raise many questions. To start, what are the mechanisms of action of these interventions? A meta-analysis by Hood et al suggests that multicomponent interventions targeting emotional, social, or family processes that facilitate diabetes management are more potent than interventions that target a single direct behavioral process.[28] Identifying active ingredients and determining the necessary doses of those ingredients would allow both clinicians and patients to focus resources on the most important areas of an intervention. How can we maintain lasting behavioral changes once they have been initiated? Results from many weight loss interventions highlight the need for more consideration of behavior maintenance strategies.[29] Lastly, how can we effectively disseminate interventions to the larger diabetic population? Even the most effective interventions are useful only to the point that patients have access to them. The internet, telemedicine, peers and community health workers, and mobile electronic devices all hold promise in this regard.

The magnitude of the behavioral diabetes research agenda is impressive, although much work is still needed to determine the optimal approach to diabetes management. Until then, the lifestyle interventions discussed give patients the behavioral technology they need to more effectively navigate their world with diabetes. They also give healthcare providers greater ability to inform and support their patients with diabetes. Encouraging patients to self-manage their disease, as well as engaging all stakeholders in the necessary behavioral changes, can positively influence the long-term treatment outcomes of patients with diabetes.

Finally, educating physicians and allied health professionals on the power of lifestyle changes through diet, exercise and physical activity, and mindfulness is a critically underestimated and underfunded approach. Because of minimal nutrition training in medical school and the lack of exposure to lifestyle medicine, many healthcare providers do not counsel, implement, or coach patients to make these changes. Recently, the American College of Cardiology hosted a half-day intensive within its 2016 Annual Scientific Sessions that solely focused on lifestyle modification. Education from leading experts in the realm of lifestyle and nutrition was delivered with an incredibly positive response to a standing room-only audience. The intensive session started with a debate about commonly held nutrition misconceptions and was followed by sessions on the latest in behavioral modification and motivational interviewing, smoking cessation, and scientific evidence around the topics of mindfulness, stress reduction, love, and connection. Overall comments from the audience showed a true desire to learn more about these topics and ways to implement them in common practice.

In summary, treatment for diabetes and the associated CVD has come a very long way. Behavioral intervention, in the form of lifestyle medicine, is an approach that both minimizes cost and maximizes yield in dealing with both. Now is the time for the medical community, as a whole, to become aware of this approach and review the research that has often been ignored despite excellent results. While implementation is the major barrier, along with patient compliance and uptake, the time and effort required leads to lasting results that are well worth the initial investment. ◆

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ORIGINAL RESEARCH

Differential Weight Loss Effects on Type 2 Diabetes Remission Among Adults

Virender Kumar, PhD; William Encinosa, PhD; Hena Thakur; and Kisha Thakur

continued from cover

ABSTRACT

INTRODUCTION: Little is known about the variation in the effect of nonsurgical weight loss among obese and nonobese individuals on the incidence of type 2 diabetes (T2D) remission.

METHODS: Using data from a nationally representative healthcare survey, we analyzed the differential effect of weight loss on the relationship between obesity and the incidence of T2D remission over the span of 1 year among 3755 adults. Anyone who reported having T2D in the first year, but not in the subsequent year, was considered to be in remission. Changes in a person's weight were measured as change in the body mass index. Data gathered between 2009 and 2013 were analyzed in 2016.

RESULTS: The incidence of self-reported remission was 5.22% (P <.001). Among obese individuals (BMI≥30), those who experiences a 3% drop in weight, at minimum, were 2.1 percentage points more likely to report remission than those who lost less than 3% bodyweight (P <.05). Comparing all individuals who lost more than 3% of their weight with those who lost less than 3% of their weight, obese individuals were 3.7 percentage points more likely than nonobese individuals to report being in remission (P <.05). Furthermore, after accounting for demographic and clinical information, we found that T2D remission was negatively associated with the duration of a T2D diagnosis and diabetes medication type, and was positively associated with being African American.

CONCLUSIONS: T2D is reversible, and the relationship between obesity and T2D remission varies with weight loss.

