

RSSDI Indian Diabetes

EDUCATOR JOURNAL



Theme of the Month

Diabetes RRR- Reversal, Remission & Relapse

To keep Members Diabetes Care team abreast about
DSME /DSMS - (Diabetes Self management Education / Support) Concepts

2015

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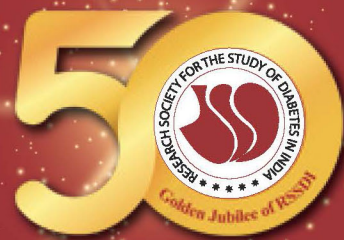
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FOREWORD

Research Society for the Study of Diabetes in India (RSSDI) founded by Prof MMS Ahuja in the year 1972 is the biggest scientific association of healthcare professionals involved in promoting diabetes education and research in India. RSSDI is happy to collaborate with USV to support their endeavour to make India the 'Diabetes care capital of the world'. Through this collaboration, RSSDI would like to strengthen the cadre of diabetes educators by empowering them with recent updates in diabetes management helping bridge the gap between the physician and the patient. Today, the rule of 50% is prevailing in terms of awareness, detection, treatment and control in T2DM. Our aspiration is to achieve 90-90-90-90 i.e. 90% of people with diabetes should be made aware, 90% should be detected, 90% of those detected should be treated, and 90% of those treated should reach their goals.

Indian Diabetes Educator Journal (IDEJ) is the first of its kind in India, and the longest running monthly diabetes educator journal since April 2015 & continues its endeavour to spread awareness, knowledge and enable healthcare teams to manage individuals with diabetes and empower them for self-care. RSSDI IDEJ will continue to keep the members of diabetes care team abreast with concepts of Diabetes Self-Management Education/Support (DSME/S) with a reach of 44000 doctors and diabetes educators digitally.

Type 2 diabetes mellitus (T2DM) has always been thought of as a chronic progressive condition. However, in recent times there has been a shift in this paradigm with the focus being on reversing diabetes or achieving remission. Given the presence of enough evidence for T2DM reversal, and its acceptance in guidelines as well, this month's IDEJ aims to propagate information based on the latest research about ways and means to achieve diabetes remission. We hope this journal will enable diabetes educators to actively engage in counseling patients about diabetes reversal, remission, and relapse.

We sincerely thank our contributors for making this issue delightful reading for our readers. We dedicate this journal to all the healthcare professionals who are working relentlessly towards making "India–The Diabetes Care Capital of the World."

Sincere Regards,

Dr. Sanjay Agarwal
RSSDI Secretary

Disclaimer: This Journal provides news, opinions, information and tips for effective counselling of people with diabetes. This Journal intends to empower your clinic support staffs for basic counselling of people with diabetes. This journal has been made in good faith with the literature available on this subject. The views and opinions expressed in this journal of selected sections are solely those of the original contributors. Every effort is made to ensure the accuracy of information but Hansa Medcell or USV Private Limited will not be held responsible for any inadvertent error(s). Professional are requested to use and apply their own professional judgement, experience and training and should not rely solely on the information contained in this publication before prescribing any diet, exercise and medication. Hansa Medcell or USV Private Limited assumes no responsibility or liability for personal or the injury, loss or damage that may result from suggestions or information in this book.

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RSSDI Indian Diabetes

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Cover Story: Defining the 3 R's of Diabetes



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Type 2 diabetes mellitus (T2DM) is a complicated, heterogeneous metabolic condition with most patients requiring progressively intensive therapy to control hyperglycemia over time. It is generally considered as an irreversible condition that advances inevitably in over 50% of patients to insulin-dependence state within 9-10 years and

needs a continuous titration of medications. However, in the last few years, there has been a drastic change in the strategies to manage diabetes. The concept of T2DM remission and the reversal of glucose levels to normal by intense dietary and lifestyle changes or metabolic surgery has gained momentum. It is no longer considered to be a progressive disorder, but efforts are being made to reverse the disorder completely. But, does T2DM really get reversed or can it get relapsed after remission is achieved? To understand this concept it is important to understand what these terms actually mean.

What are the 3 R's of diabetes?

Reversal: Diabetes reversal is a term that usually refers to a significant long-term improvement in insulin sensitivity and maintaining HbA1c below 6.5% without taking diabetes medication.

Remission: The International Expert Group organized by the American Diabetes Association (ADA), proposed that the term “remission” is preferable to “reversal,” and is defined as a return of HbA1c to <6.5% and/or fasting glucose to <126 mg/dL, either following an intervention or spontaneously, and which persists for at least 3 months in the absence of glucose-lowering medications.

“Partial remission” is when a person with T2DM achieves an HbA1c of <6.5% and/or fasting glucose levels between 100-125 mg/dL and is off all medications for diabetes for more than 1 year.

“Complete remission” is when a person with T2DM achieves an HbA1c of <5.6% and/or fasting glucose levels below 100 mg/dL and is off all medications for diabetes for more than 1 year.

“Prolonged remission” is when a person with T2DM achieves an HbA1c of <5.6% and/or fasting glucose levels below 100 mg/dL and is off all medications for diabetes for more than 5 years.

Relapse: Relapse is defined as the recurrence of diabetes medication use and/or HbA1c $\geq 6.5\%$.

Is diabetes remission and reversal the same?

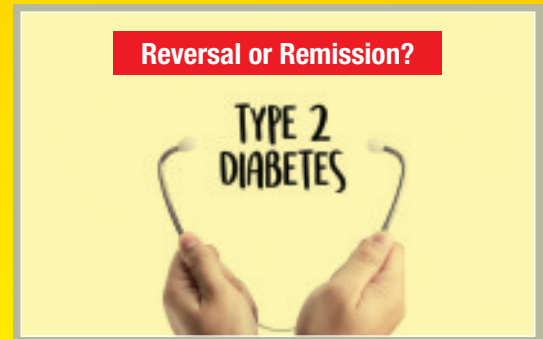
Clinicians and patients frequently use these two terms interchangeably. However, there's a distinction between the two. Reversal implies that the condition is completely cured and will not return. This gives a false feeling of security that diabetes has gone never to come back.

Remission means that the condition has got better temporarily and will remain dormant as long as the patients continue to meet specific requirements. For instance, maintaining a healthy weight is essential to prevent the recurrence of diabetes. Hence, the word remission is better than reversal when it comes to diabetes as it implies that the patient still needs to adhere to the diet and lifestyle changes and needs to follow-up with the doctor. It also reminds the doctor that the individual who has achieved remission will require long-term follow-up, motivation, and close monitoring to avoid relapse.

The key behind diabetes remission is weight loss, however, long-term data on sustainability are still needed. Significant weight loss is achieved by radically altering food and lifestyle which results in a drastic reduction in body fat and improves insulin sensitivity, or by using therapeutic methods such as bariatric surgery, a very low-calorie diet, a diet that restricts carbohydrates, and exercise.

It must be emphasized that only people with T2DM and pre-diabetes can undergo diabetes remission. Since type 1 diabetes is an autoimmune disorder requiring insulin therapy to survive, there is currently no evidence that the condition may be reversed or can go into remission. With some patients, insulin withdrawal attempts can be dangerous and even fatal.

It is important to realize that even though T2DM can enter remission, relapse may occur if lifestyle and dietary restrictions are not followed. The key to the overall effectiveness of diabetes remission may be choosing the best educational assistance strategy. Longer-term research is required to ascertain the long-term viability of diabetes remission.



