# Diabetes & Obesity
## RESEARCH REVIEW™

Making Education Easy

Issue 151 – 2021


## In this issue:



# Welcome to issue 151 of Diabetes and Obesity Research Review.

This extended issue begins with a stepped-wedge RCT proving that interventions can be effective in reducing the amount of higher energy foods purchased at worksite cafeterias. On similar lines, interventions of lottery-based financial incentives and environmental change strategies were less successful for achieving meaningful weight loss among employees from three large US companies. Other included research has compared SGLT-2 inhibitors with GLP-1 receptor agonists for differential CV benefits among patients with type 2 diabetes according to the presence or absence of pre-existing CV disease. SGLT-2 inhibitors have also been compared with DPP-4 inhibitors for their capacity to reduce all-cause and CV-related mortality and hospitalisations for heart failure and CKD in patients with type 2 diabetes with or without established CV and/or renal disease.

We hope you enjoy the research selected. We appreciate feedback and suggestions from our readers, so please keep sending them.

Best regards,


**Professor Jeremy Krebs**
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## Impact of decreasing the proportion of higher energy foods and reducing portion sizes on food purchased in worksite cafeterias

**Authors:** Reynolds JP et al.


**Summary:** Nineteen worksite cafeterias in the UK serving 20,327 employees introduced the replacement of higher energy products with lower energy products ('availability') and also introduced reductions in portion sizes of higher energy products ('size') in this stepped-wedge randomised trial, with the availability intervention implemented first and maintained and the size intervention added to the availability intervention; intervention categories included main meals, sides, cold drinks, snacks and desserts. There were overall reductions from baseline in energy purchased from intervention categories during both the availability and size interventions of 4.8% and 11.5% ($p<0.001$ for both), with the difference between the two interventions reaching statistical significance ($p<0.001$).


**Comment:** It is widely recognised that to turn around the obesity epidemic, multiple strategies are required that include both individual and population level interventions. Ultimately to achieve weight loss, individuals need to reduce their total energy intake. Anything that helps facilitate this should be embraced. Manipulating the energy density of food and portion sizes are two obvious ways to achieve this and form the basis of many weight management programmes. What this study investigated is the effect of doing this at a population/food environmental level by restricting the availability of food items in a work cafeteria. The study shows that it is possible to reduce the total energy purchased. It wasn't able to confirm that this necessarily reduced the energy consumed or weight of individuals. There are many obvious ways that might have prevented that. However, it is a promising outcome that warrants further investigation.


***Reference: PLoS Med 2021;18:e1003743***
Abstract


**Abbreviations used in this issue**

**CGM** = continuous glucose monitoring
**CKD** = chronic kidney disease
**CSII** = continuous subcutaneous insulin infusion
**CV** = cardiovascular
**DPP** = dipeptidyl peptidase
**GDM** = gestational diabetes mellitus
**GLP** = glucagon-like peptide
**$HbA_{1c}$** = glycosylated haemoglobin
**HR** = hazard ratio
**MDI** = multiple daily injections
**RCT** = randomised controlled trial
**SGLT** = sodium glucose cotransporter



## Quantity and variety of food groups consumption and the risk of diabetes in adults

**Authors:** Liu M et al.

**Summary:** Relationships between variety and quantity of 12 major food groups with new-onset diabetes were explored in a prospective cohort of 16,117 individuals free of diabetes at baseline in this research from China. Over a median 9.0 years of follow-up, 1088 of the participants were diagnosed with new-onset diabetes. A significant inverse association was reported between a dietary variety score and new-onset diabetes risk (HR for each 1-point incremental increase, 0.85 [95% CI 0.80, 0.90]), with significant U-shaped associations for refined grains, whole grains, nuts, red meat, poultry, processed meat, dairy products and aquatic products, and significant L-shaped associations for legumes, vegetables, fruits and eggs.