To our knowledge, the above mentioned study is the lone community-based remission incidence study. However, this study lacks generalizability to the US population. Therefore, we used the Medical Expenditure Survey (MEPS), a national survey of the US noninstitutionalized civilian population, to study the differential effect of weight loss among obese and nonobese adults in remission without bariatric surgery.

Methods

Data Sample. MEPS, an annual nationally representative survey, employs an overlapping panel design and includes a new panel each year. The survey collects health status, healthcare expenditures, and health insurance coverage information for each member of a sampled household for a period of 2 calendar years, through 5 rounds of interviews. In the Priority Condition (PC) section, each household member entering the survey for the first time is asked to indicate whether or not he or she has diabetes. In the third and fifth follow-up rounds, a person who reported having been told by a doctor or other healthcare professional that he/she had diabetes is asked to complete a self-administered Diabetes Care Survey (DCS). At that point, if a patient says that the earlier response was an error or that he or she no longer has diabetes, the variable indicating diabetes diagnosis is reset to "No". Otherwise, the respondent is asked to fill out the DCS survey in which he or she will be asked to indicate receipt of diabetes diagnosis. If a respondent reports being unaware of having diabetes, that person is not assigned a positive DCS weight. This weight adjusts for DCS nonresponse and standardizes to the number of persons with diabetes in the US civilian noninstitutionalized population.

The age of a diabetes diagnosis was not made available until the 2009 MEPS public use files. Therefore, this study includes individuals in panels 14 to 17 who reported having diabetes during the first-year PC survey section, as well as in the DCS, and who fully participated in both years of data collection. About 5% of these individuals had missing values for body mass index (BMI) and/or age when they received their diabetes diagnosis. We used a multiple imputation method to assign the missing values of these 2 variables. Furthermore, the final analytic sample excluded those who had any of the following characteristics: (1) bariatric surgery or related surgical complications during the 2 years of their respective panels, (2) the absence of positive diabetic survey weight in the first year of their panel, (3) a BMI below 20 and/or age younger than 30 years when diagnosed with diabetes, and (4) use of an insulin-only medication regimen. A total of 3755 adults were in the analytical sample and 191 (5%) of them had an imputed BMI or age at which they were diagnosed for diabetes. Data gathered between 2009 and 2013 were analyzed in 2016.

Measures. Anyone who reported a diabetes diagnosis in both the PC section of the survey and in his or her first year of the DCS, but reported the absence of a diabetes condition (second year diabetes indicator variable = 2 ["No"]) in the subsequent year's DCS, was considered to be in diabetes remission.

Individuals with a BMI less than 30 were categorized as nonobese. A change in an individual's weight was measured in terms of a change in his/her BMI. A dichotomous indicator variable indicating a drop of more than 3% in BMI between the first and second year was constructed. The age reported in the latest round of the first year was used to categorize individuals into 3 age groups: 18 to 44 years, 45 to 64 years, and 65 years or older; 3 categorical variables indicating the years since initial T2D diagnosis were used. Next, the self-reported medication use in the DCS survey at the end of first year was used to construct 4 dummy variables to indicate if an individual was taking: (1) any medicine, (2) an oral agent only, (3) insulin only, or (4) a combination of insulin and oral agents. Anyone with a self-reported diagnosis of coronary heart disease, myocardial infarction, or stroke was designated as having cardiovascular disease. Other indicator variables included hypertension, gender, and race/ethnicity (Asian, African American, and other races).

Statistical Analysis. This study used Stata SE 14.1 (Stata Corporation, College Station, Texas) to predict T2D remission using a logistic regression model that accounted for the complex survey design. The DCS weights were used in the analysis. To assess model fit, the goodness-of-fit test accounting for survey design suggested by Archer and Lemeshow was conducted.[13] Interaction effects and standard errors were computed as suggested by Norton, Wang, and Ai,[14] but only after accounting for the complex survey design.

