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REVIEW

Could Dietary Modification Independent of Energy Balance Influence the Underlying Pathophysiology of Type 2 Diabetes? Implications for Type 2 Diabetes Remission

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ABSTRACT

High-quality clinical trial data demonstrate that remission is possible for people living with type 2 diabetes (T2D) if they lose a large amount of weight (≥ 10 kg). Durable remission appears predicated on the long-term maintenance of weight loss. Unfortunately, long-term follow-up data from lifestyle-based weight loss programmes show that, on average, most people regain at least some of the weight lost. In addition, restoration of a diminished first-phase insulin response also appears necessary for durable remission, and this becomes less likely as T2D progresses. A pragmatic approach to enhance the effects of weight loss on durable remission is to consider whether dietary components could help control blood glucose, independent of caloric balance. This manuscript reviews current evidence on weight-neutral effects of diet on blood glucose, including high-protein, low-carbohydrate, high-fibre and plant-based diets, with a particular focus on the effect of nutrition on the underlying pathophysiology of T2D, including the first-phase insulin response. The importance of mechanistic data in enhancing our understanding of dietary strategies in T2D remission is described, and suggestions are made for future advances in remission research.

Keywords: Glucose; Type 2 diabetes; Protein; Carbohydrate; Ketogenic; Fibre; Plant-based

Key Summary Points

Remission of type 2 diabetes (T2D) is now possible for many people living with T2D if they are able to lose and maintain > 10% weight loss and have T2D of short duration.

This excludes many people if they do not want to, or are unable to lose and maintain that much weight loss. It also potentially excludes people who have T2D of longer duration. Dietary strategies which could help lower glycaemia independent of weight loss could help more people achieve normalisation of glucose concentrations.

This manuscript reviews the evidence for different weight-neutral dietary strategies to help support optimal management of T2D and describes a way forward for remission research.

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INTRODUCTION

The aim of type 2 diabetes (T2D) management is to control cardiovascular (CV) risk factors, including glucose, altered lipid profile and blood pressure. The pinnacle of T2D management can be considered remission [1]—the normalisation or achievement of blood glucose concentrations under the diabetic threshold in the absence of hypoglycaemic medications, which is often associated with reduction in blood pressure and improvement in the lipid profile [1, 2].

It is currently accepted that remission can be achieved via marked weight loss following caloric restriction achieved through diet or bariatric surgery [1, 3]. In the UK, a total diet replacement approach used in the seminal Diabetes Remission Clinical Trial (DiRECT) is being piloted across 12 sites in the UK [4]. While the evidence shows that body weight (an imperfect proxy for adiposity) is the most important factor in T2D development [5], remission [6] and relapse [6], other dietary strategies could help lower blood glucose [7, 8] and manage some T2D risk factors [9, 10] in ways that could be independent of energy balance. The use of such strategies could be a useful addition to T2D remission programmes, but also to prevention programmes.

It is important to note that dietary interventions often require an individual to make changes to nearly all aspects of their lives—from shopping, to cooking, to eating—and that these changes may need to be continued for most meals that person eats. For these and other reasons, no one diet will ever be appropriate for everyone, regardless of whether it is physiologically efficacious or not. Nevertheless, a better quality evidence base which can allow us to make more precise statements about what nutrients and diets can and cannot do will enable us to inform our patients of what works, how it works and possibly in whom it works.

The dearth of mechanistic and well-controlled studies in individuals with T2D to date mean that we are largely unable to give patients more specific guidance than "lose weight in whatever way you are able to sustain" [11]. Even the most up-to-date guidance for T2D is based on free-living weight loss interventions which use different dietary patterns to achieve this weight loss. As such, recommendations for specific dietary strategies are understandably weak [12]. As I described in this review, there is growing evidence that there are dietary strategies which can indeed influence key aspects of T2D physiology and lower blood glucose independent of caloric balance.

This manuscript will examine how dietary strategies could influence the underlying pathophysiology of T2D beyond caloric restriction and describe a way forward for T2D remission research. Since this article is based on previously conducted studies and does not contain any new studies with human participants, ethical approval was not sought.