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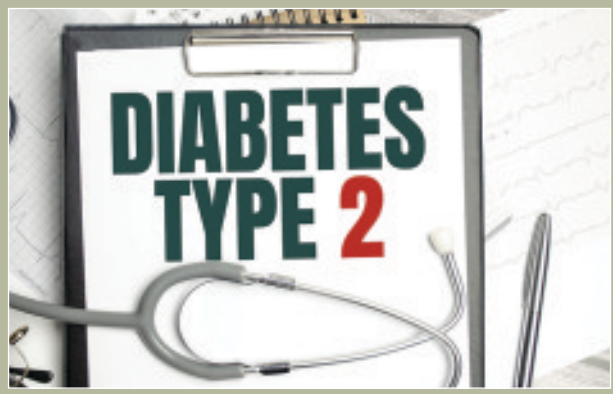
Frequently Asked Questions

1. My 10-year-old daughter has had type 1 diabetes for the past 2 years. Lately, there have been a lot of talks online about curing & reversing diabetes, and I know of a person who has reversed his diabetes. Is it possible to do the same for my daughter? Can we reverse her diabetes?

Ans: The most common question people with type 1 diabetes ask, is 'if there is a cure, or can it be reversed?' The reversal that you are referring to is known as 'Diabetes Remission', which is basically reversing the HbA1c to below 6.5% and/or fasting plasma glucose to <126 mg/dL and being able to maintain it without medications. This is possible in type 2 diabetes with intense diet and lifestyle modification resulting in significant weight loss.

There is currently no evidence that suggests type 1 diabetes can be reversed or put into remission. Type 1 diabetes is an autoimmune disorder that requires insulin therapy to survive, which if withdrawn can be fatal to the person. However, it can be controlled with the help of a well-planned diet, a healthy lifestyle as well as regular physical activity.

2. I am a 41-year-old individual with type 2 diabetes for the past 10 years. Recently I have come across various programs which claim to 'reverse' or 'cure' diabetes. I was wondering if this was actually true. Can diabetes be cured?



Ans: To answer your question, diabetes mellitus, be it type 1 or type 2 is not completely curable. An individual who achieves diabetes remission does not simply get 'cured' of diabetes. Remission is basically reversing your HbA1c and fasting blood glucose to the normal level and maintaining it without the aid of medicines. It is a state in which diabetes is not present but which nonetheless requires continued observation as chances of a re-occurrence are high. Weight gain, stress from other forms of illness, and continuing decline of β -cell function can all lead to the recurrence of type 2 diabetes.

In order to achieve remission one has to follow a very strict dietary regimen alongside regular physical activity and lifestyle modification life-long in-order to maintain the diabetes remission. If unable to do so, the chances of a "Re-reversal" or "Relapse" of type 2 diabetes are seen. Also, research shows that the chances of remission are highest when the time from diagnosis is up to 6 years. So what you can aim for is not to 'cure' your diabetes but achieve good glycemic control for living well with diabetes.

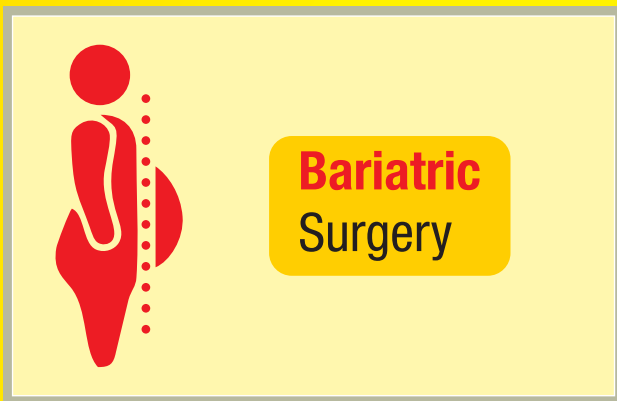


3. I am 56 years old and was diagnosed with type 2 diabetes 12 years ago. My blood glucose levels were uncontrolled, hence I was switched to insulin from OHA 4 years ago. I have heard about diabetes remission and its benefits. I also read that it is very effective, especially in type 2 diabetes. Is it possible for me to achieve remission?

Ans: Yes, diabetes remission is very beneficial and much more achievable for people with type 2 diabetes. In diabetes remission, the individuals follow a set of diet and exercise guidelines, while going off medications. It should be noted that reaching remission becomes more challenging the longer you have type 2 diabetes. The pancreatic β -cells eventually "burn out," or stop being able to produce insulin. After a given amount of time, it might be impossible to resume normal insulin production. Therefore, diabetes remission chances are low for you, but you can follow a similar dietary & exercise regimen to regularize your blood glucose levels and improve your overall quality of life.



4. I am a 48-year-old male with a BMI of 40 kg/m^2 . I was diagnosed with diabetes and hypertension 7 years ago. I am advised to opt for bariatric surgery to get my diabetes as well as weight under control. Will it be beneficial for me?



Ans: Yes, bariatric surgery is a recommended option if lifestyle and pharmacological interventions fail to achieve the desired weight loss and metabolic health. There are various procedures that are possible and your bariatric surgeon will help you decide which procedure will work best for you. There is enough evidence to show that these procedures help in significant weight loss as well as diabetes remission in most individuals and improve metabolic health. However, bariatric surgery means that your dietary patterns will change drastically from what it was before the surgery to post-surgery. A post-bariatric surgery diet will include being on fluids for a period of time before shifting to whole meals. You will have to

maintain small portion sizes for a lifetime. Sometimes these diets are not sustainable for long durations and people opt out, which could lead to weight gain and re-occurrence of diabetes. So before you opt for surgery, talk to your doctor and dietitian about the post-surgery lifestyle and go for it when you are mentally prepared to get maximum benefits out of it.

How Diabetes Remission Occurs



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The concept of remission was introduced in 2009 to express a phenomenon observed in type 2 diabetes mellitus (T2DM) patients with persistent normal blood glucose levels who underwent metabolic surgery, intense therapeutic intervention, or major lifestyle modification also confirming the restoration of functional β -cell mass to a normal level. The

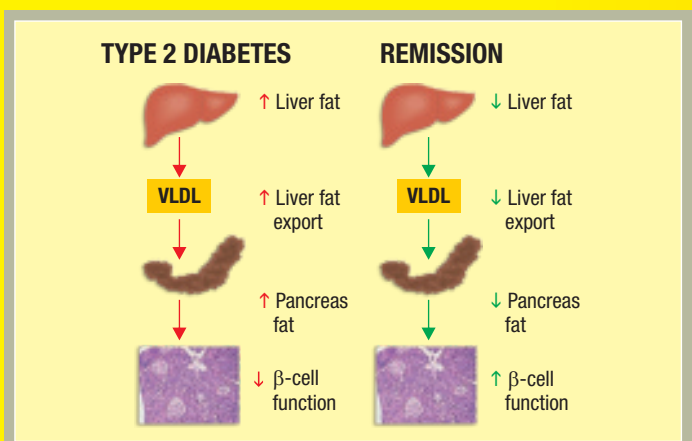
consensus expert groups from the United States and Europe defined the remission of type 2 diabetes mellitus in 2021 when HbA1c concentrations of $<6.5\%$ (48 mmol/mol) are achieved after weight loss and at least six months later without the use of any anti-diabetic drugs. The consensus guideline lays out three requirements for the remission of type 2 diabetes:

1. Weight loss
2. Fasting plasma glucose $<126 \text{ mg/dL}$ ($<7.0 \text{ mmol/L}$)
3. Estimated glycosylated hemoglobin $<6.5\%$, derived by results from continuous glucose monitoring

The twin cycle hypothesis

According to current scientific thinking, type 2 diabetes remission is most likely driven by weight loss. The deposition of more fat in the liver and pancreas than the body can handle is a characteristic feature of type 2 diabetes. One theory in 2008, the “**Twin Cycle Hypothesis**,” postulated that when extra fat is deposited in the liver due to weight gain, fat accumulates in the pancreas and impairs insulin-producing β -cells. Thus, overall weight loss, and reducing fat in the pancreas help restore normal insulin production.

