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ADS
ABSTRACT BOOK

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Australian Diabetes Society

A Case of Type 1 Diabetes Mellitus with Multiple Acyl-CoA Dehydrogenase Deficiency – A Management Conundrum

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Introduction/Aim: Multiple Acyl-CoA Dehydrogenase Deficiency (MADD) is a rare inherited disorder of fatty acid oxidation with associated hypoketotic hypoglycemia, particularly during periods of metabolic stress (e.g. starvation). Patients with Type 1 Diabetes Mellitus (T1DM), typified by insulin deficiency, rely on fatty acid oxidation for ketogenesis and thus energy production. The coexistence of these disorders is novel and presents a metabolic conundrum.

Method: We present a rare case of a patient with longstanding T1DM who was later diagnosed with MADD.

Results: A 50-year-old woman with known T1DM presented with intermittent confusion, myalgia and fatigue following a self-limiting diarrhoeal illness. Preceding this event, she had been following a low-calorie diet in an attempt to lose weight. On admission, her blood glucose was within normal range and her ketones were not raised. Regular blood investigations, magnetic resonance imaging of her brain and cerebrospinal fluid analysis were all normal.

Her intermittent confusion prevented her from working. Outpatient investigations revealed abnormalities in the acylcarnitine profile with elevated C5DC, C8, C10 and C10:1 level. A diagnosis of MADD was entertained, and she was started on regular riboflavin and carnitine. She experienced significant improvement in her symptoms which enabled her to return to work.

The management of T1DM together with MADD required significant input from a multidisciplinary team including endocrinologist, specialist dietitian and the inborn error of metabolism specialist. Specific concerns relating to high carbohydrate diets recommended for MADD, insulin adherence to avoid excessive lipolysis, and issues with impaired ketogenesis required review.

Conclusion: Management of T1DM requires a cautious balance between insulin administration and carbohydrate intake. With concurrent MADD, regular complex carbohydrate and insulin is also imperative to avoid excessive lipolysis, which may impair ketogenesis. Specialist care, insulin adherence and strict dietary attention are crucial to prevent a metabolic crisis - whilst preventing complications from diabetes, including diabetic ketoacidosis

A community-led, trauma-informed, psychosocial intervention for paediatric patients with type 1 Diabetes: towards the development of a protocol for the Wellbeing-T1D study

Lombardi K[1,2,3], Coombs S[1], Paciente R[1], Milroy H[1], Bebbington K[1,5], Roby H[1], Taplin C[1,5,6], Rose S[6], Wickens N[1], Woolard A[1,4]

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Aim: Improvements in medical treatments have led to better physical outcomes for young people with Type 1 Diabetes however, the psychological impact associated with experiencing such a chronic condition have mostly been overlooked. We are using a codesign framework, collaborating with young people living with Type 1 Diabetes (T1D), their families, and clinicians, to develop and pilot an intervention that addresses the trauma experienced in this population, with the aim of improving wellbeing, resilience and coping skills.

Method: This project will offer a new psychosocial intervention for children and young people living with T1D, and their parents which seeks to directly address the psychological outcomes relating to potential traumatic T1D-related events. This intervention will have the capacity to test the effectiveness of the previously developed medical trauma intervention and will help direct future psychological interventions directed specifically to families who have been impacted by a T1D diagnosis. In Phase 1, we will conduct three focus groups with each participant group (with 5 adolescents (13-17 years) and 5 young adults living with T1D (aged 18-30 years), 10 caregivers whose child is living with T1D, and 10 clinicians with experience in helping young people manage their T1D). First, we seek to understand their mental health experiences with T1D through a trauma-sensitive lens from which we will develop a psychosocial intervention. Second, we will present a prototype of an intervention for appropriateness based on needs. Third, we will present the finalised intervention. Phase 2 will pilot and evaluate the intervention.

Conclusion: This project will be the first project to create a community-led, trauma-informed, specific psychosocial intervention to improve mental health for young people living with T1D. The results of this study will lay the foundation for an evidence-based, trauma-informed approach to clinical care for paediatric burn survivors and their families in Western Australia.

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A Hospital-Wide Electronic Glucose Management Worklist to Improve Blood Glucose Management in High-Risk Surgical Patients at Royal North Shore Hospital.

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Background/Aim: Surgical patients remain at high risk of perioperative complications related to blood glucose level (BGL) control. Royal North Shore Hospital utilises the Glucose Control Team (GCT), including endocrinology registrar, diabetes educator, ward junior medical officer, and endocrinology staff specialist, to pro-actively screen inpatients and oversee their glucose management. The NSW eHealth Cerner application, Glucose Management Worklist (GMW), was introduced within RNSH in April 2024 with the aim to improve user efficiency and patient outcomes.

Methods: Previously, the GCT generated a MS Excel spreadsheet of patients to be seen by the GCT, based on criteria that included: surgical ward admission, BGL < 4mmol/L or > 10mmol/L, utilising the electronic medical record (eMR) to determine GCT suitability. Comparatively, the GMW, integrated within the eMR, allows for pre-set filters which automatically generates a list of patients with the desired parameters. The patients are then reviewed by the GCT as necessary.

Results: Using the older method, the GCT list acquisition required an average of 4 work hours per session. Since the introduction of the GMW, work time has reduced to an average of 1 hour per session. As a result of the changed workflow, the GCT new patient review can occur thrice weekly, as compared to twice weekly previously.

Discussion and Conclusion: The GMW has streamlined processes by reducing data handling time and the risk of transcription errors. Its integration into the eMR has allowed patients to be reviewed more seamlessly, whilst reducing potential privacy issues when creating a manual list. Ultimately, patients are reviewed more frequently and earlier**.** Improved glucose control is likely to lead to decreased hospital complications such as infections. With better resource utilisation, there is further potential to identify patients with undiagnosed diabetes and implement strategies such as Patient-General Practitioner-Endocrinologist Case Conferences to ensure seamless care transition on discharge.

A Low Volume Exercise Intervention Alters the Type-2 Diabetic Lipidome, Reducing Circulating Toxic Deoxyceramides

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Aim: High intensity interval training (HIIT) has recently gained interest as a potential intervention for improving outcomes in people with type-2 diabetes mellitus (T2DM) and prediabetes (PD). Previous studies by our laboratory conducted on the randomised control trial PACE-G have shown that a low-volume combined supervised HIIT and progressive resistance training (exercise) intervention over 12 weeks improved liver fat. This study aims to determine: (1) how the baseline plasma lipidome differs between participants with normal glucose (NG), PD or T2DM, and (2) the effect of exercise intervention on circulating lipids.

Methods: PACE-G study participants (n=160) with a BMI >25 kg/m^2 encompassing newly diagnosed T2DM (n=26), PD (n=60) and NG (n=74) were randomised to either a stretching or exercise protocol. Fasted plasma was collected at baseline and after a 12-week intervention period. Untargeted lipidomics was performed using LC-MS/MS on a Thermo Q-Exactive HF-X and Vanquish HPLC and analysed with LipidSearch software.

Results: At baseline, the groups were matched for age and sex, however the T2DM group displayed higher BMI, liver fat and triglycerides. 635 total lipids across 22 functional lipid classes were quantified. At baseline, 96 lipids were significantly altered between the three groups by one-way ANOVA following age, sex, and BMI adjustment, and false discovery rate correction (Benjamini-Hochberg, 5%). T2DM participants displayed significantly lower levels of sphingomyelin (SM) and lysophosphatidylcholine (LPC) species and higher levels of diacylglycerol (DAG) and deoxyceramide (mCer) species relative to NG and PD. PD participants had significantly lower levels of LPC and SM species compared with NG participants. Following 12 weeks of intervention, levels of mCers, a ceramide subclass thought to exert cytotoxic effects, were significantly reduced in T2DM participants randomised to the exercise intervention.

Conclusion: This study specifically identifies elevated circulating toxic mCers in T2DM, with novel reduction in their levels by an exercise intervention.

A Multi-country Study of Trends in the Incidence of End-stage Kidney Disease among people with Diabetes

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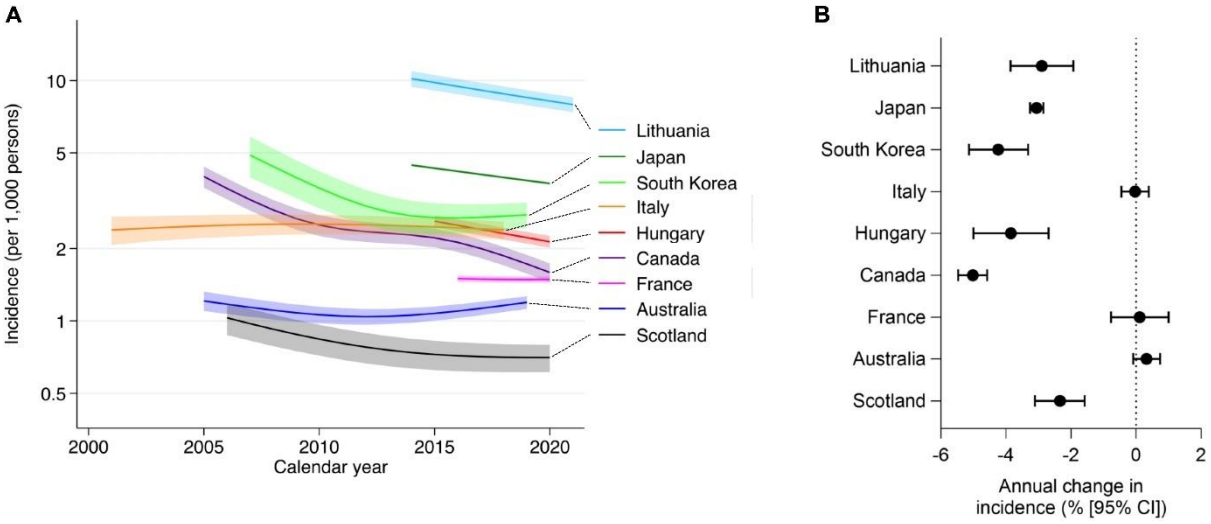
Aim: Escalating worldwide prevalence of end-stage kidney disease (ESKD) is well-known, but the incidence of ESKD among people with diabetes is a more relevant metric for monitoring diabetes-related ESKD risk. This multi-country study examined trends over time in the incidence of ESKD treatment.

Methods: Nine high-income jurisdictions contributed registry/administrative diabetes population data linked to the outcome of treated ESKD (initiation of kidney replacement therapy [KRT]) for different periods spanning the early 2000s to 2021. Incidence rates were derived from age-period-cohort Poisson models. Average annual percent changes in age-standardised rates were determined overall, and by sex.

Results: Incident cases of KRT totalled 288,668 during ~98 million person-years of follow-up. Age-standardised incidence rates (Figure part A) showed geographic variation throughout the study period, but decreased over time in six of the nine jurisdictions (Figure part B). The exceptions (Australia, France and Italy) were among the jurisdictions with the lowest KRT incidence at their respective study start dates and showed relatively unchanged rates over time. Trends were similar for men and women.

Conclusion: Incidence of KRT among people with diabetes has been declining in most participating jurisdictions. Continued surveillance may be important with the expected emerging impact of newer drugs (e.g. sodium-glucose cotransporter 2 inhibitors) at the population level.



A new subtype of Type 1 Diabetes

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Background: Fluctuating insulin requirements suggestive of ketosis prone type 2 diabetes (T2D) or "Flatbush" diabetes, has been well-described in individuals of African/Asian ancestry. Similar presentations in Caucasian individuals remain difficult to classify with unclear treatment strategies. Current type 1 diabetes (T1D) guidelines recommend monitoring C-peptide 3 years following diagnosis. This results in ineligibility for appropriate therapies, compounded by clinician and patient doubt regarding classification.

Methods: We describe three cases of Caucasian adults who present with weight loss, elevated HbA1c, mild ketosis, negative islet autoantibodies detectable low range C-peptide concentrations who initially required insulin therapy (see table). After several months, they were successfully weaned off insulin and continued to have persistent detectable low range C-peptide.

Conclusion: Whether such cases should be classified as T1D or atypical T2D remains keenly debated. We propose a novel subgroup "autoantibody negative T1D in remission" in this cohort. The threshold for insulin recommencement in such patients should remain low long-term, to avoid ketoacidosis. Accurate classification from diagnosis has important treatment implications as eligibility to PBS-subsidised therapies will be subject to initial diagnosis. Further, early commencement of beta-cell trophic agents should be considered in this group, in an attempt to delay the rate of decline in beta-cell function.

Table:

Case	1	2	3
Age at diagnosis (years)	55	41	27
Ethnicity	Caucasian	Caucasian	Caucasian
BMI (kg/m2)	23.3	30.0	27
HbA1c at diagnosis (%)	10.2	12.4	11.8
Latest HbA1c (%)	5.9	6.4	6.6
Fasting C-peptide (nmol/L)	0.2	0.2	0.3
Stimulated C-peptide (nmol/L)	0.6	0.3	0.5

A Novel Structured Telehealth Education Program improves Knowledge and Confidence in Carbohydrate counting

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Aim: Knowledge and self-perceived confidence in carbohydrate (CHO) counting is fundamental in optimising glycaemia for people with type 1 diabetes (T1D). We implemented a novel, telehealth delivered, structured and concise carbohydrate counting education program. We aimed to evaluate changes in knowledge and patient-reported confidence of carbohydrate counting pre-and-post participation in the program.

Method: Three 30-minute structured education sessions were delivered either individually or in a small group up to four. Participants were invited to complete questionnaires pre-and post-education; evaluating (i) CHO counting competency as determined by ability to recognise CHO containing foods, knowledge of CHO content in common foods and meals and accuracy of label reading and (ii) self-reported confidence in CHO counting for fresh, packaged and restaurant/takeaway foods.

Results: Fifty-six people with T1D received CHO counting education. Twenty-four completed the knowledge assessment pre-and-post participation in the education program. Fourteen were female (58%); median (IQR) age was 32.5 years (24.5, 46), and median years with diabetes was 13 (3.5, 19.5). Nine people received group education and 15 received individual counselling.

Knowledge assessment (n=24)	Pre-education (n,%) correct answer	Post-education (n,%) correct answer
Sausage roll	19 (80%)	24 (100%)
Banana	18 (75%)	24 (100%)
Cheese	19 (80%)	22 (92%)
1 cup low fat milk	17 (71%)	24 (100%)
1 cup pasta	17 (71%)	20 (83%)
1 cup rice	14 (58%)	24 (100%)
Biscuits in 1 serve	22 (92%)	24 (100%)
Grams of CHO per serve	20 (83%)	23 (96%)
Grams of CHO in 10 biscuits	11 (46%)	20 (83%)
Grams of CHO in meal	14 (58%)	16 (67%)

Of these 24 participants, 14 (58%) completed the self-reported confidence questionnaire pre-and-post the education program. The proportion of individuals who reported confidence in CHO counting fresh foods increased from 21% to 71%, packaged foods 54.5% to 89% and restaurant/takeaway foods 17% to 57%.

Conclusion: Following participation in the novel CHO counting education program a greater proportion of patients were able to accurately identify CHO containing foods, determine the CHO content of meals and read food labels. A greater proportion of participants reported being confident in CHO counting fresh foods, packaged foods and restaurant/takeaway foods following the program.

A Qualitative Exploration of Barriers and Solutions to Optimal Diabetes Foot Care in Western Australia: Perspectives of Patients and Healthcare Professionals

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Aim: A multidisciplinary high risk foot clinic in the Perth North Metropolitan Area Health Service (NMAHS) observed patients with diabetic foot disease were frequently more clinically advanced. In partnership with a diabetes community-based organisation, a qualitative investigation commenced to explore issues, barriers, and solutions.

Method: A qualitative thematic analysis was conducted through semi-structured interviews with a credentialled diabetes educator (CDE). Patients with diabetic foot disease and heath care professionals (HCP's) across the NMAHS catchment were invited to share their experience and barriers with diabetes care, particularly relating to feet.

Results: 25 people with diabetes and 52 HCP's consented to interviews. The themes identified by the patients were broken down into categories of personal determinants including attitude towards health, knowledge and health literacy, and behavioural factors including lack of engagement with GP and diabetes self-management behaviours. The themes identified by the health professionals were divided into personal determinants including lack of time, low risk perception, knowledge gaps and clinical fatigue from low patient engagement, and behavioural factors including not completing neurovascular foot assessments, and limited collaboration with other services.
The interviews revealed variance in perceived quality of care provided and sub-optimal support systems in place, such as referral pathways, funding, availability of time, and access to hospital services.

Conclusion: General Practitioners (GP's) play a crucial role to prevent and identify diabetes-related foot diseases, and that providing a supporting network of HCP's around the GP could help overcome the identified barriers. Embedding more CDE's and upskilling Practice Nurses to be better utilised in chronic disease management could increase support for the GP, and potentially lead to prevention or timely treatment for diabetic foot disease.
Referral pathways must be clarified and disseminated among primary care HCPs, including Health Pathways localised referral and information resources outlining local diabetes service providers and high-risk foot services.

A Qualitative Investigation of Young People's Trauma and Trauma-sensitive care for Type 1 Diabetes through the lens of a Paediatric multidisciplinary team.

Paciente R[1], Coombs S[1], Lombardi K[1,2,3], Milroy H[1], Bebbington K[1,5], Roby H[1], Taplin C[1,4,6], Rose S[6], Wickens N[1], Woolard A[1,4]

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Aim*:* The psychological burden of Type 1 Diabetes (T1D) on young people can be immense and may stem from the potentially traumatic nature of T1D diagnosis and ongoing management. The rigidity of T1D management and the nature of clinical practice make clinicians important informants for trauma informed interventions for children and young people. We aim to uncover clinicians' perspectives of the mental health of young people with T1D, engagement with their clinical practice, and trauma-informed approaches that may be beneficial to embed in clinical practice.

Methods: We utilised a qualitative descriptive approach to investigate our aim. We recruited clinicians across the multidisciplinary team from the Perth Children's Hospital Endocrinology department and held focus groups. These focus groups were recorded, transcribed, and analysed using Reflexive Thematic Analysis, through a medical trauma-sensitive lens. The study is currently ongoing.

Results: The preliminary findings of this study pertain to the overarching theme of 'deficits in trauma-informed practice'. Firstly, clinicians acknowledged the mental health impacts and the traumatic nature of T1D. They identified grief and the need for control among young people, and their parents alike, which manifests certain coping mechanisms and behaviours. This includes hypervigilance in management, for younger people avoidance of certain clinical practices, and manifestation of disordered eating. However, clinicians also noted that some of their practices inherently exacerbate trauma responses which is reflected in the invasive nature of the care they need to provide. Clinicians point to the need for patient-centred care to "give power back" to young people, which is consistent with trauma-sensitive care.

Conclusion: The diagnosis and management of T1D can be traumatising for children, young people and their families. Although clinicians are best placed to assist with their management, their practices may exacerbate traumatic responses. Reinforcing trauma-sensitive practice where applicable is paramount to improve engagement and improve psychological safety in clinical care.

A Retrospective Audit of Admissions for Ketosis at Gosford District Hospital

Flannery W[1], Heidegger D[1], Snape L[1], Fenton B[1], Do K[1], Joshi T[1], Layton M[1]
[1]NSW Health

Aims: Audit of the admissions with starvation ketosis and euglycemic ketosis and their associated complications

Methods: A retrospective audit was conducted to assess the admission pathway for patients with starvation ketosis or euglycemic ketosis to assess frequency of missed diagnosis and associated complications.

Results: 152 admissions with ketosis were identified, of which 74% were correctly diagnosed, 13% were incorrectly diagnosed, and 13% were missed. 94% of patients received appropriate initial management in the emergency department (ED), with 8% of patients requiring admission to ICU. Complications included acidosis (20%), decreased level of consciousness (11%), tachycardia or bradycardia (16%), and acute kidney injury (21%). Of the 129 patients with starvation ketosis, 47% had ketones between 1-2.9mmol/L, 11% had ketones 3 – 5mmol/L, and 12% had ketones greater than 5mmol/L, with a period of fasting occurring in 80%. This population had significant comorbidities in 87% of patients, and a macrovascular event was responsible for the presentation to the ED in 17% of patients. 3% of these patients were admitted under the endocrinology team. Euglycemic ketosis was identified in 12 patients, 100% of whom had a prior diagnosis of T2DM and were on empagliflozin or dapagliflozin. Of the patients with euglycemic ketosis, 50% had ketones between 1 - 2.9mmol/L, and 50% had ketones 3 – 5.9mmol/L, with 33% of these patients having a concomitant acidosis. None of these patients were admitted under the endocrinology team, and endocrinology input was sought in 58% of patients.

Conclusion: Ketosis is an important complication of intercurrent illness and may occur secondary to a plethora of illnesses. The diagnosis of euglycemic ketosis and starvation ketosis are often misdiagnosed or missed, and may contribute to acidosis, decreased level of consciousness and haemodynamic instability. Involvement of the inpatient endocrinology team is currently not routine with management often guided by the admitting team.

A Retrospective Audit of the Incidence and Management of SGLT2 Inhibitor Associated Ketosis

Flannery W[1], Mowbray J[1], Randall H[1], Hariharan S[1], Do K[1], Clifford L[1], Layton M[1], Joshi T[1]
[1]NSW Health

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Conclusion: Ketosis is an important complication of intercurrent illness and may occur secondary to a plethora of illnesses. The diagnosis of euglycemic ketosis and starvation ketosis are often misdiagnosed or missed, and may contribute to acidosis, decreased level of consciousness and haemodynamic instability. Involvement of the inpatient endocrinology team is currently not routine with management often guided by the admitting team.

A Retrospective Audit of the management of DKA in the Emergency Department

Clifford L[1,2], Heidegger D[3], Medveczky D[4], Snape L[3], Fenton B[3], Do K[5], Flannery W[4], Joshi T[3,6], Layton M[3]

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Aims: Audit of the diagnosis and management of diabetes ketoacidosis (DKA) in the Emergency Department (ED)

Method: A retrospective audit was conducted over a 5-year period to assess the diagnosis and management of DKA, and assess the adherence to the DKA protocol in the ED.

Results: Of the 143 cases, 84% were correctly diagnosed, with 3% completely missed. 79% received intravenous fluids within 60 minutes of admission, and 79% received fluids at a rate of 1L/hour. Time to subcutaneous insulin was 3.5 ± 5.9 hours from resolution. Only 68% received IV potassium if required. Average time to resolution was 19.1 hours ±13.6, with average length of stay (LOS) 6.9 ± 9.5 days. Most common cause of DKA was missed insulin (24%), followed by infection (22%). Complications included hypokalaemia (24%) and hyperkalaemia (18%). Factors affecting LOS included age ($p<0.001$) and HCO3 level ($p= 0.083$). BGL was the only factor that trended towards significance with respect to time to resolution ($p = 0.053$). An independent t sample test was performed to explore the variables in DKA, and HCO3 was the only one that trended toward significance ($p =0.066$). A Pearson's coefficient test demonstrated that pH was significantly associated with age, as well as HCO3, potassium, and the BGL. LOS and time to resolution were not impacted by the degree of acidosis in this study. Time to consult Endocrine was 4.9 ± 8 hours.

Conclusion: DKA remains an important hyperglycaemic emergency. Management involves a combination of fluid resuscitation with potassium replacement, as well as a fixed rate insulin infusion initially. These patients can be very fluid deplete and require large amounts of fluid resuscitation. This audit demonstrates the importance of guideline-based management for DKA in the acute setting, and early Endocrine involvement.

A Retrospective Audit of the Management of HHS in the Emergency Department

Clifford L[1,2], Davies K[3], Kim A[3], Snape L[3], Fenton B[3], Do K[4], Flannery W[5], Joshi T[3,6], Layton M[3]
[1]Bankstown-Lidcombe Hospital, [2]University of New South Wales, [3]Gosford District Hospital, [4]Nepean Hospital, [5]Royal North Shore Hospital, [6]University of Newcastle

Aims: Audit of the diagnosis and management of hyperglycaemic hyperosmolar state (HHS) in the Emergency Department (ED)

Methods: A retrospective audit was conducted over a 5-year period to assess the diagnosis and management of HHS, and to determine an appropriate treatment algorithm for HHS in the ED.

Results: Of the 49 cases, 74% were correctly diagnosed, with 4% completely missed. 4% were mixed DKA/HHS. Only 45% received IV fluids within 60 minutes of admission, and 71% received fluids at a rate of 1L/hour. Average time to resolution was 22 ± 15 hours, with average length of stay (LOS) 9.5 ± 8.2 days. Complications included hypokalaemia (35%), hyperkalaemia (31%), and pulmonary oedema (2%). Of note, whilst 92% met the criteria for an admission to ICU, only 43% were admitted. The most common causes of HHS were unknown (43%) and missed insulin (16%). Average HbA1c was 102 ± 26mmol/mol, 11.6 ± 1.9%. An independent t sample test demonstrated that males were more acidotic ($p = 0.028$) and females had an HbA1c more above target ($p = 0.019$). Factors influencing time to resolution were not significant. A Pearson's coefficient test showed that age was significantly associated with pH, BGL, and LOS. LOS didn't correlate to HbA1c ($p = 0.925$). Time to Endocrine contact was 1.8 ± 54.7 hours.