Results

A total of 3755 individuals from 4 panels (14 to 17) constituted our study sample. Among these individuals, 5.91% were in remission, 56.5% were obese, 45% were male, 33.7% saw more than a 3% drop in BMI in 1 year, 46.8% were 45 to 65 years old, 10.4% were given a T2D diagnosis within the last 2 years, and about 11% reported taking no T2D medication (**Table 1**). Those who reported being diagnosed for hypertension or cardiovascular conditions in their lifetime represented 77.6% and 34.1% of the sample, respectively.

Table 2 presents the results of the logistic regression analysis. The goodness-of-fit test indicated that the model was a good fit {F(9,180)=0.425 and P>F = .92}. Both nonobesity and weight loss (BMI loss) were positively associated with remission (P<.05). The relationship between the likelihood of remission and weight loss varied with obesity, in that nonobese individuals who lost weight »

ENCINOSA

H. THAKUR

William Encinosa, PhD, is with the Center for Delivery, Organization and Markets, Agency for Healthcare Research and Quality (AHRQ), Rockville, Maryland; and the McCourt School of Public Policy, Georgetown University.

Hena Thakur is a medical student at Boston University Medical School.

KUMAR

K. THAKUR

Virender Kumar, PhD, is with survey operations of Westat, Inc, Rockville, Maryland.

Kisha Thakur is an undergraduate in biology, University of Maryland, College Park, Maryland.

TABLE 1. Characteristics of the Study Sample

	PERSONS (n = 3755)	PERCENT OF TOTAL RAW	PERCENT OF TOTAL WEIGHTED
Diabetes remission in second year			
Yes	222	5.91	5.22
No	3533	94.09	94.78
Baseline obesity			
Nonobese	1634	43.52	42.38
Obese	2121	56.48	57.62
Weight loss in 1 year			
>3% of weight	1264	33.66	32.18
<3% or no weight loss/ weight gain	2491	66.34	67.82
Interactions			
Nonobese and lost >3% of weight	457	12.17	11.46
Others	3298	87.83	88.54
Age group			
18 to 44 years	485	12.92	10.73
45 to 65 years	1780	47.40	46.80
65 years and older	1490	39.68	42.46
Years since diagnosed with diabetes			
Less than 2 years	391	10.41	10.85
2 to 10 years	1744	46.44	42.72
10 or more years	1620	43.14	46.43
Diabetes medicine at baseline			
None	410	10.92	10.92
Oral agents only	2327	61.97	62.96
Insulin only	298	7.94	7.91
Oral agents and insulin	720	19.17	18.21
Gender			
Male	1690	45.01	49.42
Female	2065	54.99	50.58
Race/ethnicity			
White/Hispanic	2555	68.04	79.39
Asian	222	5.91	4.24
African American	978	26.05	16.37
Ever diagnosed as having high blood pressure other than during pregnancy?			
Yes	2914	77.60	77.42
No	841	22.40	22.58
Ever diagnosed as having cardiovascular disease?			
Yes	1279	34.06	36.25
No	2476	65.94	63.75

A1C indicates glycated hemoglobin; PWD, patient with diabetes.

TABLE 2. Likelihood of Remission After 1 Year From Baseline

CHARACTERISTICS	COEFFICIENT
Baseline obesity	
Nonobese	**0.460**[a]
Obese	Ref
Weight loss in 1 year	
>3% of weight	**0.496**[a]
<3%, didn't loss or gained	Ref
Interactions	
Nonobese and lost >3% of weight	**–0.873**[a]
Others	Ref
Age group	
18 to 44 years	**0.449**
45 to 65 years	Ref
65 years and older	**0.306**
Years since diagnosed diabetic	
Less than 2 years	**1.204**[c]
2 to 10 years	0.460
10 or more years	Ref
Diabetic medicine at baseline	
None	Ref
Oral agents only	**–2.230**[c]
Insulin only	**–2.767**[c]
Oral agents and insulin	**–3.167**[c]
Gender	
Male	–0.034
Female	Ref
Race/ethnicity	
White/Hispanic	Ref
Asian	0.556
African American	**0.503**[a]
Ever diagnosed as having high blood pressure other than during pregnancy?	
Yes	–0.275
No	Ref
Ever diagnosed as having cardiovascular disease?	
Yes	0.177
No	Ref
Constant	**–2.193**[c]