Insulin resistance is brought on by excess liver fat, which completely resolves when liver fat levels return to normal range. Once this occurs, insulin can function normally once again, controlling the release of glucose into the blood and rapidly reducing fasting blood glucose levels back to normal. This decrease in liver fat causes the high rate of triglyceride supply to fall to normal. When the fat levels inside the pancreas decrease gradually, insulin response to eating is restored to normal. Studies have pointed out that around 15 kg weight loss causes a high level of liver and pancreas fat to come to normal ranges which decreases hepatic glucose output and improves pancreatic β -cell function. However, research also says that in the case of long-standing diabetes, patients' metabolic profiles are less likely to respond to changes in weight.



Weight loss with low-calorie diet: Strategy for T2DM remission

In another randomized controlled trial in primary care of a low-calorie diet with scheduled follow-up where 7 primary care nurses or dietitians worked with the patients, approximately 30% of participants showed an average weight loss of 14.5 kg and 36% of them achieved remission for two years. This trial referred to as **DiRECT (Diabetes Remission Clinical Trial)** also demonstrated that after initial rapid weight loss, individuals in remission may achieve normal functional β -cell mass provided they maintained their weight. Over a third of persons with type 2 diabetes mellitus who participated in the DiRECT trial retained their remissions after 24 months. The degree of long-term weight decrease was associated with sustained remission.



Hypothesis: T2DM as an intestinal disease

Various studies have reported that more than half of patients can achieve remission with current treatment strategies that result in active glycemic control and significant weight loss. The excess intra-organ fat can be eliminated with any sustained reduction in calorie consumption. This was shown by **Rubino**, a surgeon, specializing in metabolic surgery, who described diabetes as an operative intestinal condition. He focused on the improvement of diabetes and its mechanism following bariatric surgery. Within days of having bariatric surgery, glycemic control improved significantly. This rapid shift could not be explained by weight loss alone. As a result, it was proposed that the structural change in the intestine was a mechanism for improving blood glucose control. The change brought about by food bypassing the proximal part of the small intestine is called the **foregut hypothesis** and the **hindgut hypothesis** describes the change brought on by food moving rapidly toward the small intestine's distal end. Incretins, an intestinal hormone, plays a significant role in these changes.

Bariatric surgery and T2DM remission



By using the same underlying principles as intentional dieting, a sudden decrease in food consumption following bariatric surgery results in remission. The ADA has recognized that some individuals with type 2 diabetes may benefit from having bariatric surgery, especially if they have a higher BMI (body mass index). A variety of bariatric surgical procedures have been found to be more effective than medical management for T2DM control, some of them showing the highest remission rates. A long-term study of Swedish individuals showed that 72% of people who underwent surgery were in remission two years after the procedure, and 30% were still in remission 15 years thereafter.

Intensive glycemic control in T2DM lowers the problems associated with the condition and enhances the likelihood of remission at an earlier stage of the condition. Indian populations have also demonstrated pre-diabetes remission through weight loss and exercise, with notable changes in insulin resistance and β -cell function. Diabetes remission is a new concept that requires a lot of research to understand and evidence to support its lasting effect. While in many situations, blood glucose levels can start to increase, it becomes crucial to keep up with regular healthcare follow-ups even in remission. Remission may seem like a fairytale. However, this is real provided the efforts one takes to make it happen.

Resources:

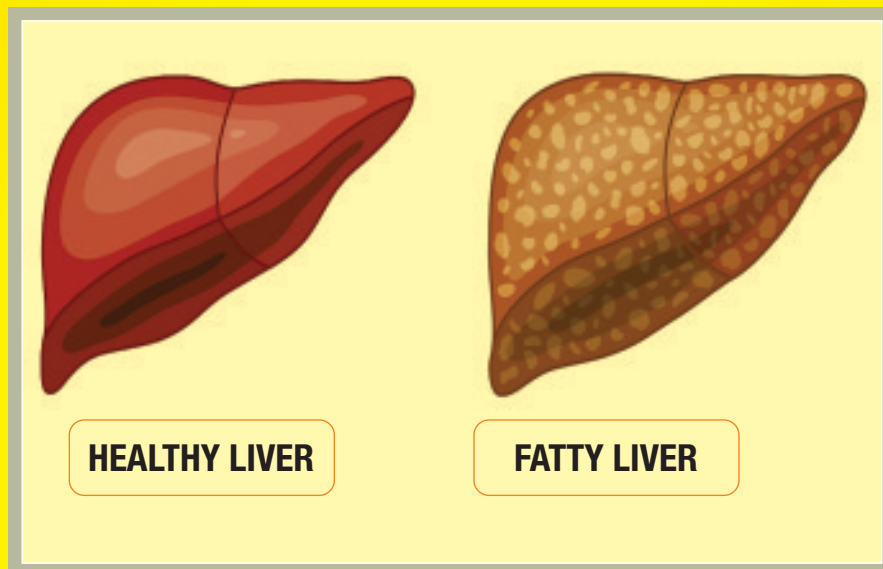
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Did You Know?

Type 2 diabetes remission is possible in people with normal weight too.

Type 2 diabetes mellitus (T2DM) is usually associated with obesity and high BMI levels. However, data shows that 15% of newly diagnosed cases of T2DM are within the normal BMI range. Research has shown that a significant weight loss in obese individuals with diabetes, helps in achieving diabetes remission. But what if the individual with diabetes is already in the healthy BMI range or just above the normal cut-off? This was investigated by Prof. Roy Taylor in the Reversal of Type 2 Diabetes upon Normalization of Energy Intake in the Non-obese (ReTUNE) trial. He studied individuals diagnosed with diabetes who were at a healthy BMI (below 27 kg/m²) and put them on a low-calorie diet. The results showed that 70% of participants with lower body weights achieved type 2 remission through diet-induced weight loss, even though they were not obese. The underlying mechanism of diabetes remission in these individuals was reducing fat in the liver and pancreas. At baseline even at lower body weight, individuals with diabetes had 2.5 times higher fat in the liver as compared to their matched control group, which with calorie restriction reduced drastically. This led to improved insulin secretion and sensitivity and therefore normalized glucose levels. This study shows that regardless of weight, people with diabetes have more fat levels than their body can cope with and there is a high chance of remission for people with a BMI of below 27 kg/m² if they lose around 10% of their starting weight.



