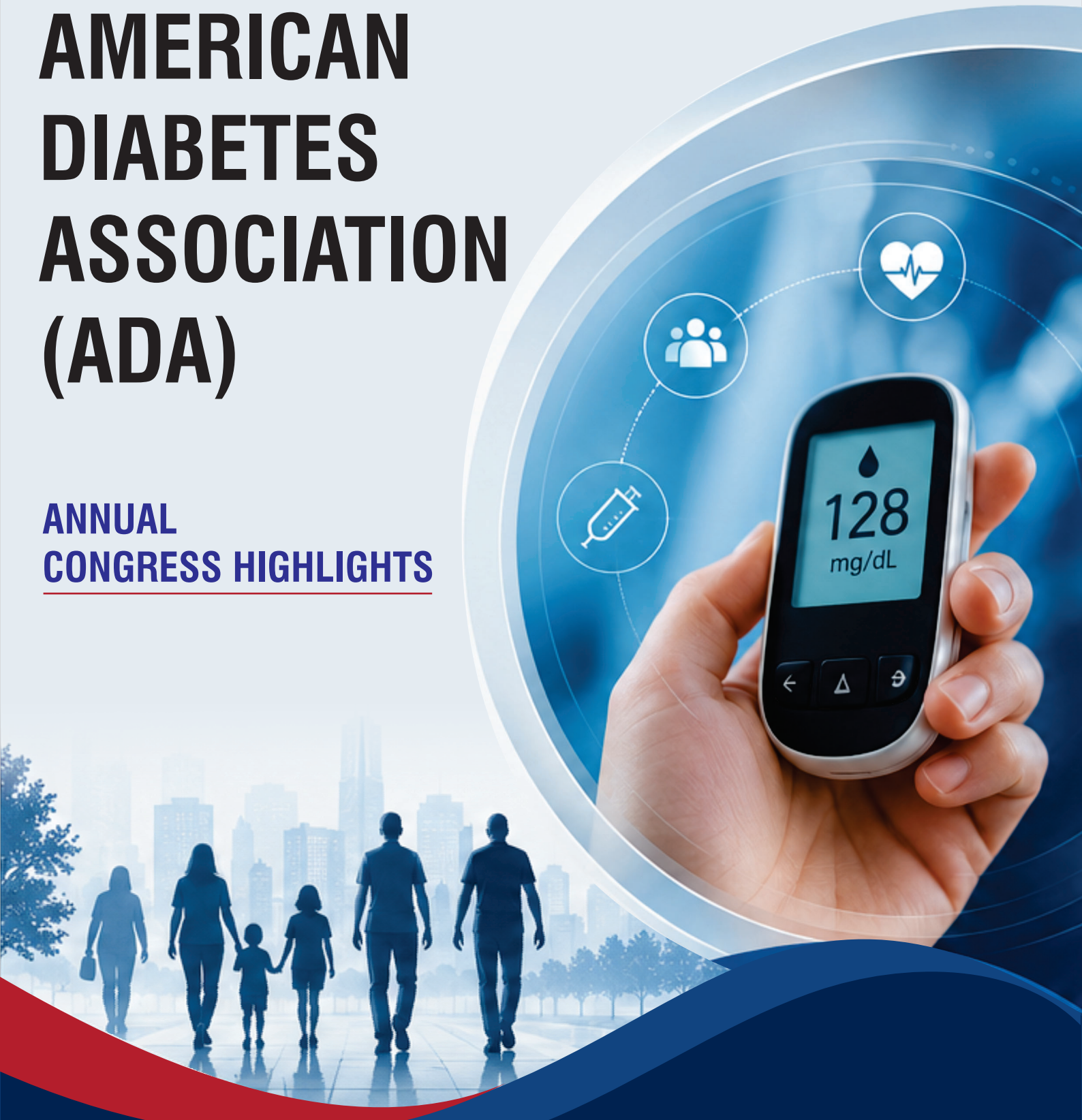
AMERICAN DIABETES ASSOCIATION (ADA)

ANNUAL CONGRESS HIGHLIGHTS



86th Scientific Sessions

June 5-8, 2026
New Orleans

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A. Complications-Hypoglycemia

Rural–Urban Disparities in Post-Crisis Follow-Up Care in Diabetic Adults: A Retrospective Cohort Study

Herges J et al.

Introduction and Objective:

- To evaluate rural–urban differences in outpatient follow-up with primary care physicians (PCPs) and endocrinologists among adults with diabetes following an emergency department (ED) visit or hospitalization for hyperglycemic or hypoglycemic crisis.

Methods:

- Retrospective cohort study utilizing electronic health record (EHR) data from a large integrated U.S. Upper Midwest healthcare system (January 1, 2020 – October 1, 2024).
- Adults (≥18 years) with diabetes presenting with a primary diagnosis of hypo- or hyperglycemic crisis were stratified by rurality (rural: population <20,000 vs. non-rural/urban).
- PCP and endocrinology follow-up rates were quantified at 30, 60, and 90 days post-discharge.

Results:

- A total of 1,258 individuals were identified (rural: 23.1%, n=291; urban: 76.9%, n=967).
- At 30 days post-discharge, rural residents demonstrated significantly lower PCP visit rates (39.5% vs. 49.3%, P=0.003) and endocrinology visit rates (8.6% vs. 16.3%, P=0.001) compared to urban counterparts.
- This rural deficit in follow-up persisted at 60 and 90 days.

CONCLUSION:

- **Post-crisis follow-up — critical for preventing recurrence — is significantly lower in rural diabetic adults versus urban counterparts for both PCP and endocrinology care.**
- **Suboptimal utilization was evident even in urban populations.**
- **Targeted interventions including telehealth, team-based care models, and population health tools are urgently warranted, particularly in rural settings.**

B.Complications-Kidney-Clinical and Translational Research

High-Dose Semaglutide Preserves Renal Function in Non-Diabetic Obesity: Evidence from the STEP UP Trial

Rossing P, et al.

Introduction and Objective:

- Post hoc analysis of STEP UP trial evaluating renal function and hsCRP changes from baseline to week 72 in obesity (without diabetes) with semaglutide (sema) 7.2 mg, sema 2.4 mg, or placebo (pbo).

Methods:

- eGFR calculated via CKD-EPI 2021 creatinine (eGFRcre) and creatinine-cystatin C (eGFRcre-cys). Outcomes: eGFRcreeGFRcre-cys, category shifts (<60, 60–<90, ≥90 mL/min/1.73 m^2), and hsCRP at week 72 (on-treatment data).

Results:

- n = 1,005 (sema 7.2 mg), 201 (sema 2.4 mg), 201 (pbo).
- Baseline eGFRcre ≥90 mL/min/1.73 m^2: 67.3%, 70.6%, 69.7%, respectively.
- Estimated outcomes are described in Table 1.

Table 1: Key Efficacy Outcomes at Week 72

Outcome	Sema 7.2 mg vs Pbo	Sema 2.4 mg vs Pbo
$eGFR_{cre}$ ETD (mL/min/1.73 m^2)	−0.40 (−2.01, 1.21); p=0.83	0.46 (−1.71, 2.62); p=0.87
$eGFR_{cre\text{-}cys}$ ETD (mL/min/1.73 m^2)	3.21 (1.08, 5.33); **p=0.001**	3.42 (1.63, 5.00); **p<0.001**
hsCRP ETR vs pbo	0.42 (0.36, 0.50); **p<0.001**	0.47 (0.38, 0.58); **p<0.001**

ETD = estimated treatment difference; ETR = estimated treatment ratio

- eGFRcre was comparable across groups; eGFRcre-cys and hsCRP improved significantly with both sema doses vs pbo .

CONCLUSION:

Sema 7.2 mg and 2.4 mg significantly improved eGFRcre-cys (weight-loss independent) and reduced hsCRP vs pbo, demonstrating preserved renal function and reduced systemic inflammation in non-diabetic obesity.

CKD Screening Rates and GDMT Utilization in T2D: A Retrospective Analysis

Harrigfeld S, et al.

Introduction:

- Guideline-directed medical therapy (GDMT) shows improvement in type 2 diabetes (T2D) complicated by chronic kidney disease (CKD), yet remains underutilized, potentially attributable to suboptimal CKD screening rates in clinical practice.

Objective:

- To evaluate eGFR (estimated glomerular filtration rate) and UACR (urine albumin-to-creatinine ratio) screening rates and GDMT prescribing patterns in T2D patients, stratified by CKD status.

Methods:

- Retrospective analysis of an electronic health record (EHR)-based T2D registry (n=34,471) at a large urban tertiary care center.
- Inclusion criteria: active patients with a completed office visit and recorded SBP between 02/27/2023 and 02/26/2026.
- CKD was defined by ICD-10 code or active EHR problem list diagnosis.
- Rates of eGFR and UACR screening and GDMT use were described and stratified by CKD status.

Results:

- Mean age: 59 years; female: 55.8%; mean SBP: 133 mmHg; mean A1C: 7.2%; CKD prevalence: 24.7%.
- Both eGFR and UACR screening rates were suboptimal in T2D patients regardless of CKD status (Figures 1a–1c).
- eGFR: 1. T2D without CKD (52.5%); 2. T2D with CKD (65.7%)
- UACR: 1. T2D without CKD (26.6%); 2. T2D with CKD (42.1%)
- All T2D: eGFR <60 mL/min/1.73m^2 (14.7%), UACR >30 mg/g (12.8%), 6.7% met criteria for high-risk CKD (CKD and UACR >30)
- Across all GDMT classes (RASi, SGLT2i, GLP-1RA, nsMRA), prescribing rates in CKD patients remained below 60%.

Figure 1a. Rate of eGFR and UACR measurement in people with T2D with and without CKD

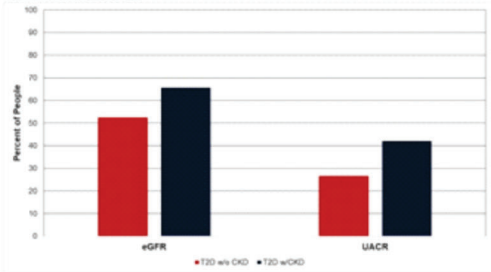


Figure 1b. Rate of GDMT prescribing among people with T2D

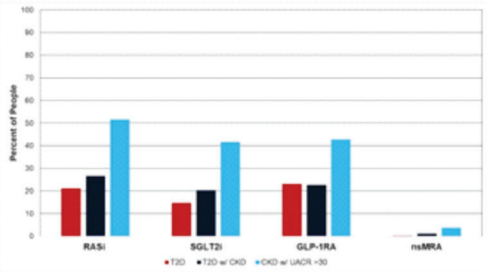
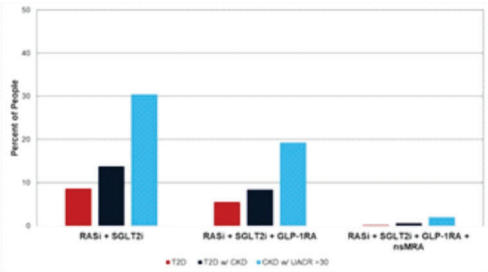


Figure 1c. Rate of combination therapy prescribing among people with T2D



Abbreviations: T2D, type 2 diabetes; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate (mL/min/1.73m^2); UACR, urine albumin-to-creatinine ratio (mg/g); GDMT, guideline-directed medical therapy; RASi, renin-angiotensin system inhibitor; SGLT2i, sodium-glucose co-transporter 2 inhibitor; GLP-1RA, glucagon-like peptide-1 receptor agonist; nsMRA, nonsteroidal mineralocorticoid receptor antagonist

CONCLUSION:

- **eGFR and UACR screening rates are inadequate in T2D patients with and without CKD. GDMT utilization in CKD remains substantially below recommended targets.**
- **Systematic initiatives to improve CKD screening and GDMT prescribing are essential in T2D populations.**

C. Complications-Macrovascular-Atherosclerotic Cardiovascular Disease and Human Diabetes

Metabolic Profile Supersedes Disease Duration in Determining Complication Risk in Type 2 Diabetes Mellitus

Bagri SA et al.

Background:

- Diabetes duration alone fails to predict complication onset; metabolic dysregulation may be a dominant independent driver.

Objective:

- To determine whether triglycerides (TG) and BMI override disease duration as primary complication determinants in community-based T2DM.

Methods:

- 400 T2DM patients stratified by duration (<5y, n=142; 5–10y, n=158; >10y, n=100) and metabolic phenotype — optimal (TG<150 + BMI<26) vs. poor (TG>200 or BMI>30).
- Endpoints: neuropathy, bone density, dyslipidemia.
- Key subgroups: short-duration/poor-metabolic (n=38) vs. long-duration/optimal-metabolic (n=28).

Results:

- Significant duration–metabolic interaction ($p<0.001$).
- Short-duration/poor-metabolic patients: 71% complication prevalence vs. 32% in long-duration/optimal-metabolic ($p<0.001$; $\Delta=39\%$).
- Poor metabolics conferred 4.2-fold risk within <5y cohort (OR 4.18, 95% CI 1.89–9.24).
- Paradox case: 3y-TG 220-BMI 32 → 78% complications vs. 15y-TG 125-BMI 24 → 28% ($p<0.01$).
- Duration effect within optimal metabolics: negligible (<5y 17%, 5–10y 22%, >10y 32%; $p=0.18$).
- Regression: TG>200 OR 5.8 (CI 3.2–10.4); BMI>30 OR 4.2 (CI 2.4–7.3); 5y-duration OR 1.4 (CI 1.1–1.8).

CONCLUSION:

- **Metabolic profile — not disease duration — is the primary complication driver in T2DM.**
- **Poor TG and BMI elevate complication risk 3–4× over long-standing diabetics with optimal metabolics.**
- **Duration-based risk stratification is insufficient; aggressive metabolic intervention at diagnosis is mandated regardless of disease chronology.**

D. Complications-Neuropathy

Wearable Sensory Prosthesis for Plantar Sensory Restoration in Diabetic Peripheral Neuropathy: Real-World Effects on Physical Function

Oddsson L et al.

Background:

- Diabetic peripheral neuropathy (PN) causes plantar sensory loss, impairing balance and increasing fall risk, with few effective interventions.

Objective:

- To assess real-world effects of Walkasins (HCPCS L8720/L8721) — an ankle-worn device delivering direction-specific haptic feedback from in-shoe plantar pressure sensors — on self-reported physical function over 12 weeks

Methods:

- US-wide registry (2022–2025) of type 1 or type 2 diabetes (T1D/T2D) adults with confirmed PN, plantar sensory loss, and gait/balance deficits.
- Physical function assessed via phone-administered Patient-Specific Functional Scale (PSFS) at baseline and 12 weeks; compared by Wilcoxon signed-rank test (α=0.05).

Results:

- Registrants- 2,998 with diabetes; Completers- 722 (46 states)
- T2D- 96.5%; mean age- 76.2±8.1 yr; Adherence- 92% ≥3 days/week
- Table 2 describes the PSFS outcomes.

Table 2: PSFS outcomes at baseline vs. 12 weeks

Timepoint	PSFS mean ± SD	p-value
Baseline	3.36 ± 1.92	<0.001
12 weeks	6.94 ± 2.24	
Change	+3.58 (~107%)	—

- Top functional concerns (n=620, 85.6% of completers) — all walking-related were: Walking across a room, Walking without support, Walking on uneven ground

CONCLUSION:

- **Walkasins use was associated with statistically significant, clinically meaningful improvements in self-reported physical, predominantly in walking tasks.**
- **Findings support Walkasins as an effective patient-centered intervention for diabetic PN.**

E. Foot Care-Lower Extremities

GLP-1 Receptor Agonism and Diabetic Foot Ulcer Incidence: A Meta-analysis

Yao J et al.

Background:

- GLP-1 receptor agonists (GLP-1 RAs) provide cardiovascular and metabolic benefits in T2DM, yet their effect on diabetic foot ulcer (DFU) risk remains unclear.

Objective:

- To assess the association between GLP-1 RA therapy and DFU incidence, with secondary outcomes of lower limb amputation (LLA), DFU-related hospitalization, and all-cause mortality in T2DM adults.

Methods

- PRISMA-compliant systematic review and meta-analysis different databases. Included: RCTs and cohort studies comparing GLP-1 RAs vs. other glucose-lowering agents.
- Pooled HRs (95% CIs) computed using random-effects models; subgroups stratified by treatment duration (≤400 vs. >400 days).

Results

- 31 studies (18 RCTs, 13 cohorts; n = 826,412) were analyzed.
- GLP-1 RA use reduced DFU incidence by 19% vs. controls.
- Secondary outcomes also improved significantly (all p < 0.001) as described in Table 3.

