

Diabetes

Current Awareness Bulletin

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1. Challenges in implementing nationwide epidemiological studies on metabolic noncommunicable diseases in low-income and middle-income countries

Anjana R.M., Elangovan N, Pradeepa R, et al. *Lancet Diabetes & Endocrinology*, 2023, 11(12), pp.889-891.

[Metabolic non-communicable diseases (NCDs), such as diabetes, hypertension, and cardiovascular disease, are leading causes of morbidity and mortality worldwide. Planning and implementation of preventive and therapeutic measures to stop the global pandemic of metabolic NCDs require accurate epidemiological data on the magnitude of the problem. However, there are numerous challenges to conduct these studies, especially in low-income and middle-income countries (LMICs), where the majority of individuals with NCDs reside. 1 The challenges include insufficient financial resources and technical facilities, socio-cultural beliefs and practices, adverse climate conditions and inaccessible terrain, and political instability. Additionally, recruitment and training of personnel for the conduct of these studies are difficult, on account of low levels of literacy and educational attainment (panel). We experienced many of these challenges firsthand when performing the ICMR-India Diabetes (ICMR-INDIAB) study, 2 which included urban and rural areas of every state of India.]

2. IDF leadership voices dismay and concern at ongoing situation in the Middle East

Hussain A, Schwarz P, Ceriello A. Diabetes Research and Clinical Practice 2023, 206: 110995.

[The harrowing reports emerging from Israel and the Gaza strip over recent weeks have provided a bleak and horrific account of an area in the throes of a humanitarian disaster. Beside the War we are currently experiencing humanitarian crisis in Israel, The Westbank and Gaza. In war, it is the innocents who bear the brunt of the horror – nearly a third of all deaths are reported to be among children. Moreover, there are about 500 children with type 1 diabetes in Gaza. Disruption of supply of insulin to these children for days or even hours may lead to certain death as an indirect consequence of this war. Due to the destruction of infrastructure in Gaza, the supply chains to deliver insulin to these patients are interrupted. The health system has all but collapsed.]

3. Metabolic non-communicable diseases in India: time to act

Habeeb S, Thankappan K.R. Lancet Diabetes & Endocrinology, 2023, 11(12), pp.897-898.

[The Article by Ranjit Mohan Anjana and colleagues 1 non-communicable disease (NCDs) burden in India, which is much higher than previous reports. For example, in this Article, the number of people with diabetes is estimated to be 101 million, 36% higher than the 74·2 million reported by the International Diabetes Federation. 2 The hypertension prevalence of 35·5% is much higher than the 28·5% reported in the National NCD Monitoring Survey (NNMS), based on a nationally representative sample of adults aged 18–69 years. 3 As the authors report, inclusion of older adults in the sample could be one of the reasons for the higher prevalence of NCDs. In addition, most studies, including the NNMS, 4 used only fasting capillary glucose for identifying people with diabetes, whereas in Anjana and colleagues' study 1, the oral glucose tolerance test was used to identify people with diabetes. What proportion of diabetes will be missed when only fasting capillary glucose is used to detect people with diabetes is not mentioned in the Article, but could be useful information.]

4. Metabolic non-communicable diseases in India: time to act

Nag S, Shrivastava S, Chakma T. Lancet Diabetes & Endocrinology, 2023, 11(12), pp.896-897.

[Amidst the global COVID-19 pandemic, health-care sectors have primarily focused on combating infectious diseases, given their immediate impact on morbidity and mortality. However, it is essential to acknowledge that there has also been a tremendous increase in the prevalence of metabolic non-communicable diseases (NCDs) during this period, which remains overshadowed by the pandemic.]

5. Metabolic non-communicable diseases in India: time to act – Authors' reply

Anjana R.M., Unnikrishnan R, Pradeepa R, et al. *Lancet Diabetes & Endocrinology*, 2023, 11(12), pp.898-899.

[We thank Shikha Nag and colleagues for their interest in our Article reporting on metabolic noncommunicable diseases (NCDs) in India. 1 While we appreciate their concern that the ICMR-INDIAB study does not encompass the entirety of India's population (particularly the underprivileged indigenous tribes), we would like to emphasise that the study sample is representative of the nation with respect to distribution in area of residence (30% urban, 70% rural) and sex (47% male, 53% female). This study has covered all the states and union territories of India and is representative of the country in terms of geographical distribution, population size, and socioeconomic status. Therefore, we have some tribal populations also included in the study. However, we do acknowledge that ICMR-INDIAB, not being a study specifically conducted on tribal populations, does not provide too much detail on this population.]

6. Tackling the diabetes surge in sub-Saharan Africa through novel youth-centric strategies

Chilunga F.P, Mtintsilana A, Aovare P, et al. *Lancet Diabetes & Endocrinology*, 2023, 11(12), pp.886-889.

[Over the past few decades, diabetes cases in sub-Saharan Africa have shown a substantial increase. According to a recent Global Burden of Disease Study, published in *The Lancet*, the age-standardised prevalence of diabetes in sub-Saharan Africa rose by 83% between 1990 and 2021, reaching 4248 cases per 100 000 individuals. 1 Furthermore, projections predict a 57% increase in diabetes in sub-Saharan Africa from 2021 to 2050, reaching a prevalence of 6688 cases per 100 000 individuals. 1 These statistics depict a worrisome picture of an impending public health crisis that demands immediate attention.]

7. Trends in health behaviors of US adults with and without Diabetes: 2007–2018

Shah M.K., Gandrakota N, Bullard K.M., et al. *Diabetes Research and Clinical Practice* 2023, 206: 110990.

[**Aims**: Understanding health behaviors of people with diabetes can inform strategies to reduce diabetes-related burdens.]

Children with diabetes

8. Glucagon fill rates and cost among children and adolescents with type 1 diabetes in the United States, 2011–2021

Benning T.J., Heien H.C., Herges J.R., et al. *Diabetes Research and Clinical Practice* 2023, 206: 111026.

[**Aims**: To characterize glucagon fill rates and costs among youth with type 1 diabetes mellitus (T1DM).]

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

Cardiovascular Disease

9. ACMSD mediated de novo NAD + biosynthetic impairment in cardiac endothelial cells as a potential therapeutic target for diabetic cardiomyopathy

Zeng F, Zhou P, Wang M, et al. *Diabetes Research and Clinical Practice* 2023, 206: 111014.

[Object: The highly conserved α -amino- β -carboxymuconate- ϵ -semialdehyde decarboxylase (ACMSD) is the key enzyme that regulates the de novo NAD + synthesis from tryptophan. NAD + metabolism in diabetic cardiomyopathy (DCM) was not elucidated yet.]

10. Association of cumulative blood glucose load with cardiovascular risk and all-cause mortality

Tian X, Chen S, Zhang Y, et al. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2023;17(12): 102900.

[**Background**: Incorporation both the magnitude and duration of exposure to elevated fasting blood glucose (FBG) into a single risk parameter (cumulative FBG load) for future diseases is intuitively appealing, although a data-based demonstration of the utility of this metric is not available. This study aimed to investigate the associations with cumulative FBG load with the risk of cardiovascular diseases (CVD) and all-cause mortality in the general population.]

11. Clinical Features, Cardiovascular Risk Profile, and Therapeutic Trajectories of Patients with Type 2 Diabetes Candidate for Oral Semaglutide Therapy in the Italian Specialist Care.

Morieri M.L., Candido R, Frontoni S, et al. *Diabetes Therapy* 2023, 14(12): 2159-2172.

