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Diabetes

Current Awareness Bulletin

June 2026

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- **Quickfire health literacy: communicating with patients more effectively**
  30 minutes. Learn about the communication barriers patients may encounter, and ways to ensure they get the most from their care.

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Book a session today at https://forms.office.com/e/HyiSXfDaYV (these sessions will be held on a monthly basis)

General

Risk of recurrence after successful surgery for Cushing's disease and association with *USP8* genotype and tumour size: an international, retrospective, longitudinal cohort study

Zhang Q., Cai Y., Liu Y., et al. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.327-336.

[**Background**: Recurrence after successful pituitary surgery remains a challenge in the management of patients with Cushing's disease, with no reliable predictors of long-term outcome. Pathogenic somatic *USP8* variants are found in one third of cases and their association with recurrence is unclear. The aim of this study was to determine the association between *USP8* status and postoperative outcome.]

Specific cortisol blockade in Cushing's syndrome

Grossman A. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.276-277.

[Cushing's syndrome is most frequently seen in patients on exogenous glucocorticoids (ie, steroids) for immune-related conditions (eg, rheumatoid arthritis and asthma) and specific haematological cancers. Endogenous Cushing's syndrome is rare, with the excess glucocorticoids arising from the adrenal cortex. The majority of cases are adrenocorticotropic hormone (ACTH)-dependent, most often pituitary-dependent Cushing's syndrome (Cushing's disease), which was first described by Harvey Cushing in 1932. [1] These are generally small corticotroph tumours, although 5–10% are macroadenomas. Over the past 2 years, an increasing proportion of ACTH-dependent Cushing's syndrome has been identified as arising from neuroendocrine tumours, causing ectopic ACTH syndrome, many from small bronchial carcinoids. For ACTH-independent Cushing's syndrome, these could be due to adrenal adenomas or carcinomas, as well as rare bilateral micronodular or macronodular adrenal hyperplasia. [2]]

***USP8* genotype and tumour size as predictors for recurrence in Cushing's disease**

Lodish M.B. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.280-281.

[The study by Qilin Zhang and colleagues published in *The Lancet Diabetes & Endocrinology* evaluates the risk of recurrence following successful surgery for Cushing's disease and examines its association with *USP8* genotype and tumour size. [1] With 435 patients included, it represents one of the largest

investigations to date exploring genotype–phenotype associations in Cushing's disease. The findings suggest a robust and clinically relevant predictor of long-term outcomes, which is particularly important given that disease recurrence following initially successful transsphenoidal surgery remains a substantial clinical challenge. The ability to stratify recurrence risk more accurately is essential to inform personalised postoperative management strategies and optimise follow-up care.]

Children with diabetes

Cognitive skills in children and adolescents with type 1 diabetes: a scoping review and meta-analysis

Arman D., Haynes E., Brussoni M., et al. *BMJ Open Diabetes Research and Care* 2026;14: e005635

[Type 1 diabetes (T1D) complications may impair cognitive development, but evidence on cognitive skills in children and adolescents with T1D is inconsistent. This study aimed to document measures and outcomes used to assess cognitive skills in children with T1D and to examine the relationship between T1D and cognitive skills. A systematic literature search was conducted across five databases to identify studies that administered cognitive assessments to children and adolescents aged ≤19 years with T1D. Study characteristics, cognitive skills assessments and outcomes and comparisons to non-T1D peers where available were synthesized on an evidence map. Random-effects meta-analysis was used to assess differences in Wechsler Full Scale Intelligence Quotient (IQ) test scores between T1D and non-T1D groups. From 2464 studies, 129 were included. Five main cognitive categories were identified, with comparisons to non-T1D peers—where available—yielding mixed results: academic performance (n=37; n=7/22 worse T1D), executive function (n=101; n=31/48 worse T1D), intelligence (n=73; n=22/37 worse T1D), language (n=30; n=7/20 worse T1D) and memory and learning (n=84; n=31/48 worse T1D). Large-scale studies (n≥1000) did not find significant differences between groups for academic performance (n=0/6 worse T1D) and language (n=0/3 worse T1D). In the meta-analysis of 16 studies (n=1594), children with T1D had slightly lower IQ scores than peers without T1D (mean difference −3.49, 95% CI (−6.16 to −0.82); p=0.010). T1D appears to be associated with slightly lower cognitive outcomes in some areas. Further research is needed to understand the impact of these findings on daily functioning and to inform screening for at-risk children.]

Co-morbidities (find here cardiovascular, kidney disease, neuropathy, diabetic retinopathy etc)

Cardiovascular Disease

Association of life’s essential 8 with cardiovascular outcomes and mortality in adults with prediabetes: mediating role of inflammatory biomarkers

Liang J., Yang R., Liang Y., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113187.

[**Aims**: The intervention of prediabetes, with lifestyle modification as its first-line therapy, is an emerging method to prevent diabetes and cardiovascular complications. This study investigated the association of Life’s Essential 8 (LE8) with cardiovascular outcomes and mortality among individuals with prediabetes, and the mediating role of inflammation in these relationships.]

Association of remnant cholesterol with stroke risk by glycemic status: a nationwide prospective cohort study

Lu F. and Yang F. *Diabetes Research and Clinical Practice* 2026, 234: 113190.

[**Background**: The role of elevated remnant cholesterol (RC) across different glycemic status categories remains unclear.]

Cardiometabolic multimorbidity prevalence and mortality risks in Chinese old-old population: real-world evidence from continuing care retirement community

Cao Y., Wang Z., Wang F., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113164.

[**Aims**: To provide evidence on cardiometabolic multimorbidity (CMM) among very elderly Chinese.]

Combined associations of GLP-1 receptor agonists and a healthy lifestyle with cardiovascular outcomes among individuals with type 2 diabetes: a prospective cohort study

Nguyen X.M.T., Li Y., Czernichow S., et al. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.317-326.

[**Background**: The long-term combined effects of lifestyle habits and GLP-1 receptor agonists on cardiovascular outcomes are unknown. We aimed to examine the combined association of GLP-1 receptor agonist use and adherence to eight lifestyle habits with cardiovascular outcomes.]

Comment on "Effects of GLP-1 agonists on 10-year cardiovascular risk reduction in primary prevention: A 44-week open label prospective study"

Dedeepya S.D., Goel V., Desai N.N. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2026;20(4): 103418.

[Seijas-Amigo et al. report an important real-world signal: among people with Type 2 diabetes mellitus (T2DM) and obesity treated with glucagon-like peptide-1 receptor agonists (GLP-1 receptor agonists, GLP-1 RA), estimated 10-year atherosclerotic cardiovascular disease (ASCVD) risk fell by a mean 3.28 percentage points at 44 weeks [1]. The manuscript adds timely clinical data on population-level risk projection outside controlled cardiovascular outcome trials. Below I offer focused considerations intended to strengthen interpretation and next steps for translation.]

Comparison of the American diabetes association risk test, BMI, and estimated cardiorespiratory fitness with incident prediabetes and type 2 diabetes: A cohort study

Sloan R.A., Lailo J.M., Lee S.A., et al. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2026;20(4): 103421.

[**Aim(s)**: To compare associations of nonexercise estimated cardiorespiratory fitness (eCRF), the American Diabetes Association Risk Test (ADART), and body mass index (BMI) with incident prediabetes and type 2 diabetes in adults with normoglycemia.]

Corneal confocal microscopy and cardiac autonomic neuropathy in individuals with type 1 diabetes mellitus

Ziori M., Tentolouris A., Eleftheriadou I., et al. *Journal of Diabetes and Its Complications*, 2026, 40(4), Article 109290.

[**Background and aims**: Cardiac autonomic neuropathy (CAN) in diabetes is associated with increased mortality. Corneal confocal microscopy (CCM) is a non-invasive imaging modality that quantifies small fiber neuropathy. The aim of this study was to examine the association between CCM-derived corneal nerve parameters and CAN in individuals with type 1 diabetes mellitus (T1DM).]

Correction to *Lancet Diabetes Endocrinol* 2026; 14: 317–2

Lancet Diabetes & Endocrinology, 2026, 14(4), e.7.

[*Nguyen X-MT, Li Y, Czernichow S, et al. Combined associations of GLP-1 receptor agonists and a healthy lifestyle with cardiovascular outcomes among individuals with type 2 diabetes: a prospective cohort study*.]

The effect of baseline prediabetes on the relation between lipoprotein (a) and incident type 2 diabetes mellitus and cardiovascular outcomes: observations from the UK-Biobank

Chattopadhyay S., Sangha J., Sathyapalan T. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2026;20(4): 103422.

