



DIABETES IS PRIMARY

TIMELY NEWS AND NOTES FOR PRIMARY CARE PROVIDERS
from the American Diabetes Association

By Max Bingham, PhD

FROM THE JOURNALS.....

Insulin Crisis: From Readily Available Drug to Unaffordable Luxury

Even though steps are being taken to address the sky-high price of insulin in the United States, they are insufficient, according to Fralick and Kesselheim (*New England Journal of Medicine*, doi.org/dk83), and more substantial reforms will be needed to address the issue. The price of a box of certain long-acting insulin formulations can reach as much as \$700, making it far more expensive than in other countries, where pricing is more controlled. The result: hundreds of reports of Americans rationing their medication and experiencing worsening glycemic control and, in some cases, death. How did this happen and what can be done about it?

In their analysis, Fralick and Kesselheim point to two issues that have led to insulin becoming an unaffordable luxury: a lack of regulation and a lack of competition in the United States. They point to U.S. laws allowing manufacturers to price their products at whatever price they think the market will accept and to raise their prices whenever they want. With regard to competition, they point out that just three manufacturers effectively control ~90% of the U.S. market and that effective competition among them is lacking. In short, they suggest that the U.S. market for insulin has failed.

To address this crucial issue, the authors review options to increase competition with generic products, although they acknowledge that there are challenges with this plan. They also cite examples of state- and federal-level interventions that are starting to make progress. Finally, they discuss the option of simply importing cheaper insulin, although they question the viability of this course, even though there is evidence that some individuals with diabetes are already doing it.

An interview with co-author Fralick is available at doi.org/dk83.

Max Bingham, PhD, is a science writer and editor in Rotterdam, Netherlands. He can be reached on Twitter at @maxbingham.

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WHO Launches Prequalification Program for Biosimilar Insulins

Although national-level efforts will hopefully start to force insulin prices down in the United States, an editorial in *The Lancet Diabetes & Endocrinology* (doi.org/dk85) describes an initiative of the World Health Organization (WHO) intended to address poor insulin availability and high costs at a global level. WHO announced its prequalification program for human insulin in November 2019 (bit.ly/33V7wmg). The initiative will allow manufacturers of generic or biosimilar insulin products to be assessed for prequalification, ensuring that these products meet internationally accepted standards, and so should increase the confidence in their use within international agencies and health care systems.

Survey Assesses Illicit Trading of Diabetes Treatments

Communities of people with diabetes in the United States are involved in an “underground exchange” of diabetes medications and supplies, according to a survey by Litchman et al. (*Journal of Diabetes Science and Technology*, doi.org/dk86). Despite most of the respondents reporting incomes well above the poverty line and adequate health insurance, the authors found that many individuals still turned to peers with diabetes to fulfill unmet medication needs, often in times of crisis. They warn that health care providers should be aware of such activity and investigate whether it is occurring with their patients.

In the survey of 159 individuals, mostly with type 1 diabetes, who self-reported underground activities, they found that 57% reported donating some kind of supply, 35% reported receiving donations, 24% reported trading supplies, 15% reported purchasing a black-market item, and 22% reported borrowing an item. Some individuals reported engaging in multiple activities. The researchers found that this underground exchange took place variously among family members, friends, coworkers, online acquaintances, and even online strangers.

Participants reported various reasons for the practice, including experiencing financial stress, facing bureaucracy

in obtaining products, feeling a sense of altruism and a desire to help others, having excess medications on hand, finding supplies cheaper online or offshore, and even needing to gain access to treatments and supplies at all. The authors noted that the practice in some cases allows patients to try alternative medications and that there is a desire to “try before you buy” before committing to a treatment. The article includes sample quotes from survey responses, some of which describe desperate situations of life-or-death decision-making.

“People have to make a decision,” lead author Michelle Litchman said in a statement (bit.ly/39mMPS1). “Do they want to maintain their health? And, if so, what are the medications and tools they need in order to stay healthy? In some cases, people have had to go to extreme measures and find a network that can supply their health care needs.”

An interview with Litchman is also available (bit.ly/2S7GVyo).

MARKETPLACE.....

Most Diabetes Apps Lack Vital Guidance on Taking Action

A growing array of diabetes digital apps are now available that claim to enhance diabetes self-management, providing decision support when out-of-range glucose levels are recorded. In theory, timely, on-the-spot advice should help users take appropriate action. According to Lum et al. (*Diabetes Metabolism Research and Reviews*, doi.org/dk88), however, most apps do not provide evidence-based steps to guide patients during episodes of hyperglycemia or hypoglycemia. In fact, their estimates suggest that fewer than one-fifth of available apps provide action points that meet the American Diabetes Association’s guidelines for glycemic management.

