

# DRS - WCPD

DIABETES RESEARCH & SOLUTIONS

## 11<sup>TH</sup> WORLD CONGRESS ON PREVENTION OF DIABETES AND ITS COMPLICATIONS

### Theme:

Prevention of Diabetes and Prevention of Complications

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### Diabetes is Absolutely Preventable: Compelling Evidence

Successful disease prevention requires agreed-upon diagnostic criteria, understanding risk factors and natural history, affordable and acceptable screening, and influencing modifiable risk factors. Challenges in advancing type 2 diabetes (T2D) prevention include slow progress in population studies and randomized controlled trials (RCTs), lack of standardized definitions, limited use of behavioral change interventions, and delayed development of evidence-based medicine. By the time substantial research began, T2D had already reached epidemic levels in some populations.



Dr Shashank Joshi  
Mumbai

However, major RCTs on T2D prevention have shown:

- Major studies demonstrated significant and consistent relative risk reduction in T2D among high-risk individuals through lifestyle interventions.
- Positive impacts of lifestyle interventions were observed soon after implementation.
- Preventive effects were equally effective for both men and women.
- Lifestyle interventions were beneficial across all ethnic groups.

Based on RCT findings:

- The reduction in T2D incidence was consistent across all participants, regardless of baseline body mass index (BMI).
- No single intervention component was the most effective; those engaging in multiple lifestyle changes saw the greatest benefits.
- Lifestyle interventions delayed T2D progression by at least 5 years.
- Individuals with a high genetic predisposition to T2D significantly benefited from lifestyle interventions.

### AID: Arguably the Best Rx for T1DM

- Automated insulin delivery (AID) appears superior to other insulin treatment modalities with continuous glucose monitoring (CGM) and conventional insulin therapy.
- AID systems increase time-in-range across short-term and long-term interventions, benefiting both children and adults.
- AID is the fundamental right of everyone with type 1 diabetes (T1D).
- We all need to work together to make it a REALITY!



Dr Manoj Chawla  
Mumbai

### Confirming the Diagnosis of Type 1 Diabetes Mellitus: A Few Different Scenarios

- Diabetes is now perhaps the most common endocrine disorder in children and adolescents across the world.
- Several unique challenges: the differential diagnosis is wide, and the clinical course is likely to be more aggressive.
- Adolescent patients are prone to develop disease complications not only because of the long duration of hyperglycemia that they accumulate but also due to the inherently aggressive nature of the diseases and suboptimal control.
- Unfortunately, the diagnosis of diabetes is often delayed (except in T1D), leading to prolonged periods of uncontrolled hyperglycemia and consequent risk of acute and chronic complications, and misclassification occurs occasionally.
- Timely and accurate diagnosis, combined with regular follow-up and maintenance of optimal glycemic and risk factor control through judicious use of the available therapies, will ensure that these young people enjoy a long, fruitful, and complication-free life in spite of diabetes.



Dr Banshi Saboo  
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## Therapeutic Approach to DITY



**Dr Sanjay Agarwal**  
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- Type 1 diabetes mellitus was traditionally the most common form of diabetes in children and adolescents, but this trend is changing rapidly.
- There is a rising prevalence of youth-onset T2D worldwide, which parallels the obesity epidemic.
- The CDC estimates that over the next 40 years, the rate of childhood T2D could increase fourfold from the current situation.

- A WHO commission report highlights increasing obesity rates among Indians aged 5 to 19 years.
- Comprehensive care for youth with T2D should include patient education, emotional assessment, blood glucose monitoring, medical nutrition, stress management, support from family, peers, and medical professionals, and encouraging physical activity.
- Diabetic education is key to successful ambulatory care; initial education should be provided once the child and family stabilize.
- Important educational topics for diabetic care include insulin injection techniques, dose adjustments, insulin storage, diet planning, exercise, blood glucose testing, recognizing and managing hypoglycemia, and care during sick days.
- Regular review and reinforcement of diabetes education are essential for young patients.
- Management goals for youth with T2D focus on weight loss, increasing exercise capacity, normalizing glycemia, and controlling comorbidities like hypertension, dyslipidemia, nephropathy, and hepatic steatosis.
- The future of diabetes care involves increased physician awareness, newer technologies, support group initiatives, and personalized treatment approaches.

## How to Avoid Inertia in the Treatment with Noninsulin Glucose Lowering Drugs?

Type 2 diabetes is a progressive condition characterized by declining beta-cell function and worsening insulin resistance. Effective management requires timely intensification of therapy, yet clinical inertia—where health care providers delay advancing treatment—remains a significant barrier. Despite clear guidelines, many patients remain on oral antidiabetic drugs for too long, leading to suboptimal glycemic control and an increased risk of complications.



**Dr Jean Claude Mbanya**  
Cameroon

To overcome this inertia, a multifaceted approach is necessary.

- Early combination therapy should be implemented to address multiple pathophysiological defects, which can enhance treatment durability without increasing adverse effects.
- Shared decision-making between physicians and patients is crucial. This ensures that treatment choices align with the patient's needs and preferences. This process fosters collaboration and improves adherence to prescribed regimens.
- Structured education and support play a vital role in diabetes management. Providing patients with the necessary knowledge and skills to manage their condition can lead to better outcomes.
- Regular monitoring and ongoing review of treatment plans are essential to adapting to the patient's evolving needs and preventing the inertia that leads to poor outcomes.

