ENDOGEAR: AUTOMATED DIABETES CARE PRODUCTS

NOVEMBER 2024

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Endocrine news

Dimensions *in* Diabetes

- **UNSOLVED MYSTERIES:** Four decades at the bench and **Daniel Drucker, MD**, is still unlocking scientific secrets.
- **PHARMACEUTICAL PHENOMENA:** Recent studies shed light on the safety and efficacy of diabetes medications.
- **ALL THE RAGE:** Combatting counterfeit weight-loss and diabetes drugs flooding the market
- **BEATING PREDIABETES:** New research explores the impact of prediabetes on a Mexican population.

This month, *Endocrine News* focuses on the research and the researchers striving to better understand the science and treatment of diabetes.

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14 | Unsolved Mysteries

Four decades at the bench and Daniel Drucker, MD, is still unlocking scientific secrets.

The Endocrine Society's 2025 Fred Conrad Koch Lifetime Achievement Award recipient, Daniel Drucker, MD, first discovered his passion for science in high school when he learned "this is how stuff works." He's still learning to this day, and he tells *Endocrine News* about his ongoing scientific quests, the mentors who made a difference along the way, and why even old ideas are still valid. **BY GLENDA FAUNTLEROY SHAW**

22 | Pharmaceutical Phenomena

Recent studies shed light on the safety and efficacy of diabetes medications.

GLP-1 receptor agonists, SGLT2 inhibitors, and DPP4 inhibitors were all scrutinized in new research presented at **ENDO 2024**. While most of the results were good news for the impact of medications for people with type 2 diabetes, clinicians prescribing these medications should be aware of specific side effects in certain populations as well as obstacles regarding patient access.

BY KELLY HORVATH

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ENDOCRINE SOCIETY
Hormone Science to Health

Advocacy for Diabetes Care

> Regardless of the dates on which these campaigns fall around the world, the aim is generally the same: to increase awareness of the impact that diabetes has on patients and their families, the complications caused by the disease, and healthcare policies and practices needed to improve care.

In the U.S., November is designated as American Diabetes Month. The World Health Organization sets aside November 14 as Diabetes Day. And here in the U.K., we blocked out June 10 – 16, 2024, as Diabetes Week. Globally, many other countries have similar diabetes mellitus recognition events in their calendars.

Regardless of the dates on which these campaigns fall around the world, the aim is generally the same: to increase awareness of the impact that diabetes has on patients and their families, the complications caused by the disease, and healthcare policies and practices needed to improve care.

The Endocrine Society has a long history and deep commitment to tackling diabetes.

I'm always proud to let people know that scientists in our field were the ones who discovered and created diabetes treatments using insulin more than 100 years ago. And I'm equally proud to highlight our ongoing accomplishments in treating diabetes and its related causes, many of which you can read in this special diabetes-themed November issue of *Endocrine News*. Diabetes research also is the topic of our latest thematic issue from the Endocrine Society's journals.

I'd like to underscore several recent milestones in our work in the area of diabetes.

On the U.S. advocacy front, the Society was invited to an August 13 event at the White House commemorating passage of the Inflation Reduction Act. That law included a landmark provision requiring all Medicare Part D plans to charge no more than $35 per month for all covered insulin products.

The Society was the leading advocate for this remarkable legislation, which has saved countless U.S. citizens millions of dollars each year on their medication expenses. Undoubtedly, this law also has saved lives and reduced morbidity, as many people living with diabetes had previously forgone their insulin treatments due to costs.

The Endocrine Society was represented at the White House by member **Joshua J. Joseph, MD, MPH**, a professor at The Ohio State University College of Medicine and the former chair of the Society's Clinical Affairs Core Committee. Joseph is a passionate advocate for ensuring all people living with diabetes receive affordable medicines needed for their diabetes care. Our work to lower insulin costs in the U.S. will continue for individuals who receive healthcare under private insurance companies and those who are uninsured.

Moving forward, our advocacy team has launched a campaign to encourage U.S. lawmakers to reauthorize the Special Diabetes Program (SDP), which is set to

expire on December 31, 2024. The SDP is a federal program composed of two components to advance research for type 1 diabetes and provide treatment and education programs for type 2 diabetes among American Indians and Alaska Natives. I encourage you to join the Society in urging Congress to continue this program by passing legislation that would extend it for two years at $170 million per program per year.

Whether provided through government or private health programs, the Society wants to ensure all patients receive the best diabetes care possible. Our organization has partnered with the American College of Osteopathic Family Physicians to develop a holistic certificate program covering many facets of diabetes care. You can learn about it at: **https://www.endocrine.org/store/online-education/comprehensive-care-for-persons-with-diabetes-a-certificate-program**.

Society Also Leads on Obesity Care

On the diabetes-related topic of obesity, the Society also has been demonstrating its leadership in recent months.

One of the most prestigious awards in medical science is the Lasker~DeBakey Clinical Medical Research Award, which is often seen as a precursor to the Nobel prizes. Three Society members have taken home the 2024 award for their roles in the discovery and development of GLP-1-based obesity drugs, designed initially to treat diabetes. These members are:

- **Joel F. Habener, MA, MD**, chief of Laboratory of Molecular Endocrinology, Massachusetts General Hospital;
- **Lotte Bjerre Knudsen, DMSc**, chief scientific advisor and head of the GLP-1 Centre of Excellence at Novo Nordisk; and
- **Svetlana Mojsov, PhD**, research associate professor at Rockefeller University in New York.

Our fellow members are improving the health of millions of people through use of these remarkable drugs.

On a similar vein of recognition, long-time Society member **Daniel Drucker, MD**, is the recipient of the Society's highest honor, the Fred Conrad Koch Lifetime Achievement Award, this year for his role as a pioneer in advancing next-generation treatments for diabetes and weight loss. Drucker was a postdoc in Joel Habener's lab, where he made discoveries about glucagon-like peptides (GLP-1 and GLP-2) that contributed significantly to the development of new classes of drugs, including semaglutide and tirzepatide.

> **As you can see, your Society is extremely active in these important areas that affect global public health. Wherever you reside, I wish you a successful diabetes recognition event!**

I invite you to watch a series of fascinating video interviews with Drucker on the Society's Focus on Obesity webpage. Be sure to read more about Drucker's life and career in this issue on page 14.

The Society also is leading the medical field in training experts on obesity care. In late September, the Society held its second-annual Obesity Fellows Program, an in-person and online course on best practices in obesity care for endocrinology fellows. Roughly 50 fellows participated in the in-person program at the Society's headquarters in Washington, D.C.

Finally, at **ENDO 2025** in San Francisco, Calif., July 12 – 15, attendees will be treated to a master class in the field of obesity care at one of the three plenary sessions taking place from 8:00 AM to 9:15 AM (PDT) on Monday, July 14, 2025. Titled "**Innovative Approaches in Obesity Care: From Molecules to Society,**" the speakers are **Jens Holst, MD, DMSc**, who will discuss *Incretins: the silver bullet?,* and **Fatima Stanford, MD, MPH, MPA**, who will explore the changing game of obesity care across lifespans, including policies, diets, and drug innovation.

As you can see, your Society is extremely active in these important areas that affect global public health. Wherever you reside, I wish you a successful diabetes recognition event! EN

John Newell-Price, MD, PhD, FRCP
President, Endocrine Society

A Diabetes Discourse

If it's November, then it must be time for an issue of *Endocrine News* devoted entirely to the science and treatment of people living with diabetes to coincide with Diabetes Awareness Month in the United States. Each year, we highlight the work of our members around the world and the research they conduct that contributes to a better understanding of diabetes, which, hopefully, could one day lead to a cure.

One of the world's leading and much lauded researchers, Daniel Drucker, MD, is featured in **"Unsolved Mysteries"** on page 14 by Glenda Fauntleroy Shaw. No stranger to the readers of *Endocrine News* nor the members of the Endocrine Society, Drucker is the recipient of the Society's 2025 Fred Conrad Koch Lifetime Achievement Award, the highest honor that can be bestowed on an endocrinologist by the Endocrine Society. After four decades of diabetes research, Drucker has garnered more recent acclaim for his discoveries related to GLP-1s and their impact on obesity. However,

> "Each year, we highlight the work of our members around the world and the research they conduct that contributes to a better understanding of diabetes, which, hopefully, could one day lead to a cure."

that research started many years ago, and Drucker says some people still complain that he has no new ideas, a critique he takes in stride. "That's a valid criticism," he acknowledges. "But for me, to see all of these fantastic new trials showing benefits in people, I really still want to understand how these medicines work." Onward and upward.

Speaking of GLP-1s and their ilk, on page 22, Kelly Horvath uncovers recent research presented at **ENDO 2024** that sheds light on the safety

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and effectiveness of a number of diabetes medications in **"Pharmaceutical Phenomena."** GLP-1 receptor agonists, SGLT2 inhibitors, and DPP4 inhibitors were all scrutinized in these studies, and, fortunately, most of the results were good news for people with type 2 diabetes. But clinicians prescribing these medications should be aware of specific side effects in certain populations as well as obstacles regarding patient access.

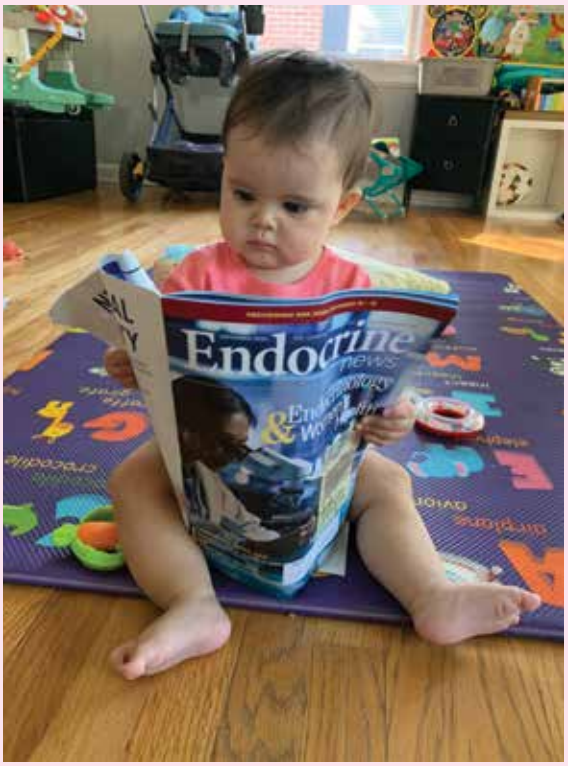
Another often confounding condition — prediabetes — was also highlighted at **ENDO 2024**, this time looking at its impact on certain Mexican populations and is discussed in **"Beating Prediabetes"** on page 32. Kelly spoke with Carlos A. Fermín-Martínez, MD, who discusses his findings and why it's important for clinicians to screen for prediabetes, especially in susceptible populations. Fermín-Martínez was part of a diabetes-focused series of press conferences at **ENDO 2024**, and his research showed that prediabetes can increase the risk of dying before the age of 75, particularly due to heart disease, kidney disease, and acute diabetic complications in these populations. "In our study, participants were initially free of diabetes," Fermín-Martínez says. "However, eventual development of diabetes likely accounts for a significant percentage of deaths, further highlighting that early detection and management of prediabetes is crucial to reduce mortality and cardiometabolic disease."

On page 28, Eric Seaborg looks into the steps clinicians can take to combat the abundance of counterfeit weight-loss and diabetes drugs that have flooded the market thanks to an onslaught of email spam and online pop-up ads. In **"All the Rage,"** Eric discusses the phenomenon that GLP-1s have become as they garner celebrity endorsements and an ever-increasing demand from consumers looking for a quick weight-loss solution. Moreover, many insurance companies will not cover the cost of the drugs for the people who need them, so they're forced to find online pharmacies with more affordable prices. "This is a challenging situation," says Priyanka Majety, MD, assistant professor, Division of Endocrinology, Diabetes, and Metabolism at the Virginia Commonwealth University in Richmond, Va. "We encounter patients every day who would greatly benefit from these medications, but their insurance won't cover them. So, while it's unfortunate that some patients are turning to unregulated online pharmacies to get these medications, it's not entirely surprising." Sadly, this article will be the last Eric will write for us since he has decided to dive into retirement. All of us at *Endocrine News* and the Endocrine Society wish him well and happy trails!

As always, if you have any questions, comments, or suggestions for topics you would like to see covered in *Endocrine News*, feel free to contact me at: **mnewman@endocrine.org**.

— Mark A. Newman, Executive Editor, *Endocrine News*

Reader of the Month



No, this is not a new intern at *Endocrine News*, it's Amelia, the eight-month-old daughter of Endocrine Society member Claudia Villatora, MD, PhD, clinical instructor at the Division of Endocrinology, Metabolism, and Lipid Research at Washington University in St. Louis, Mo., who shared this adorable photo online. Amelia likes birds and, judging from her concentration, learning about reproductive endocrinology from our September issue!

Newest Scientific Statement Reviews Research on Opioids' Effect on Bone, Adrenal Health

A new Scientific Statement published by the Endocrine Society highlights research gaps associated with the negative effects of opioid use on the endocrine system.