HISTORY OF DIET-INDUCED MEDICATION WITHDRAWAL/ REMISSION IN T2D

Following observations from bariatric surgery that normalisation of blood glucose and medication withdrawal was possible in patients with T2D before any significant weight loss had occurred, multiple investigative groups examined the independent effect of marked caloric restriction alone on T2D pathophysiology.

A series of mechanistic physiological studies [13–17] demonstrated that marked energy restriction (intake of 400–800 kcal/day) over the short term (2 days to 8 weeks) favourably alters key aspects of T2D pathophysiology and leads to substantial reductions in or even normalisation of blood glucose. However, in all of these studies, the follow-up tests were carried out immediately following the energy restriction, and the durability of these glucoregulatory improvements was unknown [18]. Further research demonstrated that the remission achieved with marked weight loss (in the order of 10–15 kg) can be maintained up to 2 years in a large proportion of people, provided weight regain is limited or prevented [2, 6, 19].

Another key aspect of our understanding of remission is that durable remission achieved with diet-induced marked weight loss is

dependent upon the return of a key aspect of beta-cell function, called the first-phase insulin response [19, 20]. This marked post-meal insulin spike is critical physiologically to suppress hepatic glucose output and lipolysis of peripheral adipose tissue, and to promote the uptake of glucose and fatty acids into skeletal muscle [21]. The first-phase insulin response declines over the course of T2D, and data from lifestyle trials and bariatric surgery consistently show an inverse relationship between duration of T2D and likelihood of remission [19–21].

In summary, our current understanding is that remission of T2D via diet can be achieved contingent on: (1) the return of the first-phase insulin response, which itself is reliant on achieving and sustaining significant weight loss, and (2) T2D being of relatively short duration.

The next sections review how other dietary strategies could optimise T2D remission programmes, with a focus on how diet affects the underlying physiology of the disease. The discussion points are summarised in Table 1 and in Fig. 1.

HIGH PROTEIN

In healthy individuals, the pancreas is able to precisely control blood glucose by releasing just the right amount of insulin required to keep blood glucose within a narrow range [22]. One of the most important qualitative properties of the insulin secretory response is the ability of the beta-cells [22] to respond to the rapid rises in blood glucose following a carbohydrate load by acutely and rapidly increasing the amount of insulin released [21]. In clinical terms, this "insulin spike" is referred to as the "early" or "first-phase" insulin response [21, 23].

The physiological importance of the first-phase insulin response is demonstrated by studies in which its experimental reduction results in impaired suppression of hepatic glucose output, hyperglucongaemia, post-prandial lipaemia, higher maximal glucose concentrations and prolonged hyperglycaemia which may last for several hours [21, 24, 25]. Conversely, experimental restoration of the absent early insulin response in T2D normalises glucose tolerance without increasing the overall insulin demand [21, 25].

Protein has long been known to potentiate the insulin response to a carbohydrate load [26], such that increasing the amount of protein in a meal acutely can more than double the amount of insulin produced [27–29], and lead to a reduction in post-prandial glucose concentrations [26, 30, 31]. This insulinogenic response likely occurs via direct stimulation of amino acids on the beta-cell [32, 33] and an enhanced incretin effect [34].

Of particular relevance to T2D, while glucose-stimulated insulin secretion declines markedly as T2D progresses, amino acid-stimulated insulin secretion appears to remain relatively intact [35]. In fact, the insulinotrophic effect of protein may be greater in people with T2D [28, 29] than in people with normal glucose tolerance. Given that a potent prandial insulin response is necessary for optimal control of post-prandial glucose concentrations [20, 25], and that the glucose-stimulated insulin response declines in T2D [21], this raises the question of whether increasing the amount of protein in the diet could help lower blood glucose concentrations, independent of weight loss.