[**Aims**: To explore the effect of prevalent prediabetes (preDM) on relation between lipoprotein (a) Lp(a) and incident diabetes mellitus (T2DM) and cardiovascular outcomes.]

Elevated FIB-4 index as a risk marker within the KDIGO framework in patients with type 2 diabetes and hypertension

Fu H., Xing C., Wang H., et al. *BMJ Open Diabetes Research and Care* 2026;14: e005880

[**Background and aims**: The Kidney Disease: Improving Global Outcomes (KDIGO) 2024 guideline recommends risk stratification for chronic kidney disease (CKD) management; however, patients within the same KDIGO category may still experience heterogeneous outcomes. Hypertension and type 2 diabetes mellitus (T2DM) are predominant causes of CKD, and hepatic fibrosis is highly prevalent in

this population, but not integrated into current KDIGO risk assessment. The Fibrosis-4 (FIB-4) index, a widely validated noninvasive marker of hepatic fibrosis, may capture residual risk not reflected by KDIGO stratification. This study aims to explore whether FIB-4 can identify residual risk beyond KDIGO stratification in patients with T2DM and hypertension.]

Liver fibrosis scores predict cardiovascular outcomes in myocardial infarction and non-obstructive coronary arteries patients with and without diabetes or prediabetes

Abdu F.A., Shi T., Liu L., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113182.

[**Aims**: We aimed to investigate the association between liver fibrosis scores (LFS) and major adverse cardiovascular events (MACE) in patients with myocardial infarction and non-obstructive coronary arteries (MINOCA), particularly in those with and without diabetes (DM) or prediabetes (pre-DM).]

Low uptake and disparities in therapeutic inertia of cardiorenal protective diabetes medications for patients with type 2 diabetes and above-target hemoglobin A1c

German J., Huang W.A., Brucker A., et al. *BMJ Open Diabetes Research and Care* 2026;14: e005546

[**Introduction**: Therapeutic inertia (failure to initiate or intensify therapy when therapeutic goals are unmet) contributes to poor glycemic control and diabetes-related complications. We assessed the extent of therapeutic inertia, defined as a lack of new prescription orders for sodium-glucose cotransporter-2 inhibitors (SGLT2i) or glucagon-like peptide-1 receptor agonists (GLP-1RA), among patients with type 2 diabetes and above-target hemoglobin A1c who had clinical indications for use, were not currently using these medications, and had no contraindications. We also examined whether prescribing patterns differed by race and ethnicity.]

Mechanisms in diabetes mellitus: Relationships to metabolism and/or neoplasia

D'Elia J.A., Roshan B., Weinrauch L.A. *Journal of Diabetes and Its Complications*, 2026, 40(4), Article 109289.

[Insulin resistance and diabetes mellitus are associated with increased atherosclerotic thromboembolic events, decreased immune competence, and elevated neoplasia event rates compared with euglycemic populations. Insulin signals cellular metabolism to activate adenosine monophosphate protein kinase (AMPK) for energy generation and transduces insulin-like growth factor to promote cell growth and proliferation. Diabetes renders inhibition of genes for tumor suppression, thereby promoting cell growth and proliferation. Since insulin resistance may increase expression of cell growth and proliferation, it is a target for therapeutic interruption. Metformin and pioglitazone have been found to promote metabolic (mTOR2) while inhibiting neoplastic (mTOR 1) pathways of the AMPK signaling network.]

Optimising lipid monitoring interval for primary prevention of cardiovascular disease in patients with type-2 diabetes: A target trial emulation study

Wang B., Tse E.T.Y., Chui C.S.L., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113156.

[**Background**: Guidelines differ on how often to monitor lipid profiles in adults with type 2 diabetes mellitus (T2DM) without established cardiovascular disease (CVD), and randomized evidence is lacking. This study aimed to optimise lipid monitoring intervals for type-2 diabetes mellitus (T2DM) patients at various LDL-C levels.]

Dementia

Management of diabetes when comorbid with dementia.

Dening K.H. *British Journal of Community Nursing* 2026;31(4):162-167.

[Dementia is a syndrome caused by progressive neurological conditions. The majority of people will be diagnosed with late-onset dementia and will be over the age of 65 years, though a significant number may also be diagnosed before this age, termed young-onset dementia. People with dementia, especially late-onset, are more likely to have other comorbid conditions, and often multiple health conditions, more so in number than age-equivalent populations without dementia. One of the common comorbid conditions experienced by people with dementia is diabetes, which may have been present before any diagnosis of dementia is made, or onset may also be after the person's diagnosis of

dementia. The ongoing management of diabetes as a person's dementia progresses can often raise significant anxiety in both health and care professionals and family carers alike. This article discusses some of the issues to consider in the management of diabetes in a person with dementia.]

Diabetic Neuropathy

Hyperglycaemia-induced metabolic stress and epigenetic imprinting in the inflammatory pathogenesis of diabetic neuropathy

Razi F.B., Ashraf H., Singhal S., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113172.

[Diabetic neuropathy (DN), a major microvascular complication of diabetes mellitus, results from a complex interplay among oxidative stress, inflammation, and persistent epigenetic modifications. Hyperglycemia-induced mitochondrial dysfunction increases reactive oxygen species (ROS), which activate redox-sensitive inflammatory cascades, including NF-κB, JAK/STAT, and the NLRP3 inflammasome. These pathways amplify cytokine release and neuronal sensitisation, while reciprocal feedback between ROS and inflammation mediated by Nrf2 suppression further perpetuates nerve damage. Damage-associated molecular patterns (DAMPs), including HMGB1, S100A8/A9, mitochondrial DNA, and extracellular ATP, act as key amplifiers of neuroinflammation. By engaging receptors such as RAGE, Toll-like receptors (TLRs), and NOD-like receptors (NLRs), particularly NLRP3, these DAMPs trigger glial activation and nociceptive signalling, contributing to axonal degeneration and pain hypersensitivity in DN. Epigenetic dysregulation, including DNA methylation drift, histone modification imbalance, and aberrant non-coding RNA expression, constitutes a critical mechanism underlying metabolic memory, wherein prior hyperglycemic exposure leaves lasting molecular imprints. Persistent histone acetylation (H3K9ac), altered methylation (H3K4me1/Set7, H3K9me3/SUV39H1), and stable 5-methylcytosine patterns sustain inflammatory and oxidative pathways, even after glucose normalisation. Therapeutically, DNMT and HDAC inhibitors, miRNA modulators, and agents targeting RAGE/TLR4/NLRP3 pathways show promise in reversing these molecular imprints. Antioxidants and anti-inflammatory compounds with epigenetic effects further represent potential disease-modifying strategies. Future research must focus on longitudinal human studies, nerve-specific epigenomics, and multi-omics integration to enable personalised, mechanism-based therapy for DN. Understanding the interdependence of ROS, DAMPs, and epigenetic memory is key to breaking the cycle of chronic neuroinflammation and neuronal injury.]

Eye Diseases

Letter to the editor: “Prediction of retinopathy risk: A prospective cohort study in China”

Mehta R. and Sah R. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2026;20(4): 103415.

[We read with interest the study by Xu et al. evaluating risk prediction for retinopathy using nomograms based on baseline and longitudinal data from a large multiethnic Chinese cohort [1]. Although the combination nomogram incorporating dynamic clinical parameters represents a pragmatic advancement over static baseline models, several key limitations remain unaddressed and merit critical consideration.]

Response to Letter to the Editor regarding “Prediction of retinopathy risk: A prospective cohort study in China”

Xu X., Wang D., Alam U., et al. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2026;20(4): 103414.

[We are grateful to Dr. Rachana Mehta and Dr. Ranjana Sah for their interest in our recent publication titled “Prediction of Retinopathy Risk: A Prospective Cohort Study in China” [1]. We appreciate their thoughtful appraisal and are happy to clarify and expand upon the points raised in their letter.]

Letter to the Editor “The role of artificial intelligence in diabetic retinopathy screening in type 1 diabetes: A systematic review”

Ji L., Abudulam R., Li M. *Journal of Diabetes and Its Complications*, 2026, 40(4), Article 109155.

[Sacchini et al. [1] recently conducted a systematic review to explore the role of artificial intelligence (AI) in screening for diabetic retinopathy (DR) among individuals with type 1 diabetes (T1D). However, the

following issues need to be carefully considered.]

Response to: "Letter to the editor "The role of artificial intelligence in diabetic retinopathy screening in type 1 diabetes: A systematic review"

Cangelosi G., Sacchini F., Mancin S., et al. *Journal of Diabetes and Its Complications*, 2026, 40(4), Article 109180.