After screening just over 5,000 apps, the authors identified 371 (either for sale or free) that were designed for diabetes management and allowed users to enter their blood glucose

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TREATMENTS + THERAPIES

Lipid Profile Predicts Type 2 Diabetes Risk Better Than Obesity

A blood lipid profile common in people with type 2 diabetes predicts the risk of developing the disease many years in advance, according to Fernandez et al. (*Diabetes Care*, doi.org/dk89). Accordingly, they suggest that it might be possible to identify individuals at risk and intervene in terms of both lifestyle modification and primary prevention treatments targeting lipids and their metabolism. Further studies will be needed, but already these authors suggest that blood lipids contain enough new information to potentially predict the risk of diabetes many years in advance and beyond what is possible with the presence of obesity alone.

Based on a cohort of initially healthy individuals in the Malmö Diet and Cancer Study, the authors identified ~3,700 individuals who had suitable blood samples taken in the early 1990s and who were then followed up until the end of 2014 for incident type 2 diabetes. The samples were then subjected to lipidomics, a type of lipid profiling tool, to measure 178 molecular lipid species. Crucially, the individuals involved were randomized into a discovery set ($n = 1,868$) and a replication set ($n = 1,800$) prior to analysis.

In the discovery set, 257 individuals developed type 2 diabetes. The researchers then applied a statistical modeling tool to look at all 178 lipid species and their relationship to type 2 diabetes. From this process, they identified a profile of 77 lipid species that were linked to the risk of developing type 2 diabetes later in life. They further validated the predictive quality of the profile with the replication set (with 249 incident cases of type 2 diabetes), where they successfully predicted diabetes risk.

“In health care, the total amounts of cholesterol and triglycerides are measured, not the exact composition of the classes,” lead author Céline Fernandez explained in a statement (bit.ly/2SpH6Ux). “One class consists of several molecules, and in our study, we can see that it is good to have more of certain blood lipid molecules and less of others, and that these can be linked to lifestyle. This means that we could produce a better assessment of who had a high risk of developing type 2 diabetes.”

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Three Daily Meals (Not Six) Tied to Better Diabetes Outcomes

A three-meal approach to dietary intake in type 2 diabetes promotes weight loss and significantly improves glucose control, according to Jakubowicz et al. (*Diabetes Care*, doi.org/ggdgbk). Specifically, this approach, when used over a period of 12 weeks, appears to improve glycemic control and weight loss by about the same amount that can be expected from modern diabetes medications such as sodium–glucose cotransporter 2 inhibitors or glucagon-like peptide 1 receptor agonists.

The study, which involved 28 individuals with type 2 diabetes and obesity, randomized half to a diet that loaded nearly 50% of energy and carbohydrate at breakfast, followed by reduced intake at lunch and less still at dinner. The control group followed a six-meal approach involving three relatively smaller main meals plus three snacks, spreading energy and carbohydrate intake evenly throughout the day. Energy intake was limited to 1,500 calories per day in both groups.

The three-meal approach led to significant weight loss of ~5.4 kg and A1C reduction of ~1.2% after 12 weeks. There were also reductions in fasting, overall, and nocturnal glucose levels with the three-meal approach. The six-meal approach, in comparison, had no effect, even with the limited calorie intake.

Individuals on the three-meal plan experienced a substantial reduction in insulin requirements, and continuous glucose monitoring indicated a substantial reduction in hyperglycemia. The three-meal approach also yielded reductions in hunger and in cravings for sugar, high-carbohydrate/high-fat foods, and fast food.

“The traditional diet specifies six small meals spread throughout the day, but this diet has not been effective for glycemic control,” lead author Daniela Jakubowicz said in a statement (bit.ly/2S4MdKK). “Our research proposes shifting the starch-rich calories to the early hours of the day. We believe that through this regimen, it will be possible for [people with diabetes] to significantly reduce or even stop the injections of insulin and most antidiabetes medications, to achieve excellent control of glucose levels.”



ADA NEWS

NEW APP SUPPORTS GUIDELINES-BASED TREATMENT

The Know Diabetes by Heart A1CVD Pro professional education app is a competency-based medical education program tailored to the needs of busy health care professionals. Aimed at clinicians who treat patients with type 2 diabetes, this free tool is designed to improve clinical decision-making and understanding of current American Heart Association (AHA) and American Diabetes Association (ADA) treatment guidelines for diabetes and cardiovascular disease (CVD), taking users through a simulation experience through which they are presented with real-life case studies, given a series of treatment decisions, and guided through current practice guidelines. The new app is available in the Apple App Store and Google Play. Learn more at bit.ly/31yffpr.

NEW CONSENSUS REPORTS FOCUS ON DIABETES DIGITAL APPS, HYPERGLYCEMIA MANAGEMENT

A joint consensus report from ADA and the European Association for the Study of Diabetes (EASD) (doi.org/dk9f) reviews diabetes digital health technology and outlines recommendations for regulatory agencies, manufacturing companies, professional societies, funding bodies, researchers, health care providers, and people with diabetes.

ADA and EASD also recently published a 2019 update to their recommendations on hyperglycemia management (doi.org/gghfjw). New evidence from large cardiovascular outcomes trials led to inclusion of additional considerations for treatment with a glucagon-like peptide 1 receptor agonist or a sodium–glucose cotransporter 2 inhibitor in the setting of type 2 diabetes and established CVD.