[Introduction: This study aimed to address therapeutic inertia in the management of type 2 diabetes (T2D) by investigating the potential of early treatment with oral semaglutide.]

12. Combined exposure to multiple air pollutants and incident ischemic heart disease in individuals with and without type 2 diabetes: A cohort study from the UK Biobank

Li R, Chen J.X., Li R.Y., et al. Diabetes Research and Clinical Practice 2023, 206: 111019.

[**Background**: Air pollution and type 2 diabetes (T2D) are both associated with an increased risk of ischemic heart disease (IHD). Little is known about the combined effects of multiple air pollutants on IHD risk, especially among individuals with T2D. We sought to assess the association of combined exposure to multiple air pollutants with incident IHD and examine the modification effect of T2D.]

13. Comparative evaluation of LDL-CT, non-HDL/HDL ratio, and ApoB/ApoA1 in assessing CHD risk among patients with type 2 diabetes mellitus

Păunică I, Mihai A.D., Ștefan S, et al. *Journal of Diabetes and Its Complications*, 2023, 37(12), Article 108634.

[**Background**: Research proved the importance of dosing apolipoprotein B (ApoB) over LDL cholesterol as a predictor of cardiovascular events. In this study, we aimed to observe the input apolipoprotein A1 (ApoA1) and ApoB, primarily if its ratio could provide in patients with type 2 diabetes mellitus (T2DM) without known atherosclerotic events regarding the coronary heart disease (CHD) risk.]

14. Cumulative HbA1c exposure as a CVD risk in patients with type 2 diabetes: A post hoc analysis of ACCORD trial

Cheng Y, Zou J, Chu R, et al. Diabetes Research and Clinical Practice 2023, 206: 111009.

[**Aims**: The study aimed to investigate the relationship between cumulative HbA1c exposure and cardiovascular events in patients with type 2 diabetes (T2D).]

15. Early rhythm control on diabetes-related complications and mortality in patients with type 2 diabetes mellitus and atrial fibrillation

Lee S.R., Choi J.M., Choi E.K., et al. Diabetes Research and Clinical Practice 2023, 206: 111020.

[**Aims**: We evaluated the impact of early rhythm control (ERC) on diabetes-related complications and mortality in subjects with type 2 diabetes mellitus (T2DM) and atrial fibrillation (AF).]

16. Effects of percutaneous coronary intervention and diabetes mellitus on short- and longterm prognosis assessed by the three-vessel quantitative flow ratio

Chen Y, Zhong J, Chen L, et al. Diabetes Research and Clinical Practice 2023, 206: 111013.

[Aims: We aimed to investigate the impact of percutaneous coronary intervention (PCI) and diabetes mellitus (DM) on short- and long-term prognosis in patients with coronary artery disease using three-vessel quantitative flow ratio (3 V-QFR) assessment.]

17. GLP-1 and dual GIP/GLP-1 receptor agonists in overweight/obese patients for atherosclerotic cardiovascular disease prevention: Where are we now?

Muzurović E, Yumuk V.D., Rizzo M. *Journal of Diabetes and Its Complications*, 2023, 37(12), Article 108647.

[Obesity is a highly prevalent chronic disease characterized by an increase of body fat stores. 1 Increased adiposity (body fat), particularly abdominal/visceral fat, plays a role in altering immune and inflammatory function, developing insulin resistance (IR) and contributing to downstream metabolic risk factors (RFs) such as hyperglycemia, dyslipidemia, systemic adrenergic activity, hypertension, atherosclerosis and finally, cardiovascular (CV) disease (CVD). 2 Furthermore, visceral fat is strongly associated with increased atherosclerotic burden and the risk of recurrent atherosclerotic CVD (ASCVD), residual CV risk, and CVD mortality. 3]

18. Humanistic and Economic Burden of Patients with Cardiorenal Metabolic Conditions: A Systematic Review.

Ferdinand K.C., Norris K.C., Rodbard H.W., et al. Diabetes Therapy 2023, 14(12): 1979-1996.

[Introduction: Diabetes is associated with significant economic burden. Moreover, cardiovascular disease (CVD), including heart failure, and chronic kidney disease (CKD) are common comorbidities, leading to premature mortality. We conducted a systematic review to assess the humanistic and economic burden of cardio-renal-metabolic (CRM) conditions in individuals \geq 18 years with CVD, CKD, and type 2 diabetes mellitus.]

19. Insulin resistance and metabolic flexibility as drivers of liver and cardiac disease in T2DM

Colosimo S, Mitra S.K., Chaudhury T, et al. *Diabetes Research and Clinical Practice* 2023, 206: 111016.

[Metabolic flexibility refers to the ability of tissues to adapt their use of energy sources according to substrate availability and energy demands. This review aims to disentangle the emerging mechanisms through which altered metabolic flexibility and insulin resistance promote NAFLD and heart disease progression. Insulin resistance and metabolic inflexibility are central drivers of hepatic and cardiac diseases in individuals with type 2 diabetes. Both play a critical role in the complex interaction between glucose and lipid metabolism. Disruption of metabolic flexibility results in hyperglycemia and abnormal lipid metabolism, leading to increased accumulation of fat in the liver, contributing to the development and progression of NAFLD. Similarly, insulin resistance affects cardiac glucose metabolism, leading to altered utilization of energy substrates and impaired cardiac function, and influence cardiac lipid metabolism, further exacerbating the progression of heart failure. Regular physical activity promotes metabolic flexibility by increasing energy expenditure and enabling efficient switching between different energy substrates. On the contrary, weight loss achieved through calorie restriction ameliorates insulin sensitivity without improving flexibility. Strategies that mimic the effects of physical exercise, such as pharmacological interventions or targeted lifestyle modifications, show promise in effectively treating both diabetes and NAFLD, finally reducing the risk of advanced liver disease.]

20. Serum osmolality was non-linearly associated with the risk of all-cause and cardiovascular mortality in patients with diabetes

Hu T, Li C, Wang T, et al. BMJ Open Diabetes Research and Care 2023;11:e003826

[**Aims**: This study aimed to evaluate the relationship between both low and high osmolarity and the risk of all-cause and cause-specific mortality in diabetic population.]

21. Sex hormone-binding globulin and heart failure hospitalizations in patients with dysglycemia

Wang A, Hess S, Lee S.F., et al. Diabetes Research and Clinical Practice 2023, 206: 111010.

[Introduction: Sex hormone-binding globulin (SHBG), which binds most of circulating testosterone in blood, has been linked to dysglycemia and cardiovascular disease but the relationship with heart failure remains unclear.

Aim: To study the relation between SHBG and heart failure hospitalizations.]

Diabetic Neuropathy

22. Effects of foot and ankle mobilisations combined with home stretches in people with diabetic peripheral neuropathy: a proof-of-concept RCT.

Lepesis V, Paton J, Rickard A, et al. *Journal of Foot and Ankle Research* 2023;16(1):88. [Introduction: People with diabetic peripheral neuropathy (DPN) and limited joint mobility syndrome (LJMS) can experience increased forefoot peak plantar pressures (PPPs), a known risk factor for ulceration. The aim of this study was to investigate whether ankle and 1st metatarsophalangeal (MTP) joint mobilisations and home-based stretches in people with DPN improve joint range of motion (ROM) and reduce forefoot PPPs.]

23. Systemic biomarkers of microvascular alterations in type 1 diabetes associated neuropathy and nephropathy - A prospective long-term follow-up study

Baldimtsi E, Whiss P.A., Wahlberg J. *Journal of Diabetes and Its Complications*, 2023, 37(12), Article 108635.