The use and misuse of opioids are a growing global problem. Opioids are used to treat pain in people with cancer or other conditions (e.g., after an injury or surgery); however, they are highly addictive and people can develop opioid use disorder (OUD). The World Health Organization estimates 125,000 people died of opioid overdoses in 2019.

The use and misuse of opioids has a negative effect on our hormones and can lead to reproductive, bone, and adrenal health complications. "Exogenous Opioids and the Human Endocrine System: An Endocrine Society Scientific Statement," reviews data related to the use and misuse of opioids and the effects of these drugs on the endocrine system. The Statement discusses recent research on the clinical consequences of opioids, especially on the hypothalamic-pituitary system and bone health.

"We address the many research gaps associated with the effects and clinical consequences of opioids on the endocrine system within this Scientific Statement," says lead Statement author Niki Karavitaki, MSc, PhD, FRCP, of the University of Birmingham, Birmingham Health Partners, and the University Hospitals Birmingham National Health Service Foundation Trust in Birmingham, U.K. "We hope bringing attention to recent research in the space, including opioid use's impact on gonadal, bone, and adrenal conditions, will improve the endocrine health of people using or misusing opioids worldwide."

The authors report hypogonadism as a well-recognized side effect of opioids and provide more clarity around the drug's lesser-known effects on the hypothalamic-pituitary system and bone health. They discuss the link between opioids and the development of hyperprolactinemia and how more research is needed to understand their effect on secondary adrenal insufficiency.

The Statement authors also assessed how opioids affect the secretion of certain hormones to better understand the connection between opioid use and endocrine disease. These hormones include growth hormone, prolactin (responsible for milk production and lactation), arginine vasopressin (regulates the body's water balance and blood pressure), and oxytocin (plays a crucial role in the childbirth process).

They also reviewed research into opioid's actions on bone metabolism and their negative impact on bone mineral density and risk of fracture.

"Clinicians should monitor patients who are using opioids more closely for signs and symptoms of these endocrine health consequences," Karavitaki says.

The statement, "Exogenous Opioids and the Human Endocrine System: An Endocrine Society Scientific Statement," was published online in the Society's journal, *Endocrine Reviews*.

Endocrine Society Partners with Keystone Symposia to Advance Research and Education

The Endocrine Society and Keystone Symposia, a nonprofit host of conferences and symposia on a range of life science and biomedical topics, will jointly host a series of three conferences to advance endocrine research.

The three conferences will focus on diabetes, oncology, and cardiovascular disease — hormone-related conditions that have a major impact on public health. The conference series is slated to launch in late 2026 or early 2027 and will run for at least three years.

Each event will feature the top-flight scientific programming and luminary speakers both organizations are known for. The conferences are designed to accelerate scientific

breakthroughs, catalyzing advances in foundational science that can ultimately lead to improved clinical outcomes for patients.

"We are elated about the opportunity to collaborate with Keystone Symposia in the spirit of advancing science," says Endocrine Society President John Newell-Price MD, PhD, FRCP. "Our basic research members value the opportunity to discuss science with other leading members of the field, and this series of conferences will offer more chances for basic researchers to interact and share ideas."

Keystone Symposia specializes in holding intimate conferences in relaxed environments that encourage networking and foster connections among attendees. Building relationships with other researchers can inspire scientists to pursue new lines of inquiry and form partnerships, which can advance discoveries.

"This partnership will be instrumental in bringing together basic scientists with clinicians and clinician-scientists to accelerate translational advances that will impact patients. We are thrilled to connect with the Endocrine Society to facilitate this common goal," says Keystone Symposia President and CEO James Baumgartner, PhD. "These conferences will spur innovative perspectives and collaborations that integrate laboratory research with clinical insights, to ultimately yield breakthroughs against three of the most deadly diseases we face in modern society — cardiovascular disease, diabetes, and cancer."

The Endocrine Society and Keystone Symposia plan to hold the conferences annually for at least three years.

Endocrine Society's Obesity Fellows Program a Success

For two days in late September, the Endocrine Society's headquarters in Washington, D.C., played host to almost 50 members who attended the Society's second Obesity Fellows Program.

This blended learning experience presented the best practices in obesity care tailored exclusively for endocrinology fellows. Chaired by obesity medicine expert Amy Rothberg, MD, DABOM, the program was an exclusive application-based educational activity that offered a variety of topics, including the Current State of Obesity Management; Body Composition; Challenging Case Studies; Lifestyle Interventions to Treat Obesity; Side Effects of Pharmacologic Treatment; and much more.

This year's program welcomed 49 fellows from 20 U.S. states, Washington, D.C., and Puerto Rico, and was supported by an educational grant from Lilly and Novo Nordisk.

For more information: **https://www.endocrine.org/education-and-training/obesity-fellows-program.** EN

BY DEREK BAGLEY
Senior Editor

People with Type 2 Diabetes Who Eat A Low-Carb Diet May Be Able to Discontinue Medication

Adults with type 2 diabetes on a low-carbohydrate diet may see benefits to their β-cell function allowing them to better manage their disease and possibly discontinue medication, according to new research published in *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Barbara Gower, PhD, of the University of Alabama at Birmingham in Birmingham, Ala., point out that the possibility that the progression of type 2 diabetes can be mitigated is suggested by the return of glycemic control with bariatric surgery in patients with type 2 diabetes.

"Similarly, data obtained with very-low-calorie diet interventions have shown that severe energy restriction also can induce remission of type 2 diabetes and permit the return of first-phase insulin response," the authors write. "Autopsy studies have shown that β-cell neogenesis occurs in the pancreas of type 2 diabetes patients. Taken together, these observations suggest that remission of type 2 diabetes may be possible."

> **"Autopsy studies have shown that β-cell neogenesis occurs in the pancreas of type 2 diabetes patients. Taken together, these observations suggest that remission of type 2 diabetes may be possible."**

The authors go on to write that, as a group, African Americans have a higher prevalence of type 2 diabetes than European Americans, and that this higher risk is at least in part independent of obesity, lifestyle, and demographic variables. "Greater β-cell responsiveness early in life has been observed in African Americans and may predispose to later β-cell failure," the authors write. "It is possible that inherent β-cell vulnerability plays a primary role in the etiology of type 2 diabetes in African Americans."

"Therefore," the authors continue, "the purpose of this study was to determine if a carbohydrate-restricted diet (CR) when compared to a higher carbohydrate diet (HC), in the absence of weight loss, would improve β-cell function, as assessed from a hyperglycemic clamp and an oral glucose tolerance test (OGTT) in a population of African American and European American adults with type 2 diabetes. A secondary aim was to determine if the changes in β-cell function induced by the diet differed with self-reported race."

For this study, the researchers gathered data from 57 White and Black adults with type 2 diabetes, half on a low-carbohydrate diet and the other half on a high-carbohydrate diet and examined their β-cell function and insulin secretion at baseline and after 12 weeks.

All of the participants' meals were provided. People on the carbohydrate-restricted diet ate 9% carbohydrates and 65% fat, and participants on the high-carbohydrate diet ate 55% carbohydrates and 20% fat.

The researchers found those on a low-carbohydrate versus a high-carbohydrate diet saw improvements in the acute and maximal β-cell responses that were two-fold and 22% greater, respectively. Within each race group, Black adults on a low-carbohydrate diet saw 110% greater improvements in the acute β-cell response, and White adults had improvements in the maximal β-cell response that were 48% greater than their respective counterparts on the high-carbohydrate diet.

"Further research is needed to determine if a low-carbohydrate diet can restore β-cell function and lead to remission in people with type 2 diabetes," Gower says.

HDL Quality, Not Quantity, Contribute to the First Sign of Alzheimer's Disease in Women

Higher levels of HDL-C — known as the "good cholesterol" — have been shown to correlate with heightened risk for Alzheimer's disease, according to a study recently published in *The Journal of Clinical Endocrinology & Metabolism*.

Once women reach the menopause transition, it's a matter of the quality, rather than quantity, of the total cholesterol carried by HDL particles circulating in a woman's bloodstream, and that quality declines over time, according to a research team led by a University of Pittsburgh School of Public Health epidemiologist.

Researchers led by Samar R. El Khoudary, PhD, MPH, professor of epidemiology at Pitt Public Health, point out that women constitute almost two-thirds of Americans with Alzheimer's disease, the most common type of dementia. After midlife, women experience faster cognitive decline than men.

The authors write that for this study, they aimed to: "1) assess associations of comprehensive metrics of serum HDL at midlife and their change over midlife with future cognitive performance among women and 2) test if the associations of changes in HDL-CEC with cognitive performance are modified by changes in HDL lipid contents and subclasses. Considering alterations of HDL metrics in midlife women, we defined the baseline HDL as the midlife level and the difference between subsequent and the HDL measures at midlife as the changes over midlife. We hypothesized that smaller HDL size, higher HDL-phospholipid (HDL-PL), more apoA-1, greater total HDL-P, and higher HDL-CEC at and over midlife are associated with a better future cognitive performance."

HDL particles vary in their size, composition, and level of functioning. The team measured these features in the blood of 503 women from the Study of Women's Health Across the Nation (SWAN) HDL ancillary study. The researchers found that, over time, the number of larger HDL particles in the women's bodies increased — and these larger particles, unfortunately, did not function as well as their smaller counterparts.

The researchers conducted repeated assessments of study participants' cognitive function from 2000 to 2016 and compared these data to changes in the women's HDL particles, composition, and function as they aged.

"We were able to show that as early as midlife, women who have more of the smaller-size particles and those whose particles' concentrations of phospholipids increased over the menopause transition are more likely to experience better episodic memory later in life," El Khoudary says, adding that loss of working memory is the first sign of Alzheimer's disease.

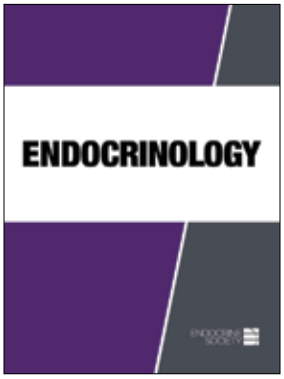
Previously, El Khoudary's team has shown that health behaviors — such as those included in the American Heart Association's (AHA) Life's Essential 8 — work to improve the quality of HDL particles, for example, by adding more of the phospholipid-rich particles in the bloodstream.

"That's the good news in this developing picture of brain health and the 'not-so-good-after-all' cholesterol," says El Khoudary. "Even though higher levels of HDL-C may not be protective as you get older, there are things you can do that might help, even as early as your 40s. The same, modifiable risk factors that the AHA is advocating for — including physical activity, ideal body weight, and quitting smoking — can help you protect your brain, too." EN

"We were able to show that as early as midlife, women who have more of the smaller-size particles and those whose particles' concentrations of phospholipids increased over the menopause transition are more likely to experience better episodic memory later in life."

CALL FOR APPLICATIONS: EDITOR-IN-CHIEF OF *ENDOCRINOLOGY*

APPLICATIONS OPEN FROM NOVEMBER 1–29, 2024



The Endocrine Society calls for applications for the next Editor-in-Chief (EIC) of *Endocrinology*, the Society's premier basic science journal, publishing continuously online on basic and translational research at molecular, biochemical, cellular, genomic, comparative, and organismal levels.

Endocrinology is ranked as one of the most authoritative and cited research journals in its field. It is the seventh most-cited journal among 187 journals in the Clarivate category "Endocrinology & Metabolism," earning more than 34,000 citations in 2023, and has the category's highest Cited Half-Life with a median of 14.8 years.

The EIC position requires a dynamic, internationally recognized researcher who has a broad background in the field and is committed to working with the Society to continue *Endocrinology's* history of forward-looking editorial leadership to maximize the journal's impact and success.

The successful candidate will receive a stipend, travel allowance, and serve for a three-year term, beginning January 2026, with preparatory work beginning in late summer/fall 2025.

RESPONSIBILITIES

Based at their home institution, the EIC reports to the Society's Publications Core Committee and works with professional publishing staff at the Society's headquarters in Washington DC, to:

- Serve as a global ambassador and advocate for *Endocrinology*, bringing high-impact authors and high-impact areas to the journal
- Advance and contribute to the Society's strategic plan for the journal and its place in the Society's publishing program
- Identify and recruit qualified experts internationally for Deputy Editor (DE), Associate Editors (AEs), Editorial Board members, and reviewers
- Oversee fast, fair, and professional peer review by the journal's DE and AEs, working to improve performance metrics
- Cover research in keeping with research trends and the Society's mission
- Be a member of the Society and remain in good standing for the duration of the term
- Maintain a professionally based institutional affiliation that provides the informational and technical resources required for full professional participation with peers

EDITORIAL STRUCTURE

The EIC will lead a team of a DE and AEs as identified by the EIC and approved by the Society, supported by an Executive Editor and others on staff at the Society.

