DIABETES IS PRIMARY

TIMELY NEWS AND NOTES FOR PRIMARY CARE PROVIDERS

from the American Diabetes Association

By Max Bingham, PhD

FROM THE JOURNALS

Definition of Type 2 Diabetes Remission Proposed

A recent consensus report jointly published by four major diabetes organizations sets out a series of criteria for defining diabetes "remission." The report was simultaneously published in *Diabetes Care* (doi.org/g4h9), *The Journal of Clinical Endocrinology & Metabolism* (doi.org/g4jb), *Diabetologia* (doi.org/g4jc), and *Diabetic Medicine* (doi.org/g4jd).

For years, there has been no agreement on what remission consists of, even though numerous therapies aim to reduce blood glucose to normal healthy levels. However, the report's 12-member writing panel proposes the use of "remission" (rather than phrases such as "reversal," "cure," or "resolution") to describe prolonged normoglycemia without the use of any glucose-lowering medication in an individual previously diagnosed with type 2 diabetes.

"Our international group of experts suggest an A1C (average blood glucose) level of less than 6.5% at least 3 months after stopping diabetes medication as the usual diagnostic criterion for diabetes remission," author and writing group chair Matthew Riddle said. "We also made suggestions for clinicians observing patients experiencing remission and discussed further questions and unmet needs regarding predictors and outcomes."

Interventions to achieve remission might include lifestyle/dietary modification, drugs, bariatric surgery, or some other means, according to the panel. The report also stresses the importance of A1C testing both before and after intervention to document continued remission.

Although the report is based on expert opinion, the authors stress that it is not intended to provide. Rather, they say their intention is to propose terminology and a structure for further research to support future clinical guidelines. Indeed, they suggest a series of key research questions that need to be resolved before guidelines can be considered. These include whether an A1C of 6.5% is the best break point to indicate remission, the validation of the timing of glycemic measurements, and the effects of other drugs during diabetes remission, among other issues.

Co-author Roy Taylor explained the importance of the report and why consensus is needed in a press release from Newcastle University (bit.ly/3jZ00js). "Previously, there was confusion about when people could say that they no longer had type 2 diabetes," he said. "This is now set out in black and white—in simple language. An international agreement gives confidence to everyone—patients, doctors, insurance companies—about when a person has returned to health. For instance, in countries where people pay for medical insurance, this can save them a lot of money, as diabetes is so expensive."

The proposed new definition will also ensure that researchers can be sure they mean the same thing when they describe diabetes as being in remission.

Reviews: Diet and Weight Loss Should Be Primary Treatment Goals

A review of clinical evidence suggests that type 2 diabetes remission achieved via intensive dietary approaches and weight loss should now be a primary treatment goal for health care providers. The review, conducted by Brown et al. (*Journal of Human Nutrition and Dietetics*, doi.org/g4jf), covers a variety of dietary approaches that might lead to remission, but in nearly all cases, the most important factor is weight loss. The review emphasizes that different dietary approaches appear to have variable success rates, but that the level of evidence is still somewhat mixed and that a personalized approach will be needed.

"Accounting for all the evidence, our review suggests remission should be discussed as a primary treatment goal with people living with type 2 diabetes," author Duane Mellor said. "There are multiple dietary approaches that have been shown to bring about . . . remission, though, at present, meal replacements offer the best-quality evidence. Low-carbohydrate diets have

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been shown to be highly effective and should also be considered as a dietary approach for remission."

Meanwhile, another review by Lingvay et al. (*The Lancet*, doi.org/gm3z9n) suggests that weight loss of 15% should be used as a primary approach to diabetes treatment. Specifically, the authors suggest that weight loss has benefits that go beyond glycemic control and that achieving it will have benefits relating to cardiometabolic health and quality of life.

"It's known that obesity contributes to the progression of diabetes," lead author Ildiko Lingvay said. "What's new is that, instead of focusing on lowering blood sugar, we recommend the primary approach to the treatment of type 2 diabetes be on the treatment of obesity."

To achieve this weight loss, the authors point to a series of approaches that might be considered, including intensive lifestyle intervention, bariatric surgery, and pharmacotherapy. They also provide a useful guide to some of the newer pharmacologic agents that are in the pipeline, including dual and triple agonists and amylin agonists. One caveat they note with all approaches is that it can be difficult to maintain weight loss in the longer term.

"It's hard to achieve sustained weight loss," Lingvay said. "Most lifestyle interventions result in progressive weight loss over 6 months, followed by a plateau and weight regain over 1–3 years. New weight loss medications and those in the pipeline will help patients succeed in managing their weight over the long term."