Table 3: Pooled outcomes — GLP-1 RA vs. controls in T2DM

Outcome	HR	95% CI	p
Incident DFU	0.81	0.74 – 0.89	< 0.001
Lower limb amputation (LLA)	0.72	0.61 – 0.85	< 0.001
DFU-related hospitalization	0.78	0.70 – 0.87	< 0.001
All-cause mortality	0.85	0.79 – 0.92	< 0.001

- Long-term use (>400 days) showed greater risk reduction (HR 0.74, 95% CI 0.66–0.83) than short-term use (HR 0.88, 95% CI 0.79–0.98).

CONCLUSION:

- **GLP-1 RA therapy significantly reduces DFU risk and associated complications (LLA, hospitalization, mortality) in T2DM.**
- **Clinical use is supported, particularly with long-term therapy.**

Correlation of VitD Status and Diabetic Foot Ulcer Risk: Meta-analysis

Yao J. et al.

Introduction and Objective:

- Diabetic foot ulcer (DFU) is a severe diabetic complication with high disability and amputation rates.
- This meta-analysis assessed the association between vitamin D deficiency and DFU risk.

Methods:

- Literature search through December 2025 for observational studies comparing vitamin D status between DFU and non-DFU patients.
- Vitamin D deficiency (VDD) and insufficiency (VDI) were defined as serum 25(OH)D <20 ng/mL and 20–29.9 ng/mL, respectively.

Results:

- 21 studies (n = 9,570) were included.
- DFU patients had significantly lower 25(OH)D levels (MD = −5.77 ng/mL; 95% CI: −7.87 to −3.66; P <0.001).
- VDD was associated with elevated DFU risk (OR = 1.82; 95% CI: 1.32–2.52; P <0.001), with severe VDD conferring greater risk (OR = 3.22; 95% CI: 2.42–4.28; P <0.001).

CONCLUSION:

- **VDD and VDI are significantly associated with increased DFU risk.**
- **Prospective cohorts and RCTs are warranted to establish causality.**
- **Routine 25(OH)D screening and supplementation in high-risk patients may reduce DFU incidence and improve prognosis.**

A. Diabetes Education

Impact of Multimodal Diabetes self-management education and Point-of-Care HbA1c Testing on Self-Management Behaviors

Ortega E et al

Introduction and Objective:

- Diabetes self-management education (DSME) is critical for optimizing glycemic control and promoting patient empowerment via lifestyle modification.
- To evaluate the efficacy of DSME integrating onsite HbA1c testing and culinary demonstrations on patient engagement and glycemic control.

Methods:

- Monthly bilingual (English/Spanish) sessions-delivered in group or 1:1 formats-covered pathophysiology, pharmacotherapy, nutrition.
- Interventions featured culturally tailored nutritional demonstrations.
- Changes in knowledge and self-efficacy were assessed via pre- and post-session surveys.

Results:

- Wilcoxon signed-rank analysis (n=41 matched pairs) demonstrated statistically significant improvements across all metrics with large effect sizes (r=.51–.92).

CONCLUSION:

Integrating practical nutritional guidance within flexible educational frameworks effectively enhances patient engagement and self-management.

Optimizing Guideline-Directed Cardiorenal Pharmacotherapy via Multi-Center Educational Implementation

Kulasa K, et al

Introduction and Objective:

- To improve sodium glucose transport protein 2 inhibitors (SGLT2i) and glucagon-like peptide-1 receptor agonists (GLP-1 RA) prescribing for T2D patients with comorbid ASCVD/CKD across five UC academic centers, addressing suboptimal real-world uptake.

Methods:

- The UC Diabetes Way Initiative (est. 2020) deployed educational frameworks and QI strategies tracking patients (age 18-75) with T2D and comorbid ASCVD, CKD, or eGFR <60.

Results:

- Implementing treatment algorithms and supporting tools such as dot phrases and smart sets increased prescribing rates among the 17,806 qualifying patients (from a total T2D cohort of 57,767): From Baseline (2020) 26.5% to Study Conclusion (2025) 68.5%

CONCLUSION:

Multimodal Quality improvement initiatives significantly improve guideline-driven cardiorenal prescribing in high-risk T2D populations through education and data tracking.

Enhancing Inpatient CGM Data Documentation

Kashat M et al.

Introduction:

- Inconsistent EMR documentation of inpatient CGM values limits glycemic trend review and raises patient safety concerns.

Objective:

- To determine whether a nursing practice alert improves inpatient CGM glucose documentation.

Methods

- Retrospective pre-post quality improvement (QI) study (Corewell Health William Beaumont University Hospital).
- Inclusion criteria: Adults ≥18 years with T1DM/T2DM admitted with functional CGM were included.
- Pre-intervention: 7/21/24–11/21/24; post-intervention: 11/21/24–04/21/25.

Results:

- Outcomes of 224 patients (34% T1DM, 66% T2DM); mean age 63±15 years; median HbA1c 7.4% (IQR 6.4–8.4) are shown in Table 4.

Table 4: Key Outcomes Pre- vs. Post-Intervention

Parameter	Pre (n=94)	Post (n=128)	p
CGM documentation rate	54.3%	68.8%	0.0389
Severe hypoglycemia (<54 mg/dL)	0.47%	0.19%	—
Mean daily CGM readings	—	~3/day	—

- Improved documentation correlated with older age, longer length of stay, and varied by hospital unit.

CONCLUSION:

A nursing practice alert significantly improved inpatient CGM documentation and reduced severe hypoglycemia, supporting system-level glycemic management strategies.

B. Exercise

Optimizing Dose and Exercise for Glycemic Control in Older Type 2 Diabetes Patients

Park Y et al.

Introduction and Objective:

- Age-related decline and cardiometabolic comorbidities in older adults with T2DM may alter glycemic responses to exercise; yet modality and dose recommendations derive from general adult data.
- This Network Meta-analysis (NMA) compared exercise modalities and dose-response relationships for glycemic control in older adults with T2DM.

Methods:

- Literature search was performed for RCTs of exercise interventions in older adults with T2DM reporting HbA1c.

Results:

- From 46 RCTs, high-intensity interval training (HIIT) produced the greatest HbA1c reduction vs. minimal-intervention control, followed by combined exercise (CE), mind-body exercise (MBE), continuous aerobic exercise (CAE), and resistance training (RT) (Table 5).

Table 5: HbA1c reduction by exercise modality vs. minimal-intervention control (Bayesian NMA)

Modality	MD in HbA1c (%)	95% CrI	Rank
HIIT	−1.02	−1.48, −0.59	1
CE	−0.60	−0.94, −0.26	2
MBE	−0.54	−0.88, −0.20	3
CAE	−0.44	−0.66, −0.23	4
RT	−0.36	−0.59, −0.15	5

MD = mean difference; CrI = credible interval. HIIT = high-intensity interval training; CE = combined exercise; MBE = mind-body exercise; CAE = continuous aerobic exercise; RT = resistance training.

- The dose-response relationship was non-linear, peaking at ~630 Metabolic Equivalent of Task (MET)s-min/week, with significant benefits observed between 390 and 840 METs-min/week.
- HIIT demonstrated the most rapid improvement gradient, while CAE and MBE showed intermediate patterns.

CONCLUSION:

- **All types of exercise effectively lower A1c levels.**
- **HIIT provides the best results, followed by combined and mind-body exercises.**
- **Aerobic and strength training also help, especially when done regularly throughout the week**

Vigorous Exercise Effects on Insulin Resistance in Post- Gestational Diabetes South Asian and Nordic Women

Kalleklev, T. L., et al.

Introduction and Objective:

- South Asians (SA) exhibit higher T2D risk than Nordics (NO), particularly post- gestational diabetes (GDM).
- Evaluate vigorous exercise impact on tissue-specific insulin resistance (IR) in SA vs. NO women with prior GDM.

Methods:

- 18 SA and 22 NO sedentary women underwent 8 weeks of supervised training (2x strength, 2x high-intensity interval training /week).
- Assessments: VO2max, body composition, 6-hour prime continuous intravenous infusion of ([6,6-D2] glucose / [1,1,2,3,3-D5] glycerol) and 2.5 g[U-13C] glucose was performed with the 75 g oral glucose tolerance test (OGTT).

Results:

- Both groups significantly ($p<0.001$) improved fitness (VO2max, strength) and body composition (□lean mass, □visceral fat) as shown in Table 6.

Table 6: Shared fitness and body composition changes post-intervention (SA vs. NO)

Parameter	SA (Δ)	NO (Δ)
VO_2max (ml/min/kg)	+3.5 ± 0.52	+3.8 ± 0.5
Chest press (kg)	+4.8 ± 0.8	+5.4 ± 0.9
Leg press (kg)	+30.8 ± 2.5	+22.8 ± 2.5
Lean body mass (kg)	+1.40 ± 0.27	+1.28 ± 0.22
Visceral fat (g)	−99 ± 33	−83 ± 25

- Muscle IR (MCR/I): South Asians (SA) showed a significant improvement of +1.0 ± 0.5 ($p=0.03$) in postprandial glucose clearance relative to insulin.
- Matsuda Index: Nordic (NO) women experienced a +12% ($p=0.04$) increase, indicating improved whole-body insulin sensitivity.
- Hepatic IR Index: Only the Nordic group showed a significant reduction of -0.2 ± 0.87 ($p=0.02$), reflecting improved liver insulin sensitivity.
- Lipolysis Suppression: South Asians demonstrated a significant +10 ± 2.44% ($p<0.001$) increase, showing better insulin control over fat breakdown.

CONCLUSION:

Supervised exercise improves fitness universally, while metabolic adaptations in IR exhibit ethnic-specific patterns.

C. Nutrition- Clinical

Type 2 Diabetes Remission and Pharmacologic De-intensification Following 12-Month Intermittent Fasting Intervention

Steger F et al.

Introduction:

- Intermittent energy restriction (IER) and time-restricted eating (TRE) are distinct intermittent fasting (IF) modalities with potential to reduce antidiabetic pharmacotherapy in type 2 diabetes (T2D).

Objective:

- To compare the effects of IER versus TRE on T2D remission and medication de-intensification.

Methods:

- A 12-month parallel trial of 57 adults with T2D overweight/obesity, weight-stable and medication-stable (≥3 months) randomized 1:1 to IER (550–800 kcal/day, 2–3 days/week) or TRE (≤8-hr window).
- Primary outcomes at 0, 3, 6 and 12 months: T2D remission (HbA1c <6.5% without therapy) and changes in medication type, count, and intensity.

Results:

- At 12 months, 67% of participants de-intensified pharmacotherapy (p=0.93) and 24% discontinued all medications (p=0.81).
- T2D remission was achieved by 14% overall (IER: 17%, TRE: 11%; p=0.48) as shown in Table 7.

Table 7: T2D pharmacologic outcomes and remission rates at 6 and 12 months

Outcome	IER (n=29)	TRE (n=28)	p-value
Pharmacologic de-intensification (among those on therapy at baseline)			
De-intensification by 12 months	18/27 (67%)	19/28 (68%)	0.93
Discontinuation of all antidiabetic medications by 12 months	6/27 (22%)	7/28 (25%)	0.81
T2D remission (HbA1c <6.5% for ≥3 months, off glucose-lowering therapy)			
Remission at 6 months	4/29 (14%)	7/28 (25%)	0.28
Remission at 12 months	5/29 (17%)	3/28 (11%)	0.48

IER = intermittent energy restriction; TRE = time-restricted eating. No statistically significant between-group differences observed. Some participants who achieved remission at 6 months regressed by 12 months.

- No statistically significant between-group differences were identified for any outcome.

CONCLUSION:

- **Both IER and TRE significantly reduce medication burden and facilitate T2D remission with comparable efficacy.**

Impact of a Very Low-Carbohydrate Breakfast Intervention on Adults with Type 2 Diabetes

Saslow L et al.

Introduction & Objective:

- Very low-carbohydrate (VLC) diets improve glycemic control in type 2 diabetes mellitus (T2DM), yet full dietary adherence remains challenging.
- Emerging evidence indicates that restricting carbohydrates at breakfast alone may confer glycemic benefit.
- This pilot study evaluated the feasibility, acceptability, and efficacy of a digital VLC breakfast-only intervention in adults with T2DM.

Methods:

- A 16-week, single-arm, pre-post intervention (baseline HbA1c ≥7.0%).
- Nutritional targets: breakfast <10g net carbs, 20-30g protein, 350-500 kcal.
- Primary outcomes: feasibility (retention), satisfaction (0-6 Likert scale), and 4-month HbA1c change analyzed via paired t-tests.

Results:

- N=119; mean age 61.1±11.1; baseline HbA1c 8.8%±1.1%.
- Retention: 97% (115/119).
- Satisfaction: 5.4±0.9.
- HbA1c Change at 4 months: -0.4% (95% CI: -0.6, -0.2; p < 0.001).

CONCLUSION:

The VLC breakfast intervention is a feasible, acceptable, and effective scalable strategy for metabolic improvement in T2D.

Impact of 8-h Time-Restricted Eating vs. Daily Calorie Restriction on Adiposity and Glycemic Metrics in T1DM

Runchey et al.

Introduction & Objective:

- Evaluate Time-Restricted Eating (TRE) efficacy and safety for weight management in T1DM with overweight/obesity compared to Calorie Restriction (CR) and controls.

Methods:

- 6-month RCT; adults (BMI 25–50 kg/m^2) randomized to TRE (in between 12:00–20:00 h eating only), CR (daily 25% energy restriction), or control.
- Primary outcome: change in body weight

Results:

- N=32 (BMI 33±7; HbA1c 7.3±1.0%).
- 6-month weight change was non-significant for TRE (-2.19% [95% CI, -5.70, -1.31]) or CR (-0.47% [-4.72, 3.78]) vs. controls.
- TRE significantly reduced HbA1c vs. CR (-0.46% [-0.80, -0.12], P=0.01).
- Insulin, euglycemia, and safety (diabetic ketoacidosis/hypoglycemia) remained stable.

CONCLUSION:

TRE safely improves HbA1c in T1DM but is not superior to CR or control for weight loss.

Impact of Beta-hydroxy-beta-methylbutyrate (HMB)-Specific Nutrition for Metabolic and Muscle Health in Type 2 Diabetes With or at Risk of Malnutrition

Garcia Almeida JM et al.

Introduction & Objective:

- Malnutrition (MN) and sarcopenia are prevalent in type 2 diabetes (T2DM) and confer adverse outcomes.
- This study assessed the impact of a high-protein, diabetes-specific nutrition formula with β-hydroxy β-methylbutyrate (HP-DSNF+HMB) on nutritional, glycemic, and musculoskeletal outcomes in T2DM outpatients with or at risk of MN.

Methods:

- 90-day prospective study (16 clinics).
- Patients (T2DM, Malnutrition Universal Screening Tool (MUST) ≥2) received exercise guidance and 2 daily HP-DSNF+HMB servings.
- Primary endpoint: change in MUST risk category.

Results:

- Cohort (n=193; 69±0.7 years; 73% male) were high MN risk (53.4% severe) as shown in Table 8.
- 64.5% improved MUST risk category ($p<0.0001$).
- While body weight remained stable, Vitamin D, Sarcopenia risk, diabetes distress, and quality-of-life significantly improved.

Table 8: Key Clinical Outcomes at 90 Days

Outcome	Change (mean ± SE)	p
MN risk category improvement	(n=166)64.5%; 66.3% (≥70% adherence)	<0.0001
Fasting blood glucose	−9.9 ± 4.2 mg/dL	0.020
HbA1c	No significant change	-
Chair stand test	+1.3 ± 0.3 rises/30s	<0.0001
Fat-free mass	+1.1 ± 0.4 kg	0.011
Phase angle	+0.5° ± 0.05	<0.0001
Body cell mass	+2.0 ± 0.3 kg	<0.0001

CONCLUSION:

Multimodal HP-DSNF+HMB intervention clinically improved nutritional, metabolic, and muscle health in T2DM patients.

D. Psychosocial/Behavioral Medicine

Remote Randomized Clinical Trial of Personalized Dietary Management in Type 2 Diabetes: The Diabetes Telemedicine Mediterranean Diet (DiaTeleMed) Study

Berube L et al.

Introduction & Objective:

- This study is done to evaluate the impact of precision nutrition and Mediterranean-based dietary management on postprandial glycemic response (PPGR) and glycemic variability (GV) in type 2 diabetes (T2D).

Methods:

- 6-month, 3-arm remote RCT (N=161; age 21–80; HbA1c 6.5–8.0%).
- Arms: Usual Care Control (UCC), Standardized (counseling), and Personalized (Standardized + algorithm-driven PPGR feedback).
- Primary metrics: Mean amplitude of glycemic excursions (MAGE) and GV via CGM.

Results:

- n=161; 60±12y; baseline HbA1c 6.77±0.6%.
- MAGE changes were non-significant across arms (UCC vs. Standardized: p=0.24; UCC vs. Personalized: p=0.13; Standardized vs. Personalized: p=0.70) (p>0.10).
- Other GV metrics were non-significantly different at 3 and 6 months.
- At 6 months, the Personalized arm showed a significant reduction in coefficient of variation (CV) vs. UCC (MD: −1.84%; 95% CI: −3.57 to −0.11; p=0.04).