[We are deeply grateful to the letter's authors for their attention and care in examining our work. [1,2] Their comments provide us with a valuable opportunity to clarify certain methodological aspects and to enrich the scientific discussion on a highly relevant topic. We are pleased to emphasize that our study was designed and conducted as a systematic review, not a meta-analysis. We are aware that the distinction may sometimes appear subtle, but we consider it fundamental, as some observations seem to be based on the assumption of a quantitative synthesis, which was not within the scope of our work. The primary objective was to systematically collect, critically analyse, and provide a comprehensive overview of the available evidence on the use of artificial intelligence (AI) in screening for diabetic retinopathy (DR) in individuals with type 1 diabetes (T1D). We are pleased to affirm that this objective was fully achieved.]

Role of retinal biomarkers in diabetes detection and risk prediction: A systematic scoping review

Kaup S., Bhat S., Reardon E.E., et al. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2026;20(4): 103405.

[**Aims**: This systematic scoping review was conducted to map and synthesize literature on retinal biomarkers associated with type 2 diabetes (T2D), including conventional and Artificial Intelligence(AI)-derived features, while considering ethnic/geographic diversity.]

Kidney Disease

Exclusive association of non-HDL/HDL ratio with albuminuria in diabetes and its nonlinear pattern in advanced CKD: Findings from NHANES 2015–2020

Ke X. *Diabetes Research and Clinical Practice* 2026, 234: 113150.

[**Objective**: To investigate the diabetes-specific association between non-HDL/HDL cholesterol ratio (NHHR) and urinary albumin-to-creatinine ratio (UACR), and its nonlinear threshold effect in chronic kidney disease (CKD) stages. **Methods:** This cross-sectional study included 10,613 U.S. adults (aged 20–70 years, estimated glomerular filtration rate ≥ 30 mL/min/1.73 m ^{2}) from NHANES 2015–2020. NHHR was calculated as the difference between total cholesterol and HDL-C divided by HDL-C. To explore the relationship between NHHR and UACR, a multivariable logistic regression model, smoothed curve fitting and subgroup analyses were employed. **Results:** Each 1-unit NHHR increase elevated UACR by 4.46 mg/g overall (95% CI: 1.13–7.78, P = 0.009). Crucially, NHHR-UACR association was exclusive to diabetics (β = 23.56 mg/g, 95% CI: 8.59–38.54, P < 0.001) with no significance in non-diabetics (P for interaction < 0.001). A nonlinear pattern emerged and intensified with declining renal function: Stage 1 showed a linear relationship (P = 0.426), Stage 2 demonstrated marginal nonlinearity (P = 0.031), and Stage 3 displayed a markedly nonlinear relationship (P < 0.001), characterized by an accelerated increase in UACR beyond an NHHR of approximately 3.5. Effect modification was significant by ethnicity (stronger in Non-Hispanic Blacks, P = 0.016) and sex (greater in females, P = 0.048). **Conclusion:** NHHR associates with albuminuria exclusively in diabetes and exhibits a nonlinear pattern in CKD stage 3. These findings indicate diabetes-specific renal injury patterns and CKD stage-dependent pathophysiological mechanisms.]

Finerenone increases the likelihood of improved KDIGO risk category in patients with CKD and type 2 diabetes: An analysis from FIDELITY

Weingold R., Filippatos G., Anker S.D., et al. *Journal of Diabetes and Its Complications*, 2026, 40(4), Article 109274.

[**Aims**: In FIDELITY, finerenone improved kidney and cardiovascular (CV) outcomes in patients with type 2 diabetes (T2D) and chronic kidney disease (CKD). The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines categorise CKD progression risk based on estimated glomerular

filtration rate (eGFR) and urine albumin-to-creatinine ratio (UACR). This FIDELITY post hoc subanalysis investigated KDIGO risk category changes associated with finerenone.]

Low uptake and disparities in therapeutic inertia of cardiorenal protective diabetes medications for patients with type 2 diabetes and above-target hemoglobin A1c

German J., Huang W.A., Brucker A., et al. *BMJ Open Diabetes Research and Care* 2026;14: e005546

[**Introduction**: Therapeutic inertia (failure to initiate or intensify therapy when therapeutic goals are unmet) contributes to poor glycemic control and diabetes-related complications. We assessed the extent of therapeutic inertia, defined as a lack of new prescription orders for sodium-glucose cotransporter-2 inhibitors (SGLT2i) or glucagon-like peptide-1 receptor agonists (GLP-1RA), among patients with type 2 diabetes and above-target hemoglobin A1c who had clinical indications for use, were not currently using these medications, and had no contraindications. We also examined whether prescribing patterns differed by race and ethnicity.]

Renal Outcomes of GLP-1 Receptor Agonists and Tirzepatide Across CKD Stages and Metabolic Phenotypes (Type 2 Diabetes and/or Overweight/Obesity): A Scoping Review

Rico-Fontalvo J., Daza-Arnedo R., Elbert A., et al. *Diabetes Therapy* 2026, 17(4): 499–528.

[**Introduction**: Diabetes mellitus is the leading global cause of chronic kidney disease (CKD) and end-stage renal disease. Although cardiovascular outcomes have improved substantially, renal risk remains high. Glucagon-like peptide 1 (GLP-1) receptor agonists and the dual GLP-1/GIP agonist tirzepatide have demonstrated potential cardiorenal benefits, but renal evidence has not been systematically mapped across CKD stages and metabolic phenotypes. This scoping review aimed to identify and describe clinical evidence on renal outcomes associated with GLP-1-based therapies in adults with type 2 diabetes and/or overweight/obesity, with or without CKD.]

Complications (find here atherosclerosis, claudication, diabetic foot, ulcers etc)

Diabetic Foot

Comparison of posterior slab cast with total contact cast in the management of diabetic foot ulcers: A randomized controlled trial

Goyal G., Bose U.B., Srivastava R., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113157.

[**Background**: Total contact cast (TCC) is the ‘reference–standard’ for off-loading plantar diabetic foot ulcers (DFU). Practical limitations, associated complications, and lack of patient acceptability, limits its widespread use. Posterior slab cast (PSC) may provide an alternate way of off-loading the foot that might be more acceptable, and better tolerated, by people with DFU.

Aim: To compare wound healing and foot related outcomes in people with plantar DFU using TCC or PSC for off-loading the foot.]

Risk factors and mortality for amputations in the diabetic foot: a nationwide cohort study

Shim D.W., Lee W., Park K.H., et al. *Diabetes Research and Clinical Practice* 2026, 234: 112435.

[**Objective**: To investigate risk factors and mortality associated with major amputations in people with diabetic foot ulcers (DFUs), and to differentiate them from minor amputations.

Diabetes and pregnancy

Differences in association between gestational weight gain and perinatal outcomes according to pre-pregnancy body mass index categories and gestational diabetes mellitus status: findings from a large Japanese cohort

Shingu K.F., Takahara M., Waguri M., et al. *BMJ Open Diabetes Research and Care* 2026;14: e005709

[**Introduction**: We aimed to examine the impact of gestational weight gain (GWG) on perinatal outcomes based on body mass index (BMI) category and gestational diabetes mellitus (GDM) status.]

Implementation of a Gestational Diabetes Virtual Care Clinic: A Before–After Comparative Study

Coveney C., Callaghan S., Rutter E., et al. *Diabetes Therapy* 2026, 17(4): 563–570.

[**Introduction**: Gestational diabetes mellitus (GDM) is common diagnosis during pregnancy and has a substantial effect on maternal and fetal morbidity. Advancements in healthcare technology, such as Bluetooth-enabled glucometers, telemedicine, and virtual clinics, have emerged as efficient tools for GDM management.]

Long-term adverse multi-system health outcomes of gestational diabetes mellitus: an analysis of real-world cohort data

Heague M.O., Henney A.E., Riley D.R., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113171.

[**Background**: There is emerging evidence that gestational diabetes mellitus (GDM) increases the risk of multi-system long-term complications such as cancer and autoimmune disease, however this evidence is scarce and conflicting. Therefore, we aim to explore the long-term health implications of GDM.]

Tight versus less tight glycaemic targets for women with gestational diabetes mellitus: a randomised controlled trial

Popova P.V., Vasukova E.A., Tkachuk A.S., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113151.

[**Aims**: To determine if tight glycemic control in gestational diabetes mellitus (GDM) reduces adverse outcomes compared to less tight targets.