**Comment:** There is a vast array of literature on associations between various dietary components and the risk of diabetes. Studies have looked at the relative effects of macronutrients and then broken these down further; for example, saturated fat versus mono- or polyunsaturated fats. Others have examined the glycaemic response to individual foods; e.g. low versus high glycaemic index. This study takes a different approach to look at variety of foods and shows that a greater variety is associated with reduced risk of diabetes. This is another twist on the concept of dietary patterns rather than individual nutrients. It raises many questions, such as combinations or relative importance of particular food items, and as alluded to in this paper, whether there are thresholds where benefits shift to risks. These are difficult issues to resolve in experimental studies.

***Reference: Clin Nutr 2021;40:5710–7***
Abstract

## Efficacy of continuous glucose monitoring on maternal and neonatal outcomes in gestational diabetes mellitus

**Authors:** García-Moreno RM et al.

**Summary:** This was a systematic review with meta-analysis of six RCTs comparing CGM with blood glucose level monitoring in a total of 482 women with GDM. Compared with blood glucose level monitoring, CGM use was associated with lower $HbA_{1c}$ levels at the end of pregnancy (mean difference, –0.22% [95% CI –0.42, –0.03]), less gestational weight gain (–1.17kg [-2.15, –0.19]) and a lower birthweight in the offspring (–116.26g [–224.70, –7.81]); there was no significant difference for any other outcome assessed.

**Comment:** The management of GDM requires intensive dietary and then often insulin therapy to achieve tight glycaemic control. Women are generally very motivated to achieve good results to achieve the best outcomes for their babies, and therefore the optimal use of newer technologies is of great interest. This paper reviewed the evidence for CGM as a tool to assist women with GDM. In a systematic review, there were very few RCTs of CGM, so the evidence base is relatively small. Despite that, the conclusion was that CGM does help women achieve better glycaemic control and also importantly less weight gain and lower birthweights, which are all associated with better pregnancy outcomes and also later metabolic outcomes for the children.

***Reference: Diabet Med; Published online Sept 24, 2021***
Abstract



## Effect of financial incentives and environmental strategies on weight loss in the healthy weigh study

**Authors:** Glanz K et al.

**Summary:** Employees with a BMI of 30–55 kg/m$^2$ and ≥1 other CV risk factor were enrolled in a 2×2 factorial randomised trial comparing the effects of 18 months of lottery-based financial incentives, environmental strategies and their combination with usual care on weight loss and maintenance; 86 participants were randomised to each of the four groups. Relative to usual care, participants assigned to the incentives, environmental strategies and combined incentives plus environmental strategies groups had mean weight losses at 18 months (primary endpoint) of 2.45kg, 1.00kg and 1.09kg, but none of these differences achieved statistical significance; similar nonsignificant differences persisted 6 months later (i.e. 6 months after the interventions had finished).

**Comment:** The main message I take from this paper is that helping people to lose weight is really hard! Most people who are obese would like to lose weight and most have tried. Sadly, few are successful, particularly in the long-term. Many barriers and facilitators have been described, and these include support from an external agent and financial incentives. These were studied in this trial, either alone or in combination. Neither were particularly effective in the way they were used here. This may be because they aren't effective or because the delivery was not intensive enough. That all feels a bit depressing doesn't it, but we mustn't give up. The DiRect study amongst others have given us clear evidence that when people do achieve meaningful weight loss, it really makes a difference to their health.

***Reference: JAMA Netw Open 2021;4:e2124132***
Abstract

## Association of habitual alcohol consumption with long-term risk of type 2 diabetes among women with a history of gestational diabetes

**Authors:** Hinkle SN et al.

**Summary:** The association of alcohol consumption with type 2 diabetes risk was explored in a US Nurses' Health Study II cohort of 4740 women with a history of GDM. Over a median 24 years of follow-up (78,328 person-years), the incidence of type 2 diabetes was 19%. Compared with no alcohol consumption, consumption of 5.0–14.9 g/day was associated with a lower risk of incident type 2 diabetes (adjusted HR 0.45 [95% CI 0.33, 0.61]), with no associations detected for other alcohol consumption ranges assessed (0.1–4.9 and ≥15.0 g/day); similar results were obtained after additional adjustment for BMI (HR for 5.0–14.9 g/day, 0.59 [0.42, 0.81]) with the other two alcohol consumption ranges still not significantly associated.