[Introduction: This study aimed to investigate circulating biomarkers associated with the risk of developing diabetic peripheral neuropathy (DPN) and nephropathy in type 1 diabetes (T1D).]

Diabetic Retinopathy

24. Effects of the ABCC8 R1420H loss-of-function variant on beta-cell function, diabetes incidence, and retinopathy

Arreola E.V., Knowler W.C., Baier L.J., et al. *BMJ Open Diabetes Research and Care* 2023;11:e003700

[Introduction: The *ABCC8* gene regulates insulin secretion and plays a critical role in glucose homeostasis. The effects of an *ABCC8* R1420H loss-of-function variant on beta-cell function, incidence of type 2 diabetes, and age-at-onset, prevalence, and progression of diabetes complications were assessed in a longitudinal study in American Indians.]

25. Predicting the risk of diabetic retinopathy using explainable machine learning algorithms

Islam M.M., Rahman M.J., Rabby M.S., et al. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2023;17(12): 102919.

[**Background and objective**: Diabetic retinopathy (DR) is a global health concern among diabetic patients. The objective of this study was to propose an explainable machine learning (ML)-based system for predicting the risk of DR.]

Kidney Disease

26. Circulating tumor necrosis factor-related biomarkers predict kidney function decline in Japanese patients with diabetes: An observational cohort study

Murakoshi M, Kamei N, Suzuki Y, et al. *Diabetes Research and Clinical Practice* 2023, 206: 111017.

[Aims: Tumor necrosis factor (TNF) receptors (TNFRs: TNFR1 and, TNFR2) are reportedly associated with chronic kidney disease (CKD) progression chiefly in Caucasian patients with diabetes. We assessed the prognostic value of TNF-related biomarkers for CKD progression in Japanese patients with diabetes.]

27. Systemic biomarkers of microvascular alterations in type 1 diabetes associated neuropathy and nephropathy - A prospective long-term follow-up study

Baldimtsi E, Whiss P.A., Wahlberg J. *Journal of Diabetes and Its Complications*, 2023, 37(12), Article 108635.

[Introduction: This study aimed to investigate circulating biomarkers associated with the risk of developing diabetic peripheral neuropathy (DPN) and nephropathy in type 1 diabetes (T1D).]

Liver Disease

28. Association between nonalcoholic fatty liver disease and type 2 diabetes: A bidirectional two-sample mendelian randomization study

Ni X, Tong C, Halengbieke A, et al. *Diabetes Research and Clinical Practice* 2023, 206: 110993. [**Objective**: The aim of this study was to explore the mutually causal relationship between NAFLD and type 2 diabetes.]

29. Effect of Policaptil Gel Retard on Liver Fat Content and Fibrosis in Adults with Metabolic Syndrome and Type 2 Diabetes: A Non-invasive Approach to MAFLD.

Guarino G, Strollo F, Corte D.T., et al. *Diabetes Therapy* 2023, 14(12): 2089-2108.

[Introduction: Non-alcoholic fatty liver disease (NAFLD) is part of a disease spectrum ranging from steatosis to steatohepatitis (NASH), fibrosis, and cirrhosis, and when associated with metabolic syndrome (MS), and overt diabetes is defined as metabolic NAFLD (MAFLD). Some easily available, inexpensive biomarkers have been validated based on common anthropometric and laboratory parameters, including the Fatty Liver Index (FLI), the Fibrosis (FIB)-4 Score (FIB-4), and the NAFLD Fibrosis Score (NFS). In people with overweight/obesity, MS, and diabetes, the pathogenesis of fatty liver involves parameters known to be positively affected by Policaptil Gel Retard (PGR), a phytocomplex already successfully used in adolescents and adults with MS and type 2 diabetes mellitus (T2DM). This study's primary outcome was to assess PGR's ability to improve indirect validated signs of liver steatosis and fibrosis, i.e., FLI, FIB-4, and NFS Scores; as the secondary outcome, we aimed to confirm PGR's positive effects on anthropometric parameters and lipid levels and to assess any eventually occurring cytolysis liver marker changes in patients with MS/T2DM and MAFLD/NASH.]

30. Insulin resistance and metabolic flexibility as drivers of liver and cardiac disease in T2DM

Colosimo S, Mitra S.K., Chaudhury T, et al. *Diabetes Research and Clinical Practice* 2023, 206: 111016.

[Metabolic flexibility refers to the ability of tissues to adapt their use of energy sources according to substrate availability and energy demands. This review aims to disentangle the emerging mechanisms through which altered metabolic flexibility and insulin resistance promote NAFLD and heart disease progression. Insulin resistance and metabolic inflexibility are central drivers of hepatic and cardiac diseases in individuals with type 2 diabetes. Both play a critical role in the complex

interaction between glucose and lipid metabolism. Disruption of metabolic flexibility results in hyperglycemia and abnormal lipid metabolism, leading to increased accumulation of fat in the liver, contributing to the development and progression of NAFLD. Similarly, insulin resistance affects cardiac glucose metabolism, leading to altered utilization of energy substrates and impaired cardiac function, and influence cardiac lipid metabolism, further exacerbating the progression of heart failure. Regular physical activity promotes metabolic flexibility by increasing energy expenditure and enabling efficient switching between different energy substrates. On the contrary, weight loss achieved through calorie restriction ameliorates insulin sensitivity without improving flexibility. Strategies that mimic the effects of physical exercise, such as pharmacological interventions or targeted lifestyle modifications, show promise in effectively treating both diabetes and NAFLD, finally reducing the risk of advanced liver disease.]

Osteoporosis

31. Medications and medical expenditures for diabetic patients with osteoporosis in Beijing, China: A retrospective study

Pan Q, Chen H, Fei S, et al. *Diabetes Research and Clinical Practice* 2023, 206: 110980.

[**Aims**: This study aimed to clarify the changes in treatment regimens and medical expenditures in diabetic patients with osteoporosis.]

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

General

32. Methyl protodioscin reduces c-Myc to ameliorate diabetes mellitus erectile dysfunction via

downregulation of AKAP12

Luo M, Hu Z, Liu Z, et al. Diabetes Research and Clinical Practice 2023, 206: 111012.

[**Background**: Diabetes mellitus erectile dysfunction (DMED) is one of common complications of diabetes. We aimed to investigate the potential efficacy of methyl protodioscin (MPD) in DMED and explored the underlying mechanism.]

Diabetic Foot

33. Comorbid status in patients with osteomyelitis is associated with long-term incidence of extremity amputation

Schmidt B.M., Keeney-Bonthrone T.P., et al. *BMJ Open Diabetes Research and Care* 2023;11:e003611

[Introduction: Osteomyelitis is associated with significant morbidity, including amputation. There are limited data on long-term amputation rates following an osteomyelitis diagnosis. We sought to determine the incidence of amputation in patients with osteomyelitis over 2 years.]

34. Decision-making processes for non-emergency diabetes-related lower extremity amputations: A scoping review

Ong E.K.M., Murray C, Hillier S, et al. *Diabetes Research and Clinical Practice* 2023, 206: 111015.