Ref indicates reference.
Boldface indicates statistical significance.
[a]*P*<.05
[b]*P*<.01
[c]*P*<.001.
Model fit test: SVYLOGITGOF F(9,180)=0.425 and (*P* >F = .92)

were less likely to have remission (*P*<.015). Remission was also negatively associated with duration since the initial T2D diagnosis and use of diabetic medication at baseline. Being African American was positively associated with remission (*P*<.05).

Our results suggest that more than 5% of individuals reported remission in 1 year (see **Table 3**). Among obese individuals, those who underwent a more than 3% drop in their weight were 2.1 percentage points more likely to report remission than those who lost less than 3% of their weight (*P*<.05). Among those who lost less than 3% of their weight, obese individuals were 1.9 percentage points less likely to report remission than nonobese individuals (*P*<.05). Comparing the average predicted probability of remission for those who lost more than 3% of their weight with those who lost less than 3% of their weight, obese individuals were 3.7 percentage points more likely than nonobese individuals to report being in remission (*P*<.05). The likelihood of remission declines with the duration of T2D diagnosis. Compared with those who had T2D for 10 or more years, those who had T2D within the last 2 years were 6 percentage points more likely to be in remission (*P*<.001) and those having T2D for more than 2 years but less than 10 years were 1.7 percentage points more likely to be in remission (*P*= .05). Those taking no medication to treat T2D were more likely to be in remission than those taking oral agents, insulin only, or both insulin and oral agents by 19.3, 20.6, and 21.2 percentage points, respectively (*P*<.001). Those taking only oral agents were 2 percentage points more likely to be in remission than those taking both insulin and oral agents (*P*<.001). Compared with whites and Hispanics, African Americans were 2.4 percentage points more likely to be in remission (*P*<.05).

Discussion

In our analysis of nationally representative survey-based data, we found that 5.2% of adults with T2D reported being in remission (without bariatric surgery) at the end of the second year. To our knowledge, this is the first analysis providing evidence of remission

TABLE 3. Predicted Probabilities of Remission and Marginal Difference at the Sample Representative Values

	PROBABILITY	MARGINAL DIFFERENCE
Overall	**0.0522**[c]	
Obesity		
Obese	**0.0483**[c]	Ref
Nonobese	**0.0551**[c]	0.0068 (0.414)
Weight loss		
≤3%	**0.0502**[c]	Ref
>3%	**0.0540**[c]	0.0038 (0.674)
Obesity and weight loss		
Obese and weight loss ≤3%	**0.0413**[c]	Ref
Obese and weight loss >3%	**0.0623**[c]	**0.0210**[a]
Nonobese and weight loss ≤3%	**0.0605**[c]	**0.0192**[a]
Nonobese and weight loss >3%	**0.0443**[c]	
Age group		
18 to 44 years	**0.0643**[c]	0.0198 (0.089)
45 to 64 years	**0.0444**[c]	Ref
65 years and older	**0.0573**[c]	0.0129 (0.156)
Years since diagnosed diabetic		10+ vs others
Less than 2 years	**0.0953**[c]	**0.0602**[c]
2 to 10 years	**0.0523**[c]	**0.0172**[a]
10 or more years	**0.0351**[c]	Ref
Diabetic medicine at baseline		
None	**0.2256**[c]	Ref
Oral agents only	**0.0328**[c]	**-0.1928**[c]
Insulin only	0.0195 (0.136)	**-0.2061**[c]
Oral agents and insulin	**0.0132**[b]	**-0.2124**[c]
Gender		
Male	**0.0514**[c]	-0.0015 (0.864)
Female	**0.0529**[c]	Ref
Race/ethnicity		
White/Hispanic	**0.0475**[c]	Ref
Asian	**0.0743**[c]	0.0268 (0.132)
African American	**0.0713**[c]	**0.0238**[a]
Ever diagnosed as having high blood pressure other than during pregnancy?		
Yes	**0.0488**[c]	-0.0124 (0.221)
No	**0.0612**[c]	Ref
Ever diagnosed as having cardiovascular disease?		
Yes	**0.0573**[c]	0.0077 (0.415)
No	**0.0573**[c]	Ref