## Clinical Impact of the Evolving Insulins and the Persisting Lacuna in Adoption



**Dr AG Unnikrishnan**  
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- 46.7% of patients with uncontrolled T2DM delay insulin therapy.
- Despite the innovations in insulins, the delay in insulinization, burden of daily injections, and needle phobia still persist.
- By reducing the frequency of injections, we can improve patient adherence and, ultimately, patient outcomes.

## Type 2 Diabetes: Primary Prevention in Real Life



**Dr Pablo Fischner**  
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In low- and middle-income countries (LMICs) with limited resources, diabetes prevention programs should focus on high-risk groups identified through locally validated, noninvasive screening tests like FINDRISC. Individuals with impaired fasting glucose may not respond as effectively to these interventions.

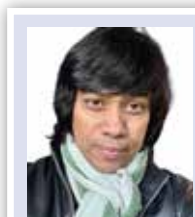
Primary prevention programs (3P) should be established before any screening initiatives. These programs can be delivered by health professionals, community workers, or through technology, with a preference for trained lifestyle coaches. Technology can help improve long-term adherence, and successful RCTs strategies should be adapted to local cultures.

Some of the common findings observed in real-world studies include:

- Most studies have achieved modest weight reduction (up to 4 kg), but aiming for a weight loss of at least 5 kg is ideal.
- Metformin is a common option but has limited success and only temporary effects.
- Primordial prevention of obesity is considered the best long-term solution.

## Type 1 Diabetes Index

The T1D Index is a pioneering tool that measures the human, public health, and economic impact of T1D globally and at the country level. It uniquely highlights the “missing people” and “healthy years lost” due to T1D. According to the Index, of India's average life expectancy of 73.5 years, only 1.2 years are spent on T1D treatment, while 4.5 years are lost to disability and complications. Overall, 44.8 healthy life years are lost due to T1D in India. This trend stems from factors such as lack of care, undiagnosed cases, limited testing, and pump/CGM usage in less than 1% of cases.



**Dr Partha Kar**  
UK

To address these challenges, the WJCF India Basic Care Pilot Trial was initiated in collaboration with the Indian government to establish pilot T1D clinics nationwide. As part of the project, researchers will create an implementation plan, set up eight pilot clinics, and foster further collaboration within the ecosystem.

The key objectives of this project are:

- Establishing basal-bolus therapy as the standard
- Promoting peer support as a standard practice
- Creating an information and education portal
- Developing a model of care based on evidence
- Integrating technology.

## How to Avoid Inertia in the Treatment with Insulin?



**Dr Nebojsa Lalic**  
Serbia

Managing T2D involves modifying its course through lifestyle changes, medications, and appropriate tools. Understanding the impact of diabetes on a patient's daily life is crucial, especially when selecting medications and recommending lifestyle changes. Clinical inertia often results in patients with T2D experiencing poor glycemic control. In such cases, insulin is a highly effective treatment option. Alternative insulin delivery methods, such as insulin pens, wearable mealtime insulin delivery patches, patch pumps, and conventional insulin pumps, can support addressing clinical inertia. Ideally, these methods should be integrated with advanced digital, patient-centered diabetes management systems to improve glycemic control and patient outcomes. Clinical studies have further confirmed these benefits.

To optimize diabetes management and reduce patient burden, people with T2D should be provided with simple solutions, straightforward treatment algorithms, dosing aids, and user-friendly insulin delivery devices.

Positive aspects of initiating insulin therapy include:

- For many patients with T2D, insulin can help restore residual beta-cell function.
- Maintain a positive attitude when discussing insulin therapy with patients.
- Initiate basal insulin therapy following current clinical guidelines.



## Background: Rationale, Pathophysiology, and Overview

Relying solely on fasting plasma glucose (FPG) and/or HbA1c to diagnose impaired glucose homeostasis (IGH) and T2D can result in missed opportunities for early detection and prevention. In contrast, 1-hour plasma glucose has emerged as a valuable tool due to its heightened sensitivity in detecting T2D. It is increasingly used in clinical practice to reduce the underdiagnosis of high-risk individuals. This approach improves the identification of individuals at high risk of micro- and macrovascular complications and mortality. 1-hour post-load hyperglycemia can result from a defective beta-cell function, impaired insulin action, accelerated gastric emptying, and increased glucose absorption in the proximal intestine.