Methods: In a single-center, open-label randomized controlled trial, 650 women with GDM (singleton pregnancies, 12–31 weeks' gestation) were randomized to tight (fasting < 5.1 mmol/L, 1-h postprandial < 7.0 mmol/L) or less tight (fasting < 5.3 mmol/L, postprandial < 7.8 mmol/L) targets. The primary outcome was the incidence of large-for-gestational-age (LGA) infants. Secondary outcomes included measures of maternal and neonatal health, analyzed by intention-to-treat.

Results: Of 650 enrolled women, 626 (96.3%) completed the trial with primary outcome data. The tight-target group had a lower incidence of LGA (19.2% vs. 26.5%; adjusted relative risk (aRR) 0.61, 95%CI 0.42–0.89; p = 0.010), lower cesarean rates (23% vs. 29.9%; aRR 0.63; p = 0.012), and reduced gestational weight gain (10.1 vs. 10.7 kg; p = 0.006). Insulin use was higher with tight targets (32.6% vs. 21.6%; aRR 1.67; p = 0.005). Serious complications and maternal hypoglycemia rates were low and comparable.

Conclusion: Tight glycemic targets in GDM lower the risk of LGA births, cesarean delivery, and excess maternal weight gain without increasing severe adverse events, though they necessitate more frequent insulin therapy.

Diabetes mellitus Type 1

Autologous and allogeneic stem cell-derived islet therapy in three recipients with type 1 diabetes and complete loss of endogenous pancreatic β-cell function pretransplant

Shi Y., Feng Y., Li T., et al. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.285-288.

[In a large population of people with type 1 diabetes, the glycaemic target might not be achieved despite insulin therapy and issues around recurrent severe hypoglycaemia caused by insulin excess can result in irreversible neurological damage or even death. [1] Clinical trials with allogeneic [2] and terminally differentiated autologous [3,4] stem cell-derived islets have provided convincing evidence that such therapies can restore durable normoglycaemic islet function in people with type 1 and type 2 diabetes. However, questions over the optimal immunosuppression regime to sustain a stem cell-derived islet-alone transplant in the setting of type 1 diabetes remain. All autologous studies reported to date have involved patients who already require full-dose immunosuppression to sustain previous kidney [3] or liver [4] transplants. We report herein the outcome of three patients with type 1 diabetes complicated by severe hypoglycaemia receiving autologous or allogeneic endoderm stem cell-derived islet-like tissue (E-islets) with differing degrees of immunosuppression (appendix).]

Automated insulin delivery systems and improved glycaemic outcomes in type 1 diabetes: what comes next?

Zaharieva D.P. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.277-278.

[Early clinical trials established the safety and feasibility of closed-loop insulin delivery, but the 2019 iDCL trial [1] marked the first large, outpatient, randomised, controlled trial to show a greater percentage of glucose time in range compared with the use of a sensor-augmented insulin pump. Over the past decade, randomised controlled trials (RCTs) and real-world studies have consistently shown that automated insulin delivery (AID) systems improve glycaemic outcomes in individuals with type 1 diabetes. [2] Clinicians, researchers, and people with type 1 diabetes and their families have seen how AID systems have transformed type 1 diabetes management. However, the majority of these studies compared AID with insulin pump therapy or sensor-augmented pump therapy, with few RCTs directly comparing AID to multiple daily injections.]

Cognitive skills in children and adolescents with type 1 diabetes: a scoping review and meta-analysis

Arman D., Haynes E., Brussoni M., et al. *BMJ Open Diabetes Research and Care* 2026;14: e005635

[Type 1 diabetes (T1D) complications may impair cognitive development, but evidence on cognitive skills in children and adolescents with T1D is inconsistent. This study aimed to document measures and outcomes used to assess cognitive skills in children with T1D and to examine the relationship between T1D and cognitive skills. A systematic literature search was conducted across five databases to identify studies that administered cognitive assessments to children and adolescents aged ≤19 years with T1D. Study characteristics, cognitive skills assessments and outcomes and comparisons to non-T1D peers where available were synthesized on an evidence map. Random-effects meta-analysis was used to assess differences in Wechsler Full Scale Intelligence Quotient (IQ) test scores between T1D and non-T1D groups. From 2464 studies, 129 were included. Five main cognitive categories were identified, with comparisons to non-T1D peers—where available—yielding mixed results: academic performance (n=37; n=7/22 worse T1D), executive function (n=101; n=31/48 worse T1D), intelligence (n=73; n=22/37 worse T1D), language (n=30; n=7/20 worse T1D) and memory and learning (n=84; n=31/48 worse T1D). Large-scale studies (n≥1000) did not find significant differences between groups for academic performance (n=0/6 worse T1D) and language (n=0/3 worse T1D). In the meta-analysis of 16 studies (n=1594), children with T1D had slightly lower IQ scores than peers without T1D (mean difference −3.49, 95% CI (−6.16 to −0.82); p=0.010). T1D appears to be associated with slightly lower cognitive outcomes in some areas. Further research is needed to understand the impact of these findings on daily functioning and to inform screening for at-risk children.]

Overview of health outcomes and care options for people with Type 1 diabetes in the Western Pacific Region

Thornton T.D., Huang M.L.H., Kodani N., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113189.

[Type 1 diabetes (T1D) affects ≈9.5 million people globally [1], with widely varying outcomes. Some die without a diagnosis, whilst others are in good health after >70 years of T1D. T1D incidence is wide-ranging in the Western Pacific Region (WPR), ranging from an annual incidence in youth (0–14 years) of 0.9 (95% CI 0.6–1.3)/100,000 people in Fiji to 23.2 (21.3–25.2)/100,000 people in Australia [2]. T1D incidence in the WPR is rising, with an annual increase ranging from 2.8% in Australia (1990–2002) to 14.2% in Shanghai (1997–2011) [2]. A systematic review of the global incidence of adult-onset T1D, which is more common in men than in women, identifies a paucity of studies, particularly from low- and middle-income countries [3]. Asian countries had the lowest and Australia had the highest incidence in the WPR. It is unclear if adult-onset T1D incidence declines with age or has changed over time [3]. Getting a T1D diagnosis correct can be challenging, particularly in older adults and without C-peptide and autoantibody tests [4]. T1D prevalence also varies greatly, influenced by incidence, life-expectancy, and health-care access [1,] which also changes the T1D population age-distribution. For example, with excellent care and high rates of adult-onset T1D, in Australia two-thirds of people with T1D are ≥40 y.o and one third are ≥60 y.o [5].]

Sex specific genomic insights into type 1 diabetes through GWAS and single cell transcriptome analysis

Qu H.Q., Ostberg K., Slater D.J., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113181.

[**Aims**: Type 1 diabetes (T1D) exhibits sex differences in genetic risk, yet most genetic studies treat sex as a covariate rather than a modifier of risk. We hypothesized that sex-stratified genome-wide association studies (GWAS) would uncover sex-specific genetic architecture and improve risk prediction. **Methods**: We performed GWAS in 6,599 T1D cases (3,483 males, 3,109 females, 7 undetermined) and 12,350 controls (6,665 males, 5,658 females, 27 undetermined) of European ancestry, testing additive models and sex-stratified analyses. For mechanistic insights, we performed scRNA-seq of PBMCs from nine matched male–female pediatric pairs. Finally, we tested male-, female-, and standard polygenic risk scores (PRS) in an independent cohort (471 T1D cases, 2,300 controls). **Results**: Sex-stratified analyses identified 215 genome wide significant SNPs ($P < 5x10^{-8}$) with heterogeneity: 119 male-specific and 94 female-specific. Integration of scRNA-seq data revealed 41 sex-specific T1D genes with cell type-specific differential expression. In the independent cohort, sex-specific PRS outperformed the combined PRS: in males, AUC = 0.668 versus 0.623 ($p < 2.2x10^{-16}$); in females, AUC = 0.719 versus 0.635 ($p < 2.2x10^{-16}$). **Conclusions**: Sex-stratified GWAS reveal novel T1D risk loci influenced by sex. Incorporating sex-specific effect sizes into PRS enhances risk discrimination, underscoring the value of sex-aware genetic analyses for precise prediction of T1D.]

Thyroid function influences insulin requirements in patients with type 1 diabetes mellitus and chronic autoimmune thyroiditis: A cross-sectional study

Cannarella R., Marino M., Condorelli R.A., et al. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2026;20(4): 103416.

[**Objective**: To evaluate the association between serum thyroid-stimulating hormone (TSH), free thyroxine (FT4), and free triiodothyronine (FT3) levels and basal and bolus fast-acting insulin doses in patients with type 1 diabetes mellitus (T1DM) and chronic autoimmune thyroiditis (CAT).]