Conclusion: HHS is an important hyperglycaemic emergency that often doesn't have well-defined treatment protocols. Management involves fluid resuscitation with electrolyte replacement in the first instance, and consideration of insulin if there is acidosis present. These patients are usually comorbid and dehydrated, often requiring complex management. The absence of consistent treatment guidelines in Australia makes management difficult and is a compelling reason to establish a treatment pathway.

A Retrospective Audit of the Management of Steroid-induced Hyperglycaemia

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[1]Bankstown-Lidcombe Hospital, [2]University of New South Wales, [3]University of Western Sydney

Background: Steroid-induced hyperglycaemia is an important complication of steroid therapy. There is a standardised protocol for monitoring BGLs in patients with diabetes and/or on steroids at our centre.

Aims: Audit of the detection and management of steroid-induced hyperglycaemia.

Method: A retrospective audit was conducted over a 12-month period to assess the management of steroid-induced hyperglycaemia and assess monitoring. Inpatients included were those admitted for management of an inflammatory requiring steroids. Patients with adrenal insufficiency or on methylprednisone were excluded.

Results: Of the 104 cases on steroid therapy, 35% developed steroid-induced hyperglycaemia, with 45% males. The most common presenting issue was dyspnoea 46% (48). 49% were on steroids pre-admission, with the most common reasons respiratory disease (46%). Average length of stay (LOS) was 16.6 ± 17.9 days, but for patients with diabetes the mean LOS was 12.7 ± 13.6 days compared to 11.6 ± 13.7 days. The most prescribed steroids were hydrocortisone (53%) and prednisone (42%). Mean steroid dose (as a 24-hour equivalent of prednisone) was 45.2 ± 26mg. Duration of hyperglycaemia was 1.88 ± 5.48 days. 72% of patients with hyperglycaemia received an Endocrine consult, with the mean time to consult was 25.5 ± 28.2 hours. Median total basal insulin was 50 units with bolus at 29 units, and age was found to correlate with both basal ($p<0.01$) and bolus ($p<0.01$) insulin. Hyperglycaemia trended towards a positive association with LOS ($p=0.058$) but didn't correlate with the pre-therapy Hb11c ($p=0.322$). There was also no correlation between the HbA1c and total amount of basal ($p=0.613$) and bolus ($p=0.655$) insulin.

N=104	Number (%)	Mean	Median (IQR)
Gender			
Male	47 (45)		
Female	57 (55)		
Age (years)		68.9 ± 20	76 (59 – 84)
Length of stay (days)		11.8 ± 13.8	7 (4 – 12)
BMI		30 ± 11.2	27 (23 – 34)
HbA1c			
%		9 ± 14.7	6.4 (5.7 – 7.0)
mmol/mol		41 ± 15.6	46 (34 – 99)
Mortality	10 (9.6%)		
Co-morbidities	99 (95)		
Admission			
Lung disease	48 (46)		
GI	15 (14)		
Arthropathy	5 (5)		
Other	36 (35)		
Steroids			
Lung disease	48 (46)		
Arthropathy	19 (18)		
IBD	14 (13)		
Other	23 (23)		
Pre-admission	51 (49)		
Prednisone dose/day		49 ± 31.2	50 (1 – 100)
Glucose Monitoring			
BGLs/day		1.9 ± 2	1 (<1 – 4)
Hypoglycaemia	8 (8)		
Hyperglycaemia (days)		1.72 ± 5.3	3 (0 – 42)
Total no. of BGLs			
Time to consult (hours)		97 ± 103.7	48 (2 – 240)

Conclusion:
Steroid-induced hyperglycaemia is a common side effect of steroid therapy, however monitoring BGLs in this context is not performed as often as dictated by policy. Subsequently, there is likely a burden of hyperglycaemia that is not being detected.

A Retrospective review of Length of Stay for Patients with Type 1 and Type 2 Diabetic Ketoacidosis.

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Aim: The study aimed to assess changes in the median length of stay (mLOS) over time among admitted inpatients (AIP) diagnosed with Type 1 (T1DM) or Type 2 diabetes (T2DM) with ketoacidosis (DKA) in a socioeconomically deprived and culturally diverse area of Western Sydney.

Methods: Conducting a retrospective descriptive analysis of routine healthcare data from January 2012 to December 2023, patients were identified through hospital discharge codes. In 2020 the medical HDU closed, and all admissions were to ICU or medical ward thereafter.

Results: Among 836 T1DM admissions for DKA between 2012 and 2023, females accounted for 57.8%, with a mean age of 37±17.2 years. AIP had a consistent mLOS of 3 days over the 12-year period, with longer stays for ICU admissions compared to the ward (p=0.0004). Younger age and admission under endocrinology were associated with reduced mLOS (p=<0.0001).

For T2DM, there were 1166 admissions with a male predominance of 58.1% and a mean age of 65±14.6 years. AIP had an mLOS of 9 days, longer for ICU and HDU admissions compared to the ward (p=<0.0001). Similarly, younger age and endocrinology admission were associated with reduced mLOS (p=<0.0001).
Notably, being of Aboriginal or Torres Strait Islander origin or born outside Australia did not affect mLOS in either population.

Type 1 Diabetes												
	2012-2015			2016-2019			2020-2023			2012-2023		
	mLOS (days)	95% CI	n	mLOS (days)	95% CI	n	mLOS (days)	95% CI	n	mLOS (days)	95% CI	n
ICU	7	4-15	29	5	4-8	26	3	3-4	143	4	3-4	198
HDU	3	3-4	128	3	3-3	137	3	2-16	5	3	3-3	270
Ward	2	1-3	148	2	2-3	101	2	2-3	119	2	2-3	368
ALL	3	3-4	305	3	3-3	264	3	2-3	267	3	3-3	836
Type 2 Diabetes												
	2012-2015			2016-2019			2020-2023			2012-2023		
	mLOS (days)	95% CI	n	mLOS (days)	95% CI	n	mLOS (days)	95% CI	n	mLOS (days)	95% CI	n
ICU	16	11-27	59	13	10-18	109	11	10-14	177	12	11-14	345
HDU	10	8-11	124	9	8-12	144	24	2-61	4	10	8-11	272
Ward	6.5	9-13	154	7	6-9	207	7	6-8	181	7	6-8	549
ALL	9	8-10	337	9	8-10	460	9	8-10	369	9	9-10	1166

Conclusion: In conclusion, this study highlights consistent mLOS patterns over time among T1DM and T2DM patients with DKA in Western Sydney, with ICU admissions and older ages correlating with prolonged LOS.

A Systematic review of Metabolic and Glycaemic outcomes in Patients with concurrent Overweight/ Obesity and Type 1 Diabetes following prolonged Glucagon-like Peptide-1 Receptor agonist treatment

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Type 1 diabetes, when complicated by overweight or obesity, significantly challenges effective glycaemic management and elevates insulin resistance highlighting the need for innovative therapeutic approaches. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are favoured for the treatment of inadequately controlled overweight/obesity and type 2 diabetes but are yet to be approved as a treatment for individuals with type 1 diabetes.

Aim: This review aims to assess the efficacy of GLP-1RAs to similarly benefit individuals with type 1 diabetes and overweight/obesity by inducing weight loss and improving glycaemic control (HbA1c).

Methods: A search of electronic databases (Medline, Scopus, Cochrane Central and Embase) was conducted in June 2023 and updated in May 2024. A meta-analysis was conducted using a random effects model to generate standardised mean difference including 12 studies with a total of 3662 participants.

Results: The baseline mean body weight and BMI for all participants was 87kg and 29.1kg/m^2 respectively. GLP-1RA treatment duration ranged from 12 to 52 weeks. GLP-1RA treatment with semaglutide (1mg/week) or liraglutide (0.6, 1.2 or 1.8mg/day) reduced body weight by 0.99kg (95% CI: -1.3456 to -0.6313, $p<0.0001$). Significant improvement was also seen in HbA1c which was reduced by 0.30% (95% CI: -0.3851 to -0.2111, $p<0.0001$).

Conclusions: These findings indicate that intervention with GLP-1RAs results in modest reductions in body weight and HbA1c. This suggests that while current GLP-1RAs can be beneficial, there may be potential for greater efficacy with newer incretin therapies, such as the GLP-1/glucose-dependent insulinotropic polypeptide receptor agonist, tirzepatide. These newer therapies could offer enhanced potency and improved outcomes when used in combination with insulin for treating individuals with type 1 diabetes and overweight/obesity.

Acknowledgments:
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A Tale of Two Funding Models: Australian access to Diabetes Technology

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Aim: Diabetes technology has improved glycaemic outcomes for individuals with type 1 diabetes (T1D), particularly when continuous glucose monitors (CGM) and insulin pumps are used in hybrid closed loop systems (HCL). The funding models for diabetes technologies are major barriers restricting access of their use.
In 2017, the Australian government fully subsidised CGM for T1D youth up to 21 years, extending this to adults in 2022. Insulin pumps, conversely, are not subsidised and in Australia are accessible via private health insurance, self-funding or philanthropy.
This study investigated diabetes technology use across the Australian socioeconomic spectrum.

Method: Data was extracted from the National Diabetes Services Scheme (NDSS), estimated to capture >90% of the Australian T1D population. The Index of Relative Socioeconomic Disadvantage (IRSD) is a census derived measure representing area-based relative disadvantage of Australian postcodes by decile. Accessibility/Remoteness Index of Australia Plus (ARIA+) classifies postcodes by geographic remoteness. Postcodes were classified by IRSD Quintile and ARIA+ (urban or rural/remote).

Results: As of March 2024, 134,940 individuals with T1D were registered with the NDSS. CGM was registered for use in 80.3%, pump in 33.3%.
CGM use was comparable across all deciles except decile 1 (most disadvantaged) with 61.8% registered to use CGM compared to 77.2-84.6% across other deciles (Figure A). Pump use increased with increasing decile and decreasing disadvantage, with 19.1% registered to use pump in decile 1 versus 42.4% in decile 10 (Figure B). CGM and pump use did not significantly differ between urban and rural/remote postcodes.

Conclusion: Australian T1D data demonstrate national funding of CGM has resulted in similar CGM use across the socioeconomic spectrum, aside from in the most disadvantaged group. Comparatively, pump use demonstrated a stepwise increase with decreasing disadvantage. Current funding models in Australia limit access to pumps, in turn limiting access to and benefits of HCL.

Figure A

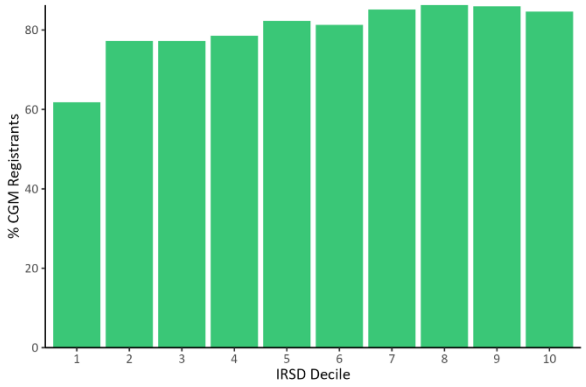
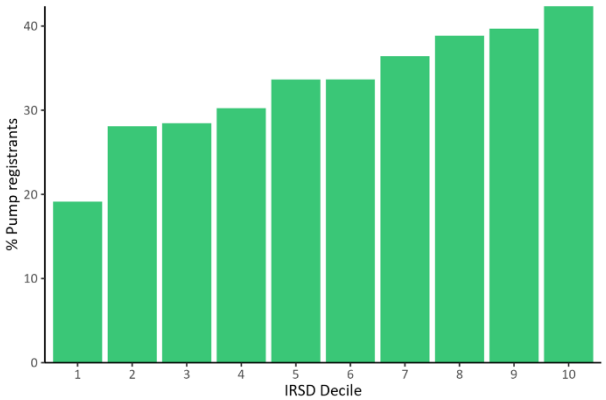


Figure B



A Value-based Care approach to determining Screening and Testing Procedures for Gestational Diabetes Mellitus: A side-by-side BE-OPEN analysis

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Aim: Value-based care (VBC) requires consideration of patient experience and outcomes, improved health of populations, cost effectiveness and health care worker experiences, though many barriers inhibit the uptake of VBC initiatives. The BE-OPEN tool was developed to assist with evaluating the value of care provided. Here we use BE-OPEN to conduct a side-by-side analysis of the current Australian gestational diabetes mellitus (GDM) screening/ diagnostic guidelines against a simplified process, implemented during the COVID-19 pandemic.

Methods: BE-OPEN examines five domains: Based on evidence, Experiences of patients, patient-reported Outcomes, Price, Effect and if No, what are the alternatives. The current GDM screening/diagnostic guideline (universal screening using a 2-hour 75g oral glucose tolerance test [OGTT]) was compared to the simplified method that uses fasting blood glucose (FBG) as a first step for GDM screening, recognises that women with an FBG <4.7 mmol/l appear to have no absolute risk for developing glycemia-related pregnancy complications. Five separate studies by the authors along with other peer-reviewed research was used to complete the analysis.

Results: This BE-OPEN analysis demonstrates that there is sufficient evidence, improved patient experience, similar patient outcomes and reduced cost to consider the simplified process as an alternative for women, particularly those with low GDM risk. Furthermore, the simplified process may remove the need for an OGTT for up to 80% of pregnant women.

Conclusion: There is an urgent need to reduce unnecessary diagnosis and overuse of healthcare services that do not provide value. Continuing to adhere to low value testing procedures can be harmful, divert care from those most likely to benefit, use precious healthcare resources and threaten the sustainability of the health system. Here we have used a systematic approach to determine the value of the current and a modified GDM screening procedure that should be considered and offered to pregnant women.

Accuracy and Feasibility of a Novel Glucose/Lactate Continuous Multi-Analyte Sensing Platform in Humans

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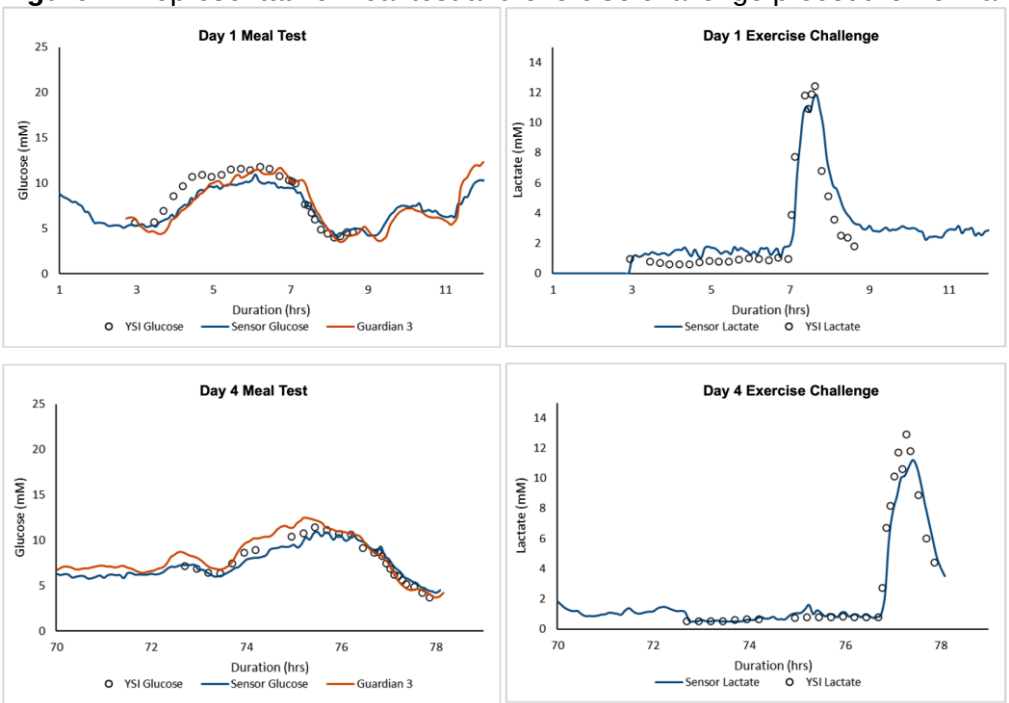
Background and Aim: Continuous glucose monitoring systems (CGM) have been commercially available for several years. However, automated insulin delivery systems may benefit from real-time inputs in addition to glucose. Continuous multi-analyte sensing platforms will meet this area of potential growth without increasing the burden of additional devices. We aimed to generate pilot data regarding safety and function of a first in human, single-probe glucose/lactate multi-analyte continuous sensor.

Methods: The investigational glucose/lactate continuous multi-analyte sensor (PercuSense, Valencia, CA) was inserted to the upper arms of 16 adults with diabetes and data was available for analysis from 11 of these (7 Female; Mean [SD] age 43 years [16]; BMI 27 kg/m^2 [5]). A commercially available Guardian 3 CGM (Medtronic, Northridge, CA) was also inserted to the abdomen for comparison. All participants underwent a meal-test followed by an exercise challenge on day 1 and day 4 of wear. Performance was benchmarked against YSI glucose and lactate values.

Results: The glucose sensor had an overall MARD of 14.5% (median 11.2%) which improved on day 4 compared to day 1 (13.9% vs 15.2%). In comparison, the Guardian 3 CGM (Medtronic, Northridge, CA) had an overall MARD of 13.9% (median 9.4%). The lactate sensor readings within 20/20% and 40/40% of YSI values were 59.7% and 83.1% respectively.

Conclusions: Our results provide initial data supporting safety and functionality of a novel glucose/lactate continuous multi-analyte sensor. Further sensor refinement will improve run-in performance and accuracy.

Figure 1: Representative meal test and exercise challenge procedure from a single participant



Accuracy of Continuous Glucose monitoring measures during Intravenous Insulin infusion in people with Type 1 Diabetes

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Aim: For patients requiring intravenous insulin infusions (IVII), frequent capillary point-of-care (POC) or blood gas (GAS) blood glucose (BG) testing to dose insulin is burdensome. We aimed to determine CGM accuracy during IVII in hospitalised individuals with type 1 diabetes (T1D).

Methods: In this multi-centre retrospective observational study, we compared CGM with POC and GAS BG pairs (time-matched within 7 minutes) during IVII in patients with T1D requiring multi-day admissions from 2020-2023 across three health networks in Melbourne. Patients with FreeStyle Libre 2, Medtronic Guardian 3, and Dexcom G6 CGMs linked to their health service's respective CGM software account were included. For each time-matched glucose pair, absolute difference between CGM and reference BG was divided by reference BG. The mean of these results determined the mean absolute relative difference (MARD)

Results: 825 time-matched glucose pairs during IVII from 45 patients over 51 admissions were analysed. Median age was 39 years (IQR 28–57), 58% were men (26/45), mean HbA1c 9.2% (SD 2.4), median length of stay 2.4 days (IQR 1.8–5.0) and median IVII duration 22.0 hours (IQR 13.7–35.4). Overall MARD was 12.7%. Accuracy metrics were assessed according to glucose strata and BG reference source (Table 1). A high proportion of glucose pairs fell within Zones A/B of the Clarke Error Grid (97.9% of CGM-POC pairs; 96.9% of CGM-GAS pairs), which was just below ISO 15197:2013 standards (≥99%).

Conclusion: In a real-world cohort of inpatients with T1DM receiving IVII, CGM measures related well to BG, however fell just short of ISO 15197:2013 standards. In most instances treatment decisions likely could be based upon CGM measures, however more real-world data is required to validate its accuracy and safety. Use of CGM during IVII would not only improve the in-hospital experience for patients but may also enable greater IVII use.

Table 1: CGM accuracy during intravenous insulin infusion, according to glucose ranges and glucose reference source

	CGM-POC glucose pairs	**CGM-GAS glucose pairs**
MARD % (glucose pairs)		
All wards	12.4% (597)	13.4% (227)
Intensive care	14.0% (106)	13.7% (119)
General ward	12.1% (491)	13.0% (108)
Blood glucose (mmol/L)		
<3.9	36.5% (12)	24.1% (3)
3.9-10.0	13.2% (342)	11.9% (123)
>10.0	10.2% (243)	14.9% (101)
Clarke Error Grid analysis *		
Zone A	80.9% (483)	82.4% (187)
Zone B	17.1% (102)	14.5% (33)
Zone C	0.5% (3)	0.4% (1)
Zone D	1.5% (9)	1.3% (3)
Zone E	0% (0)	1.3% (3)

*Where glucose results within Zone A are considered accurate (deviate from reference by no more than 20% or are <3.9mmol/L when reference is also <3.9mmol/L) and within Zone B are clinically benign (deviate from reference by >20% but would lead to benign/no treatment)

Acute Kidney injury in People Hospitalised with Diabetes-related Foot infections

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Background: High rates (approaching 50%) of acute kidney injury (AKI) have been reported amongst people hospitalised with diabetes-related foot infection (DFI). Supporting data for the Australian context is not available.

Aims: Determine the rates of AKI in people hospitalised with DFI, and differences in 1- and 5-year progression of renal disease, major amputation and mortality in those with AKI.

Methods and Materials: A retrospective study was conducted of AKI prevalence and outcomes in 129 patients admitted to Fiona Stanley Hospital Multidisciplinary Diabetes Foot Unit between 1st Feb 2015 to 31st Jan 2016. 3 patients with baseline chronic kidney disease (CKD) stage 5 were excluded from further analysis. The presence of AKI was defined using the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. CKD progression was defined as progression to CKD stages 3, 4 or 5.

Results: 36 (29%) patients experienced an AKI during hospitalisation for DFI. At 1 year, CKD progression occurred in 5 (14%) patients with AKI and 3 (3%) without AKI (p=0.028). No patients in either group required dialysis, major amputation was performed in 5 (14%) patients with AKI and 11 (12%) patients without AKI, and 5 (14%) patients with AKI and 8 (9%) patients without AKI died (all p>0.05). At 5 years 10 (28%) of AKI patients and 18 (20%) patients without AKI had CKD progression, 5 (14%) AKI patients and 8 (9%) of non-AKI patients progressed to requiring dialysis, 6 (17%) AKI patients and 11 (12%) without AKI underwent major amputation, and 9 (25%) AKI patients and 21 (23%) non-AKI patients died (all p>0.05).

Conclusion: Acute kidney injury was common amongst Australian patients hospitalised with DFI. CKD progression at 12 months was more common amongst patients who experienced AKI, but there were no other differences in 1- and 5-year outcomes.

Adapting a Bespoke Digital Diabetes Self-management Education Programme for people with Early-onset type 2 Diabetes (16-45 years)

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Background: Adults with early-onset type 2 diabetes (EOT2D; 16-45years) have high burden of disease and poorer long-term outcomes. However, evidence reports low engagement with healthcare services, possibly due to services not being tailored towards their specific needs.

Aims: To adapt and tailor an existing digital self-management education programme (myDESMOND) specifically for adults with EOT2D. This formed part of a wider NIHR-funded research programme, “M3” (NIHR201165).
Methods
We performed literature scoping and diverse patient and public involvement activities (PPI) with adults living with EOT2D to understand the landscape of existing support, with further PPI and a qualitative research study to better understand their needs and preferences. PPI group members were invited to take part in developing and reviewing new material for the adapted MyDESMOND digital programme.

Results: A tailored digital self-management programme was adapted, including lived experience media files with adults with EOT2D. These included conversations around important topics raised, such as diabetes-related stigma, men’s and women’s health and information about sleep and type 2 diabetes. A private chat forum was also developed to allow discussion of topics relevant to their lives, meeting a desire to engage and share experiences with other adults with EOT2D.

Next Steps: Our new digital programme has been included within the innovative holistic intervention developed in the M3 programme, which will be tested through a multi-site randomised controlled trial. The usability and accessibility of our digital programme for adults with EOT2D will be evaluated as part of a process evaluation embedded within this trial.

Adapting the Diabetes Education and Self-management for Ongoing and Newly Diagnosed (DESMOND) programme to support people in the D/deaf community.

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Background: People in the D/deaf community can have limited access to health education due to the need for British Sign Language (BSL) interpretation. DESMOND self-management education programme (SMEP) is designed to support people living with type 2 diabetes (T2DM) to become more confident in the management of their condition. The DESMOND team collaborated with Greater Manchester (GM) Integrated Care in the UK to adapt the programme for the D/deaf population.

Aims: To identify what adaptations are needed to deliver the DESMOND programme for the D/deaf community.

Methods: An in-person discussion group with people from the D/deaf community living with T2DM was held with the support of the Manchester Deaf Centre (MDC).

Results: 10 participants, and 2 BSL interpreters all provided feedback.
Key areas of discussion included the need for DESMOND groups to be held in-person within a local Deaf Centre and a toolkit to be created for accredited DESMOND educators, and for the BSL interpreters working in DESMOND groups to include top tips, such as the need to elongate the programme to account for additional interpretation time.
Additionally, BSL interpreters require access to the general content of the sessions before programme delivery including a glossary of terms, to help with the BSL interpretation of some clinical information.

Summary: Following these discussions with key stakeholders, two toolkits have been developed to support future rollout of Desmond groups for the D/deaf community with T2DM across GM and support the 105 other Desmond providers to adapt their delivery. The toolkits are being piloted within the MDC to refine and implement in 2024.