**Dr AK Das**  
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### Association of 1-hour post-load plasma glucose with

#### Cardiovascular Risk Factors

- ▣ Increased viscosity
- ▣ Reduced vitamin D
- ▣ Increase in proinflammatory markers
- ▣ Increase in oxidative stress markers
- ▣ Reduction in molecules with anti-inflammatory properties

#### Target Organ Damage

- ▣ Impaired insulin-stimulated myocardial glucose metabolism
- ▣ Impaired myocardial mechano-energetic efficacy
- ▣ Decline in kidney function
- ▣ Increased albuminuria
- ▣ Diabetic retinopathy
- ▣ Increased liver enzyme

Based on studies such as the San Antonio Heart Study, Botnia Study, and CATAMERI, the following conclusions have been drawn:

- ▣ Plasma glucose concentration at 1 hour during the oral glucose tolerance test (OGTT) strongly predicts future risk of T2D.
- ▣ Higher 1-hour plasma glucose values may identify an intermediate condition between normal glucose tolerance (NGT) and impaired glucose tolerance, characterized by insulin resistance and reduced beta-cell sensitivity.
- ▣ Individuals with NGT but elevated 1-hour plasma glucose (NGT-1h-high) have a higher risk of developing diabetes than those with impaired fasting glucose or lower 1-hour plasma glucose (NGT-1h-low), likely due to decreased insulin sensitivity and impaired beta-cell function.

## Use of Digital Technology in Primary Prevention and Diabetes Care



**Dr A Ramachandran**  
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Studies on the use of digital technology in prevention include the Indian SMS Study, the Post-Trial Sustainability Study, the UK-India Collaboration Study, and research on scalability using mobile technology in prevention strategies. In diabetes care, digital technology encompasses SMS and apps. Based on various studies on digital technology in diabetes prevention, the following conclusions were made:

- ▣ Mobile technology has been utilized for primary prevention in India (2010-2013).
- ▣ Post-trial effects have shown positive outcomes.
- ▣ Studies on primary prevention with mobile technology in India and the UK have revealed ethnic differences.
- ▣ Mobile technology is scalable and could support national programs by reaching many people quickly.
- ▣ Mobile technology may be beneficial for a national mDiabetes program in India.
- ▣ Both SMS and apps can educate a large number of people.
- ▣ They have a significant beneficial effect on behavior.
- ▣ Apps are useful for routine diabetes management and are cost-effective.

For instance, the digital platform Diahome can be used for comprehensive diabetes management. This app offers several features, including online consultations, queries, and follow-ups.

**Key features of Diahome include:** Clinical support; partnerships with advanced diagnostic labs across India; access to an experienced team of senior diabetologists, dietitians, counselors; electronic medical records; and pharmacists.

## SGLT2 Inhibitors and Its Combinations as First-Line Agents

- ▣ Early initiation of sodium-glucose co-transporter-2 inhibitors (SGLT2i) offers significant advantages in achieving and maintaining glycemic control in patients with T2DM. It has a favorable tolerability profile and low risk of hypoglycemia.
- ▣ SGLT2i effectively reduces cardiovascular disorders and risk factors, controls blood glucose levels, reduces glycemic variability, and improves insulin resistance.
- ▣ SGLT2i is effective in patients with T2D and chronic kidney disease (CKD) and is considered cost-effective.
- ▣ SGLT2i can help prevent cardiovascular and renal events in patients without established cardiovascular disease (CVD) or CKD. Dapagliflozin provides substantial cardiovascular and renal benefits beyond glycemic control.
- ▣ SGLT2i and their combinations are safe for use in combination therapy with other oral hypoglycemic agents.
- ▣ SGLT2i offers multiple beneficial effects but also carries some risks; therefore, clinicians should assess a patient's bone density, cardiac profile, and hepatic and renal function before initiating SGLT2i therapy.



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## How to Avoid Inertia in the Treatment of Obesity?



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Globesity is on the rise, with over 1 billion people worldwide affected by obesity—650 million adults, 340 million adolescents, and 39 million children. The World Health Organization (WHO) estimates that by 2025, approximately 167 million people, both adults and children, will experience decreased health due to being overweight or obese. Obesity is not just a matter of weight but is better understood as an adiposity-based chronic disease.

Clinical inertia in obesity can be categorized into two types: Diagnostic inertia – Failure to diagnose the disease; Therapeutic inertia – Failure to advance or de-intensify therapy when appropriate.

In therapeutic inertia, medical nutrition therapy and physical activity are often used exclusively for treating obesity despite the availability of effective adjunctive interventions, including psychological support, pharmacological treatments, and bariatric surgery. The simplistic view of obesity as a self-imposed condition with an easy solution contributes to its mismanagement compared to other noncommunicable diseases. The overestimation of the efficacy of therapeutic interventions based solely on patient education and lifestyle modifications contributes to therapeutic inertia among health care professionals. It delays the adoption of more effective strategies.

**To overcome this inertia, several interventions can be helpful:** Patient education; motivating and supporting patients in self-management; adherence to medication and guidelines; personal feedback to HCPs; effective use of information system; and developing quality measures.

## The 1-hour Plasma Glucose Concept: Cardiovascular Outcome and Mortality

Prediabetes is associated with generalized microvascular dysfunction, and growing evidence shows that it can lead to microvascular damage similar to that of diabetes. Individuals with prediabetes face a significantly higher risk compared to those with normal glucose levels: their risk of all-cause mortality is seven times higher, and their risk of composite CVD is nine times higher. The 2009-2014 NHANES survey reported that 7.5% to 16% of people with prediabetes had peripheral neuropathy, while the 2017-2020 NHANES survey found a 9.7% prevalence of CKD among those with prediabetes. According to a 2018 study, 1-hour post-load glucose (1h-PG) is a useful predictor of retinopathy risk, comparable to 2-hour post-load glucose (2h-PG), and could be considered an alternative measurement during an OGTT. Increasing evidence also links impaired glucose tolerance, based on 1h-PG, with higher risks of all-cause mortality and CVD. Studies have shown that screening with 1h-PG is cost-effective and aids in early detection, potentially delaying progression to type 2 diabetes.



