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2.5-MONTH EFFECTS OF A HIGH-INTENSITY LOW-CARBOHYDRATE INTERVENTION ON GLYCEMIC AND LIPID PROFILE: A TYPE-2 DIABETES NEAR-TO-REMISSION CASE STUDY OF A 65-YEAR-OLD INDIAN WOMAN WITH RECENT BILATERAL KNEE REPLACEMENT SURGERY.

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Abstract

This case study presents the effects of approximately 2.5 months of low-carbohydrate dietary intervention in a 65-year-old woman who had chronic type-2 diabetes for approximately 4 years and had recently undergone bilateral knee replacement surgery. The intervention's primary aim was to tackle the markers of insulin resistance and type-2 diabetes. Results have demonstrated noticeable improvements in numerous important health indicators. The glycated haemoglobin (HbA1c) levels have decreased from 7.10% to 6%. Body weight has reduced from 78 kg to 71.5 kg, and Body Mass Index (BMI) has reduced from 30.46 to 27.92 kg/m^2—these changes have occurred without employing calorie-deficit and exercises or increased physical activity, implying low-carbohydrate intervention's potential in reducing weight. The lipid profile has improved—the Triglycerides (TG) to High-Density Lipoprotein (HDL) ratio, a well-established predictor of cardiovascular disease, has reduced from 4.23 to 2.65. Collectively, the results indicate low-carbohydrate intervention's significance in managing and potentially reversing the markers of insulin resistance and type-2 diabetes.

Additionally, a positive change in eating behaviour and habits has been observed—likely because of age-friendly communication, involving family members in the consultations, encouraging positive dietary changes in the overall family members, providing various recipes, tailoring a personalised diet chart, providing guidelines to navigate through social and festive situations, and regularly repeated consultations. Although this is an approximately 2.5-month single-person case study and thus has its inherent limitations for generalisation, its results corroborate with the growing body of strong empirical evidence, suggesting the usefulness of low-carbohydrate intervention in type-2 diabetes and insulin resistance management. Furthermore, the results of this case study underline the importance of personalised dietary intervention and comprehensive support for adhering to it.

This case study adds to the current knowledge pertaining to dietary interventions by highlighting the conceivable benefits and evident relevance of a tailored low-carbohydrate dietary intervention in improving metabolic health markers and addressing insulin resistance in an older adult with chronic type-2 diabetes. In order to validate the results of this approximately 2.5-month single-person case study and to explore the broader benefits and applicability of low-carbohydrate interventions in older adults with chronic type-2 diabetes, further research with multiple participants (larger group) is needed with long-term intervention.

Keywords: Older adults, Geriatrics, Low-carbohydrate, Type-2 diabetes, Eating behaviour, Eating habits, Age-friendly communication, Diabetes remission, Weight loss, Lipid profile, Metabolic health.

1) Introduction

As Saklayen (2018) [40] reported, insulin resistance is one of the most common health disorders in the world. It concerns approximately fifty percent of all adults in countries located in North America (Menke, Casagrande, Geiss, & Cowie, 2015) [24], the Middle East (Abuyassin & Laher, 2016) [1], and Asia (Hu & Jia, 2018) [14]. Insulin resistance not only has a shockingly high prevalence, but it also raises the risk of a wide variety of non-communicable diseases, such as, but not limited to, cancer (Kasper & Giovannucci, 2006) [17], cardiovascular diseases (Wang et al., 2018) [47], and dementia (De La Monte & Wands, 2008) [8]. Therefore, considering this severe global public health challenge, it becomes clear how urgent it is to cease the worldwide rise in insulin resistance and uncover techniques that may turn the trend around.

A wide variety of pharmacological therapies are often employed in order to improve insulin sensitivity. This is primarily due to the rising prevalence of insulin resistance as well as a variety of pathophysiologies that are associated—and arrives—with it. Several of these pharmacological treatments focus on decreasing the amount of glucose absorbed by the intestinal tract (via the usage of alpha-glucosidase inhibitors, for example) or increasing the amount of glucose excreted by the kidneys (for example, Sodium-Glucose Cotransporter-2 [SGLT2] inhibitors). Side effects such as osmotic diarrhoea (Playford, Pither, Gao, & Middleton, 2013) [37] and urinary tract infections (Johnsson et al., 2013) [16] limit the enthusiasm and across-the-board adoption of these treatments, despite the varying effectiveness of these treatments in lowering blood glucose and insulin levels and increasing insulin sensitivity (reducing insulin resistance). Contrary to the use of pharmaceuticals in an effort to slow down glucose absorption or speed up glucose excretion, a more logical approach would be to cut down on the amount of (dietary) glucose consumed.

Regarding lowering insulin resistance, as Knowler et al. (2002) [20] explained, lifestyle therapy may be a well-established alternative—or can provide additional support—to current pharmacological treatments. In light of the metabolic effects and response of a dietary carbohydrate intake (which raises blood glucose and insulin levels), an efficient dietary approach may place a greater emphasis on dietary proteins and fats (Nuttall & Gannon, 1991) [32]. Dietary proteins and fats have a negligible influence, if any influence at all, on blood glucose and insulin levels (Nuttall & Gannon, 1991) [32].

The purpose of publishing this case study is to report the improvement in the markers of insulin resistance and type-2 diabetes in a 65-year-old woman subject after following approximately 2.5 months of a low-carbohydrate dietary intervention. At the starting point of the intervention, the subject was chronically type-2 diabetic (for approximately 4 years) and had then-recently (1 month earlier) undergone bilateral knee replacement surgery.

2) Material and methods

2.1) Subject

The subject (65-year-old woman) self-approached (via her 30-year-old son) Public Health India on 24th of March 2022 for a dietary consultation in order to address 2 primary issues: first, chronic (for

approximately 4 years) type-2 diabetes with elevated levels of glycated haemoglobin (HbA1c); second, overweight, which was, in effect, putting significant pressure on subject's newly operated knees, and was making the subject difficult to walk, move, or to perform any activity involving knee joints.

On 26th of March 2022, employing age-friendly communication (National Institute on Aging [NIA], 2023) [30], the subject received an online pre-consultation (half hour), familiarising her with the nature of the dietary and lifestyle changes she might go through. After the subject's positive response to the pre-consultation, and after receiving the relevant reports, i.e., body weight, Body Mass Index (BMI), HbA1c, blood glucose levels (mean and 1.5-hours postprandial), blood lipid profile, and abdominal sonography (all executed and evaluated by qualified pathologist and radiologist), a detailed assessment and comprehension of the subject's health and pathology status was accomplished by an experienced certified nutritionist. Also, the subject's health goals were appropriately understood, which were—preference-wise—addressing type-2 diabetes and reducing body weight and BMI.

In light of the aforementioned careful assessments and comprehension of the subject's health status and a thorough grasp of the subject's health goals, the same nutritionist developed a low-carbohydrate dietary intervention (timeline: 27th-29th of March 2022). Then on 29th of March 2022, the nutritionist delivered 4-5 hours of a face-to-face major-consultation to the subject (involving the subject's family), explaining the designed intervention and its rationale interactively. In this detailed consultation, along with the nutritional and lifestyle changes, robust scientific evidence, theories, practical examples, and explanations were discussed interactively. The subject was encouraged to ask questions about the low-carbohydrate dietary intervention and its science and practice, and the nutritionist addressed them. Once the subject was fully informed and satisfied with the intervention (and its rationale, design, and feasibility), the intervention was implemented on 30th of March 2022 with the informed consent.

2.2) Baseline data

During the implementation of the intervention, the subject's reports were as shown in figure 1.

Baseline data of the subject

Weight	78 kg
BMI	30.46 kg/m^2
HbA1c	7.10%
Fatty Liver status	Grade 1
Low-Density Lipoprotein (LDL)	112 mg/dl
High-Density Lipoprotein (HDL)	43 mg/dl
TG:HDL ratio	4.23

Figure 1*: Baseline data. Presented in Pathare and Chaudhary (2024).*

2.3) Intervention

After delivering the previously mentioned (see section *subject*) pre-consultation (half-hour [online]), major-consultation (4-5 hours [face-to-face]), and theoretical and practical (application-based) knowledge of the low-carbohydrate dietary intervention (collectively via pre and major consultations), the subject received a low-carbohydrate (and rich in naturally occurring proteins and healthy fats) diet plan designed by a certified nutritionist. Consistently, age-friendly communication

was employed in all interactions. As suggested by NIA (2023) [30], this consists of using a respectful tone, making the subject comfortable, avoiding hurrying and jargons, face-to-face positioning, and providing prints for more essential takeaways. Moreover, in order to improve fidelity to the intervention, the meal plan was designed by considering the ageing-related physiological, psychological, social, and cultural aspects (Appleton, 2016; Appleton, 2023; Best & Appleton, 2013; Wylie, Copeman, & Kirk, 1999; Yannakoulia et al., 2018; Zhou et al., 2018) [4, 5, 6, 49, 52, 53].