Addressing Inequalities in Foot Screening and Care for Vulnerable Populations with Diabetes

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Introduction: Despite advancements in healthcare, vulnerable people with diabetes face disparities in access to timely foot care.

Aims: To assess alignment of foot screening with best-practice guidelines in vulnerable people with diabetes. To explore barriers to care and successes of a reimagined care model.

Methods: The 'A Step Ahead' initiative was funded by the St Vincent's Health Australia Health Equity Program. Dedicated to people with vulnerability, it delivers person-centred and culturally sensitive foot care. A quality improvement database was maintained for one year commencing September 2022. Baseline individual, service and foot care characteristics are described, and groups with and without diabetes compared using Chi-squared test or odds ratio with significance at $p<0.05$.

Results: Care was delivered to 143 people, mean age 54 (SD 14), 120 (84%) were men, and 48 (34%) had diabetes. Vulnerabilities were homelessness (85%), mental illness (49%), substance misuse (43%), and Aboriginal and/or Torres Strait Islander background (13%). The majority were self-referred (55%) and attended our mobile clinic (52%).
Prior foot screening was more prevalent in those with compared to those without diabetes (48% vs 16%, $p<0.001$). None of those with diabetes reported last screening at the recommended interval (median 24 months, IQR 13-36), despite two-thirds having risk factors for foot ulceration. Diabetes was associated with higher likelihood of active ulceration (29% vs 13%, OR 2.85, 95%CI 1.2-6.8, $p=0.02$). Pre-ulcerative signs were similarly prevalent between groups (23% vs 17%).
In those with diabetes, greatest barriers to foot care were time/prioritisation (66%) and locality/accessibility (47%). Key barriers to wearing well-fitting shoes were comfort (41%) and supply/accessibility (35%). A third were deemed reliant on this initiative for ongoing podiatric care.

Conclusions: Vulnerable people with diabetes receive inadequate foot screening and care, and sustainable innovations in service delivery are required. Barriers to care will be further explored through qualitative research.

Addressing the Complexities of Diabetes Management with Impaired Vision

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Diabetic retinopathy (DR) is a primary cause of vision loss in diabetes, particularly challenging when insulin therapy is needed. Managing diabetes requires regular blood glucose monitoring, dietary adherence, and insulin injections, but these tasks become daunting for visually impaired individuals. Standard devices often lack accessibility features, hindering accurate dosing without visual cues. Many patients and healthcare providers are unaware of available technological innovations that could aid this vulnerable population.

A 54-year-old lady with longstanding history of type 1 diabetes mellitus was reviewed in the outpatient clinic. She had previous enucleation of her left eye and visual impairment in the right eye secondary to diabetic retinopathy requiring multiple laser photocoagulation surgeries. She was using Medtronic 670G insulin pump therapy but faced challenges using Medtronic sensors due to her vision impairment, opting instead to use Freestyle Libre. She also had severe gastroparesis and had frequent episodes of hypoglycaemia necessitating adjustments in the rates of basal insulin.

Several strategies can facilitate diabetes management in visually impaired individuals. Accessibility features of continuous glucose monitors and talking glucose meters provide spoken feedback, enabling individuals to monitor blood glucose levels independently. Accessible insulin delivery devices, such as insulin pens with audible clicks or tactile markers, enhance accuracy and ease of use.

Tight glycaemic control is the cornerstone in preventing the onset and progression of DR as demonstrated in the landmark Diabetes Control and Complications Trial (DCCT) and its long-term follow-up study, the Epidemiology of Diabetes Interventions and Complications (EDIC) trial. However, individualised targets may be required in advanced microvascular complications. Similarly, optimal blood pressure control and lipid lowering therapy play a pivotal role in DR prevention. However, managing diabetes effectively in these individuals necessitates comprehensive support systems, with awareness of technological advancements by healthcare providers, relatives, and community services.

Advancing Diabetes Care Through Improved Disease Surveillance: A Comprehensive Review of Global Diabetes Registries

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Aims: Registries provide a platform to improve quality of care by systematically measuring large amounts of data to identify variations. Previous reviews of diabetes registries have had limited scope. This comprehensive review aims to identify high-quality diabetes registries which can be used as the 'gold standard' template when updating or developing registries.

Methods: All active diabetes registries were identified through searching PubMed, MEDLINE and Google until February 4 2024 using the terms: diabetes AND regist* OR database AND "name of country". Quality of data collection was inferred through each registry's alignment with the 13 variables in the International Consortium on Health Outcome Measurement (ICHOM) standard set.

Results: In total, 47 national diabetes registries were identified: 25.5% collecting adult data, 34.0% collecting paediatric data, 34.0% collecting both and 6.4% unknown. Patient populations were drawn from Europe in 48.9% of registries followed by Asia (27.7%), North America (12.8%) and Australia (10.6%). Most registries captured >6 ICHOM outcomes but the depth of coverage varies significantly. The majority of registries (89.4%) collect laboratory data such as HbA1c, blood pressure or lipid profile. However, only 36.2% incorporate patient-reported outcome measures (PROMs) or wellbeing outcomes and only 38.3% collect financial barriers to accessing care. Most registries (83.0%) publish scientific reports and/or employ quality improvement initiatives. There were 11 registries found to be high-quality (capturing ≥9 ICHOM variables). Commonalities included mandatory participation, high population coverage, continuous data collection from multiple sources and care settings and successful quality improvement strategies.

Conclusions: While a large number of diabetes registries exist globally, many lack comprehensive collection of the ICHOM variables. Although Europe and North America maintain multiple high-quality registries, further work needs to be done to advance registries in Australia and other continents. More widespread reporting of PROMs and psychosocial impacts of diabetes should be a future focus for all registries.

Ageing Well with Insulin Pumps: A single-centre mixed methods study

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Aim. Information about the optimal management of older PwD (people with diabetes) using insulin pumps is limited. HPs (Health Professionals) may express concern about pump use in older PwD, for example in the context of possible cognitive decline. Therefore, the study sought to: 1) Compare PwD and HP preferences regarding topics for prioritisation during clinic discussions and 2) explore PwD perceptions of the advantages and disadvantages of pump use, in older pump users and their HPs.

Method. The study was co-designed with expert patients. PwD eligibility included use of a government funded pump; living in Canterbury, New Zealand; 65+ years. HPs caring for these PwDs were also invited to participate. Using 1000minds decision-analysis software, PwD were asked to prioritise 10 possible points for discussion at their next diabetes clinic visit by pairwise ranking them (i.e. two at a time). PwD lived experience was documented by in-person semi-structured interviews, analysed thematically using the inductive approach.

Results. 26 PwDs and 27 HPs participated. Median age of PwD was 70 (range=65-85) years, 80% (n=21) were female, 57% (n=15) used advanced hybrid closed loop technology, 11% (n=3) had pancreatic diabetes. The 26 PwD had no single preferred topic for prioritisation, from the 10 discussion points. HPs tended to prioritise statements about safety, such as hypoglycaemia minimisation and management (Kendall's W for PwD=0.17; HP=0.36). Thematic analysis of PwD interviews identified three major themes: Improved glycaemic control, quality of life and challenges. PwD commented on the advantages of pumps as self-management memory aids, and for correction of inadvertent self-management errors.

Conclusion. PwD and HPs' prioritisation of in-clinic pump discussion topics was discordant. This should be acknowledged during clinic appointments. The lived experience reported in this study mirrored previous literature findings, however it also highlighted the advantages of pump use, for those living with mild cognitive impairment.

An Audit of ward-based Intravenous Insulin Infusions at the Royal Brisbane and Women's Hospital

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Aim: Patients with diabetes are more likely to experience longer hospitalisations and suffer from complications. Intravenous insulin infusion is one aspect of hospital diabetes management and existing audits into their use are limited. This audit aimed to assess the prescription and administration of intravenous insulin on the ward at the Royal Brisbane and Women's Hospital (RBWH).

Method: The RBWH's electronic database was interrogated for patients treated with intravenous insulin infusion between June 2022 and June 2023. Individual chart review was performed and data extracted. Exemption from full ethical review was approved by the Metro North Human Research Ethics Committee A.

Results: A total of 144 patients were retrieved and the first 40 that met the inclusion criteria were included. Type 2 diabetes was seen in 22 patients (55%), while 16 (40%) had type 1 diabetes. Most patients were admitted for a surgical indication (24, 60%). Indications for insulin infusion included diabetic ketoacidosis (10, 25%), fasting (17, 43%) and ketosis without acidosis (8, 20%). While adherence to key practices was generally well observed, only 55% (608/1103) of blood glucose levels were within target range and hypokalaemia occurred in 13 cases (33%). Duration of insulin infusion was suitable in the majority of cases (36, 90%), however, cessation and transition to subcutaneous insulin was inappropriate in 10 cases (25%).

Conclusion: This audit provides a valuable basis for ongoing efforts to improve the quality of diabetes care in the hospital setting. Although practice was overall reasonably good, improving time in therapeutic range and transition from intravenous to subcutaneous insulin could be improved. Future studies should also investigate the factors contributing to hypokalaemia and suboptimal blood glucose control, and evaluate the effectiveness of interventions aimed at addressing these issues. Implementation science methodologies should be used to investigate clinician attitudes and beliefs and clinical workflows.

An overview of the FLOW trial

Perkovic V

Aim: To assess the effects of subcutaneous semaglutide 1.0 mg once weekly in preventing kidney failure, substantial loss of kidney function, and death from kidney or cardiovascular causes in people with type 2 diabetes (T2D) and chronic kidney disease (CKD).

Methods: In this double-blind, randomised, placebo-controlled, international trial, patients with T2D (glycated haemoglobin ≤10%) and high-risk CKD (estimated glomerular filtration rate [eGFR] of 50–75 ml/min/1.73m^2, and urine albumin-creatinine ratio [UACR] >300–<5,000 mg/g, or eGFR 25–<50 ml/min/1.73m^2 and UACR of >100–<5,000 mg/g) were randomised to subcutaneous semaglutide 1.0 mg weekly or placebo. The primary outcome comprised kidney failure (dialysis, transplantation or eGFR <15 ml/min/1.73m^2), ≥50% eGFR reduction from baseline, or kidney or cardiovascular death. Prespecified confirmatory secondary endpoints (total eGFR slope, major adverse cardiovascular events (MACE) incidence and all-cause death) were tested hierarchically.

Results: Overall, 3,533 randomised participants had median follow-up of 3.4 years, after early study cessation was recommended at a pre-specified interim analysis. The risk of the primary outcome was 24% lower in participants treated with semaglutide vs placebo (331 vs 410 events, hazard ratio [HR] 0.76; 95% confidence interval [CI] 0.66, 0.88, p=0.0003) with consistency across kidney specific (HR 0.79; 95% CI 0.66, 0.94) and cardiovascular death components (HR 0.71; 95% CI 0.56, 0.89). All confirmatory secondary endpoints were improved by semaglutide: annual eGFR slope was 1.16 ml/min/1.73m^2/year slower (p<0.001), the risk of MACE was 18% lower (HR 0.82; 95% CI 0.68, 0.98, p=0.03), and the risk of all-cause death was 20% lower (HR 0.80; 95% CI 0.670 .95, p=0.010). Serious adverse events were reported by fewer participants in the semaglutide group (49.6% vs placebo 53.8%).

Conclusions: Semaglutide reduced the risk of clinically important kidney outcomes and cardiovascular death, MACE, and death from any cause in participants with T2D and CKD.

Trial registration: NCT03819153.

An unusual Presentation of Diabetic Ketoacidosis and Boerhaave Syndrome

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Introduction: Effort rupture of the oesophagus with perforation, Boerhaave syndrome, is a rare but serious complication of diabetic ketoacidosis (DKA) that carries high mortality. We present a case of pneumomediastinum in a patient with T1DM who presented with DKA and severe vomiting.

Case summary: A 56 year old fisherman with long-standing poorly controlled T1DM presented with diabetes ketoacidosis and 4 day history of epigastric pain associated with excessive projectile vomiting. His vitals were significant of tachycardia (heart rate of 130beats/min) and tachypnoea with Kussmaul breathing.

Initial venous blood gas showed pH of 7.05, a bicarbonate of 5mmol/L, glucose of 29.8mmol/L and anion gap of 37mmol/L. Initial ketone level was 7mmol/L. His HbA1c was 11.5%. The patient was started on intravenous insulin infusion and intravenous fluids as per the local hospital protocol and was transferred to intensive care. CT abdomen was done showing inflammatory changes in the duodenum suggestive of duodenitis complicated by gastric outlet obstruction.

Repeat CT chest with oral contrast study were done due to ongoing clinical concern of vomiting, which showed moderate mediastinal air in the subcarinal space suggestive of pneumomediastinum and moderate bilateral pleural effusion with bilateral ground glass opacities. An upper endoscopy demonstrated necrotic appearing distal oesophagus at 30-40cm with no ulcers. The patient was conservatively managed with IV antibiotics and antifungals. His feeding was slowly upgraded with nasojejunal feeding post being kept nil by mouth. He underwent intense diabetes re-education and was discharged with multiple daily injections regimen.

Discussion: Forceful vomiting can lead to increase in intra-luminal oesophageal pressure resulting in transmural oesophageal tear. Spontaneous oesophageal perforation resulting in secondary pneumomediastinum known as Boerhaave's syndrome is a serious complication that is rarely seen as a complication of DKA. This should be considered in those with pneumomediastinum seen on the initial investigations and clinical presentations.

Analysis of Glucose Biomarkers in Phase I and Phase II Studies of Survodutide in People with Type 2 Diabetes or Living With Overweight/Obesity

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Aim: Survodutide, a glucagon receptor/glucagon-like peptide-1 receptor (GCGR/GLP-1R) dual agonist, elicited greater HbA1c reduction up to –1.71% vs semaglutide 1 mg (–1.47%) in a Phase 2 trial in patients with type 2 diabetes. This analysis evaluated changes in insulin sensitivity, pancreatic islet cell function, and glucose biomarkers from three Phase I/II trials of survodutide.

Methods: Descriptive statistics were derived from a Phase 2 trial in patients living with obesity/overweight without diabetes (NCT04667377), a Phase 2 trial in patients with type 2 diabetes (NCT04153929), and a Phase 1 study in patients living with obesity/overweight (NCT03591718).

Results: High survodutide doses improved insulin sensitivity as reflected in a decrease in mean absolute HOMA-IR scores from baseline (BL) to the end of treatment (EOT), in contrast to no change or increase with placebo (PBO): NCT04667377, –1.1 (4.8 mg QW) vs –0.2 at Week 46; NCT04153929, –0.9 (1.8 mg twice weekly [BIW]) vs 0.9 at Week 17; and NCT03591718, –1.0 (2.4 mg BIW following up titration) vs 0.3 at Week 16. Survodutide improved HOMA-β, with mean percentage change from BL to EOT consistently higher vs PBO: NCT04667377, 8.6% vs –1.1%; NCT04153929, 88.0% vs 18.0%. In NCT04667377, change from BL to Week 46 in FPG with survodutide vs PBO was 0.4 vs 0.0 mmol/L. Change from BL in insulin and non-fasting plasma glucose levels with survodutide 4.8 mg vs PBO, was –23.4 vs 0.4 pmol/L and –0.0 vs 0.6 mmol/L, respectively. Additionally, mean change from BL to Week 46 in adiponectin, glucagon, and c-peptide levels with survodutide 4.8 mg vs PBO was 1.9 vs –0.15 mg/L, –15.2 vs –0.8 pmol/L, and –0.1 vs 0.0 nmol/L, respectively.

Conclusion: Survodutide treatment showed improvement in markers of insulin sensitivity, pancreatic islet cell function, and glucose biomarkers, in patients living with obesity/overweight and those with type 2 diabetes.

Application of a Trauma-sensitive Lens to the Mental health experience of young people living with Type 1 Diabetes: a qualitative study.

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Aim: Despite the various traumatic events that a young person living with Type 1 Diabetes (T1D) may experience, little is formally investigated about the burden and manifestation of traumatic stress in this population. Though mental health outcomes have been explored generally, a trauma-sensitive approach to understanding these experiences remain limited. To fill this gap, we seek to discuss with young people living with T1D how T1D has impacted their mental health through a trauma-sensitive lens.

Methods: We utilised a qualitative descriptive approach to investigate our aim. We interviewed young people aged 13-30 living with type 1 diabetes. These interviews were recorded, transcribed, and analysed using Reflexive Thematic Analysis through a medical trauma-sensitive lens. The study is currently ongoing.

Results: Two preliminary themes have been generated: 1) 'The pathway to post-traumatic growth through adolescence: grief, acceptance, and resilience' and 2) 'Waning resilience and the impact of getting older'. The initial diagnosis and early stages of management involved grieving and rejection of the diagnosis and management. However, the conscious processing of these difficult emotions led to acceptance enabling the young people to cope with the demands of management. The second theme pertains to the participants' experiences of their resilience waning once they became cognizant of their self-stigma surrounding T1D and how the added pressures of life contributed to the difficulty in managing diabetes rather than diabetes management being inherently difficult.

Conclusion: Application of the trauma-sensitive lens to these experiences shows that perhaps acute stress in diagnosis and initial rejection of the management are normal responses to T1D. What the young people have provided is a framework surrounding resilience and post-traumatic growth. From here, we can develop a trauma-informed psychosocial intervention to prevent progression into more adverse mental health outcomes based on the needs expressed by the young people.

Application of a Validated Prognostic Protein Biomarker test for Renal Decline in Type 2 diabetes to Type 1 Diabetes: The Fremantle Diabetes Study Phase II

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PromarkerD is a validated biomarker-based blood test developed for predicting renal decline over four years in type 2 diabetes (T2D). This study assessed whether PromarkerD has similar clinical utility as a prognostic test in type 1 diabetes (T1D).

PromarkerD scores were measured at baseline in 137 participants with T1D from the community-based Fremantle Diabetes Study Phase II. Plasma protein concentrations (ApoA4, CD5L, IGFBP3) measured by ELISA were combined with the concomitant age, serum HDL-cholesterol and eGFR to provide PromarkerD scores (0 to 100%). Scores were categorised as low-, moderate- or high-risk as determined by pre-specified cut-offs. Renal decline was defined as incident chronic kidney disease (CKD) (eGFR <60 mL/min/1.73m² in people without CKD at baseline) or an eGFR decline of ≥30% over the next four years. Performance was assessed using the area under the receiver operating characteristic curve (ROC AUC).

At baseline, the 137 participants (mean age 45 years, 53% males, median diabetes duration 20 years) had a mean PromarkerD score of 5.1%, with 83% categorised low-risk, 10% moderate-risk and 7% high-risk for renal function decline. Of these, 92 (67%) had renal function assessed at the four-year review, with 9 (9.8%) developing outcomes. The biomarkers ApoA4 and CD5L were significantly elevated at baseline in the people with prespecified renal outcomes while IGFBP3 showed no significant difference. The PromarkerD test scores were substantially higher in those with incident renal outcomes; the ROC AUC was 0.93 (95% CI 0.87–0.99), with sensitivity 78%, specificity 98%, PPV 50% and NPV 97%.

The present data suggest that PromarkerD has strong clinical utility in identifying people with T1D at risk of adverse renal outcomes. Further validation studies are needed to confirm this promising performance of the PromarkerD test for predicting CKD in T1D, as has previously been shown for T2D.

Are Age and Gender associated with Diabetes and Weight Stigmas among adults with type 2 diabetes? Results from the second Diabetes MILES–Australia (MILES-2) Study

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Structured Abstract:

Aim: Limited research explores age and gender differences in stigma among adults with type 2 diabetes (T2D). We aimed to examine whether age and gender are independently associated with diabetes and weight stigmas among adults with T2D in Australia.

Method: Data were from Diabetes MILES-2, an online, cross-sectional survey of adults with diabetes in Australia. Eligible participants (mainly recruited via NDSS) self-reported T2D. Validated measures assessed experienced and internalised diabetes stigma (DSAS-2 total score and subscales: blame and judgment; treated differently; self-stigma), and internalised weight stigma (WSSQ total score and subscales: fear of enacted stigma; self-devaluation). Across scales, higher scores indicate greater experience. Cross-sectional associations were tested using (un)adjusted linear regression (confounders: BMI, diabetes-related complications, diabetes duration).

Results: Participants (*N*=1,264) were aged 61±9 years (range 22-75), including 43% women and 57% men; with a diabetes duration of 11±7 years, BMI of 31±7kg/m^2; and 57% reporting ≥1 diabetes-related complications. Age and gender together explained between 6-13% of the variance in DSAS-2 and WSSQ total and subscale scores (excluding WSSQ self-devaluation). Across models, age was a stronger predictor than gender (β≤-0.32 vs β≤-0.18). DSAS-2 scores were lower for older participants (total and all subscales) and for men (total and blame and judgment subscale only). WSSQ scores were lower for older participants and men (total and fear of enacted stigma subscale only). Observed independent associations were retained after adjusting for confounders, while BMI became the strongest predictor of WSSQ total and subscale scores.

Conclusion: These results suggest differential experiences of diabetes and weight stigmas by age and gender among adults with T2D. Younger adults and women with T2D may have greater unmet needs relevant to their experiences. In addition to interventions and healthcare supports which address stigma among those most vulnerable, qualitative exploration to better understand their lived experience is warranted.

Are Wound Healing Trajectories obtained from Individual Diabetic Foot Ulcers useful for Real world Point-of-care Decision making?

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Background. Wound healing rates are predictors of complete wound healing. For DFU (diabetic foot ulcers), only three wound surface area data points are needed to support statements such as: “A 50% decrease of wound area at 4 weeks is a strong predictor of healing at 12 weeks”. Current electronic wound imaging technology allows the capture and interpretation of detailed wound healing trajectories in real time. This may then aid point-of-care health professional decision making, aimed at optimising DFU healing management by the health professional team.

Aim. This single centre study determined the percentage of DFU (diabetic foot ulcers) with four or more images captured during routine diabetes podiatry outpatient visits, available for calculation of a complete healing trajectory. A DFU was considered healed if complete wound closure was documented by six months. Images were captured and in-clinic trajectories (serial change in cm^2) calculated using e-wound imaging hardware and software (Silhouette; ARANZ Medical, NZ).

Results. 533 DFU and 9258 associated images, collected over 3.5 years, were reviewed. DFU trajectories from initial presentation to complete wound closure were available on 103 (19%) of wounds. 67/103 trajectories showed non-linear healing. Slowing of healing rate was often associated with a DFU infection. Data needed for populating trajectory calculations was frequently incomplete due to a mix of predominantly modifiable and predominantly non-modifiable factors. Examples include lack of e-data capture capability among all of the health providers caring for the person with diabetes across secondary and community care (modifiable); or the person with diabetes undergoing amputation, or dying (non-modifiable).

Conclusion. Point-of-care review of DFU healing trajectories is a promising clinical decision support tool. Consistent, standardised data capture and better data sharing (network effect) across all the health provider teams caring for the person with a DFU, is however required before this promise can be realised.

Asking The Right Questions: Codesigning a pre-consultation assessment tool to meet the needs of people with diabetes in Western Sydney

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Background: Diabetes remains a leading global health burden. Western Sydney, a diabetes hotspot, has over half of the population with or at risk of having type 2 diabetes. With the growing prevalence, integrated, value-based and patient-centred care is essential for both patients and the healthcare system. While community-facing digital interventions have improved care, few have been co-designed to meet patient specific needs. Western Sydney Diabetes (WSD) developed a pre-consultation assessment tool for specialist team to gather patient information to enhance consultations and diabetes care plans. This study aims to: (1) co-design the tool with patients and health care professionals and (2) evaluate the feasibility and acceptability of the prototype.

Methods: A co-design process was conducted: (1) five focus groups with patients and diabetes health professionals to identify key needs and concerns; and (2) end-user testing interviews to understand and improve the acceptability of the tool. Data were analysed in stages to assess the acceptability and make iterative improvements to better identify needs and priorities.

Results: Focus group data (n=18) suggested improvements for the tool: reordering to prioritise important questions, shortening to reduce completion time, and adopting a non-overwhelming format. Participants valued completing the tool for management of their diabetes, and emphasized including questions on diabetes complications, especially mental health, for holistic care. Co-design process assisted in identifying and balancing the needs of both patients and providers, ensuring the tool is simple for patients and thorough for providers. Offering the tool in multiple ways, online and paper-based, might increase uptake. These findings informed the redevelopment of the tool on an integrated care platform, a patient care portal providing diabetes education content shared between General Practices and specialist teams in Western Sydney.

Conclusion: The Co-design led to more acceptable content that met two different user groups and informed the roll-out of a new digital format. This tool will inform pre-clinic processes and discussions by multi-disciplinary health care teams, facilitating tailored, patient-centred integrated care. Further research is needed to test the refined tool's impact on diabetes management and quality of care.

Assessing Diabetes Distress Levels Among Adults Attending a Multidisciplinary Type 1 Diabetes Tertiary Hospital Clinic

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Background: Living with type 1 diabetes (T1D) can impact psychosocial well-being and may lead to diabetes-related distress. The five-item Problem Areas in Diabetes (PAID) questionnaire, PAID-5, is a validated screening tool for diabetes-related emotional distress. PAID-5 scores range from 0–20; scores ≥8 indicate possible diabetes-related distress warranting further assessment.