[Living with a diabetes-related foot ulcer has significant lifestyle impacts. Whilst often considered a last resort, amputation can overcome the burden of ulcer management, for an improved quality of

life. However, limited research has been conducted to understand how the decision to amputate is made for people with a chronic ulcer when amputation is not required as a medical emergency. Therefore, the aim was to identify and map key concepts in the literature which describe the decision-making for diabetes-related amputations. This review followed Arksey and O'Malley's PRISMA scoping review framework. Five electronic databases and grey literature were searched for papers which described clinical reasoning and/or decision-making processes for diabetes-related amputation. Data were extracted and mapped to corresponding domains of the World Health Organisation's International Classification of functioning, Disability and Health (ICF) framework. Ninety-four papers were included. Personal factors including emotional wellbeing, quality of life, and treatment goals are key considerations for an elective amputation. It is important to consider an individual's lifestyle and personal circumstances, as well as the pathology when deciding between amputation or conservative management. This highlights the importance of a holistic and shared decision-making process for amputation which includes assessment of a person's lifestyle and function.]

35. Global healthcare pathway of people living with diabetes prior to wounding is associated with a decreased risk of amputation

Bonnet J.B., Nicolet G, Papinaud L, et al. *Diabetes Research and Clinical Practice* 2023, 206: 111007.

[Aims: Diabetic foot ulcer (DFU) has a poor prognosis and high amputation rate. We previously used the French National Health Data System (Système National des Données de Santé: SNDS) to analyze the impact of deprivation and healthcare access on DFU prognosis. The purpose of this ancillary study was to explore the relationship between the global care pathway (care consumption) the year before and after DFU and the risk of amputation.]

36. Perceptions of primary and secondary care clinicians treating diabetic foot: A pan India study and quantitative analysis

Tayade A, Kumar P, Kumar S, et al. Diabetes Research and Clinical Practice 2023, 206: 111008.

[Aim: The study quantifies clinicians' perceptions and challenges during different stages of diabetic foot treatment. Diabetic neuropathy (DN), which is a major consequence of diabetes, significantly increases the risk of lower limb amputation. This can be prevented to a large extent by foot care, early detection, and lesion treatment.]

Diabetic Ketoacidosis

37. Comparative study of diabetic ketoacidosis in the elderly and non-elderly patients: A nine-year experience from an academic hospital in North India

Pannu A.K., Kiran R, Kumar A, et al. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2023;17(12): 102903.

[**Background and aims**: Despite an increasing prevalence of the aged population with diabetes in low-middle-income countries, there is limited literature on geriatric hyperglycemic emergencies. The present study aimed to compare the spectrum and outcomes of diabetic ketoacidosis (DKA) between elderly and non-elderly adult patients in India.]

Diabetes and pregnancy

38. Considering gestational diabetes and gestational hypertension history across two pregnancies in relationship to cardiovascular disease development: A retrospective cohort study

Mussa J, Rahme E, Dahhou M, et al. *Diabetes Research and Clinical Practice* 2023, 206: 110998.

[Aims: Gestational diabetes (GDM) and hypertension (GHTN) occurrences signal elevated cardiovascular disease (CVD) risk. There is little study of occurrence and recurrence of these conditions in relationship to CVD. Among women with two singleton pregnancies, we aimed to quantify CVD risk in relationship to the number of GDM/GHTN occurrences.]

39. A Simplified Screening Model to Predict the Risk of Gestational Diabetes Mellitus in Pregnant Chinese Women.

Duo Y, Song S, Qiao X, et al. *Diabetes Therapy* 2023, 14(12): 2143-2157.

[Introduction: This study aimed to develop a simplified screening model to identify pregnant Chinese women at risk of gestational diabetes mellitus (GDM) in the first trimester.]

40. Various screening and diagnosis approaches for gestational diabetes mellitus and adverse pregnancy outcomes: a secondary analysis of a randomized non-inferiority field trial

Tehrani F.R., et al. BMJ Open Diabetes Research and Care 2023;11:e003510

[Introduction: We evaluate which screening and diagnostic approach resulted in the greatest reduction in adverse pregnancy outcomes due to increased treatment.]

Diabetes mellitus Type 1

41. C-peptide and metabolic outcomes in trials of disease modifying therapy in new-onset type 1 diabetes: an individual participant meta-analysis

Taylor P.N., Collins K.S., Lam A, et al. Lancet Diabetes & Endocrinology, 2023, 11(12), pp.915-925.

[**Background**: Metabolic outcomes in type 1 diabetes remain suboptimal. Disease modifying therapy to prevent β -cell loss presents an alternative treatment framework but the effect on metabolic outcomes is unclear. We, therefore, aimed to define the relationship between insulin C-peptide as a marker of β -cell function and metabolic outcomes in new-onset type 1 diabetes.]

42. Characteristics associated with having a hemoglobin A1c \leq 7 % (\leq 53 mmol/mol) among adults with type 1 diabetes using an automated insulin delivery system

Wu Z, Talbo M, Lebbar M, et al. Diabetes Research and Clinical Practice 2023, 206: 111006.

[**Background**: We aim to investigate which characteristics are associated with having an HbA1c ≤ 7 % (≤53 mmol/mol) among adult automated insulin delivery (AID) users living with type 1 diabetes (T1D).]

43. Evaluation of a novel eating disorder prevention program for young women with type 1 diabetes: A preliminary randomized trial

Stice E, Wisting L, Desjardins C.D., et al. *Diabetes Research and Clinical Practice* 2023, 206: 110997.

[**Objective**: Evaluate whether the *Body Project* prevention program adapted for young women with type 1 diabetes (*Diabetes Body Project*) reduces eating disorder (ED) risk factors and symptoms.]

44. Impact of disease-modifying therapy on β -cell function and metabolic control in newly diagnosed type 1 diabetes

Knip M. Lancet Diabetes & Endocrinology, 2023, 11(12), pp.881-882.

[Type 1 diabetes is an immune-mediated disease and therefore immunotherapy is a potential modality for halting β -cell destruction and attenuating C-peptide loss after the diagnosis of clinical diabetes. From the beginning of this century, a series of intervention trials have been done to assess whether immunotherapy could affect the loss of β -cell function and metabolic control in people with newly diagnosed type 1 diabetes. As part of the Trial Outcome Markers Initiative, Peter

Taylor and colleagues 2 have now carried out an individual participant meta-analysis of C-peptide and metabolic outcomes in 21 trials of disease-modifying therapy including 1315 adults (ie, those 18 years and older) and 1396 children (ie, those younger than 18 years).]

45. Interpreting with caution of the higher occurrence of pediatric new-onset type 1 diabetes during the COVID-19 pandemic

Cai Y, Zhang Y.F., Wu S.Q., et al. Diabetes Research and Clinical Practice 2023, 206: 111030.

[**To the Editor**, Recently, a retrospective multicenter study from Malaysia showed that new-onset type 1 diabetes (T1D) increased during the COVID-19 pandemic (109 versus 71 cases), with a greater proportion of severe diabetic ketoacidosis (DKA) than the pre-pandemic period (46.8 % versus 28.2 %) [1]. Despite several limitations have been listed by authors, the above findings should be interpreted with caution due to the following, at least, 7 confounding factors.]

46. Longitudinal associations of physical activity with inflammatory markers in US adults with and without type 1 diabetes

Richardson L.A., Basu A, Chien L.C., et al. *Diabetes Research and Clinical Practice* 2023, 206: 110978.

[**Aims**: To investigate the longitudinal associations of different levels of moderate-to-vigorous physical activity (MVPA) with C-reactive protein (CRP), plasminogen activator inhibitor-1 (PAI-1), and fibrinogen.]

47. Sars-Cov-2 Infection in People with Type 1 Diabetes and Hospital Admission: An Analysis of Risk Factors for England.

Heald A.H., Jenkins D.A., Williams R, et al. *Diabetes Therapy* 2023, 14(12): 2031-2042.