Furthermore, to aid the adherence to the intervention, the subject received meticulous and consistent guidance, support and assistance from a certified nutritionist and a qualified public health professional throughout the tenure of the intervention (approximately 2.5 months [30th of March 2022 to 11th of June 2022]). The endeavours mentioned above include 2 follow-up meetings per week (online and telephonic) by a certified nutritionist; and 1 major mid-tenure face-to-face consultation (4th of May 2022| 3-4 hours long | involving the subject's family) by a qualified public health professional to address the intervention-related and general health-related broader queries that the subject and her family harboured.

Along with the previously mentioned meal plan, weekly follow-up meetings and mid-tenure major-consultation, the subject also periodically received educational materials. All these supporting and comprehensive efforts (discussed so far) were undertaken to edify and concentrate on the reasoning and execution of a central intervention (see the subsequent text), and to provide the subject with an explanation of how adherence to a low-carbohydrate diet helps maintain low insulin levels and, in effect, can help reduce insulin resistance. The central intervention, i.e., a low-carbohydrate diet, more specifically, was as follows: the dietary intake (in terms of calorie percentage) of carbohydrates, proteins, and fats (naturally occurring) should be approximately 5%, 20-25%, and 70-75%, respectively (as opposed to the subject's usual macronutrient composition—calculated through self-reported dietary pattern—which was as follows: carbohydrates: 60%; proteins: 10%; and fats: 30% [mostly unsaturated]). An essential part and ground rule of the dietary intervention was limiting carbohydrate consumption to no more than 30 g per day; moreover, even within this limit, the subject was guided and encouraged to prefer non-starchy vegetables.

Free consumption (as per hunger and appetite) of naturally occurring proteins and fats through real food was encouraged—this included mainly dairy and poultry. Furthermore, nuts such as almonds, walnuts, and cashews were to be consumed as snacks. Homemade low-carbohydrate high-fat shakes using reliable whey protein powder were also allowed. However, these shakes were encouraged to consume only on rare occasions, in case of, for example, the subject's time constraints. Caloric restriction was strictly not adopted due to its number of well agreed serious side effects, such as—but not limited to—fatigue, muscle loss, low metabolism, hair fall, semi-starvation neurosis, and character neurosis (Taubes, 2020) [45].

At the starting point of the intervention, the subject had then-recently (1 month earlier) undergone bilateral knee replacement surgery (see *introduction* section). Therefore, the physical activities/exercises involved in the subject's routine were almost absent. The only exception to this was the physical exertion involved in daily household routine, and that too was much less due to the bilateral knee replacement surgery. Therefore, the intervention did not involve mandatory physical activity but was kept to the subject's choice, comfort, and threshold. Accordingly, physical exercise was not a part of the central or peripheral intervention.

2.4) Outcomes

Key variables included body weight, BMI, HbA1c, mean blood glucose, 1.5-hours postprandial blood glucose, and Triglycerides (TG) to High-Density Lipoprotein (HDL) ratio. The TG to HDL ratio was measured twice, i.e., in the beginning and after approximately 2.5 months of the intervention. The remaining investigations mentioned above were done thrice, i.e., in the beginning, after approximately 1 month, and after approximately 2.5 months of the intervention. A trained pathologist conducted all evaluations.

3) Results

3.1) Body weight and BMI

At the beginning of the intervention (30th of March 2022), the subject's body weight and BMI were 78 kg and 30.46 kg/m^2, respectively. Within the intervention's first month, as re-measured on 26th of April 2022, the body weight and BMI dropped to 75.5 kg and 29.48 kg/m^2, respectively. Furthermore, within the intervention's approximately 2.5 months, as measured on 11th of June 2022, the subject's body weight and BMI dropped to 71.5 kg and 27.92 kg/m^2, respectively. Therefore, this suggests a significant reduction in the subject's body weight and BMI over approximately 2.5 months of intervention.

3.2) Glycated haemoglobin (HbA1c)

As HbA1c levels are one of the most relevant indicators of long-term glycemic control, they indicate the severity of type-2 diabetes. When blood glucose levels remain raised for an extended period, glucose may bind to haemoglobin proteins in the bloodstream in a manner that does not need enzymes. The widely accepted range for HbA1c in diabetes has been 6.5% or above (with 5.7% to 6.4% being prediabetic). Consequently, a primary objective of the strategies used to address type-2 diabetes is to get the elevated HbA1c values—lower than or—as close to the threshold (6.5%) as possible.

The subject was diagnosed with type-2 diabetes for approximately 4 years. The HbA1c levels were on progressive increment despite the prescribed long-term pharmacological treatment—metformin 500 mg. At the beginning of (or just before) the intervention, as measured on 24th of March 2022, the HbA1c level of the subject was 7.10%. Interestingly, after approximately 1 month of the intervention, as measured on 26th of April 2022, the HbA1c levels dropped to 6.4%. Furthermore, within approximately 2.5 months of the intervention, as measured on 11th of June 2022, the HbA1c levels dropped to 6%. Therefore, within approximately 2.5 months of the intervention, the HbA1c dropped from diabetic to prediabetic range. These results are presented in figure 2.

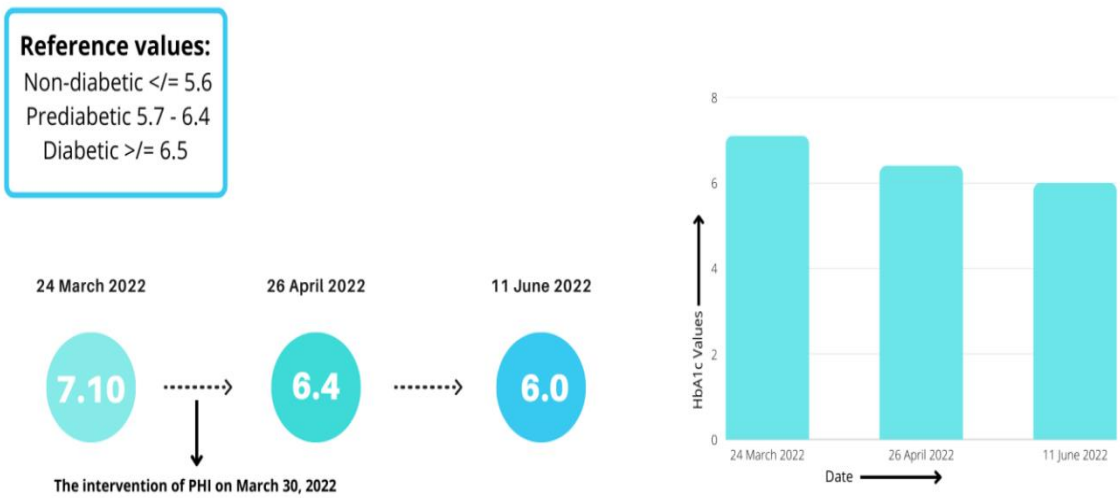


Figure 2: *Reduction in HbA1c within approximately 2.5 months of low-carbohydrate intervention (65-year-old woman). Presented in Pathare and Chaudhary (2024).*

A growing body of robust evidence demonstrates that a low-carbohydrate diet—by improving insulin sensitivity, regulating blood glucose levels, and promoting fat loss—can reduce the need for medication, leading to a healthier, natural, and medication-free lifestyle (Yancy, Foy, Chalecki, Vernon, & Westman, 2005) [51]. Therefore, diabetes medications, while on low-carbohydrate diets, need to be adjusted carefully. Metformin, however, is considered safe to continue on a low-carbohydrate approach (Cucuzzella, Riley, & Isaacs, 2021) [7], as there is no hypoglycemia associated with metformin. Another benefit of continuing metformin on a low-carbohydrate approach may be that it helps address insulin resistance and also provides cardiovascular benefits (Kelly, Unwin, & Finucane, 2020) [18], corroborating and optimising the effects of low-carbohydrate diets.