- *Endocrinology* has a distributed decision-making structure among its DE and AEs, intended to distribute workloads more broadly and speed time to decision and publication
- Manuscript submissions typically go directly to the DE and AEs, each of whom is responsible to the EIC for managing peer-review and making final decisions on manuscripts submitted to their areas of responsibility

APPLICATIONS

Applicants should submit:

- Description of qualifications (up to two pages)
- Views on the present status of the journal, opportunities for growth and enhancement, and plans to achieve goals (up to three pages). An information packet for prospective applicants summarizing the journal's current status is available from the Society at the email address below
- *Curriculum vitæ*

In evaluating candidates, the Search Committee will consider the following criteria:

- Ideas about novel approaches and receptivity to innovation during a time of great change in the scientific publishing field
- The capacity to build on an established record of success, while continuing to evolve a leading journal in the field and take it to the next level
- Demonstrated ability to lead colleagues and work with staff
- Previous editorial leadership experience
- Adequate time flexibility to take on the responsibilities of EIC
- A distinguished record of research in endocrinology-related fields
- Demonstrated ability to work with online manuscript submission and peer-review systems. The Society uses Editorial Manager™
- Recognized service to and leadership in the science community

All members of the Endocrine Society are encouraged to consider applying and to share this announcement with suitable candidates. Applications should be sent to: Richard O'Grady, Chief Publications Officer, Endocrine Society, at rogrady@endocrine.org. The deadline for receipt of completed applications is November 29, 2024.

ENDOCRINE SOCIETY

> That's the thing about basic science. It sometimes literally will take a decade or even longer, to become apparent what the real relevance and potential is. Back in those days, none of us foresaw the current landscape with regard to obesity. **We thought GLP-1 might be useful as a diabetes treatment, and after 15 or 20 years, that turned out to be the case, but I think the obesity story was not really apparent to anybody in the 1980s. That came much later."**

Daniel Drucker, MD, the recipient of the Endocrine Society's 2025 Fred Conrad Koch Lifetime Achievement Award, discussing the impact of the GLP-1 discovery decades later in **"Unsolved Mysteries"** on page 14.

40%

The percentage of pregnant women who suffer from Short Sleep Duration — sleeping fewer than seven hours per night due to hormonal changes, frequent urination, and other factors — putting them at a higher risk of having children with neurodevelopmental delays.

— **SOURCE:** *THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM*

65%

The percentage of insulin users in the U.S. who had adopted continuous glucose monitoring by the end of 2023, a 38% increase from 2019.

— **SOURCE:** DIABETES TECHNOLOGY SOCIETY

60,000,000

The number of American adults predicted to be diagnosed with diabetes by 2060.

SOURCE: CDC "PROJECTION OF THE FUTURE DIABETES BURDEN IN THE UNITED STATES" REPORT

10%

While 40% of adults living in the U.S. are currently classified as obese, nearly 10% of the population is considered "severely obese," significantly raising the risk for diabetes, metabolic syndrome, and additional endocrine and cardiovascular complications.

SOURCE: NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

20%

Women taking estrogen-only hormone therapy after age 65 were 20% less likely to die than those who had never taken or who had quit taking it.

SOURCE: *FORTUNE*

30 to 45 MINUTES

In healthy individuals, the majority of cortisol secretion occurs within several hours surrounding morning awakening, with the most active secretory period, known as the cortisol awakening response (CAR), taking place in the first 30 to 45 minutes after waking up. **SOURCE:** *ENDOCRINE REVIEWS*

ENDO 2025

We hope to see you at **ENDO 2025**, taking place July 12 – 15, 2025, in San Francisco, Calif. With more than 7,000 attendees, nearly 2,000 abstracts, and more than 200 other sessions, **ENDO** is the top global meeting on endocrinology research and clinical care. **ENDO** provides the opportunity to collaborate with an unparalleled list of endocrinologists, healthcare practitioners, and leading scientists from around the world. Through sharing our experience, advice on patient care, and new advances in research, we move the needle forward in hormone health and science.

Our outstanding slate of world-renowned speakers will showcase the most cutting-edge advances in research and medicine, with presentations spanning the spectrum of science, clinical care, and social implications.

https://www.endocrine.org/meetings-and-events/endo-2024

Abstract Submission period:
December 5, 2024 – January 30, 2025

26th Davidson Mestman Intensive Course

Miami, Florida
December 11 – 14, 2024

Presented entirely in Spanish, the main objective of this intensive course is to provide physicians with specialized and advanced training in the diagnosis, treatment, and comprehensive management of patients with endocrine disorders, diabetes, and associated cardiovascular diseases, obesity, and endocrine cancers. The program will focus on updating and honing participants' clinical skills, enabling them to deliver cutting-edge, personalized medical care in these specialized areas.

https://www.cursodavidsonmestman.com/

Lab Manager's Innovating the Future Digital Summit

Virtual Event
December 11 – 12, 2024

At *Lab Manager's* Innovating the Future Digital Summit, business leaders will discuss the most recent advancements in lab technology, automation, and services as well as what lies ahead in the immediate and long term. Register for this free event, which will provide you with knowledge and practical experience to help you create a lab that is optimized and future-proof. Following each presentation, audience members will be given the opportunity to ask the speakers questions in order to get guidance on their individual labs and circumstances.

https://www.labmanager.com/innovating-the-future-digital-summit-31347

2025 CDEI 60th Annual CME Conference

Vail, Colorado
January 24 – 28, 2025

The Clinical Diabetes and Endocrinology Institute 60th Annual CME Conference will be a dynamic, interactive experience with highly relevant clinical endocrinology sessions including the fast-changing landscape of type 2 and type 1 diabetes, diabetes technology, prevention of type 1 diabetes, obesity, hypercortisolism, disorders of thyroid function, thyroid cancer, diabetes complications including kidney disease, lipid disorders, and cardiovascular risk, bone health including osteoporosis and hypoparathyroidism, acromegaly, genetic testing for endocrine neoplasms, and vasopressin disorders. The faculty are nationally and internationally renowned experts who will present sessions filled with the latest research, clinical insights, and practical tips for the clinician and also highlight clinical guidelines.

https://www.eventsquid.com/event.cfm?id=24172

NASIT 2025

Washington, D.C.
January 31 – February 1, 2025

The North American Society for Interventional Thyroidology (NASIT) is the largest, multidisciplinary group in the United States dedicated to the field of interventional thyroidology. The

society was created to promote safe integration of ablative thyroid technologies into clinical practice and a collaborative environment that supports education and research efforts in interventional thyroidology. NASIT holds an annual meeting that includes 1.5 days of expert panel sessions, scientific presentations, and the most up-to-date information on innovative technologies in the field.
https://nasit.org/event-5795114

AAES 2025 Annual Meeting

Milwaukee, Wisconsin
May 17 – 19, 2025

American Association of Endocrine Surgeons 2025 Annual Meeting attendees can look forward to dynamic speakers, presentations of innovative research, opportunities to connect with colleagues, and informative panel discussions. The AAES Annual Meeting is dedicated to the advancement of the science and art of endocrine surgery through exchange of knowledge and fostering collaboration. The upcoming 2025 event promises to deliver innovative programming that will enrich attendees' clinical practices, provide networking opportunities, and facilitate scholarly pursuits. We cordially invite you to join us in Milwaukee for this exciting event. It will be an excellent opportunity to dive into new topics, share expertise, and connect with peers who share similar interests.
https://www.endocrinesurgery.org/2025-annual-meeting

INTERNATIONAL **ITINERARY**

EuroPit 2024

Annecy, France • November 18 – 20, 2024

EuroPit is a unique, multidisciplinary course in Europe that provides a foundation in the diagnosis and management of pituitary disorders for young doctors and includes pathologists, neurosurgeons, and endocrinologists from countries across Europe to provide a comprehensive perspective of pituitary disorders management. Courses will cover the management of pituitary disorders: pathology, investigation, treatment options, and the development of optimized care in the future.
https://www.ese-hormones.org/education-and-training/events-key-dates/europit-2024/

Reproductive Endocrinology 2024

London, U.K. • December 3, 2024

Reproductive Endocrinology 2024 has partnered with the open-access journal, *Endocrine Connections* and its special collection, "New Avenues in Male Reproductive Health." This timely special collection will pull together an array of research focused on improving the treatment of male reproductive disorders. Submissions of original research or reviews are welcomed for inclusion.
https://www.endocrinology.org/events/reproductive-endocrinology/reproductive-endocrinology-2024/

SIMBA Adrenal 2025

Birmingham, U.K. • February 6 – 7, 2025

The conference will feature scenario-based assessments based on the SIMBA model (Simulation via Instant Messaging Birmingham Advance), providing a realistic and interactive learning experience. There will also be lectures focusing on glucocorticoid-induced adrenal insufficiency, pheochromocytoma/paraganglioma, primary aldosteronism, and adrenal cancer. Attendees will also benefit from opportunities to network in a peer-focused environment, fostering professional growth and collaboration.
https://www.ese-hormones.org/education-and-training/events-key-dates/simba-adrenal-2025/

Obesity and Adipose Tissue

Banff, AB, Canada • February 23 – 26, 2025

Obesity is a major risk factor for type 2 diabetes, nonalcoholic fatty liver disease, cardiovascular disease, and many types of cancer. Collectively, these associated diseases are the leading causes of morbidity and mortality worldwide. A deeper understanding of the biology of adipose tissue and pathophysiology of obesity will be critical to address this major threat to human health. This conference will be held jointly with the Keystone Symposium on MASH Pathogenesis and Therapeutic Approaches to encourage cross-disciplinary insights and collaborations toward understanding underlying mechanisms of how obesity leads to liver disease.
https://www.keystonesymposia.org/conferences/conference-listing/meeting?eventid=7106

UNSOLVED Mysteries

Four decades at the bench and Daniel Drucker, MD, is still unlocking scientific secrets.

The Endocrine Society's 2025 Fred Conrad Koch Lifetime Achievement Award recipient, Daniel Drucker, MD, first discovered his passion for science in high school when he learned "this is how stuff works." He's still learning to this day, and he tells *Endocrine News* about his ongoing scientific quests, the mentors who made a difference along the way, and why even old ideas are still valid.

BY GLENDA FAUNTLEROY SHAW

Daniel Drucker, MD, knows the enormous impact his discoveries have made to the lives of those living with diabetes and obesity, but after 40 years of scientific research, he believes there's still more mysteries for him to unlock.

Drucker, the 2025 recipient of the Endocrine Society's Fred Conrad Koch Lifetime Achievement Award, is a professor of medicine at the Lunenfeld Tanenbaum Research Institute of Mt. Sinai Hospital and the University of Toronto in Toronto, Canada, and is recognized for his ground-breaking contributions to the understanding of the physiology and pharmacology of glucagon-like peptides (GLPs) and their use for the benefit of patients. His discoveries of GLP-1, GLP-2, and dipeptidyl peptidase-4 (DPP-4) activity provide the foundation for some of the largest sectors of drugs for obesity, gut disorders, and type 2 diabetes.

His spark for science was first ignited in high school after Drucker — born to European immigrants in Montreal, Canada — and his family moved to Ottawa when he was 13 years old.

"It just sort of appealed to me, the fact there were laws governing scientific processes, whether it was in physics or chemistry, that one can explain how stuff happens, and I think that was

Daniel Drucker, MD

> “It’s the most exciting time yet to be doing science related to GLP-1. So, it’s quite a privilege, to be honest, to be working in a field that has remained so fresh and so exciting for so many years. You really don’t see that that often in biomedical science.”
>
> — DANIEL DRUCKER, MD, PROFESSOR OF MEDICINE, LUNENFELD TANENBAUM RESEARCH INSTITUTE OF MT. SINAI HOSPITAL AND THE UNIVERSITY OF TORONTO, TORONTO, CANADA

very attractive to me,” he recalls. “Maybe I was insecure in my ability to deal with the humanities and English literature and more abstract processes, whereas the science was ‘this is how stuff works.’”

Drucker received his medical degree from the University of Toronto and later took a research fellowship position at the Massachusetts General Hospital lab of another renowned endocrinologist, Joel Habener, MD. Habener, too, has played a pivotal role in the early discovery of GLP hormones. Habener, too, is no stranger to accolades from the Endocrine Society; he received the 2018 Outstanding Mentor Laureate Award.

Life Is Often Full Circle

Habener’s lab was a very interesting place, Drucker recalls.

“It was very well funded at the time, with multiple NIH grants and funding from Howard Hughes,” he says. “That was really a luxury, in that we didn’t have to worry every day about where can we get the money to buy this, or can we possibly afford to do the next experiment?”

“It was a wonderful environment because there were some really smart people from all over the world who were attracted to Mass General and to Harvard and certainly, to Joel’s lab, and I think that was really important because you went to work every day, and there’s so many other people surrounding you who have great ideas and who are worth listening to and are role models themselves,” Drucker says. “That was the environment that I found myself in, and Joel was an ideas person.”

“It was a little intimidating for me,” Drucker continues. “I didn’t have a strong scientific background, and to be honest, I didn’t really know what I was doing the first few months, but it was a great place to learn, and that’s where I had the opportunity to learn science.”

Who could have guessed that the two of them would come together years later on the GLP-1 discovery?

“That’s the thing about basic science,” Drucker says. “It sometimes literally will take a decade or even longer, to become apparent what the real relevance and potential is. Back in those days, none of us foresaw the current landscape with regard to obesity. We thought GLP-1 might be useful as a diabetes treatment, and after 15 or 20 years, that turned out to be the case, but I think the obesity story was not really apparent to anybody in the 1980s. That came much later.”

Biggest Health Story of 2024?