Aim: To evaluate diabetes distress among adults attending a dedicated T1D service in a tertiary hospital to facilitate holistic, multidisciplinary care provision.

Methods: From October 2023 to April 2024, all patients attending a multidisciplinary T1D clinic at a single tertiary centre were screened using the PAID-5 during their initial consultation. Data were analysed using generalised linear modelling.

Results: Ninety-eight adults completed the PAID-5 (median age 36 years [IQR 29–51]; T1D duration 17 years [4–24]; HbA1c mean±SD 8.4±2.1%; n=53 [54%] women). Current insulin therapy was via injection for n=77 (79%) and pump for n=20 (20%); one individual was not treated with insulin. PAID-5 median score was 8 [IQR 4–12]**.** Fifty-one individuals (52%) had PAID-5 score ≥8, with two individuals (2%) reporting the maximum score of 20. No single PAID-5 item scored significantly higher than others; PAID-5 scores did not differ by age, sex, T1D duration, HbA1c or insulin modality.

Conclusion: We identified a high burden of possible diabetes-related distress among adults attending this T1D service, across all five PAID-5 items and unrelated to their clinical demographics. Clinicians addressed these results with patients during their review. We propose these high rates may be related to the multifaceted psychosocial aspects of living with T1D, and the self-care burden with current therapies. These findings highlight the importance of psychological assessment and support for people living with T1D, and the need for further advancement of diabetes therapies to reduce the burden of living with T1D.

Assessing the Impact of a New Cardiometabolic multidisciplinary Clinic at a Tertiary hospital

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Background: With a growing population of patients with comorbid cardiovascular and metabolic conditions resulting in adverse health outcomes, a new dual-specialty-led (Cardiology/Endocrinology) multidisciplinary clinic was started in a tertiary hospital in Western Australia to optimise primary and secondary cardiovascular prevention. This study aimed to assess its impact in management of a high cardiovascular risk population, with a particular focus on patients with complex dyslipidaemia.

Methods: A retrospective analysis of clinic patients seen between 18 January 2023 to 30 April 2024 was performed. Data including demographics, laboratory parameters and Dutch Lipid Clinic Network Score (DLCNS) were collected during clinic visits. All attendees were seen by a clinical nurse specialist and cardiologist/endocrinologist/advanced trainee, and pharmacist, dietician or diabetes educator as required. Frequency of genetic tests and pharmacotherapy changes were analysed.

Results: 205 patients were reviewed, with age 51.9±14 years, 50.2% female, body mass index 28.35±4.34kg/m^2, waist circumference 98.3±17.0cm (Male) and 94.4±14.5cm (Female). Blood pressure was 136.4±19.0/85.0±11.1mmHg. Common comorbidities were hypertension (41.0%), ischaemic heart disease (19.3%), obesity (28.3%), diabetes (16.6%), others included hepatic steatosis (7.8%), chronic renal failure (3.4%) and pancreatitis (3.4%).
144 patients (70.2%) had hypercholesterolaemia, 58 mixed dyslipidaemia (including 21 severe hypertriglyceridemia). Total cholesterol was 6.27±2.14mmol/l, low-density lipoprotein cholesterol (LDL-C) 3.97±1.94mmol/l and triglycerides 2.70±2.60mmol/l. 56 (36.4%) had elevated lipoprotein(a), 107 (69.5%) had elevated apolipoprotein B.
Based on DLCNS, 50 patients had probable familial hypercholesterolaemia (FH), 20 had definite FH. 56 genetic tests for FH were conducted, with 15/44 (34.1%) positive. Lipid-lowering therapy was intensified in 78 patients (38.0%) comprising: increased statin dose (n=11), initiation of statin (n=34), ezetimibe (n=16), fibrate (n=3), evolocumab (n=15) and inclisiran (n=5). 79 (38.5%) underwent dietician review.

Conclusion: A multidisciplinary approach facilitated appropriate FH screening and genetic testing, and escalation of pharmacological therapy to improve LDL-C. A tenth of the cohort were initiated on evolocumab or inclisiran.

Assessment of Biomarkers associated with Renal Decline in the Detection of incident Neuropathy in Type 2 Diabetes: The Fremantle Diabetes Study Phase II

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PromarkerD is a validated biomarker-based blood test that predicts the onset of chronic kidney disease (CKD) and rapid decline in renal function in type 2 diabetes (T2D) utilising a panel of plasma proteins and routinely available clinical variables. This study aimed to determine whether PromarkerD and/or the component proteins could be used to predict incident peripheral sensory neuropathy (PSN), another microvascular complication of T2D.

Plasma proteins (ApoA4, CD5L, IGFBP3) were measured by ELISA in baseline fasting plasma from 151 Fremantle Diabetes Study Phase II participants without PSN at baseline, of which, half remained free of PSN, while half developed incident PSN during four-years' follow-up. PSN was defined using the clinical portion of the Michigan Neuropathy Screening Instrument (MNSI), which includes biothesiometry (for vibration sense), presence of ankle reflexes, presence of foot ulceration, and appearance for abnormalities such as callus and Charcot's foot deformity. Incident PSN was defined as MNSI score >2 in either foot in individuals without PSN at baseline. Protein biomarker concentrations were combined with age, serum HDL cholesterol and eGFR to provide PromarkerD scores (0-100%) categorised as low-, moderate- or high-risk of adverse renal outcomes. Logistic regression determined whether individual proteins or PromarkerD score were associated with incident PSN. The performance of PromarkerD for detecting incident PSN was assessed using the area under the receiver operating characteristic curve (ROC AUC).

At baseline, of the 151 participants (mean age 69 years, 56% males, median diabetes duration 10 years) 56% were categorised by PromarkerD as low-risk, 20% moderate-risk and 24% high-risk for renal function decline. PromarkerD score was not significantly associated with incident PSN (ROC AUC 0.52). Similarly, individual biomarkers were not associated with outcome.

PromarkerD and its constituent biomarkers were not significantly associated with incident PSN. Future studies to screen for novel proteomic candidate protein biomarkers is warranted.

Assessment of malnutrition among elderly people with type 2 diabetes.

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Introduction: Malnutrition is a highly prevalent condition in older adults, and poses a substantial burden on health, social, and aged-care systems. Older adults are vulnerable to malnutrition due to age-related physiological decline, reduced access to nutritious food, and comorbidity.

Aim: To see the nutritional status of elderly people with type 2 diabetes and different factors related to malnutrition.

Method: This cross-sectional study was conducted at the National Institute of Diabetes and Endocrinology (NIDE) a tertiary care diabetes center in Karachi Pakistan from November 2021 till December 2023. People with elderly (more than 60 years) type2 diabetes attending the outpatient department of NIDE were included in the study after taking informed consent. A questionnaire was used to know the general characteristics. Nutritional assessment was also done by a validated mini nutritional assessment form. Total score of nutrition screening and assessment were 24-30 for normal nutrition status, 17- 23 .5 for risk of malnutrition, and less than 17 for malnourished.

Results: Three hundred diabetic patients (65.7±5.5 years; 42.3% male; body mass index: 26.2±4.9 kg/m^2) were included in this study. Nutritional assessment of older diabetic patients according to the MNA® revealed that 203 (67.7%) patients were at risk of malnutrition whereas 51 (17%) were malnourished. Patients with lower BMI (22.6±3.6 kg/m2 were malnourished; 26.8±4.8 kg/m2 were at risk and 27.3±4.3 kg/m2 were found normal nutrition status with p-value of <0.001). Consumption of protein was significantly associated with nutritional status (p-value< 0.001) as proportion of being malnourished was high in those patients who consumed ≤ 1 serving of protein daily (n=28, 54.9%) as compared to those who consumed two or more serving of protein every day (n=7, 13.7%).

Conclusion: Majority of elderly people with diabetes are at risk of malnourishment, it is important that reasons should be addressed and proper individualized dietary counseling sessions should be done with caregivers and elderly people to improve their nutrition status.

Association between Different Obesity indices and Carotid Intima-media thickness in Patients with Type 2 Diabetes assessed by a decision Tree model and logistic regression

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Objective: To explore the relationship between different obesity indicators and carotid intima-media thickness (CIMT), so as to provide a scientific basis for the selection of early warning indicators for CIMT thickening.

Methods: The samples were collected from patients with type 2 diabetes (T2DM) who visited the department of endocrinology of two Grade A tertiary hospitals in Jiangsu Province from 2019 to 2022. A decision tree model combined with logistic regression analysis were used to compare the effects of different obesity indicators on CIMT thickening in T2DM. And subgroup analysis was performed by patient age to explore the association between obesity indicators and CIMT in the young, middle-aged, and elderly groups.

Results: A total of 2676 patients with T2DM were enrolled, and 900 cases of CIMT thickening were detected. The CHAID decision tree model screened 7 significant factors influencing CIMT thickening, the most significant one was age. Binary Logistic regression showed that after adjusting for confounding variables, VFA [OR=1.023, 95%CI (1.011,1.036)], NC [OR=1.231, 95%CI (1.074,1.411)] and VAI [OR=2.500, 95%CI (1.392,4.488)] in the young group, High CAVI [OR=1.041, 95%CI (1.024,1.059)] and low SFA [OR=0.994, 95%CI (0.989,0.999)] in the middle-aged group, and high NC [OR=1.041, 95% CI (1.024,1.059)] in the elderly group had a statistically effect on CIMT thickening.

Conclusion: The traditional obesity indicators are not good predictors of CIMT thickening. VFA, NC and VAI in the youth, CAVI and SFA in the middle-aged, and NC in the elderly T2DM patients independently influenced CIMT.

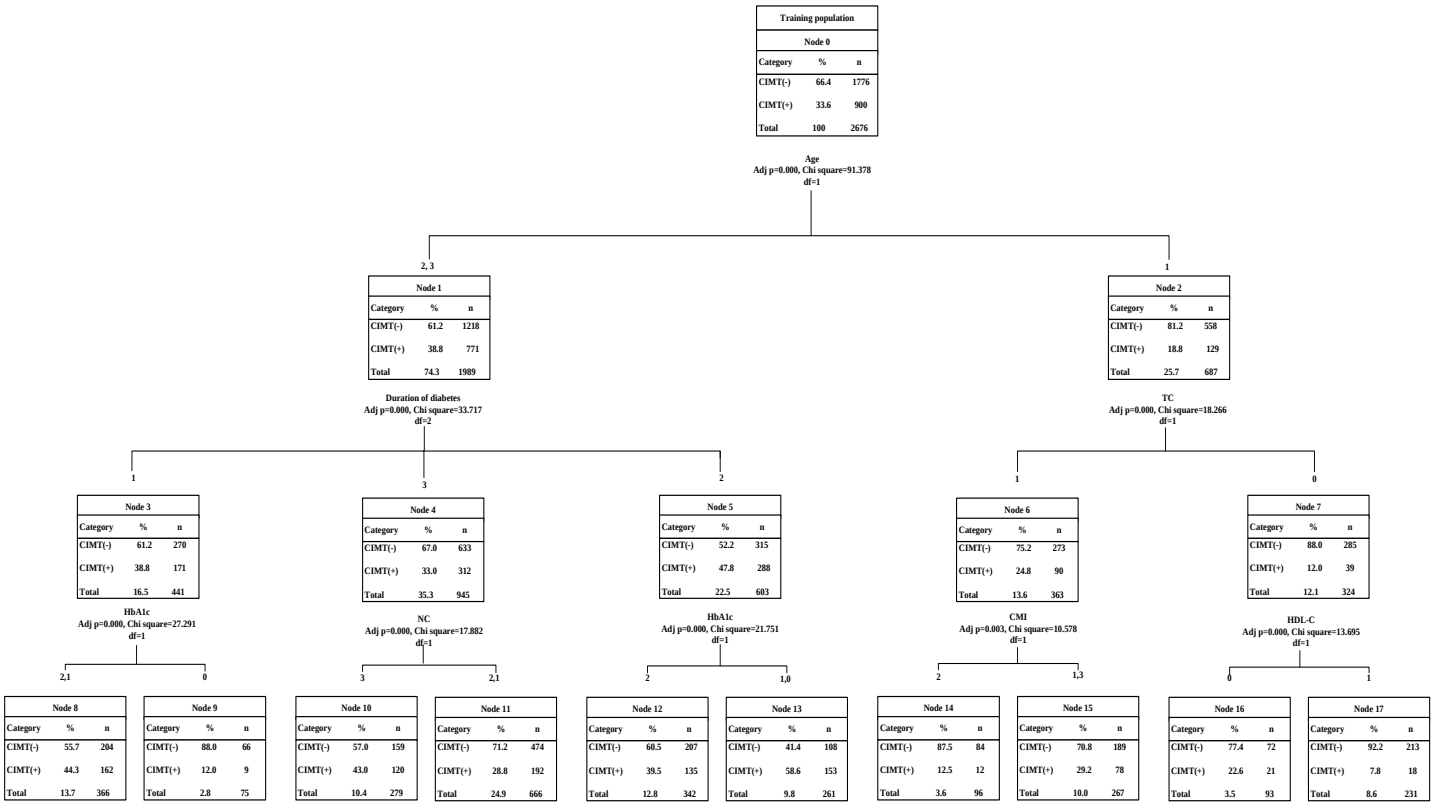

Figure 1 Training dataset of decision tree model

Association between Unstable Housing and Diabetes-related Emergency presentations in a Large Metropolitan Hospital

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Aim: The management of Diabetes Mellitus (DM) requires pro-active case detection, a multidisciplinary and multifaceted approach, strong therapeutic relations and a high degree of self-management. This is complex at the best of times, but exceedingly challenging for people in unstable housing including homelessness. Patients from this population have poorer glycaemic control, a higher complication rate and more frequent hospital presentations. This leads to increased pressure on health care facilities and costs for the health care system. Some of these presentations are potentially avoidable if appropriate and accessible community-based care would be available. To assess the impact of unstable housing on DM-related hospital presentations, and to better understand the medical, social and cultural needs and barriers of care for these patients, an audit will be undertaken of DM-related emergency department (ED) presentations to a major Metropolitan Brisbane hospital.

Method: This audit involves a retrospective review of all DM-related ED presentations to the Princess Alexandra Hospital in Brisbane over a three-month period in 2023. Cases were selected based on available coding data. Relevant demographic data (including housing conditions, cultural background, usual primary care provider) and clinical information (diabetes medications, HbA1c, prior ED presentations, concurrent mental health diagnoses and disposition) were extracted. The health outcomes of people living in unstable housing conditions will be compared against the general population.

Results: This audit is in progress and its outcomes will be presented. It is hypothesised that the results will show people in unstable housing are represented disproportionately in DM-related ED presentations, that they have poorer glycaemic control, higher complication rates and less firmly established community-based care relations

Conclusion: This study will provide insight into the impact of unstable housing on DM-related ED presentations and the medical and social care needs of patients in this population to inform the development of effective community-based care pathways.

Association of a Community Food Hub Model with Food security in individuals with and at high-risk of Type 2 Diabetes

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Aim: Food insecurity is a risk factor for type 2 diabetes (T2D) and the development of complications in those with T2D. Limited evidence exists for accessible, affordable, sustainable, and scalable food systems in Australia. Community food hubs shorten supply chains by sourcing produce locally, reducing transport costs and increasing food security through improved access and affordability of high-quality, fresh, healthy foods. We aimed to explore the association of a community food hub-model on food security levels in people with, or at high-risk of T2D, in NSW and parts of ACT.

Method: The food hub model we assessed offered fruit, vegetables (F&V), dairy, meat, seafood, and pantry items at prices on average less than supermarkets, near user's homes. An online questionnaire invite was emailed to >11,000 registrants of the food hub model. Questions inquired about the participants self-reflected changes in levels of food security (as a scale of 1 (low) to 6 (high)). Changes in food security in participants with prediabetes, T2D, and no diabetes from before joining a hub to the present were explored using ANOVA.

Results: Out of 2789 survey responses, 1972 participants had sufficient data for analyses (n=79, prediabetes; n=57, T2D; and n=1836, no diabetes). There was a significant difference in change in food security scores between the groups ($F=4.139$, $p<0.05$), with food security scores increasing by: 0.94 (SD1.65) in those with prediabetes, increasing from 36.7%-61.1% of participants food secure; 0.89 (SD1.58) in those with T2D, from 28.1%-52.6%; and 0.59 (SD1.24), increasing from 51.3%-73.6% in those without diabetes.

Conclusion: Participants with prediabetes, T2D, and no diabetes all reported reduced food insecurity from using a community-led food hub, with greatest benefit in those with prediabetes, highlighting the potential of these food access models for diabetes prevention.

Association of Fat Mass and other Body Composition indices with Cardiometabolic Characteristics and Cardiovascular Disease risk in Adults with Type 1 diabetes

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Background: Body mass index (BMI) is routinely used. However, BMI does not delineate adiposity, which may have stronger association with cardiometabolic characteristics and cardiovascular disease (CVD) risk in adults with type 1 diabetes (T1D).

Aim: Assess associations between body composition indices and:
1) Cardiometabolic characteristics.
2) Steno T1 Risk Engine (ST1RE) CVD risk.
3) Coronary artery calcium (CAC).

Method: Participants were prospectively recruited from an Australian tertiary hospital T1D clinic. Inclusion criteria were age 20-60 years, statin-naïve, not pregnant and no prior CVD. Dual-energy X-ray absorptiometry was performed for body composition. Non-contrast cardiac computed tomography was performed for CAC and liver density (Hounsfield units). CVD risk was assessed using ST1RE. Non-parametric and parametric ANOVA was used to compare sex-specific tertiles and $p<0.05$ was considered statistically significant.

Results: Overall, 85 patients were enrolled: mean age 35.4±10.3 years, 49 (57.6%) male, HbA1c 8.3±1.5% and diabetes duration T1D 17.0±10.1 years. Table 1 shows variables associated with fat mass index (FMI). BMI tertiles were associated with low-density lipoprotein cholesterol ($p=0.039$) but not total daily dose (TDD) of insulin, high-density lipoprotein cholesterol (HDL-C) or triglycerides. Visceral adipose tissue (VAT) tertiles were associated with age ($p=0.004$) and diabetes diagnosis age ($p=0.007$), but not TDD, nephropathy or hypertension. Upper FMI ($p=0.049$) and VAT ($p=0.002$) tertiles were associated with higher CAC, whilst FMI ($p<0.001$), BMI ($p=0.001$) and VAT ($p=0.019$) tertiles were associated with higher ST1RE risk.

Table 1. Characteristics according to FMI tertile.

Characteristic	Tertile			p-value
	Lower (n=28)	Middle (n=28)	Upper (n=29)	
TDD (unit/kg/day)	0.67±0.26	0.54±0.20	0.70±0.24	0.032
Nephropathy	17.9%	14.3%	41.4%	0.036
Hypertension	25.0%	10.7%	51.7%	0.003
HDL-C (mmol/L)	1.4 (1.3-1.8)	1.6 (1.3-1.9)	1.3 (1.0-1.5)	0.030
Triglycerides (mmol/L)	1.0 (0.7-1.2)	0.9 (0.6-1.5)	1.2 (0.9-2.1)	0.033
Liver density (HU)	66.0±11.3	63.0±9.5	58.0±10.0	0.007

Conclusion: FMI was associated with many cardiometabolic characteristics, ST1RE and CAC in adults with T1D.

Associations between Inflammation, Oxidative stress, Vascular disease related miRs, Glucose variability and Insulin delivery modality in Youth with Type 1 Diabetes.

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Background and Aims
For the same mean HbA1c insulin delivery by pump (CSII) vs. multiple daily injections (MDI) has ≈40% less Type 1 diabetes (T1D) complications, potentially due to lower insulin, glucose variability, inflammation and oxidative stress. In 27 T1D youth with similar glycaemia, C-peptide and complication-associated miRNAs at baseline, we published (Scott E, Sci Rep, 2021) no changes in HbA1c or C-peptide but significant improvements in 1,5-AG and 11 miRNAs with CSII. Aim: In this cohort to determine associations between inflammation, oxidative stress, glucose variability, miRNAs and insulin delivery modality.

Methods
Subjects: T1D, mean(SD) age 14.1(1.3), <3-months T1D on MDI, allocated CSII (n=12) or MDI (n=15), followed (median, LQ-UQ) 535, 519-563 days).
Biochemistry 2-4 time-points. Inflammation: CRP (high sensitivity turbidimetry; Roche); Interleukin-6 (IL6), sVCAM-1, sICAM-1, sE-selectin (ELISA; RnD). Myeloperoxidase (MPO ELISA; Mercodia). Glycaemia: HbA1c, 1,5-anhydoglucitol (1,5-AG; Glycomark). miRNAs, RT-PCR.
Statistics: Variability by SD and CV. Descriptive statistics, Spearman correlation coefficients, two-way RM-ANOVA, significance at $p<0.05$.

Results
CRP mean and variability correlated significantly with HbA1c, sE-selectin and IL6 (r: 0.394-0.627) but not MPO. 6/11 miRNA changes correlated with sVCAM-1 (r:0.41-0.519); 8/11 miRNA changes correlated with IL6 variability (r:0.426-0.715) all $p<0.05$, but were unrelated to MPO or glycaemia.

Conclusions
In T1D youth inflammatory measures and vascular damage miRNAs positively correlate, but are unrelated to oxidative stress. Few metrics relate to insulin delivery modality.
Acknowledgements: Study participants and staff. Drs Anand Hardikar and Mugdha Joglekar for training. Grant: Rio Tinto Children's Diabetes Centre (MH).

Associations of Neuropathic pain, Diabetes distress and Depression in people with Type 2 Diabetes in Bangladesh

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Aims: Neuropathic pain occurs frequently in type 2 diabetes (T2D), can interfere with daily activities, and leads to psycho-social impairment as well as reduced quality of life. Both diabetes distress and depression, are also common in T2D and associated with poor quality of life. There is little information, however, about the relationships between neuropathic pain, diabetes distress, and depressive symptoms, particularly in low-income countries, including those in South Asia. We evaluated these relationships in a community setting in Bangladesh.

Methods: 448 participants (T2D: N = 227, female: 65.2%, mean age: 50.9±0.74 years, BMI: 24.6±0.22 Kg/m^2, duration diabetes: 6.3±0.34 years, random blood glucose: 13.0±0.54 mmol/L and non-diabetic 'controls': N = 221, females: 57.9%, mean age: 42.9±0.92 years, BMI: 23.9±0.23 Kg/m2, random blood glucose: 6.7±0.28 mmol/L) were recruited from community in Bangladesh. Each completed validated questionnaires to evaluate neuropathic pain (DN4), diabetes distress (DDS-17) and depression (PHQ-9), where scores of >4, ≥2 and ≥10 respectively were considered abnormal. Results are shown as mean±SEM with a P value ≤0.05 indicating statistical significance.

Results: The prevalence of neuropathic pain was much higher in people with T2D than controls (42.5.0% vs. 16.3%, P<0.001). The score for neuropathic pain score was higher in those with diabetes distress (4.2±0.15 vs 3.6±0.31, P<0.05) and depression (4.6±0.13 vs 2.6±0.12, P<0.001). Furthermore, in both groups (T2D: 57.3% vs 30.1%, P<0.001 and controls: 27.7% vs 13.2%, P<0.05) the prevalence of significant neuropathic pain was higher in those with depression. The score for neuropathic pain was also related directly to both diabetes distress (R=0.25, P<0.001) and depression (T2D: R=0.39, P<0.001, controls: R=0.52, P<0.001).

Conclusions: Among people with T2D in Bangladesh neuropathic pain occurs frequently and is associated with both diabetes distress and depression. Strategies which reduce neuropathic pain may accordingly have beneficial effects on both distress and depression in this groups.

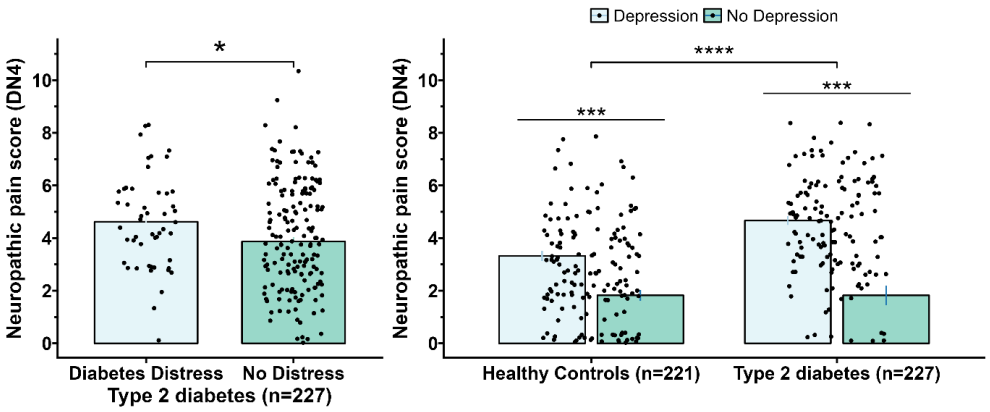

Fig 1: Score for neuropathic pain in type 2 individuals with and without diabetes distress (DDS-17: ≥2) and both type 2 individuals and healthy controls with depression (PHQ-9: ≥10)
[*: P<0.05; **:P<0.01; ***: P<0.001]

Associations of Telomere length and its change over time with Risk factors and Mortality in Type 2 Diabetes: The Fremantle Diabetes Study Phase II

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Aims: Relative telomere length (rTL), a marker of aging, has been implicated in type 2 diabetes (T2D) complications. We aimed to identify (a) associates of rTL and 4-year rTL change (∆rTL), and (b) if they predict mortality in Fremantle Diabetes Study Phase II (FDS2) participants.