Nevertheless, metformin can be gradually and carefully eliminated in some cases, especially when the subject's diabetes is in remission (Diabetes UK, n.d.) [9]. Since this case study's subject's diabetes was observed to be progressing towards remission, the subject—gradually and carefully—exhibited discontinuation of metformin. Another vital rationale behind discontinuing metformin was that the subject reported experiencing discomfort after administering metformin and was willing to manage diabetes through dietary and lifestyle changes. It is important to note that metformin can sometimes demonstrate serious side effects in some cases (Nasri & Rafieian-Kopaei, 2014) [29], and appropriate lifestyle changes can help reduce and eliminate the metformin doses (Fallabel, 2023) [12].

Most importantly, to continue metformin-free (or, in general, medicine-free) diabetes management, it is crucial to sustain the lifestyle and dietary changes that have been employed. Therefore, the subject of this case study has received careful counselling, encouraging strict adherence to lifestyle and dietary interventions. The subject has also been advised to contact the healthcare provider in case of any lifestyle or dietary changes so that, if necessary, the medicine doses can be reintroduced and carefully regulated.

3.3) Mean blood glucose levels

The reference value for the mean blood glucose level is 70 mg/dL to 100 mg/dL. At the beginning of (or just before) the intervention, as measured on 24th of March 2022, the mean blood glucose level of the subject was 157.07 mg/dL. Interestingly, after approximately 1 month of the intervention, as measured on 26th of April 2022, the level dropped to 136 mg/dL. Furthermore, within approximately 2.5 months of the intervention, as measured on 11th of June 2022, the mean blood glucose level dropped to 125 mg/dL. Therefore, within approximately 2.5 months of the intervention, the mean blood glucose dropped from 157.07 to 125 mg/dL. These results are presented in figure 3.

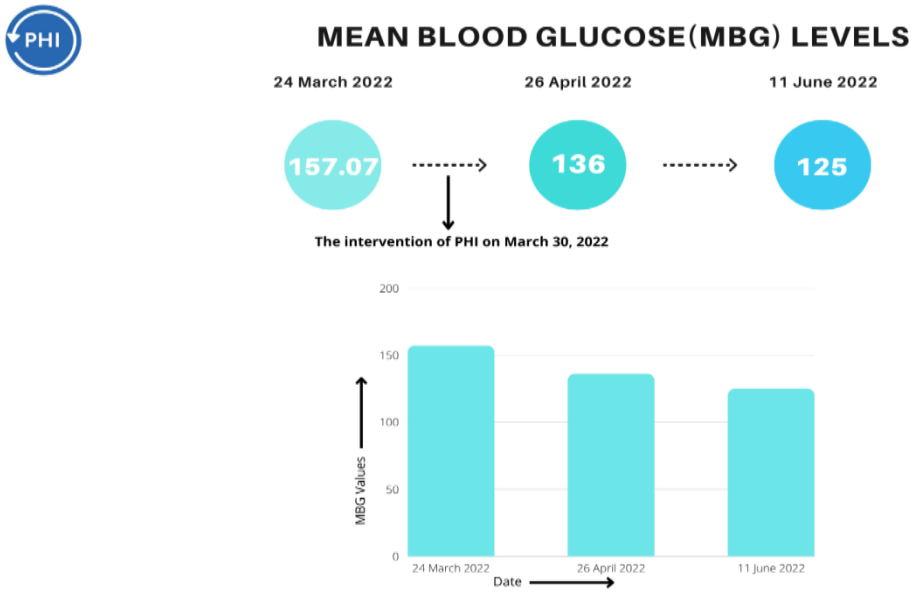


Figure 3: *Reduction in mean blood glucose levels within approximately 2.5 months of low-carbohydrate intervention (65-year-old woman). Unit: mg/dL. Presented in Pathare and Chaudhary (2024).*

3.4) 1.5-hours postprandial blood glucose levels

At the beginning of (or just before) the intervention, as measured on 24th of March 2022, 1.5-hours postprandial blood glucose level of the subject was 145 mg/dL. Interestingly, after approximately 1 month of the intervention, as measured on 26th of April 2022, the level dropped to 133 mg/dL. Furthermore, within approximately 2.5 months of the intervention, as measured on 11th of June 2022, it dropped to 128 mg/dL. Therefore, within approximately 2.5 months of the intervention, 1.5-hours postprandial blood glucose levels dropped from above-normal to normal range. These results are presented in figure 4.

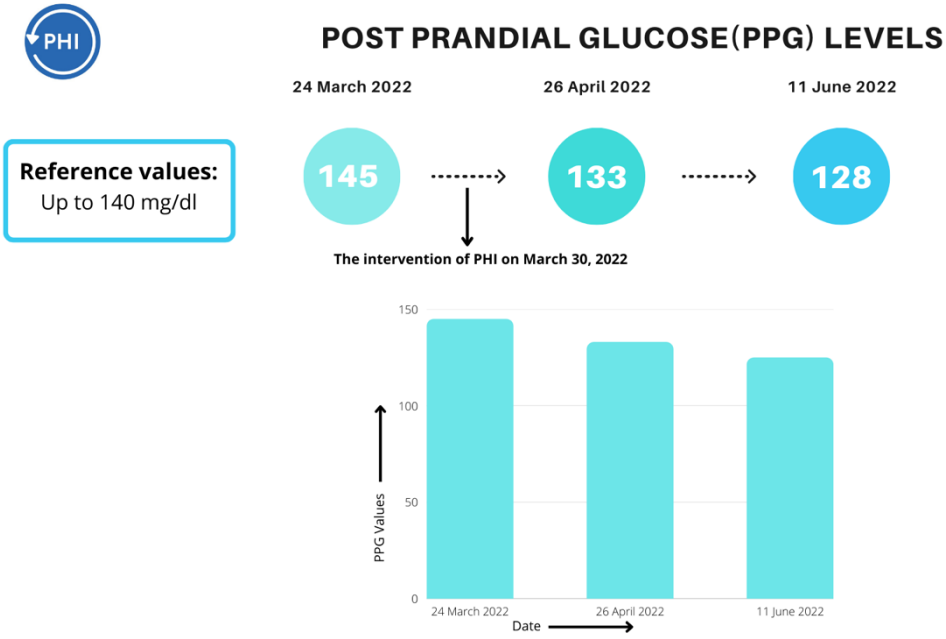


Figure 4: *Reduction in 1.5-hours postprandial glucose levels within approximately 2.5 months of low-carbohydrate intervention (65-year-old woman). Presented in Pathare and Chaudhary (2024).*

3.5) Blood lipids

Blood tests are the standard method for determining levels of lipids like Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL), Very Low-Density Lipoprotein (VLDL) and Triglycerides (TG), which are all important types of blood lipids. As per the conventional view, each of these above-mentioned lipids has been regarded to influence the risk of cardiovascular diseases to differing degrees. Notably, the connection between blood lipids and the glycemic profile seems reasonably comprehensible because, as Reaven (1999) [38] highlighted, cardiovascular diseases commonly prevail in people with type-2 diabetes. Interestingly, the intervention's effect on the subject's blood lipids was meaningful, just as with the HbA1c levels.

At the beginning of (or just before) the intervention, as measured on 24th of March 2022, the subject's lipid profile was as follows: Low-Density Lipoprotein (LDL) level was 112 mg/dL and High-Density Lipoprotein (HDL) level was 43 mg/dL; the Triglycerides (TG) level was 182 mg/dL; consequently, the TG to HDL ratio was 4.23. After approximately 2.5 months of the intervention, as measured on 11th of June 2022, the lipid profile observed was as follows: Low-Density Lipoprotein (LDL) level was 138 mg/dL, and High-Density Lipoprotein (HDL) level was 49 mg/dL; the Triglycerides (TG) level was 130 mg/dL; consequently, the TG to HDL ratio was 2.65.