Resources:

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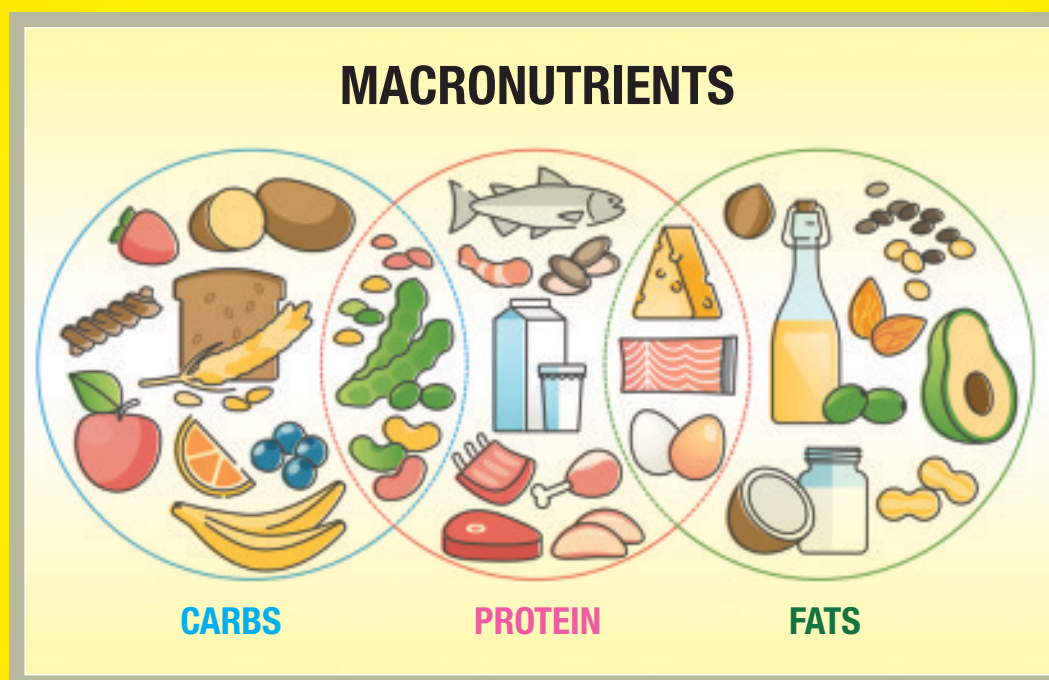
Facts and Figures

The recent macronutrient recommendations (% of total energy) for diabetes remission and prevention of diabetes in Asian Indians are as follows:

	Carbohydrate (%)	Protein (%)	Fat (%)
Newly diagnosed diabetes	49-54	19-20	21-26
Prediabetes to normal glucose tolerance	50-56	18-20	21-27
Prevention of progression of pre-diabetes to diabetes	54-57	16-20	20-24
Prevention of progression of normal glucose tolerance to diabetes	56-60	14-17	20-24

Resources:

- Anjana RM, Srinivasan S, Sudha V, *et al.* Macronutrient Recommendations for Remission and Prevention of Diabetes in Asian Indians Based on a Data-Driven Optimization Model: The ICMR-INDIAB National Study [published online ahead of print, 2022 Aug 18]. *Diabetes Care*. 2022;dc220627. doi:10.2337/dc22-0627



What's Trending? Do Keto Diets Help to Reverse Diabetes?



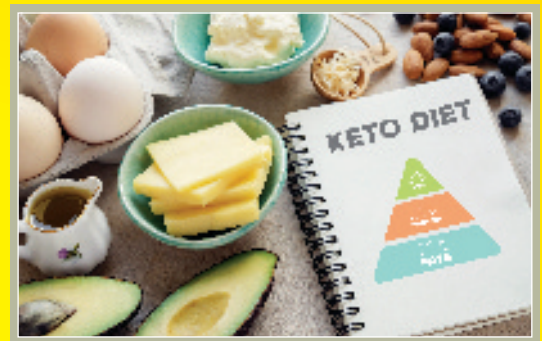
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According to international diabetes society guidelines, the management of diabetes involves making lifestyle changes in addition to pharmacological interventions. Nutrition treatment recommendations frequently place an emphasis on reduction in excessive carbohydrate intake as well as restricting fat intake to 20-35% of total calories, with a particular emphasis on the decrease in saturated fats.

Some diets advocate substantially reducing the intake of carbohydrates while increasing the intake of fats, which become the main source of calories. These diets are known as ketogenic diets (KD), as the severe carbohydrate restriction (less than 50 g/day) and the excess of free fatty acids cause ketosis. With an increase in liver fatty acid oxidation and ketone body synthesis, this combination causes a fundamental shift in energy metabolism. This leads to energy-producing ketone compounds acetoacetate (AcAc) and 3-hydroxybutyrate (BHB), as well as acetone, which is produced upon spontaneous decarboxylation of acetoacetate.



A ketogenic diet has been shown to help individuals with type 2 diabetes mellitus (T2DM) to lose significant weight and improve their glycemic control. There is recent evidence to show that KD help to reduce HbA1c and glycemic variability in individuals with T2DM. Several studies have also observed a reduction in glucose-lowering medications following a KD diet.

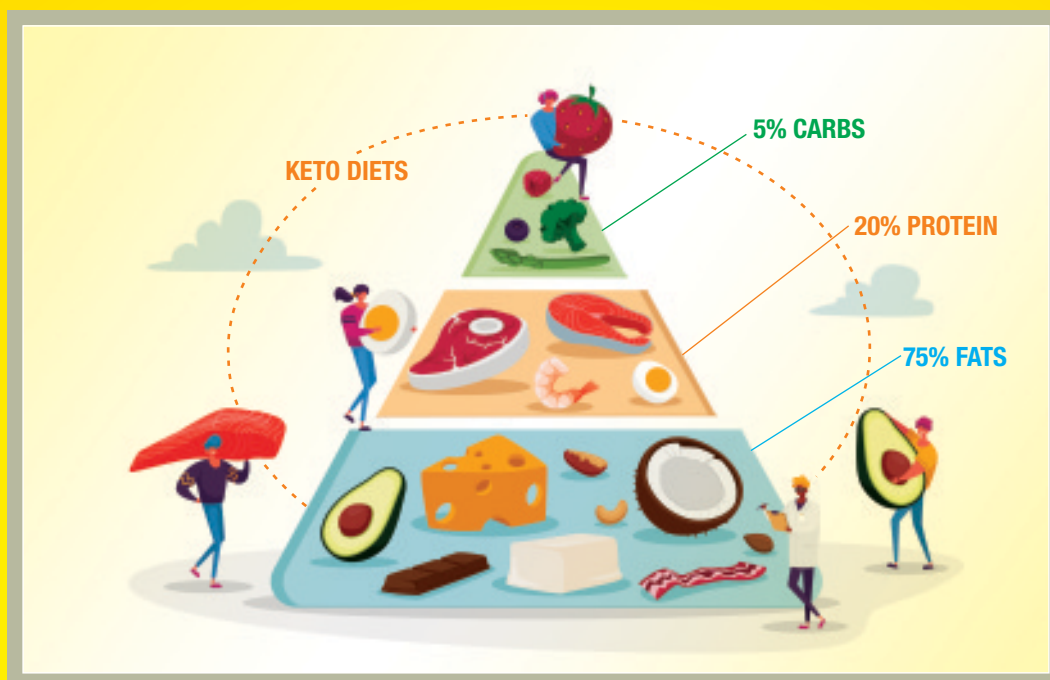
However, ketogenic diets might not be suitable for everyone. It is important to weigh the advantages of weight loss and better glycemic control against the potential increase in cardiovascular risk brought on by the unfavorable lipid profile seen with ketogenic diets, especially in people with type 2 diabetes. These diets have the potential to enhance metabolic regulation, although caution is advised due to the risk of diabetic ketoacidosis (DKA), nephrolithiasis, the possibility of worsening the lipid profile, and hypoglycaemic episodes if the glucose-lowering therapy is not adjusted. Because ketogenic diets can significantly drop blood glucose levels, people with diabetes wanting to embark on a ketogenic diet must only do so under strict medical supervision which includes medication adjustment and frequent blood glucose monitoring to avoid hypoglycemia. Again, adhering to a KD is challenging due to its restrictive pattern and increased cost. Compliance seems to improve with psychological support, motivation, and reinforcing mindful eating.