While scientists may have been aware of the possibilities in the late 1980s that GLP-1 could do more than treat diabetes, for the mainstream public, Ozempic and Wegovy seem to hit the news in 2024 like a lightening bolt.

“In 1996, there were three papers published that showed that GLP-1 inhibited food intake, and one of them was from my lab in Toronto,” Drucker explains. “So, we had

Drucker (far right) grabbing coffee with his sons, Aaron, Jeremy, and Mitch while the family was in Jerusalem where Drucker received the 2023 Wolf Prize in Medicine "for pioneering work in elucidating the mechanisms and therapeutic potential of enteroendocrine hormones."

a sense that here's something that not only lowers blood sugar for diabetes, but also reduces food intake, and then it took 18 years from 1996 to 2014, to when the world's first GLP-1 medicine was approved for the treatment of obesity."

The first drug approved in 2014 was liraglutide, but liraglutide didn't become the topic of conversation at everyone's dinner table and didn't take social media by storm, recalls Drucker. "The turning point was once we got semaglutide for the treatment of obesity, which really showed the potential for GLP-1 to produce much more profound weight loss than we'd seen before." Drucker says that for researchers in the specialty, GLP-1 medicines are like a gift that keeps on giving.

"We started with type 2 diabetes, and then we moved to obesity," he says. "Then we got really good data showing that GLP-1 reduces heart disease and strokes, and more recently, we have very exciting data showing that it reduces kidney disease and severity of sleep apnea. And it's now in clinical trials for metabolic liver disease, peripheral artery disease, Parkinson's disease, and for Alzheimer's disease."

"It's the most exciting time yet to be doing science related to GLP-1," Drucker adds. "So, it's quite a privilege, to be honest, to be

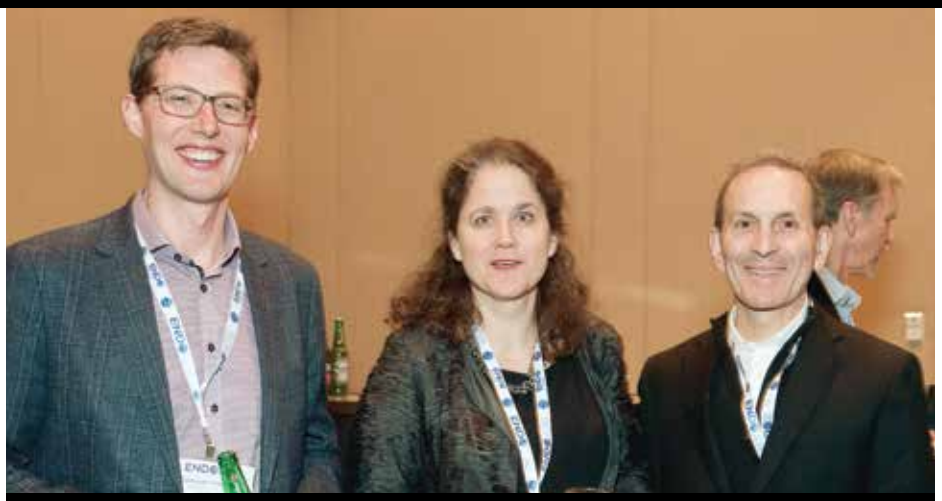
Accolades and Then Some

Aside from the 2025 Koch Lifetime Achievement Award, Drucker is also a past recipient of the Endocrine Society's 2009 Clinical Investigator Award Lecture and the 1993 Richard E. Weitzman Memorial Award. Earlier this year, he — along with Habener and Svetlana Mojsov, PhD, research associate professor at Rockefeller University in New York – was recognized by *TIME* magazine in its 100 Most Influential People of 2024 issue for their collective involvement in the development of GLP-1 medications.

In 2020, Drucker and Habener received the Warren Alpert Foundation Prize for their discoveries about the function of key intestinal hormones, their effects on metabolism, and the subsequent design of treatments for type 2 diabetes, obesity, and short bowel syndrome — the first time in many years that this prestigious award has gone to investigators in the field of endocrinology.

Drucker has served the Endocrine Society in various capacities, including on the Board of Directors. Most recently, he was an editorial board member for the *Journal of the Endocrine Society*, served with distinction as the editor-in-chief of *Endocrine Reviews* from 2018 to 2021, and served as a member of the Society's Nominating Committee.

The Fred Conrad Koch Lifetime Achievement Award Medal will be presented to Drucker at **ENDO 2025** in San Francisco, Calif., next July.



While in Chicago, Ill., for **ENDO 2018**, Drucker (right) chats with Gregory Steinberg, PhD, (far left) an associate editor of *Endocrine Reviews* during Drucker's term as editor-in-chief, and Mary Elizabeth Patti, MD, an editorial board member of the *Journal of the Endocrine Society*.

working in a field that has remained so fresh and so exciting for so many years. You really don't see that that often in biomedical science."

But has there been an enormous branding fail in marketing GLP-1 as a weight-loss drug? Did scientists finally discover the drug that cures obesity, only to have people ashamed to admit using it? Why are overweight and obese people still being called "cheaters" for not just exercising and dieting to lose weight?

"There's clearly a stigma surrounding obesity that we don't see with many other chronic medical conditions, and I think many folks, including, healthcare professionals and scientists, harbor the opinion that you should be able to control your own body weight, and it's a moral failing or a lack of discipline," Drucker says. "We tend to make judgements about someone's inability to lose weight, even though there's an abundance of evidence and science that shows that obesity is a disease, and your brain becomes wired differently."

Obesity fights a person's attempts to lose weight, Drucker adds, and many people are not willing to acknowledge that.

"We would never say to someone with Crohn's disease, or arthritis, with a horrible infection 'why can't you just get better yourself?'" he emphasizes. "People would be appalled if you

Members of the Drucker Lab (from left to right): Eloisa DaSilva, Susanna Fang, Dianne Matthews (seated), Rui Shang, Rola Hammoud, Maria Gonzalez, Daniel Drucker, Fiona Cui (seated), Kyle Medak, Xiemin Cao, Jacqueline Koehler, Bernardo Yusta (seated), Chi Kin Wong, and Wenran Ren.

Drucker, his wife Cheryl Rosen Drucker, and their grandchildren, Benjamin, Madeline, Miles, Hallie, Brendan, and Kyle.

said that, but for some reason, it tends to be what some segments of society do say when confronted with this challenge surrounding weight loss."

"With the GLP-1 medicines, many people can lose 10%, 15%, 20%, or more of their weight, and they can proudly look at their colleagues, their family members, and people who may have been questioning them and say, 'you see, I just needed help.'"

For people needing the GLP-1 weight-loss drugs, however, a large barrier to access is the drugs' high cost, but Drucker says changes are on the horizon.

"I have no doubt that the medicines will become much more affordable, and there's several reasons why," he says. "First, there will be competition with many new types of GLP-1 medicines, and some of them will be pills that are much easier and cheaper to make, so that alone will bring down the cost of the medicine."

"Also, right now, we have Novo Nordisk and Eli Lilly and no one else," Drucker continues. "But in five years, there's going to be half a dozen other companies involved that will also bring pressure on the price. Then we also have Congress, which is examining the prices of medicines and asking Medicare and Medicaid to look carefully at negotiating price discounts. In September, the CEO of Novo Nordisk said that he believes that Ozempic will be the subject of price discounts mandated by Medicare/Medicaid negotiations in a couple of years."

During a September session before the Senate Committee on Health, Education, Labor, and Pensions, the CEO of Novo Nordisk indeed faced tough questions about the high

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From **ENDO 2018** in Chicago, Ill., Drucker (center) is pictured with Patricia Brubaker, PhD, from the University of Toronto (left), and 2018 Endocrine Society President Susan Mandel, MD, MPH.

prices for its drugs Ozempic and Wegovy. A report issued by the Committee showed the cost of Wegovy is significantly less in European countries — from $140 a month in Germany to $92 a month in the United Kingdom. Americans pay about $1,349 a month for the exact same drug. According to news reports of the Senate hearing, Novo Nordisk CEO Lars Fruergaard Jorgensen agreed to meet with pharmacy benefit managers to discuss lowering the costs of the two drugs.

Grandkids and Golf?

Drucker says that there are days when he thinks that after 40 years of scientific research, maybe it's time to just play more golf and spend more time with his grandchildren. But he laughs and says he does plenty of both already, and there's still time left to spend in the lab.

So, what's his next scientific mystery to uncover?

"This may sound silly, but we really work on the same things today that we would've worked on 10 or 15 years ago, which is how do these GLP hormones work?"

"We know GLP-1 does all these really cool things, but we don't really understand how. You know, there's a new medicine tirzepatide, or Mounjaro, and it's just fantastic, developed by Eli Lilly, and it activates both GLP-1 and GIP, but we don't completely understand how that works."

Drucker says in his basic science lab they use molecular and cellular biology and mouse genetics to be able to ask these questions: How is this medicine working? Where is it working? Which cell types is it targeting? How does that magic happen?"

But Drucker says he hears the criticisms from some who say he's been doing the same research for decades and questions why he doesn't have any new ideas.

"That's a valid criticism," he acknowledges. "But for me, to see all of these fantastic new trials showing benefits in people, I really still want to understand how these medicines work." EN

> "In 1996, there were three papers published that showed that GLP-1 inhibited food intake, and one of them was from my lab in Toronto. So, we had a sense that here's something that not only lowers blood sugar for diabetes, but also reduces food intake, and then it took 18 years from 1996 to 2014, to when the world's first GLP-1 medicine was approved for the treatment of obesity."
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— SHAW IS A FREELANCE WRITER BASED IN CARMEL, IND. SHE IS A REGULAR CONTRIBUTOR TO *ENDOCRINE NEWS* AND WRITES THE MONTHLY LABORATORY NOTES COLUMN.

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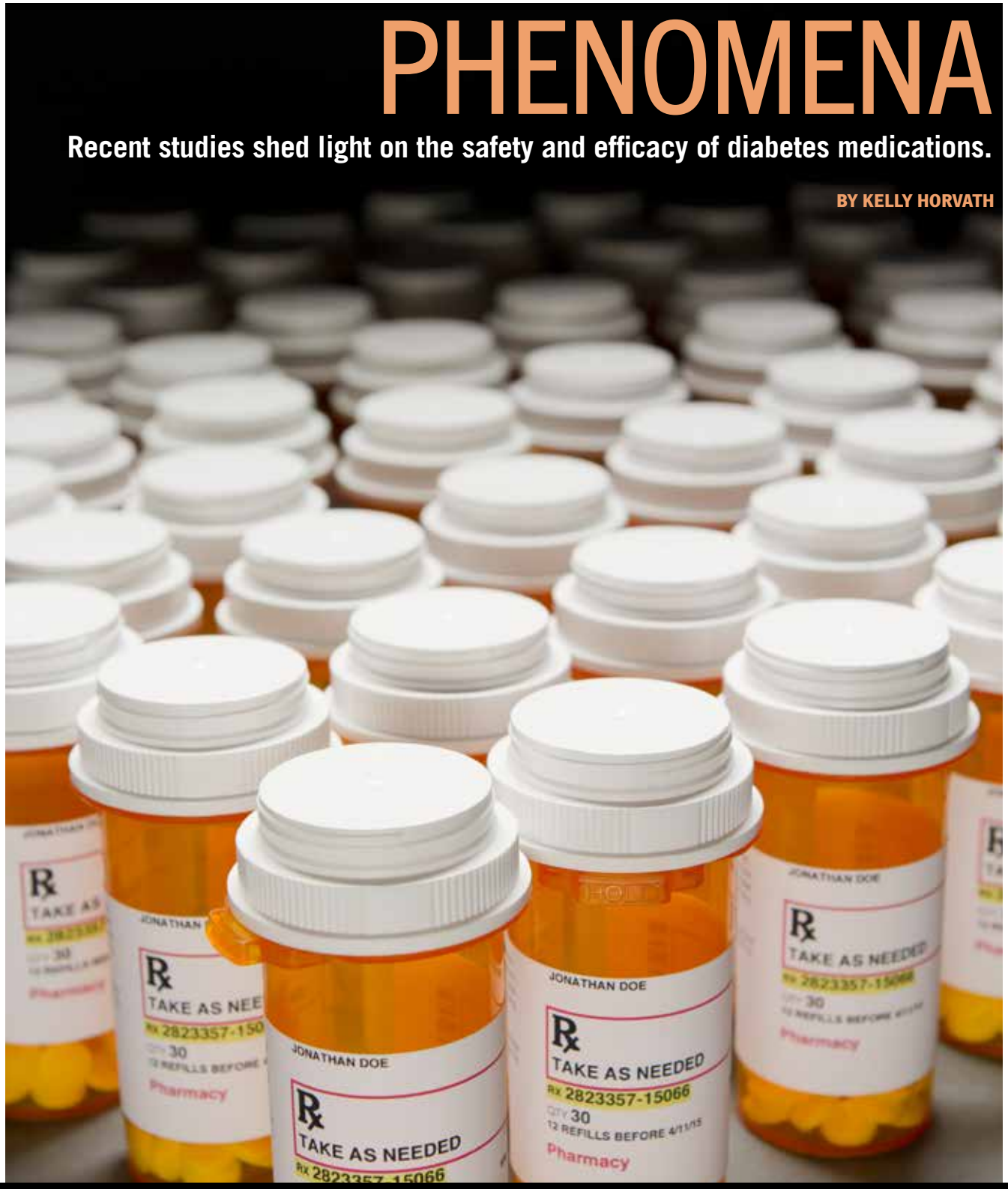
ENDOCRINE SOCIETY

Pharmaceutical PHENOMENA

Recent studies shed light on the safety and efficacy of diabetes medications.