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## Two Goals in One Shot: Degludec in OP and IP



**Dr RK Singh**  
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Insulin degludec outperforms other basal insulins like glargine U100 due to its longer duration of action. While glargine U300, a concentrated form of glargine U100, extends its half-life, it sacrifices bioavailability, requiring higher doses for similar HbA1c control. Degludec provides superior glycemic control in type 1 diabetes, with less day-to-day variability than glargine U100. It also exhibits a flatter profile than glargine U300, though study results can vary. Clinically, degludec leads to lower overall, nocturnal, and severe hypoglycemia rates, as confirmed by RCTs like SWITCH-2 and DEVOTE. It offers unique dosing flexibility, allowing intervals of 8 to 40 hours between doses.

Real-world data, such as the CONFIRM study, supports degludec's significant hypoglycemia reduction compared to glargine U300. In hospital settings: Degludec achieves rapid glucose control within 24 hours without increasing hypoglycemia risks, with observational studies backing its inpatient efficacy. Despite its ultra-long duration, degludec has a fast onset, making it highly effective in hospitals. The EXPECT trial found it non-inferior to detemir regarding maternal and fetal outcomes in type 1 diabetes.

## Treatment of Obesity in People with Type 2 Diabetes: Will Bariatric Surgery Become Unnecessary?

In the management of obesity in individuals with type 2 diabetes (T2D), bariatric surgery has long been a key strategy for significant weight loss and reducing comorbidities like cardiovascular disease. However, advancements in anti-obesity medications (AOMs) are reshaping treatment approaches.



**Dr Juan Pablo Frias**  
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Medications like semaglutide and tirzepatide have demonstrated substantial weight loss outcomes comparable to surgical interventions. Studies reveal that greater weight loss is linked to improved health outcomes, including T2D remission, reduced cardiovascular risk, and enhanced metabolic health.

Semaglutide, a once-weekly GLP-1 receptor agonist, and tirzepatide, a dual GIP and GLP-1 receptor agonist, have been incredibly effective. They promote significant weight loss and improve glycemic control and cardiovascular risk factors, offering superior results over many nonsurgical methods.

While these advancements are promising, bariatric surgery will likely remain a crucial option for some patients. This is because: Patients require a variety of treatment options; some may not respond to or tolerate GLP-1 RA-based therapies; certain individuals may not be eligible for surgery or may experience insufficient weight loss or regain after surgery; a combination of both medical and surgical therapies may be needed in some cases

## Understanding Lipid Profile Minutely



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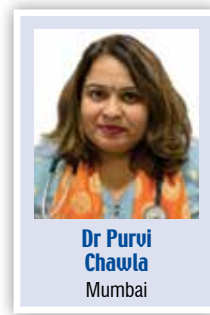
A comprehensive lipid profile includes several key parameters that offer detailed insights into cardiovascular risk. Low-density lipoprotein (LDL) cholesterol is often the primary focus due to its strong link to atherosclerosis and cardiovascular disease. However, LDL cholesterol (LDL-C) alone may not fully capture lipid-related risk. Non-HDL cholesterol provides a broader assessment of atherosclerotic risk, especially when LDL-C levels are very low, such as in secondary prevention. Apolipoprotein B (ApoB) is a more precise marker of cardiovascular risk. Since each atherogenic particle, including LDL, carries one ApoB molecule, ApoB reflects the total number of such particles in circulation.

Research from the FOURIER and IMPROVE-IT trials indicates that Non-HDL-C and ApoB are similarly associated with future myocardial infarction, with adjusted hazard ratios of 1.16 and 1.19, respectively. However, when adjusted for each other, ApoB appears to be a slightly better predictor of risk, though both markers provide similar predictive values due to their high correlation. Lipoprotein(a) [Lp(a)] is a genetically determined variant of LDL with additional proteins and elevated Lp(a) levels are linked to increased cardiovascular risk, independent of lifestyle factors. Thus, Lp(a) is important for evaluating genetic predispositions to heart disease.

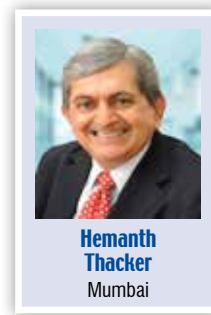
## Drug, Diet & Diabetes: A Discussion on Weight Centric Approach in T2DM



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**Dr Purvi Chawla**  
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**Hemanth Thacker**  
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### Importance of Weight Management:

- Weight loss is critical for improving metabolic parameters in type 2 diabetes.
- Even modest reductions in weight (3-7%) can significantly improve glycemia and cardiovascular risk factors.
- Sustained Weight loss of >10% usually confers greater benefits, such as disease-modifying effects and type 2 diabetes remission.
- Achieving and maintaining a healthy weight (Goal: >5-7%) is essential for long-term diabetes management and reducing the risk of complications.