In type 1 diabetes mellitus (T1DM), there is an absence of evidence to show that KD or low carbohydrate diets can delay or prevent its onset. In T1DM, there is an increased risk of DKA, worsening of lipid profile, and also the risk of negative impact on the growth and development of children. Therefore, KD should not be the choice of dietary strategy to control T1DM.

To conclude, ketogenic diets can be an effective option in people with T2DM, as it helps in improving glycemic control although they are not the only available dietary approach for such individuals. Ketogenic diets, if chosen should be tailored to individual needs and accompanied by structured long-term support by dietitians and treating physicians to avoid adverse effects and to adjust glucose-lowering medications.

Resources:

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Selection of the Right Candidate for Diabetes Remission



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Diabetes mellitus (DM) has a significant impact on human life and health and is rapidly emerging as a critical public health issue.

Recently, the focus has shifted significantly towards trying to reverse diabetes. There is growing evidence that some patients with type 2 diabetes may be able to achieve remission.

Reversal of blood glucose levels into the normal

range can be accomplished through treatment techniques like bariatric surgery or by drastically altering food and lifestyle to achieve profound weight loss that culminates in drastic reductions in body fat, which in turn improves insulin sensitivity.

How to select the right candidate for remission?

The most appropriate candidates are people with type 2 diabetes ideally within 2 years of diagnosis, preferably males, who have better glycemic control, take fewer anti-diabetes medications, have a good β -cell function and insulin secretion, have less visceral fat, and lastly, have good mental health. The ABCDEF algorithm can be used to determine which T2DM patients are most likely to achieve remission.

A: A1c or HbA1c- The likelihood of remission is higher in people with A1c levels that are not significantly elevated.

B: Body weight- Higher body weight increases the likelihood of remission (15 kg or more weight loss is required to achieve T2DM remission).

C: C-peptide- Better C-peptide levels are associated with increased remission possibility.

D: Diabetes duration- Having diabetes for a lesser duration (up to 6 yrs) increases the likelihood of remission.

E: Enthusiasm- Remission requires a lot of motivation.

F: Frequent follow-ups- People should be eager and ready to follow-up with the medical staff.

A further point that has to be made is that 'only people with T2DM and pre-diabetes can experience a diabetes remission.' There is currently no evidence for type 1 diabetes remission or reversal. Type 1 diabetes is an autoimmune illness that requires insulin therapy for survival. With these patients, insulin withdrawal attempts can be risky and potentially fatal. Last but not least, it is important to realize that while type 2 diabetes can enter remission, relapse may occur if lifestyle and dietary control are not maintained. Thus, for long-term success, comprehensive programs assisting individuals in obtaining remission must be provided together with ongoing support and follow-ups from the multidisciplinary healthcare team, particularly an experienced nutritionist and psychologist.



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Dietary Strategies for Remission of Type 2 Diabetes Mellitus



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With an increase in the type 2 diabetes mellitus (T2DM) epidemic, the perspective on its management has changed. The focus has shifted from the classical upward titration of medications towards a better and more sustainable management that elicits remission. Nutritional management of T2DM has traditionally focussed on improving blood glucose levels and weight/fat loss, without specifically aiming to achieve remission.

What is remission?

Diabetes remission means blood glucose levels are below the diabetes threshold (in the normal range) which persists for a period of time without the need for medications. American Diabetes Association (ADA), defines remission as, *“return of HbA1c to <6.5% and/or fasting plasma glucose to <126 mg/dL either spontaneously or following an intervention, and that persists for at least 3 months in the absence of glucose-lowering pharmacotherapy.”*

With the aid of various treatment modalities, including bariatric surgery, a strict diet, and lifestyle changes, blood glucose levels can be brought back into the normal range. Profound weight loss results in a significant decrease in body fat, especially hepatic fat, which improves insulin sensitivity. Dietary strategies involved in diabetes remission are as follows:



1. Low-calorie and very low-calorie diets:

Calorie restriction approaches for T2DM remission involve the use of either low-calorie diets (LCDs) or restricting calories even further called very low-calorie diets (VLCDs) in order to achieve weight reduction. Calorie restriction leads to a reduction in liver and pancreatic fat, reducing insulin resistance and enhancing insulin secretion. They are classified as:

Low-calorie diet	1000-1500 kcal/day
Very low-calorie diet	<800 kcal/day

In a VLCD regime, typically regular food is replaced with a liquid diet formula providing nearly 400 to 800 kcal/day for a period of 12–16 weeks in a clinical setting. This is followed by the second phase of structured solid food reintroduction tailored for the maintenance of weight loss. These VLCD liquid formulations comprise approximately 50–60% of calories coming from carbohydrates (maltodextrins and sucrose) to prevent ketosis, high-biological-value proteins of 1.2–1.5 g/kg body weight to preserve lean body mass, and essential fatty acids to meet the daily requirements. They contain very little fiber, artificial sweeteners, and are fortified with vitamins and minerals. However, obese individuals are often suggested multivitamins and multimineral

supplements on a VLCD to meet the requirements. Several studies have shown that LCDs and VLCDs help achieve diabetes remission. In VLCDs, weight loss of 15 kg or greater, and maintenance of weight loss is the main driver and predictor of remission. Two years of follow-up of the well-known and one of the largest trials – the DiRECT trial, showed that more than a third of people with T2DM were demonstrated to sustain remission. Continued remission was found to be linked to the extent of sustained weight loss. On the contrary, it must also be noted that two-thirds of participants of the DiRECT trial, despite VLCDs, remission could not be maintained beyond 2 years even in a structured clinical trial mode. Hence, in a real-life situation, sustained remission may be much more difficult to achieve. Also, self-efficacy along with compliance is an integral part and determines the success of any dietary intervention.

2. Low-carbohydrate and very low-carbohydrate diets:

Low-carbohydrate diets (LCBD) predominantly work on the hypothesis that in a LCBD, decreased carbohydrate supply to the liver reduces the synthesis of fatty acids from excessive carbohydrates, and increases lipolysis (fat breakdown). There is also a reduction in plasma insulin levels that decrease fat storage in adipose tissue. Thus, LCBD promotes calorie utilization by increasing lipolysis and reduces fat storage which in turn facilitates remission. They are classified as:

Low-carbohydrate diet	<26% calories from carbohydrates or <130 g carbohydrates/day
Very low-carbohydrate diet	<10% calories from carbohydrates or 20-50 g carbohydrates/day

LCBD has shown a reduction in fat mass and remission of T2DM for up to 6 months. If LCBD is sustained, T2DM remission is seen to be maintained in the absence of weight loss. Long-term studies with LCBD in the sustenance of T2DM remission are warranted as the efficiency of LCBD on weight loss and metabolic benefits beyond 6 months is found to be unsatisfactory. These could be due to high fat intake especially saturated fat and low dietary fiber intake as part of the LCBD. Limitations of LCBD include sustainability in the long run due to restrictions on food choices. These diets can be nutritionally deficient, especially when done without medical supervision. Relapse is likely to occur if carbohydrate restriction ceases. Restricting carbohydrates to as low as 10-26% can be a challenge in a country like India where the carbohydrate intake is around 60-65%.