To date, five well-controlled studies [8, 10, 36–38] by two independent research groups have shown that increasing the protein content of the diet from 15% to 30% kcal lowers blood glucose in T2D. These studies carefully controlled body weight, provided full food provision throughout each dietary intervention and measured multiple parameters of glycaemic control. The reduction in glucose is clinically significant: up to a reduction of 2–5 mmol/L during the 4-h period after a meal. In each of these studies the carbohydrate was also reduced and represented between 20 and 40%kcal. Therefore, the relative contribution of increased protein and carbohydrate restriction to the improvements in glycaemia are unknown. It is also important to reference studies [39, 40] which tested a similar dietary composition and did not find any superiority on glucose lowering while also noting that these studies did not

Table 1 Summary of the emerging evidence for the effect of dietary components on glucose and the physiological drivers underlying glucose concentrations in type 2 diabetes independent of calorie restriction

Dietary components	First-phase/ early insulin response	Hepatic glucose output	Increase glucose uptake	Glucose
Increasing dietary protein	Increases	No acute effect, long-term effect unknown	Conflicting data	Lowers, may need to be combined with carbohydrate restriction
Reducing dietary carbohydrate	Unknown	May reduce output, but likely depends on degree of reduction	Unknown—likely depends on the degree of reduction	Unknown—likely depends on the degree of reduction
Increasing dietary ketones	Unknown	Reduces	Unknown	Lowers
Increasing fibre	Increases[a]	Reduces[a]	Increases[a]	Reduces[a]
Increasing polyunsaturated fatty acids:saturated fatty acids ratio	Unknown	Reduces acutely	Unknown	No effect
Increasing plant-based components eg phytonutrients	Unknown	Unknown	Unknown	Unknown

[a]Depends on the physicochemical properties of the fibres, and the dose. Large differences in fibre are needed to see a significant effect

provide the dietary protocol or control the confounding variables, including body weight.

As convincingly shown by the DiRECT trial investigators [2], marked weight loss can restore the first-phase insulin response in people with T2D of short duration (< 4 and < 6 years)[19, 20]. However, therapeutically it is important to understand if there are other ways to restore the early insulin response that could be effective in people with T2D of longer duration, or without necessarily requiring such marked weight loss. If the beta-cells are able to produce a large post-prandial insulin response to amino acids, this could be a clinically useful strategy to help manage glycaemia in T2D of long duration.

With respect to the effect of additional protein on other underlying drivers of glucose homeostasis, evidence suggests high intakes of protein do not increase hepatic glucose output acutely [41], but the longer-term impact is not known. There is conflicting data on whether high-protein diets influence peripheral glucose uptake [42, 43]. However, the reduction in blood glucose with a high-protein (alongside a reduced-carbohydrate) diet is large enough that if there are changes in hepatic glucose output or glucose uptake, these may not be significant enough to counteract the glucose-lowering effect of the enhanced insulin secretion.

CARBOHYDRATE RESTRICTION

There has been immense interest in the role of a low-carbohydrate diet on glycaemia because carbohydrate is the macronutrient with the greatest effect on acute glycaemia [44]. Since the greater the glycaemic load of a meal, the greater the post-prandial glucose rise, it has become conventional wisdom that simply reducing the carbohydrate load of the diet will lower blood