Tubeless automated insulin delivery versus multiple daily injections in children and adults with type 1 diabetes with elevated HbA_{1c} (RADIANT): a multicentre, international, parallel-group, open-label, randomised, controlled trial

Wilmot E.G., Beltrand J., Guerci B., et al. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.305-316.

[**Background**: Automated insulin delivery (AID) systems have been shown to improve glycaemic outcomes in people with type 1 diabetes managed with insulin pump therapy. No randomised studies have evaluated the benefits of tubeless AID in both adults and children with suboptimal glycaemia compared with multiple daily injections. We aimed to evaluate the safety and efficacy of a tubeless AID system compared with multiple daily injections in this population.]

Diabetes mellitus Type 2

Chronic complication risk and benefits of fenofibrate in type 2 diabetes by a PPARα polymorphism (rs6008845, C/T): a FIELD trial substudy

Januszewski A.S., Huang M.L.H., Mangani A.S., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113168.

[**Objective**: Peroxisome proliferator-activated receptor α (PPARα) regulates lipid metabolism, cardiac energy balance, vascular inflammation and cell differentiation. We examined whether a PPARα gene variant (rs6008845, C/T) is associated with risk of chronic complications and death, and with benefit of fenofibrate (a PPARα agonist) in adults with type 2 diabetes.]

Concurrent management of gout and type 2 diabetes mellitus: combined therapy insights

Wang H., Wang B., Zhang J., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113169.

[Gout and type 2 diabetes mellitus (T2DM) are prevalent metabolic disorders with a significant bidirectional association. The review article focuses on the interplay between serum uric acid and glucose/lipid metabolism, innate immunity, inflammation, and gut microbiota, proposing simultaneous

treatment strategies. Gout, caused by monosodium urate crystal deposition due to hyperuricaemia, and T2DM, induced by high-fat, high-sugar diets disrupting metabolic balance, share common pathological mechanisms. Elevated uric acid levels contribute to lipid and glucose metabolic disorders, activate inflammatory pathways like the nucleotide-binding oligomerization domain-like receptor 3 inflammasome, and trigger innate immune responses. The gut microbiota also plays a significant role in both metabolic diseases, with dysbiosis affecting uric acid excretion and insulin resistance. This review article highlights promising therapeutic approaches, including the use of sodium-glucose cotransporter-2 inhibitors which reduce serum uric acid and lowers gout risk alongside glycaemic control. Additionally, targeting inflammatory pathways such as interleukin-1β offers potential benefits for both conditions. Combined pharmacological therapies, dietary adjustments, and gut microbiota interventions present new directions for simultaneous management. This review article provides a comprehensive analysis of the links between gout and T2DM, offering novel insights for clinical practice and future research.]

Efficacy and Safety of Once-Weekly IcoSema Versus Once-Daily IDegLira in People with Type 2 Diabetes: Systematic Literature Review and Network Meta-analysis

Kandalam S., Benamar M., Le Reun C., et al. *Diabetes Therapy* 2026, 17(4): 547–561.

[**Introduction**: For people with type 2 diabetes (T2D), combination therapy with a basal insulin and a glucagon-like peptide 1 receptor agonist (GLP-1 RA) can improve glycaemic control, lower hypoglycaemia risk, and improve adherence. IcoSema is the first once-weekly combination of basal insulin and GLP-1 RA in a single injection. To compare once-weekly IcoSema and once-daily IDegLira for the management of T2D in the absence of head-to-head trials, we performed a network meta-analysis (NMA).]

Gut Microbiota and Metabolic Health: From Dysbiosis to Therapeutics

Pillai S.S. and Ashraf A.P. *Diabetes Therapy* 2026, 17(4): 483–497.

[The gut microbiota (GM) is a pivotal regulator of host metabolism and a contributor to the pathophysiology of obesity, type 2 diabetes (T2D), and metabolic syndrome (MS). Disruptions in GM composition and function are collectively termed dysbiosis. This review synthesizes current evidence on GM dysbiosis, moving beyond simple taxonomic associations, to examine functional drivers of metabolic dysfunction. Dysbiosis impairs metabolic health through several interconnected pathways: enhanced dietary energy extraction, compromised intestinal barrier integrity leading to metabolic endotoxemia, chronic low-grade “meta-inflammation,” and the disruption of circadian rhythms and neuro-immune signaling. Beyond bacteria, dysbiosis of the gut virome and mycobiota may further modulate metabolic risk. Animal and emerging human studies indicate that reduced virome diversity and altered phage–bacteria interactions can amplify dysbiosis, promote inflammatory signaling, and impair metabolic homeostasis. Recognition of GM dysbiosis as a contributor to metabolic disease has prompted development of therapeutic strategies aimed at restoring microbial balance and function. These interventions span a spectrum from established clinical approaches with indirect microbiota effects to experimental therapies designed to directly manipulate microbial composition or activity. We evaluate the clinical readiness of GM-targeted therapies, including dietary patterns, prebiotics, probiotics, and fecal microbiota transplantation. While established metabolic treatments such as glucagon-like peptide-1 (GLP-1) receptor agonists and bariatric surgery significantly reshape the GM, direct microbial manipulations often yield variable results in human trials. We conclude that the future of metabolic management lies in personalized microbiomics, utilizing artificial intelligence and precision-based interventions to restore specific functional microbial deficits tailored to the individual host profile.]

Interaction patterns among risk factors for bladder cancer in adults with type 2 diabetes managed in primary care: a retrospective cohort study

Yau S., Leung E.Y.M., Hung C.T., et al. *BJGP Open* 2026;:BJGPO.2025.0028.

[**Background**: Previous studies have shown that patients with type 2 diabetes have a higher risk of developing bladder cancer than the general population. However, little is known about how different risk factors interact to influence the risk of bladder cancer among patients with diabetes.

Aim: To explore the interaction patterns among factors associated with the risk of bladder cancer incidence among patients who received diabetes management in primary care.]

Reuniting diabetes through the islet coordinate framework

Jagannathan R., Staimez L.R., Narayan K.M.V. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.282-284.

[For nearly a century, type 2 diabetes has been understood and managed as a single clinical entity. However, converging discoveries now point to type 2 diabetes as a constellation of subtypes defined by genetic, metabolic, and phenotypic diversity. [1,2] Insights into pathways involving pancreatic β-cell deficiency, insulin resistance, adipose dysfunction, and, more recently, α-cell dysregulation reveal distinct molecular profiles. When clinical risk is defined only by downstream end products, such as hyperglycaemia, these upstream forces are obscured, clinical phenotyping loses resolution, misclassification occurs, and opportunities for prevention and targeted treatment are diminished. Evidence from multiple fields now suggests that the biological architecture of type 2 diabetes is grounded in federated pathways, defined as decentralised biological processes spanning cellular, metabolic, structural, and regulatory levels, with divergent trajectories. This raises an important question: how can we reconcile this mechanistic dissonance of type 2 diabetes within a unified conceptual model that informs clinical phenotyping and translation? To address this, we synthesised key evidence from clinical and population studies, integrated advances in cellular and islet biology, and propose an islet-centred conceptual framework that treats type 2 diabetes as one disease with multiple mechanistic expressions.]

The role of small, dense lipoproteins in type-2 diabetes and maturity-onset diabetes of the young (MODY): What's new

Zeljkovic A., Vekic J., Elrayess M.A., et al. *Journal of Diabetes and Its Complications*, 2026, 40(4), Article 109233.

[Although diabetic dyslipidemia is a well-known and extensively studied phenomenon, its features continue to attract significant attention from both researchers and clinicians. Given that lipid profile abnormalities are associated with an increased risk of cardiovascular disease, [1,2] considerable efforts have been devoted to elucidating the underlying mechanisms through which these pathophysiological alterations contribute to elevated cardiovascular morbidity and mortality in patients with diabetes. Moreover, specific components of diabetic dyslipidemia are being studied for their potential as diagnostic or therapeutic tools.]

Diagnosis

Feasibility of using OGTT 1-h PG as a diagnostic criterion for diabetes and pre-diabetes

Chen L., Bian B., Ran H., et al. *BMJ Open Diabetes Research and Care* 2026;14: e005689

[**Aims**: To investigate whether oral glucose tolerance test (OGTT) 1-hour plasma glucose (1-h PG) concentration can be used as the criterion for diagnosing diabetes mellitus (DM) and pre-diabetes.]