**Comment:** Women with a history of GDM are at greater risk of developing type 2 diabetes later in life than women who do not develop GDM. The actual increase in risk varies across studies, and is of course influenced by other individual risk factors, such as weight, family history and exercise. It is worth noting that in this study of nurses in the US, the rate of developing diabetes was 19% over a median of 24 years. This paper reported on the association between level of habitual alcohol use and risk of developing type 2 diabetes in women with a history of GDM. It may come as a relief to many that, as has been reported in other situations, a low level consumption of alcohol was associated with a reduced risk of type 2 diabetes. That glass of chardonnay as you are preparing the kids' meals may be just the answer. Of course there are many other considerations, and the slippery slope of the second and third glasses that can so easily happen!

***Reference: JAMA Netw Open 2021;4:e2124669***
Abstract



## Sodium-glucose cotransporter-2 inhibitors versus glucagon-like peptide-1 receptor agonists and the risk for cardiovascular outcomes in routine care patients with diabetes across categories of cardiovascular disease

**Authors:** Patorno E et al.

**Summary:** These researchers investigated the differential CV benefits of SGLT-2 inhibitors versus GLP-1 receptor agonists in population-based propensity score-matched cohorts of patients with type 2 diabetes with (52,901 pairs) and without (133,139 pairs) CV disease. Compared with starting a GLP-1 receptor agonist, starting an SGLT-2 inhibitor was associated with a lower risk of myocardial infarction or stroke in the presence of CV disease (HR 0.90 [95% CI 0.82, 0.98]) but not in its absence (1.07 [0.97, 1.18]), and also a lower risk of hospitalisation for heart failure, this time in patients with and those without CV disease (0.71 [0.64, 0.79] and 0.69 [0.56, 0.85], respectively).

**Comment:** Now that we have access to a funded SGLT-2 inhibitor and a GLP-1 agonist for many people with type 2 diabetes, the obvious question is when is one agent better than the other? Unfortunately, we do not have any large RCTs with hard outcome measures comparing the two classes to inform this question. From the existing placebo controlled trials within each class, there are some apparent differences. For example, SGLT-2 inhibitors have strong evidence to support a reduction in heart failure admissions, which GLP-1 agonists do not. GLP-1 agonist appear to reduce the risk of stroke, which is not necessarily supported for SGLT-2 inhibitors. This paper reports matched individuals starting either class of drug, and outcomes according to previous CV disease. The key thing here is that they were not randomly allocated to the drug, but they are real-world patients. The data support the difference in risk of heart failure and possibly a small benefit to SGLT-2 inhibitors in CV disease for those with existing CV disease. In the absence of heart failure, I think we can say for now that the decision between agents may best be informed by patient choice and side-effect profile.

***Reference: Ann Intern Med 2021;174:1528–41***
Abstract

## Use of continuous subcutaneous insulin infusion versus multiple daily injections in emerging adults with type 1 diabetes is associated with better clinical engagement but not glycaemic control

**Authors:** Chai TYL et al.

**Summary:** These researchers assessed glycaemic control and utilisation of services for a retrospective cohort of 318 emerging adults with type 1 diabetes on MDIs or CSIIs; 176 of the patients were receiving MDIs, 121 were receiving CSIIs and 21 switched from MDIs to CSIIs. There was no significant difference between CSII versus MDI recipients for aggregated mean $HbA_{1c}$ level (9.1% vs. 9.3% [p=0.23]); however, CSII users had a significantly greater mean change in $HbA_{1c}$ level at 3 years of 0.55% (p<0.01) while MDI users had no significant change. CSII recipients also exhibited improvements in clinic visits compared with MDI recipients (2.8 vs. 2.5 per year [p=0.02]), whereas admissions for diabetic ketoacidosis were similar at 3.6 per 100 patient-years.