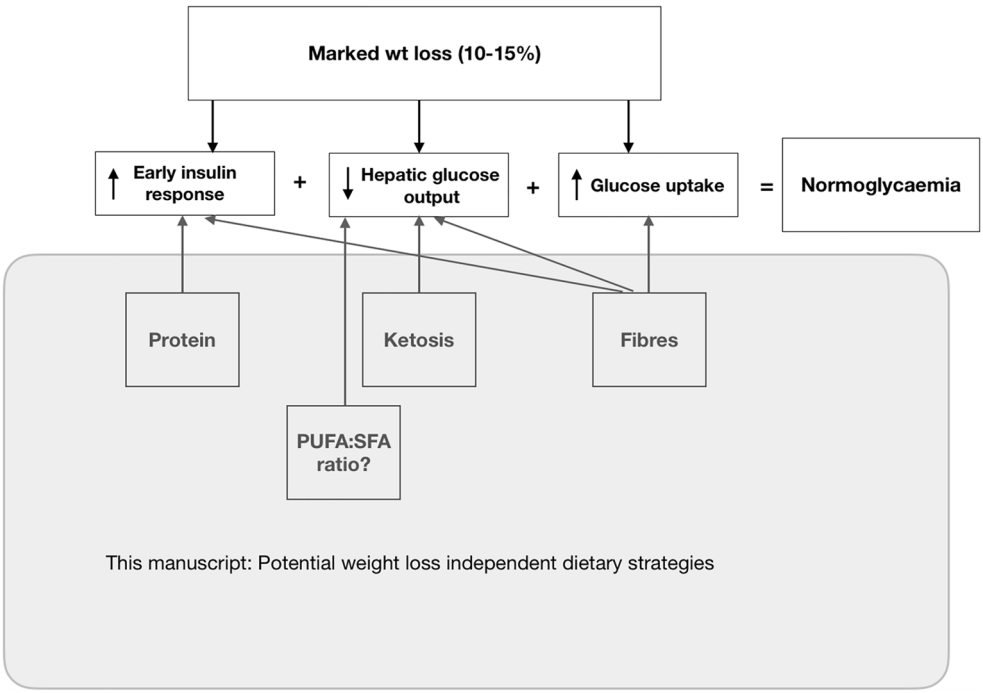

Fig. 1 Graphic overview of proposed mechanisms of actions of protein, nutritional ketosis, fibre and the PUFA/SFA ratio on the underlying drivers of type 2 diabetes remission. *PUFA* Polyunsaturated fat, *SFA* saturated fat

glucose concentrations. However, this is an oversimplication and ignores physiological changes which occur in the body in response to a reduction in carbohydrate intake, including an increase in gluconeogenesis [45] and possibly the development of insulin resistance [46] and down-regulation of insulin secretion [47]. In fact, some of the earliest studies in T2D show that increasing the amount of carbohydrate in the diet lowers plasma glucose concentrations [48]. Equally, while carbohydrate restriction may alter insulin signalling in some tissues, the net effect on long-term CV risk of an increase in muscle-specific insulin resistance when considered against other homeostatic counter-alterations in glucose homeostasis is unclear [49]. In fact, some studies show improvement in classical CV risk factors with a low-carbohydrate diet [50, 51]. Thus, whether and how physiological changes occur in T2D in response to varying degrees of carbohydrate intake has been largely unexplored [52].

Despite the existence of multiple meta-analyses of trials investigating the effect of dietary carbohydrate restriction on glycaemia in T2D [53, 54], it is important to note that the heterogeneity of these trials makes them very difficult to compare. The trials are confounded by differences in weight loss, protein, fibre, fat type and the presence, type and dose of diabetes medications both within the interventions themselves and between the intervention and control groups. Nevertheless, there is scientific data available which provide insight into the potential role of carbohydrate restriction per se on glycaemia, and this will now be reviewed.

While moderate carbohydrate restriction—independent of protein [36, 55, 56] or weight loss—may not alter glucose concentrations in T2D [57, 58], there is evidence that reducing the carbohydrate intake to levels likely to increase ketogenesis does have weight-independent effects on glucose [45, 59].

In a randomised crossover trial which compared two very low-energy weight loss diets in patients with obesity and T2D that were carefully matched for calorie and protein content, a diet containing 28% kcal from carbohydrate lowered fasting and post-prandial glucose to a greater extent than the diet with 78% kcal

carbohydrate [60]. The plasma ketones were 1–2 mmol/L higher in the 28% kcal carbohydrate diet than in the 78% kcal diet, and a significant relationship was observed between plasma ketones and hepatic glucose output. These results support data from experimental physiological studies showing a suppressive effect of plasma ketones on endogenous glucose production and glucose concentrations in people with and without T2D [61–63], as well as data showing that a 0% kcal (89% kcal from fat, 11% kcal from protein) carbohydrate diet suppresses glucose appearance to a greater extent compared to an 89% kcal carbohydrate diet (0% kcal from fat, 11% kcal from protein) in T2D [45].