Ref indicates reference.
Boldface indicates statistical significance.
[a]$P<.05$
[b]$P<.01$
[c]$P<.001$.
Model fit test: SVYLOGITGOF F(9,180)=0.425 and (P >F = .92)

among diabetic adults using data from a national survey representing the US noninstitutional population. Remission was highest among those not using any medication (23%) and occurred much less often among those using oral agents and insulin (1.3%). Our study further supports findings from earlier studies that indicate T2D is reversible in some cases.

Similar to 2 previous studies,[9,12] the incidence of remission in our cohort was positively associated with fewer years since diagnosis, the absence of glucose-lowering medication intake, and being African American. In our study, we found no variation in remission with regard to an individual's age. In addition, our study shows that the relationship between weight loss and diabetic remission differs between obese and nonobese individuals. Between those who lose more than 3% of weight and those who don't, obese persons with T2D are more likely to report remission than nonobese adults with T2D.

Limitations

There are some limitations to our study. First, the presence and absence of T2D is based on self-reports, and therefore, the information is prone to errors. However, the findings of this study are in line with the findings of 2 previously published studies. In addition, both BMI and age values were missing in less than 5% of the sample. We used a multiple-imputation method to impute the missing BMI and age values. The results of our model did not change when individuals with missing BMI and age values were excluded from the analysis. ◆

DISCLOSURES

Author Information: Virender Kumar, PhD, is with survey operations of Westat, Inc, Rockville, Maryland. William Encinosa, PhD, is with the Center for Delivery, Organization and Markets, Agency for Healthcare Research and Quality (AHRQ), Rockville, Maryland; and the McCourt School of Public Policy, Georgetown University. Hena Thakur is a third-year medical student at Boston University Medical School and a fellow with the National Institutes of Health, Rockville, Maryland. Kisha Thakur is an undergraduate in biology, University of Maryland, College Park, Maryland. The authors received no financial support from any institution. The views herein do not represent the views of AHRQ or HHS.

Corresponding Author:
William Encinosa, PhD.
Georgetown University
Old North Suite 100, 37th and O Streets, N.W.
Washington D.C. 20057
301-427-1437
wee4@georgetown.edu

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Reaching Beyond the Exam Room: How Technology-backed Lifestyle Intervention Is Improving Health Outcomes for Diabetes and Hypertension Management

Andreas Michaelides, PhD, and Ed Pienkosz, MS

MICHAELIDES

PIENKOSZ

Andreas Michaelides, PhD, is chief psychology officer for Noom, Inc.

Ed Pienkosz is the director of Business and Coach Development for Noom, Inc.

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of programs in clinical settings, they defined chronic disease management as:

> *An organized, proactive, multi-component, patient-centered approach to healthcare delivery that involves all members of a defined population who have a specific disease entity (or a subpopulation with specific risk factors). Care is focused on, and integrated across, the entire spectrum of the disease and its complications, the prevention of comorbid conditions, and relevant aspects of the delivery system.*[1]

This definition certainly describes the approach to addressing chronic disease at that time and in many cases today. For decades, the medical community has designed chronic disease management programs to fit within the clinical patient care setting, whether or not it was convenient for the patient. For individuals who do not need care in a clinical setting, there are numerous chronic disease self-management education programs (CDSMPs). These programs extend beyond the traditional educational, knowledge-centered approach to include knowledge application in real-world situations, self-monitoring, problem solving, utilization of external resources, and application to behavior change in real world situations.[2] They are typically provided in a community setting to minimize the clinical feel. However, CDSMPs require participants to show up at a specific time and location and adjust their life to the provider rather than meeting them where they are.