[Introduction: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus (coronavirus disease 2019 [COVID-19]) pandemic revealed the vulnerability of specific population groups in relation to susceptibility to acute deterioration in their health, including hospital admission and mortality. There is less data on outcomes for people with type 1 diabetes (T1D) following SARS-CoV-2 infection than for those with type 2 diabetes (T2D). In this study we set out to determine the relative likelihood of hospital admission following SARS-CoV-2 infection in people with T1D when compared to those without T1D.]

48. Self-management of type 1 diabetes in young adults: Is it impeded by aspects of everyday life? A scoping review

Shiel E.V., Hemingway S, Burton K, et al. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2023;17(12): 102918.

[**Background and aim**: For people with type 1 diabetes, self-management is a necessity. However, self-management can be impeded by aspects of everyday life, which may impact young adults moving to independence. However, it is not yet clear which aspects are most relevant, nor what knowledge gaps remain.]

Diabetes mellitus Type 2

49. 24-h ambulatory blood pressure readings and associations with albuminuria in youth with type 2 diabetes: A cross sectional analysis from the iCARE cohort

Dart A.B., Sellers E.A.C., McGavock J, et al. *Journal of Diabetes and Its Complications*, 2023, 37(12), Article 108633.

[**Aims**: To evaluate associations between 24-h ambulatory blood pressure monitor (ABPM) data vs. single casual blood pressure (BP) and albuminuria in youth with type 2 diabetes.]

50. Colonic L-cell impairment in aged subjects with type 2 diabetes leads to diminished GLP-1 production Wang Q.Y., Zhang W, Zhao Y, et al. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2023;17(12): 102907.

[Aims: Glucagon-like peptide 1 (GLP-1) is produced by the L subtype of enteroendocrine cells (EECs). Patients with type 2 diabetes (T2D) exhibit reduced incretin effect, but the pathophysiology and functional change of the L-cells remain unclear. Deciphering the mechanisms of the biological changes in L-cells under T2D conditions may assist in the research of gut-based strategies for T2D therapy.]

51. Effect of Policaptil Gel Retard on Liver Fat Content and Fibrosis in Adults with Metabolic Syndrome and Type 2 Diabetes: A Non-invasive Approach to MAFLD.

Guarino G, Strollo F, Corte T.D., et al. *Diabetes Therapy* 2023, 14(12): 2089-2108.

[Introduction: Non-alcoholic fatty liver disease (NAFLD) is part of a disease spectrum ranging from steatosis to steatohepatitis (NASH), fibrosis, and cirrhosis, and when associated with metabolic syndrome (MS), and overt diabetes is defined as metabolic NAFLD (MAFLD). Some easily available, inexpensive biomarkers have been validated based on common anthropometric and laboratory parameters, including the Fatty Liver Index (FLI), the Fibrosis (FIB)-4 Score (FIB-4), and the NAFLD Fibrosis Score (NFS). In people with overweight/obesity, MS, and diabetes, the pathogenesis of fatty liver involves parameters known to be positively affected by Policaptil Gel Retard (PGR), a phytocomplex already successfully used in adolescents and adults with MS and type 2 diabetes mellitus (T2DM). This study's primary outcome was to assess PGR's ability to improve indirect validated signs of liver steatosis and fibrosis, i.e., FLI, FIB-4, and NFS Scores; as the secondary outcome, we aimed to confirm PGR's positive effects on anthropometric parameters and lipid levels and to assess any eventually occurring cytolysis liver marker changes in patients with MS/T2DM and MAFLD/NASH.]

52. Effect of weight loss on proteinuria in adults with type 2 diabetes: A real-world study

Ren W, Gong Y, Zhen Q, et al. *Diabetes Research and Clinical Practice* 2023, 206: 111021.

[**Aims**: To assess the impact of weight loss on proteinuria in patients with type 2 diabetes (T2DM) in real-world settings.]

53. Prevalence of sarcopenia and its determinants in people with type 2 diabetes: Experience from a tertiary care hospital in north India

Shahi A, Tripathi D, Jain M, et al. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2023;17(12): 102902.

[**Objectives**: Changes in skeletal muscle mass and quality are associated with type 2 Diabetes (T2D) and its complications. We evaluated the prevalence of sarcopenia in patients with T2D and its association with various anthropometric and metabolic parameters.]

54. Unexpected evolution of a monster case of insulin-induced skin lipohypertrophy

Gentile S, Guarino G, Strollo F. Diabetes Research and Clinical Practice 2023, 206: 110994.

[In this journal, in 2020, we published the case of a 74-year-old female outpatient with type-2 diabetes mellitus who self-injected insulin four times a day according to the basal-bolus regimen, with an high glycemic variability and an high rate of severe hypoglycemic episodes. Three years before, we had found two extraordinarily large skin lipohypertrophies, with large underlying fluid collections with high insulin concentration. A long educational and intensive training completely repaired the skin lesions with the disappearance of the subcutaneous insulin reservoirs. Glycemic variability has been reduced dramatically, severe hypoglycemia has almost completely disappeared and the daily dose of insulin has been reduced by 38%. However, this extraordinary, albeit unexpected, result was achieved in five years.]

Glucose monitoring and control

55. Comparing the effectiveness of glucose-lowering agents: real-world data to emulate a four-arm target trial

Ahmed A, Anker S.D., Butler J, et al. Lancet Diabetes & Endocrinology, 2023, 11(12), pp.892-894.

[We read the study by Yan Xie and colleagues 1 with interest. Findings of this observational retrospective cohort study suggest that both SGLT2 inhibitors and GLP-1 receptor agonists are associated with a lower risk of major adverse cardiovascular events compared with DPP-4 inhibitors or sulfonylureas. The authors concluded that these "results provide evidence of the real-world comparative effectiveness of the four most commonly used second-line antihyperglycaemics and could guide choice of antihyperglycaemic therapy." 1]

56. Comparing the effectiveness of glucose-lowering agents: real-world data to emulate a four-arm target trial

Ceriello A, Prattichizzo F, Berra C.C., et al. *Lancet Diabetes & Endocrinology*, 2023, 11(12), pp.894-895.

[SGLT2 inhibitors have a protective effect for the cardiovascular system and for the kidney. 1 It is recommended to add these drugs in the treatment of type 2 diabetes when cardiovascular disease or kidney disease is prevalent. However, a matter of debate is the possible usefulness of using this class of drugs in the absence of such conditions, especially in people with a recent diagnosis of type 2 diabetes.]

57. Comparing the effectiveness of glucose-lowering agents: real-world data to emulate a four-arm target trial

Keskinler M.V., Caklili O.T., Oguz A. Lancet Diabetes & Endocrinology, 2023, 11(12), p.894.

[We read the study by Yan Xie and colleagues 1 with great interest. The study filled a gap in the evidence for the cardiovascular effects of diabetes medications by using an original method of emulation of a randomised pragmatic clinical trial. The findings of the study showed that SGLT2 inhibitors and GLP-1 receptor agonists were superior to DPP-4 inhibitors in reducing major adverse cardiovascular events (MACE) and that DPP-4 inhibitors reduced MACE more than sulfonylureas. Since the effects of four different agents on MACE were compared with themselves, no judgment can be made as to how much they reduce MACE compared with placebo. The general perception in the interpretation of this study 1 is that sulfonylureas are neutral, DPP-4 inhibitors are more favourable than sulfonylureas, and SGLT2 inhibitors and GLP-1 receptor agonists are superior.]

58. Comparing the effectiveness of glucose-lowering agents: real-world data to emulate a four-arm target trial – Authors' reply

Xie Y, Al-Aly Z. Lancet Diabetes & Endocrinology, 2023, 11(12), pp.895-896.