Social determinants of health and recommended A1C monitoring among women with postpartum-onset diabetes: results from a retrospective cohort

Boychuk N.A., McCarthy K.J., Liu S.H., et al. *BMJ Open Diabetes Research and Care* 2026;14: e005745

[**Introduction**: Diabetes is increasingly prevalent in reproductive-aged women, but the association between social determinants of health (SDOH) and access to A1C monitoring after diagnosis are poorly understood. We explored SDOH and receipt of recommended follow-up A1C testing among postpartum women with diabetes.]

Glucose monitoring and control

Continuous Glucose Monitoring Before and After Simultaneous Pancreas–Kidney Transplantation: Insights from a Real-World Clinical Setting

Amor A.J., Solà C., Ventura-Aguiar P., et al. *Diabetes Therapy* 2026, 17(4): 617–626.

[**Introduction**: Simultaneous pancreas–kidney (SPK) transplantation normalizes glycemia in patients with diabetes and end-stage kidney disease, yet data on continuous glucose monitoring (CGM) remain scarce.]

Cost-Effectiveness of Highly Effective Glucose-Lowering Agents: Do Current Practices Optimize Clinical and Economic Outcomes?

Hoog M., Minghetti A., Valentine W.J. *Diabetes Therapy* 2026, 17(4): 571–585.

[**Introduction**: Advances in type 2 diabetes (T2D) treatment have expanded therapeutic options, but evidence on optimal treatment sequencing for long-term outcomes remains limited. This study evaluated six common T2D treatment pathways in the US using long-term modeling.]

Glycaemic control remains central in type 2 diabetes mellitus management: key learnings from the latest International Diabetes Federation guidelines

Chan J.C.N., Deerochanawong C., Khunti K., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113173.

[The 2025 International Diabetes Federation (IDF) guidelines recognise global disparities in healthcare access, with ~ 80% of people with type 2 diabetes mellitus (T2D) living in low-to-middle–income countries (LMICs). A panel of international experts discussed the evidence underlying these updated guidelines. Randomised trials demonstrate cardiovascular-kidney protection with sodium–glucose cotransporter 2 inhibitors (SGLT2is) and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) in high-risk people with T2D, although their role among those with low-risk disease remains less clear. Whilst advocating for the need to improve access to newer glucose-lowering drugs (GLDs) in LMICs, the IDF guidelines propose two standards-of-care ('optimal' or 'basic'), with the following key messages: (i) early glycaemic control using conventional GLDs prevents complications and preserves quality of life; (ii) multifactorial management using effective GLDs and organ-protective drugs (e.g. statins and renin–angiotensin–aldosterone system inhibitors) improve outcomes; (iii) individualised regimens with shared decision-making and treatment persistence maximises benefits and minimises harm; (iv) metformin is a foundation therapy, with no evidence supporting first-line SGLT2i or GLP-1 RA monotherapy in low-risk individuals; (v) sulphonylureas are highly effective and affordable GLDs, making them important options (particularly in low-resource settings); and (vi) initial combination therapy achieves early glycaemic control with increased durability versus stepwise GLD addition.]

Improved Glycaemic Control with IDegLira in Chinese Adults with Type 2 Diabetes in Real-World Settings: A Retrospective, Database Cohort Study

Wang S., Sun B., Zhu D., et al. *Diabetes Therapy* 2026, 17(4): 603–616.

[**Introduction**: This study aimed to investigate glycaemic control and safety in Chinese adults with type 2 diabetes (T2D) receiving fixed-ratio combination of insulin degludec and liraglutide (IDegLira) in real-world clinical practice.]

Letter to the editor-The predictive value of estimated glucose disposal rate for all-cause and cardiovascular mortality in the US non-diabetic population aged ≥60 years: A population-based cohort study

Li L., Qin Z., Wang C. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2026;20(4): 103419.

[We are writing in response to the article "The predictive value of estimated glucose disposal rate for all-cause and cardiovascular mortality in the US non-diabetic population aged ≥60 years: A population-based cohort study"recently published in your journal [1]. This study provides important insights into the potential value of eGDR in predicting mortality outcomes in non-diabetic older adults. The article uses nationwide data from the National Health and Nutrition Examination Survey (NHANES), providing a solid empirical foundation for the application of eGDR as a tool for predicting mortality risk.]

Sex differences in glycemic outcomes: a systematic review and meta-analysis of diabetes treatments

Liu C., Mujahid O., Beneyto A., et al. *BMJ Open Diabetes Research and Care* 2026;14: e005808

[Sex differences in glycemic outcomes following insulin therapy remain underexplored despite biological and psychosocial factors that may influence individual responses. This systematic review examines sex-specific differences in glycemic control to guide personalized diabetes care and promote health equity. We searched PubMed, Scopus, Cochrane Library, and Google Scholar (August 2014–

December 2025) for randomized and observational studies involving adults of both sexes on insulin. Twenty-four studies were included, with certainty of evidence assessed using GRADE. In type 1 diabetes, women showed no significant difference in achieving HbA1c <7% (RR 1.05, 95% CI 0.91 to 1.22; very low certainty) and toward higher time-in-range (SMD 0.78, −0.01 to 1.57; moderate certainty). In type 2 diabetes, men were more likely to achieve HbA1c targets (RR 0.86, 95% CI 0.72 to 1.03; low certainty), while women required higher weight-adjusted insulin doses (SMD 0.55, 0.23 to 0.86; very low certainty). Hypoglycemia risk showed opposing trends in inpatient (RR 0.78, 95% CI 0.33 to 1.83; very low certainty) versus outpatient settings (RR 1.08, 95% CI 0.61 to 1.89; low certainty) with substantial heterogeneity (I2>70%). These findings suggest that sex-related differences in glycemic outcomes vary by diabetes type and treatment context. Given the low certainty and heterogeneity of current evidence, results should be interpreted as hypothesis-generating. This review supports the consideration of biological sex within a broader, individualized diabetes management framework and highlights the need for future sex-stratified analyses with rigorous control of lifestyle and physiological factors.]

Hyperglycaemia

Hyperglycaemia-induced metabolic stress and epigenetic imprinting in the inflammatory pathogenesis of diabetic neuropathy

Razi F.B., Ashraf H., Singhal S., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113172.

[Diabetic neuropathy (DN), a major microvascular complication of diabetes mellitus, results from a complex interplay among oxidative stress, inflammation, and persistent epigenetic modifications. Hyperglycemia-induced mitochondrial dysfunction increases reactive oxygen species (ROS), which activate redox-sensitive inflammatory cascades, including NF-κB, JAK/STAT, and the NLRP3 inflammasome. These pathways amplify cytokine release and neuronal sensitisation, while reciprocal feedback between ROS and inflammation mediated by Nrf2 suppression further perpetuates nerve damage. Damage-associated molecular patterns (DAMPs), including HMGB1, S100A8/A9, mitochondrial DNA, and extracellular ATP, act as key amplifiers of neuroinflammation. By engaging receptors such as RAGE, Toll-like receptors (TLRs), and NOD-like receptors (NLRs), particularly NLRP3, these DAMPs trigger glial activation and nociceptive signalling, contributing to axonal degeneration and pain hypersensitivity in DN. Epigenetic dysregulation, including DNA methylation drift, histone modification imbalance, and aberrant non-coding RNA expression, constitutes a critical mechanism underlying metabolic memory, wherein prior hyperglycemic exposure leaves lasting molecular imprints. Persistent histone acetylation (H3K9ac), altered methylation (H3K4me1/Set7, H3K9me3/SUV39H1), and stable 5-methylcytosine patterns sustain inflammatory and oxidative pathways, even after glucose normalisation. Therapeutically, DNMT and HDAC inhibitors, miRNA modulators, and agents targeting RAGE/TLR4/NLRP3 pathways show promise in reversing these molecular imprints. Antioxidants and anti-inflammatory compounds with epigenetic effects further represent potential disease-modifying strategies. Future research must focus on longitudinal human studies, nerve-specific epigenomics, and multi-omics integration to enable personalised, mechanism-based therapy for DN. Understanding the interdependence of ROS, DAMPs, and epigenetic memory is key to breaking the cycle of chronic neuroinflammation and neuronal injury.]

Hypoglycaemia

Control of nocturnal hypoglycemia by CGM-based AI-enabled nocturnal hypoglycemia prediction: A retrospective analysis of real-world data

Bogaarts G., Mitter M., Bailey T.S., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113188.

[**Aims**: To evaluate the effect of the Accu-Chek® SmartGuide Predict app Night Low Predict (NLP) feature use on nocturnal hypoglycemia in people with diabetes in a real-world setting.]