These post-2.5-month-intervention lipid readings suggest an interesting pattern as follows: although the Low-Density Lipoprotein (LDL) and (slightly) the High-Density Lipoprotein (HDL) levels have increased, the Triglycerides (TG) levels have shown a noticeable decrement. These alterations, in effect, have substantially reduced the TG to HDL ratio. Importantly, in their seminal study, Luz, Favarato, Faria-Neto Junior, Lemos, and Chagas (2008) [22] found that the TG to HDL ratio is a more accurate predictor of cardiovascular disease than the Low-Density Lipoprotein (LDL) levels. Luz et al. (2008) [22], moreover, found that the elevation in the TG to HDL ratio was the single most powerful predictor of extensive coronary heart disease among all the lipid variables examined.

4) Discussion

The purpose of presenting and publishing this case study is to report the improvement in the markers of insulin resistance and type-2 diabetes in a 65-year-old woman subject after following a short-term (approximately 2.5 months) low-carbohydrate dietary intervention. At the starting point of the intervention, the subject was chronically type-2 diabetic (for approximately 4 years) and had then-recently (1 month earlier) undergone knee replacement surgery on both knees. Most significantly, we found that a low-carbohydrate high-fat diet in which carbohydrates constituted around just 10% of calories, generated a noteworthy decline in HbA1c, i.e., from 7.10% to 6%, turning from the diabetic to the prediabetic—but near-normal—range, and this drop occurred in approximately only 2.5 months. In addition, the low-carbohydrate high-fat dietary intervention led to a substantial improvement in different cardiometabolic markers, including mean and 1.5-hours postprandial blood glucose levels, body weight, BMI, and, most importantly, the TG to HDL ratio.

The type of research we have documented in this manuscript is a "case study". Therefore, this section (discussion) is drafted by keeping some of the most characteristic limitations of the case study in mind, i.e., lack of generalisability, single-subject (no opportunity for bigger sample size or randomisation), and risk of overinterpretation. One of the potential limitations of our case study is that it is based only on a single subject; nevertheless, this limitation can be alleviated when evidence from more prolonged and more extensive research studies (indicating that restricting carbohydrates causes likely similar outcomes to that we have presented in this manuscript) is considered. The results of our case study accord with the results of the recent clinical case series by Walton, Perry, Hart, Berry, and Bikman (2019) [46]. Walton et al. (2019) [46] reported significant improvements in eleven 18-45 aged women—with recently diagnosed type-2 diabetes—after 90 days of low-carbohydrate

ketogenic dietary intervention. All participants with an average HbA1c level of 8.9% and a BMI of 36.3 kg/m^2 consented to engage in an intensive dietary intervention limiting carbohydrate intake to less than 30 g per day for 90 days. Participants dropped a large amount of body weight, from 85.7 ± 3.2 kg to 76.7 ± 2.8 kg, and HbA1c descended to 5.6%. Triglycerides (TG) levels decreased dramatically from 177.0 ± 19.8 to 92.1 ± 8.7 mg/dL, and the TG to HDL ratio also decreased significantly from 4.7 ± 0.8 to 1.9 ± 0.2; this shows an overall improvement in blood lipids. In an open-label, non-randomised, controlled study by Hallberg et al. (2018) [13], it was observed that (over 1 year of carbohydrate-restricted intervention) participants' HbA1c, body weight, Triglycerides (TG), and other lipids dropped considerably, depicting a noticeable improvement in overall metabolic health. Furthermore, the type-2 diabetes medication prescription, except metformin, declined from 56.9 ± 3.1% to 29.7 ± 3.0%, and insulin therapy was reduced or eliminated in 94% of users. This study, however, was not randomised. Westman, Yancy, Mavropoulos, Marquart, and McDuffie (2008) [48] showed similar results in their randomised trial. Over just 24 weeks, the low-carbohydrate, ketogenic diet group (<20 g of carbohydrate daily) showed a considerably more significant decrease in HbA1c (-1.5% vs. -0.5%) and body weight (-11.1 kg vs. -6.9 kg) than the group consuming high-carbohydrate (55% of daily caloric intake), low glycemic index, reduced-calorie diet. Additionally, diabetes medications were reduced or eliminated in 95.2% of the low-carbohydrate, ketogenic diet participants (as opposed to only 62% in the higher carbohydrate consumption participants).

In a crucial sense, what these so far discussed past research (Hallberg et al., 2018; Walton et al., 2019; Westman et al., 2008) [13, 46, 48] and our current case study have in common is the degree of attention provided to the participants/subjects involved, regardless of the mode—online or in-person—of the interaction. This careful and sustained attention may be necessary for the positive results that other researchers and we have reported; this may be because, as observed by Iqbal et al. (2010) [15], a low-carbohydrate intervention with little instructions (i.e., low-intensity intervention) seems to have no effect on HbA1c when compared to a low-fat group with the same number of instructions (although the low-carbohydrate group lost a lot more weight [1.5 kg] than the low-fat group [0.2 kg]). However, carbohydrate restriction as a therapy for diabetes is now adequately acknowledged and validated. For example, the American Diabetes Association [ADA, 2019] [3], in its recently issued *Standards of Medical Care in Diabetes*, has stated the following: "...research indicates that low-carbohydrate eating plans may result in improved glycemia and have the potential to reduce antihyperglycemic medications for individuals with type-2 diabetes".

Although we have been looking at insulin resistance, the fact that this case study did not measure plasma insulin levels prevents us from coming to any definitive conclusions on insulin resistance. Therefore, in future research, our research team will try addressing this shortcoming so that the outcomes of low-carbohydrate high-fat intervention on insulin sensitivity could be investigated in more profundity. However, it is imperative to note that the TG to HDL ratio is considered a surrogate for insulin resistance (Kim-Dorner, Deuster, Zeno, Remaley, & Poth, 2009; Salazar et al., 2017) [19, 41], and this ratio has been significantly reduced (from 4.23 to 2.65) in the subject of our case study; this, therefore, suggests an insulin sensitising effect.

Numerous traditional clinical therapies aim to reduce glucose and HbA1c levels by raising insulin via insulin therapy or insulin secretagogues (for example, sulfonylureas) because of the well-accepted/established significance of HbA1c in diabetes-associated disease outcomes, such as (notably) cardiovascular disease (Selvin, Wattanakit, Steffes, Coresh, & Sharrett, 2006) [42], nephropathy (Liu et al., 2013) [21], and neuropathy (Xu et al., 2014) [50]. However, hyperinsulinemia is already a common condition associated with type-2 diabetes, in which the blood insulin amounts are higher than the average. Therefore, in such circumstances, although the intention is to address HbA1c levels and achieve glycemic control, intensive attempts to decrease glucose and HbA1c by

artificially increasing insulin above the existing (type-2 diabetes-associated) hyperinsulinemia result in increased mortality (Action to Control Cardiovascular Risk in Diabetes Study Group [ACCRDSG, 2008]) [2]. Additionally, pharmacological interventions for raising insulin levels may have potential side effects such as increased blood pressure (Roumie et al., 2012) [39] and weight gain (Ness-Abramof & Apovian, 2005) [31]. On the other hand, a low-carbohydrate diet can reduce HbA1c levels without aggravating hyperinsulinemia; therefore, this is a crucial component of a low-carbohydrate dietary intervention as a feasible method to control glycemia. Therefore, carbohydrate restriction (via a high-intensity low-carbohydrate dietary intervention) makes reasonable sense and works effectively for achieving the objectives of diabetes management.

4.1) Eating behaviour and habits

Changing eating behaviour and habits, especially in older adults, is considered a challenging task (Yannakoulia et al., 2018) [52], and the specific guidelines related to this age group to communicate or encourage a change in eating behaviour or habits is limited in India. This case study, interestingly, has made some meaningful observations related to eating behaviour and how to communicate or encourage positive changes in eating behaviour. The subject of this case study successfully made positive changes in eating behaviour and habits.

The dietary intervention implemented in this case study was significantly different than the regular dietary patterns and habits of the subject. The usual pattern of macronutrient composition in the subject's food had been high in carbohydrates and poor in proteins and healthy fats. On the other hand, the intervention was low in carbohydrates and rich in proteins and healthy fats. Notably, despite this significant variation in the macronutrient compositions of the meals, the eating behaviour and habits of the subject were observed to be successfully changed. There could be several factors/reasons that facilitated these positive changes: involving family members in consultations, encouraging positive dietary changes in the overall family members (for example, the husband and the son of the subject), providing intervention-specific recipes, tailoring a personalised diet chart (flexible according to various situations and occasions such as social functions and festivals), and providing regular/repeated consultations, followed by regular follow-up calls.