CONCLUSION:

Algorithmic PPGR feedback did not significantly improve MAGE or primary GV metrics compared to standard Mediterranean counseling or usual care.

Real-World Efficacy of AI-Enabled Weight Management in Type 2 Diabetes Adults

Huntriss et al.

Introduction & Objective:

- AI-powered mobile apps for weight management are increasingly deployed in T2D, yet real-world efficacy data remain sparse. This study evaluated weight loss at 12 and 26 weeks and assessed whether AI coaching chat engagement predicted weight loss outcomes.

Methods:

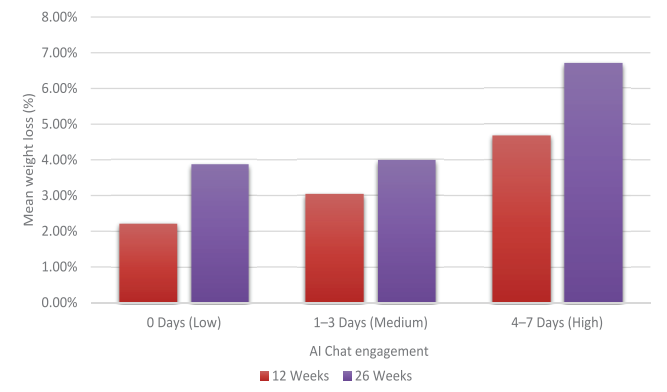
- Retrospective study assessing % weight loss at 12 and 26 weeks. AI engagement was categorized by usage (0, 1–3, or 4–7 days/week).
- Multivariable regression adjusted for age, sex, baseline BMI, and total app activity.

Results:

- At 12 weeks (n=444; BMI 36.2), mean weight loss was 3.63±4.16%.
- At 26 weeks (n=263), loss was 4.54±6.20%.

- Mean weight loss (%) by AI chat engagement frequency is depicted in Figure 2.

Figure 2: Mean Weight Loss (%) by AI Engagement



- Higher engagement associated with greater loss; association non-significant after multivariable adjustment.

CONCLUSION:

- **AI-enabled mobile apps facilitate clinically meaningful weight loss in T2D.**
- **Chat engagement correlates with weight loss but likely serves as a proxy for overall program adherence.**

Dexcom CGM Use During Ramadan in Diabetes: Confidence and Behavioral Adaptation

Crawford et al.

Introduction:

- Ramadan fasting alters eating patterns, medication timing, and self-management routines in people with diabetes (PWD), potentially affecting glycemic outcomes and fasting confidence.

Objective:

- To assess behavioral impact and confidence associated with Dexcom CGM use in T1D and T2D adults during Ramadan.

Methods:

- Analysis of CGM metrics and surveys from Ramadan 2025 (Middle East), stratified by diabetes type, T2D insulin use, and perceived CGM impact on fasting.
- Between-group differences assessed.

Results:

- Included 141 T1D, 10 T2D+insulin, and 47 T2D-no insulin participants.
- ≥80% reported increased confidence; 25% adjusted medication doses.
- Table 9 clearly highlights how increased confidence correlates with significantly better Time in Range (TIR).

Table 9: Impact of Confidence on CGM Metrics

Metric	Increased Confidence	No Increase	p-value
TIR (70-180 mg/dL)	71 ± 23%	54 ± 25%	<0.05
CGM Wear Time	76 ± 30%	57 ± 34%	0.1

CONCLUSION:

- **CGM facilitates safe Ramadan participation via enhanced confidence and personalized behavioral adaptation.**

Psychosocial and Quality of Life Outcomes of GLP-1 Therapy in Adults with Comorbid Obesity and T2D.

Levent A, et al.

Introduction:

- GLP-1 receptor agonists (GLP-1 RAs) are widely used for obesity and T2D management; however, their effects on psychosocial and behavioral outcomes remain inadequately characterized.

Objective:

- To evaluate GLP-1-associated patient-reported outcomes (PROs), specifically confidence, social engagement, and food-related cognitive burden, beyond traditional glycemic and weight metrics.

Methods:

- Analysis of 1,370 US GLP-1 users via the Ipsos Obesity Consumer Monitor (Oct-Nov 2025).
- Quality of Life (QoL) indicators were assessed using a 7-point Likert scale.

Results:

- Key findings are summarized below in Table 10.

Table 10: QoL Outcomes by Patient Cohort

Metric (Mean Score)	Obesity + T2D (n=53)	Comparative Cohorts* (n=404)
Energy Levels	4.85**	4.20 – 4.38
Healthy Eating	4.78	4.26 – 4.53
Exercise	4.64	3.90 – 4.29
Self-Confidence	4.57	4.01 – 4.50

*Includes obesity alone, T2D alone, and multiple comorbidities.
**Significant at $p < 0.05$.

CONCLUSION:

- **Patients with concurrent obesity and T2D demonstrate superior psychosocial improvements on GLP-1 therapy compared to single-condition cohorts.**
- **These findings suggest clinical utility for setting QoL expectations beyond weight loss.**

Efficacy of CGM-Based Digital Intervention for Glycemic Regulation in Adults with Prediabetes

DAVID BLACK

Introduction & Objective:

- To evaluate the clinical impact of My Control! —a community health worker (CHW)-led, CGM-informed digital education intervention —on glycemic control within a Latino prediabetic population.

Methods:

- Trial 1 (NCT06472297) (N=20 CHWs): 20-day CGM wear (high glucose alert: 140 mg/dL; low alerts disabled) with daily video reflections to develop 14 AI-assisted educational modules.
- Trial 2 (NCT06883812) (N=30): Experimental AB design (10-day masked vs. 10-day unmasked CGM) paired with daily intervention videos. Primary metrics: Mean glucose and Time Above Range (TAR >140mg/dL).

Results:

- Trial 1: 100% CGM completion rate; 95% valid data on ≥83% of study days. Generated 723 minutes of video content □ 14 My Control! videos.
- Trial 2: Masked□unmasked transition yielded significant reductions in both glycemic outcomes (Table 11).

Table 11: Glycemic Outcomes: Masked vs. Unmasked CGM Phase (Trial 2; N=30)

Outcome	Median Change	Q1, Q3	p-value	Responders (>criterion)
TAR >140 mg/dL (%)	−6.4%	−11.6, 1.4	.02	52% (14/27); criterion: >5% reduction
Mean Glucose (mg/dL)	−3.7	−10.6, 3.6	.049	—

CONCLUSION:

My Control! is a feasible, biosensor-integrated behavioral model that facilitates clinically meaningful glycemic self-regulation in prediabetes.

A.Clinical Therapeutics-Diabetes Prevention

Impact of Early Oral Antidiabetics on Biphasic Insulin Secretion in Prediabetes: A Hyperglycemic Clamp Analysis

Zaitoon H, et al.

Objective:

- Compare long-term effects of distinct antidiabetic classes on β-cell function (BCF) in prediabetes (PreDM)

Methods:

- 60 age/BMI-matched PreDM subjects received Metformin (MET), Pioglitazone (PIO), Saxagliptin (SAXA), or Dapagliflozin (DAPA) (n=15/group) for 2 years.
- Hyperglycemic clamps (+125 mg/dL) assessed first-phase (0-15 min) and second-phase (15-120 min) insulin secretion (ISecr) and sensitivity (glucose infusion rate during the steady state (GIR 90-120)).

Results:

- Overall (n=60): FPG declined (107□104 mg/dL; $p<0.05$); HbA1c unchanged. First-phase ISecr increased (949□1174 μU/mL; $p<0.001$); second-phase ISecr unchanged. GIR 90–120 improved (6.1□7.2 mg/kg·min; $p<0.05$).
- Treatment-specific: MET, SAXA, and PIO each increased first-phase ISecr ($p<0.05$). GIR 90–120 improved with MET ($p<0.05$), DAPA ($p<0.05$), and PIO ($p=0.05$). Second-phase ISecr and disposition index (ISecr × GIR) were unchanged across all groups. MET reduced weight ($p<0.005$); PIO increased weight ($p<0.001$).

CONCLUSION:

Early pharmacological intervention in PreDM enhances first-phase BCF and maintains second-phase ISecr, potentially modifying the trajectory toward Type 2 Diabetes.

B. Clinical Therapeutics-Incretin-Based Therapies

Monthly Subcutaneous Delivery of Tirzepatide and Retatrutide via Novel Long-Acting Injectable (LAI)

Lee J et al.

Introduction & Objective:

- Weekly tirzepatid and retatrutide injections impose significant patient burden.
- Transitioning to monthly administration via long-acting injectable (LAI) formulations would improve adherence and convenience.
- To minimize injection burden, high-drug-loading long-acting injectables (LAIs) were developed to enable monthly subcutaneous (SC) administration of tirzepatide and retatrutide.

Methods:

- LAIs were fabricated using biodegradable polymers via emulsion-based processes and characterized by HPLC.
- Pharmacokinetics (PK) were evaluated in male Sprague-Dawley rats.

Results:

- Formulations achieved high encapsulation efficiency and spherical morphology. Initial burst release was controlled at <5% within 24 hours.
- PK data confirmed sustained plasma concentrations exceeding one month post-injection.

CONCLUSION:

High-loading LAIs optimize PK profiles while reducing microsphere mass, enhancing clinical feasibility and patient adherence for monthly peptide therapy.

Phase 2 Trial: Oral Ribupatide (HRS9531) for Obesity

Bi Y, et al.

Objective:

- To assess the efficacy and safety of oral GLP-1/GIP dual agonist ribupatide for weight management in non-diabetic adults with obesity.

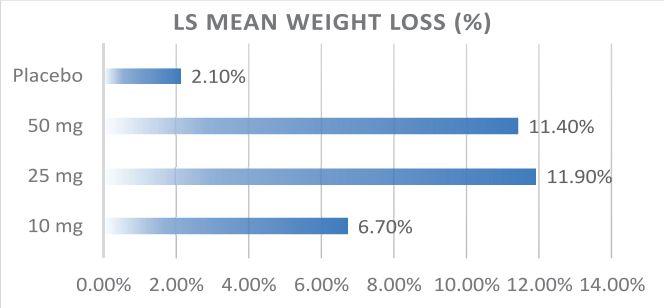
Methods:

- 26-week randomized (1:1:1:1) trial (10, 25, 50 mg vs. placebo); BMI 28–40 kg/m^2.
- Primary endpoint: % weight change at W26.

Results:

- Weight Loss Outcomes at W26 are described in Figure 3.

Figure 3: Body Weight Change at Week 26



Secondary Metrics & Safety:

- Threshold Achievement: Up to 38.6% of participants achieved ≥15% weight loss.
- Adverse Events (Aes): Most common were mild-to-moderate gastrointestinal symptoms (nausea, diarrhea, vomiting).
- Discontinuations: 0% (none led to treatment discontinuation or down-titration).

CONCLUSION:

Oral ribupatide yields significant weight reduction with a favorable safety profile and no observed efficacy plateau at W26

Semaglutide in Type 2 Diabetes and Advanced Chronic Kidney Disease: Efficacy and Safety Study

Elnour S et al.

Introduction and Objective:

- GLP-1 receptor agonists (GLP-1 RAs) offer cardio-renal benefits in T2DM, but data for advanced chronic kidney disease (CKD) are limited.
- This study assessed semaglutide safety and efficacy in T2DM with CKD stages 4–5.

Methods:

- Retrospective analysis of 45 patients (CKD stage 4/5) over 12 months.
- Primary endpoints: HbA1c and eGFR changes.
- Secondary endpoints: weight, BMI, safety, and discontinuation.

Results:

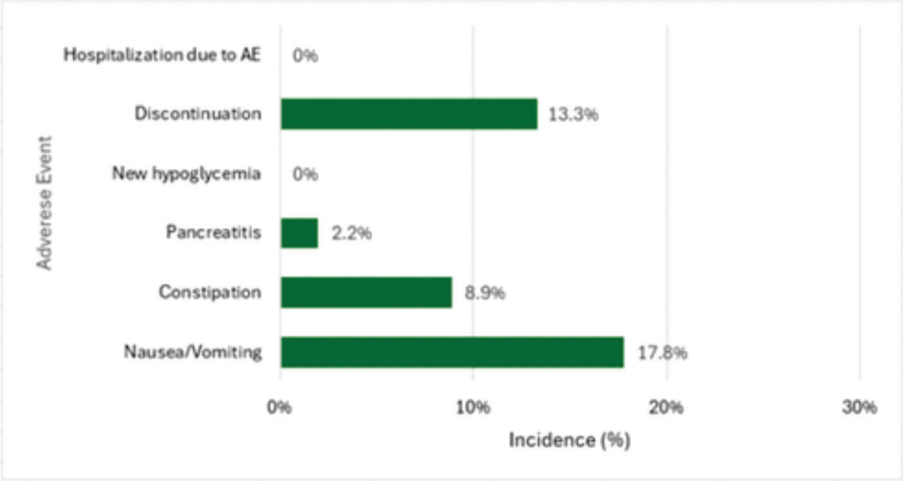
- Cohort: mean age 69.1±10.9 years; 57.8% female.
- Primary outcomes are described in Table 12.

Table 12: Glycemic, renal, and anthropometric outcomes at baseline vs. 12-month follow-up

Parameter	Baseline	Follow-up	p-value
HbA1c (%)	8.3 ± 1.7	7.6 ± 1.5	< 0.001
eGFR (mL/min/1.73 m^2)	25.5 ± 10.2	25.3 ± 10.4	0.305
Weight (kg)	77.6 ± 16.6	77.2 ± 16.5	0.496

- Figure 4 shows safety data of Semaglutide

Figure 4: Adverse event incidence; nausea/vomiting most frequent (17.8%), with 0% new hypoglycemia and 0% hospitalizations



CONCLUSION:

Semaglutide demonstrates significant glycemic efficacy and an acceptable safety profile in advanced CKD, warranting prospective validation.

Longitudinal Evolution of GLP-1RA and SGLT2i Prescribing Patterns in T2D Patients with Cardio-Renal Indications

Torres HA, et al.

Introduction:

- Glucagon-like peptide-1 receptor agonists (GLP-1RA) and sodium-glucose transporter 2 inhibitors (SGLT2i) are guideline-recommended therapies for type 2 diabetes (T2DM) with cardiovascular disease (CVD) or diabetic kidney disease (DKD), yet early adoption remains suboptimal.

Objective:

- To evaluate the longitudinal association (2016–2023) between clinical indications (CVD, DKD, obesity, hyperglycemia) and GLP-1RA/SGLT2i adoption in T2DM.

Methods:

- Retrospective analysis of EHR data from a large regional health system.
- Included adults with T2DM and ≥1 indication: CVD/DKD, obesity, or HbA1c >8%.
- Cluster-robust linear probability models assessed GLP-1RA/SGLT2i prescription probability by indication, with interaction terms for 3 time periods (2016–2018, 2019–2021, 2022–2023).
- N = 7,917 patients; 12,667 patient-time-periods.

Results:

- CVD/DKD, obesity, and HbA1c >8% increased prescription probability by 6.4%, 12.6%, and 16.3% respectively ($p<0.001$).
- By 2022–2023, rates for obesity (50.9%) and high HbA1c (50.7%) significantly exceeded CVD/DKD (46.7%).

CONCLUSION:

Prescribing for high-risk cardio-renal patients remains suboptimal compared to obesity or glycemic indications, necessitating targeted clinical decision support.

Glycemic Durability Following GLP-1 Discontinuation in a Real-World Remote Monitoring Diabetes Program (RMDP)

James RA, et al.

Introduction:

- A systematic review reported clinically significant metabolic rebound post–GLP-1 RA discontinuation (ΔHbA1c: +0.58% T1D; +0.65% T2D), with greater worsening over longer follow-up.

Objective:

- To evaluate the impact of GLP-1 adherence and the sustainability of glycemic control following therapy discontinuation within a RMDP.

Methods:

- This retrospective cohort analysis (N=10,654 adults (≥18 years); baseline A1c ≥7%) utilized 24-month follow-up data.
- Participants were stratified by 12-month adherence (proportion of days covered [PDC] ≥0.8 vs. <0.8) and compared to non-users.
- Outcomes measured age-adjusted eA1c reduction via Nathan's method.

Results:

- N = 10,654 (45.4% female; mean age 60.9 ± 10.5 yr); 47.8% initiated GLP-1s in Year 1, of whom 76.3% were adherent (PDC ≥0.8).
- Key Glycemic outcomes are explained in Table 13.

Table 13: Baseline and 24-Month Glycemic Outcomes by GLP-1 Use and Adherence

Group	Baseline eA1c (%)	Adjusted ΔeA1c at 24 mo (%)	SD
GLP-1 Adherent (PDC ≥0.8)	8.9	−2.6	2.4
GLP-1 Nonadherent (PDC <0.8)	9.0	−1.8	2.6
No GLP-1 Use	8.6	−1.1	2.3

- Adherent members who discontinued therapy (2.5%) showed no significant metabolic rebound, with a mean A1c change of only +0.10% (p=0.43) after 12 months.