Insulin therapies

Adipose tissue expression of Notch signaling genes in relation to insulin sensitivity and obesity in humans

Karczewska-Kupczewska M., Matulewicz N., Stefanowicz M., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113183.

[**Aims**: Notch signaling may regulate adipogenesis. The objective of the present study was to analyze the role of the Notch pathway in the development of insulin resistance and metabolic complications of obesity. We analyzed subcutaneous (SAT) and visceral adipose tissue (VAT) expression of Notch genes in relation to insulin sensitivity, obesity, and metabolic syndrome (MS).

Automated insulin delivery systems and improved glycaemic outcomes in type 1 diabetes: what comes next?

Zaharieva D.P. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.277-278.

[Early clinical trials established the safety and feasibility of closed-loop insulin delivery, but the 2019 iDCL trial [1] marked the first large, outpatient, randomised, controlled trial to show a greater percentage of glucose time in range compared with the use of a sensor-augmented insulin pump. Over the past decade, randomised controlled trials (RCTs) and real-world studies have consistently shown that automated insulin delivery (AID) systems improve glycaemic outcomes in individuals with type 1 diabetes. [2] Clinicians, researchers, and people with type 1 diabetes and their families have seen how AID systems have transformed type 1 diabetes management. However, the majority of these studies compared AID with insulin pump therapy or sensor-augmented pump therapy, with few RCTs directly comparing AID to multiple daily injections.]

From survival to freedom: redefining success in type 1 diabetes

Piemonti L. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.356-362.

[Type 1 diabetes has shifted from a condition once associated with early mortality to a chronic disease owing to the development of intensive insulin therapy, continuous glucose monitoring, and hybrid closed-loop systems. Despite near-normoglycaemia becoming an attainable target, residual excess mortality and cardiovascular risk persist. These outcomes are thought to reflect the long-term biological legacy of earlier dysglycaemia, including metabolic and epigenetic memory associated with inflammatory and vascular vulnerability. As survival for people with type 1 diabetes lengthens, morbidity increasingly shifts towards cognitive decline, depression, infections, and cancer, whereas the lived burden of daily disease management remains high. As evidence suggests that further reductions in HbA_{1c} do not translate into proportional improvements in outcomes at the population level, the next therapeutic frontier becomes physiological resilience: interventions that restore endogenous regulation, reduce glycaemic variability, and dampen inflammatory stress, thereby approximating a more physiological metabolic state. β-cell replacement—via pancreas or islet transplantation and emerging stem cell–derived implants—should be judged less by mean HbA_{1c} and more by durability, safety, C-peptide preservation, time in (tight) range, and validated patient-reported outcomes. Regulatory and economic frameworks must consequently embrace multidimensional benefits. Within this evolving framework, success is measured not only by longer survival, but also by improved physiological control achieved with minimal toxicity and reduced cognitive burden. This Personal View argues for reframing therapeutic success in type 1 diabetes by shifting the focus from glycaemic metrics alone to the restoration of endogenous regulation and physiological resilience—outcomes operationalised as sustained metabolic stability, protection from severe hypoglycaemia, and a substantial reduction in cognitive and therapeutic burden.]

Insulin Pen Needle Reuse in U.S. Adults with Diabetes: A Cross-Sectional Survey Study on Patterns, Motivations, and Educational Implications

Guzman S., Bellini N., Hughes L., et al. *Diabetes Therapy* 2026, 17(4): 529–546.

[**Introduction**: Effective insulin therapy relies on proper injection technique and the correct use of insulin delivery devices. Despite recommendations for a single-use device, the pen needle reuse remains common. This study explored pen needle reuse patterns, reasons for reuse, and motivators to changing reuse behavior, in order to provide actionable insights for clinical education and patient-support interventions.]

Tubed or tubeless insulin pumps? A retrospective real-world analysis of national French health data

Hanaire H., Vimont A., Bonin A., et al. *BMJ Open Diabetes Research and Care* 2026;14: e005860

[**Background**: Tubeless insulin pumps, introduced in France in 2016, have been associated with higher user satisfaction than tubed pumps, primarily due to reduced interference with daily tasks. Whether this translates to greater treatment persistence remains uncertain. This study evaluates persistence among people with type 1 diabetes initiating tubed or tubeless pump therapy in France.]

Tubeless automated insulin delivery versus multiple daily injections in children and adults with type 1 diabetes with elevated HbA $_{1c}$ (RADIANT): a multicentre, international, parallel-group, open-label, randomised, controlled trial

Wilmot E.G., Beltrand J., Guerci B., et al. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.305-316.

[**Background**: Automated insulin delivery (AID) systems have been shown to improve glycaemic outcomes in people with type 1 diabetes managed with insulin pump therapy. No randomised studies have evaluated the benefits of tubeless AID in both adults and children with suboptimal glycaemia compared with multiple daily injections. We aimed to evaluate the safety and efficacy of a tubeless AID system compared with multiple daily injections in this population.]

Management of diabetes (diet, exercise, lifestyle)

Additional benefits of combining GLP-1 receptor agonist use with lifestyle modification

Del Prato S. and Solini A. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.278-280.

[GLP-1 receptor agonists have largely contributed to revolutionising pharmacological therapy of type 2 diabetes. They are among the most potent glucose-lowering agents, while also eliciting bodyweight reduction—an effect that, before their introduction, was reached only through lifestyle intervention. Moreover, and more importantly, these medications have shown unprecedented cardiorenal protection in both randomised controlled trials [1] and real-world studies. [2] A further confirmation of these beneficial effects is reported by Xuan-Mai T Nguyen and colleagues in this issue of *The Lancet Diabetes & Endocrinology.* [3] In a large population drawn from the US Veterans Affairs Million Veteran Program, when comparing GLP-1 receptor agonist users with non-users, they reported a hazard ratio (HR) for major adverse cardiovascular events (MACE) of 0·84 (95% CI 0·76–0·92). Of note, this estimate is similar to that reported in the most recent meta-analysis of ten cardiovascular outcome trials including more than 70 000 people with type 2 diabetes (0·86, CI 0·81–0·90). [3] Altogether, these findings have increased optimism regarding the possibility of reducing the burden of cardiovascular complications in type 2 diabetes.]

Erratum to "Associations between disease acceptance and dietary adherence in patients with type 2 diabetes mellitus in China: a cross-sectional study". [DIAB 224 (2025) 112196]

Liu X., Zhang Q., Huang L., et al. *Diabetes Research and Clinical Practice* 2026, 234: 112950.

[The publisher regrets to inform that the article was incorrectly published as a review paper. This paper should be categorized as a Research article.]

Mental health and diabetes

Association between GLP-1 receptor agonist use and worsening mental illness in people with depression and anxiety in Sweden: a national cohort study.

Taipale H., Taylor M., Lähteenvuo M., et al. *The Lancet Psychiatry* 2026;13(4): 327-335.

[**Background**: People with diabetes have an elevated risk of developing depression, anxiety, and suicide. GLP-1 receptor agonists are licensed to treat diabetes and obesity, but data on whether these medications alleviate or exacerbate anxiety, depression, and self-harm are mixed. We studied the risk of worsening mental illness in people already diagnosed with depression, anxiety, or both who were prescribed antidiabetic medications including GLP-1 receptor agonists.]

Diabetes and mental health

Pouwer F., Ehrmann D., Strandberg R.B., et al. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.337-355.

[This Review summarises the research into five common mental health problems that can affect adults living with type 1 diabetes, type 2 diabetes, or gestational diabetes: fear of hypoglycaemia, diabetes distress, depression, disordered eating, and sleep disorders. Mental health problems are common among adults with diabetes and can substantially decrease the quality of life and self-care, and increase the risk of adverse health outcomes, such as high HbA_{1c}, comorbidities, and premature mortality. Many mental health problems are bi-directionally linked to diabetes. Randomised controlled trials have shown that psychological interventions are effective in reducing symptoms in the short term, including cognitive behavioural therapy, mindfulness-based cognitive therapy, and stepped care, which can also be offered digitally as a first step. However, diabetes distress, depression, and other mental health problems are known to recur and the longer-term outcomes of prevention or treatments are unclear. In general, mental health problems are understudied in diabetes, particularly gestational diabetes. People with diabetes want to talk with their diabetes health professionals about the emotional side of living with and managing diabetes. These findings support the integration of routine monitoring and psychological support into clinical practice. Health-care policy makers should ensure that diabetes health-care professionals are well equipped to discuss mental health and refer to appropriate digital health tools and mental health specialists when needed.]