### Nutritional Interventions:

- Diabetes-specific nutritional formulas play a key role in managing weight and controlling diabetes.
- These formulas provide balanced nutrition and can be used as meal replacements or supplements based on individual patient needs and goals.
- They are designed to offer a balanced mix of calories, modified carbohydrates (Low GI), proteins, and modified fats (monosaturated fatty acids), often fortified with essential vitamins and minerals.
- May reduce the need for additional insulin to maintain good glycemic control.

### Physical Activity Recommendations:

- The American Diabetes Association (ADA) recommends at least 150 minutes of moderate to vigorous aerobic activity per week, ideally spread across the week.
- For additional health benefits, exceeding 300 minutes per week is suggested.
- Physical activity should be a regular part of diabetes management to enhance overall health and support weight management.

Children and Adolescents—A minimum of 60 minutes of daily physical activity is recommended for those under 18 with type 1 or type 2 diabetes.

### Practical Tips:

- Simple activities like walking, climbing stairs, and using standing desks can contribute effectively to meeting physical activity goals.
- For those finding the 10,000 steps per day goal daunting, starting with 4,000 steps can be a manageable initial target.

### When to Consider Drugs or Surgery for Weight Management:

#### Pharmacotherapy:

- Lifestyle Interventions Alone Are Insufficient:** Consider medication if the patient does not achieve adequate weight loss with lifestyle changes alone, especially if bariatric surgery is not an option.
- BMI Considerations:** Pharmacotherapy is appropriate for patients with a BMI >30 kg/m<sup>2</sup> or between 27 and 29.9 kg/m<sup>2</sup> who have obesity-related comorbidities.
- Recommended Medications:** Options include liraglutide, semaglutide, and tirzepatide, which have shown efficacy in managing weight and improving metabolic health.

#### Surgery:

- Severe Clinical Obesity:** Consider bariatric surgery for patients with severe obesity, defined as a BMI ≥40 kg/m<sup>2</sup> or ≥35 kg/m<sup>2</sup> with obesity-related comorbidities.
- Ineffectiveness of Conventional Methods:** Surgery may be suitable for individuals who have not successfully lost weight through conventional methods, such as diet and exercise.
- High Risk for Obesity-Related Complications:** Surgery is a consideration for those at elevated risk for severe health issues or death related to obesity.



## Detection of Prediabetes and Diagnosis of Type 2 Diabetes with 1-Hour v/s Fasting Glucose and 2-Hour Glucose

Various methods to measure glycemia include 2-hour plasma glucose, FPG, and HbA1c. However, studies have shown that 1-hour plasma glucose during the OGTT strongly correlates with beta-cell function and outperforms other models and indexes in predicting the risk of T2D. It has been observed that a 1-hour cut-off point of 155 mg/dL effectively stratifies individuals into high- and low-risk categories for T2D development.



Additional benefits of 1-hour plasma glucose can be summarized as follows:

- ▣ 1-hour plasma glucose is a useful and cost-effective tool for screening undetected prediabetes and T2D.
- ▣ Lifestyle interventions are more effective in reducing T2D progression in individuals with elevated post-challenge glucose detected by 1-hour plasma glucose.
- ▣ It allows for earlier detection of elevated postprandial glucose and timely intervention.
- ▣ A 1-hour plasma glucose level of  $\geq 11.6$  mmol/L or 12.0 mmol/L is the optimal threshold for diagnosing T2D, while  $\geq 8.6$  mmol/L indicates prediabetes.
- ▣ Using 1-hour plasma glucose as the primary measurement simplifies the diagnostic process and reduces confusion with current criteria.
- ▣ Shortening the OGTT from 2 hours to 1 hour is more practical and clinically acceptable.

## Managing Type 1 Diabetes Mellitus in Limited Resource Settings



Indian T1DM patients face many challenges, including a lack of free supply of insulin, glucose measuring devices, blood glucose test strips, and other consumables, lack of structured diabetes education, lack of psychosocial support, and inadequately trained health care workers. We embarked upon developing, implementing, and evaluating a health program for the management of T1DM in the state of West Bengal.

The program aims to provide comprehensive health care services (detection, management of disease and complications, appropriate referral, and even rehabilitation) for T1DM patients, utilizing the existing health care delivery system and building up a registry of T1DM patients for careful monitoring and follow-up of care services.

The highlights of the significant results revealed are:

- ▣ The HbA1c fasting and postprandial glycemia came down.
- ▣ Over a period of 1-year, diabetic ketoacidosis rate, overall hypoglycemia rates, infections, hospitalizations, diabetic neuropathy, and foot ulcers have come down to zero.
- ▣ Clinical and psychological well-being, diabetes and health-related quality of life, and family life have all improved.
- ▣ Health expenditure has also reduced.