CONCLUSION:

- **GLP-1 adherence yields superior long-term glycemic reduction.**
- **RMDP participation may mitigate the metabolic rebound typically observed after therapy discontinuation**

Safety Profiles of Semaglutide and Liraglutide Across Clinical Indications

Fisch SA et al.

Introduction:

- Glucagon-like peptide-1 (GLP-1) receptor agonists semaglutide and liraglutide received FDA approval in 2017 for type 2 diabetes mellitus (T2DM) and obesity.
- Expanding clinical use has prompted pharmacovigilance evaluation of indication-specific adverse event (AE) profiles.

Objective:

- To compare adverse event (AE) signals for semaglutide and liraglutide in type 2 diabetes (T2D) and obesity via FAERS to differentiate drug-specific vs. disease-related risks.

Methods:

- Disproportionality analysis of 2017+ FAERS reports (n=53,176) using reporting odds ratio (ROR), proportional reporting ratio (PRR), information component (IC), and empirical Bayesian geometric mean (EBGM).
- Class comparisons included metformin and orlistat.

Results:

- Semaglutide T2D reports (15,515) and obesity reports (5,567) exceeded liraglutide counts.
- Key semaglutide signals included:
  - T2D: Brain fog (ROR 12.78), optic ischemic neuropathy (12.11), impaired gastric emptying (9.57), suicidal ideation (4.69).
  - Obesity: Malnutrition (10.92), ileus (6.98), insomnia (2.76) visual impairment (2.38)

CONCLUSION:

- **Consistent AE signals across indications suggest drug-specific mechanisms.**
- **Class-level comparisons with metformin and orlistat corroborated these findings.**
- **Spontaneous reporting precludes causal inference.**

Pioglitazone–Exenatide Combination vs. Conventional Therapy: Effects on Body Composition and Bone Mineral Density

Abdelgani S et al.

Objective:

- To evaluate the 3-year effects of exenatide/ pioglitazone combination therapy on body composition and BMD in T2DM patients.

Methods:

- Newly diagnosed T2DM patients received Triple Therapy (metformin/pioglitazone/ exenatide; n=71) or Conventional Therapy (metformin/glipizide/glargine; n=68) for 3 years.
- DEXA scans were performed at baseline and year 3.

Results:

- Triple Therapy yielded superior, more durable HbA1c reduction (-2.4±0.2% vs. -1.5±0.2%; p<0.01).
- Although mean weight was stable, 1/3 of patients gained weight; the negative impact of weight gain on HbA1c was 2.5-fold higher in the Conventional group.
- Triple Therapy was associated with a 3.5% BMD decrease in women >50; no significant changes were noted in men or younger women.

CONCLUSION:

GLP-1 RA/pioglitazone combination provides superior glycemic durability and weight maintenance but is associated with BMD loss in postmenopausal women.

Efficacy and Tolerability of Utreglutide (GL0034) Escalation Regimens in Overweight and Obese Type 2 Diabetes (T2DM.

Thennati R, et al.

Introduction and Objective:

- Interim evaluation of GL0034, a novel once-weekly GLP-1 receptor agonist (GLP-1RA) safety and efficacy in T2DM patients on metformin ± SGLT2i.

Methods:

- 16-week, double-blind, placebo-controlled trial; participants randomized to two weekly GL0034 dose-escalation regimens or placebo.

Results:

- Both regimens were well-tolerated with comparable TEAE incidence (Table 14).
- GL0034 cohorts showed significant reductions in HbA1c, SMPG, peak postprandial glucose, body weight, and waist circumference versus placebo.
- No significant efficacy differences were observed between the two dose-escalation cohorts.

Table 14: Tolerability and efficacy outcomes at week 16 (mean±SD)

	Cohort 1 (n=16)	Cohort 2 (n=16)	Placebo (n=16)
Tolerability			
Symptom Score	4.25±9.63#	2.09±3.01*	0.69±1.56
GI AEs (Number/participant)	2.38±2.22*	2.25±2.24*	0.94±1.88
Incidence of all TEAEs	87.5%	87.5%	87.5%
Efficacy (change from baseline to week 16)			
Body weight (% change)	-7.7±5.3*	-6.5±4.4*	-0.7±2.2
Waist circumference (cm)	-8.8±6.2#	-5.7±5.1	-0.2±3.8
HbA1c (%)[1]	-0.88±0.39#	-1.09±0.63*	0.01±0.55
- Participants reaching HbA1c<6.5%	84.2%[2]		18.2%
Mean Daily SMPG (mg/dL)	-25.54±16.63#	-44.89±25.77*	0.84±55.78
Peak Glucose in meal test (mg/dL)	-76.8±31.1*	-67.4±34.5*	-14.5±58.9

Data are mean±SD; *p<0.05; #p<0.01; *p<0.001 vs. Placebo
[1]Small n-numbers (6, 13, and 11 for cohort 1, cohort 2, placebo, respectively); [2]pooled data from cohorts 1 and 2

Doses of GL0034 (mg/week)

Weeks	1-2	3-4	5-6	7-8	9-10	11-12	13-16
Cohort 1	0.3	0.6	1.0	1.4	1.8	2.4	3.0
Cohort 2	0.4	0.4	0.8	0.8	1.6	1.6	2.4

Symptom Score

GI-AE Points	Intensity Points
Vomiting 5	Mild 0.5
Nausea 2	Moderate 1
Other GI-AEs 1	Severe 3
Leading to discontinuation 10	

The final symptom score is calculated by multiplying GI-AE points with intensity points

CONCLUSION:

Weekly GL0034 (max 2.4/3.0 mg) effectively reduces weight and improves glycemic control with favorable tolerability in T2DM.

Semaglutide 2mg Titration vs. Tirzepatide Switch in Semaglutide 1mg-Treated T2D: Cardiometabolic Outcomes

Fang G, et al.

Objective:

- To evaluate the clinical noninferiority and superiority of semaglutide (SEMA) 2mg titration versus switching to tirzepatide (TZP) in T2D adults previously treated with SEMA 1mg.

Methods:

- Retrospective cohort study (2018–2025) utilizing Inverse Probability of Treatment Weighting (IPTW) balanced Cox proportional hazard models to assess HbA1c <7% and ≥5% weight loss.

Results:

- HbA1c cohort (n=64,888) and body weight cohort (n=56,852) had mean age 58 (SD 12) and 59 (SD 12) yrs; 52% and 60% White, respectively, with balanced baseline characteristics.
- Detailed outcomes are presented in Table 15.

Table 15: Cardiometabolic Outcomes: SEMA 2mg Titration vs. TZP Switch in T2D Adults

Outcomes	Treatment	Estimate type	Estimate	95% CI	*P* value	Noninferiority (margin)*	Superiority (margin)*
HbA1c <7%	Titration to SEMA 2mg (n=55,550)	Event rate at 1 year (360 days)	74.7%	73.3%-76.2%	<0.001		
	Switch to TZP (n=9,338)		75.1%	74.0%-76.2%	<0.001		
	Titration to SEMA 2mg vs switch to TZP	Risk difference	-0.4%	-1.1%-0.4%	0.343		
		NNT	~				
		Hazard ratio	0.98	0.94-1.02	0.343	Yes (0.93)†	No (1.07)†
Weight loss ≥5%	Titration to SEMA 2mg (n=48,596)	Event rate at 1 year (360 days)	60.5%	58.7%-62.3%	<0.001		
	Switch to TZP (n=8,256)		55.3%	53.9%-56.7%	<0.001		
	Titration to SEMA 2mg vs switch to TZP	Risk difference	5.2%	4.1%-6.3%	<0.001		
		NNT	19				
		Hazard ratio	1.19	1.15-1.24	<0.001	Yes (0.92)†	Yes (1.09)†

Noninferiority and/or superiority of titration to SEMA 2mg vs a switch to TZP in HbA1c goal achievement (<7%) and ≥5% body weight loss among patients with T2D treated with SEMA 1mg.
*2-sided alpha=0.05, power=0.80. For noninferiority the upper bound of the 95% CI is above the clinical margin and for superiority the lower bound of the 95% CI is above the clinical margin. †Assuming a 5% risk difference at 1 year.
HbA1c, glycated hemoglobin; SEMA, semaglutide; T2D, type 2 diabetes; TZP, tirzepatide.

CONCLUSION:

- **SEMA 2mg titration is noninferior for glycemic control and superior for weight reduction compared to a TZP switch.**

25 mg Oral Semaglutide vs 14 mg in T2D Metformin-Monotherapy: PIONEER PLUS Post Hoc Analysis

Xie L, et al.

Introduction and Objective:

- Post hoc analysis of PIONEER PLUS (NCT04707469) comparing efficacy of 25mg vs 14mg oral semaglutide (SEMA) in T2D adults previously treated with metformin monotherapy.

Methods:

- Randomized participants (N=262; HbA1c 8.0–10.5%; BMI ≥25.0) 1:1:1 to once-daily oral SEMA 14, 25, or 50 mg for 68 weeks and were evaluated for changes in weight and HbA1c from baseline to week 52 using an ANCOVA model.

Results:

- Baseline characteristics were comparable.
- At week 52, 25mg SEMA demonstrated significantly greater weight loss; HbA1c reduction was numerically greater but not statistically significant (Table 16).

Table 16: Clinical Outcomes at Week 52

Parameter	14mg (n=128)	25mg (n=134)	Difference	p-value
Weight Change	-4.5 kg	-7.9 kg	-3.4 kg	0.0002
HbA1c Change	-1.9%	-2.1%	-0.19%	0.2454

CONCLUSION:

Oral SEMA 25mg provides superior weight reduction with comparable glycemic control versus the 14mg dose in metformin-treated adults.

Semaglutide's Impact on MACE and Incident OSA: SELECT Post Hoc Analysis

Inzucchi S, et al.

Objective:

- To evaluate the effect of semaglutide 2.4mg on major adverse cardiovascular events (MACE) risk by Obstructive sleep apnea (OSA) status and its impact on incident OSA in patients with obesity and cardiovascular disease (CVD).

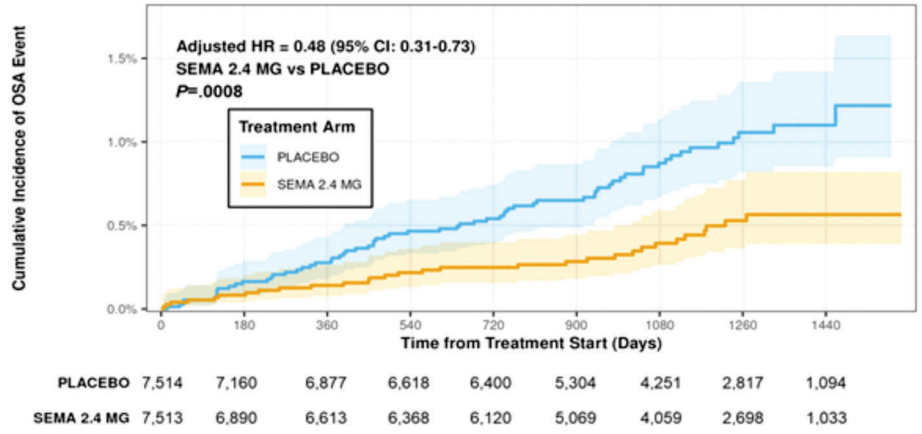
Methods:

- Post hoc analysis of SELECT trial participants (Age ≥45, BMI ≥27, CVD, no diabetes).
- Baseline OSA was identified via questionnaire; incident OSA was captured through adverse event reports.
- MACE risk (composite of non-fatal myocardial infarction, non-fatal stroke, or CV death) was assessed by OSA status.

Results:

- At baseline, 2,550 (14.5%) participants reported OSA.
- MACE reduction was consistent across groups (OSA: HR 0.93 [0.72-1.20]; non-OSA: HR 0.78 [0.69-0.88]; P-interaction=0.203).
- Semaglutide significantly reduced the risk of incident OSA (HR 0.48 [0.31-0.73]) (Figure 5).

Figure 5: Cumulative Incidence of Incident OSA (Competing Risk: Death) — Participants Without Baseline OSA



Cumulative incidence function estimated using the Aalen-Johansen estimator for competing risks analysis. Subjects may experience OSA event (event of interest) or death without OSA (competing risk). Subjects without events were censored at the end of their in-trial period. Cause-specific HR from Cox proportional hazards model adjusted for age, sex, baseline BMI categories, and region. Treatment comparison: Sema 2.4 mg vs Placebo (reference). Population: FAS population without OSA at baseline. Total OSA events: 95 (Placebo: 65, Sema 2.4 mg: 30). FAS, full analysis set; HR, hazard ratio; OSA, obstructive sleep apnea.

CONCLUSION:

- **CV benefits of semaglutide are consistent regardless of OSA status, and therapy is associated with a 52% reduction in incident OSA.**

PT403, Monthly poly (lactic-co-glycolic acid) (PLGA)-Encapsulated Semaglutide-Preclinical Efficacy and Pilot Safety

Choi MJ, et al.

Introduction:

- GLP-1 receptor agonists (GLP-1RAs) are efficacious in type 2 diabetes (T2DM) and obesity; however, frequent injections compromise adherence.

Objective:

- To evaluate PT403, a once-monthly biodegradable PLGA-microsphere semaglutide formulation, for improved treatment adherence and GI tolerability.

Methods:

- Semaglutide was encapsulated via ultrasonic spray-drying for sustained release.
- Testing included high-fat diet-induced obesity (DIO) mouse models and a randomized human pilot (N=16) comparing a single subcutaneous 4mg PT403 dose to 0.5mg weekly semaglutide over 57 days.

Results:

- In mice, PT403 (Q2W/Q3W) achieved -30% weight reduction by week 4.
- In humans, PT403 demonstrated a superior safety profile compared to weekly semaglutide, showing fewer total adverse events and a complete absence of gastrointestinal issues like nausea and vomiting (Table 17).

Table 17: Pilot Safety and Tolerability Comparison

Metric	PT403 (n=8)	Weekly Semaglutide (n=8)
Total Adverse Events	27	33
ADR Intervention Rate	29.6%	45.5%
GI (Nausea/Vomiting)	0%	Reported

CONCLUSION:

- **PT403 demonstrates sustained efficacy and superior tolerability, supporting its potential as a long-acting GLP-1RA.**

C. Clinical Therapeutics-Insulins

Comparing Insulin Glargine 300 U/mL (Gla-300) vs. Icodec in Type 2 Diabetes: Systematic Review and Network Meta-analysis

Ritzel R, et al.

Objective:

- Compare efficacy and safety of daily Gla-300 vs. weekly Icodec in insulin-naïve People with Type 2 Diabetes (PWT2D) on oral antidiabetic drugs (OADs).

Methods:

- Meta-analysis of RCTs (MEDLINE, Embase, CENTRAL; searched July 2025) evaluating treatment effects at ~6 months using Bayesian/frequentist models.

Results:

- 5 RCTs (N = 3,246; Gla-300: n = 2,411; icodec: n = 835)
- Gla-300 showed significantly lower Level 1, 2, and combined 2/3 hypoglycemia risk vs. Icodec.
- Glycemic outcomes (HbA1c, weight) were similar, though Gla-300 had lower <7% HbA1c attainment and smaller FPG reductions (Table 18)

Table 18: Bayesian model summary — Gla-300 vs. icode

Outcome		Number of Trials‡	Time point (Weeks)	Statistic (Gla 300 vs Icodec)	Bayesian Model: Estimate (95% CrI) Under FE Model ** (Gla 300 vs Icodec)
Level 1 (≥ 54 mg/dL and < 70 mg/dL)‡ 24-hr hypoglycemia	Incidence	5	23–29	Risk Ratio	* 0.74 (0.64, 0.86)
Level 2 (< 54 mg/dL)‡ 24-hr hypoglycemia	Incidence	2	23–29	Risk Ratio	* 0.43 (0.22, 0.85)
Combined level 2 (< 54 mg/dL)‡ or level 3 24-hr hypoglycemia	Incidence	5	23–29	Risk Ratio	* 0.43 (0.27, 0.70)
Level 3 (severe) 24-hr hypoglycemia†	Incidence	5	23–29	Risk Ratio	0.72 (0.16, 3.50)
Level 1 (≥ 54 mg/dL and < 70 mg/dL)‡ 24-hr hypoglycemia	Event Rate	5	23–29	Rate Ratio	* 0.37 (0.32, 0.42)
Level 2 (< 54 mg/dL)‡ 24-hr hypoglycemia	Event Rate	2	23–29	Rate Ratio	* 0.23 (0.13, 0.42)
Combined level 2 (< 54 mg/dL)‡ or level 3 24-hr hypoglycemia	Event Rate	5	23–29	Rate Ratio	* 0.42 (0.28, 0.61)
Level 3 (severe) 24-hr hypoglycemia†	Event Rate	5	23–29	Rate Ratio	1.56 (0.20, 16.64)
Change in HbA1c (%)		5	23–29	Mean Difference	0.09 (-0.13, 0.32)
HbA1c <7% achievement		5	23–29	Risk Ratio	* 0.86 (0.76, 0.99)
HbA1c <7% achievement, Without severe or confirmed (< 54 mg/dL)‡ hypoglycemia		2	23–29	Risk Ratio	0.84 (0.68, 1.05)
Change in FPG (mg/dL)		5	23–29	Mean Difference	* 8.15 (1.55, 14.73)
Change in body weight (kg)		5	23–29	Mean Difference	-0.46 (-1.07, 0.14)
Final daily insulin dose (U/day)		5	24–26	Mean Difference	* 11.86 (7.02, 16.67)
Final daily insulin dose (U/kg)		5	24–26	Mean Difference	0.17 (-0.04, 0.38)
Any AE		4	23–29	Risk Ratio	0.89 (0.76, 1.06)
Any SAE		4	23–29	Risk Ratio	1.25 (0.57, 2.80)
Discontinuation due to an AE†		5	23–29	Risk Ratio	1.01 (0.34, 3.42)

* : 95% credible intervals do not cross the null.
** : Normal(0, 10,000) prior distribution applied to the effect size.
‡ : 54 mg/dL = 3.0 mmol/L; 70mg/dL = 3.9 mmol/L
† : continuity correction applied for zero-event cells.
‡ : continuity correction not applied because zero counts were appropriately accommodated by the Poisson likelihood used in the event rate analysis.
§ : The full network of five RCTs included EDITION 3, EDITION AP, BRIGHT, ONWARDS 3, and NN1436-4383.