ONLINE EDUCATIONAL RESOURCES AVAILABLE

Diabetes and Hypertension Webcast

ADA, AHA, and the Association of Black Cardiologists recently partnered to present a live discussion on “The Management of Type 2 Diabetes and Hypertension.” The program reviewed current guidelines, barriers to hypertension and diabetes management, and clinical solutions to reduce those barriers. A webcast of the program can be viewed at bit.ly/373qBmc.

Diabetes Prevention Program Webcast Series

ADA offers a free webcast series focusing on identifying and treating people with prediabetes, understanding the benefits of structured lifestyle change programs, and making referrals to a National Diabetes Prevention Program in your community. Continuing education credits are available. Register at bit.ly/33VChHS.

Self-Assessment Program on CVD Risk Reduction

Self-assessment programs, which consist of multiple-choice clinical problem-solving questions and educational explanations for each answer, are designed to assess and strengthen knowledge of evidence-based care for type 2 diabetes. The latest such program, on CVD risk reduction in type 2 diabetes, explains how to estimate a patient’s risk of atherosclerotic CVD, the clinical importance of diabetes-specific risk enhancers for CVD, and the appropriate management of blood pressure and cholesterol for people with diabetes. Continuing education credits are available. The program can be accessed at bit.ly/2vb6uoQ.

Continuing Education for Primary Care Providers

ADA offers free continuing education activities designed for primary care providers. Current topics include:

- Patient-Centered Care: What This Means for PCPs (available from bit.ly/2Sjbr7f)
- Talking Nutrition in Primary Care (available from bit.ly/371gTRt)
- Exercise in Primary Care (available from bit.ly/2SpjTSx)
- Caring for Asian Americans, Pacific Islanders, and Native Hawaiian Populations (available from bit.ly/2UuJnR8)
- PCP Survival Guide to Diabetes Technology (available from bit.ly/2v7mmJj)

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levels. Using predetermined blood glucose values indicative of hyperglycemia and hypoglycemia, they then tested each app to determine the appropriateness of the suggested response according to care guidelines. Inappropriate responses were defined as not being aligned with the guidelines or providing advice that was non-specific or too general to be useful.

Of the 371 apps they identified, 217 and 216 alerted users about hypoglycemia and hyperglycemia, respectively. Of these, 45 (of 217, or 20.7%) provided action prompts with respect to hypoglycemia, and 33 (of 216, or 15.3%) did so for hyperglycemia.

Of the apps providing such prompts, the authors rated 86.7% as giving appropriate advice and 24.4% as giving inappropriate advice in relation to hypoglycemia. For hyperglycemia, 97% were found to give appropriate advice, while 33% gave nonspecific or unhelpful advice.

“This study highlighted the low presence of appropriate action prompts for patient self-management of out-of-range blood glucose in diabetes apps,” the authors conclude. “Better app design processes and standards to ensure appropriate, evidence-based action prompts for patient self-management of out-of-range blood glucose should be required for diabetes apps.”



CONFERENCE SPOTLIGHT

Basic Clinical and Laboratory Measurements Can Predict Chronic Kidney Disease Risk

A study presented at the American Society of Nephrology Kidney Week in November 2019 and simultaneously published in the *Journal of the American Medical Association* will likely have immediate relevance to primary care. According to Nelson et al. (doi.org/dk9c), identifying chronic kidney disease (CKD) risk from common clinical and laboratory measurements is possible and may be useful in ordinary clinical practice to help patients avoid this complication.

The authors combined data from 34 multinational cohorts within the CKD Prognosis Consortium that included ~5.2 million individuals over the period from 1970 to 2017. Their main outcome was progression to an estimated glomerular filtration rate (eGFR) indicative of CKD. Significantly, they split their analysis between individuals with and without diabetes.

Individuals without diabetes had an incident rate of ~15% for reduced eGFR, whereas 40% of those with diabetes experienced

the same outcome. From this finding, the authors developed risk models that predicted kidney outcomes based on factors as simple as height, weight, and regularly collected clinical and laboratory-derived measurements. After further validation, they concluded that their approach offers predictive ability up to ~5 years before reduced eGFR occurs.

"With the risk equations that we've developed, physicians should be able to determine with high accuracy who will or won't develop chronic kidney disease in the next few years, and our analyses suggest that they can maintain that accuracy in a variety of clinical settings globally," senior author Josef Coresh said in a statement (bit.ly/2Owsn9d).

The authors have since published a series of online apps allowing clinicians to input basic data such as urinary test values, demographics, and geographic location to get a prediction on whether individual patients, including those with diabetes, might be at elevated risk for various kidney diseases or even kidney failure. The models and online calculators are available at www.ckdpcrisk.org.

To learn more about ADA's continuing education opportunities, including Diabetes Is Primary events in your community, please visit **professional.diabetes.org/ce**.