**Comment:** This paper caught my eye, mainly because I was curious what an emerging adult was! Images of cocoons came to mind. Anyway, this very real-world retrospective audit of a young adult diabetes clinic makes some interesting observations. There is often a belief that insulin pumps are somehow the holy grail of diabetes management, and I think both patients, parents and members of the diabetes team sometimes can forget that they are just a tool to deliver insulin. For some people who use the tool to its best advantage, there is no doubt that they can achieve much better results in managing their glucose levels than they could with multiple injections. However, this paper reminds us that that is not the case for everyone. It also reminds us that the group of 'emerging adults' pose many challenges to trying to achieve tight glycaemic control and reducing the risks of complications.

***Reference: Intern Med J; Published online Sept 24, 2021***
Abstract

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## Effects of intranasal oxytocin in food intake and craving

**Authors:** Chen C-Y et al.

**Summary:** This was a meta-analysis of twelve clinical trials in 266 non-psychiatric and 157 psychiatric participants reporting on the effects of intranasal oxytocin on food intake, craving, anxiety and stress reduction. Single-dose intranasal oxytocin induced significant reductions in food intake in non-psychiatric participants (standardised mean difference, –0.66 [95% CI –1.18, –0.14]), but there was no significant effect seen in those with anorexia nervosa, bulimia nervosa/binge eating disorder or schizophrenia. Additional analyses on leisure foods also showed there was a reduction in chocolate biscuit consumption in non-psychiatric participants. Intranasal oxytocin had no significant impact on food craving or hunger compared with placebo for the non-psychiatric participants or those with bulimia nervosa/binge eating disorder or schizophrenia, nor did it significantly affect anxiety or stress in any subgroup.

**Comment:** The hormonal regulation of appetite is complex, and we keep discovering new players and complex interactions. Oxytocin may be one of these. This meta-analysis looked at whether intranasal oxytocin had an effect on food behaviours. It is somewhat complicated by patient populations studied, and divides the results between those with psychiatric disease and those without. Oxytocin did reduce food intake as a single dose in those with no psychiatric disease, and could be further explored as a treatment strategy for obesity. Of course there is a major difference between single doses and ongoing regular treatment, particularly whether there is effect modification with repeated dosing. However, this does look promising.

***Reference: Clin Nutr 2021;40:5407–16***
Abstract

## Association of body mass index and its long-term changes with cardiometabolic diseases

**Authors:** Guo J et al.

**Summary:** Relationships of BMI and its long-term changes with cardiometabolic diseases, and the role of familial background and a healthy lifestyle on these associations, were explored in 36,622 individuals aged ≥40 years who were free of cardiometabolic disease and with 25–35 years of follow-up from baseline from the Swedish Twin Registry; 44.2% of the participants had a BMI ≥25 kg/m$^2$ (i.e. overweight/obese) and 30.6% developed cardiometabolic diseases during follow-up. Compared with BMIs 20–25 kg/m$^2$, individuals with a BMI of ≥25 kg/m$^2$ were at significantly increased risk of developing any cardiometabolic disease (HR 1.52 [95% CI 1.45, 1.58]). Compared with individuals who had a stable BMI of 20–25 kg/m$^2$, the risk of developing a cardiometabolic disease was increased in those who were overweight/obese in early life only, in later life only and both early and later life (respective HRs 1.28 [95% CI 1.02, 1.59], 1.33 [1.24, 1.43] and 1.69 [1.55, 1.85]). Stratified Cox analyses for cardiometabolic disease-discordant twin pairs revealed a significant association between overweight/obesity and increased cardiometabolic disease risk (HR 1.37 [95% CI 1.18, 1.61]), and a joint effect analysis revealed that the increased cardiometabolic diseases risk related to overweight/obesity was attenuated by 32% for those who adopted favourable lifestyle choices (1.51 [1.44, 1.58]) compared with those who did not (2.20 [2.03, 2.38]).