We thank Ali Ahmed and colleagues for their interest in our study of the comparative effectiveness of four antihyperglycaemics on the risk of major adverse cardiovascular events (MACE). 1 However, they do not seem to appreciate the merit of the target trial emulation approach in general and that we leveraged this approach to address a major knowledge gap that has not been answered by any randomised controlled trial (RCT). 23 Target trial emulation is a novel approach in pharmacoepidemiology that seeks to replicate the design of an RCT using observational data. 23 It is a major advance in causal inference. 23 One of its principal strengths is the ability to harness extensive, real-world data, such as those from high quality electronic health records, to answer questions that might be logistically challenging, ethically questionable, or economically infeasible to address through RCTs. By emulating the design, execution, and analysis stages of an RCT, target trial emulation seeks to minimise biases commonly associated with observational studies. Therefore, this methodology combines the rigour of RCT design with the breadth and depth of realworld observational data, offering a robust mechanism for generating evidence, especially in scenarios in which conventional RCTs are unattainable. Furthermore, by leveraging existing data sources, target trial emulation can provide timely insights when rapid decision making is essential, such as in post-market drug safety evaluations or during public health emergencies. 45 RCTs and target trial emulation are complementary approaches in addressing the evidence gap and informing clinical decision making. It is important to note that target trial emulation is the standard terminology used to describe and report these analyses. We celebrate this progress in causal inference and

pharmacoepidemiology and issue an invitation to adopt it as best practice in pharmacoepidemiologic analyses using real-world data.]

59. The effect of sodium-glucose cotransporter 2 inhibitors as an adjunct to insulin in patients with type 1 diabetes assessed by continuous glucose monitoring: A systematic review and meta-analysis

Li M, Liu Z, Yang X, et al. Journal of Diabetes and Its Complications, 2023, 37(12), Article 108632.

[Aims: Patients undergoing insulin-based therapy for type 1 diabetes often experience poor glycemic control characterized by significant fluctuations. This study was undertaken to analyze the effect of sodium-glucose cotransporter 2 inhibitors (SGLT2Is), as an adjunct to insulin, on time in range (TIR) and glycemic variability in patients with type 1 diabetes, using continuous glucose monitoring (CGM). In addition, we examined which type of SGLT2I yielded a superior effect compared to others.]

60. Glycaemic fluctuations across the menstrual cycle: possible effect of the brain

Hummel J, Kullmann S, Wagner R, et al. *Lancet Diabetes & Endocrinology*, 2023, 11(12), pp.883-884.

[Epidemiological research has identified a lower risk for type 2 diabetes and cardiovascular disease in women who are premenopausal than in men. 12 However, after menopause, women have a higher risk for these diseases than men do. 12 The effect of the menstrual cycle on glycaemia is thought to contribute to this phenomenon. Lin and colleagues 3 recently made use of the latest advancements in continuous glucose monitoring to better characterise changes in glycaemia across the menstrual cycle in 49 individuals with natural menstrual cycles. They detected dynamic cycle-phase specific glucose fluctuations: following a drop during menstruation (day 1), daily median glucose declines to its nadir in the late-follicular phase (around day 14), followed by an increase during ovulation and a final glucose peak in the luteal phase (around day 25). 3 A further strength of this study is the daily measurement of sex hormones from urine, which was used to ensure correct allocation of data to cycle phase and for correlational analyses. Here, higher urinary oestradiol metabolites (as is typically present in the late-follicular phase) were associated with lower glucose concentrations. 3]

61. Glycemic outcomes of a family-focused intervention for adults with type 2 diabetes: Main, mediated, and subgroup effects from the FAMS 2.0 RCT

Nelson L.A., Spieker A.J., Greevy R.A., et al. *Diabetes Research and Clinical Practice* 2023, 206: 110991.

[Aims: Family/friend Activation to Motivate Self-care (FAMS) is a self-care support intervention delivered via mobile phones. We evaluated FAMS' effects on hemoglobin A1c (HbA1c) and intervention targets among adults with type 2 diabetes in a 15-month RCT.]

Hypoglycaemia

62. Daytime hypoglycemic episodes during the use of an advanced hybrid closed loop system

Rossi A, Montefusco L, Reseghetti E, et al. *Diabetes Research and Clinical Practice* 2023, 206: 111011.

[Aims: The use of advanced hybrid closed loop systems is spreading due to the beneficial effects on glycometabolic control obtained in patients with type 1 diabetes. However, hypoglycemic episodes can be sometimes a matter of concern. We aim to compare the hypoglycemic risk of an advanced hybrid closed loop system and a predictive low glucose suspend sensor augmented pump.]

63. Incidence rate and risk factors for hypoglycemia among individuals with type 1 diabetes or type 2 diabetes in China receiving insulin treatment

Chen S, Lu J, Peng D, et al. *Diabetes Research and Clinical Practice* 2023, 206: 110987.

[**Aims**: We investigated the real-world incidence of hypoglycemic events among patients with type 1 or type 2 diabetes (T1DM or T2DM) receiving insulin in routine clinical practice in China.]

64. Validation of the hypoglycemia awareness questionnaire to assess hypoglycemia awareness in patients with type 2 diabetes treated with insulin

Henao-Carrillo D.C., Sierra-Matamoros F.A., Algarra A.J.C., et al. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2023;17(12): 102917.

[Aims: Given the implications of impaired hypoglycemia awareness in patients with type 2 diabetes (T2D), it is necessary to identify reliable and valid instruments for its measurement. The Hypoglycemia Awareness Questionnaire (HypoA-Q) measures impaired awareness, symptom severity, and symptom frequency. The present study evaluated the HypoA-Q validity for assessing awareness of hypoglycemia in patients with T2D treated with insulin.]

Insulin therapies

65. Addressing Insulin Injection Technique: A Follow-up Study of Canadian Patients with Diabetes.

Bari B, Corbeil M.A., MacNeill G, et al. Diabetes Therapy 2023, 14(12): 2057-2074.

[Introduction: Proper insulin injection technique is important for optimal glycaemic control, yet patients with diabetes often inject insulin incorrectly. Previous studies identified common errors in insulin injection in Canada, and this article seeks to evaluate the current insulin injection technique practices among patients and explore the effectiveness of feedback and education in improving their technique.]

66. Characteristics associated with having a hemoglobin A1c \leq 7 % (\leq 53 mmol/mol) among adults with type 1 diabetes using an automated insulin delivery system

Wu Z, Talbo M, Lebbar M, et al. Diabetes Research and Clinical Practice 2023, 206: 111006.

[**Background**: We aim to investigate which characteristics are associated with having an HbA1c ≤ 7 % (≤53 mmol/mol) among adult automated insulin delivery (AID) users living with type 1 diabetes (T1D).]

67. Chronicling insulin from discovery to crisis

Burki T. Lancet Diabetes & Endocrinology, 2023, 11(12), p.900.

[It took a while for Stuart Bradwel to get accustomed to the idea that he had type 1 diabetes. "Insulin therapy involved a great deal more than just doing injections", notes Bradwel, in the preface to *Insulin: A Hundred Year History*. "Much more challenging was what it did to my sense of self". Bradwel was diagnosed in 2009, when he was 19 years old. "Diabetes threatened the very core of my being by stripping away part of my identity and replacing it with something that was, somehow, not me", he writes. Bradwel felt that he was no longer the person he had been, nor could he become the person he was planning to be: "if the things that made me recognise myself were gone, then who was I?".]