Methods: T2D participants (n=819) had baseline and Year-4 blood samples assayed for rTL by qPCR (intra- and inter-assay CVs 0.56% and 2.69%, respectively). ∆rTL was categorised as: Shortening (<–2.69%), Unchanged (–2.69% to +2.69%), and Lengthening (>+2.69%). Multiple logistic regression identified significant baseline determinants of rTL Shortening vs. Not Shortening. rTL and ∆rTL (continuous/categorical variables) were added to the most parsimonious Cox regression model of baseline predictors of cardiovascular disease (CVD) death and all-cause mortality over 11.5±2.1 years of follow-up.

Results: Baseline rTL and age correlated inversely (*b*= –0.016, *P*<0.001). Shortest vs. longest rTL-tertile subjects were older with worse liver function (increased AST/ALT and alpha-2 macroglobulin) and lower CRP. rTL shortened in 25.5% subjects, lengthened in 64.0% and was unchanged in 10.5%. rTL Shortening vs. Not-Shortening differed by baseline factors (**Table**).

Table. Independent baseline associates of telomere Shortening vs. Not Shortening

	Odds ratio (95% CI)	*P*-value
Age (increase of 10 years)	1.35 (1.12, 1.62)	**0.002**
Male	1.72 (1.13, 2.61)	**0.011**
Baseline rTL (increase of 1)	4.23 (3.24, 5.53)	**<0.001**
Ex-smoker	1.54 (1.04, 2.27)	**0.029**
Central obesity (by waist circumference)	1.57 (1.02, 2.43)	**0.042**
On lipid-modifying medication	1.83 (1.19, 2.80)	**0.006**
Ln(Platelets ($x10^9$/L))[a]	2.41 (1.12, 5.20)	**0.025**
Ln(Bilirubin (umol/L))[a]	0.54 (0.33, 0.89)	**0.016**

[a] An increase of 1 in ln(x) equates to a 2.72 increase in x.

Unadjusted Cox regression indicated that a unit increase in baseline and Year-4 rTL was associated with reduced risk of all-cause mortality ((HR (95% CI): 0.87 (0.75, 0.996), *P*=0.043, and 0.914 (0.855, 0.997), *P*=0.008, respectively). Increased Year-4 rTL and ∆rTL were associated with reduced risk of CVD death ((HR: 0.880 (0.807, 0.959), *P*=0.004, and 0.989 (0.979, 0.9996), *P*=0.042, respectively). After age and sex adjustment, only Year-4 rTL remained a significant predictor of CVD death (*P*=0.046). Neither ∆rTL (continuous/categorical variable) nor rTL improved prediction of all-cause mortality (*P*≥0.268).

Conclusion: In T2D adults rTL and ∆rTL were associated with cardiometabolic factors. rTL do not always shorten over time. rTL and ∆rTL were indicators of mortality but did not improve mortality prediction models that included traditional risk factors.

Attainment of Traditional Risk Factor Targets in Adults with Type 1 Diabetes.

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Background and aim: Optimal management of traditional risk factors can ameliorate the micro- and macro-vascular complications of diabetes. We aimed to assess risk factor levels of adults with Type 1 diabetes.

Methods: An ethics committee approved cross-sectional study of adults with T1D attending the Baker Heart and Diabetes Institute Diabetes Clinics in the last 10-years was conducted. Data were analysed in EXCEL and GraphPad Prism 10 using descriptive statistics and non-parametric tests with significance at $p<0.05$. The percent meeting each risk factor and the median number of recommended targets met calculated.

Results: There were 1480 adults with T1D: 56.2% male, median age 50 yrs, 22 years T1D. The percentage meeting risk factor targets were: 29% HbA1c<7% (<53mmol/mol); 46% systolic BP<130mmHg; 52% diastolic BP<80 mmHg; 49% BMI<27.5 kg/m^2; 31% LDL-C<2mmol/l; 23% LDL-C<1.8mmol/l; and for secondary CVD prevention: 6.6% LDL-C<1.4mmol/l; 83% TG<2mmol/l; 85.6% HDL-C>1mmol/l; 83% eGFR>60 ml/min/1.73m^2; 81% urine ACR (<3.5 for women, <2.5 for men); 95% non-smoking.

Of 10 risk factors the median (25-75th percentile) number of targets met was 7 (5-8). Pump-users and CGM-users met more risk factor targets than non-users both 7 vs. 6, p=0.0002 and p<0.0001, respectively. The secondary CVD prevention group attained less risk factor targets than those without CVD, 6 vs. 7 p=0.036.

The table shows median (25-75th percentile) values for all subjects and difference significance by age, sex, device use and CVD status. Blank cells: p>0.05

Risk Factor	All	Age <40, 40-60, >60	Sex M, F	Pump MDI	CGM, No CGM	No CVD, +ve CVD
HbA1c (%)	7.6 (6.9-8.5)		p=0.013 7.5 (6.9-8.4) 7.7 (7-8.6)	p<0.0001 7.4 (6.8-8.1) 7.7 (7-8.7)	p<0.0001 7.5 (6.9-8.3) 7.9 (7.1-14.8)	p=0.0029 7.5 (6.9-8.5) 7.8 (7.2-8.8)
SBP (mmHg)	129 (118-140)	p<0.0001 120 (111-130) 129 (119-139) 129 (118-140)	p<0.0001 131 (121-141) 124 (113-136)	p<0.0001 125 (115-138) 130 (120-140)		p=0.0037 128 (118-140) 132 (120-143)
DBP (mmHg)	77 (70-84)	p<0.0001 78 (71-85) 79 (72-85) 72 (65-80)				p<0.0001 77 (70-84) 73 (63-81)
BMI (kg/m2)	26.6 (23.8-29.9)	p=0.0003 25.8 (23.2-29.4), 27.1 (24.4-30.4), 27.0 (23.9-29.5)				
Urine ACR (mg/mmol)	1 (0.5-2.2)	p<0.0001 0.8 (0.4-1.6) 1.0 (0.5-2) 1.3 (0.7-3.5)	p=0.0483 1 (0.5-2), 1 (0.6-2.3)		p=0.03 1 (0.6-2.2) 1 (0.4-2.1)	p<0.0001 0.9 (0.5-1.9) 1.9 (1-7.5)
eGFR (ml/min/1.73m^2)	90 (78-90)	p<0.0001 90 (90-90) 90 (82-90) 75 (58-87)		p=0.004 90 (82-90) 90 (76-90)		p<0.0001 90 (81-90), 72 (53.5-89)
LDL-C (mmol/L)	2.3 (1.7-2.9)	p<0.0001 2.5 (2-3.1) 2.4 (1.9-3.1) 1.9 (1.4-2.4)				p<0.0001 2.4 (1.8-3), 1.8 (1.4-2.1)
TG (mmol/L)	1.1 (0.8-1.5)		p<0.05 1.1 (0.8, 1.6) 1.0 (0.7, 1.5)	p<0.001 1.0 (0.7, 1.4) 1.1 (0.8, 1.6)		

HDL-C (mmol/L)	1.6 (1.3-2)		p<0.001 1.5 (1.2,1.8) 1.8 (1.5,2.2)	p<0.05 1.7(1.4, 2.1) 1.6(1.3, 2.0)	p<0.01 1.63 (1.3, 2.0) 1.6 (1.2, 1.9)	p<0.0001 1.6(1.4, 2.0) 1.4(1.2,1.7)

Conclusion: Traditional risk factor control was suboptimal in adults with T1D. Improvement is merited.

Audit of Real-World Continuous Glucose Monitoring(CGM) Use in Young Adults(YA) with Type 1 Diabetes Attending a South-Western Sydney Local Heath District Young Adults Clinic(YAC)

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Background: CGM has demonstrated real-world improvements in glycaemic outcomes among individuals with type 1 diabetes (T1D) and is now recommended as best practice. Despite the provision of fully subsidised CGM technology to YA with T1D, uptake remains low.
Aim: An audit of current CGM use in the YAC as well as evaluating patients' experiences and glycaemic metrics.

Methods: Yas aged 18-34 using CGM devices and sharing data were included in this retrospective audit. Basic demographics were collected at baseline. CGM metrics were collected at baseline, 3 months, and 6 months. Perceptions of CGM user experience were self-reported using a 26-question Likert-style online survey.

Results: Data were available for 29 CGM users between November 2017 and June 2023. 55% were female; median age and diabetes duration was 24 (Interquartile Range(IQR) = 4) and 13 (IQR = 10) years, respectively. Glucose management indicator (GMI) was [mean ± SD] 7.7% ± 0.9% at baseline with no significant change (7.8%) at both follow up time points. The majority of CGM users failed to meet international consensus recommendations for metrics of time in range and time above range throughout the study period, with no statistically significant differences overall between baseline and follow-up. 18 respondents completed the survey from March to June 2023. Most users (72%; n = 13) perceived that use of CGM had a positive impact on their lifestyle, with cost identified as the only barrier to continued CGM use. Skin site reactions(n=2) and loss of signal (n=5) were other reported barriers.

Conclusions: The majority of CGM users failed to meet recommended clinical targets despite engagement with technology, however displayed comparatively favourable GMI metrics at baseline. This highlights that service engagement may be key in the ongoing challenge of improving real-world outcomes in YAs with T1D.

Table 3. Continuous Glucose Monitoring Metrics in an Audit of Continuous Glucose Monitoring (CGM) Use in Young Adults (YAs) with Type 1 Diabetes (T1D) attending a South-Western Sydney Local Health District (SWSLHD) Young Adults Clinic (YAC)

	Baseline	3 months after	P-value	6 months after	P-value
GMI, mean (SD), %	7.7 (0.9)	7.8 (0.9)	0.27	7.8 (0.7)	0.26
Active time, mean (SD), %	90.5 (14.2)	93.4 (16.0)	0.26	94.5 (12.7)	0.20
Time In Range, (3.9 – 10.0mmol/L), mean (SD), %	51.9 (20.4)	50.9 (20.7)	0.33	48.1 (15.8)	0.14
Time Above Range (> 10.0 mmol/L), mean (SD), %	46.5 (21.4)	47.5 (21.2)	0.34	49.3 (19.0)	0.14
- **Time Above Range (10.1 – 13.9 mmol/L l), mean (SD), %**	26.6 (10.9)	25.7 (8.4)		28.0 (0.6)	
- **Time Above Range, (>13.9 mmol/L) mean (SD), %**	19.9 (15.7)	19.7 (17.3)		20.6 (13.6)	
Time Below Range (<3.9 mmol/L), mean (SD), %	1.6 (2.2)	1.5 (1.6)	0.37	1.3 (1.5)	0.30
- **Time Below Range (3.0 – 3.8 mmol/L), mean (SD), %**	1.3 (1.7)	1.4 (1.4)		1.1 (1.1)	
- **Time Below Range (<3.0 mmol/L) mean (SD), %**	0.2 (0.7)	0.1 (0.3)		0.2 (0.6)	
Glucose, mean (SD), mmol/L	10.3 (2.0)	10.4 (2.2)	0.28	10.4 (1.6)	0.06
Coefficient of variation*, mean (SD), %	34.5 (6.8)	35.1 (6.3)	0.35	36.3 (5.5)	0.07

GMI: glucose management indicator; SD: standard deviation
**Target < 36%[15].*

Australian Trial of an Automated Insulin Delivery (AID) System: Results Support Benefit for Many Australian Adults With Type 1 diabetes.

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Background: Less than one in five Australians with type 1 diabetes (T1D) meet recommended HbA1c targets. Automated Insulin Delivery (AID) systems, now recommended by international consensus groups as gold standard T1D care are associated with the best glucose outcomes. Aims: To determine if baseline factors are associated with trial-end glycaemia in a 6-month Australian AID clinical trial.

Methods: A post-hoc analysis of the 55 subjects who completed the 6-month AID (Minimed 670G, Medtronic, Northridge, CA) intervention arm of the adult Australian JDRF Closed Loop trial ((ACTRN12617000520336). As published, relative to those randomised to standard care (MDI or an insulin pump without CGM), 6-months of AID use improved all aspects of glycaemia, including the primary end-point of glucose time-in-range (TIR 3.9-10 mmol/l) >70%, time above and below the recommended targets, HbA1c, and glucose variability, as well as diabetes-related quality of life and well-being. Subject characteristics, glucose metrics and psychological, social, sleep and cognition were assessed at baseline and trial-end.

Results: Achievement of TIR>70% and correlations with trial-end TIR did not differ by age, sex, diabetes duration, body mass index, socioeconomic status, microvascular or macrovascular complication status, C-peptide, total daily insulin dose, diabetic ketoacidosis or severe hypoglycaemia in the past 12-months, hypoglycaemia awareness, pre-trial insulin delivery (MDI or insulin pump without CGM), cognition, sleep quality, and most aspects of psychological well-being. Those with better baseline or randomisation glycaemia tended to also achieve the best trial-end glycaemia. The greatest HbA1c and TIR improvements were achieved by those with the highest HbA1c and lowest TIR at baseline. The only other baseline factor associated with better glycaemia outcomes was greater diabetes-specific positive well-being.

Conclusion: Our trial shows a wide spectrum of Australian adults with T1D can achieve recommended glucose targets and improve well-being. Insulin pumps are not subsidised for T1D adults. We advocate change.

Both Plasma and Monocyte NOX5 expression are excellent Biomarkers of Multimorbidity and Complications in the Cardiovascular Kidney Metabolic (CKM) syndrome.

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Aim: To measure NOX5 levels in plasma and circulating immune cells in relation to the occurrence of cardiometabolic complications in a cross-sectional study of subjects undergoing coronary angiography.

Methods: We invited adults having coronary angiograms to provide a blood sample to measure metabolites as well as peripheral blood mononuclear cells (PBMCs). We quantified NOX5 in plasma by ELISA and by flow cytometry on PMBCs (CD45+) and Monocytes (CD45+/CD14+). Cardiac biomarkers and a complete metabolic profile were determined. To estimate the total burden of atherosclerosis, we calculated the Gensini score as a measure of CAD severity, which reflects the number, location, and degree of coronary lesions.

Results: The study population (n=200) consisted of 79% males, with a median age of 67 years (IQR 58-74). People with diabetes (DM=43%) and BMI>30kg/m^2 (High-BMI=43%) had significantly higher plasma NOX5 levels compared to those without diabetes (*median* 246.5 ug/mL vs 174.8 ug/mL, p=0.0049) or normal weight (*median* 238.3 ug/mL vs. 170.1 ug/mL, p=0.0005).
NOX5+/PBMCs were increased in acute coronary syndromes (ACS=31%) vs. non-acute ACS, (*median* 16.0% vs. 7.58 %, p<0.001). NOX5 in plasma was correlated with the severity of the CAD burden (Gensini score) r=0.24 95%CI (0.09-0.36) p<0.001, and eGFR r=0.57 95%CI (0.46-0.66) p<0.0001. A NOX5 concentration >287.3 ug/mL had an AUC/ROC=0.83, 95%CI (0.71-0.95) p<0.0001, for the identification of Stage 3 (subclinical CVD) and Stage 4 (clinical CVD) of the Cardiovascular Kidney Metabolic (CKM) syndrome. A NOX5+/CD14+ cell-count >15.48%, had an AUC/ROC=0.74 95%CI (0.64-0.84) p<0.001, in distinguishing people requiring CABG vs. Medical-therapy (MT). The same was true for CABG vs. PCI, but not PCI vs. MT.

Conclusion: Plasma and PBMCs NOX5 levels are potential biomarkers for excess CVD risk in diabetes, elevated BMI, CKD and the related CKM syndrome, detecting patients at risk of adverse coronary outcomes, as well as identifying individuals with unstable CAD requiring invasive non-medical approaches.

Can Continuous Glucose Monitoring improve glucose management for Aboriginal and Torres Strait Islander peoples with type 2 diabetes? A protocol for a randomised controlled trial.

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Background: Aboriginal and Torres Strait Islander peoples are disproportionately impacted by type 2 diabetes. Continuous glucose monitoring (CGM) technology (such as Abbott Freestyle Libre 2, previously referred to as Flash Glucose Monitoring) offers real-time glucose monitoring that is convenient and easy to use compared to self-monitoring of blood glucose (SMBG). However, this technology's use is neither widespread nor subsidised for Aboriginal and Torres Strait Islander peoples with type 2 diabetes.

Aims: to assess the effect of CGM compared to SMBG on (i) haemoglobin A1c (HbA1c), (ii) achieving blood glucose targets, (iii) reducing hypoglycaemic episodes; and (iv) cost-effective healthcare in an Aboriginal and Torres Strait Islander health setting.

Methods: This is a non-masked, parallel-group, two-arm, individually randomised, controlled trial (ACTRN12621000753853). Aboriginal and Torres Strait Islander adults with type 2 diabetes on injectable therapy and HbA1c≥7.5% (n=350) will be randomised (1:1) to CGM or SMBG for 6 months. The primary outcome is change in HbA1c level from baseline to 6 months. Secondary outcomes include i) CGM-derived metrics, ii) frequency of hypoglycaemic episodes, iii) health-related quality of life, and iv) incremental cost per quality-adjusted life year gained associated with the CGM compared to SMBG.

Results: The trial is ongoing with +20 clinical trial sites (Aboriginal Community Controlled Organisations, Aboriginal Medical Services, primary care centres, and tertiary hospitals) across urban, rural, regional, and remote Australia. Over 190 participants have been screened, 146 randomised and 105 completers.

Conclusion: The trial will assess the effect of CGM compared to SMBG on HbA1c for Aboriginal and Torres Strait Islander people with type 2 diabetes in Australia. This trial could have long-term benefits in improving diabetes management and providing evidence for funding of CGM in this population.

Keywords
Type 2 diabetes, Aboriginal and Torres Strait Islander peoples, Indigenous Australians, First Nations, continuous glucose monitoring, flash glucose monitoring, HbA1c, randomised controlled trial, Freestyle Libre 2.

Cardiorenal Effectiveness of Empagliflozin vs. GLP-1 Receptor Agonists in Patients with Advanced Chronic Kidney Disease: Results from the EMPRISE study

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Aim: Patients with chronic kidney disease (CKD) are at an increased risk of cardiovascular disease, heart failure, and mortality. We reported the final year results of the EMPRISE study program in patients with type 2 diabetes (T2D) and advanced CKD.

Method: Using Medicare, Optum, and Marketscan data (2014-2019), we identified 10,930 pairs of 1:1 propensity score-matched patients aged >18 years with T2D and CKD stage 3-4, who initiated empagliflozin (EMPA) or a glucagon-like peptide-1 receptor agonist (GLP-1RA). Primary outcomes were hospitalisation for heart failure (HHF), a composite of myocardial infarction (MI) or stroke, and end-stage renal disease (ESRD). Secondary outcomes were MI, stroke, and all-cause mortality. We estimated hazard ratios (HR) and rate differences (RD), adjusting for 143 baseline covariates.

Results: Compared to GLP-1RA, EMPA was associated with a reduced risk of HHF (HR 0.68 [0.55-0.85]; RD -9.44 [-14.78, -4.10]), and ESRD (HR 0.70 [0.56-0.87]; RD -9.01 [-14.30, -3.72]), and a trend towards reduced risk for the composite outcome (HR 0.88 [0.72-1.07]; RD -3.84 [-9.60, 1.93]). Estimates for the secondary outcomes were: MI (HR 0.78 [0.61-1.00]), stroke (HR 1.16 [0.83-1.62]), and all-cause mortality (HR 1.08 [0.86-1.36]).

Conclusion: In patients with T2D and advanced CKD in routine care, we observed risk reductions for cardiorenal outcomes with EMPA vs. GLP-1RA.

Empagliflozin vs. GLP1RA			
	Empagliflozin (N = 10,930)	**GLP1RA (N = 10,930)**	
Patient characteristics[1]	**Mean (SD) or n (%)**	**Mean (SD) or n (%)**	**Stand. Diff.**
Age, mean (SD)	72.15 (7.37)	72.12 (7.39)	-0.0041
Gender male, n (%)	4,823 (44.1%)	4,771 (43.7%)	-0.0081
Cardiovascular disease history, n (%)	6,683 (61.1%)	6,703 (61.3%)	0.0041
Acute myocardial infarction, n (%)	533 (4.9%)	544 (5.0%)	0.0046
Stroke, n (%)	1,616 (14.8%)	1,596 (14.6%)	-0.0056
Heart failure, n (%)	2,743 (25.1%)	2,799 (25.6%)	0.0115
Acute kidney injury, n (%)	1,643 (15.0%)	1,746 (16.0%)	0.0276
Number of diabetes medications at index date, mean (SD)	1.48 (0.96)	1.52 (0.95)	0.0419
Current use of metformin; n (%)	4,992 (45.7%)	5,079 (46.5%)	0.0160
Current use of insulin; n (%)	2,659 (24.3%)	2,753 (25.2%)	0.0209
HbA1c, mean (SD)[2]	8.83 (2.30)	8.80 (2.25)	-0.01319
eGFR, mean (SD)[2]	53.38 (16.00)	49.92 (15.88)	-0.21706

Outcomes	**N events (IR/1000 PY)**	**N events (IR/1000 PY)**	**HR (95% CI)**	**RD (95% CI)**
Myocardial infarction (MI), Ischaemic or Haemorrhagic Stroke[3]	176 (26.9)	208 (30.7)	0.88 (0.72-1.07)	-3.84 (-9.60, 1.93)
MI	107 (16.3)	144 (21.2)	0.78 (0.61-1.00)	-4.93 (-9.56, -0.29)
Ischaemic or haemorrhagic stroke	73 (11.1)	65 (9.5)	1.16 (0.83-1.62)	1.59 (-1.85, 5.02)
All-cause mortality	143 (21.6)	137 (20.0)	1.08 (0.86-1.36)	1.66 (-3.21, 6.53)
HHF[4]	132 (20.1)	200 (29.5)	0.68 (0.55-0.85)	-9.44 (-14.78, -4.10)
ESRD	130 (19.8)	195 (28.8)	0.70 (0.56-0.87)	-9.01 (-14.30, -3.72)

1. Baseline characteristics measured during 12 months before drug initiation (cohort entry)
2. Measured only for a subset of populations in Optum and Marketscan. Not used in PS matching.
3. MI and stroke are measured in the inpatient setting (primary or secondary discharge positions) – an algorithm shown to have high specificity.
4. HF hospitalisation in primary discharge position – algorithm shown to have high specificity.

Cardiovascular risk management in adults with diabetes: Findings from the Australian National Diabetes Audit

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Aim: To assess cardiovascular risk management in terms of glucose, blood pressure and lipid control, as well as lifestyle factors, in Australian adults with diabetes using a contemporary national audit of health services providing diabetes care.

Method: A retrospective analysis of the 2022 Australian National Diabetes Audit (ANDA) data on adults (≥18 years) with type 1 (T1D), type 2 (T2D), other types or unstated/unknown diabetes attending primary, secondary and tertiary diabetes centres across Australia was undertaken. Cardiovascular risk management was assessed by benchmarking cardiovascular risk factors against evidence-based clinical targets. Sub-analyses by diabetes type (T1D vs. T2D) and cardiovascular disease (CVD) status were also performed.

Results: Among 4,641 adults with diabetes, 26.0% met the HbA_{1c} target of ≤7% (or 53 mmol/mol), 45.2% met the low-density lipoprotein cholesterol (LDL-C) target of <2 mmol/L, 43.6% met the systolic blood pressure target of <130 mmHg, 20.5% met the body mass index target of <25 kg/m^2, 30.5% met the physical activity target of ≥150 mins/week of moderate-to-vigorous intensity, and 84.9% were non-smokers. Moreover, only 49.0% of patients met three or more of the six risk factor targets. Patients with T2D were less likely to meet targets compared to patients with T1D. Patients with CVD were less likely to meet targets compared to patients without CVD.

Conclusion: Cardiovascular risk management in adults with diabetes is suboptimal, with less than half of all people with diabetes achieving evidence-based clinical guideline targets for glucose, blood pressure, and lipid control. Improving multi risk factor management is imperative in order to improve health outcomes for people with diabetes, and reduce the overwhelming health and economic burden of disease. Workforce support for diabetes services at all levels is an important initiative in improving cardiovascular risk management.