## Redefining Obesity Management with Contemporary Anti-Obesity Medications

- ▣ The pillars of obesity management include lifestyle recommendations (medical nutrition therapy, physical activity), behavioral interventions (for achieving 5% weight loss through behavior modification, cognitive behavioral therapy, and counseling), pharmacotherapy (for 5%-15% weight loss), and endoscopic or surgical interventions (12%-30% weight loss).
- ▣ Endoscopic procedures can result in 12%-20% weight loss, while bariatric surgery can lead to 20%-30% weight loss.
- ▣ Lifestyle changes are foundational for managing any chronic disease, including obesity; however, similar to hypertension or diabetes, pharmacotherapy is needed to address the biological aspects of obesity and should be part of a long-term treatment strategy.
- ▣ Effective pharmacotherapies for obesity should combine weight loss efficacy, long-term safety, weight loss maintenance, and the reduction of complications.
- ▣ GLP-1 RA have demonstrated robust clinical evidence as anti-obesity medications to meet the current unmet needs in obesity care.
- ▣ Pharmacological options for weight management available in India include orlistat, which works by causing energy wastage, and semaglutide 2.4 mg, which reduces appetite.
- ▣ Semaglutide is the latest anti-obesity medication in the arsenal of obesity management, with evidence showing up to 17% weight reduction in the STEP trials.



## Overview of Algorithms in Clinical Practice

The BMI-centric approach to diagnosing and managing obesity has limitations, so it is recommended to use both BMI and waist circumference (WC). A complication-centric approach to obesity management can help personalize care, optimize patient outcomes, and improve the cost-effectiveness of interventions.



Pharmacotherapy is crucial for weight loss, long-term weight maintenance, weight regain prevention, and protection of end organs. The proposed algorithm assists in comprehensive assessment and appropriate treatment selection in primary care settings.

- ▣ Step 1: Anthropometric Evaluation – During the initial visit, measure height, weight, BMI, WC, hip circumference, waist-to-height ratio (WHtR), and waist-to-hip ratio (WHR).
- ▣ Step 2: Clinical Evaluation – Assess comorbidities and physiological and psychological impacts, conduct endocrine evaluations if necessary, and consider socioeconomic status.
- ▣ Step 3: Risk Stratification and Management – Categorize patients as “normal weight” or “overweight/obesity” based on anthropometric data. Manage normal-weight patients with preventive care. For overweight/obesity, use the Edmonton Obesity Staging System (EOSS) for clinical stage assessment. Lifestyle modifications apply to all stages. Initiate pharmacotherapy for stage 1 patients with BMI  $\geq 27$  kg/m<sup>2</sup> if lifestyle interventions are ineffective and for stages 2 and above (BMI  $\geq 25$  with comorbidities). Bariatric surgery may be considered for BMI  $\geq 32.5$  kg/m<sup>2</sup> in stage 2 and for stages 3 and 4.
- ▣ Step 4: Follow-up – Schedule follow-ups at 2, 3, or 6 months, tailored by stage and treatment approach. Adjust the plan based on outcomes, with long-term follow-up needed for all patients.

## Type 1 Diabetes Prevention: Wishful Thinking or Reality?

Type 1 diabetes progresses through distinct stages. It begins with a genetic predisposition, where no autoimmunity is detectable, followed by immune activation marked by the appearance of islet cell autoantibodies. As the disease advances, beta cell dysfunction occurs, leading to overt hyperglycemia and the eventual clinical diagnosis of diabetes. Nonlinear beta cell loss is a hallmark of T1D, with immunological phases classified into immune activation, acceleration, and chronicity. The “acceleration phase” represents a therapeutic window for intervention.



Primary prevention strategies focus on modulating the early immune response through dietary modifications, vitamin D supplementation, and antigen-specific oral insulin therapy to delay the onset of autoimmunity.

Secondary prevention targets individuals with existing islet autoantibodies, aiming to prevent progression to clinical diabetes by inducing immune tolerance or modulating autoimmune responses with agents like nicotinamide, insulin, or potent immunotherapies. Tertiary prevention focuses on recent-onset cases, aiming to preserve residual beta cell function and delay disease progression using immunomodulatory therapies.

For example, anti-CD3 monoclonal antibodies like teplizumab modulate T-cell activity to protect beta cells. Clinical trials show that a single course of anti-CD3 therapy can significantly slow the decline in C-peptide levels, particularly when administered early. These strategies and ongoing research promise to improve outcomes, reduce complications, and enhance the quality of life for individuals with T1D.

## Sarcopenia in Young Adults

- Sarcopenia and poor muscle quality are associated with severe obesity in young and middle-aged adults.
- Even in young adults, changes are observed in all parameters related to strength, muscle mass, and muscle function, negatively impacting these areas.
- Possible etiologies of sarcopenia in young adults include metabolic syndrome, physical inactivity, inadequate nutrition, inherent and perinatal factors, vitamin D deficiency, endocrinopathy, gut microbiota imbalance, neuromuscular diseases, organ failure, malignancy, and other inflammatory disorders.
- The diagnostic approach to sarcopenia includes screening with the SARC-F questionnaire, assessing muscle strength through grip strength and chair stand tests, confirming muscle mass with MRI, CT, DXA, or BIA, and evaluating severity.
- Muscle quality is an important risk factor for functional disability and should be considered in sarcopenia assessments.
- A study that evaluated 108 volunteers of both sexes with grade II to III obesity (mean age 43.1 years); found that 2% had dynapenia, and 33% had low leg muscle strength.
- The prevalence of sarcopenia varied between 11.1% and 13.9%, corresponding to low muscle quantity and low muscle quality, respectively, with a higher impact on middle-aged women.
- Treatment for sarcopenia involves sufficient protein and energy intake, branched-chain amino acids, vitamin D and calcium supplementation, omega-3 fatty acids, antidiabetic drugs, and physical exercise.
- There is a need to standardize criteria for assessing sarcopenia in young adults with severe obesity, as prevalence rates vary widely.