68. LIVE INDIA: Effectiveness of Gla-100 in a Post hoc Pooled Analysis of FINE ASIA and GOAL Registries.

Deshmukh V, Chaudhury T, Chadha M, et al. *Diabetes Therapy* 2023, 14(12): 2075-2088.

[Introduction: Real-world evidence on insulin glargine 100 U/ml (Gla-100) initiation in Indian type 2 diabetes mellitus (T2DM) individuals is limited. The present study aimed to evaluate the effectiveness of Gla-100 in insulin-naïve T2DM participants from India.]

69. Quantification of insulin adherence in adults with insulin-treated type 2 diabetes: A systematic review

Nørlev J.T.D., Hejlesen O, Jensen M.H., et al. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2023;17(12): 102908.

[Aims: This systematic review aims to identify current methods used for the assessment of insulin adherence in adults with insulin-treated type 2 diabetes. The primary goal is to offer recommendations for clinical practice to improve quantification of adherence.]

Management of diabetes (diet, exercise, lifestyle)

70. Balancing hormonal shifts: exploring the impact of ageing and dietary restriction

Twigg S.M., Fontana L. Lancet Diabetes & Endocrinology, 2023, 11(12), pp.884-886.

[In the recent Scientific Statement of the Endocrine Society, Anne R Cappola and colleagues presented a comprehensive overview of ageing's impact on various hormonal axes, highlighting crucial areas for future research. 1 As individuals age, all major endocrine systems undergo simultaneous adjustments. Typically, following the peak secretion experienced in puberty or early adulthood, there is a steep decline in serum concentrations of growth hormone (secretion amplitude), insulin-like growth factor 1 (IGF-1), testosterone, dehydroepiandrosterone sulphate (DHEAS), and triiodothyronine. Conversely, cortisol and insulin levels and insulin resistance measures tend to rise with age. 1 The extent to which these alterations are caused or contribute to the molecular, metabolic, physical, and cognitive adaptations associated with accelerated ageing and its comorbid conditions remains to be fully understood.]

71. Beyond pounds: What else could be lost?

Idrees T, Umpierrez G.E. Journal of Diabetes and Its Complications, 2023, 37(12), Article 108649.

[Worldwide, obesity has reached pandemic dimensions, affecting 800 million individuals. Obesity is projected to affect 50 % of the US population by 2030 and >1 billion humans globally. 1 Substantial evidence links obesity with medical conditions including cancer, cardiovascular disease, and type 2 diabetes. 2 Thus, the discovery of powerful weight loss agents is welcomed by healthcare providers globally.]

72. Diabetes education self-management intervention in improving self-efficacy for people with type 2 diabetes in the Gulf Cooperation Council countries: A systematic review

Alharbi T.A.F., Alhumaidi B, Alharbi M.N., et al. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2023;17(12): 102906.

[Aims: This research aims to evaluate the effectiveness of diabetes education self-management intervention for improving self-efficacy for people with type 2 diabetes mellitus in the Gulf Cooperation Council countries.]

73. The effects of the ketogenic diet for the management of type 2 diabetes mellitus: A systematic review and meta-analysis of recent studies

Choy K.Y.C., Louie J.C.Y. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* 2023;17(12): 102905.

[**Objective**: To systematically review the effects of the ketogenic diet on glycaemic control, body weight, cardiovascular risk factors, and liver and kidney function in patients with type 2 diabetes.]

Mental health and diabetes

74. Making adjustments: diabetes and developmental disability

Burki T. Lancet Diabetes & Endocrinology, 2023, 11(12), pp.901-902.

[On Sept 15 2023, WHO and UNICEF released a joint report on children with developmental disabilities. It stated that individuals with such disabilities are vulnerable to stigmatisation, prejudice, and social exclusion; they face barriers to accessing care and experience worse health outcomes

and a higher risk of premature mortality than the general population. When admitted to hospital as inpatients, they tend to stay for longer and are more vulnerable to adverse events. The new report described itself as a "call for action." It urged countries to invest in systems of care that are responsive to the needs of people with developmental disabilities.]

75. The prevalence of diabetes distress in Chinese patients with type 2 diabetes: A systematic review and meta-analysis

Tang F.Y., Guo X.T., Zhang L, et al. *Diabetes Research and Clinical Practice* 2023, 206: 110996.

[**Objective**: To systematically evaluate the prevalence of Diabetes Distress (DD) in type 2 diabetes mellitus (T2DM) patients in China.]

76. Recognising the impact of diabetes on mental health

Hussain A. Diabetes Research and Clinical Practice 2023, 206: 111028.

[Managing diabetes and its complications can be a challenging task for the millions of people around the world living with the condition, particularly for those without access to the best available treatment, education, and support. The latest figures from the International Diabetes Federation (IDF) show that 537 million adults now live with diabetes, with close to half not yet diagnosed. The number is predicted to rise to 643 million by 2030.]

Pharmacological management of diabetes

77. Budget Impact Analysis of Intensification with iGlarLixi Compared to Alternative Treatment Strategies Among Patients with Type 2 Diabetes Mellitus.

Ken-Opurum J, Srinivas S.S.S., Jain D, et al. *Diabetes Therapy* 2023, 14(12): 2109-2125.

[Introduction: The clinical benefits of treating patients with type 2 diabetes mellitus (T2DM) with fixed-ratio combination of insulin iGlar (iGlar) plus lixisenatide (iGlarLixi) were demonstrated in clinical trials and real-world evidence studies; however, its cost impact to healthcare payers is unknown.]

78. Challenging Clinical Perspectives in Type 2 Diabetes with Tirzepatide, a First-in-Class Twincretin.

MacIsaac R.J., Deed G, D'Emden M, et al. Diabetes Therapy 2023, 14(12): 1997-2014.

[Tirzepatide is a first-in-class GIP/GLP-1 receptor agonist ('twincretin')-a single molecule that acts as an agonist at both glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) receptors. In the SURPASS clinical trial program in type 2 diabetes mellitus (T2D), tirzepatide was associated with unprecedented reductions in HbA1c, clinically significant weight loss and other metabolic benefits, combined with low rates of hypoglycaemia across a wide range of patient characteristics. The safety and adverse event rate for tirzepatide appears comparable to that of GLP-1 receptor agonists. Although results from dedicated cardiovascular (CV) and kidney trials are currently not available, information to date suggests that tirzepatide may have CV and kidney benefits in people with T2D. Tirzepatide has been approved for the treatment of T2D in the USA, United Arab Emirates, European Union, Japan and Australia. Here, we review how tirzepatide will fit into the T2D treatment continuum. We also consider future directions with tirzepatide in T2D, including its potential for targeting cardio-renal-metabolic disease in T2D, and discuss how tirzepatide-and other co-agonists in development-may challenge current approaches for management of T2D.]

79. Cost per Patient Achieving Treatment Targets and Number Needed to Treat with Tirzepatide Versus Semaglutide 1 mg in Patients with Type 2 Diabetes in the United States.

Mody R.R., Meyer K.L., Ward J.M., et al. *Diabetes Therapy* 2023, 14(12): 2045-2055.

[Introduction: Achieving glycemic control can help reduce complications of type 2 diabetes (T2D). This study compared the pharmacy cost per responder and number needed to treat (NNT) of

tirzepatide 5 mg, 10 mg, and 15 mg versus semaglutide 1 mg to achieve glycemic, weight loss, and composite treatment endpoints in patients with T2D in the United States.]