It must be highlighted that both dietary strategies work only for a targeted population and careful selection of the candidate needs to be done by healthcare professionals. Both LCD and LCBD need continuous support and follow-up by a multi-disciplinary healthcare team to prevent weight regain and re-reversal of diabetes. The implementation of these dietary interventions is seen to be more effective in a clinical setting and appears to be most appropriate for candidates with less than 6 years and ideally within 2 years of diagnosis of T2DM, those with better glycemic control, who are on fewer anti-diabetes drugs, those with good β -cell function and insulin secretion, those with less visceral fat, and lastly with good mental health.

Strategies to optimize the avoidance of weight regain in the long term are required to be developed.

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Source: 1. JAPI 2020;68:51-55 2. Data on File, 3. Cureus 2020; 12(9): e10.7759/cureus.1070 4. Diabetes Technology & Therapeutics 2019; 21:79-84 5. Kaino, et al.: Sulfonylurea and combinations: International Task Force Indian J Endocr Metab 2018;22:132-57.

Prescribing Information

Information: Metformin hydrochloride (as prolonged release) and glimepiride tablets. Glycomet-GP 0.5/Glycomet-GP 0.5 Forte/ Glycomet-GP 1/ Glycomet-GP 1/050/ Glycomet-GP 2/ Glycomet-GP 2/050/ Glycomet-GP 3/ Glycomet-GP 3/050/ Glycomet-GP 4/ Glycomet-GP 4/050/ Glycomet-GP 1 Forte/ Glycomet-GP 2 Forte/ Glycomet-GP 3 Forte/ Glycomet-GP 4 Forte Abridged Prescribing Information. **Composition:** Glycomet-GP 0.5mg: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500mg and glimepiride IP 0.5mg. Glycomet-GP 1 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 0.5mg. Glycomet-GP 1: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 1 mg. Glycomet-GP 1/050: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 1 mg. 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Glycomet-GP 2 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 2mg. Glycomet-GP 3 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 3mg. Glycomet-GP 4 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 4mg. **Indications:** Glycomet-GP is indicated for the management of patients with type 2 diabetes mellitus (T2DM) when diet, exercise and single agent (metformin hydrochloride or glimepiride alone) do not result in adequate glycaemic control. **Dosage and Administration:** Dosage of Glycomet-GP should be individualized on the basis of effectiveness and tolerability while not exceeding the maximum recommended daily dose of glimepiride 4mg and metformin 2000 mg. **Initial dose:** 1 tablet of Glycomet-GP should be administered once daily during breakfast or with the first main meal. Do not crush or chew the tablet. In several cases the tablet may remain intact during transit through the gastrointestinal (GI) tract and will be eliminated in faeces as hydrated mass (ghost matrix). Patients should be advised that this is normal as all drug components have already been released during GI transit. **Contraindications:** In patients hypersensitive to glimepiride, other sulfonylureas, other sulfonamides, metformin or any of the excipients of Glycomet-GP; pregnancy and lactation; diabetic ketoacidosis, diabetic pre-coma, in patients with eGFR <30 ml/min/1.73 m², acute conditions with the potential to alter renal function (dehydration, severe infection, shock, intravascular administration of iodinated contrast agents), acute or chronic disease which may cause tissue hypoxia (myocardial infarction, shock, cardiac/respiratory failure) hepatic insufficiency, acute alcohol intoxication, alcoholism. **Warnings:** Keep out of reach of children. Patient should be advised to report promptly exceptional stress situations (e.g. trauma, surgery, febrile infections). Blood glucose regulation may deteriorate and a temporary change to insulin may be necessary to maintain good metabolic control. In case of lactic acidosis, patient should be hospitalized immediately. **Precautions:** In the initial weeks of treatment, the risk of hypoglycaemia may be increased and necessitates especially careful monitoring. Serum creatinine levels should be determined before initiating treatment and regularly thereafter; at least annually in patients with normal renal function. Intravascular contrast studies with iodinated materials can lead to acute alteration of renal function. In patients in whom such study is planned, Glycomet-GP should be temporarily discontinued at the time of or prior to the procedure, and withheld for 48 hours subsequent to the procedure and reintroduced only after renal function has been re-evaluated and found to be normal. 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Role of Bariatric Surgery in Diabetes Remission



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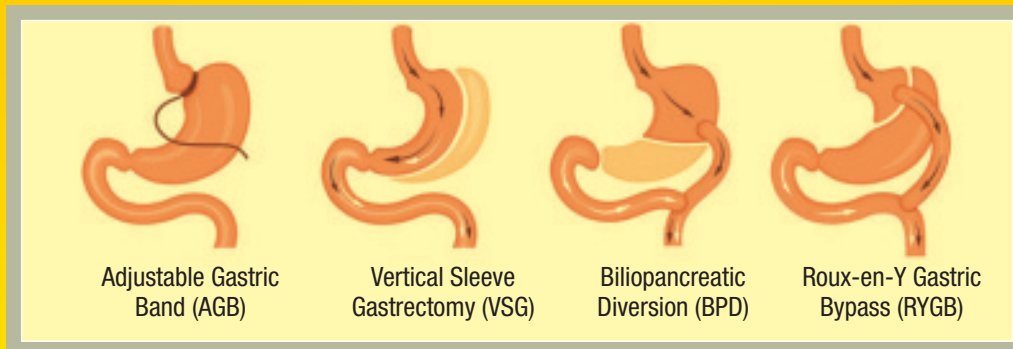
Obesity has become an epidemic over the past few decades, affecting both the developing and developed worlds. The burden of obesity-related comorbidities [such as type 2 diabetes mellitus (T2DM), hypertension, etc.] has directly increased as a result. There has been a significant paradigm shift recently in favor of attempting to reverse T2DM.

A growing body of research indicates that some people may be able to achieve T2DM remission. Although modifying one's lifestyle is the cornerstone of treatment for both obesity and diabetes, prolonged success with this approach is a huge practical challenge. Bariatric surgery has been used as a treatment modality for many years now for morbidly obese individuals and diabetes reversal or remission was first seen as an outcome of bariatric surgeries before it could be studied in depth.

Types of bariatric procedures used for diabetes remission:

Currently, bariatric surgery is more broadly categorized as 1) restrictive procedures, which drastically lower the size of the stomach to limit gastric capacity and encourage early satiety but do not change the anatomy of the intestines, or 2) gastrointestinal diversionary procedures, which bypass portions of the small intestine.

Procedure	Description
Restrictive Procedures	
Adjustable gastric banding (AGB)	An inflatable silicone band is placed around the gastric fundus to create a 30-cc pouch; gastric anatomy remains intact.
Vertical sleeve gastrectomy (VSG)	75% of the stomach is removed, including virtually all of the fundus; no rearrangement of the small bowel.
Gastrointestinal diversionary procedures	
Biliopancreatic diversion (BPD)	A partial gastrectomy is performed to create a 150- to 200-cc gastric sleeve, which is anastomosed to the small intestine. The excluded portion of the small intestine that serves as the conduit for bile and pancreatic juices is attached 100 cm proximal to the ileocecal valve. In the duodenal switch variation, the gastric antrum, pylorus, and a short portion of the duodenum are left intact.
Roux-en-Y gastric bypass (RYGB)	A gastrectomy is performed to create a 30-cc pouch, to which the distal jejunum is anastomosed. The proximal jejunum is reattached 75–150 cm below the gastro-jejunal anastomosis.



Mechanisms of T2DM remission following bariatric surgery:

Weight loss: One mechanism is a decrease in calorie intake, which eventually results in a large reduction in weight and enhanced glucose sensitivity. This is accomplished by the bariatric surgery's restrictive and/or malabsorptive qualities.