BY KELLY HORVATH



GLP-1 receptor agonists, SGLT-2 inhibitors, and DPP4 inhibitors were all scrutinized in new research presented at **ENDO 2024**. While most of the results were good news for the impact of medications for people with type 2 diabetes, clinicians prescribing these medications should be aware of specific side effects in certain populations as well as obstacles regarding patient access.

Research presented at **ENDO 2024** in June shed more light on new or overlooked effects — mostly good — of medications prescribed to combat diabetes, such as GLP-1 receptor agonists, SGLT-2 inhibitors, and DPP4 inhibitors. Spoiler alert: The GLP-1 receptor agonists may be emerging as the best in show.

The researchers highlighted here were unanimous in their praise of the meeting, citing the quality of the sessions, the excellent networking opportunities, and the numerous resources the meeting makes available.

GLP-1 Receptor Agonists and SGLT-2 Inhibitors

Good news on the diabetes medications front comes from Alexander Kutz, MD, MPH, MSc, a research fellow in the Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, at Brigham and Women's Hospital and Harvard Medical School in Boston, Mass., and team who aimed to understand the effectiveness of glucagon-like peptide-1 (GLP-1) receptor agonists and sodium-glucose cotransporter-2 (SGLT-2) inhibitors in reducing cardiovascular and liver events in patients with type 2 diabetes and metabolic dysfunction-associated steatotic liver disease (MASLD).

"This is crucial as MASLD is becoming more prevalent and poses significant health risks, yet has few effective treatment options," Kutz explains. "The scarcity of therapies highlights the need to explore antidiabetic medications' potential benefits for MASLD, aiming to expand the therapeutic spectrum and improve patient outcomes."

Their large cohort design study used data from Medicare and a major U.S. health insurance database from 2013 to 2022 to compare the effectiveness of GLP-1 receptor agonists, SGLT-2 inhibitors, and dipeptidyl peptidase-4 (DPP4) inhibitors among a diverse population of patients with type 2 diabetes and MASLD.

"A weighting approach was employed to balance patient characteristics across study groups, effectively emulating two target trials," Kutz says. "The data analysis focused on the impact of these medications on cardiovascular and liver-related events, ensuring robust and reliable results that provide valuable insights into the therapeutic potential of these antidiabetic drugs for patients with MALSD."

ALEXANDER KUTZ, MD, MPH, MSC

RESEARCH FELLOW, DIVISION OF PHARMACOEPIDEMIOLOGY AND PHARMACOECONOMICS, DEPARTMENT OF MEDICINE, BRIGHAM AND WOMEN'S HOSPITAL AND HARVARD MEDICAL SCHOOL, BOSTON, MASS.

"GLP-1 receptor agonists improve glycemic control, reduce inflammation, and have beneficial effects on weight and lipid profiles. SGLT-2 inhibitors reduce blood glucose levels … which lowers blood pressure, reduces body weight, and decreases cardiovascular stress. **Both drug classes also exhibit direct protective effects on the liver by reducing fat accumulation … and inflammation, which are not observed with DPP4 inhibitors. These combined benefits may explain their superior outcomes in preventing cardiovascular and liver-related events."**

They found that those using GLP-1 receptor agonists or SGLT-2 inhibitors had fewer cardiovascular and severe liver events than those using DPP4 inhibitors. Other types of adverse events occurred with similar frequency among the three drug classes, suggesting that the GLP-1 receptor agonists and SGLT-2 inhibitors are overall safe in the setting of MASLD.

Multiple mechanisms are probably at play in why and how GLP-1 receptor agonists and SGLT-2 inhibitors are more effective than DPP4 inhibitors in preventing heart and liver-related events in diabetes and MASLD. "GLP-1 receptor agonists improve glycemic control, reduce inflammation, and have beneficial effects on weight and lipid profiles," Kutz says. "SGLT-2 inhibitors reduce blood glucose levels by promoting glycosuria, which lowers blood pressure, reduces body weight, and decreases cardiovascular stress. Both drug classes also exhibit direct protective effects on the liver by reducing fat accumulation (induction of lipolysis) and inflammation, which are not observed with DPP4 inhibitors. These combined benefits may explain their superior outcomes in preventing cardiovascular and liver-related events."

Clinicians should be aware of the significant benefits of GLP-1 receptor agonists and SGLT-2 inhibitors when prescribing diabetes medications. "As the prevalence of MASLD continues to rise, it's crucial for clinicians to incorporate these drugs into treatment plans for high-risk patients to mitigate long-term health risks and improve overall patient outcomes," Kutz says. Moreover, a growing body of evidence is revealing other health benefits these drugs confer, providing even more support for including them in a diabetes management toolkit.

"Additionally, it will be interesting to see how effective these drugs will be as compared with the recently approved thyroid β-receptor agonist," Kutz says.

GLP-1 Receptor Agonists and Pancreatitis Risk

Yet, another study by Mahmoud Nassar, MD, PhD, Department of Medicine fellow in the Division of Endocrinology, Diabetes, and Metabolism in the Jacobs School of Medicine and Biomedical Sciences at the University at Buffalo in Buffalo, N.Y., and team looked at the effects of GLP-1 receptor agonists prescribed for type 2 diabetes and obesity on pancreatitis recurrence, using TriNetX, a database comprising information from more than 100,000,000 patients in 15 countries.

"This study was motivated by my interest in research and commitment to using current resources and technologies to improve patient care and support evidence-based medicine," Nassar says. "TriNetX is an exceptional tool with a vast database of patients, providing an invaluable resource for answering clinical questions." Specifically, the researchers identified 638,501 individuals with a history of acute pancreatitis and taking either a GLP-1 receptor agonist, an SGLT-2 inhibitor, or a DPP4 inhibitor to compare their risk of acute pancreatitis recurrence, having noted that some of these patients were potentially missing out on the benefits of GLP-1 receptor agonists. The GLP-1 group showed a lower risk of

acute pancreatitis recurrence (15.2% and 14.4%, respectively) compared with 24.0% in the SGLT-2 inhibitor group and 23.3% in the DPP4 inhibitor group. Among patients not taking any of these medications, recurrence risk was 51.6% compared to 14.5% in those taking SGLT-2 inhibitors.

"Currently, GLP-1 receptor agonists are contraindicated in patients with a history of pancreatitis due to post-marketing reports suggesting an increased risk of acute pancreatitis when using these medications," Nassar says. "This led to caution in prescribing these drugs to such patients. Therefore, this study aimed to assess the risk of recurrent acute pancreatitis in this population, with the goal of informing safer prescribing practices and ensuring that these patients could also benefit from GLP-1 receptor agonists."

The mechanism underlying GLP-1 receptor agonists' potentially safer profile as compared to SGLT-2 and DPP4 inhibitors may stem from their anti-inflammatory properties, especially the reduction of hyperglycemia-induced inflammation, and their benefits in weight loss, explained Nassar. "Collectively, this may contribute to a lower risk of acute pancreatitis recurrence," he says.

MAHMOUD NASSAR, MD, PHD

DEPARTMENT OF MEDICINE FELLOW, DIVISION OF ENDOCRINOLOGY, DIABETES, AND METABOLISM, JACOBS SCHOOL OF MEDICINE AND BIOMEDICAL SCIENCES UNIVERSITY AT BUFFALO, BUFFALO, N.Y.

"GLP-1 receptor agonists are contraindicated in patients with a history of pancreatitis … suggesting an increased risk of acute pancreatitis when using these medications. This led to caution in prescribing these drugs to such patients. **Therefore, this study aimed to assess the risk of recurrent acute pancreatitis in this population, with the goal of informing safer prescribing practices and ensuring that these patients could also benefit from GLP-1 receptor agonists."**

AT A GLANCE

- **GLP-1 receptor agonists and SGLT-2 inhibitors have shown superior outcomes in reducing cardiovascular and liver-related events compared to DPP4 inhibitors in patients with type 2 diabetes and MASLD.**
- **GLP-1 receptor agonists may be a safer option for managing type 2 diabetes and obesity in patients with a history of acute pancreatitis than previously thought.**
- **Insurance denied prescriptions for GLP-1 receptor agonists in 64% of teenage patients with obesity and 32% of teenage patients with type 2 diabetes, which restricts access for these patients to medications that could improve their health.**

This could be big news for this drug class, potentially leading to expanded use of GLP-1 receptor agonists. Nassar moreover believes that the findings may warrant reassessment of current guidelines and could translate into more personalized treatment approaches.

GLP-1 Receptor Agonists in the Pediatric Population

Amidst all the hype about GLP-1 receptor agonists, Gabriel Castano, MD, of Texas Children's Hospital Baylor College of Medicine in Houston, Texas, and team shared some less positive findings — not about the medications themselves but rather about access and adherence.

They studied 599 patients with an average age of 15 years who had been prescribed a GLP-1 receptor agonist from 2019 to 2023 for type 2 diabetes and weight management, reviewing insurance approval rates, adherence, dose titration, and side effects. Castano says they undertook this descriptive study because "there are no real-world studies that have looked at children; all that we know is what the clinical trials tell us, and real life is not a clinical trial."

They found that private insurance denied coverage of 37% of the prescriptions for type 2 diabetes, and Medicaid denied 27%. In patients with obesity only, private insurance denied 64% of prescriptions and Medicaid 70%. The upshot is that, without this insurance coverage, patients may not be able to afford a medication that could improve their health.

However, Castano says that lack of insurance coverage is not the only barrier for pediatric patients to take GLP-1 receptor agonists because many pediatric patients struggle with medication adherence; others are lost to follow up. On these points, he urges clinicians to have a system in place to be able to track and motivate patients.

GABRIEL CASTANO, MD

TEXAS CHILDREN'S HOSPITAL BAYLOR COLLEGE OF MEDICINE, HOUSTON, TEXAS

"There are no real-world studies that have looked at children; **all that we know is what the clinical trials tell us, and real life is not a clinical trial."**

Dose titration is another potential barrier when it is not well understood by patients and leads to lower treatment doses and ultimately less overall efficacy, especially because the intended effects of GLP-1 receptor agonists are dose-dependent. "Lastly," says Castano, "we need to be on the lookout for side effects like pancreatitis, which is an associated risk in type 2 diabetes, as well as some that have not been described, and reported them if observed." It should be noted that most patients in the study experienced mild to no side effects." EN

Metformin in Pregnancy

Metformin is the most commonly prescribed oral medication for type 2 diabetes. With recent findings, Deep Dutta, MD, DM, director of endocrinology at CEDAR Superspeciality Healthcare in Dwarka, New Delhi, India, shows that this important tool is not only safe to use in pregnancy, but also confers no adverse effects on the mother or offspring in the long term.

Dutta and team analyzed data from seven studies, comprising 10,117 pairs of mothers and their offspring and found that, at age nine years, the children of mothers who took metformin during pregnancy had similar body mass index and body fat amount and distribution as children of mothers who took insulin during pregnancy.

This study is the first to examine the long-term effects of metformin during pregnancy on mothers with diabetes and their offspring.

– HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. SHE WROTE ABOUT ORAL TESTOSTERONE REPLACEMENT THERAPY FOR MEN IN THE OCTOBER ISSUE.

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All the Rage

Combatting counterfeit weight-loss and diabetes drugs flooding the market

As online ads abound for diabetes and obesity medications, endocrinologists should be prepared to talk to patients who may be attracted to GLP-1 drug lookalikes and supplements from questionable sources.

BY ERIC SEABORG

GLP-1 agonists are a cultural phenomenon. Celebrity and social media influencer comments hyping the drugs' weight-loss success have led to demand outstripping supply, resulting in shortages for some patients who could benefit the most. High costs and limited insurance coverage have led patients to look for more affordable alternative sources.

The success and notoriety have opened an attractive opportunity for imitators and quick-buck artists. With many consumers turning to online sources, the U.S. Food and Drug Administration (FDA) has warned potential customers about the dangers of these products and written warning letters to many companies with websites that market these drugs and supplements.

Illegal Online Pharmacies

The authors of a recent research letter in *JAMA* ("Safety and Risk Assessment of No-Prescription Online Semaglutide Products" by Ashraf AR, Mackey TK, Schmidt J, et al.) did online searches for semaglutide and found that about 42% of the results "belonged to

illegal pharmacy operations." When the researchers ordered products from six of these vendors, three of them failed to deliver a product and instead engaged in scams requesting additional payments. Analysis of the products that did arrive revealed problems with potential contamination, purity, and semaglutide content. The authors note that "U.S. poison control centers have reported a 1,500% increase in calls related to semaglutide."

"The main message here is that alternative sources of drugs, particularly counterfeit options, are not regulated, and we do not have certainty of the quality of the product or whether this is the true medication," says Rodolfo J. Galindo, MD, associate professor of medicine at the University of Miami Miller School of Medicine, Miami. Fla.

