### The Weight of the Matter in Diabetes Care

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#### **A**BSTRACT

The weight of the matter in diabetes care challenges the traditional glucose-centric model of diabetes management and argues for a paradigm shift toward prioritizing weight—specifically fat reduction—as the central lever in achieving metabolic health. Drawing insights from landmark trials such as SURMOUNT and Diabetes Remission Clinical Trial (DiRECT), as well as real-world Indian experience with agents like oral semaglutide, the article emphasizes that visceral adiposity is a root cause driving insulin resistance, beta-cell dysfunction, and multiorgan complications. Addressing weight early can lead to improved glycemic control, cardiorenal protection, and even disease remission—outcomes that far exceed glucose lowering alone. In the Indian context, where the "thin–fat" phenotype and central obesity present unique challenges, this weight-first approach demands culturally sensitive strategies and redefined success metrics beyond body mass index (BMI) or hemoglobin A1c (HbA1c). With the advent of incretin-based therapies, clinicians now have the tools to treat upstream rather than manage symptoms downstream. The piece calls for a unified therapeutic strategy that targets excess adiposity to deliver both glycemic and vascular legacy benefits—reframing weight not merely as a number but as a powerful determinant of risk, response, and recovery.

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## THE WEIGHT OF THE MATTER IN DIABETES CARE: PRIORITIZING WHAT TRULY MATTERS

At a recent national diabetes conference, a thought-provoking debate took place on a pressing question: what should be the main focus in managing diabetes—glucose, weight, or vascular protection? The discussion featured leading experts from across the country, and the final consensus—both from the panel and the audience—favored weight as the most crucial factor.

This piece builds on those arguments, aiming to reflect the clinical reality many of us face. It suggests that by giving timely attention to weight management—especially fat reduction—we may not only achieve better sugar control but also improve long-term heart, kidney, and liver health.

# FROM GLUCOSE NUMBERS TO FAT LOSS: A SHIFT IN THINKING

For years, diabetes control meant managing sugar levels—hemoglobin A1c (HbA1c), fasting, and postmeal glucose. That approach still matters, but it no longer tells the full story. Increasingly, we are learning that excess fat—especially around the liver and pancreas—is what drives insulin resistance and disease progression. The underlying issues go beyond sugar to include adiposity, low-grade inflammation, and early beta-cell stress.<sup>1</sup> This change in understanding has

been reinforced by newer evidence. The SURMOUNT-1 and SURMOUNT-2 trials, which studied tirzepatide, a glucose-dependent insulinotropic polypeptide (GIP)/glucagon-like peptide-1 (GLP-1) dual agonist, showed that people with obesity—even without diabetes—experienced up to 22.5% weight loss and marked health improvements. More strikingly, among those with prediabetes, over 95% returned to normal glucose levels, suggesting that remission is possible if weight is addressed early.<sup>2</sup>

This is not about choosing one number over another. It is about facing the real cause and treating it before complications take root.

## WHY WEIGHT WINS: THE CLINICAL CASCADE

#### **Glucose Control**

Losing 10–15% of body weight can set off a positive chain reaction.<sup>2</sup> It reduces liver glucose production, improves insulin sensitivity, and helps restore beta-cell function. In early diabetes, this shift may work as well as—or sometimes better than—starting medication. In the SURMOUNT-1 trial, participants who lost ≥15% of their weight showed meaningful HbA1c improvements, even if they were not diabetic to begin with.

#### Cardiorenal Benefits

Obesity is no longer just a background risk factor—it is a direct contributor to heart and kidney disease.<sup>2</sup> Medications like tirzepatide, which help with weight loss, also lower

inflammation, improve blood vessel health, and protect multiple organs. This broader benefit makes them more than just glucoselowering agents.

#### **Remission is Realistic**

Several studies now suggest that with enough weight loss, diabetes remission is possible—especially in the first few years after diagnosis. In SURMOUNT-1, over 95% of people with prediabetes returned to normal glucose levels. Results from calorie restriction trials like Diabetes Remission Clinical Trial (DIRECT) and real-world programs like the Indian Diabetes Prevention and Remission Program with Calorie Restriction (I-DAPA CR) support this idea: targeting weight early may help reverse the disease altogether.

"Weight is the lever. When you shift it, everything downstream—glucose, kidneys, heart, liver—aligns."