Insulin sensitivity: Early on after bariatric surgery, there is a significant reduction in insulin resistance, which is one of the most critical variables influencing increased glucose tolerance. When measured using a homeostatic model assessment of insulin resistance, insulin resistance actually falls by around 50% in the first week after surgery and approaches the typical range reported in individuals who can tolerate glucose well. Improvements in liver insulin sensitivity are accompanied by an increase in insulin clearance, which is assumed to result from a reduction in caloric intake, which in turn lowers the amount of fat in the liver. By lessening the harmful effects of glucose, these combined effects reduce baseline glucose concentration and are suggested to promote pancreatic β -cell function.

Foregut/hindgut hypothesis: The foregut-hindgut hypothesis states that because the foregut is bypassed, there is a greater amount of partially digested food supplied to the distal intestine. In turn, this activates specialized β -cells that help release peptide YY and glucagon-like peptide-1 (GLP-1), both of which have been linked to weight loss. Both also have positive effects on pancreatic cells that result in improved insulin sensitivity. It's interesting to note that days after bariatric surgery stimulates pancreatic β -cells, GLP-1 levels rise sharply. A temporary early rise in plasma glucose levels, which later results in higher insulin release, amplifies this effect of β -cell stimulation.

Bile acids: Following bariatric surgery, circulating bile acid (BA) levels also rise and are associated with enhanced glucose sensitivity. This is believed to happen as a result of a decreased mixing of partially digested nutrients and BAs after surgery, which raises the concentration of free-circulating BAs. This, in turn, causes a decrease in the generation of hepatic glucose as well as gluconeogenesis in the portions of the gut lacking BAs.

Evidence for bariatric surgery and diabetes remission:

Observational data suggest that, depending on the method, bariatric surgery is associated with a 45-95% incidence of diabetes remission. Diabetes was resolved in 78% and improved in 87% of the 3,188 individuals with type 2 diabetes who underwent bariatric surgery in the largest meta-analysis to date. BPD, RYGB, and finally AGB had the greatest rates of weight loss and diabetes remission. A meta-analysis of the effects of bariatric surgery versus traditional medical therapy on weight loss and type 2 diabetes

mellitus (T2DM) remission was carried out by Ribaric G, *et al.*, 2014. Comparing the surgical group to the conventional group, the total T2DM remission rate was 63.5 vs. 15.6% (p 0.001). In a meta-analysis, Buchwald *et al.*, 2009 assessed the impact of bariatric surgery on 135,246 patients' weight loss and comorbidities associated with obesity. Individual rates related to each procedure varied, however, an overall excess weight loss of 55.9% was reported for all surgeries. It has been discovered that bariatric surgery often causes a body mass index decrease of 10-15 kg/m² and a weight loss of 30-50 kg.

Remission and improvement in type 2 diabetes associated with various bariatric procedures

	AGB	RYGB	BPD
Excess weight loss (%)	46.2	59.7	63.6
Remission of type 2 diabetes (%)	56.7	80.3	95.1

After bariatric surgery, the glycemia improvement and cardiovascular advantages continue for years. However, new data suggests that a significant percentage of patients do have a relapse of diabetes. Studies conducted over a longer period of time indicate an even higher likelihood of diabetes return, particularly in patients who had RYGB surgery. In a case series of 157 individuals who had previously undergone RYGB and had initially experienced remission from their diabetes, 68 (43.1%) of them developed the disease again. Less early weight loss and more weight gain were shown to be linked to a higher risk of diabetes recurrence.

Bariatric surgery results in significant changes in glucose homeostasis. The efficacy of the four approved weight reduction and T2DM remission therapies are as follows: BPD >RYGB >SG >AGB. Long term studies are required to evaluate the impact of bariatric surgery in diabetes remission, its durability, and more precisely determine the rate of relapse, long-term studies are required.

Resources:

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Diabetes Educator Tip of the Month



Contributed by
Name: Ms. Tamanna Shaikh

Bachelor's in Applied Nutrition

Low carbohydrate snack- Peanut chaat

This recipe is made with peanuts that provide protein and healthy fats. It includes vegetables that are packed with micronutrients and condiments to enhance the taste. This recipe is low in carbohydrates (as low as 5 g) making it an ideal snacking option for people with diabetes.

Serves: 1

Ingredients	Amount
Boiled peanuts	½ cup
Onions, finely chopped	1 tbsp
Tomatoes, finely chopped	1 tbsp
Sweet corn, boiled	¼ cup
Raw mango, finely chopped	1 tsp
Lemon juice	1 tbsp
Coriander, finely chopped	¼ cup
Salt	To taste
Red chili powder	2 pinch

1 cup: 200 mL; 1 tablespoon: 15 mL; 1 teaspoon: 5 mL



Method

- In a bowl, add all the ingredients.
- Mix them well and garnish with a few coriander leaves.

Superfood: Almonds

The almond tree, *Prunus dulcis*, is a member of the Rosaceae family and is indigenous to Central Asia, California, and Australia. It is primarily grown in Mediterranean regions. It is grown and consumed all over the world due to its wide range of health advantages.

Variety of nutrients in almonds, including phytosterols, polyphenols, antioxidants, micronutrients, and healthy fats [Monounsaturated fatty acids (MUFA)-62% and polyunsaturated fatty acids (PUFA)-24%] are linked to the health benefits of almonds.



Nutritional benefits

- Rich in vitamins and minerals such as vitamin E, riboflavin, magnesium, manganese, copper, and phosphorus as well as potassium and zinc.
- Low in carbohydrates.
- Good source of protein and fiber.
- Antioxidant property.

Health benefits

Weight management

Almonds have a low glycemic index and are high in protein and fiber, all of which are known to increase satiety and inhibit hunger, hence reducing caloric intake. Consuming nuts is also known to lead to higher energy expenditure. Almonds are therefore helpful for controlling weight.

Diabetes management

Almonds are known to improve insulin sensitivity. Almonds include unsaturated fatty acids that are known to make it easier for glucose receptors to migrate to the cell surface and so improve insulin sensitivity. The efficacy of β -cell function is increased by the stimulation of glucagon-like peptide (GLP-1) release by unsaturated fatty acids.

Almonds are low in carbohydrates (10 g/100 g) and have a low glycemic index, which could lower the glycemic index of ingested foods and possibly slow down the rate of glucose absorption as they are high in fiber and high in healthy fats. A fistful of almonds can replace a carbohydrate-rich snack which will help in better glucose control.

Cardiovascular management

Almonds contain a lot of phytosterols, which prevent the body from absorbing cholesterol and support normal cholesterol levels. As almonds are also high in MUFA, which are likewise known to lower low-density lipoprotein (LDL) cholesterol, they are beneficial in the management of cardiovascular disease.

Anti-oxidant effect

Dietary flavonoids are well-known antioxidants that can lower the chance of developing chronic diseases. Almond skin shows the presence of bioavailable flavonoids, which work in combination with vitamin E and vitamin C to boost the antioxidant effect.

How to consume?

Almonds can be eaten raw, soaked, roasted, or added to a variety of culinary preparations, such as almond bread, almond cookies, almond crackers, and so on. Almond milk is used as a low-carbohydrate lactose-free alternative to regular milk.

Recommended dosage

As a component of a healthy diet, it is advised to consume 30 to 50 g of almonds daily.

Resources:

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Recipe: Strawberry Almond Milk Smoothie

Serves: 1

Ingredients	Amount
Strawberries	½ cup
Greek yogurt	½ cup
Almond milk	½ cup
Chia seeds (optional)	2 tsp
Vanilla essence	1 drop
1 cup: 250 mL; 1 tablespoon: 15 mL; 1 teaspoon: 5 mL	



Method

1. Put all the ingredients (except chia seeds) in a blender and blend till you get a smooth mixture. Keep in the refrigerator to cool for sometime.
2. Pour the smoothie into a tall glass and garnish with fresh strawberries and some chia seeds if desired, serve chilled.