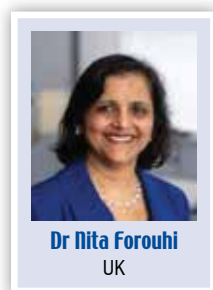
**Dr Rakesh Sahay**  
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- Thiazolidinediones (TZDs), like pioglitazone, prevent the progression from impaired glucose tolerance to T2DM.
- The 2023 ADA & EASD Position Statement noted that pioglitazone showed a modest benefit on cardiovascular events as a secondary outcome in a large trial involving patients with overt macrovascular disease.
- The PROactive study investigated the effects of pioglitazone (45 mg/day) on macrovascular outcomes in 5,238 patients with T2DM and pre-existing CVD.
- In patients with a previous myocardial infarction, pioglitazone significantly reduced the risk of a subsequent myocardial infarction by 28% and acute coronary syndrome by 38%. In patients with a previous stroke, pioglitazone reduced the risk of a second stroke by 48%.
- Pioglitazone is the only available agent that effectively treats insulin resistance and preserves beta-cells, offering cardiovascular protection through various mechanisms, including increasing HDL levels.
- Pioglitazone benefits liver histology by improving inflammation, ballooning, necrosis, steatosis, and fibrosis.
- A recent study involving over 600,000 T2DM patients showed that pioglitazone use significantly decreased the risk of liver cancer, with stronger effects at higher dosages and longer treatment durations. It was also associated with a decreased risk of colorectal cancer in patients using TZDs compared to those not using TZDs.
- Favorable effects of pioglitazone include reducing insulin resistance, preserving beta-cells, durable glucose lowering, improving lipid profiles, anti-inflammatory effects, potential reduction in cardiovascular events, and improvement in nonalcoholic fatty liver disease.
- Unfavorable effects of pioglitazone include weight gain, congestive heart failure, bone fractures, possible bladder cancer, and macular edema.
- Minimizing the side effects of PPAR- $\gamma$  agonists can be achieved by using lower doses, avoiding use with insulin in high-risk patients, avoiding use in those at high-risk for fractures, reducing salt and calorie intake, and avoiding calcium channel blockers.
- The combination of pioglitazone with metformin and SGLT2 inhibitors or glucagon-like peptide 1 receptor agonists (GLP-1RAs) can be the best approach for managing T2DM.



**Dr Mangesh Tiwaskar**  
Mumbai

## Hot on the Plate: Low Carbohydrate Diets and Type 2 Diabetes – Good, Bad, or Balanced?



**Dr Nita Forouhi**  
UK

It has been observed that there is a dose-response relationship between carbohydrate intake and the risk of T2D. In Asian populations, a sharp linear increase in T2D risk is seen when carbohydrate intake exceeds 70% of total energy.

Therefore, based on several studies, clinicians recommend a low-carbohydrate diet as an effective short-term option (up to 6 months) for improving glycemic control in overweight or obese adults with T2D. A low-carb diet can help balance T2D management.

### Key points include:

- Low-carb diets are effective in short-term T2D management and weight control.
- Long-term effects require more research, as some epidemiological evidence suggests potential adverse health impacts.
- For the general population, a carbohydrate intake of around 45% to 50% of total energy appears optimal.
- In populations with very high carbohydrate intake, prioritizing quality and type of carbohydrates is important.
- Focusing solely on carbohydrate quality is insufficient; food sources matter—there are both good and bad carbohydrate sources.
- The replacement nutrients also matter, including choosing healthy protein and fat sources.
- Dietary advice should consider personal dietary preferences, health literacy, available resources, food access, cost, and support for adherence.
- Government support for changes in the food environment is also essential.

## The Curious Case of Painful Diabetic Peripheral Neuropathy

A 36-year-old male with type 3c diabetes for 4 years presented with severe pain, burning, shocks, and pricking sensations for 6 weeks. The present illness was subacute in onset and slowly progressive, with difficulty getting up from a squatting position, buckling of knees while walking, and difficulty climbing stairs.

The patient had a flail-type weakness with no difficulty gripping footwear, mixing food, or lifting the hand above the head (e.g., combing hair). There were no signs of muscle thinning or twitching, no intake of naturopathic or alternative medicines, no diurnal variation, cognitive issues, or cranial nerve dysfunction.

The patient reported bilateral numbness in the feet and frequent pins and needles sensations for the past few years, with no other sensory complaints. There was not any history of incoordination, involuntary movements, abnormal sweating, dryness of skin, or dizziness upon standing. Examination revealed absent monofilament sensations, vibration perception threshold of 30 mV, indicating neuropathy, ankle-brachial index of 1.0 bilaterally, and HbA1c of 10.5%. The patient was diagnosed with painful diabetic peripheral neuropathy (DPN).