What if a lifestyle intervention and management program was designed to address the risk factors associated with the condition, enhance knowledge, and lead to sustainable behavior change in a way that allowed participants to attend when and where it was convenient for them? More importantly, what if the program allowed participants to engage when they were truly "present" and not merely in a state of presenteeism? Now, with the proliferation of mobile technology, such programs exist.

Bringing together innovative technologies and clinically validated curricula expands reach outside of the physician exam room and/or community-based setting into the daily lives of patients. This powerful combination can significantly enhance the prevention of lifestyle-related chronic conditions to improve health outcomes further upstream. The potential of this approach is extensive, with benefits related to prevention of the condition and/or symptom improvement, as well as a reduction in healthcare costs.

Overview and Business Case

Recently, a large private employer and health system in the Midwest identified a significant rise in type 2 diabetes and hypertension in their patient population. This trend was mirrored closer to home, among the health system's own employees. Although the system offered multiple disease management and prevention programs, including physician referrals for these services, their care-related costs were increasing, productivity was declining, and the overall well-being of their employee population was suffering.

Faced with this data, the health system decided to divert from a traditional chronic disease management approach to a new model. In 2016, it created a partnership with Noom, Inc, a leader in mobile health coaching, to deploy an innovative chronic disease management solution designed to address these issues. The year-long initiative leveraged technology and human coaching to improve practical knowledge of the diagnosed condition and modify lifestyle behaviors, with a goal of decreasing associated risk factors. The initiative maintained positive aspects of traditional and self-management education programs while simultaneously reducing common barriers to engagement. This included high-touch support from a health coach alongside a structured clinically validated program delivered via their employees' smartphones. This approach also increased the reach and efficiency of the program by reducing the number of required staff resources per participant from 1:15 to 1:42.

Noom's technology and its structured diabetes and hypertension management programs were utilized for this initiative. The health system's coaches supported participants in real time, utilizing Noom's coaching tools which reveal trends, patterns, and individual actions to enable timely intervention. Eligible participants used Noom's mobile application to log their meals, track physical activity, and monitor biometric readings with integrated glucometer and blood pressure monitors. They also received structured, condition-specific curriculum; group support from a virtual group of peers; and feedback from their coach at moments of greatest impact, such as during a vacation or family celebration.

Employee eligibility was determined using data available in the health system's EPIC database. Once identified, individuals were made aware of the opportunity to participate via a series of communications and allowed to seamlessly self-enroll via their smartphones. No incentives were given to interested employees. All participants were guided through an initial onboarding period that explained the components of the initiative and the use of Noom's mobile application, set expectations for coach and participant responsibilities, and gathered baseline participant metrics. The 2 health coaches employed by the health system were also trained by Noom on how to use the Noom platform, including the mobile application functionalities, curriculum delivery in a virtual environment, the use of a coach dashboard, and foundational behavior change techniques.

When the initiative launched, participants received virtual delivery of condition-specific curriculum via their mobile device, virtual human coaching, and a combination of four 1-on-1 in-person meetings, scheduled coach check-in phone calls, and access to daily 2-way messaging via the mobile application. Participants also used the mobile application to log their food and beverage intake, physical activity, blood glucose, and/or blood pressure (as appropriate for their condition); completed in-app motivation and mood surveys at scheduled intervals; and were provided with program satisfaction surveys at 4-week intervals.

Using the Noom mobile application, participants took advantage of a proprietary food database that includes more than 3.7 million unique food-portion pairings to log all their meals. This

emphasized awareness and self-monitoring throughout the program. In addition, participants monitored and logged blood pressure and blood glucose, weight, and physical activity, and received ongoing support from a health coach and group of peers.

Eighty-two employees were enrolled in the program, with the majority being female (83%) between 50 and 64 years old (65%). Depending on eligibility, participants were placed in either diabetes management (20%), hypertension management (65%), or comorbid diabetes and hypertension management (15%) programs. A majority of baseline weights fell within the obese (20%) and morbidly obese (48%) classifications based on CDC guidelines and body mass index (BMI) categories. See the **Figure** and **Table** for a more detailed summary of baseline characteristics.