Dia-Games

True or False

1. Reversal of blood glucose levels into the normal range can be accomplished through bariatric surgery which in turn improves insulin sensitivity.
2. The remission state of diabetes is defined as when a patient achieves an HbA1c level below 6.5% while also being able to discontinue all diabetes medications for at least 3 months.
3. People with type 2 diabetes require <10kg weight loss to achieve remission.
4. Low-calorie, as well as low-carbohydrate diets, work well to achieve diabetes remission.
5. Reversal is defined as the recurrence of medication use and/or HbA1c $\geq 6.5\%$.
6. The likelihood of remission is higher in people with A1c levels that are not significantly elevated.
7. Lowering of fat levels in the pancreas leads to better β -cell functioning.
8. Gastric banding is considered to be the most efficient bariatric surgery for achieving diabetes remission.

Answer: 1. True, 2. True, 3. False, 4. True, 5. False, 6. True, 7. True, 8. False

Patient Speaks

I am Manoj, a 52-year-old man having diabetes for the last 7 years. My blood glucose levels are well maintained now with the advice from my doctor and diabetes educator (DE). I am now very committed to following a healthy lifestyle which includes regular exercise and good eating habits.

Initially post my diagnosis I did not take my doctor's recommendations seriously and was not careful at all. Neither did I visit my doctor regularly nor did I do any of the follow-up tests recommended for me. I was not even regular with my prescribed medications. I was in denial and did not feel the need to take any specific care.

On the other hand, my sister was also diagnosed with diabetes in the same year as me. She was very particular post her diagnosis and followed all her doctors' recommendations. She was particular about her medications as well as took the help of her DE to make healthy lifestyle changes. She immediately went to a qualified dietitian and made changes in her diet and at the same time began exercising daily, losing over 16 kg of weight over 4 years. She also checked her blood glucose levels regularly by self-monitoring based on her DE's recommendations. She visited her doctor and did the follow-up tests to monitor her blood glucose levels. Her glucose control was excellent and in a span of 4 years her diabetes went into remission, and she went off all medication. She has managed to keep her sugars in the normal range and has maintained weight loss with regular exercise and a healthy eating pattern.

Seeing my sister's success, I decided to follow her example. I started consulting my HCP regularly. I also met a diabetes educator who patiently explained to me more about my condition and the importance of going to the doctor regularly, doing my tests as well as following a healthy lifestyle with exercise. She made me understand the complications that I could develop if my blood glucose levels were not in control. I got myself a diet plan from a qualified dietitian. These steps helped me to get my blood glucose under control.

The next time I went to my DE, I was very happy as my reports showed that my efforts had paid off. I am very thankful to my doctor and my DE for guiding and supporting me in living a healthier lifestyle and following treatment plan with regular follow ups.



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For screening people with High & Moderate Risk of Diabetes

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Glycomet[®]-GP 1/2

Metformin Hydrochloride 500 mg SR + Glimepiride 1/2 mg



Source: 1. JAPI 2020 68,51-55 2. Data on File, 3. Cureus 2020; 12(9): e10.7759/cureus.1070 4. Diabetes Technology & Therapeutics 2019,,2,79-84 5. Kalra, et al.: Sulfonylurea and combinations: International Task Force Indian J Endocr Metab 2018;22:132-57.

Prescribing information

Information: Metformin hydrochloride (as prolonged release) and glimepiride tablets. Glycomet-GP 0.5/Glycomet-GP 0.5 Forte/ Glycomet-GP 1/ Glycomet-GP 1/850/ Glycomet-GP 2/ Glycomet-GP 2/850/ Glycomet-GP 3/ Glycomet-GP 3/850/ Glycomet-GP 4/ Glycomet-GP 4/850/ Glycomet-GP 1 Forte/ Glycomet-GP 2 Forte/ Glycomet-GP 3 Forte/ Glycomet-GP 4 Forte Abridged Prescribing Information **Composition:** Glycomet GP 0.5mg: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500mg and glimepiride IP 0.5mg. Glycomet GP 0.5 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 0.5mg. Glycomet GP 1: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 1 mg. Glycomet GP 1/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 1 mg. Glycomet GP 2: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 2 mg. Glycomet GP 2/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 2 mg. Glycomet GP 3: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 3 mg. Glycomet GP 3/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 3 mg. Glycomet GP 4: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 500 mg and glimepiride IP 4 mg. Glycomet GP 4/850: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 850 mg and glimepiride IP 4 mg. Glycomet GP 1 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 1mg. Glycomet GP 2 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 2mg. Glycomet GP 3 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP 3mg. Glycomet GP 4 Forte: Each uncoated tablet contains metformin hydrochloride IP (as prolonged release form) 1000mg and glimepiride IP mg. **Indications:** Glycomet GP is indicated for the management of patients with type 2 diabetes mellitus (T2DM) when diet, exercise and single agent (metformin hydrochloride or glimepiride alone) do not result in adequate glycemic control. **Dosage and Administration:** Dosage of Glycomet GP should be individualized on the basis of effectiveness and tolerability while not exceeding the maximum recommended daily dose of glimepiride 8mg and metformin 2000 mg. **Initial dose:** 1 tablet of Glycomet GP should be administered once daily during breakfast or with the first main meal. Do not crush or chew the tablet. In several cases the tablet may remain intact during transit through the gastrointestinal (GI) tract and will be eliminated in feces as hydrated mass (ghost matrix). Patients should be advised that this is normal as all drug components have already been released during GI transit. **Contraindications:** In patients hypersensitive to glimepiride, other sulfonylureas, other sulfonamides, metformin or any of the excipients of Glycomet GP; pregnancy and lactation; diabetic ketoacidosis, diabetic pre-coma, in patients with eGFR<30 ml/min/ 1.73 m2, acute conditions with the potential to alter renal function (dehydration, severe infection, shock, intravascular administration of iodinated contrast agents), acute or chronic disease which may cause tissue hypoxia (myocardial infarction, shock, cardiac/respiratory failure) hepatic insufficiency, acute alcohol intoxication, alcoholism. **Warnings:** Keep out of reach of children. Patient should be advised to report promptly exceptional stress situations (e.g. trauma, surgery, febrile infections). Blood glucose regulation may deteriorate and a temporary change to insulin may be necessary to maintain good metabolic control. In case of lactic acidosis, patient should be hospitalized immediately. **Precautions:** In the initial weeks of treatment, the risk of hypoglycemia may be increased and necessitates especially careful monitoring. Serum creatinine levels should be determined before initiating treatment and regularly thereafter: at least annually in patients with normal renal function. Intravascular contrast studies with iodinated materials can lead to acute alteration of renal function. In patients in whom such study is planned, Glycomet GP should be temporarily discontinued at the time of or prior to the procedure, and withheld for 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal. Use of Glycomet GP should be discontinued 48 hours before any surgical procedure. **Adverse reactions:** For glimepiride - hypoglycaemia; temporary visual impairment; GI symptoms like nausea, vomiting, abdominal pain, diarrhoea may occur; increased liver enzymes, cholestasis and jaundice may occur; allergic reactions may occur occasionally. For metformin - GI symptoms like nausea, vomiting, abdominal pain or discomfort may occur.

In case of any adverse events, kindly contact: pv@usv.in

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