This suggests that making or encouraging positive changes in the eating behaviour and habits of older adults needs a multifaceted approach involving family members and providing comprehensive guidance, including how to deal with different social and festive situations.

4.2) Weight loss achieved independent of calorie-deficit and exercises: Effect explained

According to conventional wisdom, a long-standing advice for decreasing body weight and BMI is to reduce the overall calorie intake (also known as the calorie-deficit approach) combined with increased physical activity or exercise. However, the intervention in this case study comprised neither calorie-deficit nor exercises nor increased physical activity. The rationale behind not recommending caloric-deficit is due to its adverse—physical, psychological, and behavioural—effects, as explained by Taubes (2020) [45]. The reason why exercises or increased physical activity were not recommended or encouraged (apart from some preliminary exceptions such as physical movements involved in daily life routine) is the practical limitations due to the then-recent knee replacement surgery performed on both knees of the subject.

Nevertheless, the subject's body weight and BMI demonstrated a reasonable decrement within approximately 2.5 months of low-carbohydrate dietary intervention. Simultaneously, the subject conveyed improved energy levels. Moreover, the subject also received numerous metabolic health benefits, as thoroughly discussed in this case study. This effect (losing weight without caloric control and exercises or increased physical activity) observed in this case study corroborates with the growing body of evidence in the existing low-carbohydrate-related literature, such as Malhotra, Noakes, and Phinney (2015) [23], Pathare (2021) [33], and Ebbeling et al. (2012, 2018) [11, 10].

This weight loss effect is likely due to the stabilisation effect of low-carbohydrate diets on blood glucose and associated insulin levels. Before the intervention, the dietary pattern of the subject was dominant in carbohydrates. High-carbohydrate diets increase blood glucose and insulin levels, which, in the long-term, promote body fat storage, reduce body fat breakdown, promote visceral fat accumulation (including liver), and increase cravings and hunger—these effects, as explained by Taubes (2007, 2011, 2020) [43, 44, 45], can be reversed on the low-carbohydrate approach, as it stabilises the elevated blood glucose and associated insulin levels. This, most likely, is the reason why the subject's weight and BMI switched towards the healthy range without indulging in calorie-deficit and exercises or increased physical activity.

Interestingly, the subject reported that because of the reduction in body weight (and the associated improved energy levels), mobility and physical activities became convenient—this, in effect, increased the subject's propensity towards a physically active lifestyle.

4.3) A note on Non-Alcoholic Fatty Liver Disease (NAFLD)

In the pre-intervention investigations, the subject was diagnosed with grade-1 NAFLD. There is a plethora of evidence, as documented by Pathare and Chaudhary (2022) [35], which suggests that low-carbohydrate dietary interventions have noticeable positive health effects on the liver, improving the liver functions of individuals with NAFLD. One of the limitations of this case study is that the length of the intervention was likely too short to remark on the improvements in light of the subject's fatty liver condition. This, therefore, keeps us from making any comment on the subject's NAFLD. Therefore, in future research, our research team will try to address this limitation by conducting long-term interventions.

5) Conclusion

In conclusion, this case study highlights the noticeable improvements in the markers of insulin resistance and type-2 diabetes in a 65-year-old woman after approximately 2.5 months of a low-carbohydrate dietary intervention. The subject of this case study, who was suffering from type-2 diabetes for approximately 4 years and had recently undergone bilateral knee replacement surgery, has experienced remarkable improvements in the essential health indicators.

Over the intervention period, the glycated haemoglobin (HbA1c) levels have dropped from 7.10% to 6%, turning from the diabetic to the prediabetic—but near-normal—range. This reduction in HbA1c indicates the significance of a personalised low-carbohydrate dietary approach in type-2 diabetes management and remission. Moreover, the body weight and Body Mass Index (BMI) have shown a noticeable decrement without indulging into calorie-deficit and exercises or increased physical activity. Body weight has dropped from 78 kg to 71.5 kg, and the BMI has dropped from 30.46 to 27.92 kg/m^2. This reduction—independent of calorie-restriction and exercise—implies the potential of low-carbohydrate intervention in reducing body weight and improving metabolic health.

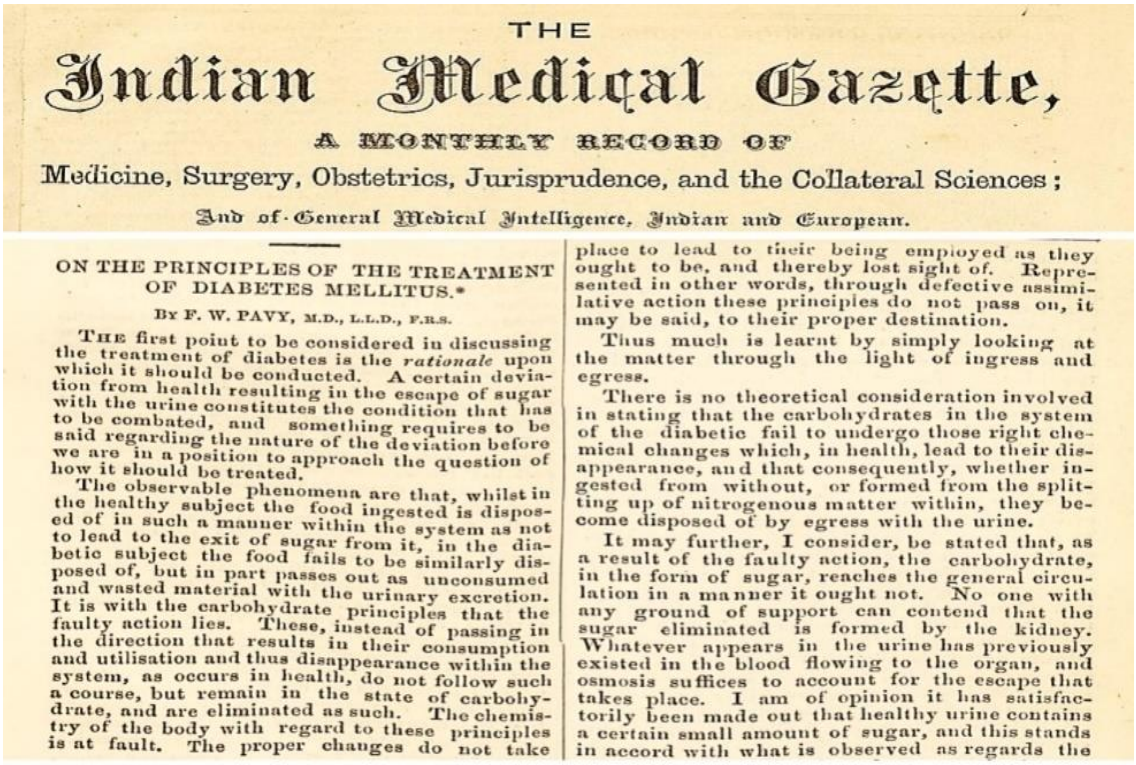
Moreover, as the Triglycerides (TG) to High-Density Lipoprotein (HDL) ratio, a well-established predictor of cardiovascular disease, has reduced from 4.23 to 2.65, the cardiovascular health of the subject has been observed to be improved. This suggests the potential of low-carbohydrate intervention in improving cardiovascular health. Furthermore, eating behaviour and habits have been observed to be positively changed, which is likely because of age-friendly communication, involving family members in the consultations, providing various recipes, tailoring a personalised diet chart, encouraging positive dietary changes in the overall family members, providing guidelines to navigate through social and festive situations, regularly repeated consultations, and consistent follow-ups.

This case study provides important insights into applying the low-carbohydrate approach in addressing insulin resistance and type-2 diabetes. However, due to the small sample size (only 1 subject/participant), short-term intervention (approximately 2.5 months), and the lack of measuring plasma insulin levels, the generalisability of the results is subject to limitations. Interestingly, the results of this case study accord with the growing body of strong empirical evidence, suggesting the

significance of low-carbohydrate intervention in managing type-2 diabetes and insulin resistance. Moreover, well-designed studies (in light of older adults) with a larger group, long-term intervention (at least six months), and plasma insulin measurements can be reasonable topics for future research.