Case Report Of A Family With GCK-MODY Overlapping With Type 1 and Type 2 Diabetes

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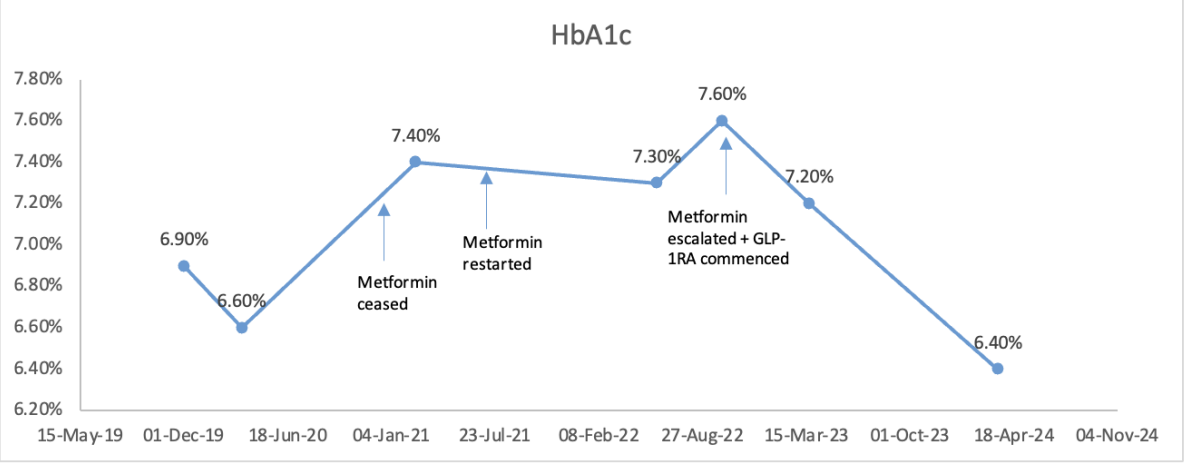
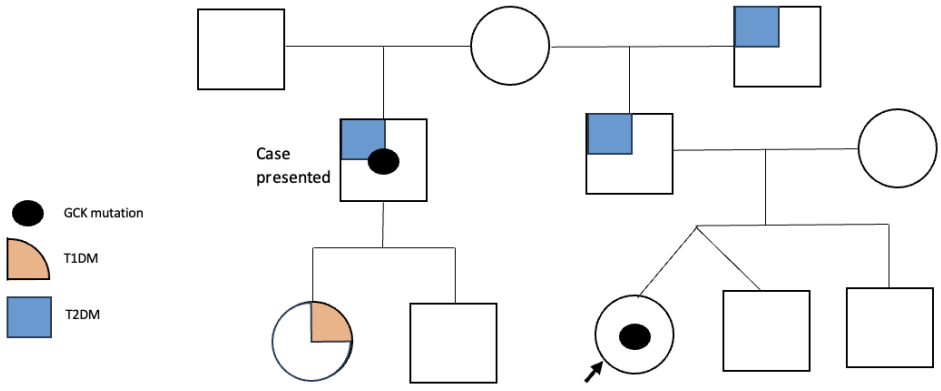
Abstract title (max. 25 words):

Outline of the case: A 54yo male with an underlying diagnosis of T2DM referred to Endocrine clinic after he was found to have a GCK mutation on cascade testing from a distant relative. On initial assessment, he had an associated metabolic syndrome with BMI 40kg/m2, dyslipidaemia and diabetes. HbA1c with the GP was 6.9% and there was a mild response to 6.6% on metformin. Metformin was ceased when the GCK mutation was detected and an OGTT was undertaken. HbA1c rose to 7.4% one-month post cessation of metformin, fasting C-peptide was 3629pmol/L and an OGTT demonstrated a BGL rise to 11.9mmol/L from 7.7mmol/L (>3mmol/L). HbA1c peaked at 7.6%, but with up titration of metformin to 2g daily and initiation/escalation of semaglutide to 1mg weekly, his HbA1c improved to 6.4%, fasting C-peptide reduced to 1448pmol/L and weight dropped from 144kg to 108kg. Overall, this gives a convincing picture of T2DM in addition to his GCK-MODY. He has a daughter who is yet to have genetic testing for a GCK mutation but has confirmed T1DM with significantly elevated anti-GAD antibodies and BGL peaks at 20mmol/L.





Intended discussion points: Can you have GCK-hyperglycaemia in addition to type 1 or type 2 diabetes? Our case highlights the emerging phenomenon of 'double diabetes', which is expected to increase with rising BMI in the general population. A diagnosis of double diabetes carries certain management implications and further research may help to develop evidence-based assessment and treatment algorithms that incorporate patient genotype.

Case Report of early onset diabetes with heterozygous missense mutation in WFS1 with exaggerated response to semaglutide

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Background: Wolfram syndrome is an autosomal recessive condition due to biallelic WFS1 loss of function (LoF) mutation resulting in **d**iabetes **i**nsipidus, early onset **d**iabetes **m**ellitus, **o**ptic **a**trophy and **d**eafness (also known as DIDMOAD syndrome). Recently, a milder, more variable 'non-classical' WFS1 phenotype has been described in association with heterozygous WFS1 variants, whereby individuals only have one or a few of the features of Wolfram syndrome, and to a milder degree (e.g., adult onset rather than childhood onset diabetes). The mechanism of diabetes mellitus in WFS1 heterozygotes appears to be, at least in part, impaired GLP1-induced insulin secretion.

Case: We report the case of a 27-year old man with a heterozygous WFS1 missense variant, who presented with prolonged hypoglycaemia following the addition of semaglutide to his pre-existing regimen of metformin, empagliflozin and insulin for management of his diabetes mellitus. He was admitted to hospital, where he was shown to have a substantial reduction in his insulin requirement (>300 units per day prior to admission). He was subsequently discharged without insulin, although he later required the re-introduction of insulin in the following months.

Conclusion: This and related cases in the literature highlight the variable expressivity of WFS1-related diabetes mellitus and a putative interplay between WFS1 variants and GLP1RA.

Causal associations between Adiposity markers and Nuclear magnetic Resonance Spectroscopy-measured Lipids in Plasma: a Mendelian randomisation study in 110,000 Mexican adults

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Background: The genotyped Mexico City Prospective Study (MCPS) cohort enables causal effects of adiposity on lipids to be explored in an overweight Hispanic population with scarce statin use.

Methods: MCPS participants aged 35-84 years, with nuclear magnetic resonance-measured blood lipids, and not on lipid-lowering therapy were included. Genetic scores for body-mass index (BMI) and waist-hip-ratio (WHR) were derived using SNPs reported by the GIANT consortium (European ancestry). Using the Mendelian randomisation one-sample ratio method, univariable and multivariable models estimated the unadjusted and mutually-adjusted effects of BMI and WHR on six lipids: total cholesterol (TC); low-density lipoprotein cholesterol (LDL-C); high-density lipoprotein cholesterol (HDL-C); triglycerides; apolipoprotein A1 (ApoA1); apolipoprotein B (ApoB). Interactions by age, sex and diabetes were explored.

Results: Among 110,669 participants (mean 52 years), mean(SD) BMI and WHR were 29.0(4.9) kg/m^2 and 0.90(0.07), respectively. Each 5kg/m^2 higher genetically-predicted BMI (772 SNPs, 3.0% variation) was associated with 0.19SD higher triglycerides (95%CI 0.15-0.22), 0.14SD lower HDL-C (0.11-0.18), 0.11SD lower LDL-C (0.07-0.15), 0.06SD lower ApoA1 (0.02-0.09) and 0.03SD lower ApoB (-0.01-0.07). By contrast, each 0.075 unit higher genetically-predicted WHR (398 SNPs, 0.9% variation) was associated with 0.66SD higher triglycerides (0.57-0.74), 0.29SD lower HDL-C (0.21-0.37), 0.13SD lower LDL-C (0.05-0.20), 0.04SD lower ApoA1 (-0.03-0.12) and 0.10SD higher ApoB (0.03-0.18). Higher BMI was associated with 0.09SD lower TC (0.05-0.12) and WHR was associated with 0.04SD lower TC (-0.03-0.12). Adjustment of BMI for WHR (or vice-versa) had little impact on effect estimates. Associations were similar in men and women, and irrespective of diabetes. Associations of BMI and WHR with triglycerides were substantially stronger at younger than at older ages.

Conclusion: In Mexican adults not on lipid-lowering therapy, genetically-predicted general and particularly central adiposity are associated with substantially higher triglycerides but moderately lower cholesterol. Triglycerides may be a more important lipid mediator of adiposity-associated atherosclerosis than cholesterol.

Challenges in Early-onset Diabetes Classification: A case report

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Case: A 28-year-old woman presented with symptomatic hyperglycaemia (glucose 30.3mmol/L) and ketosis (ketones 1.7mmol/L) without acidosis. Given the degree of hyperglycaemia (HbA1c 13%), she was considered to have type 1 diabetes and insulin therapy was continued on discharge. Fasting C-peptide eventually returned normal (0.47nmol/L) and islet auto-antibodies were negative. Her diabetes was re-classified as type 2 diabetes, resulting in commencement of metformin and gliclazide.

Given the atypical course and strong family history of diabetes (affecting mother, siblings, and maternal grandmother), maturity-onset diabetes of the young (MODY) was considered. A 50% risk was identified on the MODY risk calculator. Multigene panel tests for MODY returned negative. Imaging investigations, unexpectedly, demonstrated pancreatic dorsal agenesis and bilateral renal cortical scarring and cysts, typically observed in *HNF1B*-MODY. Recently, a 17q12del mutation (associated with *HNF1B* mutation) was detected in her brother with early-onset diabetes and end-stage renal failure. The woman has been re-referred for chromosomal microarray analysis.

Discussion: This case highlights the challenges in accurate classification of diabetes in young adults. MODY accounts for 0.5-5% of diabetes but the true prevalence is likely underestimated.[1] In addition to diabetes, *HNF1B*-MODY may manifest with pancreatic atrophy, renal abnormalities, and insufficiency.[2] Multigene panel tests is the standard approach to diagnose MODY. More comprehensive tests such as chromosomal microarray should be considered in suspected *HNF1B*-MODY cases.[3]

To date, there is no consensus guidelines on appropriate use of genetic testings in early-onset diabetes. Traditionally, MODY criteria include dominant-inheritance pattern, onset before 25 years of age, lack of insulin dependence and absence of obesity.[4] However a proportion of MODY patients will be missed by these criteria.[1] While commonly used, the MODY probability calculator[5] has its limitations. Given the implications on genetic counselling, targeted treatment, and prognostic prediction, further work to enhance the detection of MODY in the general population is essential.

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Change in Adult Body composition 12-months post Cystic Fibrosis Modulator therapy initiation

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Aims: For many adults living with Cystic fibrosis (CF), management has been revolutionized by CF modulator therapies like Elexacaftor/Tezacaftor/Ivacaftor (ETI). These agents have been shown to significantly improve pulmonary function, however, rapid weight gain within the first year of ETI use has raised concerns regarding overweight and obesity in adults with CF. We aimed to evaluate changes in body composition and their relationship with metabolic parameters in adults with CF.

Methods: We conducted a prospective study to assess pre and up to 12-months post-ETI changes using dual x-ray absorptiometry derived body composition, HbA1c, and blood pressure. Categorical variables were summarised as frequency (percentage). Continuous variables were summarised as mean (SD) if approximately normally distributed otherwise median (IQR). Changes over time were analysed using mixed effects linear regression or paired t-tests, with statistical analysis performed using Stata software.

Results: Data from 12 adults with CF (median age: 29.5 years IQR 23-39) were analysed and the majority were homozygote for the F508del mutation (67%). A third had pre-existing CF-related diabetes. There was a significant increase in mean body weight (baseline: 73.4kg(12.5) to post-ETI: 76.8kg(12.6), Δ3.3kg(4.3), p=0.020) and truncal fat (8987g to 11424g, p=0.014). Mean HbA1c level notably increased post-ETI initiation (baseline: 4.8% to 6 months: 7.0% to 12 months: 7.3%). Systolic blood pressure remained stable, while lung function improved.

Conclusion: We found initiation of ETI in adults with CF was associated with rapid weight gain and significant increase in truncal fat. This was associated with an adverse metabolic profile, specifically hyperglycaemia as evidenced by rising HbA1c. The relationship between worsening glycaemia and increase in truncal fat may point to involvement of mechanisms typically seen in type 2 diabetes. The impact of ETI on increased abdominal adiposity in adults with CF and the associated cardio-metabolic health implications requires more research.

Change in Cardiovascular risk profile in Patients with Type 1 Diabetes Mellitus over 20 years

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Aim: The management of type 1 diabetes mellitus (T1DM) has evolved in recent decades. Despite widespread uptake of continuous glucose monitoring and insulin pumps, cardiovascular risk optimisation remains challenging. This study compares cardiovascular risk factors and microvascular complications in people with T1DM between 2003 and 2023.

Method: We performed a retrospective audit comparing 96 individuals with T1DM managed in a non-specialised clinic in 2003 and 186 individuals attending a specialised multidisciplinary clinic in 2023 at the same tertiary referral teaching hospital.

Results: Mean age (44.1 vs. 44.0 years), sex (47% vs. 58% male) and mean duration of T1DM (22.9 vs. 21.5 years) was similar in 2003 and 2023. HbA1c < 7.0% was more frequently achieved in 2023 (46% in 2023 vs. 13% in 2003; p<0.0001). Antihypertensive medication use was not different between groups (27% in 2023 vs. 35% in 2003; p=0.44). Of patients prescribed antihypertensives, a similar proportion achieved the American Diabetes Association Standards of Diabetes Care (ADA) blood pressure target <= 130/80 mmHg (23% in 2023 vs. 29% in 2003; p=0.99). There was no difference in use of lipid-lowering therapy (29% in both 2023 and 2003; p=0.99); of these patients, a similar proportion achieved the 2003 ADA target LDL level < 2.6 mmol/L (56% in 2023 vs. 60% in 2003; p=0.99). Retinopathy was less common in 2023 (19% in 2023 vs. 52% in 2003; p <0.0001), and prevalence of nephropathy was similar (4% in 2023 vs. 9% in 2003; p=0.28).

Conclusion: A higher proportion of people with T1DM achieved recommended glycaemic targets in 2023 vs. 2003. However, there has been no change in the likelihood of achieving blood pressure and serum lipid targets. Greater focus is required to reduce therapeutic inertia of antihypertensive and lipid-lowering therapies in T1DM in order to reduce cardiovascular risk.

Characterising D6PV, a Novel Peptide that Inhibits and Reverses Type 1 Diabetes.

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Aims: D6PV is an apolipoprotein-mimetic peptide with anti-diabetogenic properties. We have established that D6PV enhances the expression of the β-cell survival gene pancreatic duodenal homeobox 1 (Pdx1) and stimulates insulin production in INS-1E insulinoma cells. This study asks whether D6PV delays diabetes onset and preserves β-cell mass in mice with autoimmune β-cell loss.

Methods: Female 8-week-old NOD/ShiLtJ (NOD) mice (n=10-20/group) were treated twice/week for 16 weeks with D6PV (40 mg/kg i.p) or PBS. Diabetes onset was evaluated by measuring blood glucose levels (two consecutive fed blood glucose readings ≥ 13.5mM). A separate cohort of female NOD mice were treated with D6PV or PBS twice/week for 4 weeks after they developed diabetes. Glycaemic control was evaluated by glucose tolerance test (1 g/kg i.p). Islet insulin content was quantified by immunostaining of paraffin-embedded, formalin-fixed pancreatic tissue. Expansion of CD8+ T-cells was analysed *ex vivo* from OTI-TCR transgenic mouse splenocytes and healthy human donors following stimulation via IL-7/15 and incubation ± D6PV.

Results: D6PV treatment for 16 weeks decreased fed and fasted blood glucose levels ($p < 0.05$ for both) and delayed diabetes onset in NOD mice (80% vs 30%, $p<0.05$). This was accompanied by increased insulin postive islet area in the D6PV treated, but not the PBS treated animals (0.02276±0.0244% vs 0.3367±0.2940%, $p<0.05$). D6PV treatment also reduced lymphocyte infiltration into islets but increased lymphocytic migration to the basement membrane (0.2±0.1% vs 1.8±1.7%, $p<0.05$). When NOD mice with diabetes were treated with D6PV, glucose tolerance improved (AUC 1167±341 vs 543±328, $p<0.01$). Treatment of both mouse and human cytokine-activated isolated CD8+ T-cells with D6PV suppressed T-cell expansion ($p<0.001$).

Conclusions: D6PV treatment delays diabetes onset, improves glycaemic control in mice with established disease, increases pancreatic insulin expression and inhibits T-cell expansion in NOD mice. D6PV is a potential treatment option for type 1 diabetes.

Characteristics associated with Diabetic Kidney Disease among young adults with type 2 diabetes in a multi-ethnic population in New Zealand

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Introduction: Young adults in NZ with Type 2 Diabetes (T2D) are at high risk of Diabetic Kidney Disease (DKD). This study compared the characteristics of New Zealand European (NZE), Māori, and Pasifika young adults (aged 18-40 years) based on a composite Urine Albumin:Creatinine Ratio (UACR) and Estimated Glomerular Filtration Rate (eGFR) variable in order to better stratify DKD progression risk.

Methods: A secondary analysis of entrants into a longitudinal primary-care T2D audit (DCSS:1994-2018). Ethnic comparisons used Chi-square or ANOVA with post-hoc Tukey for each DKD risk group defined by the composite UACR and eGFR threshold. This composite UACR/eGFR threshold classifies participants based on a 9-part matrix comprising three categories of eGFR (≥120, 90-119, <90 mL/min/1.73m^2) across three categories of UACR (<3, 3–30, >30 mg/mmol). A stepwise logistic regression was performed to predict the odds ratio (95% CI) of DKD risk based on the results of the bivariate analyses.

Results: Of 2184 young-adults, (mean age 33.9±4.9 years, BMI 38.0±8.7 kg/m^2, 54.2% female) 170 NZE (18.2%), 281 Māori (30.1%), and 484 Pasifika (51.8%) were at higher-risk for DKD progression (p<0.001). After adjusting for variables that were significant during bivariate analyses, the odds of being at higher-risk of DKD was: 1.75 (1.43-2.15) for those prescribed antihypertensives versus not; 1.77 (1.38-2.77) for Pasifika versus NZE; 1.32 (1.16-1.50) for each unit increase in the log odds of TG:HDL ratio as a measure of insulin resistance; 1.04 (1.02-1.05) for each year increase in age; 1.01 (1.01-1.02) for each mmol/mol increase in HbA1c; 1.01 (1.00-1.01) for each mm Hg increase in systolic blood pressure; and 0.70 (0.57-0.87) for Māori versus Pasifika.

Conclusions: Significant ethnic differences exist in socio-demographic and clinical characteristics among young adults with T2D. Using a composite UACR/eGFR allows more precise DKD risk assessment than utilising these variables individually.

Characteristics of Sodium Glucose Co-Transporter 2 Inhibitor Associated Ketoacidosis in Hospitalised People with Diabetes: A 2022 to 2023 analysis

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Background: SGLT2is are popular for glycaemic control and cardiac and renal protection. DKA, a metabolic emergency, is an increasingly known complication of SGLT2i use.

Aim: Clinical characteristics of inpatients with T2DM on SGLT2i, who had SGLT2i-DKA during admissions at Liverpool Hospital Sydney, were reviewed and assessed to identify ways to improve care.

Methods: Between 1 April 2022 to 31 December 2023, data was collected on T2DM patients on SGLT2is who had SGLT2i-DKA and referred to the Endocrinology service. SGLT2i-DKA severity was classified mild vs moderate-to-severe to facilitate multiple logistic regression modelling (Stat software R) exploring relationships between severity and underlying clinical precipitants.

Results: 47 SGLT2i-DKA cases were noted: with mean age 66±12 years; 55% male; HbA1c 8.8%; on empagliflozin 85% vs dapagliflozin 15%; 64% insulin.

Of SGLT2i-DKA events: mild 62%, 23% moderate, 15% severe. Median time from detection to resolution was 14 hours.

Findings suggest those not directed to fast had 5 times (95% CI: 1.28 to 19.35, p = 0.02) odds of moderate-severe SGLT2i-DKA compared to directed fasting. This remained significant after pre-existing insulin use, infection and choice SGLT2i agent adjustments. There was no association between SGLT2i-DKA severity and age, HbA1c or other clinical events. Importantly, SGLT2i-DKA cohort had no deaths.

Conclusion: SGLT2i-eDKA occurred in medical and surgical inpatients with poor glycaemic control. Once detected and treated (guided by the inpatient endocrinology service), it promptly resolved without any deaths.

Greater odds of moderate-to-severe SGLT2i-DKA were seen in *non-directed fasting* versus *periprocedural fasting*. Higher awareness exists surrounding risk of SGLT2i-DKA around procedures with formalised instructions to withhold medications. Despite being a quaternary hospital, instructions regarding withholding SGLT2is in poor oral intake, delirium and sepsis are not firmly established.

Exploration of SGLT2i-DKA events in other health institutions will determine if findings hold or reveal other areas where care for people with diabetes can be improved.

Chronic Complication Risk and Benefits of Fenofibrate in Type 2 diabetes by a PPARα polymorphism: A FIELD trial substudy

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Aim: To determine if a peroxisome proliferator-activated receptor alpha (PPARα) gene variant (rs6008845, C/T) is associated with chronic complication (CX) risk and benefit of fenofibrate (a PPARα agonist) in adults with Type 2 diabetes (T2D).

Methods: PPARα SNP was assessed (RT-PCR) in 8167 Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) trial participants. Microvascular CX (first occurrence or progression of neuropathy, nephropathy, retinopathy or minor amputation) and macrovascular CX (first occurrence of cardiovascular event [non-fatal myocardial infarction (MI), non-fatal stroke, death], silent MI, major amputation or peripheral revascularisation) were evaluated using Cox proportional hazard models, adjusted for baseline age, sex, and CX status.

Results: CC, TC and TT genotype frequences were: 15.7%, 48.0% and 36.3% respectively. On-trial micro-, macro-vascular or any CX occurred in 2,005 (24.6%), 1,364 (16.7%) and 2,936 (35.9%) participants respectively.

HR for each additional T allele effect on CX outcome in treatment arms, adjusted for sex, age and baseline CX.

	Micro CX	Macro CX	Any CX
Placebo	1.11(1.02, 1.21) **p=0.02**	1.02(0.91, 1.13) p=0.78	1.08(1.01, 1.16) **p=0.03**
Fenofibrate	1.09(0.99, 1.20) p=0.09	0.97(0.86, 1.08) p=0.55	1.02(0.95, 1.10) p=0.58
All	1.10(1.04, 1.18) **p=0.003**	0.99(0.92, 1.07) p=0.86	1.06(1.00, 1.12) **p=0.037**

HR for a treatment effect on CX outcome by PPARα genotype, adjusted for sex, age, and baseline CX.

	Micro CX	Macro CX	Any CX
CC	0.80(0.64, 0.99) **p=0.049**	0.91(0.70, 1.18) p=0.48	0.84(0.70, 1.01) p=0.06
TC	0.79(0.70, 0.91) **p=0.0006**	0.90(0.77, 1.05) p=0.17	0.84(0.75, 0.93) **p=0.001**
TT	0.77(0.67, 0.89) **p=0.0003**	0.83(0.70, 0.99) **p=0.042**	0.77(0.69, 0.87) **p<0.0001**
All	0.79(0.72, 0.86) **p<0001**	0.87(0.79, 0.97) **p=0.01**	0.81(0.76, 0.87) **p<0.0001**

Conclusions:
PPARα genotype (more T alleles) is associated with higher risk of microvascular CX and any CX, but all genotypes benefitted from fenofibrate.

Clinical outcomes in Patients with Diabetes-related Foot Ulceration admitted to a Large Regional Hospital.

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Background: Clinical outcomes for diabetes-related foot ulceration (DFU), including amputation rates, have been reported in a variety of Australian hospital settings although there are relatively less data from regional hospitals. In metropolitan hospitals, amputation rates have ranged from 33 to 50% (1-3). In regional hospitals amputations rates appear to be more variable and range from 32 to 78% (4, 5).

Aim: To determine the outcomes of patients admitted to a regional hospital for DFUs, including amputation rates, mortality, length of stay and readmission.

Method: Retrospective observational study of patients admitted to a large regional hospital over an 18-month period (June 2022 – November 2023). Medical admissions with ICD coding for diabetic foot ulcer as the principal diagnosis were audited using a scanned electronic medical record (Bossnet). Patient demographics, characteristics and clinical outcome data was collected using a Redcap© database. Major amputation was defined as an amputation above the ankle and minor amputation as an amputation below the ankle.

Preliminary Results: To date, 71 patients have been assessed with mean age of 67 years and 77% were men. In relation to amputation outcomes, 37% had a minor amputation whilst 8% had a major amputation. Mortality rate was 0% at 30-days and 2% at 90-days. Median length of stay was 12 days [Interquartile range: 10, 14], 30-day readmission rate was 25% and 90-day readmission rate 18%. Of those with minor amputations, 30% required readmission by 30 days and 19% at 90-days, while major amputations had corresponding readmissions of 17% and 33%.