Endogenous glucose production (EGP) is the formation of glucose from non-glucose precursors. EGP prevents hypoglycaemia from occurring during the fasting and interprandial periods. In healthy people, EGP can be suppressed for several hours following the consumption of even a small amount of carbohydrate (e.g. 25 g) [64]. In T2D, EGP is elevated in the fasting state, and its suppression can be impaired following a meal [65], leading to relative hyperglycaemia in the fed and fasting states.

The effect of nutrients per se on EGP may be particularly important because weight loss-induced suppression of EGP may not be durable in the long term: it is known that a reduction in fasting glucose during energy restriction in T2D occurs within the first week [15] and that this is closely correlated to the reduced EGP that can be achieved with caloric restriction [13, 15, 66]. Unfortunately, once a patient returns to a eucaloric diet (as they inevitably must do at some point and which usually occurs in practice after 6–12 months), EGP returns to its baseline rate, even before any weight gain occurs [67]. Christiansen and colleagues even found that the suppression of EGP with caloric restriction is transient only and that it returns to its high baseline rate even during a hypocaloric diet [67].

Weight loss-induced suppression of EGP may be maintained following extreme weight loss (> 50% of excess body weight, approx. 20 kg) [68], but this magnitude of weight loss is difficult to achieve with diet. EGP continued to be suppressed in a cohort of patients with T2D and obesity who had lost a mean of 20 kg over an average of 17 weeks (range: 4–35 weeks). However, the follow-up tests were taken as soon as patient reached their 50% excess weight loss target and therefore may have still been measured in a calorie-deficit state.

In summary, dietary approaches which could suppress endogenous glucose production independent of caloric balance may help enhance durable glycaemic control, and this may be particularly critical as the patient moves from weight loss to weight maintenance.

WHOLE-FOOD, PLANT-BASED DIET

Dietary patterns (Mediterranean, vegetarian etc.) recommended for the management of T2D have in common the inclusion of whole, intact foods from plant-based sources. While these type of diets are also associated with weight loss, there is good evidence they have beneficial effects independent of their energy density. Components of these diets for which there is evidence for weight-neutral effects on glycaemic control include fibre, polyphenolic compounds and a high proportion of saturated versus unsaturated fats.

Fibre

Dietary fibres are a group of carbohydrates which cannot be digested and absorbed in the upper gastrointestinal tract. Various factors contribute to the digestibility of carbohydrates, including the type of starch (amylose or amylopectin), rate of digestion, cooking or processing method and fibre content [69]. If the structure of the carbohydrate is such that the rate or degree of digestion is slowed, the carbohydrate is less available/"glycaemic". For example, the open structure and absence of fibre secondary to the processing used in the manufacture of white rice renders the glucose monomers rapidly and fully available. Conversely, the rigid and tight structure secondary to the retrogradation of the starch in pasta

which has been cooked and cooled makes this glucose less readily available.

The concept of the glycaemic index has formed part of T2D management for decades [70], but the effect size of a low versus high glycaemic index diet in trials is fairly modest (glycated haemoglobin [HbA1c] approx. 0.4–0.5% [4–6 mmol/mol]) [71, 72]. This suggests that "extraglycaemic" properties of carbohydrate play an important role in the relationship between indigestible carbohydrates and T2D control.

Of particular relevance to T2D may be fermentability. Indigestible fibres pass intact to the colon where they are fermented by resident gut bacteria. The products of fermentation include the short-chain fatty acids (SCFA) acetate, butyrate and propionate. These SCFA are ligands for receptors located on L cells within the colon [73, 74] that secrete enteroendocrine hormones, including glucagon-like peptide-1 (GLP-1), which augments glucose-simulated insulin secretion, and peptide YY (PYY), which slows gastric emptying. Despite promising results from animal studies, the data currently available do not suggest a significant effect of fermentable carbohydrate consumption (at 10–35 g/day intakes) on GLP-1 secretion in humans ([75, 76]. Nevertheless, a number of studies using both oral and intravenous measures of insulin secretion suggest that fermentable carbohydrates could help increase the early insulin response in people with and without T2D [77, 78], possibly secondary to a direct effect of SCFA on the beta-cell [79].

