JANUARY 2020

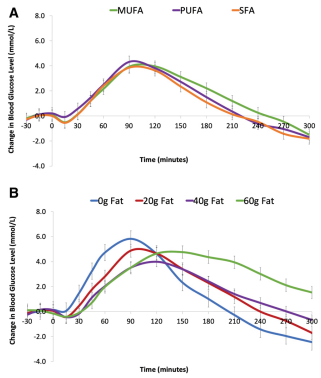
Diabetes Care®

In This Issue of *Diabetes Care*

By Max Bingham, PhD

Dietary Fat Affects Postprandial Glucose Levels—Implications for Insulin Dosing in Type 1 Diabetes

While dietary fat type has no effect on postprandial glycemia in type 1 diabetes, the amount of any fat has a significant effect, according to Bell et al. (**p. 59**). They show that insulin delivery patterns and possibly also total dose should be adjusted according to the amount of fat being consumed to avoid early hypoglycemia and later hyperglycemia. The findings come from a study of individuals with type 1 diabetes who use insulin pump therapy and who were exposed to meals with fixed levels of carbohydrate but varying types and amounts of fat. The authors found that with a fixed insulin dose, increasing amounts of fat resulted in a significant dose-dependent reduction in glucose in the early postprandial phase but an increase in the later phase. Peak glucose levels were also achieved at a later time point at higher fat levels, while nadir glucose levels were reached earlier. Increasing amounts of fat also led to lower incidence of hypoglycemia to the point where there were no episodes at the highest fat intake. In terms of insulin dosing, mealtime insulin needed to be given as a dual wave and increased by up to ~20% on average at the highest fat intake to achieve glycemic control. Based on the findings, the authors go on to recommend varying patterns of insulin dosing according to fat intake. They also suggest that support systems, possibly implemented as smartphone apps, might be developed to help optimize diet and glycemic control. Commenting further, author Kirstine Bell told us: "For years the type 1 diabetes community has been telling us about the glycemic effects of dietary fat. This paper validates their insights and gives the first practical mealtime insulin dosing solution. Managing type 1 diabetes is difficult enough, and we need to be able to respond with immediate solutions to their day-to-day concerns as well as investigating ways to make life easier in the future."



Postprandial glucose profiles for varying types (*A*) and amounts (*B*) of fat in adults with type 1 diabetes using insulin pump therapy.

Bell et al. Amount and type of dietary fat, postprandial glycemia, and insulin requirements in type 1 diabetes: a randomized within-subject trial. Diabetes Care 2020;43:59–66

U.K. NHS DPP: Improvements in Weight and HbA_{1c} Consistent With Recent Trial Evidence, Retention an Issue in Certain Groups

Early outcomes from the first 2.5 years of the NHS England Diabetes Prevention Programme (DPP) suggest that modest reductions in weight and HbA_{1c} have been achieved. And, according to Valabhji et al. (**p. 152**), their program might be on course to reduce diabetes incidence in the future. However, they also highlight the notable issues of engagement, retention, and adherence in the approach. Between June 2016 and December 2018, just under 325,000 individuals were referred to the program and, of these, ~153,000 attended an initial assessment and ~96,000 attended at least one group-based intervention session. Out of ~33,000 individuals who attended at least one session and had sufficient time to complete the program, ~17,000 actually completed, which the authors defined as attending over 60% of sessions. According to an intention-to-treat analysis, mean weight loss was 2.3 kg and HbA_{1c} reduction was 0.12%. In those who completed the program, mean weight loss was 3.3 kg and HbA_{1c} reduction was 0.19%. The authors rightly point out that because the analysis is uncontrolled (i.e., there was no parallel group that received usual care alone), confounders cannot be excluded and there may have been external factors influencing the result. They note that alterations have already been put in place in terms of DPP providers and their incentives to increase retention and adherence, and they are reportedly also piloting digital methods for delivering the program. Author Jonathan Valabhji said: "We have been able to demonstrate that a type 2 diabetes prevention program can be implemented at scale nationally over a short time period—just in excess of 2 years to achieve universal coverage in England. It is highly encouraging that the resulting weight and HbA_{1c} changes in these real-world settings are consistent with those seen in recent pragmatic studies, suggesting likely future reductions in participant type 2 diabetes incidence."