"The study emphasizes the urgent need for increased awareness and regulation to address the sale of these dangerous counterfeit drugs," agrees Priyanka Majety, MD, assistant professor in the Division of Endocrinology, Diabetes, and Metabolism at Virginia Commonwealth University, Richmond, Va. "The National Association of Boards of Pharmacy, representing state pharmacy regulators, has identified over 40,000 online pharmacies operating illegally or in ways that are not recommended."

Counterfeiters

The potentially lucrative market has attracted large-scale counterfeiting networks with ties to organized crime. The World Health Organization has reported finding counterfeit Ozempic in several countries, including the U.S.

The FDA has said it has seized thousands of units of counterfeit Ozempic — including in the legitimate drug supply. Some of these counterfeit products have been found to contain insulin, with obvious serious health risks.

Physicians should be on the lookout for these, says Osama Hamdy, MD, PhD, medical director of the Obesity Clinical Program at Joslin Diabetes Center and associate professor of medicine at Harvard Medical School, Boston, Mass.: "There are ways to identify counterfeit medications. These can include small irregularities, such as spelling mistakes on the packaging or flimsy labels that don't adhere properly to the pen. Both the FDA and Novo Nordisk have provided helpful information, including photos, to help differentiate genuine from counterfeit products."

Eli Lilly has also expressed concern about the proliferation of counterfeit versions of its tirzepatide medications and says it is "filing several legal actions against med-spas, wellness centers, and other entities selling unapproved compounded products containing what they claim is tirzepatide."

Online Marketing

Consumers can be exposed to pitches from these suppliers without even looking for them. On the local website Nextdoor, posts asking for help in finding lost pets or recommendations

Osama Hamdy, MD, PhD

"I recently saw a patient for the first time regarding thyroid concerns. Toward the end of the visit, she mentioned that she had been using Wegovy, which she purchased from an online pharmacy, for the past few months, paying a significant amount out of pocket. **She hasn't experienced much success with weight loss and wanted to know if the severity of her nausea and vomiting was normal. She's been spending a lot of money without any weight-loss results but is dealing with all the side effects."**

— OSAMA HAMDY, MD, PHD, MEDICAL DIRECTOR, OBESITY CLINICAL PROGRAM, JOSLIN DIABETES CENTER; ASSOCIATE PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL, BOSTON, MASS.

Priyanka Majety, MD

> This is a challenging situation. We encounter patients every day who would greatly benefit from these medications, but their insurance won't cover them. **So, while it's unfortunate that some patients are turning to unregulated online pharmacies to get these medications, it's not entirely surprising."**
>
> — PRIYANKA MAJETY, MD, ASSISTANT PROFESSOR, DIVISION OF ENDOCRINOLOGY, DIABETES, AND METABOLISM, VIRGINIA COMMONWEALTH UNIVERSITY, RICHMOND, VA.

for appliance repairs are interspersed with advertisements from companies like FuturHealth, which feature slim young women in form-fitting clothes brandishing injection pens that appear to be Ozempic. A click on the ad takes the viewer to a short questionnaire where one can qualify for the company's weight-loss programs, with promises of prescriptions. If you click on the Nextdoor ad, you can look forward to future ads popping up on your news feed from the same company with a picture of what looks like an Ozempic package emblazoned with the claim: "Ozempic prescription — 5 mins — no insurance needed."

Social media influencers and people famous for being famous have also climbed on the GLP-1 bandwagon. For example, Kourtney Kardashian has a website that markets "Lemme GLP-1 Daily Capsules," which are a "GLP-1 Support, Appetite & Weight Management Supplement … formulated with clinically-tested ingredients."

Talking with Patients

Majety recommends being proactive in talking to patients about these drugs: "Asking in a non-judgmental manner if patients are using any supplements or medications for weight loss not only builds trust but also allows us to better assist them. If we don't ask, we may never know. Patients can sometimes be hesitant to share this information with their doctors, fearing it may affect trust."

"It's essential to have an open conversation about the risks of using unregulated medications," Hamdy agrees. "I recently saw a patient for the first time regarding thyroid concerns. Toward the end of the visit, she mentioned that she had been using Wegovy, which she purchased from an online pharmacy, for the past few months, paying a significant amount out of pocket. She hasn't experienced much success with weight loss and wanted to know if the severity of her nausea and vomiting was normal. She's been spending a lot of money without any weight-loss results but is dealing with all the side effects."

Compounding the Problem

An additional complicating wrinkle is that the FDA put semaglutide and tirzepatide on its shortage list in 2022, which enabled compounding pharmacies to legally market their own versions. Even so, the FDA notes that "compounded drugs are not FDA-approved or evaluated for safety and effectiveness," and that the manufacturers do not face the same level of scrutiny as regular pharmaceutical manufacturers.

Furthermore, although marketers often say that their product contains the "same active ingredient" as semaglutide, an FDA notice says: "Patients should be aware that some products sold as 'semaglutide' may not contain the same active ingredient as FDA-approved semaglutide products. In some cases, the compounders may be using salt forms of semaglutide, including semaglutide sodium and semaglutide acetate. The salt forms are different active ingredients than is used in the approved drugs, which contain the base form of semaglutide," and have not been evaluated for effectiveness.

"The FDA has received adverse events reports after patients used compounded semaglutide. Patients should not use a compounded drug if an approved drug is available," the FDA says.

In early October, the FDA took tirzepatide off the shortage list, meaning compounding pharmacies could no longer dispense it. But the FDA kept semaglutide on the shortage list.

Galindo says that "recommending non-FDA regulated drugs may not be safe for patients," so he advises his patients on the lack of regulatory and scientific information on quality, quantity, or safety of alternative sources of drugs.

"This is a challenging situation," says Majety. "We encounter patients every day who would greatly benefit from these medications, but their insurance won't cover them. So, while it's unfortunate that some patients are turning to unregulated online pharmacies to get these medications, it's not entirely surprising."

"The 1,500% increase in calls to U.S. poison centers related to semaglutide highlights the growing need for stronger pharmacovigilance, particularly regarding the risks of purchasing drugs online," Majety concludes. EN

Editor's Note: As of this issue's publication date, the FDA is reevaluating its decision to remove tirzepatide from its drug shortage list.

Resources

FDA on Counterfeit Semaglutide:
https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-consumers-not-use-counterfeit-ozempic-semaglutide-found-us-drug-supply-chain

FDA on Compounded Semaglutide:
https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/medications-containing-semaglutide-marketed-type-2-diabetes-or-weight-loss

Novo Nordisk on Spotting Counterfeits:
https://www.novonordisk-us.com/media/news-archive/news-details.html?id=166119

Eli Lilly on Counterfeit, Fake, and Untested Compounded Products:
https://www.lilly.com/safety/real-medicine

– SEABORG IS A FREELANCE WRITER IN CHARLOTTESVILLE, VA. IN THE OCTOBER ISSUE, HE WROTE ABOUT THE INCREASED AWARENESS SURROUNDING POLYCYSTIC OVARY SYNDROME (PCOS).

AT A GLANCE

- Shortages and high costs have led many consumers to seek alternative sources of semaglutide and tirzepatide, including ordering them from unregulated online sources, with no way to know what these products actually contain.
- Fake and counterfeit versions of popular weight-loss and diabetes drugs have been found in many countries, even within the legitimate drug supply. The FDA and pharmaceutical manufacturers have issued guidance on spotting them.
- The FDA continues to include semaglutide on its shortage list, enabling compounding pharmacies to legally market versions, while simultaneously cautioning consumers about the use of compounded products.

Beating *Prediabetes*

New research explores the impact of prediabetes on a Mexican population.

Carlos A. Fermín-Martínez, MD, discusses his research study as part of a series of diabetes press conferences during **ENDO 2024** in Boston, Mass.

According to a study presented at **ENDO 2024**, prediabetes increases the risk of dying before the age of 75, particularly due to heart disease, kidney disease, and acute diabetic complications in Mexican populations. The study's author, **Carlos A. Fermín-Martínez, MD**, discusses his findings and why it's important for clinicians to screen for prediabetes, especially in susceptible populations.

BY KELLY HORVATH

Carlos A. Fermín-Martínez, MD

> “Overweight, obesity, and dyslipidemia are also major public health concerns among the Mexican population, which could be attributed to a detrimental lifestyle (accentuated by socioeconomic health determinants) and genetics (e.g., variants in *SLC16A11*). **All of this in turn predisposes our population to a higher risk of prediabetes and diabetes.”**
>
> — CARLOS A. FERMÍN-MARTÍNEZ, MD, PHD STUDENT, NATIONAL AUTONOMOUS UNIVERSITY OF MEXICO; NATIONAL INSTITUTE OF GERIATRICS; MEXICO CITY, MEXICO

According to the World Health Organization, more than half a billion people worldwide are living with diabetes, and most of those live in low- and middle-income countries, including Latin America, where the prevalence rate is higher than the global prevalence rate and projected to increase dramatically. Likewise, the global burden of prediabetes is close to a half a billion people and growing, expected to increase to 10% of the worldwide population in fewer than 20 years, according to the International Diabetes Federation (using the impaired glucose tolerance [IGT] definition).

The urgency here is that, not only are those with prediabetes at high risk of developing type 2 diabetes, but they are also at higher risk for all-cause, cardiovascular, renal, and acute diabetic mortality. Compounding this issue, most people (80%) with prediabetes are unaware of their status and therefore unable to make timely interventions to prevent type 2 diabetes development and other deleterious health effects.

Prediabetes in the Mexico City Prospective Study

Carlos A. Fermín-Martínez, MD, of the National Autonomous University of Mexico and the National Institute of Geriatrics in Mexico City, Mexico, and his research team, seeking to better understand the epidemiology of diabetes and metabolic diseases, identified a lack of evidence regarding the epidemiology of prediabetes in the Mexican population. “We recently described the changes in the prevalence of prediabetes in the last seven years in Mexico and its potential determinants. We figured that the next step should be to describe the long-term effects of this condition, particularly on mortality,” explains Fermín-Martínez.

Importantly, besides that the prevalence is rising in the Latin American population, this population may have other factors that predispose them to the development of prediabetes/diabetes. “Overweight, obesity, and dyslipidemia are also major public health concerns among the Mexican population,” Fermín-Martínez says, “which could be attributed to a detrimental lifestyle (accentuated by socioeconomic health determinants) and genetics (e.g., variants in *SLC16A11*). All of this in turn predisposes our population to a higher risk of prediabetes and diabetes.”

In the study titled, “Prediabetes as a Risk Factor for All-Cause and Cause-Specific Mortality in 115,919 Adults Without Diabetes in Mexico City,” the researchers undertook a secondary analysis from the Mexico City Prospective Study (MCPS), examining 110,405 participants ages 35 to 74 years old who did not have diabetes during the study recruitment phase from 1998 to 2004. Exclusion criteria included individuals with previously diagnosed diabetes, individuals who used glucose-lowering pharmacotherapy regardless of prior diagnosis, and individuals with undiagnosed diabetes

Diabetes: ENDO 2024 Press Conference

Here, Fermín-Martínez fields questions from reporters at the end of the diabetes-focused press conferences at ENDO 2024 where he was grateful to be able to connect with students and other early-career researchers like himself.

but a glycosylated hemoglobin (HbA1c) level 6.5% or higher as well as those with self-reported chronic comorbidities at baseline (e.g., ischemic heart disease, stroke, chronic kidney disease, chronic obstructive pulmonary disease, cirrhosis, or cancer).

Participants were followed up to January 1, 2021. Of these participants, more than a quarter (26%, or 28,852 individuals) met the American Diabetes Association (ADA) criterion for prediabetes of an HbA1c level between 5.7% and 6.4%. Because there is still controversy regarding the definition of prediabetes, however, Fermín-Martínez also used an HbA1c level between 6.0% and 6.4% to define prediabetes, which is from the International Experts Committee (IEC) who were asked to adjudicate a definition of A1C use for diagnosing diabetes in 2008. The number of participants meeting the IEC criterion dropped to 7% (7,203 individuals).

With these two distinct cutoffs, the team looked for associations with all-cause and cause-specific mortality using Cox regression analysis after adjusting for common confounders (e.g., municipality of residence — Coyoacán or Iztapalapa, education level, physical activity, smoking, alcohol consumption, and adiposity levels).

The sociodemographic, health-related, and lifestyle data were collected by questionnaire under nurse supervision. Height, weight, hip and waist circumference, and blood pressure measurements were obtained using calibrated instruments and standard protocols. Non-fasting venous blood samples were taken, and HbA1c levels were measured using a validated high-performance liquid chromatography method.