Conclusion: Outcomes for DFUs in a large regional hospital suggest a comparable amputation rate to previous Australian hospital studies. However, length of stay and readmission rates appears to be greater than tertiary metropolitan hospitals. These differences in clinical outcomes could relate to differences in service provision (6-8).

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Clinical utility and acceptability of FreeStyle Libre 2 in people with Insulin-treated Type 2 Diabetes Mellitus following Hospitalisation with diabetes-related Foot disease: Follow up study.

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Introduction: Patients hospitalised with diabetes-related foot disease (DFD) often have suboptimal glycaemic control, typically improving with interdisciplinary inpatient management. Capillary blood glucose monitoring (CBGM) provides limited assessment.

Aim: To determine clinical utility, acceptability and durability of intervention with FreeStyle Libre 2 (FSL2) flash glucose monitoring system in people with insulin-treated type 2 diabetes mellitus (T2DM) following DFD hospitalisation.

Methods: A prospective observational pilot study of 22 patients admitted to Fiona Stanley Hospital Multidisciplinary Diabetes Foot Unit. FSL2 sensors were applied peri-discharge, providing ≤28 days monitoring. Eligibility criteria included insulin-treated T2DM, no active psychiatric / cognitive condition, and technological proficiency.

Glucose-lowering therapy was adjusted approximately 14- and 28-days post-discharge. Follow up HbA1c was performed.

Acceptability was quantified using the Glucose Monitoring Satisfaction Survey (GMSS) T2DM version. Baseline score assessed CBGM and 4-week score FSL2.

Abbott provided FSL2 devices.

Results: Twenty-two patients completed 2-week and 21 patients 4-week follow-up. Median [IQR] age 55 [50-59] years, 90.9% male, 4.5% Indigenous. 72.7% utilised a phone, 31.8% utilised FSL2 readers.

Median [IQR] admission HbA1c was 10 [8.45-12.1] %. At 4 weeks, mean (±SD) Glucose Management Indicator was 7.4 (±1.0) %, mean (±SD) time in range (3.9-10 mmol/L) 57.7 (±27.8) % and median [IQR] time below range (<3.9mmol/L) 0 [0-0.75] %.

Mean (±SD) baseline GMSS score 3.07 (±0.67), and 4-week score 4.09 (±0.45); ($p<0.001$).

Follow up median [IQR] HbA1c (n=20) was significantly lower than baseline (8.3 [7.4-10.5] % vs 10.0 [8.4-12.4] %; $p=0.015$) assessed at 141 [123-163] days post-discharge.

Conclusion: Utilisation of FSL2 in combination with intensive diabetes management may optimise glycaemic control and minimise hypoglycaemia in high-risk patients with insulin-treated T2DM recently hospitalised for DFD. There is durability of intervention effects in the medium-term, although glycaemic benefits are lower than during the intervention period. Patient satisfaction was greater using FSL2 than CBGM.

Co- Design of a Thermal Imaging Device to predict Healing of Diabetes related Foot Ulcers

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Background: Diabetes-related foot ulcers (DFUs) are common in people living with diabetes and are a major cause of poor quality of life and disability. If not treated in a timely and appropriate way, they could lead to amputation and early death. Currently, feasible and validated methods to predict healing trajectory of DFUs have not been translated into clinical practice.

Aims: To codesign a computer-aided, non-touch test to predict DFU healing trajectory using texture analysis of thermal imaging for use in clinical practice that is fit for purpose and acceptable to both those being tested and users of the device.

Methods: Co-design and development of the prototype of a thermal imaging device involved a participatory action, codesign approach, engaging key stakeholders: specialist clinicians, adults living with or have a history of a DFU and biomedical engineers through facilitated focus groups, online surveys and individual discussions.

Results: Codesign was undertaken with nine clinicians (podiatrists, prosthetist-orthotists and an endocrinologist), two biomedical engineers and two clinician researchers. We identified the practical aspects to support device usage within a clinic setting, including device charging, device sterilisation and the robustness of the device. The device was considered to have greatest potential benefit for community health services, GP clinics and services located in rural and remote regions with limited access to timely specialist services, rather than in specialist services where dedicated, expert, multidisciplinary teams exist. Engaging up to ten people living with diabetes was undertaken alongside validation data collection. This was to ensure their improved understanding of the purpose and use of the device, enabling them to provide useful feedback that improves communication of device use and its outcomes with people with DFUs, when used in a clinical setting.

Conclusions: Adjustment to the device incorporating findings from codesign have been undertaken and validation of the device continues.

Co-designing a Comprehensive Multi-disciplinary Diabetes Service for Adults with Cystic Fibrosis: A single centre experience

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Aims: The clinical landscape for adults with cystic fibrosis (CF) has undergone significant transformation with introduction of CF modulator therapies, leading to notable reduction in respiratory symptoms. Consequently, the focus on metabolic health has gained prominence. At our centre, we introduced a co-developed 'ideal' model of care (MOC) for CF-related diabetes, aiming to address these evolving needs. Here, we present insights gathered from end-users to enhance the MOC in the post-modulator era.

Methods: This quality improvement initiative (EX/2023/MNHB/103775) was completed at the Adult Centre for Cystic Fibrosis (ACFC), The Prince Charles Hospital, Queensland, serving around 400 adults with CF. Implementation of the 'ideal' MOC commenced in June 2023 and underwent evaluation after six months. This evaluation involved a consumer survey to identify priority areas to enhance satisfaction and engagement with the MOC, coupled with state and future workshops to refine the MOC from a healthcare provider perspective.

Results: In total 72 consumers completed the survey. Most consumers were aged between 19-45 years (51% females), majority on CF modulator therapies (80%) and 25% (n=17) had CF-related diabetes. For consumers with confirmed CF-related diabetes, key concerns encompassed access to emerging diabetes technology, safe insulin titration, understanding healthy nutritional goals and exercise, and mental health support. Diabetes-related complications, weight management, and cardiovascular health were perceived as comparatively less important. Consumer satisfaction with the MOC was high. End-user workshops with healthcare providers identified several areas for improvement, including refining diabetes screening and referral procedures, enhancing connections with community-based healthcare providers, establishing pathways to risk stratify cardio-metabolic disease, developing CF-specific educational materials for consumers and healthcare providers, advocating for equitable access to diabetes technology, and fostering collaborative refinement of the MOC within ACFC.

Conclusion: Through diverse end-user engagement, we successfully implemented and continue to refine a co-designed MOC tailored for adults with CF-related diabetes.

Co-designing a New Clinical pathway to support Western Australian (WA) Families with Children Identified as having Early-stage Type 1 Diabetes (T1D)

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Background: Early stage diabetes is characterised by persisting autoimmunity without (stage 1) or with (stage 2) evidence of dysglycaemia . Licensing of the first disease-modifying therapy has accelerated global screening efforts to identify children with early stage T1D. These children and families now live with the knowledge of increased risk of clinical progression, but with no established clinical pathway to receive monitoring and support.

Aim: To co-design a new clinical pathway for WA children with early-stage diabetes.

Method: A clinical pathway will be developed using a Community-Based Participatory Research (CBPR) co-design process within a consolidated framework for implementation research (CFIR). The first step in this process was facilitated community conversations conducted with the T1D community and health care professionals (HCPs). Attendance was voluntary and via open invitation. Qualitative analysis identifying common themes via an inductive approach was performed.

Results:
Community members, including those living with and those screened for T1D were recruited via email, newsletter and flyers. 16 participated in the community conversation. 36 HCPs (13 doctors, 10 nurse educators, 2 social workers, 3 dietitians, 1 mental health nurse, 5 administrative staff, 2 clinical research staff) participated in the HCP community conversation.

Key themes identified in both community and HCP conversations, included education (access to reliable evidenced-based interactive resources and guidelines for families), communication strategies to navigate impact of uncertainty (need for psychosocial and counselling support), access to clinical trials and/or disease modifying therapy, and financial considerations. The HCPs specifically identified a need for clinical pathways stratified by T1D stage.

Conclusion: Common themes were observed across the T1D community and HCPs who care for children with T1D in the domains of education, psychosocial support and intervention access. Findings from these initial conversations will be utilised to progress next steps in the process towards implementation of this clinical model.

Combined effects of Time Restricted Eating and Exercise on Short-term Glycaemic management in individuals with Type 2 Diabetes: The TREx study

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Aim: This study investigated the acute (14 h) effects of reducing the daily eating window from 12 h (CON) to 8 h (time restricted eating; TRE), with and without a post-meal bout of exercise (CON+Ex and TRE+Ex), on blood glucose and insulin concentrations in people with type 2 diabetes (T2D).

Method: Seventeen participants were recruited for this randomised crossover study; 15 (5 F,10 M; HbA1c: 7.6 ± 1.0%) completed the four conditions: CON (eating window, 0800-2000 h), CON with exercise (CON-Ex; 0800-2000 h + 15 min walking at 60% peak aerobic capacity, 45 min post-meals), TRE (eating window 1000-1800 h), and TRE with exercise (TRE+Ex, 1000-1800 h + 15 min walking as per CON+Ex). Standardised meals were provided the evening prior to each trial and during each condition. Venous blood samples (5 mL) were collected at 25 time points (30 min-hourly, 0800-2200 h) during each condition. Plasma glucose and insulin concentrations were measured and used to calculate total area under the curve (AUC). Statistical analysis was two-way repeated measures ANOVA with significance set at $P<0.05$.

Results: There was no effect of changing the eating window on glucose (P=0.72) or insulin (P=0.67) AUC. However, there was a main effect of exercise reducing insulin AUC (P=0.009, -57 μIU/Lx14 h, 95%CI: -103 – -11 μIU/Lx14 h), but no effect of exercise on glucose AUC (P=0.97). There were no eating window × exercise interactions.

Conclusion: Whilst 8 h TRE did not improve acute (14 h) glucose or insulin concentrations compared to an extended eating (12 h) window, post-meal exercise reduced daily insulin AUC, irrespective of the eating window. As AUC does not elucidate patterns of hyperglycaemia or insulinemia, further post-meal period analysis will be performed. Future work should focus on longer interventions of meal timing and exercise for improving glycaemia in people with T2D.

Community Involvement in Paediatric Type 1 Diabetes Research: Shifting the paradigm

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Aim: Community involvement in Type-1-Diabetes (T1D) research is essential for the recognition of real-life experiences of families living with T1D in the planning, delivery, monitoring and evaluation of T1D research. Community involvement helps direct research into areas of greatest need and facilitate the translation and implementation of research into clinical practice. The JDRF Global Centre of Excellence sought to develop a framework for the integration of the lived experience to the fundamental research program of the Centre.

Method: A literature review examined quality community involvement in health research and T1D research. Definitions to determine what was considered "quality involvement" were reviewed and benchmarked against the NHMRC of Australia's Statement on Consumer and Community Involvement in Health and Medical Research. Consultation with those living with T1D and T1D healthcare professionals was conducted to provide an understanding of previous involvement activities and what they considered quality involvement.

Results: Review and consultation revealed that quality community involvement in T1D was generally ad-hoc and lacking in structure. Research governance structures did not have significant community involvement and failed to authentically embed the lived experience. A Community Involvement Framework (Framework), Community Involvement Guidelines (Guidelines) and a Stakeholder and Community Involvement Plan (Plan) was developed.
A Community Engagement Officer leads the program, with strong collaboration with the National Community and Consumer Involvement Committee, with members embedded in other working groups of the Centre. Community engagement extends to include committee participation, project specific research buddies and reference groups, grant reviews, guideline review, Community Forums, Community consultations/conversations, and contributions to parliamentary submissions.

Conclusion: The Community Involvement program of the JDRF Centre of Excellence, through a clear framework and Governance structure is successfully providing the voice of lived experience. This approach could be adopted for other T1D and Health research programs to enhance engagement and translation or research.

Components of Weight loss following 12 months in a Metabolic program in people with class 3 obesity with and without Type 2 Diabetes

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Aim: This study aimed to compare the weight loss following 12 months of an intensive non-surgical multidisciplinary metabolic program in people with class 3 obesity with and without Type 2 Diabetes (T2D), and to compare the fat mass and fat free mass (FFM) weight loss components.

Methods: All adults enrolling in a single public hospital-based outpatient metabolic program in Sydney between April 2019 and April 2024 had their bioelectrical impedance analysis (BIA) performed at baseline and after 12 months using a Marsden MBF-6010 Body Composition Scale with no footwear. After testing for normality, data was compared using student T test or Mann-Whitney U test/Wilcoxon signed-rank test.

Results: There were 340 people with baseline BIA data, 40% had T2D (n=135). Those with T2D were older (52.7±10.8 vs 43.4±13.6 years, p<0.001) with lower baseline weight (142.6±29.6kg vs 153.9±31.4kg, p=0.001) and lower BMI (51.3±10.3 vs 54.1±10.2kg/m^2, p<0.015). There was no significant difference in baseline body fat percentage (44.5±8.9% vs 46.2±8.4%, p=0.067). At 12 months, 69 patients had BIA measurements, 50.7% with T2D (n=35). Total weight loss was similar in T2D compared to non-T2D (6.0±7.0% vs 6.0±5.8%, p=0.492). T2D group had a significant reduction in body fat percentage of (Mean [CI]:1.85 [0.07,3.64], p=0.007) while non-T2D group did not (Mean [CI]:1.29 [-0.4,2.98]; p=0.127). Comparing weight loss component at 12 months, the T2D group lost 6.5±8.4kg fat mass and 1.9±9.4kg FFM (22.6% of total weight loss was FFM), whereas the non-T2D group lost 5.6±7.2kg fat mass and 3.2±7.9kg FFM (36% was FFM).

Conclusion: People with class 3 obesity with and without T2D had similar baseline body fat percentage, and both lost similar amounts of weight following 12 months of multidisciplinary weight management. However, there seemed to be a greater preservation of fat free mass in people with T2D.

Continuous Glucose Monitoring Glycaemic Outcomes in Type 1 Diabetes by different Insulin Delivery Systems in a Tertiary Diabetes Centre

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Aim: Automated insulin delivery (AID) systems can improve glycaemia in people with type 1 diabetes (T1DM), compared with multiple daily injections (MDI). At our tertiary diabetes centre, we reviewed continuous glucose monitoring (CGM) glycaemic outcomes, according to insulin delivery modality.

Method: In this cross-sectional study, we audited CGM data for adults with T1DM attending the RPA Diabetes Centre over a three-month period (February-April 2024). The primary outcome was the comparison of time in target range, according to insulin delivery modality groups, (MDI, Medtronic 780G, CamAPS FX, Control IQ {CIQ}) made based on affordability and choice.

Results: During the three-month audit, 209 individuals with T1DM using CGM were seen. 134 were on MDI (64%), 75 used pumps (36%) (39 Medtronic 780G, 20 CIQ, 13 CamAPS FX, 2 Omnipod DASH looping, 1 Medtronic 780g manual pump). Compared to MDI users, pump users were younger (38.0±14.5 vs 45.3±14.7 years), had a higher proportion females (55% vs 38%), lower HbA1c (7.0±0.8 vs 7.8±1.3%), more time in range (69.8±11.4 vs 55.6±21.3%), and less time in high range (21.9±8.7 vs 27.3±11.7%). Similar CGM outcomes were observed across the three AID systems, including GMI (Medtronic 780G 7.1±0.4%, CIQ 7.2±0.5%, CamAPS FX6.9±0.3%) and time in range (Medtronic 780G 69.4±10.5%, CIQ 67.2±13.1%, CamAPS FX75.0±7.5%) ($p<0.05$ one-way ANOVA).

Conclusion: Users of AID systems have greater time in range than MDI users. Given the increasing use of CGM, clinical audits utilising CGM metrics can complement data obtained from the Australian Diabetes Quality Audit (ADCQR), as a quality assurance activity to improve quality of diabetes care delivery. Although AID systems can offer significant benefits to individuals with T1DM, access is restricted to those who can afford the technology. This heralds the need for funding model revision for technology access, to address health inequity in Australia.

Continuous Glucose monitoring in Pregnant women with Type 1 Diabetes: A single tertiary centre's early experience

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Aim: To explore the uptake of continuous glucose monitoring (CGM) in pregnant women with type 1 diabetes (T1DM) using multi-daily injections (MDI) and examine its impact on glycaemic and obstetric outcomes.

Methods: We conducted a retrospective audit at a single tertiary care site. We included all women with established T1DM who were pregnant between March 1st 2020 to Dec 31st 2022. The start date coincided with the commencement of fully subsidised continuous and flash glucose monitoring.
We included women using MDI and excluded those using insulin pumps. We classified women into the CGM group if use was at least one trimester. We collected demographic data, glycaemic, obstetric, and foetal outcomes.

Results: There were 115 women with T1DM and of these 46 women met the inclusion criteria. 33 women used CGM, and 13 women used blood glucose self-monitoring (SMBG) alone. The main reasons for SMBG were late antenatal care or local reactions to the CGM. There was a trend to improved glycaemic control in the CGM group compared to the SMBG group. Amongst the CGM users, the Time in Range (TIR) and Glycaemic Variability (GV) improved from the first to the third trimester (first vs third trimester: TIR 77.5% vs 84%; GV 34.7% vs 31.6%). The rate of pre-term delivery, caesarean section, admission to Neonatal Intensive Care Unit (NICU) or Special Care Nursery (SCN), macrosomia and incidence of neonatal hypoglycaemia were no different between the two groups.

Conclusion: Early use of CGM during pregnancy demonstrated some improvement in glycaemic control in pregnancy. Uptake was generally high, with approximately 2/3 of women using CGM. In this small study, there was no difference in obstetric or foetal outcomes with the use of CGM compared with SMBG.

Continuous Glucose Monitoring results pre-and-post Carbohydrate Counting Telehealth Education Program

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Aim: Evidence shows a meaningful decrease in glycated haemoglobin (HbA1c) when bolus insulin is matched to carbohydrate (CHO) intake in people with type 1 diabetes (T1D). Accurately quantifying CHO intake to determine insulin dose is complex and errors in estimation can lead to either post-prandial hypo- or hyperglycaemia. We aimed to assess the impact of a novel structured CHO counting telehealth education program on glucose levels.

Method: Patients of a tertiary hospital who were referred for CHO counting education were offered to undertake the novel education program. For those who consented, three 30-minute structured telehealth sessions were delivered by a diabetes dietitian. A retrospective audit of Continuous Glucose Monitoring (CGM) Time in Range (TIR 3.9-10.9mmol/L) data for patients who completed the education program were compared pre-and-post education. Fourteen days of TIR data was included up to three months before education and 1-month post. The most recent HbA1c results recorded pre-and-post assessment dates were also included.

Results: Fifty-six people with T1D received CHO counting education. Twenty-eight were female; median (IQR) age was 30.5 (24,41); and median time since diagnosis was 15.5 (4, 23.5) years. Fourteen people received group counselling (maximum 4 participants per group) and 42 people received individual counselling. Fifty-three (95%) people with T1D were utilising multiple daily injections and three (5%) an insulin pump. Pre-and post CGM data were available for 44 individuals. OF these 44, HbA1c results pre-and-post education were recorded for 20 individuals.

Glucose measure n=44	Prior to education Mean (SD)	Post-education	p-value
CGM TIR (%)	47.9 (23.0)	54.6 (25.0)	0.004
CGM mean blood glucose level (mmol/L)	10.9 (3.1)	10.3 (3.7)	0.06
CGM usage time (%)	85 (20.8)	84 (26)	0.35
HbA1c (%) n=20	8.7 (2.2)	7.9 (1.9)	0.08

Conclusion: We observed a trend in improved average CGM TIR for the cohort of individuals where CGM data was available pre-and-post participation in the education program. HbA1c results could have been influenced by parallel changes to insulin management. Concise CHO counting programs may be of merit and require more evaluation.

Core competencies for Diabetes Specialist Nurses: Finding common approaches across different countries

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Aims: Explore APN's role in shaping a healthier, more equitable approach in diabetes care, an identified area for action is to improve workforce capacity, and provide a contribution to an international understanding of clear competencies for the diabetes specialist nurses (DSNs). The review undertaken compiles international currently identified core competencies for DSNs and compares different competency frameworks across different countries.

Methods: A systematic electronic literature search was conducted in January 2024, encompassing publication databases including CINAHL (EBSCO), Embase, PubMed, Scopus, and Web of Science from their inception. The search was conducted using the following keywords or search terms: ‘Nurse Specialists’, ‘specialist nurses’, ‘Disease Management’, ‘core competencies’, ‘core competencies framework’, ‘Professional Competence’, ‘educators’, ‘Diabetes Mellitus’ and ‘diabetes’. Additionally, a manual search was performed on the official websites of organizations, such as the national diabetes associations of different countries. Initial search identified 982 studies and documents.

Results: A total of (n=7) publications comprising two peer-reviewed studies and five professional organizations (grey literature) were selected for review. Competency frameworks of UK and New Zealand are both designed focusing on specific clinical dimensions of diabetes care. Additionally, frameworks from USA and China extend beyond traditional clinical aspects, including Communication and Advocacy, Person-Centered Care and Counseling Across the Life Span, Research and Quality Improvement and so on. A guideline from USA solely focusing on professional competencies for diabetes technology highlights the importance of diabetes technology use in practice. Additional studies also investigate cultural competency levels for diabetes care.

Conclusions: Given the central role of DSNs in diabetes care, it is imperative that DSNs possess competencies in diabetes education and management. The review identified international gaps and the need to develop a globally applicable core competency framework for DSNs.

Cost-benefit Analysis of Fenofibrate for the Prevention of Diabetes-related Amputations

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Cost-benefit analysis of fenofibrate for the prevention of diabetes-related amputations

Introduction: There are more than 4,400 diabetes-related amputations and more than 10,000 hospital admissions for diabetes-related foot ulcers in Australia. It is estimated that the cost to treat diabetic foot disease is $875 million per year. Clinical evidence from the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study demonstrated that fenofibrate can play a role in preventing diabetes-related foot disease and reduce the risk of amputation. This study sought to investigate the cost-effectiveness of using fenofibrate to prevent amputations in an Australian clinical setting.

Methods: The Australian National Diabetes Audit Report 2022 from Monash University was used as basis to simulate number of amputations in an Australian diabetes cohort treated with fenofibrate over a 20-year time horizon. The effectiveness of fenofibrate was taken from the FIELD study. Total cost of treating amputations was calculated over the 20-year time horizon. Input data was obtained from the Australian Refined-Disease Related Groups (AR-DRG) and the Australian Pharmaceutical Benefits Scheme.

Results: The model estimated that patients taking fenofibrate resulted in 38 amputations per 1000 people at a total cost of $2.5M. Patients not taking fenofibrate would result in 72 amputations per 1000 people at a cost of $4.8M. Cost of fenofibrate treatment was estimated to be $3.1M and the cost of other diabetes complications were estimated to be $10.0M for fenofibrate and $12.4M for people not taking fenofibrate. Thus, a cost savings of [$4.8M+$12.4M=$17.2M] - [$2.5M+$3.1M+$10.0M=$15.6M] = $1.6M per 1000 patients was observed.

Conclusion: Use of fenofibrate in Type 2 diabetes patients is estimated to result in a cost savings in an Australian setting due to less diabetes complications such as amputations.

Cost-Effectiveness of Real-Time CGM (Dexcom) vs Self-Monitoring of Blood Glucose in People with Type 2 Diabetes on Intensive Insulin Therapy in Australia

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Introduction: Evidence shows RT-CGM systems improve glycaemic control in people with T2D on intensive insulin therapy (IIT). Reimbursement for RT-CGM in Australia is currently limited to people with T1D. Our analysis evaluates the cost-effectiveness of RT-CGM for people with T2D IIT in Australia.

Methods: We used the IQVIA Core Diabetes Model (CDM), comprising 17 Markov submodels for diabetes complications over a lifetime horizon, to simulate clinical outcomes and direct medical costs from an Australian public healthcare system perspective. Cohort characteristics included a mean age of 65 years, 51% male, and an average diabetes duration of 16 years. The adjusted HbA1c reduction for RT-CGM was -0.56%. Severe hypoglycemic and hyperglycemia rates were 0.04 and 0.025 PPY for SMBG and 0 PPY for RT-CGM, respectively. Utilities for avoiding fingersticks (0.03) and reducing fear of hypoglycemia (0.025) were applied to RT-CGM users. Probabilistic and deterministic sensitivity analyses were conducted.

Results: RT-CGM users are projected to gain an additional 0.621 quality-adjusted life years (QALYs) with $14,117 in incremental costs, and an incremental cost-effectiveness ratio (ICER) of $23,426, below the $50,000 willingness-to-pay threshold for Australia. Microvascular and macrovascular outcomes projections indicate that RT-CGM use results in a relative reduction in diabetes eye, renal, neuropathy, and cardiovascular complications of 17.7%, 21.1%, 8.7%, and 2.5% respectively. Sensitivity analysis scenarios of RT-CGM cost reductions of 10%, 20%, and 30% resulted in ICERs of $18,666, $13,909, and $9,153, respectively. RT-CGM remained cost-effective even when costs were increased by 30%. Using Fremantle risk equations for 100% Southern European and 100% Indigenous Australian populations resulted in ICERs of $8,085 and -$1,832 (RT-CGM is Dominant).