The temporal interplay between physical activity, emotional well-being, and health-related quality of life in individuals with recently diagnosed type 2 diabetes mellitus: a cross-lagged panel analysis

Kristoffersen S.F., Domazet S.L., Pouwer F., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113185.

[**Aims**: We investigated longitudinal, bidirectional associations between objectively measured moderate to vigorous physical activity (MVPA), health-related quality of life (HRQoL), and emotional well-being (EWB) in individuals recently diagnosed with type 2 diabetes mellitus.]

Pharmacological management of diabetes

Additional benefits of combining GLP-1 receptor agonist use with lifestyle modification

Del Prato S. and Solini A. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.278-280.

[GLP-1 receptor agonists have largely contributed to revolutionising pharmacological therapy of type 2 diabetes. They are among the most potent glucose-lowering agents, while also eliciting bodyweight reduction—an effect that, before their introduction, was reached only through lifestyle intervention. Moreover, and more importantly, these medications have shown unprecedented cardiorenal protection in both randomised controlled trials [1] and real-world studies. [2] A further confirmation of these beneficial effects is reported by Xuan-Mai T Nguyen and colleagues in this issue of *The Lancet Diabetes & Endocrinology.* [3] In a large population drawn from the US Veterans Affairs Million Veteran Program, when comparing GLP-1 receptor agonist users with non-users, they reported a hazard ratio (HR) for major adverse cardiovascular events (MACE) of 0·84 (95% CI 0·76–0·92). Of note, this estimate is similar to that reported in the most recent meta-analysis of ten cardiovascular outcome trials including more than 70 000 people with type 2 diabetes (0·86, CI 0·81–0·90). [3] Altogether, these findings have increased optimism regarding the possibility of reducing the burden of cardiovascular complications in type 2 diabetes.]

Cost-effectiveness analysis of oral semaglutide versus subcutaneous dulaglutide in patients with type 2 diabetes mellitus: A Markov model study

Hsu H.Y., and Shi H.Y. *Diabetes Research and Clinical Practice* 2026, 234: 113186.

[**Aim**: This study assessed the cost-effectiveness of oral semaglutide versus subcutaneous dulaglutide for type 2 diabetes mellitus (T2DM) from the perspective of the Taiwanese healthcare payer, considering the self-paid status of oral semaglutide and the reimbursed but injectable route of dulaglutide under the National Health Insurance (NHI).]

Efficacy and safety of relacorilant for the treatment of patients with Cushing's syndrome (GRACE): a multicentre, phase 3, double-blind, placebo-controlled, randomised-withdrawal study

Pivonello R., Arnaldi G., Auchus R.J., et al. *Lancet Diabetes & Endocrinology*, 2026, 14(4), pp.291-304.

[**Background**: Relacorilant is a selective glucocorticoid receptor modulator designed to reduce excess cortisol activity by competing with cortisol for glucocorticoid receptor binding, mitigating the clinical manifestations of endogenous hypercortisolism (Cushing's syndrome). The aim of this study was to assess the efficacy and safety of relacorilant in adults with endogenous hypercortisolism.]

Extending beyond established cardiometabolic benefits of empagliflozin in type 2 diabetes: the evolving paradigm of glycemic variability

Patoulias D., Muzurović E., Maggio V., et al. *Journal of Diabetes and Its Complications*, 2026, 40(4), Article 109276.

[Glucose management in type 2 diabetes (T2D) has traditionally focused on lowering glycated hemoglobin (HbA1c) levels. However, relevant evidence supports that glycemic variability (GV), a marker of short-term fluctuations in blood glucose levels, is a strong determinant of the occurrence of both micro- and macrovascular complications of T2D. [1] GV has been associated with the activation of oxidative stress, the enhancement of inflammation, the progression of insulin resistance and the development of endothelial dysfunction, therefore providing a substrate for the development of diabetic complications. [23] GV has been also associated with pro-inflammatory small, dense low-density lipoproteins (LDL), [4] which are the most atherogenic LDL particle and closely associated to the formation and progression of atherosclerosis. [5] Widespread utilization of continuous glucose monitoring (CGM) nowadays offers a more detailed assessment of glycemic control among individuals with diabetes; recent data have suggested that use of CGM by adults with T2D, compared to self-monitoring of blood glucose (SMBG) alone results in a significant improvement in glycemic control, without any difference in the occurrence of severe hypoglycemia or macrovascular complications. [6]]

Geographical variation in the use of glucose-lowering drugs in type-2 diabetes in Denmark: A nationwide drug utilization study.

Rasmussen L., Andersen J.H., Kofoed-Enevoldsen A., et al. *British Journal of Clinical Pharmacology* 2026;92(4):1156-1166.

[**Aims**: To analyse geographical variation in use of glucose-lowering drugs (GLDs) for type-2 diabetes (T2DM) in Denmark.]

Glucagon-like peptide-1 receptor agonists and the risk of obesity-related cancers: a systematic review and meta-analysis

Ateiwi Y.A., Mahmood R., Wong H.J., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113158.

[**Background**: Type 2 diabetes mellitus (T2DM) and obesity are increasing and are established risk factors for malignancy. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are widely used for T2DM and obesity, but their association with cancer risk remains uncertain. We assessed the association between GLP-1RA use and obesity-related cancers.]

Quest for the holy grail: an effective drug for obesity

Burki T. *Lancet Diabetes & Endocrinology*, 2026, 14(4), p.290.

[Aimee Donnellan has been a correspondent for Reuters since 2017. Her patch includes the pharmaceutical industry. *Off the Scales* is her first book. In brisk and breezy terms, it recounts the history and impact of the GLP-1 receptor agonist semaglutide (Ozempic). Perhaps because of her background in business journalism, Donnellan does not characterise the development of GLP-1 receptor agonists as a quixotic quest to improve public health. Her protagonists are motivated by all kinds of drivers, including the desire to hold onto their jobs, make money, and garner accolades.]

Real-World Cohort Study of Semaglutide in Adults with Type 2 Diabetes Using an Electronic Health Records Database in Tianjin, China

Wang S., Hu P., Shen Z., et al. *Diabetes Therapy* 2026, 17(4): 587–602.

[**Introduction**: The aim of this study was to evaluate changes in clinical parameters among adults with type 2 diabetes (T2D) after initiating subcutaneous semaglutide in Chinese clinical practice.]

Thiazolidinedione and reduced epilepsy risk: A population-based study using target trial emulation

Zhao H., Zhuo L., Zhang B., et al. *Diabetes Research and Clinical Practice* 2026, 234: 113184.

[**Objective**: No epidemiological studies have yet explored the relationship between TZD use and epilepsy incidence within a population context. This study aimed to evaluate the association between TZD use and risk of epilepsy in a Chinese population by using a target trial emulation framework with active-comparator new-user (ACNU) design.]

Teenagers with diabetes

Cognitive skills in children and adolescents with type 1 diabetes: a scoping review and meta-analysis

Arman D., Haynes E., Brussoni M., et al. *BMJ Open Diabetes Research and Care* 2026;14: e005635

[Type 1 diabetes (T1D) complications may impair cognitive development, but evidence on cognitive skills in children and adolescents with T1D is inconsistent. This study aimed to document measures and outcomes used to assess cognitive skills in children with T1D and to examine the relationship between T1D and cognitive skills. A systematic literature search was conducted across five databases to identify studies that administered cognitive assessments to children and adolescents aged ≤19 years with T1D. Study characteristics, cognitive skills assessments and outcomes and comparisons to non-T1D peers where available were synthesized on an evidence map. Random-effects meta-analysis was used to assess differences in Wechsler Full Scale Intelligence Quotient (IQ) test scores between T1D and non-T1D groups. From 2464 studies, 129 were included. Five main cognitive categories were identified, with comparisons to non-T1D peers—where available—yielding mixed results: academic performance (n=37; n=7/22 worse T1D), executive function (n=101; n=31/48 worse T1D), intelligence (n=73; n=22/37 worse T1D), language (n=30; n=7/20 worse T1D) and memory and learning (n=84; n=31/48 worse T1D). Large-scale studies (n≥1000) did not find significant differences between groups for academic performance (n=0/6 worse T1D) and language (n=0/3 worse T1D). In the meta-analysis of 16 studies (n=1594), children with T1D had slightly lower IQ scores than peers without T1D (mean difference −3.49, 95% CI (−6.16 to −0.82); p=0.010). T1D appears to be associated with slightly lower cognitive outcomes in some areas. Further research is needed to understand the impact of these findings on daily functioning and to inform screening for at-risk children.]