Abbreviations: AE, adverse event; CrI, credible interval; FE, fixed-effects; FPG, fasting plasma glucose; Gla-300, insulin glargine 300 U/mL; SAE, serious adverse event.

CONCLUSION:

- **Gla-300 provides superior hypoglycemia safety with comparable glycemic efficacy vs. Icodec in insulin-naïve T2D.**

Temporal Pharmacodynamic Profiles of Inhaled Technosphere Insulin vs. Subcutaneous Lispro

Kaiserman K, et al.

Objective:

- To analyze insulin action timing using cumulative percentage of total pharmacodynamic (PD) effect to distinguish early versus late action for inhaled Technosphere Insulin (TI) vs. subcutaneous insulin lispro.

Methods:

- Randomized crossover clamp study (type 1 diabetes (T1D) adults) comparing TI 12 U and subcutaneous lispro 8 U.
- Glucose infusion rate (GIR)-time profiles were normalized to total GIR- area under the curve (AUC) at 60, 90, and 120 minutes.

Results:

- TI 12 U delivered a substantially greater proportion of its total PD effect earlier than lispro 8 U at all time points (Table 19).

Table 19: Cumulative PD Effect (% of Total GIR-AUC) and Remaining Effect (%) for TI 12 U vs. Lispro 8 U

Time Point	TI 12 U (Cumul. %)	TI 12 U (Remain. %)	Lispro 8 U (Cumul. %)	Lispro 8 U (Remain. %)	Diff. (pp)	Fold
60 min	53%	47%	10%	90%	+43	5.3×
90 min	75%	25%	27%	73%	+48	2.8×
120 min	88%	12%	45%	55%	+43	2.0×

GIR-AUC = glucose infusion rate area under the curve; pp = percentage points; TI = Technosphere Insulin

CONCLUSION:

- **TI completes the majority of its PD effect within 60 minutes.**
- **This rapid onset and earlier offset may reduce risks of insulin stacking and post-prandial hypoglycemia compared to lispro.**

D. Clinical Therapeutics-Other Therapeutic Agents

SGLT2i/GLP-1RA Combination and Fracture Risk in T2D: A Trial Emulation

Jia X, et al.

Objective:

- To assess if dual SGLT2 inhibitor (SGLT2i) and GLP-1 receptor agonist (GLP-1RA) therapy increases fracture risk compared to monotherapy in type 2 diabetes (T2DM) patients.

Methods:

- Target trial emulation using the Tianjin Diabetes and Health Cohort.
- 1:1 propensity score matching was applied to parallel cohorts: (1) GLP-1RA background (add SGLT2i vs. continue GLP-1RA) and (2) SGLT2i background (add GLP-1RA vs. continue SGLT2i).
- Primary outcome: composite major fractures (hip, pelvis, humerus, or forearm)

Results:

- 10,280 pairs (GLP-1RA cohort; mean age 54.2 years) and 13,664 pairs (SGLT2i cohort; mean age 57.3 years) were matched.
- Baseline covariates were well balanced (SMD <0.1 for all).
- Fracture incidences compared are described in Table 20.

Table 20: Fracture Incidence and Hazard Ratios by Cohort

Cohort	Combination IR (per 1,000 PY)	Monotherapy IR (per 1,000 PY)	HR	95% CI
GLP-1RA background	1.08	1.25	1.02	0.40–2.58
SGLT2i background	1.19	0.82	1.80	0.81–4.01

IR = incidence rate; PY = person-years; HR = hazard ratio; CI = confidence interval. No significant difference in secondary outcomes (non-major fractures) in either cohort (P >0.05)

CONCLUSION:

Combined SGLT2i and GLP-1RA therapy does not significantly increase fracture risk, supporting its skeletal safety in clinical practice.

E. Clinical Therapeutics-SGLT Inhibitors

TTT1 Phase 3 Trial: Insulin, Semaglutide, and Dapagliflozin Triple Therapy in Type 1 Diabetes

Ghanim HA, et al.

Objective:

- To evaluate efficacy and safety of weekly semaglutide (GLP-1RA) and daily dapagliflozin (SGLT2i) as insulin adjuncts in overweight adults (BMI >25 kg/m^2) with T1D (HbA1c 7.5–11.0%).

Methods:

- Period 1 (Weeks 1–26): 2:1 open-label randomization to standard of care (SOC) ± weekly semaglutide (1.0 mg).
- Period 2 (Weeks 26–52): Semaglutide cohort randomized double-blind to 10 mg dapagliflozin or placebo.
- Primary endpoint: HbA1c change in Period 2
- Key safety outcomes: hypoglycemia and diabetic ketoacidosis (DKA)

Results:

- N=78 (Period 1), N=36 (Period 2).
- Baseline: 45±13.7 yrs, HbA1c 8.3±0.7%, BMI 33±6.1 kg/m^2.
- Period 1: Semaglutide vs. SOC reduced HbA1c by 0.45% (p=0.0072) and weight by 10.2 kg (p<0.0001).
- Period 2: Dapagliflozin vs. placebo further reduced HbA1c by 0.46% (p=0.003); weight change was non-significant (-1.0 kg, p=0.2219).
- Safety: Level 2 hypoglycemia was higher with semaglutide (IRR 2.6, p=0.0047). One DKA event (placebo group).
- Efficacy endpoints are summarized in Table 21.

Table 21: Glycemic and Weight Efficacy Summary

Period	Comparison	ΔHbA1c (95% CI)	ΔWeight (95% CI)	p-value
Period 1	Semaglutide vs SOC	-0.45% (-0.78, -0.13)	-10.2 kg (-12.8, -7.7)	<0.01
Period 2	Dapagliflozin vs PBO	-0.46% (-0.78, -0.14)	-1.0 kg (-2.72, 0.66)	0.003

CONCLUSION:

Weekly semaglutide reduces HbA1c and weight in overweight T1D; adding dapagliflozin provides incremental glycemic benefit.

F. New Technology—Glucose Monitoring and Sensing

24-Hour Continuous Glucose Monitoring Profiles in Non-Diabetic Older Men

Griffen C, et al.

Introduction and Objective:

- CGM use is rising in non-diabetic populations for health monitoring.
- Study was done to establish normative 24-hour continuous glucose monitoring (CGM) profiles in healthy older males, addressing the data gap for non-diabetic populations.

Methods:

- 33 non-diabetic men (Age: 67±4; BMI: 25.4±2.5; HbA1c <6.5%) were monitored for 24 hours in a metabolic chamber with a controlled isocaloric diet (~45% carbohydrate, ~20% protein, ~35% fat) and standardized exercise bouts- 3 × 30 min step exercise bouts at 75 steps/min (~6,750 steps/24 hours).

Results:

- Participants maintained euglycemia (54–120 mg/dL) 80.9±12.6% of the time and a tight range (TITR; 70–140 mg/dL) 89.7±8.1% of the time.
- Time above 140 mg/dL was 7.4±6.6%.
- Mean glucose: 100±11 mg/dL.
- Additional CGM metrics are summarized in Table 22.

Table 22: 24-Hour CGM Glucose Metrics

Metric	Mean±SD
% time 54-120 mg/dL (3.0-6.6 mmol/L)	80.9±12.6
% time 70-140 mg/dL (3.9-7.8 mmol/L)	89.7±8.1
% time 70-180 mg/dL (3.9-10.0 mmol/L)	95.7±5.7
% time >140 mg/dL (>7.8 mmol/L)	7.4±6.6
% time >180 mg/dL (>10.0 mmol/L)	1.4±3.0
% time <70 mg/dL (<3.9 mmol/L)	2.9±5.0
% time <54 mg/dL (<3.0 mmol/L)	0.2±1.1
Mean glucose [mg/dL (mmol/L)]	100±11 (5.6±0.6)
CV (%)	21.7±7.3

CONCLUSION:

This study provides baseline 24-hour glycemic benchmarks for non-diabetic older men under controlled conditions.

Real-World Continuous Glucose Monitoring- Based Glycemic Management During Ramadan in Patients with Diabetes

Hassanein MA, et al.

Introduction and Objective:

- Ramadan fasting poses dysglycemia risk in people living with diabetes (PLWD).
- Study was done to evaluate real-world glycemic management in people living with diabetes (PLWD) across pre-, intra-, and post-Ramadan fasting periods using continuous glucose monitoring (CGM).

Methods:

- Retrospective analysis of 103 Dexcom users (≥18 years) in Arab Gulf countries, Jordan, and Lebanon (2020–2025).
- CGM metrics were compared across three periods, with subgroup analyses for diabetes type, insulin therapy, age, and gender.

Results:

- Among 103 participants (70% CGM utilization), mean Level 1 hypoglycemic events per week significantly decreased during Ramadan ($p < 0.05$). Demographics are summarized in the Table 23.
- No other significant metric differences were observed. MDI users exhibited higher CV and rebound hyperglycemia across all periods.

Table 23: Participant Demographics and Glycemic Outcomes

Demographics
Age: 38.2 years (12.5); **Gender:** Female: n=55 (53%); Male: n=48 (47%)
Diabetes duration: 12.3 years (10.4); **Dexcom CGM duration**: 2.5 years (1.2)
Diabetes type: T1D: n=71 (69%); T2D: n=20 (19%); Not reported: n=12 (12%)
Insulin therapy: Pump: n=15 (14%); MDI: n=74 (72%); Basal insulin only: n=3 (3%); Not reported: n=11 (11%)

Metric	Before Ramadan	During Ramadan	After Ramadan	p value (Before vs. During)	p value (During vs. After)	p value (Before vs. After)
TIR 70-180 mg/dL (%)	65.4 (21.0)	64.6 (21.1)	65.3 (20.6)	0.65	0.64	>0.99
TITR 70-140 mg/dL (%)	43.9 (20.4)	42.5 (21.3)	43.6 (21.0)	0.36	0.39	0.97
TAR >180 mg/dL (%)	30.8 (21.2)	31.5 (21.5)	30.4 (21.3)	0.69	0.38	0.93
TAR >250 mg/dL (%)	11.8 (14.9)	12.7 (15.1)	11.3 (14.3)	0.35	0.12	0.80
TBR <70 mg/dL (%)	3.9 (5.4)	3.9 (6.3)	4.3 (5.5)	>0.99	0.43	0.24
TBR <54 mg/dL (%)	1.3 (2.7)	1.5 (3.1)	1.6 (2.5)	0.66	0.88	0.25
Mean glucose (mg/dL)	161.3 (39.5)	163.9 (40.5)	159.8 (38.5)	0.28	0.05	0.78
GMI (%)	7.2 (0.9)	7.2 (1.0)	7.1 (0.92)	0.28	0.06	0.78
CV (%)	30.5 (9.3)	30.3 (9.1)	30.1 (8.7)	0.84	0.82	0.36
GRI	57 (4)	59 (4)	58 (4)	0.37	0.59	0.95
Level 1 hypoglycemic events/week (n)	4.8 (5.2)	4.0 (4.8)	4.7 (5.3)	0.01	0.02	0.94
Level 2 hypoglycemic events/week (n)	1.2 (2.1)	1.2 (2.2)	1.4 (2.3)	>0.99	0.25	0.31
Nocturnal hypoglycemic events/week (n)	1.7 (2.0)	1.6 (2.0)	1.8 (2.3)	0.81	0.31	0.67
Extended hypoglycemic events/week (n)	0.4 (1.3)	0.5 (1.6)	0.5 (1.4)	0.23	0.95	0.14
Rebound hyperglycemic events/week (n)	2.6 (3.7)	2.2 (3.7)	2.4 (3.5)	0.18	0.52	0.52
Rebound hypoglycemic events/week (n)	2.4 (3.4)	2.0 (3.6)	2.2 (3.8)	0.13	0.52	0.64
n (%) users with TIR 70-180 mg/dL >70%	46 (44.7)	47 (45.6)	45 (43.7)	>0.99	0.69	>0.99
n (%) users with TIR 70-180 mg/dL <70% and TBR <70 mg/dL >4%	19 (18.4)	18 (17.5)	20 (19.4)	>0.99	0.73	>0.99

Data are means (SD) or counts (%). Only the latest year of Ramadan data was used for each user. Statistical significance was defined as $p<0.05$. P values for continuous data were estimated using the mixed model for repeated measures (MMRM) model adjusted for family wise error. P values for categorical data were estimated using McNemar's Test. CV, coefficient of variation; GMI, glucose management indicator; GRI, glycemia risk index; MDI, multiple daily injections; T1D, Type 1 Diabetes; T2D, Type 2 Diabetes; TAR, time above range; TBR, time below range; TIR, time in range; TITR, time in tight range. Level 1 and level 2 hypoglycemic events per week were calculated as a CGM sensor value of <70 mg/dL and <50 mg/dL, respectively, for >15 minutes. Nocturnal hypoglycemic events per week were calculated as Level 1 and Level 2 hypoglycemic events that occurred between 00:00 and 06:00. Extended hypoglycemic events per week were calculated as Level 1 and Level 2 hypoglycemic events that occurred for >120 minutes. Rebound hyperglycemic events per week were calculated as a CGM sensor value <70 mg/dL for >15 minutes followed by a sensor value >180 mg/dL for >15 minutes within 120 minutes. Rebound hypoglycemic events per week were calculated as a CGM sensor value >180 mg/dL for >15 minutes followed by a sensor value <70 mg/dL for >15 minutes within 120 minutes.

CONCLUSION:

- **Glycemic management was successfully maintained before, during, and after Ramadan fasting with the use of CGM.**

Photo-Based Food Diary and CGM Integration in Type 2 Diabetes: A Pilot RCT

Brown K, et al.

Objective:

- To evaluate the glycemic efficacy of 'Undermyfork' (UMF), an mHealth application linking meal photography to continuous glucose monitoring (CGM) excursions in patients with Type 2 Diabetes (T2D)

Methods:

- A 4-month, 2-arm RCT compared CGM alone (Arm 1) to UMF+CGM (Arm 2) in 49 randomized adults (HbA1c >7.7%, time-in-range (TIR) <70%).
- Primary CGM endpoints: mean glucose and TIR at Day 20.
- Secondary endpoints: HbA1c, patient-reported outcomes (PROs), and diabetes medication dosage at 4 months.

Results:

- Of 91 enrolled (mean age 62.2; 59.3% male; A1c 9.0%), 49 met randomization criteria.
- Mean glucose significantly decreased post-unblinding (p=.023).
- Despite higher baseline metabolic burden in Arm 2 (higher BMI, poorer diet quality, higher mean glucose), glycemic improvements were comparable between arms (Table 24). Arm 2 showed faster daily TIR gains.

Table 24: Primary and Secondary Glycemic Outcomes by Treatment Arm

Outcome	Arm 1: CGM (n=25)	Arm 2: UMF+CGM (n=24)
Δ Mean glucose at Day 20 (mg/dL)	−11.0	−13.2
p-value (between groups)	0.84	—
Δ HbA1c at 4 months (%)	−0.94	−0.78
p-value (between groups)	0.69	—
Mean glucose change (blinded→unblinded), both arms	Significant (p=0.023)	—
TIR trajectory over 20 days	Upward	Steeper upward trend

CONCLUSION:

UMF-CGM integration achieves glycemic improvements comparable to CGM alone, even in higher-risk cohorts, by enhancing behavioral responses to meal-specific excursions.