80. The Effects of Sodium-Glucose Cotransporter 2 Inhibitors on Body Composition in Type 2 Diabetes Mellitus: A Narrative Review.

Jahangiri S, Malek M, Kalra S, et al. Diabetes Therapy 2023, 14(12): 2015-2030.

[Body composition is related to cardiometabolic disorders and is a major driver of the growing incidence of type 2 diabetes mellitus (T2DM). Altered fat distribution and decreased muscle mass are related to dysglycemia and impose adverse health-related outcomes in people with T2DM. Hence, improving body composition and maintaining muscle mass is crucial in T2DM. Sodium-glucose cotransporter 2 (SGLT2) inhibitors are novel glucose-lowering medications gaining popularity because of their cardiorenal-protective effects and weight-lowering characteristics. However, reports on myopathy secondary to SGLT2 inhibitor treatment raised a safety concern. The importance of maintaining muscle mass in people with T2DM necessitates further investigation to explore the impact of novel medications on body composition. In this review, we discussed current evidence on the impact of SGLT2 inhibitors on body composition in people with T2DM.]

81. Empagliflozin in adults hospitalised with COVID-19: a (null) hypothesis for RECOVERY

Garofolo M, Penno G. Lancet Diabetes & Endocrinology, 2023, 11(12), pp.880-881.

[Soon after the onset of the COVID-19 pandemic, it became apparent that diabetes, obesity, hypertension, underlying cardiovascular, and kidney diseases were associated with an increased mortality rate. Since then, there have been consistent efforts to identify treatments that could lend some degree of protection. Among the many options, within the metabolic setting, SGLT2 inhibitors raised much attention given their cardiorenal protective effect demonstrated in people with and without diabetes. 1]

82. Empagliflozin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial

RECOVERY Collaborative Group. Lancet Diabetes & Endocrinology, 2023, 11(12), pp.905-914.

[**Background**: Empagliflozin has been proposed as a treatment for COVID-19 on the basis of its anti-inflammatory, metabolic, and haemodynamic effects. The RECOVERY trial aimed to assess its safety and efficacy in patients admitted to hospital with COVID-19.]

83. Once-weekly semaglutide use in glucagon-like peptide-1 receptor agonist naïve patients with type 2 diabetes in North Macedonia: Real-world data from the MIRAGE study

Milenkovikj T, Mitreva B.C., Mishevska S.J., et al. *Diabetes Research and Clinical Practice* 2023, 206: 111018.

[Aims: The MIRAGE study aimed to evaluate the real-world use of once weekly (OW) subcutaneous semaglutide in glucagon-like peptide-1 receptor agonist naïve type 2 diabetes patients in routine clinical practice in North Macedonia.]

84. Protective Effects of Home T2DM Treatment with Glucagon-Like Peptide-1 Receptor Agonists and Sodium-Glucose Co-transporter-2 Inhibitors Against Intensive Care Unit Admission and Mortality in the Acute Phase of the COVID-19 Pandemic: A Retrospective Observational Study in Italy.

Monda V.M., Voci C, Strollo F, et al. Diabetes Therapy 2023, 14(12): 2127-2142.

[Introduction: Type 2 diabetes mellitus (T2DM) is a relevant risk factor for severe forms of COVID-19 (SARS coronavrus 2 [SARS-CoV-2] disease 2019), and calls for caution because of the high prevalence of T2DM worldwide and the high mortality rates observed in patients with T2DM who are infected with SARS-CoV-2. People with T2DM often take dipeptidyl peptidase-4 inhibitors (DPP-4is), glucagon-like peptide-1 receptor agonists (GLP-1ras), or sodium-glucose co-transporter-2 inhibitors (SGLT-2is), all of which have clear anti-inflammatory effects. The study aimed to compare (i) the severity and duration of hospital stay between patients with T2DM categorized by pre-hospitalization drug class utilization and (ii) the COVID-19-related death rates of those three

85. Treatment Satisfaction and Quality of Life with Tirzepatide Versus Dulaglutide Among Japanese Patients with Type 2 Diabetes: Exploratory Evaluation of the SURPASS J-mono Trial.

Ishii H, Oura T, Takeuchi M. Diabetes Therapy 2023, 14(12): 2173-2183.

[Introduction: Treatment satisfaction in diabetes management is vital to achieving long-term clinical outcomes. This analysis evaluated treatment satisfaction among patients with type 2 diabetes (T2D) after 52 weeks of treatment with once-weekly tirzepatide (5, 10, and 15 mg) compared with dulaglutide 0.75 mg.]

86. Understanding the mechanisms mediating cardio-renal benefit of empagliflozin in type 2 diabetes mellitus

Patoulias D, Eid A.H., Rizzo M. *Journal of Diabetes and Its Complications*, 2023, 37(12), Article 108630.

[In a recently published, post-hoc analysis of the hallmark EMPA-REG OUTCOME trial, Krämer et al. 1 assessed whether changes in cardiac and haemodynamic markers achieved with empagliflozin in subjects with type 2 diabetes mellitus (T2DM) may mediate its significant benefits across a number of surrogate cardiovascular and kidney outcomes. They have demonstrated 1 that empagliflozin treatment resulted in a significant decrease in pulse pressure (PP), mean arterial pressure (MAP) and cardiac workload, compared with placebo; at week 12, placebo-adjusted mean changes from baseline were – 2.5 mmHg for PP, –2.2 mmHg for MAP and – 315 mmHg x beats per minute (bpm) for cardiac workload (p < 0.0001 for all). They have also found that such benefits were present for both empagliflozin groups (10 mg and 25 mg) combined, while treatment differences were maintained throughout to week 164. 1]

Prevention of diabetes (diet, exercise, lifestyle)

87. Diabetes: knowing your risk matters

The Lancet Diabetes & Endocrinology. Lancet Diabetes & Endocrinology, 2023, 11(12), p.879.

[In the third year of the Access to Diabetes Care campaign, World Diabetes Day on Nov 14 highlights the importance of knowing your risk of type 2 diabetes. Under the slogan—Know your risk, Know your response—people are encouraged to use the online type 2 diabetes risk assessment tool developed by the International Diabetes Federation (IDF) to identify and understand their individual risk factors and, where possible, take positive steps to reduce those risks. Not all risk factors for type 2 diabetes are modifiable (age, ethnicity, and family history of diabetes) but many of the key drivers are (such as overweight and obesity, an unhealthy diet, and physical inactivity). By empowering people to adopt and maintain healthy lifestyle habits, type 2 diabetes can, in many cases, be prevented or delayed, or even go into remission, and diabetes-related complications avoided or reduced.]

88. How effective are referrals to the NHS Diabetes Prevention Programme? NIHR Evidence: 2023.

https://evidence.nihr.ac.uk/alert/how-effective-are-referrals-to-the-nhs-diabetes-prevention-programme/

[A referral to the NHS Diabetes Prevention Programme reduces someone's chance of developing type 2 diabetes by 20%, research found. In a related paper, the same team made suggestions to improve the programme. These include better communication between professionals and service users (about the goal of the programme, for instance) and ensuring different providers all deliver consistent digital content. The findings provide reassurance to commissioners, clinicians and patients that referral to the programme can reduce the risk of type 2 diabetes.]

Teenagers with diabetes

89. Glucagon fill rates and cost among children and adolescents with type 1 diabetes in the United States, 2011–2021

Benning T.J., Heien H.C., Herges J.R., et al. *Diabetes Research and Clinical Practice* 2023, 206: 111026.

[**Aims**: To characterize glucagon fill rates and costs among youth with type 1 diabetes mellitus (T1DM).]