TREATMENTS + THERAPIES

Screening Recommendations Change for Prediabetes and Type 2 Diabetes

Adults with overweight or obesity should now be screened for high blood glucose and diabetes starting at the age of 35 years, according to new recommendations from the U.S. Preventive Services Task Force (USPSTF). Previously, the organization recommended screening starting at 40 years of age.

Importantly, the USPSTF also recommends that individuals diagnosed with prediabetes be immediately referred to a program of "effective preventive interventions." The new recommendations, which are published in *JAMA* (doi.org/gm5cnm), will make 40% of the U.S. adult population eligible for screening, with an estimated one-third of those meeting the criteria for referral to a diabetes prevention program.

Based on a systematic review (*JAMA*, doi.org/g4jn), the USPSTF says it has "moderate certainty" that screening adults with overweight or obesity (aged 35–70 years) for prediabetes and type 2 diabetes and offering appropriate referral would have a "moderate net benefit."

"Fortunately, there are interventions that are effective for preventing prediabetes from progressing to diabetes and in helping people with prediabetes improve their health," USPSTF vice-chair Michael Barry said. "The task force encourages clinicians to screen adults over age 35 with overweight or obesity and work with them to determine if an intervention is needed."

As is pointed out in an accompanying editorial (*JAMA*, doi.org/g4jp), the systematic review concludes that there is little evidence that screening directly improves outcomes in diabetes. Rather, the recommendation is based on the rationale that screening allows the introduction of interventions after diagnosis. It is the evidence for the effectiveness of those interventions that swung the decision to recommend screening. This, says Edward Gregg and Tannaz Moin in the editorial, raises three issues that will need to be addressed if screening is to have beneficial outcomes for patients, and they all come down to implementation.

"The USPSTF recommendations to act early and identify and prevent diabetes may have their greatest value if they can reach young and vulnerable adults through a more diverse range of effective options for prevention," they write. "For individuals identified with recently diagnosed diabetes, addressing barriers and expediting access to risk factor management is the clearest route to prevent complications."

CONFERENCE SPOTLIGHT

EASD Meeting: Trial Data, Weight Loss, COVID-19, and Trouser Sizes

The European Association for the Study of Diabetes (EASD) held its again-virtual annual conference at the end of September 2021, and it featured the now-usual mix of new trial data and COVID-19 implications to chew over.

The meeting offered a first look at data from the TriMaster study, which looked at how individual clinical characteristics, including patient preferences, might be used in deciding which therapies a patient receives. Medscape had the full story (wb.md/3GMpGtt), and as chief investigator Andrew Hattersley told the outlet, "We proved a precision medicine approach worked using predefined clinical criteria to define groups of patients where one drug is better than another. This is the first-ever proof of a precision medicine approach in type 2 diabetes." Data from the trial are expected to be submitted for publication soon.

Weight loss may be the key approach to treating type 2 diabetes, but when it was discussed at the EASD conference, great attention was paid to a 15% weight loss target and whether that was appropriate for patients, according to the readout reported by Medscape (wb.md/3q3dOxk). Given the apparent positive reactions of leaders from various professional interest groups, we may well see a series of endorsements for this approach in the coming months.

Meanwhile, we also learned that even when individuals manage to achieve a healthy weight following obesity, it is still hard to completely escape all the effects in the longer term. Most notably, the risk for diabetes remained elevated, although still somewhat reduced, after weight loss (Abstract 84, bit.ly/3k0ND6O)

The interaction between COVID-19 and diabetes was always going to be a focus of discussion at the conference, as it was at the American Diabetes Association's virtual 81st Scientific Sessions earlier in 2021. One study, however, laid out the sheer devastation the pandemic has had on the usual care of individuals with diabetes and particularly on diabetes diagnosis.

According to the study (bit.ly/3nTjxD8) reported on by Dave Holland from The Benchmarking Partnership in the United Kingdom, many millions of tests for diagnosing diabetes and prediabetes were likely missed over a 6-month period in 2020 because of the pandemic, with the result being many thousands of individuals likely did not receive a diagnosis or appropriate care in that period. Medscape reported on the session (wb.md/3mEylGE).

And finally, the most quotable quote from the conference probably came from Roy Taylor describing the outcomes of a small study that looked at how weight loss, and specifically fat loss, can still result in diabetes remission even in those who are not considered overweight or to have obesity.

"As a rule of thumb, your waist size should be the same now as when you were 21," he said in a statement (bit.ly/3pWPJIr). "If you can't get into the same size trousers now, you are carrying too much fat and therefore at risk of developing type 2 diabetes, even if you aren't overweight." Predictably, the study received substantial media interest.