6) Statement of purpose and uniqueness

While searching for India-specific historical accounts of the low-carbohydrate approach in light of diabetes in the mainstream medical literature, the historical traces of the low-carbohydrate approach's effectiveness in addressing diabetes can be found in the 19th century. Referring to the Indians in Bengal and Madras, Dr TG McGann—a surgeon major from Mysore in 1885—raised the question of whether diabetes was common among the "rice-eating natives" of India (Mohan et al., 2021) [28]. In 1890, Frederick William Pavy, a British physiologist, published an article titled "On the principles of the treatment of diabetes mellitus" in the "Indian Medical Gazette" (see Pavy [1890] [36]). Pavy made studying "carbohydrate metabolism and diabetes" his principal work in his era; however, today, Pavy is a largely forgotten pioneer in the Indian, and perhaps global, low-carbohydrate community.



THE

Indian Medical Gazette,

A MONTHLY RECORD OF

Medicine, Surgery, Obstetrics, Jurisprudence, and the Collateral Sciences;

And of General Medical Intelligence, Indian and European.

ON THE PRINCIPLES OF THE TREATMENT OF DIABETES MELLITUS.*

By F. W. PAVY, M.D., L.L.D., F.R.S.

THE first point to be considered in discussing the treatment of diabetes is the *rationale* upon which it should be conducted. A certain deviation from health resulting in the escape of sugar with the urine constitutes the condition that has to be combated, and something requires to be said regarding the nature of the deviation before we are in a position to approach the question of how it should be treated.

The observable phenomena are that, whilst in the healthy subject the food ingested is disposed of in such a manner within the system as not to lead to the exit of sugar from it, in the diabetic subject the food fails to be similarly disposed of, but in part passes out as unconsumed and wasted material with the urinary excretion. It is with the carbohydrate principles that the faulty action lies. These, instead of passing in the direction that results in their consumption and utilisation and thus disappearance within the system, as occurs in health, do not follow such a course, but remain in the state of carbohydrate, and are eliminated as such. The chemistry of the body with regard to these principles is at fault. The proper changes do not take place to lead to their being employed as they ought to be, and thereby lost sight of. Represented in other words, through defective assimilative action these principles do not pass on, it may be said, to their proper destination.

Thus much is learnt by simply looking at the matter through the light of ingress and egress.

There is no theoretical consideration involved in stating that the carbohydrates in the system of the diabetic fail to undergo those right chemical changes which, in health, lead to their disappearance, and that consequently, whether ingested from without, or formed from the splitting up of nitrogenous matter within, they become disposed of by egress with the urine.

It may further, I consider, be stated that, as a result of the faulty action, the carbohydrate, in the form of sugar, reaches the general circulation in a manner it ought not. No one with any ground of support can contend that the sugar eliminated is formed by the kidney. Whatever appears in the urine has previously existed in the blood flowing to the organ, and osmosis suffices to account for the escape that takes place. I am of opinion it has satisfactorily been made out that healthy urine contains a certain small amount of sugar, and this stands in accord with what is observed as regards the

Figure 5: *Pavy's historical article on treating diabetes with carbohydrate elimination (Pavy, 1890) [36]. Presented in Pathare and Chaudhary (2024).*

Pavy's historical article (see figure 5), explaining the mechanism of carbohydrate action, clarifies how to treat diabetes by eliminating dietary carbohydrates. He explicitly suggests that removing carbohydrates from the diet will not only ensure the downward progression of the condition but also bring the patient's health and strength back. During the pre-independence era, the "Indian Medical Gazette" was perhaps the most preferred mainstream journal through which medical practitioners and researchers used to communicate essential contemporary medical practices. This article by Pavy is perhaps one of the first India-specific mainstream medical records to support removing dietary carbohydrates to address the root cause of diabetes and to regain health and strength. Therefore, Pavy's article is a unique read for current health practitioners and researchers dealing with diabetes and metabolic health.

While we have discussed one of the most historical mainstream records on the low-carbohydrate dietary approach, it becomes essential to note the recent landmark event in the same context. Recently, on 27-29 September 2023, a conference was held named "Metabolic Health Conference: India's first mega virtual low-carb conference". This conference was lead-organised by Shashikant Iyengar and Anup Singh and was lead-hosted by Ira Sahay. Because of this conference, for the first time in the history of the Indian low-carbohydrate movement, around 47 leading speaking-participants—doctors, health professionals, and organisations—gathered from around 15 countries to discuss the low-carbohydrate approach in the Indian medical and public health context.

Therefore, Metabolic Health Conference 2023 is a unique resource for not only health professionals but also health authorities, providing them with critical insights into a conventionally and culturally less accepted dietary approach. The archives of this conference are available on YouTube (for links, see Metabolic Health India [2022a, 2022b, 2022c] [25, 26, 27]).

Now, we will explain our purpose behind publishing this article (a case study). Between the before-mentioned period, i.e., from Pavy (1890) [36] to the Metabolic Health Conference 2023, there must be a plethora of studies—or scholarly articles—published in the mainstream medical and public health journals on the topic of low-carbohydrate approach in light of India or Indian participants. However, these low-carbohydrate-specific publications are relatively much less than the pharmaceutical-intervention-specific publications. This suggests that publishing India-focused low-carbohydrate-related studies in scholarly journals should be encouraged in order to increase the footprints of this approach in the scholarly/academic literature—this encouraged us to publish this article (a case study), and, to our knowledge, this article is rare of its kind for the following reasons.
This article (a case study) serves perhaps as one of the first India-specific scholarly records where the results—and results' discussion—of a high-intensity low-carbohydrate intervention on the metabolic health of an Indian older adult with then-recent bilateral knee replacement surgery are systematically documented and published. Therefore, we hope this article (a case study) serves as an encouragement for low-carbohydrate practitioners in India to systematically document their results and try to publish them in scholarly journals because these journals are effective mediums for health practitioners and researchers to communicate essential practices that inform the contemporary public health issues—this can help improve the acceptability of the low-carbohydrate approach in the overall scientific community.

7) Authors' contribution

Both authors contributed equally to this manuscript. Abhinav V Pathare wrote the initial manuscript, contributing to the manuscript's conception, design, literature search, and interpretation. Anup B Chaudhary contributed analytical components, revised the initial manuscript, provided critical feedbacks, and made an intellectual contribution. Both authors were involved in carefully proofreading the content and approved the manuscript for publication.

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9) Ethical statements

This article (a case study) intended not to experiment but to convey the results of an adequately acknowledged and validated dietary intervention. The results are conveyed transparently. A comprehensive and transparent elaboration of the intervention and the potential publication of the results was provided to the subject and the subject's family members in an interactive way before the intervention started. Informed consent was obtained directly from the subject of the case study before

the intervention started. This result-conveying publication (a case study) intends to establish scientific communication in order to contribute to the existing health literature and scientific community's knowledge. Special care was taken to protect the privacy and confidentiality of the subject throughout the publication. The subject's test reports and data were handled with privacy and confidentiality. The subject was allowed to withdraw from the intervention at any time without facing any adverse consequences.

10) Conflict of interest

There is no conflict of interest.

11) Dedication statement

We, the authors of this article, dedicate this article to a *Senior Lecturer in Public Health*, who, during the higher studies of the Corresponding Author (Abhinav V Pathare), played an essential role in equipping him with the skills required for cautiously navigating his low-carbohydrate-related research/career interest.

11.1) Disclaimer regarding the dedication statement

The responsibility for all the contents of this manuscript is solely borne by the authors and not by any other individuals or organisations. Therefore, the *Senior Lecturer in Public Health* mentioned in the dedication statement is not associated with any aspect of this case study or its publication.

The dedication statement solely intends to express gratitude and acknowledge the valuable contribution of the mentioned *Senior Lecturer* to the Corresponding Author's (Abhinav V Pathare's) skill development during his higher studies.

The article's co-author, Anup B Chaudhary, who equally contributed to the manuscript, happily consented to add the dedication statement to the manuscript.

12) Acknowledgement

First and foremost, we (the authors of this case study) are thankful to the subject whose outcomes are conveyed in this case study. The challenges faced by older adults in India can be complex and multifaceted (see Pathare, 2023 [34]); thus, adherence to dietary interventions—especially when they are significantly different from the usual dietary pattern—can be intricately difficult. Therefore, the co-operation of the 65-year-old woman subject of this case study is highly appreciable.