Some soluble fibres such as guar gum possess two separate physicochemical properties which could theoretically be of benefit in T2D: their viscosity helps form a gel which slows glucose absorption via the gastrointestinal tract, and the intact fibres are fermentable in the colon. Despite the theoretical promise of such fibres, trials do not consistently show reductions in glucose concentrations in T2D, and again, any effect is small in magnitude [80, 81].

In summary, the effects of individual fibres on glucose concentration appears to be small, and large differences in intakes are probably required to achieve a clinically relevant reduction in glucose concentrations [82–86]. Since the physiological effects of these different fibres on glucose homeostasis are distinct, it is perhaps not surprising that combining them might achieve larger reductions in plasma glucose. For example, a low-glycaemic, legume-rich diet with approximately 60 g/day fibre can lower glucose by > 2 mmol/L even compared to a reduced-carbohydrate, high-monounsaturated-fat diet [87].

Non-Nutritive Compounds

Foods which are naturally high in dietary fibre also contain multiple compounds which themselves may help lower glycaemia. For example, bioactive proteins, polyphenolic compounds and other phytochemicals [88] found in fruits, vegetables and legumes have varying effects on glucose metabolism, including inhibiting carbohydrate digestive enzymes, although again the effect size of even concentrates of these compounds when tested in human trials is modest (< 1 mmol/L) [89, 90].

Fatty Acid Composition

Plant-based dietary patterns also tend to be higher in unsaturated fats, including linoleic acid and oleic acid. These fats, and the foods high in them, improve insulin sensitivity when they replace an isocaloric quantity of saturated fat, such as from butter [91–93]. Again, it is important to note that these improvements in insulin sensitivity do not necessarily translate into clinically significant reductions in glucose [94], and large differences in intakes of unsaturated versus saturated fat may be needed to observe a difference.

Plant-Based Dietary Patterns

To summarise, it is unlikely that any single element of a plant-based diet can lower glucose on its own to a magnitude which could influence the achievement of remission. However, here it is important to note that some of the proposed mechanisms of effect of the glycaemic index, soluble and fermentable fibres, polyphenolic compounds and unsaturated:saturated fat

ratio on glucose homeostasis are distinct. Thus, it might be reasonable to expect that the effects of these foods combined on any given outcome would be additive. If each approach lowers glucose by approximately 0.7 mmol/L, the overall effect of a diet high in plant-based foods independent of weight change could theoretically reach > 3 mmol/L.

WHY MECHANISTIC RESEARCH MATTERS

Understanding the mechanism of how diet affects glycaemia (and other risk factors) in T2D is important because if a number of dietary changes each influence insulin sensitivity, EGP or insulin secretion via separate mechanisms, their combined effect could then be additive. For example, if a plant-based diet was formulated to also be a high-protein diet, the complementary mechanisms (improved insulin sensitivity, reduced glucose absorption, low glycaemic load of the plant-based diet vs. insulinogenic effects of amino acids) of each of these two dietary approaches could lead to a greater reduction in glucose than each approach alone.

Similarly, understanding how nutrients affect the underlying pathophysiology of disease is important in designing dietary trials. If amino acids stimulate insulin secretion via the same molecular pathways as a sulfonylurea, those participants receiving this medication in a trial may get no benefit from a high-protein diet. Similarly, it is interesting to note that in two inpatient studies, the same low-carbohydrate, high-monounsaturated-fat dietary intervention lowered glucose in people with T2D on insulin [95], but had no effect in diet-controlled T2D [96]. These methodological nuances represent significant barriers in our current understanding of dietary management of T2D.

In addition, understanding the mechanism of effect of foods also enables a dietitian or healthcare practitioner to tailor physiologically effective dietary recommendations to an individual based on what foods they like and can access and afford. This empowers the dietitian to provide guidance beyond the typical advice to reduce portion size in order to reduce calorie intake. This could include simple swaps, such as replacing rice with lentils, or butter with rapeseed oil, or choosing a high-protein snack, such as a yoghurt with fruit, etc.