Multisite Study of CGM in Gestational Diabetes (GDM) Management

Valent AM, et al.

Introduction and Objective:

- A gestational diabetes (GDM) gestational diabetes (GDM).
- This study assessed the impact of real-world continuous glucose monitoring (CGM) on self-management and patient experience in GDM.

Methods:

- Multi-center observational study of 50 GDM patients using Dexcom G7.
- Outcomes included CGM metrics and postpartum satisfaction surveys.

Results:

- Participants (n=50; BMI 31.0; 84% CGM-naive) demonstrated 93% adherence.
- Group A1 (no medication n=18) and A2 (medication use n=32) showed significant differences in nocturnal metrics (Table 25).

Table 25: CGM-Derived Glycemic Profiles in GDM by Treatment Category

CGM metric	Overall n=48*	A1 (n=17)	A2 (n=31)	Difference 95% CI	Adjusted P value
Day (06:01-23:59)					
Mean glucose, mg/dL	111.1 (11.3)	106.5 (7.8)	113.7 (12.2)	-13, -1.3	**0.04**
CV, %	19.4 (4)	18.4 (2.9)	19.9 (4.5)	-3.7, 0.6	0.18
pTIR 63-140 mg/dL	87.1 (12.2)	91.1 (7.8)	85 (13.6)	-0.1, 12.4	0.07
>140 mg/dL	11.9 (12.2)	7.7 (8.2)	14.2 (13.6)	-12.8, -0.2	0.06
<63 mg/dL	0.9 (0.9)	1.1 (0.9)	0.8 (0.9)	-0.2, 0.9	0.27
Night (00:00-06:00)					
Mean glucose, mg/dL	103.7 (14.1)	96.3 (7.4)	107.8 (15.3)	-18.2, -4.9	**0.004**
CV, %	16.6 (4.4)	14.8 (3.6)	17.6 (4.5)	-5.2, -0.4	**0.04**
pTIR 63-140 mg/dL	89.7 (10.8)	95.1 (3)	86.7 (12.4)	3.6, 13.1	**0.004**
>140 mg/dL	7.8 (11.1)	2 (2.4)	10.9 (12.6)	-13.7, -4.2	**0.004**
<63 mg/dL	2.5 (3.4)	2.9 (2.8)	2.3 (3.7)	-1.3, 2.5	0.54

Data are presented as mean (SD). *n=48 with sufficient CGM data; pTIR: pregnancy time in range. Bolded p values are significant after adjustment for multiple comparisons.

- Satisfaction was high (88%), with users reporting improved quality of life (QoL) despite some alarm fatigue and data anxiety.

CONCLUSION:

CGM improves self-management and QoL in GDM; however, targeted education is necessary to address user-reported challenges and optimize medication therapy.

G. Pediatrics—Obesity and Type 2 Diabetes

Early vs. Late Time-Restricted Eating (TRE) in Pediatric Obesity: A Randomized Trial

Bakhsh JA, et al.

Introduction and Objective:

- Time-restricted eating (TRE) is a low-cost dietary intervention; however, the influence of eating window timing on efficacy remains unclear.
- This trial compared the efficacy of early (eTRE) vs. late (lTRE) 8-hour windows on %BMIp95 reduction in adolescents with obesity.

Methods:

- Randomized parallel-group trial (n=94, ages 12–20 years) comparing eTRE (07:00–15:00) vs. lTRE (12:00–20:00) over 24 weeks.
- Adherence was assessed via logs and CGM.
- Primary endpoint: change in %BMIp95.
- Secondary outcomes: eating behaviors, sleep quality, metabolic markers, and body composition.

Results:

- 85% of participants completed the study with high adherence (eTRE: 5.0; lTRE: 6.0 days/week).
- Both cohorts achieved significant %BMIp95 reductions (eTRE: −4.6% [95% CI, −6.4 to −2.9]; lTRE: −2.8% [95% CI, −4.6 to −1.1]).
- Between-group difference (1.84%) was non-significant.
- Secondary metabolic and caloric markers showed no significant inter-group variance.

CONCLUSION:

- **Early and late TRE are feasible and effectively reduce adiposity in adolescents.**
- **Early timing showed numerically greater, but not statistically significant, improvements.**

Real-World Pediatric SGLT2 Inhibitor Safety and Efficacy

Kelly SR, et al.

Objective:

- To assess adverse events (AEs) and clinical outcomes of Sodium-glucose cotransporter-2 inhibitors (SGLT2i) in a large pediatric cohort.

Methods:

- Retrospective review (2019–2025) of 195 pediatric patients (177 initiators).
- Analysis focused on AE incidence, indications (cardiac vs. metabolic), and HbA1c changes over a median 19.3-month duration.

Results:

- Among 177 initiators, 78.5% remained on therapy. Indications were primarily cardiac (46.9%) and metabolic (37.3%).
- AE incidence is detailed in Table 26.

Table 26: Incidence of Prespecified Adverse Events (N=177 Initiators)

Adverse Event	Incidence (n=177 initiators)
Acute kidney injury (AKI)*	6.2%
Urinary tract infection	5.1%
Symptomatic hypoglycemia	1.7%
Fracture	1.7%
Mycotic infection	0.6%
DKA / Death / Amputation / Fournier's gangrene / Volume depletion	0%

*AKI events confined to the heart failure subgroup.

- Mean HbA1c decreased by 0.62% overall (n=105) and by 0.79% in the metabolic subgroup (n=76).

CONCLUSION:

- **Low AE rates and significant glycemic improvements support the expanded, cautious use of SGLT2i in pediatric populations.**

Mid-Sleep Timing and Insulin Secretion in Overweight Youth

Hitt T, et al.

Objective:

- To evaluate the relationship between delayed sleep phase and insulin regulation in overweight adolescents and young adults (AYA).

Methods:

- Secondary analysis of CHAriSmA, an observational metabolic risk study in overweight South Asian (SA), White (W), and African American (AA) AYA. A subset underwent: actigraphy, DXA for visceral fat (VF), and 180-min OGTT to assess insulin sensitivity (Si) and secretory rate (ISR).
- Linear regression (adjusted for sex and VF) examined MST–insulin associations in the combined cohort. Secondary analyses were stratified by ancestry.

Results:

- Later mid-sleep time (MST) was associated with higher total AUC ISR (p=0.006) and static AUC ISR (p=0.004).
- Ancestry-specific effects were observed in the White cohort (ISR p=0.002; Si p=0.017) but not in South Asian (Avg. MST 5:49am) or African American groups.

CONCLUSION:

- **Later sleep timing in overweight AYA correlates with increased compensatory insulin secretion.**
- **Findings suggest that ancestry and sociocultural factors may influence diurnal rhythms and metabolic dynamics.**

T2D Polygenic Risk Modulates Glycemic Benefits of Physical Activity in Youth

Harnois-Leblanc S, et al.

Objective:

- To investigate if T2D polygenic risk scores (PRS) modify the association between early adolescent lifestyle (activity/diet) and subsequent glycemic traits.

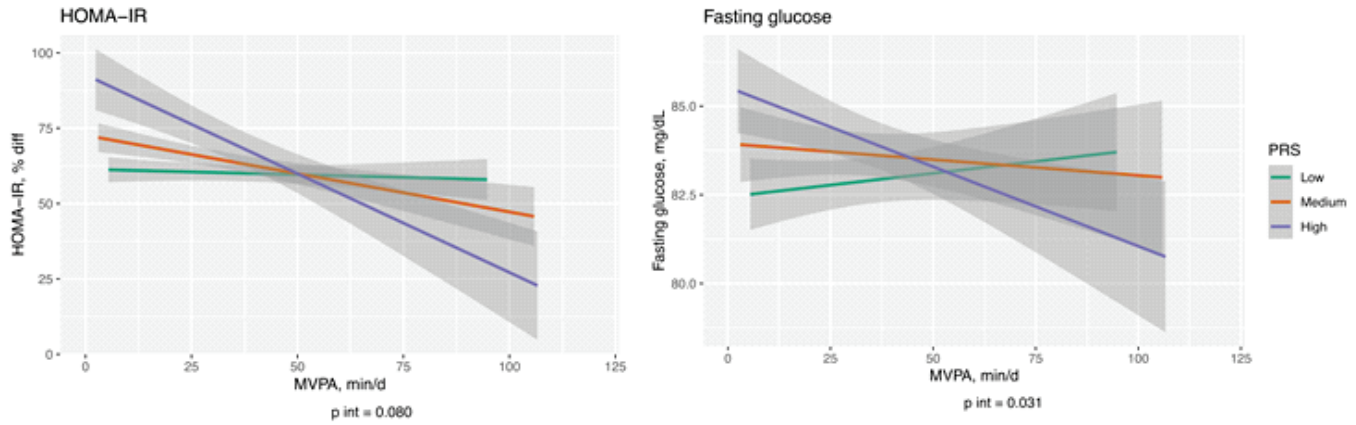
Methods:

- Longitudinal analysis of 516 youth (Project Viva).
- T2D-PRS, moderate-to-vigorous physical activity (MVPA, min/d) assessed by accelerometry, and diet assessed at age 13; fasting glucose, insulin, and HbA1c measured at age 18.
- Linear regression models adjusted for demographics and socioeconomic factors.

Results:

- Higher MVPA significantly lowered HOMA-IR and glucose, with effects amplified in individuals with higher T2D-PRS (Figure 6).

Figure 6: MVPA–Glycemia Dose-Response by T2D-PRS Tertile



Linear regression lines (with 95% CI) showing inverse MVPA–HOMA-IR and MVPA–fasting glucose associations, stratified by T2D-PRS tertile (Low, Medium, High) in 516 adolescents

- Fast-food intake (≥1x/week) increased HOMA-IR by 14.20% (95% CI: 0.05, 28.35) regardless of genetic risk. No other dietary-PRS interactions were significant.

CONCLUSION:

Youth with high genetic T2D risk gain disproportionate benefits from MVPA, whereas fast-food restriction is universally beneficial.

H. Pediatrics—Type 1 Diabetes

ADA-Recommended CGM Target Literacy Gaps in Adolescents with Diabetes

Cobry E, et al.

Objective:

- To evaluate adolescent proficiency in identifying ADA-recommended continuous glucose monitoring (CGM) targets and metric definitions.

Methods:

- Survey-based assessment of 39 adolescents (ages 14–17) regarding knowledge of time in range (TIR), time below range (TBR), glycemic variability, and A1c goals.

Results:

- Despite high CGM (95%) and AID (74%) adoption, significant knowledge gaps remain (Table 27).

Table 27: Adolescent Responses to ADA CGM Metric Goals and Definitions

ADA CGM Metric	Responses, n (%)
ADA goal of A1c <7%	**Correct: 24 (62%)** Incorrect: 9 (23%) Unsure: 6 (15%)
Defining target glucose range as 70-180mg/dL	**Correct: 18 (46%)** Incorrect: 21 (54%)
ADA goal for percentage *Time in Range* (TIR, 70-180mg/dL) as >70%	**Correct: 22 (56%)** Incorrect: 13 (33%) Unsure: 4 (10%)
ADA goal for average sensor glucose as <154mg/dL	**Correct: 6 (15%)** Incorrect: 31 (79%) Unsure: 2 (5.1%)
Defining low glucose as <70 mg/dL	**Correct: 28 (72%)** Incorrect: 10 (26%) Unsure: 1 (2.6%)
ADA goal for percentage *Time Below Range* (TBR, <70mg/dL) as <4%	**Correct: 4 (10%)** Incorrect: 27 (69%) Unsure: 8 (21%)
Defining very low glucose as <54 mg/dL	**Correct: 13 (33%)** Incorrect: 24 (62%) Unsure: 2 (5.1%)
ADA goal for percentage *Time Very Low* (<54 mg/dL) as <1%	**Correct: 26 (67%)** Incorrect: 6 (15%) Unsure: 7 (18%)
ADA goal for glycemic variability (CV) as <36%	**Correct: 4 (10%)** Incorrect: 4 (10%) Unsure: 31 (79%)

- While 72% correctly defined hypoglycemia, fewer could identify specific ADA targets for TIR or "very low" glucose.
- Males and those with >10 years of diabetes duration showed higher accuracy for specific metrics.
- No significant correlations were found between correct responses and race, insurance, or device usage.

CONCLUSION:

- **High device utilization does not equate to metric literacy.**
- **Continuous, adolescent-specific education is necessary to transition care successfully from parents to patients.**

A. Epidemiology—Cardiovascular Disease

T2D and Obesity as Predictors of Incident Atrial Fibrillation: A Large-Scale Cohort Study

Russo P, et al.

Objective:

- To quantify incident atrial fibrillation (AF) and cumulative burden within a T2D and obesity cohort, recognizing these as independent risk factors where obesity accounts for approximately 20% of AF prevalence.

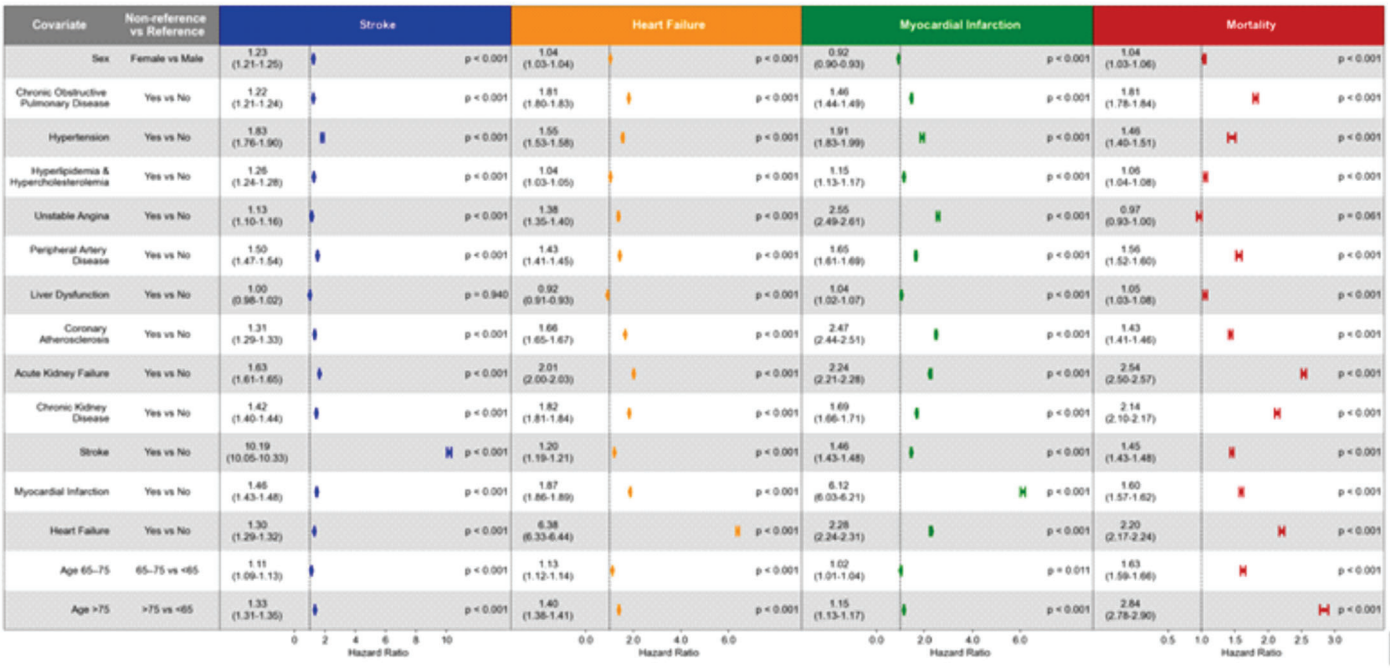
Methods:

- A retrospective real-world evidence (RWE) cohort study (2018–2025) of 8,166,278 adults with concurrent obesity and T2D, ≥12 months of continuous enrollment, and no prior AF diagnosis.
- Kaplan-Meier and Cox regression models estimated incident AF rates and post-AF mortality risks.

Results:

- AF developed in 7.8% of the cohort (n=635,233; incidence rate 1.886/100 patient-years).
- Cumulative incidence increased from 1.5% (6 months) to 12.9% (84 months).
- Key mortality predictors included age ≥75 (HR 2.84), heart failure (HR 2.20), and CKD (HR 2.14).
- Forest plot displaying HR and 95% CI for four post-AF outcomes across 15 covariates; all estimates adjusted via multivariable Cox regression shown in Figure 7.

Figure 7: Forest Plot — HR for Stroke, Heart Failure, Myocardial Infarction, and Mortality Post-AF



CONCLUSION:

- **High AF incidence in this population supports routine screening in diabetes clinics to facilitate early intervention for cardiovascular and renal risks.**

Prognostic Value of CGM Metrics vs. HbA1c for CVD and Mortality: GRADE-CGM Substudy

Tang M, et al.