**Comment:** Nature or nurture – the age old debate. If there was any health parameter to which this debate is relevant, then weight and obesity is surely the best example. Twin studies have classically been the model used to try and answer the relative contributions of genetics versus environment. This paper reports on the association between obesity and cardiometabolic disease using data from the Swedish Twin Registry, to try to tease out the relative effects of obesity from other genetic factors. What do you know, its complex! There is almost certainly an interaction between genetics and environment, with lifestyle factors either attenuating or exacerbating the underlying genetic risk. You can't choose your parents, but you can choose your dinner.

***Reference: Clin Nutr 2021;40:5467–74***
Abstract

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## Different effects of lifestyle intervention in high- and low-risk prediabetes

**Authors:** Fritsche A et al.

**Summary:** This trial conducted in 1105 individuals with prediabetes randomised those with a high-risk phenotype to a conventional lifestyle intervention or an intensified version in which the exercise requirements were doubled; those with a low-risk phenotype were randomised to a conventional lifestyle intervention or a control group, and 82% of participants completed the study. In the high-risk group, a significant difference was seen between the intensified versus conventional lifestyle intervention for reductions in postchallenge glucose level (–0.29 mmol/L [p=0.025]), liver fat (–1.34 percentage points [p=0.002]) and CV risk (p=0.007). Moreover, the likelihood of glucose level tolerance normalisation was greater in the intensive intervention group over 3 years of follow up (p=0.008).

**Comment:** If we think type 2 diabetes is very heterogeneous, then prediabetes is an even greater quagmire! We have three different ways of defining it, with fasting glucose levels, oral glucose tolerance tests and $HbA_{1c}$ levels, which overlap but do not identify the same people, nor the same risk of progression to diabetes. Furthermore, some people regress to 'normal' or never progress beyond very low levels of $HbA_{1c}$ or glucose. Therefore, developing policies for interventions is challenging to balance the investment in individual interventions versus public health approaches. This would be made easier if it were possible to identify individuals who were most at risk of progression to diabetes or adverse outcomes for whom targeted intensive interventions could be directed. This study takes a somewhat crude approach to this and shows that there is merit in following this path. What is needed is a simple tool to identify individuals with prediabetes at greatest risk that can be easily applied in primary care.

***Reference: Diabetes; Published online Sept 16, 2021***
Abstract

## The effect of discontinuing continuous glucose monitoring in adults with type 2 diabetes treated with basal insulin

**Authors:** Aleppo G et al., for the MOBILE Study Group

**Summary:** Adults with type 2 diabetes receiving basal without bolus insulin were initially randomised to real-time CGM or blood glucose level monitoring for 8 months, which was followed by an additional 6 months during which the blood glucose level monitoring group continued their assigned treatment (n=57) and the CGM group was rerandomised to continue CGM (n=53) or discontinue CGM and resume blood glucose level monitoring (n=53). In the initial CGM group, there was an improvement in mean time in glucose level range (70–180 mg/dL) from 38% prior to CGM initiation to 62% after 8 months of CGM, and for those who then discontinued CGM, it had fallen significantly to 50% at 14 months (p=0.01), whereas it remained stable (1% change) for those who continued CGM use; the difference between the initial CGM recipients who continued versus discontinued CGM at this time was –6% (p=0.20).