The time has come to move away from chasing sugar numbers alone. A weight-first approach addresses the root so the rest can follow.

### WEIGHT AS THE COMMON DENOMINATOR

When we look at the triad—glucose, weight, and vascular protection—it is clear that weight sits at the root.<sup>4</sup> Glycemia often shows up late in the course of metabolic dysfunction, while adiposity, especially visceral fat, is an early and active driver of the disease process. Addressing weight early can lead to wide-ranging benefits: better insulin action, preserved beta-cell function, and improvements in blood pressure, lipid levels, and inflammatory markers. It helps us tackle several problems at once—without treating them in isolation.

Glycemic legacy produced by conventional hypoglycemic agents or vascular legacy produced by antihypertensives can be achieved by agents like glucagon-like peptide-1 receptor agonist (GLP-1RAs)

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or GIP/GLP-1 dual agonism, which target body weight, especially visceral/ectopic adiposity, over and beyond reduction in subcutaneous adiposity, thus reducing the ongoing inflammation and endothelial damage.

In everyday clinical practice, weight tends to be the first domino. Once we manage it well, sugar control and vascular health often improve alongside. This does not mean glucose or cardiovascular care takes a backseat, but it does suggest that weight may be the one thread that ties them all together.

Put simply, weight is not just another number; it is the multiplier.

### Beyond Glucose: Reframing The Indian Weight Narrative

In India, the challenge is not just about how much weight is gained; it is also about where and how fat is stored.<sup>4</sup> Many patients appear lean on the outside but carry high levels of visceral fat and develop insulin resistance early. This "thin-fat" phenotype calls for a shift in thinking, one that moves beyond conventional body mass index (BMI) cutoffs and embraces more culturally and biologically relevant measures. Medications like tirzepatide show promise, but alongside pharmacological tools, personalized lifestyle strategies—such as bite counting, mindful eating, meal sequencing, and early satiety cues—can play a major role, especially when rooted in Indian habits and food patterns.

Doctors may need to help patients redefine success, not just in terms of blood sugar levels, but in terms of sustainable fat loss that delivers long-term health gains. The revised Indian guidelines on obesity now highlight that central adiposity in Asian Indians carries a higher metabolic risk, even at lower BMIs. This calls for early, tailored

interventions that go beyond generic targets and speak to the patient's unique risk profile.

## REAL-WORLD ECHOES: ORAL SEMAGLUTIDE IN INDIAN PRACTICE

This shift toward weight-first strategies is not just theoretical; it is being reflected in real-world Indian practice as well. Our clinical experience with oral semaglutide mirrors outcomes seen in the PIONEER study series, demonstrating both meaningful glycemic control and sustained weight loss. Among Indian patients with early diabetes or metabolic syndrome, these effects are translating into tangible clinical gains. Oral agents with weight benefits may soon play a more prominent role in practical remission strategies, complementing newer GLP-1 receptor agonists and dual incretin therapies.

### FINAL WORD: THE WEIGHT OF THE MATTER IN DIABETES CARE

This shift in thinking is more than academic—it reflects the lived reality of clinicians managing a complex and progressive disease. It reminds us that while sugar levels deserve attention, weight remains the upstream lever. Though microvascular complications are linked to the duration of dysglycemia, the macrovascular clock starts ticking even before diabetes is diagnosed. This means we must act upstream—targeting excess adiposity early to prevent both micro- and macrovascular damage downstream.

Rather than addressing each cardiometabolic complication in isolation, targeting weight—particularly visceral and ectopic adiposity—offers a unified therapeutic pathway. Agents such as GLP-1 receptor agonists and dual GIP/

GLP-1 agonists do not just lower glucose or blood pressure—they address the root metabolic disturbance. In doing so, they replicate the glycemic legacy of older hypoglycemics and the vascular legacy of antihypertensives—but by acting earlier and deeper through anti-inflammatory and endothelial-restorative pathways.

Diabetes care must evolve from symptomatic control to root-cause targeting. We now have the evidence, the tools, and the clinical insight to shift gears.

Because in the end, weight does not just measure mass—it predicts risk, reveals opportunity, and signals a chance at reversal. By acting on it early, we may finally tip the balance—not just toward control but toward long-term healing and remission.

In diabetes, chasing sugar may win the battle, but losing weight wins the war.

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