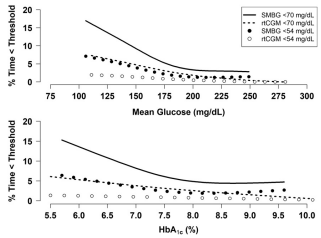
Valabhji et al. Early outcomes from the English National Health Service Diabetes Prevention Programme. Diabetes Care 2020;43:152–160

JANUARY 2020

Diabetes Care®

Real-time Continuous Glucose Monitoring Reduces Hypoglycemia in Type 1 Diabetes

Real-time continuous glucose monitoring (rtCGM) may be able to flatten the relationship between glucose control and hypoglycemia, according to Oliver et al. (**p. 53**). Specifically, rtCGM usage appears to be able to lower mean glucose in individuals with type 1 diabetes using multiple daily injections of insulin and at the same time lower the risk for hypoglycemia. The conclusions come from an analysis of two previous trials (DIAMOND and HypoDE) and comparison of CGM data from individuals who used rtCGM and control subjects who used self-monitoring of blood glucose. The authors also looked at the relationship between glucose control according to HbA_{1c} and mean rtCGM values and percentage time spent below two specific blood glucose thresholds (70 and 54 mg/dL). They found that, at baseline, mean glucose was associated with time spent below both thresholds but that the relationship did not appear linear and indicated that lower blood glucose was associated with longer time spent below the thresholds for hypoglycemia. Use of rtCGM flattened the relationship in terms of both glucose levels and HbA_{1c}, indicating reduced exposure to hypoglycemia at all thresholds. The most marked impact of rtCGM occurred at the lowest values of mean glucose and HbA_{1c}. Hypoglycemia exposure varied across all levels of glucose and HbA_{1c}, but the relationship was much weaker in the group using rtCGM. Commenting further, author Nick Oliver told us: "This analysis shows that the long-established fear that intensive glucose control increases exposure to hypoglycemia can be overcome with the use of continuous glucose monitoring with alerts and alarms, and most importantly, that this is true for people living with type 1 diabetes who self-manage with multiple insulin injections and for those at highest risk of hypoglycemia. It reassures us that we can support people to achieve an HbA_{1c} in the target range without excessive concern about hypoglycemia risk when real-time data are available."



Time spent in hypoglycemia as a function of mean glucose and HbA_{1c} by treatment arm at follow-up.

Oliver et al. Continuous glucose monitoring in people with type 1 diabetes on multiple-dose injection therapy: the relationship between glycemic control and hypoglycemia. Diabetes Care 2020;43:53–58

Diagnosing MODY: Testing for Autoantibodies and Family History Are Key

Recognizing who to test for maturity-onset diabetes of the young (MODY) is greatly helped by basic clinical measures at diagnosis, a lack of autoantibodies, a low HbA_{1c}, and family history, according to Carlsson et al (**p. 82**). Genetic testing of patients with these criteria would then definitively determine if the patient has MODY and the specific type. Recruiting from a national prospective cohort in Sweden, the authors included just under 4,000 individuals with diabetes aged 1–18 years in the analysis. At diagnosis all individuals had clinical data, islet autoantibodies, HLA type, and C-peptide collected. Out of these, 46 patients with the three common types of MODY could be identified via either clinical or research genetic sequencing of *GCK*, *HNF1A*, and *HNF4A*. According to the authors, a key finding was that no patients with islet autoantibodies had MODY. In contrast, when they tested for all four autoantibodies (GADA, IA-2A, ZnT8A, and IAA) at diagnosis, up to 88% of individuals with diabetes had at least one autoantibody, indicating that the individuals had extremely low risk of MODY. They note that increasing the number of tests for autoantibodies resulted in sequentially fewer individuals being identified. The strongest clinical characteristics at diagnosis that discriminated for MODY included lower HbA_{1c}, lower random plasma glucose, parental diabetes, and absence of diabetic ketoacidosis. They note that glycemia at diagnosis and/or family history are key in selecting individuals for genetic testing following establishment of autoantibody negativity. Author Andrew Hattersley added: "This study emphasizes that testing multiple autoantibodies at diagnosis greatly helps identify MODY at diagnosis of diabetes in the pediatric age range. Testing antibody-negative patients who have a low HbA_{1c} (<7.5%) at diagnosis or a parental history of diabetes is a very effective way to identify 96% of MODY cases. Adopting this systematic approach will mean MODY is diagnosed more often and more rapidly."

Carlsson et al. Absence of islet autoantibodies and modestly raised glucose values at diabetes diagnosis should lead to testing for MODY: lessons from a 5-year pediatric Swedish national cohort study. Diabetes Care 2020;43:82–89

https://doi.org/10.2337/dc20-ti01