Objective:

- To determine if CGM-derived time in range (TIR) and glucose management indicator (GMI) provide prognostic value for cardiovascular disease (CVD) and all-cause mortality beyond HbA1c in T2D.

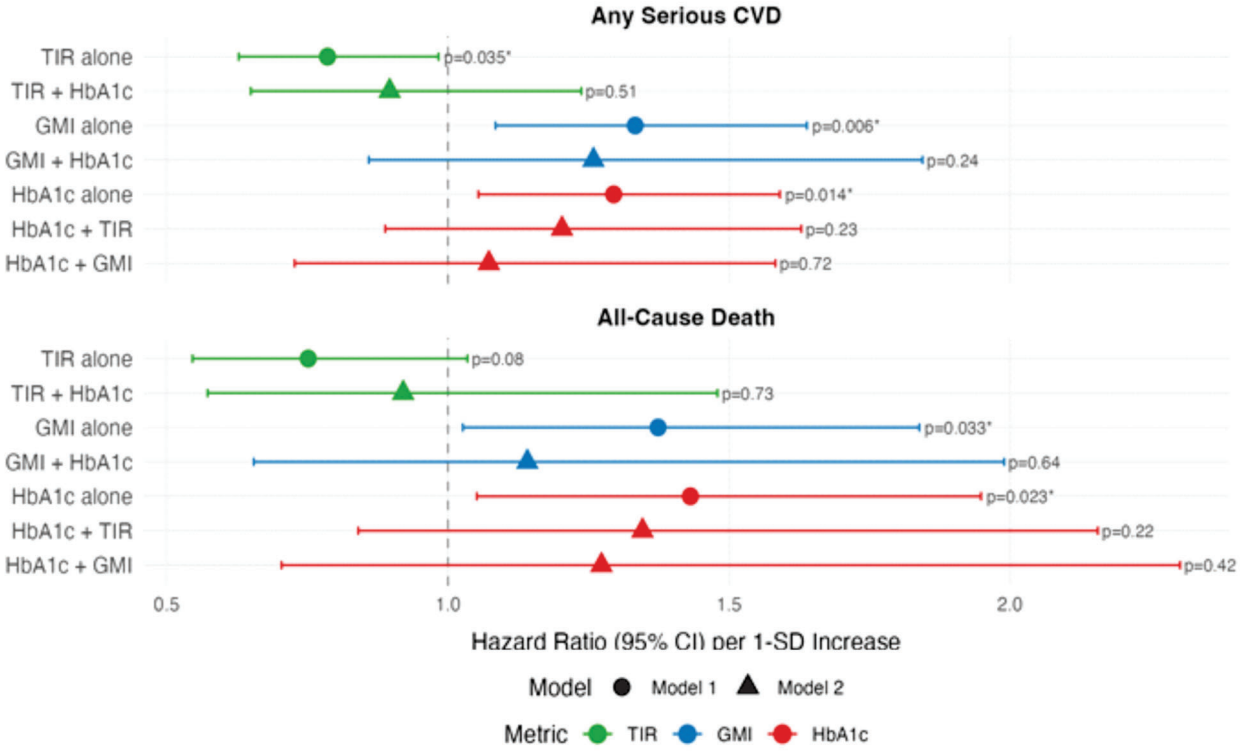
Methods:

- Analysis of 1,363 participants (GRADE (Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness) study) with 10-day CGM.
- Outcomes: serious CVD (MACE-Major Adverse Cardiovascular Events, heart failure hospitalization, angina, revascularization) and all-cause mortality
- Cox models estimated Hazard Ratios (HR) per 1-SD.
- Model 1 adjusted for baseline demographics (age, sex, race/ethnicity, treatment, diabetes duration); Model 2 mutually adjusted for CGM metrics and HbA1c.

Results:

- Over 2.3 years (59 CVD, 26 deaths), higher GMI (CVD HR 1.34; death HR 1.36) and HbA1c (CVD HR 1.30; death HR 1.42) predicted outcomes (Model 1).
- Higher TIR was protective for CVD (HR 0.78).
- Model 2 showed all associations attenuated post-mutual adjustment as shown in Figure 8.

Figure 8: Forest plot of HR (95% CI) per 1-SD increase in TIR, GMI, and HbA1c for serious CVD and all-cause death (Model 1 vs. Model 2)



Circle = Model 1 (single metric + covariates); Triangle = Model 2 (mutually adjusted with HbA1c or CGM metric).
All models adjusted for age, sex, race/ethnicity, treatment, diabetes duration.
* $p < 0.05$. N = 1,363.

CONCLUSION:

- **GMI and HbA1c offer overlapping rather than additive prognostic value.**
- **TIR's protective CVD association is not independent of HbA1c.**

Life's Essential 8 Metrics, Mortality Risk, and Life Expectancy in T2D and Cardiometabolic Multimorbidity

Yuan Y, et al

Objective:

- To quantify associations between Life's Essential 8 (LE8) scores, mortality, and life expectancy gains in individuals with T2D, coronary heart disease (CHD), stroke, or cardiometabolic multimorbidity (CMM).

Methods:

- Prospective analysis of UK Biobank data (N=24,479; mean age 59.8).
- Cohorts included T2D (n=11,745), CHD (n=4,748), stroke (n=4,891), and CMM (n=3,095).
- Mortality risk and life expectancy were assessed via Cox models and flexible parametric survival models- risk per LE8 category (low: 0–49; moderate: 50–79; high: 80–100).

Results:

- Each 10-point LE8 increase significantly reduced all-cause mortality: T2D (HR 0.90), CHD (HR 0.79), stroke (HR 0.89), and CMM (HR 0.87).
- Smoking was the primary protective component.
- Survival gains at age 65 reached 1.18 (T2D), 5.38 (CHD), 2.41 (stroke), and 2.40 (CMM) years (Figure 9).

Figure 9: Age-Dependent Life Expectancy Gains by CVH Level and Cardiometabolic Disease Group

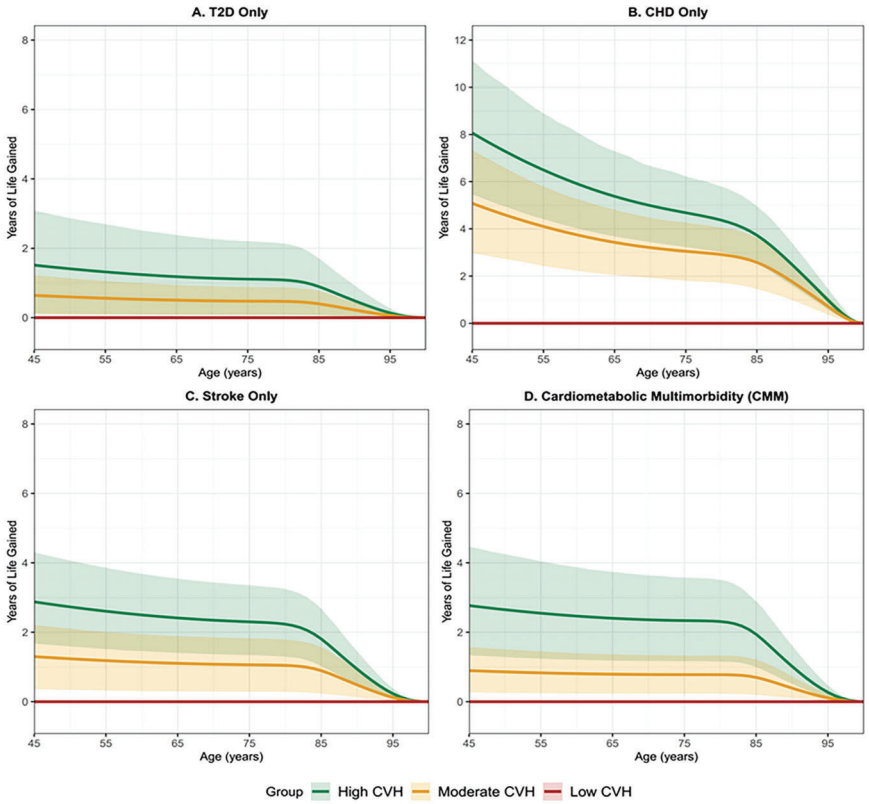


Figure: Estimated years of life gained by maintaining higher CVH across cardiometabolic disease profiles. The panels display the age-dependent impact of moderate (LE8 score 50–79; yellow line) and high (LE8 score 80–100; green line) CVH levels, compared to a low CVH reference (LE8 score 0–49; red line). Shaded areas represent 95% confidence intervals. Improving CVH was associated with significant survival gains across all groups, with younger individuals deriving the greatest extension.

At age 45, maintaining high CVH resulted in life expectancy gains of 8.07 years for CHD (5.08 years for moderate CVH), 2.88 years for stroke, 2.77 years for CMM, and 1.52 years for T2D. These benefits persisted at age 65, with high CVH extending lifespan by 5.38 years for CHD, 2.41 years for stroke, 2.40 years for CMM, and 1.18 years for T2D.

CONCLUSION:

- **Higher LE8 adherence is strongly associated with reduced mortality and substantial life expectancy extension across cardiometabolic conditions.**

B. Epidemiology—Diabetes Complications

Serum 25(OH)D Concentrations and Risk of Cardiovascular–Kidney–Metabolic (CKM) Syndrome

Abudukeranmu A, et al.

Objective:

- To evaluate the association between serum 25-hydroxyvitamin D [25(OH)D] and cardiovascular-kidney-metabolic (CKM) syndrome stages (0-4) in a nationally representative US cohort.

Methods:

- NHANES analysis (2001–2018; n=16,285) using harmonized 25(OH)D data and 2023 American Heart Association (AHA) CKM criteria (stages 0–4).
- Serum 25(OH)D was quantified by radioimmunoassay (2001-2006) and standardized liquid chromatography-tandem mass spectrometry (LC-MS/MS) (2007-2018)
- Weighted multinomial logistic regression and restricted cubic splines assessed dose-response relationships.

Results:

- Vitamin D Status distribution: 33.8% sufficient, 39.9% insufficient, 26.3% deficient.
- Vitamin D deficiency (<50 nmol/L) was significantly associated with higher risk across all CKM stages: Stage 1 (OR 1.32 [1.03–1.69]), Stage 2 (OR 2.55 [2.07–3.15]), Stage 3 (OR 2.62 [1.87–3.68]), and Stage 4 (OR 3.36 [2.52–4.48]).
- Relationships were linear for Stage 1, while Stages 2–4 exhibited nonlinear L- or J-shaped curves ($p < 0.01$).

CONCLUSION:

Vitamin D deficiency is an independent predictor of CKM progression, with association strength increasing at advanced stages.

CGM Utilization and Incident MASLD Outcomes in T2D: A Propensity-Matched Cohort Study

Liang YC, et al.

Objective:

- To evaluate the association between continuous glucose monitoring (CGM) use and metabolic dysfunction-associated steatotic liver disease (MASLD) outcomes in adults with Type 2 Diabetes (T2D).

Methods:

- Retrospective TriNetX cohort study (2017–2021) using propensity score matching (PSM) to analyze 22,928 matched pairs.
- Outcomes included 5-year incidence of NAFLD/NASH (Nonalcoholic Fatty Liver Disease/ Nonalcoholic Steatohepatitis), liver fibrosis, and hepatocellular carcinoma (HCC).

Results:

- CGM use was associated with reduced risk of NAFLD/NASH (HR 0.896; 95% CI 0.830–0.967) and liver fibrosis (HR 0.793; 95% CI 0.682–0.922).

- The greatest reduction in fibrosis risk occurred in patients with baseline HbA1c ≥10% (HR 0.547).
- Repeated CGM use further strengthened the association with reduced NAFLD/NASH risk (HR 0.794).
- No significant association was found for HCC.

CONCLUSION:

CGM use correlates with a lower risk of MASLD-related outcomes, particularly liver fibrosis in patients with suboptimal glycemic control.

BMI-Specific Glycemic Outcomes in the LANDMARC Study

Joshi S, et al.

Objective:

- To evaluate the impact of Body mass index (BMI) on glycemic control and macro/microvascular outcomes in an Indian cohort with Type 2 Diabetes (T2D) over 36 months.

Methods:

- Longitudinal subgroup analysis of 6,203 evaluable participants stratified by BMI (underweight to obese).
- Clinical assessments, cardiovascular (CV) risk factors, and insulin requirements were analyzed across 7 visits over a 3-year period.

Results:

- CV risk factors (hypertension, dyslipidemia) were identified in 58.57% of the obese group.
- While HbA1c improved from >8.0% at baseline to <7.5% by Visit 7 across all cohorts, overweight and obese participants required significantly higher basal and prandial insulin doses to achieve target levels.
- Underweight participants exhibited the lowest microvascular complication rates.
- Glycemic control improved at each visit irrespective of BMI category (Table 28)

Table 28: Vascular complications, CV risk factors, and glycemic control by BMI category at V7

BMI category	Underweight (BMI <18.0), N=44	Normal (BMI 18.0-22.9), N=902	Overweight (BMI 23.0-24.9), N=1117	Obese (BMI ≥25.0), N=4140	Total (N=6203) n (%)
Macrovascular complications (MAC) at Visit 7					
Total number of MAC	0	26	43	145	214
Total number of participants with MAC, n (%)[a]	0 (0.00%)	26 (2.88%)	39 (3.49%)	138 (3.33%)	203 (3.27%)
Cardiovascular death, n (%)[b]	0 (0.00%)	3 (11.45%)	8 (20.51%)	24 (17.39%)	35 (17.24%)
Non-fatal MI, n (%)[b]	0 (0.00%)	10 (38.46%)	16 (41.03%)	56 (40.58%)	82 (40.39%)
Microvascular complication (MIC) at Visit 7					
Total number of MIC	4	217	257	833	1311
Total number of participants with MIC, n (%)[a]	4 (9.09%)	178 (19.73%)	214 (19.16%)	724 (17.49%)	1120 (18.02%)
Neuropathy, n (%)[c]	4 (100.00%)	146 (82.02%)	171 (79.91%)	597 (82.46%)	918 (81.96%)
Nephropathy, n (%)[c]	0 (0.00%)	38 (21.35%)	44 (20.56%)	146 (20.17%)	228 (20.36%)
Retinopathy, n (%)[c]	0 (0.00%)	33 (18.54%)	42 (19.63%)	90 (12.43%)	165 (14.73%)
Participants with cardiovascular (CV) risk factors at Visit 7					
Total number of CV risk	28	552	774	3390	4744
The number of participants with CV risk, n (%)[a]	22 (50.00%)	430 (47.67%)	579 (51.84%)	2425 (58.57%)	3456 (55.71%)
Hypertension, n (%)[d]	17 (77.27%)	310 (72.09%)	436 (75.30%)	1932 (79.67%)	2695 (77.98%)
Dyslipidemia, n (%)[d]	11 (50.00%)	215 (50.00%)	295 (50.95%)	1278 (52.70%)	1799 (52.05%)
Glycemic control categories by BMI at baseline (Visit 1 and Visit 7)					
n (Visit 1)	21	631	788	3020	4460
<6.5% HbA1c	3 (14.30)	77 (12.20)	79 (10.00%)	366 (12.10%)	525 (11.80)
<7% HbA1c	8 (38.10%)	158 (25.00%)	210 (26.60%)	741 (24.50%)	1117 (25.00%)
≥7% HbA1c	13 (61.90%)	473 (75.00%)	578 (73.40%)	2279 (75.50%)	3343 (75.00%)
n (Visit 7)	21	541	640	2492	3694
<6.5% HbA1c	2 (9.50%)	78 (14.40%)	102 (15.90%)	355 (14.20%)	537 (14.50%)
<7% HbA1c	9 (42.90%)	196 (36.20%)	245 (38.30%)	903 (36.20%)	1353 (36.60%)
≥7% HbA1c	12 (57.10%)	345 (63.80%)	395 (61.70%)	1589 (63.80%)	2341 (63.40%)

Evaluable population is defined as subset of the participants in the eligible population and do not have any critical protocol violations; People with missing BMI, N=19.
[a]Percentages are based on number of participants within each BMI group in Evaluable population.
[b]Percentages are based on Total number of participants with macrovascular complications (N). Two participants were recorded to be discontinued in V1 due to CV Death. Since the date of discontinuation is after date of V1, the respective CV deaths are summarized in V2 (6 months follow-up).
[c]Percentages are based on Total number of participants with microvascular complications (N).
BMI, body mass index; CV, cardiovascular; HbA1c, glycated hemoglobin ; MAC, macrovascular complications; MI, myocardial infarction; MIC, microvascular complications ; V, visit(s).

CONCLUSION:

BMI correlates with CV risk burden and insulin requirements, reinforcing the need for BMI-tailored therapeutic strategies in T2D.

C. Epidemiology—Nutrition

BFP vs. BMI for Cardiometabolic Risk Screening in Young Adults

Mezzano L, et al.