It might be remarked that changing the macronutrient content of the diet is as challenging as losing weight. However, one of the reasons long-term weight loss maintenance is difficult is because of physiological adaptations to a caloric restriction and weight loss [97, 98]. The same is not true of macronutrient changes. In trials, some people do revert to their normal dietary patterns [99], although not always [100], and within those averages are individuals who are able to maintain dietary changes long-term.

In addition, there have been advances in the development of tools which help maintain behaviour change, including the use of apps to provide people with more intensive support and data-driven algorithms to provide personalised guidance on simple dietary switches. These developments are in their infancy, but the use of these tools could support patients in making more pronounced changes in dietary intake compared to the traditional model of care. Examples of such innovations include the Food4Me study, which used data on dietary intake collected at baseline to generate personalised recommendations for specific dietary switches for each person to make [101], and the Virta programme, which uses biofeedback to encourage patients with T2D to stick to a ketogenic diet [102].

The development of functional foods which have a lower carbohydrate or higher protein and fibre content can also be utilised to help people modify their diets to one which can more effectively help manage their diabetes.

The challenge we have currently is that we do not have data of sufficient quality to provide guidance on precisely which changes might be physiologically effective for people who are able to make larger shifts in their dietary intake. To obtain these data, the nutrition science community needs to focus on trials with greater internal validity.

ADVANCING REMISSION OF T2D

Some people would argue that we know all we need to know about how to achieve remission of T2D: lose and maintain > 10 kg in body weight. The excellent DiRECT trial showed this can be achieved in primary care [2]. Nevertheless, people who have worked so hard to lose weight do, on average, tend to regain weight regardless of which dietary approach they use [103], even in situations where they receive long-term, high-intensity specialised support [6, 104].

Since the regain of weight is, on average, inevitable and is associated with T2D relapse [6, 105], modifying the diet in such a way as to lower glucose independent of weight change seems a pragmatic approach to try and help people maintain durable glycaemic control. Moreover, some of the physiological mechanisms underlying relapse are beginning to be understood [105], which will help us design dietary and lifestyle-based remission programmes aimed at mitigating these pathophysiological responses to weight regain.

Furthermore, remission becomes much less likely if only modest weight loss (< 10 kg) is achieved [6]. There is an urgent need to develop T2D remission interventions which do not depend on achieving and maintaining > 10 kg weight loss largely because most people find it very difficult to lose and maintain > 10 kg of weight. Only in the most intensive weight loss trials does mean weight loss reach approximately 10 kg, and > 25% of people either do not lose weight or will gain weight across weight loss trials [4, 7, 8]. In addition, it is worth noting that T2D prevalence is highest (15%) in people aged > 60 years [12, 13] and that 7% of people with a body mass index (BMI) < 27 kg/m^2 have T2D [13][13]. Many of these older individuals, particularly those with a lower BMI may not feel comfortable losing as much as 10 kg. Therefore, modifying the diet using some of the strategies described in the preceding sections could help augment the effect of more feasible weight loss on glycaemia and other CV disease risk factors. It is worth noting that aspects of the dietary patterns reviewed in this manuscript have also been shown to reduce blood pressure [106, 107], lower liver fat [10, 108] and lower blood lipids independent of weight change. This is important because, of course, lowering glucose while raising apolipoprotein B-containing cholesterol may increase the risk of heart failure in patients who who are already at high risk of CV disease.

CONCLUSION

As described in this narrative review, there is evidence that elements of diets can meaningfully influence blood glucose and T2D management independent of their effect on body weight. These changes could help more people achieve remission of their T2D, both as an adjunct to traditional weight loss programmes and even as stand-alone glucose-lowering approaches. Given the incidence of weight regain following weight loss interventions, leveraging the weight-neutral effects of diet on T2D is a pragmatic approach to mitigate the pathophysiological consequences of weight regain. A greater understanding of how diet influences blood glucose can help us devise personalised diets that exploit these mechanistic effect of nutrients while meeting the tastes, preferences and needs of the patient.

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