Moreover, we are also thankful to the subject's family members for comprehensively supporting the subject (and the associated researchers). Finally, we are grateful to all those people across the globe—from diverse disciplines and professions—who dedicated their work to studying the effects of low-carbohydrate diets on human metabolic health.

13) References

1. Abuyassin, B., & Laher, I. (2016). Diabetes epidemic sweeping the Arab world. *World journal of diabetes*, *7*(8), 165. https://doi.org/10.4239%2Fwjd.v7.i8.165
2. Action to Control Cardiovascular Risk in Diabetes Study Group, Gerstein, H. C., Miller, M. E., Byington, R. P., Goff, D. C., Jr, Bigger, J. T., Buse, J. B., Cushman, W. C., Genuth, S., Ismail-Beigi, F., Grimm, R. H., Jr, Probstfield, J. L., Simons-Morton, D. G., & Friedewald, W. T. (2008). Effects of intensive glucose lowering in type 2 diabetes. *The New England journal of medicine*, *358*(24), 2545–2559. https://doi.org/10.1056/NEJMoa0802743
3. American Diabetes Association. (2019). Standards of medical care in diabetes—2019 abridged for primary care providers. *Clinical diabetes: a publication of the American Diabetes Association*, *37*(1), 11-34. https://doi.org/10.2337%2Fcd18-0105

4. Appleton, K. M. (2016). Barriers to and facilitators of the consumption of animal-based protein-rich foods in older adults. *Nutrients*, *8*(4), 187. https://doi.org/10.3390/nu8040187
5. Appleton, K. M. (2023). Barriers to and Facilitators of the Consumption of Animal-Based Protein-Rich Foods in Older Adults: Re-Analysis with a Focus on Sustainability. *Nutrients*, *15*(2), 470. https://doi.org/10.3390/nu15020470
6. Best, R. L., & Appleton, K. M. (2013). The consumption of protein-rich foods in older adults: An exploratory focus group study. *Journal of Nutrition Education and behavior*, *45*(6), 751-755. https://doi.org/10.1016/j.jneb.2013.03.008
7. Cucuzzella, M., Riley, K., & Isaacs, D. (2021). Adapting medication for type 2 diabetes to a low carbohydrate diet. *Frontiers in nutrition*. Volume 8. Article 688540. https://doi.org/10.3389/fnut.2021.688540
8. De La Monte, S. M., & Wands, J. R. (2008). Alzheimer's disease is type 3 diabetes—evidence reviewed. *Journal of diabetes science and technology*, *2*(6), 1101-1113. https://doi.org/ 10.1177%2F193229680800200619
9. Diabetes UK. (n.d.). *Metformin and diabetes*. Retrieved from https://www.diabetes.org.uk/ guide-to-diabetes/managing-your-diabetes/treating-your-diabetes/tablets-and-medication/metformin#:~:text=Some%20people%20are%20able%20to,range%20without%20needing%20any%20medication.
10. Ebbeling, C. B., Feldman, H. A., Klein, G. L., Wong, J. M., Bielak, L., Steltz, S. K., ... & Ludwig, D. S. (2018). Effects of a low carbohydrate diet on energy expenditure during weight loss maintenance: randomized trial. *bmj*, *363*. https://doi.org/10.1136/bmj.k4583
11. Ebbeling, C. B., Swain, J. F., Feldman, H. A., Wong, W. W., Hachey, D. L., Garcia-Lago, E., & Ludwig, D. S. (2012). Effects of dietary composition on energy expenditure during weight-loss maintenance. *Jama*, *307*(24), 2627-2634. doi:10.1001/jama.2012.6607
12. Fallabel. (2023). *Stopping metformin: When and how you can stop taking metformin*. Retrieved from https://diabetesstrong.com/stopping-metformin/
13. Hallberg, S. J., McKenzie, A. L., Williams, P. T., Bhanpuri, N. H., Peters, A. L., Campbell, W. W., ... & Volek, J. S. (2018). Effectiveness and safety of a novel care model for the management of type 2 diabetes at 1 year: an open-label, non-randomized, controlled study. *Diabetes Therapy*, *9*(2), 583-612. https://doi.org/10.1007/s13300-018-0373-9
14. Hu, C., & Jia, W. (2018). Diabetes in China: epidemiology and genetic risk factors and their clinical utility in personalized medication. *Diabetes*, *67*(1), 3-11. https://doi.org/10.2337/dbi17-0013
15. Iqbal, N., Vetter, M. L., Moore, R. H., Chittams, J. L., Dalton-Bakes, C. V., Dowd, M., ... & Wadden, T. A. (2010). Effects of a low-intensity intervention that prescribed a low-carbohydrate vs. a low-fat diet in obese, diabetic participants. *Obesity*, *18*(9), 1733-1738. https://doi.org/10.1038/ oby.2009.460
16. Johnsson, K. M., Ptaszynska, A., Schmitz, B., Sugg, J., Parikh, S. J., & List, J. F. (2013). Urinary tract infections in patients with diabetes treated with dapagliflozin. *Journal of Diabetes and its Complications*, *27*(5), 473-478. https://doi.org/10.1016/j.jdiacomp.2013.05.004
17. Kasper, J. S., & Giovannucci, E. (2006). A meta-analysis of diabetes mellitus and the risk of prostate cancer. *Cancer Epidemiology Biomarkers & Prevention*, *15*(11), 2056-2062. https://doi.org/10.1158/1055-9965.epi-06-0410
18. Kelly, T., Unwin, D., & Finucane, F. (2020). Low-Carbohydrate diets in the management of obesity and type 2 diabetes: a review from clinicians using the approach in practice. *International journal of environmental research and public health*, *17*(7), 2557. https://doi.org/10.3390/ijerph17072557
19. Kim-Dorner, S. J., Deuster, P. A., Zeno, S. A., Remaley, A. T., & Poth, M. (2009). Should triglycerides and the triglycerides to high-density lipoprotein cholesterol ratio be used as

surrogates for insulin resistance?. *Metabolism: Clinical and Experimental*, *59*(2), 299-304. https://doi.org/10.1016/j.metabol.2009.07.027