Introduction and Objective:

- While BMI is a standard screening tool for obesity, its inability to differentiate between adipose and lean tissue limits its diagnostic precision.
- This study evaluates whether body fat percentage (BFP), calculated via standardized formulas, offers superior sensitivity for identifying Type 2 Diabetes (T2D) risk in young adults.
- Furthermore, it assesses the incremental diagnostic utility of integrating the FINDRISK score with these anthropometric measures to optimize early cardiometabolic screening in university settings.

Methods:

- Cross-sectional analysis of 152 medical students.
- Risk was stratified using BMI, BFP (CUN-BAE formula), and FINDRISK as low, intermediate, or high risk: BMI (<25, 25-29, ≥30 kg/m^2), BFP (men: <20%, 20-25%, >25%; women: <29%, 29-35%, >35%), and FINDRISK (<7, 7-14, >14).
- Diagnostic discordance and unique case identification were analyzed ($p<0.05$).

Results:

- Among 152 students (100F, 47M), high-risk detection was significantly higher via BFP (22%) than BMI (7%).
- Overall, 41% (n=62) were categorized as intermediate/high risk by at least one metric. Notable discordance occurred in females with normal BMI but elevated BFP.
- FINDRISK uniquely identified 6.6% (n=10) of intermediate-risk cases overlooked by anthropometry.

CONCLUSION:

Multi-tool screening (BMI+BFP+FINDRISK) significantly increases diagnostic sensitivity for early cardiometabolic risk in young adults compared to BMI alone.

A. Integrated Physiology—Liver

FibroScan Measurement Reliability in Community-Based Metabolic Screening: Inter- and Intra-rater Analysis

Maldonado IH, et al.

Introduction and Objective:

- With MASLD affecting >33% of adults, early detection of steatosis and fibrosis is critical.
- This study evaluated whether trained non-ultrasonography technicians can achieve reliable FibroScan results, potentially increasing screening access in primary care settings.

Methods:

- 100 adults (≥18 years) were screened by five trained non-specialist operators using EchoSens FibroScan.
- Operators recorded liver stiffness (kPa) and Controlled Attenuation Parameter (CAP) within a 10-minute limit.
- Reliability was evaluated via Intraclass Correlation Coefficients (ICC), with 30 additional paired scans for inter-rater analysis.

Results:

- Inter-rater reliability showed good agreement for CAP (ICC 0.81, 95% CI 0.66–0.90) and excellent agreement for stiffness (ICC 0.94, 95% CI 0.89–0.97).
- Intra-rater reliability was excellent for both CAP (ICC ≈0.93) and stiffness (ICC ≈0.96). All findings reached statistical significance ($p < 0.05$).

CONCLUSION:

- **FibroScan measurements by trained non-specialist personnel are highly reliable.**
- **Implementing such programs in community settings can significantly enhance early detection and management of metabolic liver disease.**

B. Obesity—Human

Cardiovascular Outcomes of Obesity Interventions: A Network Meta-Analysis

Sarma S, et al.

Objective:

- To determine the comparative efficacy of lifestyle modification, pharmacotherapy, and bariatric surgery on major adverse cardiovascular events (MACE), heart failure (HF), and all-cause mortality in adults with obesity.

Methods:

- Systematic review and network meta-analysis (NMA) of 67 RCTs (N=205,889) from MEDLINE, Embase, and Cochrane (to June 2024).
- Frequentist random-effects NMA and CINeMA tools were utilized for outcome assessment and confidence reporting.

Results:

- Participants (mean age 63.5; BMI 32.6 kg/m^2).
- NMA findings (versus placebo) for top-ranked treatments across the three critical outcomes are presented in Table 29.

Table 29: Top-Ranked Obesity Treatments by Cardiovascular Outcome (NMA

Outcome	Treatment	OR (95% CI) vs. Placebo	P-score
MACE	**Metformin**	0.63 (0.32–1.22)	0.83
	Tirzepatide	0.71 (0.41–1.23)	0.73
	Canagliflozin	0.72 (0.56–0.93)	0.78
Heart Failure	**Bariatric Surgery**	0.24 (0.03–1.70)	0.89
	Sotagliflozin	0.50 (0.36–0.69)	0.87
	Tirzepatide	0.55 (0.33–0.92)	0.80
All-Cause Mortality	**Sotagliflozin**	0.50 (0.40–0.63)	0.98
	Empagliflozin	0.69 (0.62–0.76)	0.88
	Metformin	0.79 (0.35–1.75)	0.63

CONCLUSION:

- **Obesity treatments provide heterogeneous cardiovascular protections.**
- **Tailoring interventions is essential for optimizing outcomes-focused obesity care.**

Phase 2 Trial of UBT251 Triple GIP/GLP-1/Glucagon Agonist for Obesity

Zhou Z, et al.

Objective:

- To evaluate the efficacy and safety of UBT251, a novel triple agonist targeting glucose-dependent insulinotropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1), and glucagon (GCG) receptors, for obesity treatment.

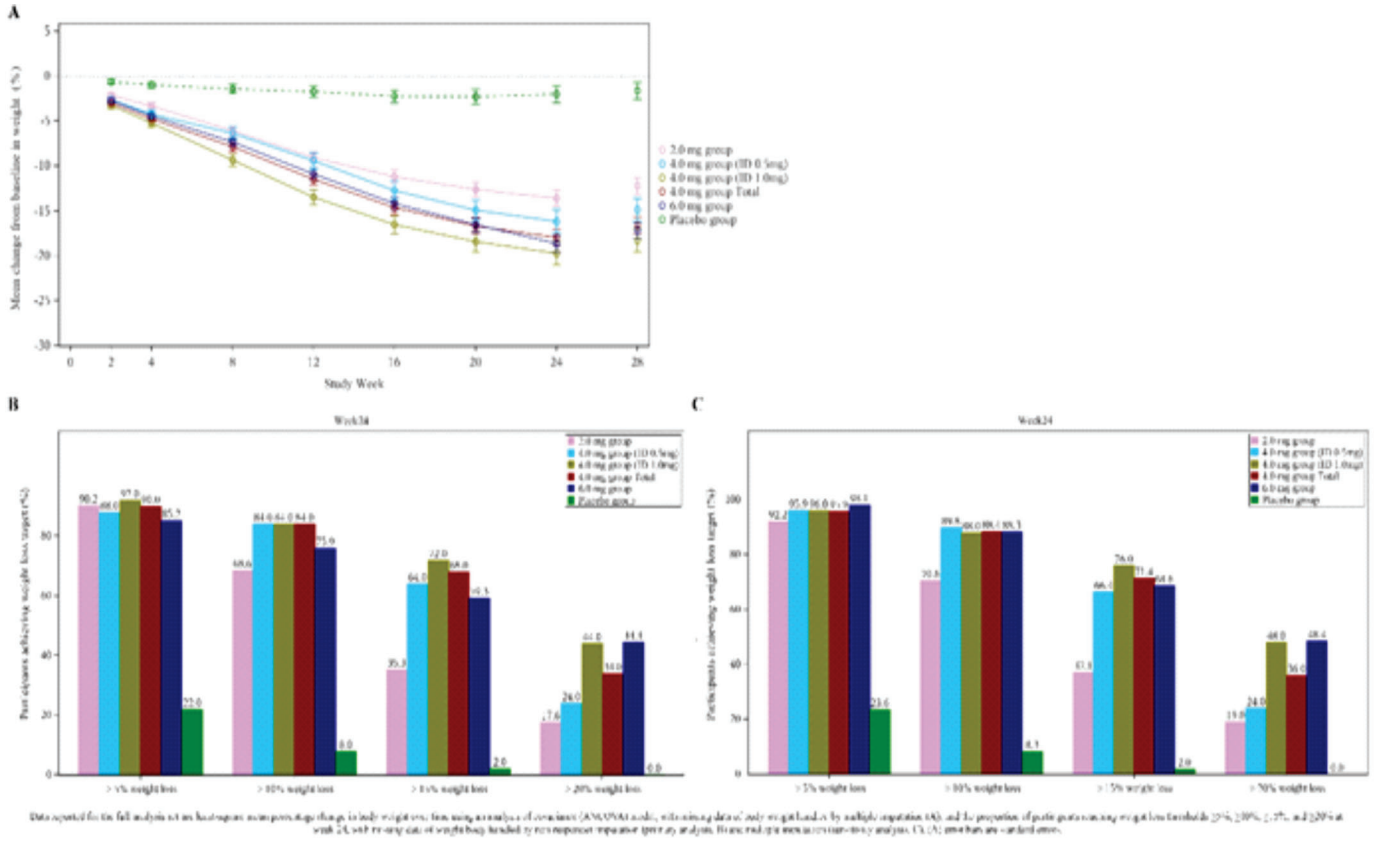
Methods:

- A 24-week Phase 2 RCT (N=205) in Chinese adults with overweight/obesity.
- Participants received once-weekly s.c. UBT251 and randomized (2:1:1:2:2) to once-weekly subcutaneous UBT251 (2.0 mg, 4.0 mg [initial dose {ID} 0.5 mg], 4.0 mg [ID 1.0 mg], or 6.0 mg) or placebo (pbo) for 24 weeks.
- Primary endpoint: Percentage weight loss (%WL).

Results:

- At week 24, UBT251 cohorts achieved significant %WL: 13.6% (2.0 mg), 16.2%–19.7% (4.0 mg), and 18.7% (6.0 mg) vs. 2.0% for placebo ($p < 0.001$).
- Absolute reductions in body weight, WC, and BMI were significantly greater with UBT251 vs. pbo (all $P<0.001$) (Figure 10).

Figure 10: Longitudinal % Weight Change and Categorical Response Thresholds Description



- Adverse events were primarily mild-to-moderate gastrointestinal symptoms.

CONCLUSION:

UBT251 produced dose-dependent, clinically significant weight loss (up to 19.7%) and demonstrated an acceptable safety profile.

Obesity Pharmacotherapy and Physical Function: A Systematic Review and Meta-Analysis

Peary A, et al.

Objective:

- To systematically evaluate the efficacy of FDA-approved obesity management medications (OMMs) on self-reported and objective physical function in adults with overweight or obesity.

Methods:

- Meta-analysis of 30 RCTs (N=25,068) investigating OMMs (orlistat, phentermine /topiramate, naltrexone/bupropion, liraglutide, setmelanotide, semaglutide, or tirzepatide us-ing PubMed, Embase, and CINAHL through August 2025.
- Random-effects models were used to estimate pooled mean differences (MD).

Results:

- OMMs significantly improved self-reported PF on both the Short-Form-36 (SF-36) and the Impact of Weight on Quality-of-Life (IWQOL) scales.
- Objective PF, assessed in three studies via the Six-Minute Walk Test (6MWT), showed modest gains vs. control (Table 30).

Table 30: Pooled Meta-analysis Results: Effect of OMMs on Physical Function Outcomes

Outcome Measure	Tool	MD (95% CI)	I^2	p-value
Self-reported PF	SF-36	1.76 (1.20–2.32)	62.5%	< 0.01
Self-reported PF	IWQOL	5.58 (4.24–6.92)	65.8%	< 0.01
Objective PF	6MWT (m)	13.95 (5.84–22.07)	31.8%	0.23

PF = physical function; SF-36 = Short-Form-36; IWQOL = Impact of Weight on Quality-of-Life; 6MWT = Six-Minute Walk Test; MD = mean difference; CI = confidence interval.

CONCLUSION:

- **OMMs effectively enhance patient-perceived physical function.**
- **Future research should incorporate more objective functional metrics to further validate treatment effectiveness.**

Metabolic Impact and Post-Discontinuation Maintenance of Oral Semaglutide: The GAROS Study

Peary A, et al.

Objective:

- To evaluate the broader metabolic effects of oral semaglutide, specifically regarding body composition, prediabetes remission, and weight maintenance following treatment cessation.

Methods:

- GAROS (Genetics of the Acute Response to Oral Semaglutide)- Prospective study (N=1,100; BMI ≥ 25).
- Participants received oral semaglutide (titrated to 42 mg/day) for 12 weeks. Assessments included DXA and OGTT at baseline and week 12, with a 6-month post-treatment follow-up.

Results:

- Mean weight loss was −8.6±4.1% (−8.9 kg; p<0.001); 81.7% achieved 5% and 34.1% achieved 10% loss.
- DXA showed 5.6 kg fat loss (63% of total) and 3.3 kg lean mass loss.

- Prediabetes remission to normoglycemia occurred in 70% of cases.
- GI adverse events were reported by 76% (nausea 64%).
- At 3 and 6 months post-discontinuation, participants remained 7.1% and 5.4% below baseline weight, respectively; 74% remained below their starting weight at 6 months.

CONCLUSION:

- **Oral semaglutide facilitates significant weight loss, improves body composition, and induces high rates of prediabetes remission, with metabolic benefits persisting 6 months post-therapy.**

Impact of Aleniglipron Initiation Dose on Gastrointestinal Tolerability in Obesity

Smith TR, et al.

Objective:

- To determine if a reduced starting dose (2.5 mg) of aleniglipron, an oral small-molecule GLP-1RA, improves gastrointestinal (GI) tolerability compared to the standard 5 mg initiation dose.

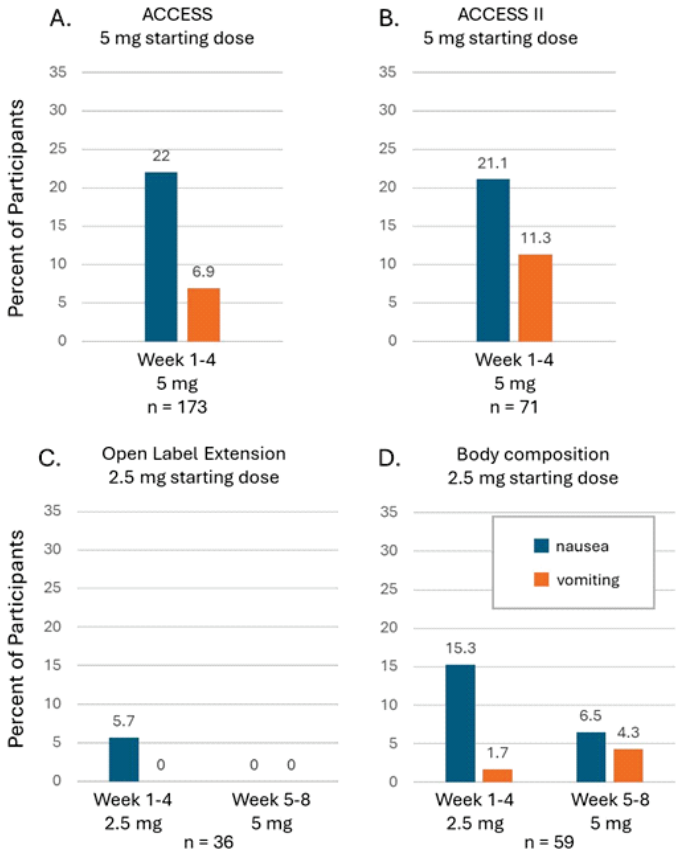
Methods:

- Interim analysis of ACCESS open-label extension (OLE) (n=36) and body composition (BC) trials (n=59) utilizing a 2.5 mg starting dose titrated to 5 mg at week 4.
- Outcomes were compared to the ACCESS (N=173) and ACCESS II (N=71) 5 mg initiation cohorts over an 8-week period.

Results:

- Starting with 2.5 mg significantly lowered the prevalence of nausea and vomiting during the first 4 weeks. No subsequent increase in nausea was observed during week 5–8 titration to 5 mg (Figure 11).

Figure 11: Nausea and vomiting prevalence (%) by study cohort and dose initiation period.



- Discontinuation due to adverse events (AEs) was 0% in the 2.5 mg group, compared to 4.6% and 9.9% in the 5 mg initiation groups.

CONCLUSION:

- **OMMs effectively enhance patient-perceived physical function.**
- **Future research should incorporate more objective functional metrics to further validate treatment effectiveness.**

MEGA We care

Makers of

Panfor SR
Metformin Hydrochloride Sustained Release Tablets 500mg/1000mg

PERGLIM
Glimepiride Tablets 1mg/2mg/3mg/4mg

PERGLIM M-1
Glimepiride and Metformin Hydrochloride SR Tablets

INSUNOVA-30/70 (Biphasic)
Insulin Injection, Biphasic Isophane Ph. Eur.

Insunova-G
Insulin Glargine Injection (rDNA)

INSUNOVA-R
Insulin Injection, Soluble Ph. Eur.

Dapiflozin
Dapagliflozin Tablets 5mg/10mg

Dapiflozin-M
Dapagliflozin and Metformin Hydrochloride Extended-Release Tablets

Amaziptin
Sitagliptin Tablet 25mg/50mg/100mg

Amaziptin-M
Sitagliptin Metformin HCl Tablet

Gly4par
Gliclazide Extended Release Tablets 30 mg/60 mg

Pansiptin
Sitagliptin Tablets 50mg/100mg