Research Findings

Although the team has a preprint of their study pending, Fermín-Martínez presented highlights at **ENDO 2024** as part of a press conference devoted to cutting-edge diabetes research. He reported that participants meeting the IEC — the stricter — definition of prediabetes had 3.4

> “In our study, participants were initially free of diabetes; however, eventual development of diabetes likely accounts for a significant percentage of deaths, further highlighting that early detection and management of prediabetes **is crucial to reduce mortality and cardiometabolic disease.”**
>
> — CARLOS A. FERMÍN-MARTÍNEZ, MD, PHD STUDENT, NATIONAL AUTONOMOUS UNIVERSITY OF MEXICO; NATIONAL INSTITUTE OF GERIATRICS; MEXICO CITY, MEXICO

times the risk of dying of acute complications of diabetes at ages 35 to 74, compared to participants with normal blood glucose levels. Their risk of dying prematurely from kidney disease was increased by 1.7 times (70%). When using the ADA definition of prediabetes, the researchers also found significant, but weaker, associations with mortality. In other words, although lower glycemic marker cutoffs may be helpful for screening for prediabetes, they may not fully reflect the associated long-term health risks.

Drilling down a bit, the absolute excess risk associated with ADA- and IEC-defined prediabetes at ages 35 to 74 years accounted for 6% and 3% of cardiovascular deaths, respectively; 10% and 5% of renal deaths; and 31% and 14% of acute diabetic deaths. They found risk ratios (RRs) to be larger at younger ages than at older ages. RRs did not vary significantly between males and females.

Implications

Prediabetes is an early-stage indicator of glycemic dysregulation, which can lead to hyperglycemia and sometimes hyperinsulinemia, which may result in inflammation, impaired lipid metabolism, and endothelial dysfunction, explains Fermín-Martínez. "These processes contribute to the development of diabetes, hypertension, and dyslipidemia that ultimately culminate in life-threatening conditions such as cardiovascular and kidney disease. In our study, participants were initially free of diabetes; however, eventual development of diabetes likely accounts for a significant percentage of deaths, further highlighting that early detection and management of prediabetes is crucial to reduce mortality and cardiometabolic disease," he says.

The takeaway is clear: Asd prediabetes increases the risk of dying from cardiovascular, renal, and acute diabetic causes as well as all causes, clinicians — particularly in Mexico — could significantly reduce premature mortality by identifying and treating prediabetes early on.

Look for the results of this important study to publish soon. Meanwhile, looking back to his presentation at **ENDO 2024**, Fermín-Martínez recalls that: "It was a very exciting and fulfilling experience; the best part was definitely the opportunity to connect with students and early-career researchers like me and having the chance to represent my research team. I am also a Society member, which so far has been very informative, as I often receive updates on conferences and research opportunities. It is undoubtedly worth it." EN

– HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. SHE WROTE ABOUT ORAL TESTOSTERONE REPLACEMENT THERAPY FOR MEN IN THE OCTOBER ISSUE.

PHOTO: Priya Darshan/Shutterstock.com

AT A GLANCE

- Latin American populations have higher rates of prediabetes and diabetes than the global average, possibly due to socioeconomic health determinants (influencing lifestyle and health trends) and genetics.
- During a follow-up period of more than 18 years, 2,282 MCPS participants with prediabetes ages 35 – 74 years died, especially due to cardiovascular causes (651), renal causes (150), and acute diabetic crises (54), with mortality rates increasing in accordance with higher HbA1c levels.
- Clinicians should screen for prediabetes to provide early treatment and potentially ward off catastrophic health sequelae.

BY GLENDA FAUNTLEROY SHAW

Rohit N. Kulkarni, MD, PhD

Setbacks and Successes

Q&A with Rohit N. Kulkarni, MD, PhD

Back row (left to right): Ling Xiao, Ava DiStefano-Forti, Shirong Wang, Garrett Fogarty, Jiang Hu, Namrata Shukla, Dario DeJesus, Joan-Sabadell, Ping Jiang, and Rohit N. Kulkarni. **Front row** (left to right): Giada Rossi, Hyunki Kim, Michael Glass, Jack McKinney, Inez Murray, Anamica Das, and Rocio Redondo Castillejo.

On the heels of receiving nearly $10 million from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), Rohit N. Kulkarni, MD, PhD, discusses how his team will use this grant to pursue new approaches to studying type 2 diabetes and obesity by exploring gene expression and regulatory activity in multiple metabolic cells.

Rohit N. Kulkarni, MD, PhD, believes without a doubt that the quality of care for people with diabetes has progressed rapidly over the past three decades. He anticipates his newly funded research will lead to new discoveries that will continue the progress to improve lives.

Kulkarni is the Diabetes Research and Wellness Foundation Endowed Chair and co-head of the Section on Islet and Regenerative Biology at Joslin Diabetes Center, Boston, Mass. He and his collaborators were recently awarded nearly $10 million from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) to take a new approach to the study of type 2 diabetes and obesity.

The five-year grant will support Kulkarni's research examining gene expression and regulatory activity in multiple metabolic cells — specifically alterations to messenger RNA (mRNA) — that lead to the development of type 2 diabetes and obesity, with the goal of identifying potential targets for innovative treatments for the chronic conditions. Kulkarni is the principal investigator on the collaborative study that includes co-principal investigators at three additional institutions: the University of Chicago, University of Kentucky, and the University of Pennsylvania. Their research project is entitled, "Epitranscriptomics in human obesity and type 2 diabetes."

Endocrine News spoke with Kulkarni about his groundbreaking collaborative research study and what he thinks about the current state of diabetes care and discovery.

Endocrine News: **An NIDDK grant award of nearly $10 million can be career changing. Can you share your initial reaction when you heard the news?**

Rohit N. Kulkarni: We were thrilled and excited because it's a very competitive grant and we've been working on the grant for some time, so it is great to know that the NIH finally appreciated the innovative nature and exciting aspect of this approach because it will potentially open new therapeutic avenues.

> "Although it's a cliché, I have realized over the years that we have to view failures and successes equally. I have also learned that when you're successful, it's a team effort and everyone deserves credit. **And when there are setbacks, I encourage people to use it as a challenge to move forward in a way that will allow us to reach our goals more effectively."**
>
> — ROHIT N. KULKARNI, MD, PHD, DIABETES RESEARCH AND WELLNESS FOUNDATION ENDOWED CHAIR AND CO-HEAD, SECTION ON ISLET AND REGENERATIVE BIOLOGY, JOSLIN DIABETES CENTER, BOSTON, MASS.

> “Our observations that RNA modifications are playing a role in the context of metabolism are exciting because it gives us an insight into an area that has not been explored at all in the context of metabolism. **And so, understanding this aspect of biology and how it contributes to the pathophysiology of both diabetes and obesity, an area that could be common for chronic conditions is very innovative.”**
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> — ROHIT N. KULKARNI, MD, PHD, DIABETES RESEARCH AND WELLNESS FOUNDATION ENDOWED CHAIR AND CO-HEAD, SECTION ON ISLET AND REGENERATIVE BIOLOGY, JOSLIN DIABETES CENTER, BOSTON, MASS.ANN ARBOR, MICH.

***EN:* You are the principal investigator (PI) and are joined on the project with four other co-PIs. Have you previously collaborated with this group of researchers?**

Kulkarni: We have been collaborating with each of the groups for various periods. With the group at the University of Chicago, my lab started some of the initial work focused on this new approach more than 10 years ago. We have collaborated with the group at Pennsylvania for more than six to eight years, and with Kentucky most recently since a few years ago. So, we have a robust collaborative approach among the teams that has been very productive. And so, it’s great that we’re now all working on this topic together.

***EN:* What are your target numbers for enrollment across the four study sites?**

Kulkarni: In terms of human samples, we are pretty ambitious. We hope to target more than 80 to 100 individuals in the context of obtaining blood samples, biopsies for skeletal muscle, and fat tissue. At the University of Pennsylvania, we are working with Professor Ali Naji to obtain human islets. From the University of Kentucky, Professor Philip Kern will assist in obtaining skeletal muscle, adipose tissue, and potentially also liver samples.

***EN:* How will your team’s research potentially impact the care and treatment of diabetes?**

Kulkarni: Many people are aware, and if not, they should be aware that insulin was discovered more than a 100 years ago. We continue to move forward in terms of finding a cure for the disease. Our observations that RNA modifications are playing a role in the context of metabolism are exciting because it gives us an insight into an area that has not been explored at all in the context of metabolism. And so, understanding this aspect of biology and how it contributes to the pathophysiology of both diabetes and obesity, an area that could be common for chronic conditions is very innovative. I feel that exploring this area in an aspect of biology, which has not been touched on before, will give us new insights.

***EN:* Can you recall the period when you knew endocrinology would be your specialty? Was it a specific occurrence that sparked your interest in this specialty or the research?**

Kulkarni: The decision was based on a combination of both excitement for research and a personal interest considering people in my own family have diabetes. When I was in medical school and subsequent training, it was impressed upon me that, in addition to patient care, one can do a little bit more

by undertaking research. This prompted me to take the extra step of getting a PhD in biochemistry when I was in England training as a physician. That provided me with a holistic view about understanding biology in a way, not only to treat individuals but also to delve into those areas that have been difficult and contribute to understanding them better so that we could finally find a cure for the disease.

***EN:* You mentioned people in your family who have diabetes. Have you seen a difference just in their care and treatment in the past 10 years?**

Kulkarni: Yes, without a doubt, the quality of care for individuals with diabetes has been progressing rapidly. For instance, trying to measure glucose levels in a less painful manner. Also having different types of insulins, which allow for different individuals for different levels of protection has emerged to be important. So, over the past two or three decades, these aspects have improved and made it relatively easier for patients to take care of their glucose levels. However, nobody likes the pain of injections or for testing glucose. So, if we can get an oral pill or something that can be curative of the disease that would be fantastic.

***EN:* Along that same line, I think the cap on insulin costs has been a big change in patients' lives. The Biden administration did it for Medicare patients, and then Lilly and other drug companies followed suit and dropped their cost.**

Kulkarni: Yes, you're correct that costs have gone down tremendously. And that is an important component because it becomes affordable, and people are much more amiable for these therapies for better glycemic control and reduce long-term complications.

***EN:* What has been the most rewarding part of making discoveries with the young researchers in your Joslin laboratory?**

Kulkarni: My lab team ranges between 12 and 15 personnel. We have about eight or nine fellows, a few research assistants, and occasional students. The most exciting, rewarding aspect of my job is waking up every day to ask new questions on how to cure the disease. And I think that is always exhilarating because of my own interest in the area, but also equally important is interacting with ambitious and energetic young trainees who come to the lab. I don't assume that I know everything. And when I get asked out-of-the-box questions from the trainees, my reaction is, "Wow, that's a very important perspective." So, I give them the credit and ensure we push ourselves to keep moving forward.

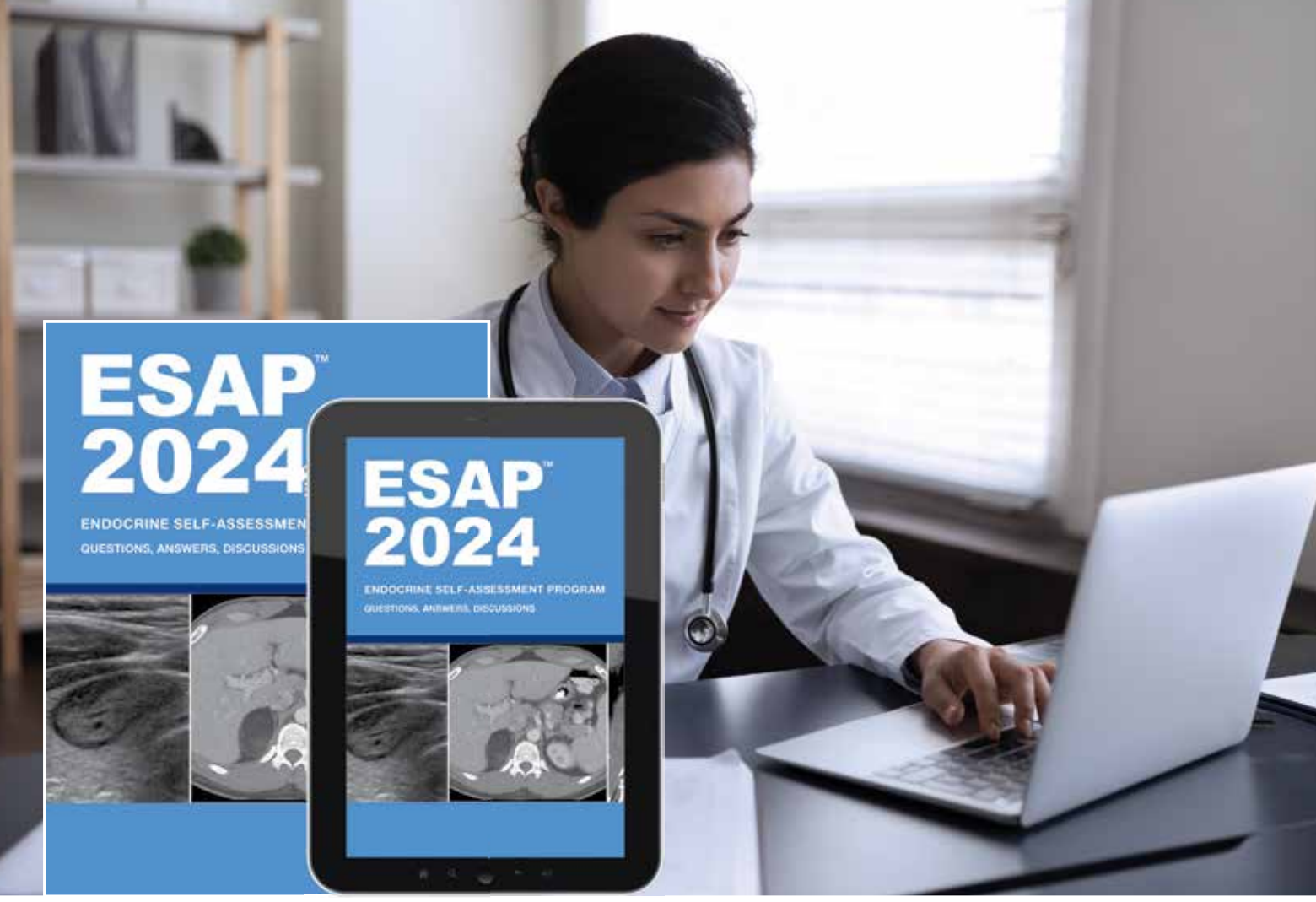
***EN:* What do you teach them about dealing with setbacks in the lab? With your long career in research, how do you tell them how to deal with it?**

Kulkarni: Although it's a cliché, I have realized over the years that we have to view failures and successes equally. I have also learned that when you're successful, it's a team effort and everyone deserves credit. And when there are setbacks, I encourage people to use it as a challenge to move forward in a way that will allow us to reach our goals more effectively. Not every success is a straight line, and I remind trainees that progress in research is mixed with setbacks and successes. When you fall down, you have to just get up and go forward again.