### Key points to remember about DPN:

- DPN affects about 50% of individuals with diabetes; half of these individuals experience pain as a symptom.
- It is a common reason for seeking medical aid and is a significant cause of morbidity and mortality.
- A “clinically relevant” response is defined as a 30% to 49% reduction in pain.
- A “robust” response is defined as a reduction of  $\geq 50\%$  in pain, with significant benefits in sleep, fatigue, depression, quality of life, function, and work.
- Efficacy of treatment should be assessed only after 2 to 4 weeks using an adequate dose.
- Choosing the appropriate treatment option for pain relief is challenging and should be guided by patient-specific factors, utilizing a multidisciplinary team approach to tailor care to each individual’s needs.



**Dr Ashu Rastogi**  
Chandigarh



## Greater Mortality with Low-Density Lipoprotein Cholesterol on Target in Adults with Diabetes not at High Risk of Cardiovascular Disease: The ELSA-Brasil Study



Lipid-lowering therapy targeting low-density lipoprotein cholesterol (LDL-C) levels below 70 mg/dL is recommended in individuals with diabetes who are not at high-risk for CVD. However, evidence from lipid-lowering trials remains inconclusive regarding all-cause mortality, and real-world studies suggest increased mortality at lower LDL-C levels. Consequently, a study was designed to assess the relationship between LDL-C levels and all-cause mortality among participants in the the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) study who had diabetes but were not considered at high cardiovascular risk.

The study included 2,098 participants from the ELSA-Brasil. These participants self-reported diabetes at baseline and had no known CVD, with a 10-year CVD risk of less than 20%. Measurements accounted for diabetes (ascertained via self-report or medication use), mortality (determined from annual follow-ups), fragility index, and phenotypic characteristics such as unintentional weight loss, exhaustion, low physical activity, slow gait speed, and weak grip strength. The findings showed that lower LDL-C levels or treatment groups were associated with higher mortality risks compared to the reference group with LDL-C levels between 100 and 160 mg/dL. Specifically, the hazard ratios (HR) for death were 1.49 for LDL-C levels between 70 and 99 mg/dL, 2.81 for levels between 55 and 69 mg/dL, and 2.69 for levels below 55 mg/dL. In contrast, the group with LDL-C levels of 130-159 mg/dL had a HR for death of 0.96.

After adjusting for statistical factors such as age, statin use, and sex, the overall risk ratios for mortality in the lower LDL-C (<100 mg/dL) group were found to be 1.67, 1.18, 1.34, and 1.49 for men and 2.01 for women. When adjusted for different causes of death, the highest HR was associated with cancer (2.55). After 5 years of follow-up, excluding deaths, the adjusted HR for fragility and phenotype were reported as 2.01 and 1.93, respectively, in the treatment arm. Based on these findings, the study concluded that in individuals with diabetes who are not at high CVD risk, mortality increases with lower LDL-C levels.

This conclusion can be attributed to: Recent declines in CVD mortality. Increased cancer risk among individuals with diabetes.

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## Clinical Management of CaReMe Syndrome: Relooking Through AHA Scientific Statement



Approaches and treatments for achieving the goals in CaReMe Stage 4.

### Heart Failure:

- Focus on the four pillars of management: Beta-blockers, angiotensin receptor/neprilysin inhibition, mineralocorticoid receptor antagonists, and SGLT2 inhibitors in heart failure with reduced ejection fraction (HFrEF) to improve outcomes/mortality.

### ASCVD

- Use of aspirin or P2Y12 inhibitor and high-intensity statins for patients with atherosclerotic cardiovascular disease (ASCVD).
- Additional LDL-lowering therapy as needed according to LDL-C levels, LDL-C reduction goals, and the presence of accompanying high-risk features.

### Obesity

- Patient-centered and nonjudgmental approach to initiate weight loss discussion.
- Weight loss through lifestyle modification to improve risk factor control among patients with obesity and ASCVD.
- Lifestyle modification, including exercise training to improve functional status in HFpEF.
- Incretin analogs (GLP-1/GLP-1 RAs) induce >15% weight loss, improve quality of life, and reduce recurrent CVD events.
- Bariatric surgery reduces recurrent CVD events and mortality by >50% in individuals with prior ASCVD and HF.

### Hypertriglyceridemia

- Statins modestly reduce triglycerides (10%-30%) and lower ASCVD risk.
- In those with hypertriglyceridemia and CVD, icosapent ethyl reduces CVD events and mortality and may be considered after statin therapy.

### Hypertension

- Blood pressure control reduces recurrent CVD events and mortality; goal, 130/80 mmHg.
- ACE/ARB in CVD with CKD or diabetes.
- Hydralazine/isosorbide after 4 pillars of GDMT in patients after HFpEF.

### Diabetes

- Lifestyle modification improves risk factor control and quality of life.
- In those with HF, SGLT2 inhibitors quality of life, reduces hospitalization, mortality risk, and worsening kidney function.
- GLP-1 RA and SGLT2 inhibitors reduce the risk for major adverse cardiovascular outcomes in patients with T2D and ASCVD.
- GLP-1 RA have more potent effects on weight and HbA1c and reduce MACE.
- In patients with ASCVD, adding LDL-lowering therapies beyond maximally tolerated statin therapy may have a more powerful clinical effect.

Dapagliflozin helps in saving patient lives suffering from CaReMe syndrome with robust clinical trial data and guideline recommendations.

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