20. Knowler, W. C., Barrett-Connor, E., Fowler, S. E., Hamman, R. F., Lachin, J. M., Walker, E. A., Nathan, D. M., & Diabetes Prevention Program Research Group (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *The New England journal of medicine*, *346*(6), 393–403. https://doi.org/10.1056/NEJMoa012512
21. Liu, F., Wu, M., Feng, Y. H., Zhong, H., Cui, T. L., Huang, Y. Q., ... & Fu, P. (2013). Influence of HbA1c on short-term blood pressure variability in type 2 diabetic patients with diabetic nephropathy. *Journal of Zhejiang University Science B*, *14*(11), 1033-1040. https://doi.org/10.1631/jzus.B1300030
22. Luz, P. L. D., Favarato, D., Faria-Neto Junior, J. R., Lemos, P., & Chagas, A. C. P. (2008). High ratio of triglycerides to HDL-cholesterol predicts extensive coronary disease. *Clinics*, *63*, 427-432. https://doi.org/10.1590%2FS18075932200800040003
23. Malhotra, A., Noakes, T., & Phinney, S. (2015). It is time to bust the myth of physical inactivity and obesity: you cannot outrun a bad diet. *British journal of sports medicine*, *49*(15), 967-968. http://dx.doi.org/10.1136/bjsports-2015-094911
24. Menke, A., Casagrande, S., Geiss, L., & Cowie, C. C. (2015). Prevalence of and trends in diabetes among adults in the United States, 1988-2012. *Jama*, *314*(10), 1021-1029. https://doi.org/10.1001/jama.2015.10029
25. Metabolic Health India. (2022a). *Metabolic health conference – Day 1*. Retrieved from https://www.youtube.com/live/nSO9v5EJwvE?feature=shared
26. Metabolic Health India. (2022b). *Metabolic health conference – Day 2*. Retrieved from https://www.youtube.com/live/rxUAaB6nPSY?feature=shared
27. Metabolic Health India. (2022c). *Metabolic health conference – Day 3*. Retrieved from https://www.youtube.com/live/y22HeshH_6g?feature=shared
28. Mohan, V., Bhavadharini, B., Mukhopadhyay, S., Nallaperumal, S., Tiwaskar, M., Anjana, R. M., & Unnikrishnan, R. (2021). Diabetes in pre-independence India: Rediscovering a forgotten era. *Journal of the Association of Physicians of India*, *69*, 80-84. PMID: 34472814
29. Nasri, H., & Rafieian-Kopaei, M. (2014). Metformin: current knowledge. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences*, *19*(7), 658. PMCID: PMC4214027
30. National Institute on Aging. (2023). *Talking with your older patients*. Retrieved from https://www.nia.nih.gov/health/talking-your-older-patients
31. Ness-Abramof, R., & Apovian, C. M. (2005). Drug-induced weight gain. *Timely topics in medicine. Cardiovascular diseases*, *9*, E31. https://pubmed.ncbi.nlm.nih.gov/16341287/
32. Nuttall, F. Q., & Gannon, M. C. (1991). Plasma glucose and insulin response to macronutrients in nondiabetic and NIDDM subjects. *Diabetes care*, *14*(9), 824-838. https://doi.org/10.2337/diacare.14.9.824
33. Pathare, A. V. (2021). Exercise Does Not Solve Obesity: The" Calorie-Burning Theory" Is Misleading And Incorrect. *International Journal Dental and Medical Sciences Research*, *3*(5), 328-333.Retrieved from http://clok.uclan.ac.uk/39920/ 1/39920%20AbhinavIJDMSR Article Editorial.pdf
34. Pathare, A. V. (2023). Improving the support for older adults in India: A multi-faceted approach for a better future. *International Journal of Paediatrics and Geriatrics*, *6*(2), 13-17. https://doi.org/10.33545/26643685.2023.v6.i2a.206
35. Pathare, A. V., & Chaudhary, A. B. (2022). Contemporary directions in fatty liver disease in light of low-carbohydrate approach: a review by public health India. European Journal of Molecular and Clinical Medicine, 9(2), 808–817. http://publichealthindia.com/wp-content/uploads/2022/04/Ejmcm-2263.1.pdf

36. Pavy F. W. (1890). On the Principles of the Treatment of Diabetes Mellitus. *The Indian Medical Gazette*. Nov;25(11):327-330. PMID: 29000506; PMCID: PMC5149308. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5149308/pdf/indmedgaz71145-0007.pdf
37. Playford, R. J., Pither, C., Gao, R., & Middleton, S. J. (2013). Use of the alpha-glucosidase inhibitor acarbose in patients with 'Middleton syndrome': Normal gastric anatomy but with accelerated gastric emptying causing postprandial reactive hypoglycemia and diarrhea. *Canadian Journal of Gastroenterology*, *27*(7), 403-404. https://doi.org/10.1155/2013/791803
38. Reaven, G. (1999). Intensive blood pressure/glucose control in type 2 diabetes: why is it so difficult to decrease coronary heart disease?. *Journal of human hypertension*, *13*(2), S19-S23. https://doi.org/10.1038/sj.jhh.1000830
39. Roumie, C. L., Liu, X., Choma, N. N., Greevy, R. A., Hung, A. M., Grijalva, C. G., & Griffin, M. R. (2012). Initiation of sulfonylureas versus metformin is associated with higher blood pressure at one year. *Pharmacoepidemiology and drug safety*, *21*(5), 515-523. https://doi.org/10.1002/pds.3249
40. Saklayen, M. G. (2018). The global epidemic of the metabolic syndrome. *Current hypertension reports*, *20*(2), 1-8. https://doi.org/10.1007/s11906-018-0812-z
41. Salazar, M. R., Carbajal, H. A., Espeche, W. G., Aizpurúa, M., Dulbecco, C. A., & Reaven, G. M. (2017). Comparison of two surrogate estimates of insulin resistance to predict cardiovascular disease in apparently healthy individuals. *Nutrition, Metabolism and Cardiovascular Diseases*, *27*(4), 366-373. https://doi.org/10.1016/j.numecd.2016.12.002
42. Selvin, E., Wattanakit, K., Steffes, M. W., Coresh, J., & Sharrett, A. R. (2006). HbA1c and peripheral arterial disease in diabetes: The Atherosclerosis Risk in Communities study. *Diabetes care*, *29*(4), 877-882. https://doi.org/10.2337/diacare.29.04.06.dc05-2018
43. Taubes, G. (2007). *Good calories, bad calories: fats, carbs, and the controversial science of diet and health*. Anchor.
44. Taubes, G. (2011). *Why we get fat: and what to do about it*. Anchor.
45. Taubes, G. (2020). *The Case for Keto: The Truth about Low-Carb, High-Fat Eating*. Granta Books.
46. Walton, C. M., Perry, K., Hart, R. H., Berry, S. L., & Bikman, B. T. (2019). Improvement in glycemic and lipid profiles in type 2 diabetics with a 90-day ketogenic diet. *Journal of diabetes research*, *2019*. https://doi.org/10.1155/2019/8681959
47. Wang, C., Li, F., Guo, J., Li, C., Xu, D., & Wang, B. (2018). Insulin resistance, blood glucose and inflammatory cytokine levels are risk factors for cardiovascular events in diabetic patients complicated with coronary heart disease. *Experimental and Therapeutic Medicine*, *15*(2), 1515-1519. https://doi.org/10.3892%2Fetm.2017.5584
48. Westman, E. C., Yancy, W. S., Mavropoulos, J. C., Marquart, M., & McDuffie, J. R. (2008). The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. *Nutrition & metabolism*, *5*(1), 1-9. https://doi.org/10.1186%2F1743-7075-5-36
49. Wylie, C., Copeman, J., & Kirk, S. F. L. (1999) Health and social factors affecting the food choice and nutritional intake of elderly people with restricted mobility. *Journal of Human Nutrition and Dietetics*, *12*(5), 375-380. https://doi.org/10.1046/j.1365-277x.1999.00177.x
50. Xu, F., Zhao, L. H., Su, J. B., Chen, T., Wang, X. Q., Chen, J. F., ... & Wang, X. H. (2014). The relationship between glycemic variability and diabetic peripheral neuropathy in type 2 diabetes with well-controlled HbA1c. *Diabetology & metabolic syndrome*, *6*(1), 1-7. https://doi.org/10.1186/1758-5996-6-139
51. Yancy, W. S., Foy, M., Chalecki, A. M., Vernon, M. C., & Westman, E. C. (2005). A low-carbohydrate, ketogenic diet to treat type 2 diabetes. *Nutrition & metabolism*, *2*(1), 1-7. https://doi.org/10.1186%2F1743-7075-2-34

52. Yannakoulia, M., Mamalaki, E., Anastasiou, C. A., Mourtzi, N., Lambrinoudaki, I., & Scarmeas, N. (2018). Eating habits and behaviors of older people: Where are we now and where should we go?. *Maturitas*, *114*, 14-21. https://doi.org/10.1016/j.maturitas.2018.05.001
53. Zhou, X., Perez-Cueto, F. J., Santos, Q. D., Monteleone, E., Giboreau, A., Appleton, K. M., ... & Hartwell, H. (2018). A systematic review of behavioural interventions promoting healthy eating among older people. *Nutrients*, *10*(2), 128. https://doi.org/10.3390/nu10020128

14) Appendix: "Near-to-remission" term's explanation and justification

According to *"Consensus report: Definition and interpretation of remission in type 2 diabetes"*, the usual diagnostic criteria for diabetes remission is when the HbA1c level is found to be below 6.5% when measured at least 3 months from the beginning of the non-pharmacological intervention, and this level should further persist at least for 3 months in the absence of diabetes medications.

However, this article (a case study) has communicated and discussed the approximately 2.5-month effects of a low-carbohydrate non-pharmacological intervention. This implies 2 things: 1) the second (improved) HbA1c report—of 6%—falls short by approximately half-month compared with the criteria mentioned by the consensus report; 2) this case study does not have an opportunity to comment on the persistence of the HbA1c levels.

Therefore, in light of the 2 implications mentioned above, the term “near-to-remission”—instead of “remission”—is used in the title of this case study. The above-mentioned consensus report can be retrieved from this link: https://doi.org/10.2337/dci21-0034