***EN:* Last question. Who has influenced you the most in your career?**

Kulkarni: I have had excellent mentors beginning with my teachers at school and then during my medical and doctoral training and post-doctoral fellowship. Each of them has provided a unique perspective that has enriched my career and life, and I am grateful for their mentoring and advice. It's important to remind oneself that it's a lifelong learning process, and the earlier one realizes that each of us would enjoy and be much more effective in what we do. EN

– SHAW IS A FREELANCE WRITER BASED IN CARMEL, IND. SHE'S A REGULAR CONTRIBUTOR TO *ENDOCRINE NEWS* AND AUTHOR OF LABORATORY NOTES.



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ENDOCRINE SOCIETY

CBO Releases Cost Estimate to Cover Anti-Obesity Medications Under Medicare

On October 8, the Congressional Budget Office (CBO) released a report with a cost estimate of covering anti-obesity medications (AOM) under the Medicare program.

The Medicare statute currently prohibits coverage of AOMs. Consequently, the Medicare law must be changed to allow coverage. For Congress to pass a law, it relies on CBO cost estimates so it can appreciate the impact to the federal budget. The CBO, which provides non-partisan cost analysis of legislation considered by Congress, estimates that authorizing coverage of AOMs in Medicare would increase federal spending by $35 billion from 2026 to 2034. The CBO estimates that covering these medications would save around $1 billion over the same time because of improved health.

Unfortunately, the CBO's cost analysis did not include an estimate of the likely savings that would result from expanding access to Intensive Behavioral Therapy (IBT) for obesity. Medicare Part B currently covers IBT for obesity, but there are

restrictions in the referral process that have resulted in low utilization. We are disappointed that the CBO did not include this in their analysis.

The Society supports the Treat and Reduce Obesity Act (TROA) originally introduced in the House and Senate, which would allow Medicare to cover anti-obesity medications and would make it easier for primary care providers to refer IBT for obesity to other qualified healthcare providers. We expect debate over coverage of AOMs will continue next year and with the new Congress, and we will continue to advocate for expanded coverage of obesity treatment and care.

Congress Returns to Washington for "Lame Duck" Session and to Complete Work for 2024

Following the November elections, Congress will return to Washington, D.C., to complete work on federal funding and a package of several pieces of health legislation including many priorities of the Endocrine Society.

Federal funding for the government expires December 20, 2024, and Congress must either complete a funding bill by that date that includes funding for the National Institutes of Health (NIH) and other health programs or pass another short-term funding bill that will allow the government to continue operating until some point in 2025. The outcome of the elections and which party holds a majority in the Senate and House will determine how it responds.

In addition, there are several pieces of health-related legislation that are set to expire or require action before January 1 that Congress will need to complete and pass. This includes legislation to reauthorize the Special Diabetes Program, legislation to extend waivers for telehealth, and legislation to avert Medicare physician payments scheduled to begin January 1, 2025. We expect Congress will complete its work by December 20 and adjourn.

Consequently, for the remainder of 2024 the Endocrine Society will conduct meetings with congressional offices to explain why it is crucial for Congress to pass a final appropriations bill and protect the NIH from funding cuts in addition to working with the Congressional Diabetes Caucus to pass reauthorization of the Special Diabetes Program with increases, and launch grassroots campaigns to urge Congress to extend telehealth waivers and avert the scheduled Medicare physician payment cuts.

For the latest information on these issues and how you can join the Society's advocacy activities, please visit: **www.endocrine.org/advocacy/take-action.**

Society Members Work to Advance Plastics Treaty

The United Nations (UN) is in the process of trying to develop a treaty to reduce plastic pollution. The Endocrine Society has served as the only professional medical organization contributing to this process by providing scientific evidence and explanation about how plastics harm not only the environment but also human health. As delegations from UN member states and participants from various international organizations prepare to travel to South Korea for the next meeting to negotiate the treaty, the Endocrine Society and our members have continued to share the latest science on the impact of chemicals on public health.

In September, scientists, policy experts, and community members gathered at a symposium in New York convened by Endocrine Society member Leonardo Trasande, MD, MPP, and the NYU Langone Center for the Investigation of Environmental Hazards (CIEH) to discuss the scientific evidence linking chemicals in plastic to human and environmental harms, as well as policy solutions at the state, federal, and international level. The meeting featured many members of the Endocrine Society as scientific contributors, including. Lindsey Trevino, PhD; Angel Nadal, PhD; Pete Myers, PhD; and Rob Sargis, MD, PhD. The event also included powerful remarks by leading policymakers including California Attorney General Rob Bonta and the Minister of Climate and Environment of Norway, Tore O. Sandvik, who spoke about the need to address plastic pollution and why recycling alone will not address this complex issue. Importantly, representatives from communities impacted directly by plastic pollution such as Jo Banner, co-founder and co-director of The Descendants Project, and Barbra Weber, co-founder and co-executive director of the Ground Score Association, shared their perspectives and identified key questions and needs from the people they represent.

> “Our overarching vision is to advance a comprehensive and ambitious treaty to address plastic pollution that includes limits on production of new plastic combined with efforts to restrict the use of hazardous EDCs and other chemicals in plastic.”

The symposium took place during the UN General Assembly meeting to debate and discuss “acting together for the advancement of peace, sustainable development, and human dignity for present and future generations.” In conjunction with the Assembly, a high-level side event to “showcase and promote best practices, innovative solutions, and collaborative efforts aimed at addressing plastic pollution” took place to further build momentum for the upcoming meeting to negotiate the plastics treaty.

Regional work to determine negotiating positions are also taking place, and Marina Fernandez, PhD, a member of the Endocrine Society’s delegation to the UN negotiating meeting, participated in a regional meeting of the Group of Latin American and Caribbean Countries (GRULAC) to have a discussion and exchange on general positions.

The Endocrine Society’s delegation of Fernandez and Trasande will participate in the negotiating meeting from November 25 through December 1 and plan to build on recent progress to ensure a health-protective treaty that reduces exposure from endocrine-disrupting chemicals (EDCs) in plastic. Since the last meeting earlier this year, member states have worked on measures to include in the treaty to address so-called chemicals of concern, and we will continue to advocate for inclusion of such measures in the treaty, alongside production limits and other health-focused provisions. Our overarching vision is to advance a comprehensive and ambitious treaty to address plastic pollution that includes limits on production of new plastic combined with efforts to restrict the use of hazardous EDCs and other chemicals in plastic. EN

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The Era of Automation

Innovations on the forefront of glucose monitoring and insulin delivery are revolutionizing the state of diabetes care.

COMPILED AND WRITTEN BY COURTNEY CARSON

Staying abreast of the latest advancements in diabetes technology is critical for improving patient care. The field of diabetes management continues to rapidly evolve with products designed to optimize glucose monitoring, insulin delivery, and patient convenience.

Next-generation continuous glucose monitors (CGMs) are becoming more accurate and user-friendly, while smart insulin pens represent an accessible step into insulin delivery without the complexity of a pump. Recent developments in insulin patches and infusion sets offer longer wear times and greater comfort. And the integration of artificial intelligence (AI) in diabetes management is transforming how patients and healthcare providers interpret data and make decisions.

Below is an overview of recent innovations that are poised to enhance diabetes management.

◂ Dexcom G7

The Dexcom G7 builds on the success of the G6 model with a smaller, all-in-one, wearable sensor and transmitter. Notable improvements include a 30-minute warm-up period (a significant reduction from the G6's two-hour warm-up) and expanded integration with wearable devices such as Apple and Android smartwatches. Easily see where glucose levels are, where they're headed, and where they've been with sensor readings as often as every five minutes.

www.dexcom.com

▼ Bigfoot Unity Diabetes Management System

The Bigfoot Unity System is designed to answer clearly and in real time, "how much insulin would my doctor recommend I take right now?" Using integrated continuous glucose monitoring system (iCGM) data, the system provides a dose recommendation based on physician instructions, which is displayed directly on the smart cap of the patient's insulin pen. Integrated with Abbott's FreeStyle® Libre 2 system, the Bigfoot Unity System is the centerpiece of the larger Bigfoot Unity program that takes a holistic approach to simplify and connect key aspects of insulin management for patients and healthcare providers.

www.bigfootbiomedical.com

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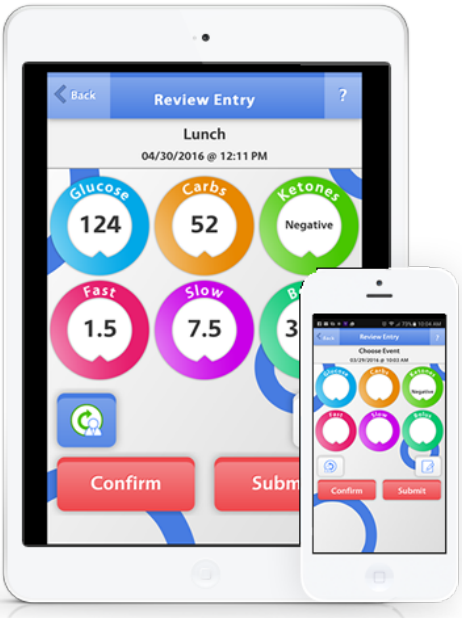
Tandem t:slim X2 with Control-IQ Technology

With a color touchscreen and sleek design, the t:slim X2 insulin pump was created to integrate seamlessly into patients' lives like any other sophisticated, modern device. The advanced algorithms of the device's Control-IQ technology use sensor values to predict glucose levels 30 minutes ahead of delivery and automatically adjusts insulin, if needed. Offering enhanced protection against hypoglycemia as well, the device can suspend insulin delivery when glucose is predicted to drop below a preset level. Personalized settings allow the user to create up to six profiles with multiple time segments to account for changing insulin needs. Featuring a convenient micro-USB port, the device can be easily charged from anywhere, and it is easy to temporarily disconnect and reconnect the insulin pump from an infusion set, allowing the patient more freedom. **www.tandemdiabetics.com**

Medtronic Extended Infusion Set

Designed to be worn for up to seven days, the Medtronic Extended Infusion Set significantly reduces the frequency of changes from every two to three days to once a week. The updated technology features new tubing and connectors aimed at creating better insulin stability, insulin absorption, and a reduced risk of occlusion. The Extended Infusion Set is created to be used exclusively with the Extended reservoir and is compatible with the MiniMed™ 780G, 770G, 670G, and 630G insulin pumps. **www.medtronic.com**



BlueLoop AI

The LOGIQ E10 by GE provides access to advanced tools in an easy-to-use design aimed at helping clinicians deliver confident care in even more places. The E10 provides enhanced precision imaging including 2D Shear Wave Elastography that enables quantitative assessment of tissue elasticity and Contrast Enhanced Ultrasound (CEUS) to help clearly visualize tissue structure and lesion vascularity for increased confidence in lesion detection and characterization. The E10 aims to create enhanced workflow by improving exam efficiency through advanced ergonomics with easy-to-reach controls (including an adjustable floating keyboard and an articulating monitor), increased mobility with an onboard battery that keeps the device ready to image at any time, and Smart Apps including Remote Control that allows system operation from an Android® tablet or phone and Photo Assistant that allows the user to acquire and include photos of relevant anatomy in reports. **www.gehealthcare.com**

The diabetes landscape continues to evolve with a focus on improving patient convenience, safety, and outcomes. From more precise CGMs to innovative insulin delivery systems and AI-driven management tools, this unprecedented growth in endocrine healthcare solutions marks an exciting time in diabetes management, pushing closer to an era of more automated and personalized care. EN

– CARSON IS A FREELANCE WRITER BASED IN BIRMINGHAM, ALA., AND HAS BEEN PROVIDING *ENDOCRINE NEWS* WITH VARIOUS TRAVELOGUES, ENDOGEAR COLUMNS, AND MORE FOR SEVERAL YEARS.

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