**Comment:** There are so many variables that determine whether a person with diabetes, type 1 or 2, achieves good glycaemic control. In people using insulin therapy, one of the most important factors is having real-time data on glucose levels. For over 30 years this has been possible with capillary glucose level monitoring, which was a major step forward from previous retrospective and very crude information from urine dipstick testing. However, finger prick testing is still invasive and there are many barriers to frequent testing. Furthermore, data are single timepoints with no trend data. For these reasons, interstitial CGM has become a very attractive option, particularly for those people who for whatever reason do very few capillary tests. In NZ where these are not funded, people decide whether they self-fund this technology or not. In clinic, I am always concerned that those who do a few tests and then trial CGMs but decide not to continue to use them will then do even fewer capillary tests. This paper to some extent confirms that concern.

***Reference: Diabetes Care; Published online Sept 29, 2021***
Abstract



### Independent commentary by Professor Jeremy Krebs MBChB, FRACP, MD

Professor Krebs is an Endocrinologist with a particular interest in obesity and diabetes. He trained in Endocrinology at Wellington Hospital in New Zealand and then did his doctorate with the Medical Research Council - Human Nutrition Research unit in Cambridge England. His thesis was on the impact of dietary factors on obesity and insulin resistance. Professor Krebs returned to New Zealand in 2002 to take up a consultant Endocrinology post at Wellington Hospital, where he was Clinical Leader of Endocrinology and Diabetes. He heads the research group and is Professor with the University of Otago, and former Director of the Clinical Research Diploma at Victoria University - which he established. As well as clinical and teaching activities, Professor Krebs maintains active research interests in the area of obesity and diabetes, with a particular focus on the association between obesity and type 2 diabetes, both from an aetiology and management perspective, with a focus on nutritional aspects, bariatric surgery and diabetes service delivery.

## Effects of empagliflozin on insulin initiation or intensification in patients with type 2 diabetes and cardiovascular disease

**Authors:** Vaduganathan M et al.

**Summary:** These researchers assessed changes in insulin use in the EMPA-REG OUTCOME trial, which randomised 7020 patients with type 2 diabetes and CV disease to receive empagliflozin 10mg, empagliflozin 25mg or placebo, and followed them for a median of 3.1 years; changes in background antihyperglycaemic therapy were permitted after 12 weeks on the study. Among 3633 trial participants not receiving insulin at baseline, empagliflozin recipients (both doses pooled) were significantly less likely to start insulin during the trial than placebo recipients (7.1% vs. 16.4%; adjusted HR 0.40 [95% CI 0.32, 0.49]). Among the 3387 participants receiving insulin at baseline, a smaller proportion of those assigned to the empagliflozin arms versus placebo arm needed to increase their insulin dose by >20% (14.4% vs. 29.3%; adjusted HR 0.42 [95% CI 0.36, 0.49]) and a greater proportion were able to sustain a >20% insulin dose reduction without impacting their $HbA_{1c}$ level (9.2% vs. 4.9%; 1.87 [1.39, 2.51]). The findings were consistent in sensitivity analyses for insulin dose changes of >10% and >30%.

**Comment:** By now you will be familiar with the EMPA-REG trial, which provides the main evidence for benefit of empagliflozin in reducing CV risk. This paper reports a secondary analysis from the EMPA-REG trial on the impact of empagliflozin on insulin requirements in this population. After 12 weeks of the study, investigators could add or adjust insulin therapy as required to achieve glycaemic control. In participants who were not using insulin at the start of the trial, there was a 60% reduction in the need to initiate insulin. In those already using insulin, there was a major reduction in the escalation of insulin dosing required. Both are important findings and benefit patients by reducing the burden of injections and of risks for hypoglycaemia and weight gain. These observations are over the mean 3-year follow-up, and of course can't tell us how sustained the effects are. The nature of type 2 diabetes is such that it is likely that many patients will still need to start insulin at some point, but any delay in that is useful.