ADA NEWS

Special Article Collection: The RISE Study of Type 2 Diabetes in Youth and Adults

The American Diabetes Association's (ADA's) clinical research journal *Diabetes Care* recently published a special collection of articles focusing on continued findings from the ongoing RISE (Restoring Insulin Secretion) study, which aims to test whether β-cell decline can be stopped in adolescents and adults with prediabetes or early type 2 diabetes and represents a unique opportunity to examine the differences in type 2 diabetes between younger and older people. The special collection includes a commentary and three original research articles offering mechanistic insights into the pathogenesis of type 2 diabetes and potential treatment pathways for adolescents. It was published in the September 2021 issue of *Diabetes Care* and is also available on the journal's website (bit.ly/3xjQsVN).

Diabetes Care Symposium Examines Diabetes and COVID-19 at 18 Months

The 2021 *Diabetes Care* Symposium, titled "Learning to Minimize Risks for People with Diabetes in the COVID-19 Pandemic," presented as part of the ADA's virtual 81st Scientific Sessions in June 2021, addressed the link between diabetes and coronavirus disease 2019 (COVID-19) morbidity and mortality, the role of diabetes in influencing COVID-19 risk, and the pandemic's impact on people with diabetes.

Looking to the future, symposium faculty recommended that longitudinal, retrievable public data be collected to further differentiate the impact of COVID-19 on people with type 1 versus type 2 diabetes and to contextualize data to inform childcare, the return to school, and extracurricular decisions for children with diabetes. They also stressed the need for multidisciplinary care for people with diabetes who contract COVID-19.

The *Diabetes Care* Symposium, hosted by the journal's editor-in-chief, is an annual event that typically focuses on a key issue or issues from the previous year. Three symposium articles were accepted for presentation, were published in the September 2021 issue of *Diabetes Care*, and are also available online as a special article collection (bit.ly/2ZeydEE).

MARKETPLACE

Artificial Pancreas Benefits People With Type 2 Diabetes and End-Stage Renal Disease, But There Are Wider Implications

An investigational artificial pancreas system has helped improve blood glucose control in adults with type 2 diabetes and end-stage renal disease (ESRD) requiring dialysis, according to a report in *Nature Medicine* (doi.org/g4jg).

The small, randomized, crossover trial found that people using the fully automated closed-loop insulin delivery system had a longer glycemic time in range (TIR) than those using standard insulin therapy (53 vs. 38%), for a mean difference of 15.1% in favor of the closed-loop approach. This difference equated to ~3.5 extra hours of TIR (ranging between 5.6 and 10.0 mmol/L [101–180 mg/dL]) compared to the control therapy. We note that the TIR used in the study was a narrower target range than the typically recommended 3.9–10.0 mmol/L (70–180 mg/dL). According to the authors, this range was chosen to account for the high risks of hypoglycemia and related adverse events that were expected in the study population.

In addition, individuals using the closed-loop system had lower overall blood glucose and less time spent in hypoglycemia. The performance of the system, and specifically its control algorithm, improved over time as it responded to individuals' glycemic patterns. Mean TIR increased from 36% on day 1 to over 60% at the end of the study period at 20 days.

"Patients living with type 2 diabetes and kidney failure are a particularly vulnerable group, and managing their condition—trying to prevent potentially dangerous highs or lows of blood sugar levels—can be a challenge," lead author Charlotte Boughton said in a statement (bit.ly/3EHSTns). "There's a real unmet need for new approaches to help them manage their condition safely and effectively."

The researchers are now trialing the approach in individuals with type 2 diabetes in outpatient care (bit.ly/3pWSMR3) and in other complex situations such as during perioperative care.

Noninvasive Blood Glucose Monitoring Devices Reviewed

A review of noninvasive blood glucose monitoring (BGM) devices reveals the sheer number of devices and technologies that are either commercially available or under development. It also reveals the many false starts and apparent difficulties some companies have had in bringing such devices to market and achieving commercial success.

Authors Shang et al. (*Journal of Diabetes Science and Technology*, doi.org/g4jj) identified 65 devices that use various technologies to achieve noninvasive or minimally invasive BGM. According to the authors, 13 products have received regulatory approval and are commercially available, whereas the remainder are still in development.

"Further refinement of these technologies is anticipated over the upcoming decade to enhance both analytical performance and adoption of these products by people with diabetes," the authors wrote in their conclusion. "Bloodless glucose monitoring products such as the ones discussed in this article are expected to become key components of novel wearable digital health tools for monitoring glucose concentrations in the diabetes market and the fitness market."