FIGURE. Gender Breakdown of Participants
All employees of health system (n = 82)
Diagnoses of type 2 diabetes, hypertension, or both

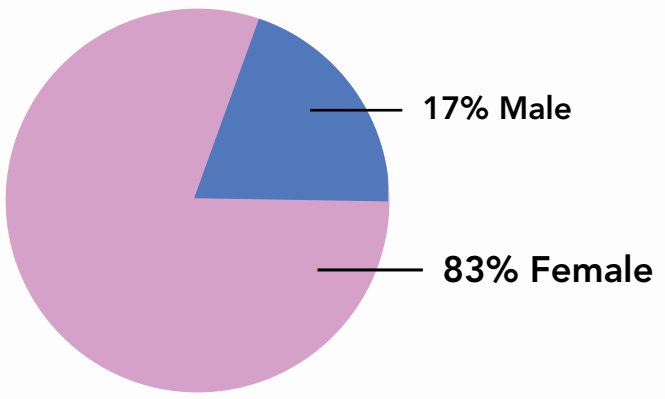

TABLE. Age, BMI of Participants

AGE BREAKDOWN	
18-34 years	5%
35-49 years	24%
65+ years	6%
BMI AT BASELINE	
Morbidly obese (BMI ≥40 kg/m^2)	48%
Obese (BMI ≥30 kg/m^2 to <40 kg/m^2	20%
Overweight (BMI ≥25 kg/m^2 to <30 kg/m^2	14%
Normal (BMI ≥18.5 kg/m^2 to <25 kg/m^2	5%
No data	13%

BMI indicates body mass index.
Source: CDC, About adult BMI. https://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html.

After just 14 weeks, participants demonstrated clinically significant outcomes and trajectories. All 82 participants remained engaged in the initiative. Of those who recorded a weight at baseline, 65% recorded weight loss, with an average loss of 3.4% of their body weight. Additionally, 21% of the cohort had already demonstrated transformative weight loss, that is, weight loss greater than 5%.[3] Sixty-seven percent of participants with diabetes or comorbid diabetes/hypertension demonstrated controlled blood glucose levels and 22% achieved normal fasting blood glucose levels as defined by the American Diabetes Association.[4]

Individuals with hypertension or comorbid diabetes/hypertension also demonstrated early improvements, 45% of whom reduced their blood pressure below 140/90 mmHg. Coaches reported, anecdotally, that the number of prescribed medications by some patients' primary care physicians went from 4 to 1 as a result of the lifestyle changes achieved.

Beyond improved health outcomes, the program scored positively among participants. Helpfulness of Coach Calls and Overall Satisfaction scored initial ratings of 4.3 and 4.2, respectively, on a 5-point Likert scale. Ninety-two percent of participants said they would recommend the program to a friend or family member. In addition, participants reported a high level of commitment to the program and increased confidence in making lifestyle changes across the board. They reported that the program was effective in addressing their specific personalized needs. Based on previously reported findings,[5] program satisfaction often predicts adoption and adherence.

TRADITIONAL IN-PERSON LIFESTYLE INTERVENTIONS STRUGGLE WITH PARTICIPATION AND LACK OF CONTEXT AND VISIBILITY.

The program will conclude in the third quarter of 2017. While the initiative is ongoing, participant progress has been significant thus far. The implications of such an initiative are paramount to helping prevent and manage potentially chronic conditions at scale. Extending beyond the examination room, institutions such as large health systems, which serve communities of hundreds of thousands of people while employing tens of thousands more, can successfully improve health outcomes and drive lasting behavior change across large populations.

Traditional in-person lifestyle interventions struggle with participation and lack context and visibility into the actions or behaviors of their population in the daily environment. However, by partnering with an innovative company like Noom, one health system was provided with a unique opportunity to meet (and help) their patients in the most convenient place imaginable—right on their mobile phone. ◆

DISCLOSURES

Author information: Andreas Michaelides, PhD, is chief psychology officer for Noom, Inc. Ed Pienkosz is the director of Business and Coach Development for Noom, Inc.

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