***Reference: Diabetes Obes Metab 2021;23:2775–84***
Abstract

## Lower risk of hospitalization for heart failure, kidney disease and death with sodium-glucose co-transporter-2 inhibitors compared with dipeptidyl peptidase-4 inhibitors in type 2 diabetes regardless of prior cardiovascular or kidney disease

**Authors:** Idris I et al.

**Summary:** These researchers assessed the relative impacts of SGLT-2 inhibitors and DPP-4 inhibitors on all-cause mortality, CV-related death and hospitalisation for heart failure or CKD in a retrospective UK primary-care cohort of individuals with type 2 diabetes with or without established CV and/or renal disease; 24,438 SGLT-2 inhibitor recipients were each propensity score matched to a DDP-4 inhibitor recipient. Compared with DDP-4 inhibitors, SGLT-2 inhibitors were associated with reductions in all-cause mortality, CV-related mortality, hospitalisation for heart failure and hospitalisation for CKD across the entire cohort; SGLT-2 inhibitors remained protective in patients with established or at high risk for CV disease for these four outcomes and hospitalisation for stroke (respective HRs 0.69 [95% CI 0.59, 0.82], 0.76 [0.62, 0.95], 0.73 [0.63, 0.85], 0.49 [0.43, 0.54] and 0.75 [0.59, 0.94]), and in patients with no history of CV and/or renal disease for all-cause mortality, hospitalisation for heart failure and hospitalisation for CKD (0.71 [0.57, 0.88], 0.76 [0.59, 0.98] and 0.75 [0.63, 0.88]).

**Comment:** The large RCTs of SGLT-2 inhibitors have provided robust evidence for benefit of this class to reduce the risk of CV disease and renal outcomes compared with placebo. However, as is always the case with these types of studies, the selection of participants often excludes many of the patients that we might consider using the drug in, and may not compare the drug with alternative agents that we might be considering. Therefore the type of study reported here, which even though limited by being retrospective and not randomised, do give very useful real-world data to inform practice. What this study shows is that compared with DPP-4 inhibitors, the SGLT-2 inhibitors have a very clear advantage in reducing the risk of hard endpoints, and therefore should wherever possible be added in to the regimen ahead of DPP-4 inhibitors. What is equally important from these data is that this applies to those who do not have existing CV or renal disease, which has not been clear from the large RCT data.

***Reference: Diabetes Obes Metab 2021;23:2207–14***
Abstract



## What are the factors associated with long-term glycaemic control in patients with type 2 diabetes and elevated glycated haemoglobin (≥7.0%) at initiation of second-line therapy?

**Authors:** Bonnet F et al.

**Summary:** This analysis of data from the global, prospective, 3-year observational DISCOVER study sought to identify factors associated with good long-term glycaemic control in 7575 participants with an $HbA_{1c}$ level of ≥7.0%, 2233 of whom had a level ≥9.0%, at initiation of second-line glucose-lowering therapy. The respective proportions of those with baseline $HbA_{1c}$ levels of 7.0–<9.0% and ≥9.0% who had achieved a level of <7.0% at 6 months were 43.7% and 24.2%, and at 3 years, the corresponding proportions were 45.8% and 29.3%. For achieving an $HbA_{1c}$ level of <7.0% at 3 years, the strongest predictor was having a level of <7.0% (vs. ≥7.0%) at 6 months (odds ratios 2.01 [95% CI 1.77, 2.27] and 2.68 [2.10, 3.41] for the respective baseline 7.0–<9.0% and ≥9.0% groups), and the likelihood was reduced by a longer duration of type 2 diabetes.

**Comment:** Clinical inertia is an important phenomenon in the management of type 2 diabetes. I have previously included studies that have looked at the patient and clinician factors which influence this. This paper reports on factors which determine the longer-term likelihood of achieving target $HbA_{1c}$ level once a second-line agent is actually introduced. It might seem intuitive that the strongest predictor of good long-term control was achieving this within 6 months, and that the higher the $HbA_{1c}$ level at the time of initiation of a second agent, the less likely that was. Both speak to the importance of early and aggressive glycaemic management.

***Reference: Diabetes Obes Metab 2021;23:2336–43***
Abstract

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