Conclusion: This study has demonstrated that using RT-CGM systems for diabetes management in people with T2D who are on intensive insulin is a cost-effective intervention. Findings support expanding reimbursement for RT-CGM in Australia.

Cystic Fibrosis Transmembrane Conductance Regulator modulation effects on Glycaemia, Body weight and Pulmonary function from a Single Tertiary Centre

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Aim: To assess changes in glycemia, body weight and pulmonary function in adults with CF before and after initiating triple combination cystic fibrosis transmembrane conductance regulator elexacaftor/tezacaftor/ivacaftor (ETI).

Method: Adults with at least one F508del, with or without CFRD, the latter with pre and post ETI OGTT glucose and insulin at 0,30,60,120 min. Primary outcomes for CFRD included HbA1c and insulin requirement. In the non-CFRD group, changes in glucose and insulin from OGTT, insulin resistance (HOMA2-IR), insulin secretion (HOMA2-%S) and beta-cell function (HOMA2-%B). Secondary outcomes in both were change in body weight and pulmonary function.

Results: The study included 38/61 individuals without CFRD with pre/post ETI OGTT and 23 with CFRD, mean age 33.4±9.5 years, mean duration ETI 13.4±7.4 months. In individuals with CFRD on ETI, insulin requirement decreased (0.1 IU/kg/day, 13 dose reduction, 3 ceased insulin) despite significant BMI increase. In the non-CFRD group there was a significant improvement in GTT classification with 11/38 IGT prior, 3/38 IGT post ETI (p=0.02) with significant reduction in 2-hour glucose. There were statistically significant improvements in HOMA2-%B but not HOMA2-IR or HOMA-%S. Mean % predicted FEV1 improved by 7% across both groups. Pulmonary function improved in both CFRD and non-CFRD groups

Conclusion: In the largest single centre analysis to date, people with CFRD on ETI improved glycemia with reduction in insulin requirement, despite increase in weight. In those without CFRD there was an improvement in glycemia and insulin secretion, despite weight gain.

CFRD	**Pre-ETI**	**Post-ETI**	**p-value**
HbA1c, %	6.70 ± 1.00	6.52 ± 1.22	0.33
Insulin total daily dose, units	19.0 ± 35.8	16.0 ± 35.5	0.50
Insulin requirement, units/kg/day	0.28 ± 0.63	0.20 ± 0.40	0.14
Body weight, kg	66.4 ± 14.5	69.2 ± 15.2	0.02
Mean BMI, kg/m^2	23.5 ± 3.8	24.6 ± 4.8	0.04
FEV1 predicted, %	55.8 ± 21.0	62.8 ± 19.0	0.02
NON-CFRD			
OGTT glucose, mmol/L			
0 min	4.70 ± 0.61	4.86 ± 0.56	0.04
30 min	8.84 ± 1.60	9.07 ± 1.94	0.50
60 min	9.61 ± 2.38	9.06 ± 3.11	0.21
120 min	6.24 ± 2.52	5.15 ± 2.03	0.01
OGTT insulin, mIU/L			
0 min	6.0 ± 4.0	5.0 ± 1.0	0.29
30 min	27.5 ± 22.8	22.0 ± 22.0	0.27
60 min	43.5 ± 37.5	32.0 ± 41.5	0.18
120 min	32.5 ± 27.5	22.5 ± 18.0	<0.01
HOMA-IR	1.6 ± 1.5	1.5 ± 1.5	0.18
HOMA-%S	88.2 ± 42.3	89.7 ± 39.6	0.84
HOMA-%B	90.8 ± 145	77.4 ± 77.0	0.05
Insulinogenic index, pmol/mmol	6.1 ± 6.05	5.0 ± 7.6	0.94
Body weight, kg	69.0 ± 13.1	72.7 ± 13.0	<0.01
BMI, kg/m^2	23.3 ± 4.0	24.6 ± 3.8	<0.01
FEV1 predicted, %	74.5 ± 26.9	81.4 ± 25.9	<0.01

Dapagliflozin reduces Insulin concentration, Body weight and Pain scores in Horses with Equine Metabolic syndrome

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Aim: Equine metabolic syndrome (EMS) shares similarities to metabolic syndrome in humans including obesity and insulin dysregulation. Hyperinsulinemia is a feature of EMS and frequently results in laminitis, a painful condition affecting the hooves. Recently, SGLT2i are being used to manage EMS but the effects of dapagliflozin have not been documented. The aim of this study was to evaluate the efficacy of dapagliflozin in the management of EMS.

Methods: Medical records of 30 horses treated with oral dapagliflozin at 0.02mg/kg once daily for a minimum of 30 days were reviewed. Pain scores were evaluated using a validated lameness scale (0-12). Comparisons between day 0 (pre-treatment) and day 30 measures were made using Wilcoxon-matched pairs signed rank tests.

Results: Between day 0 and day 30, within-horse changes (median, inter-quartile range (IQR) were: basal serum [insulin] (uU/ml) reduced from 182 (115, 270) to 28.5 (13.5, 76.5) ($p<0.0001$), pain scores reduced from 6/12 to 0/12 ($p<0.0001$), body weight (kg) reduced from 507 (285, 585) to 470 (253, 553) ($p<0.0001$), serum [triglyceride] (mmol/L) increased from 0.5 (0.3, 0.6) to 1.4 (IQR: 0.7, 2.2) ($p<0.001$) and serum [β-hydroxybutyrate] (umol/L) increased from 0.2 (0.2, 0.3) to 0.3 (0.3, 0.4) ($p<0.0001$). Adverse events included polyuria and polydipsia (20%), lethargy (7%) and mild, intermittent diarrhoea (7%).

Conclusion: Dapagliflozin treatment is associated with reductions in [insulin], body weight and pain scores in horses and may be an effective therapy for the management of EMS. Ketosis, a metabolic pathway considered unimportant in horses was induced during dapagliflozin treatment.

Data from a Diabetes Dashboard: Incidence of Hypoglycaemia among Hospitalised patients treated with Diabetes Medication

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Aim: Hypoglycaemia hospital-acquired complications are causing concern and controversy. We aimed to assess the impact of diabetes medication on the occurrence of hypoglycaemia in hospital, using data from a diabetes dashboard.

Methods: Westmead Hospital utilises a diabetes dashboard which records both capillary and formal glucose levels performed in the hospital (excluding intensive care). The dashboard also captures related information such as diabetes medications.
We examined the trough glucose level recorded for each hospital admission, and whether diabetes medications had been prescribed prior to this glucose level. The incidence of hypoglycaemia was determined for patients on Metformin, DPP4 inhibitors, SGLT2 inhibitors, GLP1 agonists in the absence of Sulphonylurea or Insulin, patients on Sulphonylureas in the absence of Insulin, and patients on Insulin (±other diabetes medications). Hypoglycaemia was divided into Level 1 (3.0-3.9 mmol/L) and Level 2-3 (<3.0 mmol/L).
Data for 2023 were analysed by chi square tests. Patients aged <16 were excluded.

Results: There were 560,671 glucose levels recorded from 32,015 admissions including 8,171 with prescription of diabetes medications. Hypoglycaemia occurred during 2,257 (7%) admissions, 1418 (63%) of which had diabetes medication prescribed. Patients who died (N=775) were more likely to have suffered hypoglycaemia than those who survived (16.0% vs 6.9%, p<0.001).
The incidence of Level 1 and Level 2-3 hypoglycaemia among patients treated with Metformin (N=2,268) was 3.4% and 0.5%, DPP4 inhibitors (N=598) 3.3% and 0.5%, SGLT2 inhibitors (N=543) 3.7% and 0.8%, GLP1 agonists (N=54) 3.7% and 0% respectively. These were not significantly different to patients on no diabetes medication (N=23,844) 3.1% and 0.4%. Patients on Sulphonylureas (N=803) had a higher incidence of hypoglycaemia (13% and 3.7%, p<0.001), as did patients on insulin (N=4701) 16.5% and 8.7%, p<0.001.

Conclusion: Hypoglycaemia is common amongst inpatients treated with sulphonylureas or insulin. Interventions focused on this may reduce hypoglycaemia hospital-acquired complications.

Data-Driven Phenotypes in Patients with Recently Diagnosed Type 2 Diabetes Mellitus: An Australian Cohort Study

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Background: Type 2 Diabetes is a heterogenous disease and previous cluster analyses have identified several novel and distinct phenotypes with unique risk profiles. However, in these studies the variables that have been used for assignment include those that are not routinely available at the clinic, such as HOMA-B and HOMA-IR, thereby precluding further study using clinical databases. As cluster analysis is dependent on candidate variable selection, it is notable that the use of commonly available, clinically relevant, routinely collected candidate variables to explore phenotypic subtypes has not been widely studied, and not previously in a multiethnic Australian context.

Aim/ Methods: Using data from the Royal Prince Alfred Diabetes Centre Clinical Database, we performed agnostic data-driven analysis (Gower Index and K-Medoids clustering analysis) of patients with type 2 diabetes, with an index visit within 2 years of diagnosis (n=6634). Clusters were based on eight variables (age, BMI, systolic and diastolic BP, total cholesterol, HDL, Triglycerides, HbA1c). Clusters are related to prospective data from patient records; Cox regression and logistic regression are used to examine the risk of diabetic morbidity and mortality.

Results: Using silhouette analysis, the optimal number of clusters was determined to be 2 or 4 clusters. Confining analysis to those for whom complete data for all variables were available (n=4309) we can describe 4 phenotypes **(Table 1)**: Cluster 1, an older- age related phenotype, with low BMI and mild metabolic derangements; Cluster 2, a mild obesity, metabolic syndrome negative phenotype; Cluster 3, a metabolic syndrome phenotype; Cluster 4, a younger obesity-related phenotype. The morbidity and mortality risk for each of these phenotypes will be presented.

Conclusions: Patients with recently diagnosed type 2 diabetes cluster into sub-groups based on routine clinical markers**.** The clinical significance of these phenotypes is discussed.

Cluster	**1**	**2**	**3**	**4**
Mean Age (yrs)	66.12	49.66	59.59	42.8
Mean BMI (kg/m2)	29.99	28.02	32.32	33.15
Mean Syst BP (mmHg)	129.04	108.97	153.37	126.53
Mean diastolic BP(mmHg)	75.23	69.87	89.14	81.58
Mean Cholesterol (mmol/l)	5.06	5.10	5.43	5.37
Mean HDL (mmol/l)	1.25	1.23	1.22	1.14

Mean Ln-Triglcerides (mmol/l)	0.58	0.53	0.73	0.77
Mean baseline HbA1c (%)	7.51	8.02	7.72	8.37

Table 1: Baseline Characteristics by Cluster

Deciphering Diabetes on Dialysis

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(Aim) Introduction: We present a case of a man with type 2 diabetes complicated by end stage kidney disease (ESKD) on peritoneal dialysis and discuss the evidence and considerations of management of insulin therapy.

(Method) Case presentation: A 65 year old man presented to the hospital following a low speed motor vehicle likely due to multifactorial delirium in the context of hypoglycaemia, multiple infections, and fluid overload. He has a background of type 2 diabetes on basal bolus insulin complicated by ESKD on overnight automatic peritoneal dialysis (APD) with glucose containing dialysate overnight and icodextrin during the day. He has frequent hypoglycaemias with impaired hypoglycaemia awareness. During the admission, overnight hyperglycaemia and daytime hypoglycaemia were noted and insulin doses were adjusted.

(Results) Management and outcome: Upon discharge, he was transitioned to temporary haemodialysis (HD) to facilitate tighter fluid balance to facilitate healing of his foot infection. Contrary to expectation, he experienced more hyperglycaemia, as noted on his continuous glucose monitor (CGM), and he reported higher appetite since transitioning to haemodialysis.

(**Conclusion) Discussion:** A number of discussion points were generated from the case in relation to diabetes management in patients on dialysis. Regarding route of administration, intraperitoneal administration has been previously advocated on peritoneal dialysis (PD) but due to adverse effects including dyslipidaemia, hepatic subscapular steatosis, and increased risk of PD peritonitis, the current recommendation is subcutaneous only. Regarding dosage, patients commencing PD usually require an increase in insulin dose, where insulin dose is usually reduced when commencing HD. There is no data on insulin adjustment when switching dialysis modalities. Self-monitoring of blood glucose (SMBG) on PD requires a glucometer compatible with icodextrin. HbA1c is inaccurate and limiting in dialysis. CGM may be a better marker that can result in more frequent treatment changes and improved glycaemic control. Insulin pump may be useful on dialysis but more research is required.

Decrease in Heart Failure Mortality lags behind Atherosclerotic Cardiovascular Disease in people with Diabetes

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Background/Aim: Reductions in cardiovascular mortality are largely attributed to improved care of atherosclerotic cardiovascular disease and reductions in smoking. We aimed to compare time trends in heart failure (HF) and atherosclerotic cardiovascular disease mortality in people with diabetes in nine jurisdictions from 2000-2020, with a particular focus on trends following the introduction of SGLT2 inhibitors, beginning in 2012-2014 and lasting until 2020.

Methods: We analysed administrative datasets from 2000-2020 for people with diabetes aged 40-89 years from nine high-income countries for mortality due to coronary heart disease (CHD) and cerebrovascular disease (CBD), and from eight countries for HF mortality. We estimated cardiovascular cause-specific mortality rates defined by the underlying cause of death using Poisson models adjusted for age and sex.

Results: There were 714,658 cardiovascular deaths over more than 67 million person-years of follow-up. From 2000-2020, the age- and sex-standardised mortality rate from CHD and CBD declined in all countries, except for CBD in the Netherlands (Figure 1A and 1B). HF mortality was stable or declined to a lesser degree in all countries. Only 2/8 countries had estimated annual percent declines in HF mortality of greater than 4%. Conversely, 7/9 and 6/9 countries had estimated annual percent declines in mortality of greater than 4% for CHD and CBD respectively. No clear evidence for an effect of the introduction of SGLT2 inhibitors on population-level HF mortality was apparent.

Conclusions: In people with diabetes, HF mortality has declined more slowly than has mortality due to atherosclerotic cardiovascular disease, and with no obvious effect of the introduction of SGLT2 inhibitors. More effective approaches to primary and secondary prevention of HF in people with diabetes are required.

A) B) C)

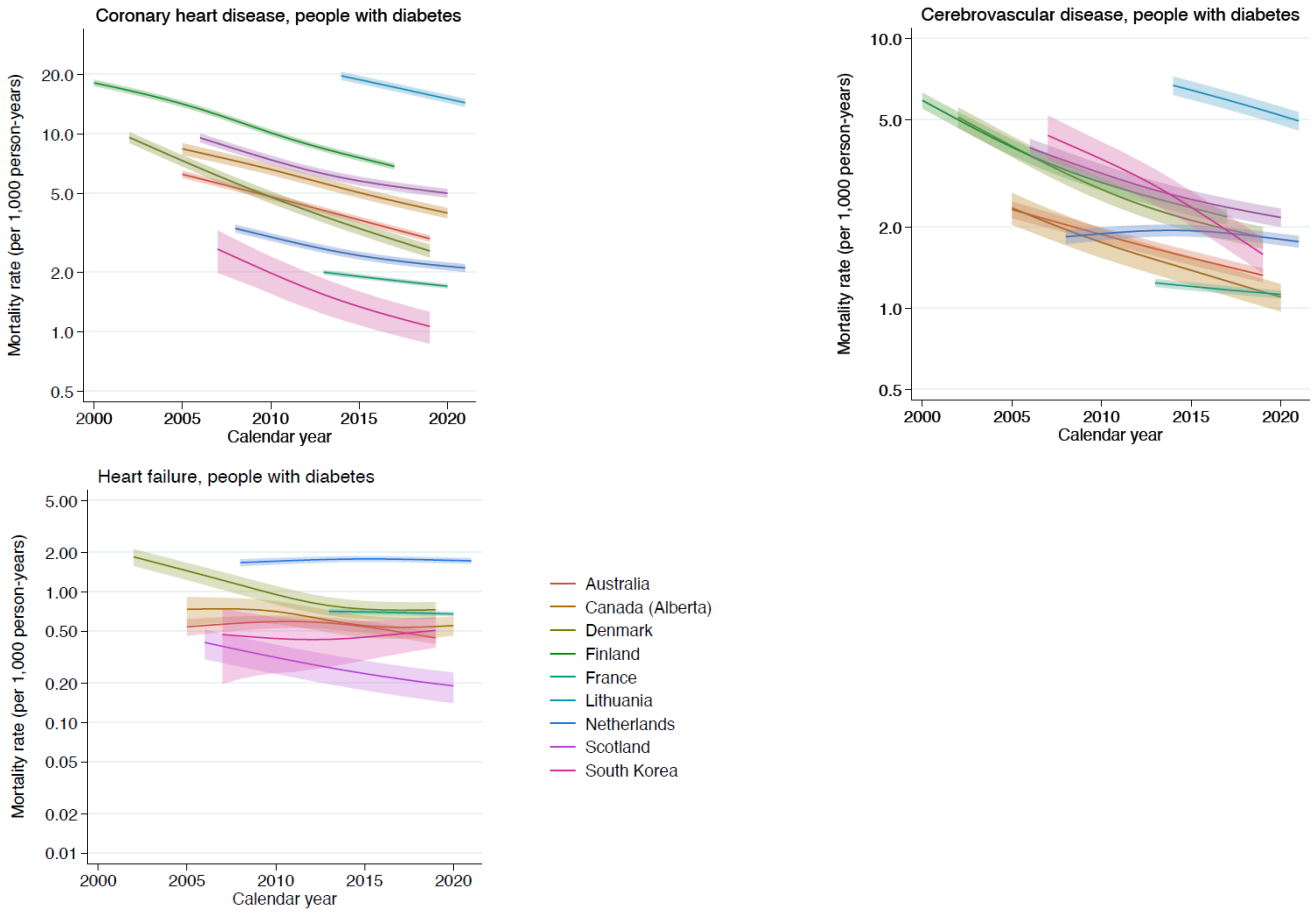

Figure 1. Age- and sex-standardised mortality rate in people with diabetes aged 40-89 years due to A) coronary heart disease, B) cerebrovascular disease, and C) heart failure, from 2000-2021.

Dedicated Aboriginal Diabetes Clinic in Mt Druitt (NSW): New initiative by Western Sydney Diabetes

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Aim: Western Sydney is a diabetes hotspot with a prevalence of 13%. Indigenous Australians shoulder a greater burden, facing a 50% higher risk of diabetes and further complications compared to non-Aboriginal people despite being younger
This study reports on the development of an Aboriginal diabetes clinic in the Mt Druitt Community Health Centre, key clinical characteristics at referral, follow-up visits, and lessons learnt.

Method: We conducted a retrospective analysis of patients from May 2023 to April 2024. The clinic operates weekly, staffed by endocrinologists, advanced trainee, RMO, nurse practitioner, dietitian, and Aboriginal healthcare worker. The clinic caters to five patients weekly with 45-minute consultations, with most patients referred from the Greater Western Sydney Aboriginal Service (GWAHS).

Results: Sixty patients (67% female) with an average age of 55 years, were reviewed across 138 case conferences. The majority (90%) had Type 2 diabetes mellitus. Referring general practitioners attended 17% of case conferences via telehealth. The non-attendance rate was 26.6%. All patients were provided with an opportunity to wear a CGM. The average time in range (baseline) was 44.47% and glucose management indicator (GMI) was 8.2%. Fifteen patients (27%) were discharged after completing treatment (1 to 4 consultations) with an average time in range of 80%. Nine patients (15%) were discharged due to failure to attend appointments (3 to 7 appointments).

Conclusion: The study identifies challenges in engaging Aboriginal communities in diabetes care, addressing logistical and cultural barriers through several initiatives. These include a dedicated phone line staffed by a nurse practitioner for better accessibility and monthly face-to-face case conferences at GWAHS with referring general practitioners. The presence of an Aboriginal healthcare worker providing culturally sensitive support has been crucial in building trust and improving service uptake. These interventions mitigate barriers, potentially reducing appointment anxiety and enhancing diabetes care outcomes for Aboriginal communities.

Delivering Excellent, Efficient, and Equitable Diabetes Care in Regional Australia and Beyond – applying Economic Evaluation to the Implementation of the expanded Diabetes Alliance Program (DAP+)

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Aim: The purpose of applied economic evaluation is to support decision makers in assessing value for money of heath expenditure. The Diabetes Alliance Program (DAP), a co-funded initiative between Hunter New England Local Health District and Hunter New England Central Coast Primary Health Network, has been operating within the region since 2017. The program's positive impacts on clinical and process outcomes for people with type 2 diabetes are established; the efficiency and equity of the program have not yet been evaluated.

The aim of this study is to evaluate the costs and consequences associated with the implementation of DAP and its recent enhancements including nutrition, physical activity, and mental health support (DAP+).

Method: The evaluation employs a staged approach consistent with the evolution of the program from DAP to DAP+. Through micro costing, stage 1 determined the costs associated with delivering care to people with diabetes through DAP, compared to diabetes outpatient services alone. In stage 2, the implementation costs associated with expanded program delivery will be prospectively identified, measured, and valued. The incremental benefit of DAP will be assessed by applying propensity score matching to the linked data within the NSW Health Lumos database.

Results: Stage 1 costing analysis showed that compared to standard outpatient services, the addition of DAP resulted in an incremental net cost saving of $108 per patient for the Local Health District with further predicted increase in the savings as the program expands.

A key driver of cost was the ratio of initial to follow up appointments. Stage 2 of the evaluation is at data collection phase.

Conclusion: DAP+ offers excellent value for money in addition to innovative and integrated diabetes care across regional, rural, and remote Australia.

Developing a Proteomics based Predictive assay for Retinopathy complicating Type 2 Diabetes: The Fremantle Diabetes Study Phase II

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Current retina scans can diagnose diabetes-related retinopathy (DR) once the eye is already damaged, but the tests cannot predict future development of disease. The aim of this study was to identify plasma protein biomarkers for prediction of disease progression in DR.

A proteomics discovery workflow was used to identify potential plasma protein biomarkers for DR. A total of 97 participants with type 2 diabetes from the Fremantle Diabetes Study Phase II were assessed. Retinopathy was graded from retinal images according to the modified Airlie House Classification system for the Early Treatment Diabetic Retinopathy Study. The severity of DR was classified as no DR, mild non-proliferative DR (NPDR), moderate NPDR, or severe NPDR. Participants were divided into four clinical groups according to DR status at baseline and year 4: (1) no DR at baseline and year 4; (2) no DR at baseline but developed DR at year 4; (3) mild/moderate NPDR at baseline and year 4; (4) severe NPDR at baseline and year 4.

A discovery experiment identified 31 candidate biomarkers that were significantly associated with DR (20 prognostic-only, 3 diagnostic-only and 8 prognostic/diagnostic). A further 10 candidates with known DR association in the literature were added to this list. A targeted mass spectrometry assay was then designed to analytically validate the candidate biomarkers. Of the 41 candidates, several were found to be differentially expressed between the different groups – 11 for Group 1 vs Group 2 ($p<0.2$), 1 for Group 1 vs Group 3 ($p=0.066$), and 7 for Group 1 vs Group 4 ($p<0.2$).

The proteins identified from this study have potential as predictive biomarkers for diabetes-related retinopathy, however, further investigation of these biomarkers in a larger cohort is required to better understand their clinical utility.

Development of a KNIME pipeline for Effective collection of International Consensus recommended Continuous Glucose Monitoring Metrics

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Aim: This study aims to develop a KNIME-based pipeline that facilitates the collection of Continuous Glucose Monitoring (CGM) metrics recommended by the 2023 international consensus statement. KNIME, an open-source platform known for its powerful data analytics capabilities and user-friendly, visually appealing interface, is chosen to facilitate this pipeline development.

Method: We conduct a comprehensive review of international consensus recommendations to identify the CGM metrics and their corresponding calculation formulas. Subsequently, we conduct a review to identify and evaluate existing software packages for CGM metric collection, focusing on their capability to process metrics endorsed by international consensus. Based on our findings, we develop the pipeline using the KNIME platform. The pipeline validation is performed for accuracy and efficiency in collecting CGM metrics.

Results: Through review we identified 15 existing software packages designed to collect CGM metrics. Our review suggests a significant gap in the integration and collection of internationally recommended CGM metrics by these tools. The newly developed, novel KNIME pipeline addresses this gap by supporting collection of all international consensus metrics and adapting to diverse data formats and sources. The pipeline is tailored to compute core, secondary, and composite endpoints for prospective clinical trials, and to visualize the Ambulatory Glucose Profile report. Validation using raw CGM data from approximately 300 patients across two clinical studies confirms the pipeline's accuracy and efficiency in collecting CGM metrics.

Conclusion: By developing this novel KNIME-based pipeline, we contribute to the advancement of diabetes research, aligning with the 2023 international consensus recommendations. This pipeline addresses the gaps in existing tools, enabling the collection and integration of international consensus recommended CGM. Tailored to compute both primary and complex endpoints for clinical trials and to visualise the Ambulatory Glucose Profile report, the pipeline may serve as a useful prospective tool for facilitating diabetes research in clinical settings.

Development of a risk prediction model for postpartum onset of Type 2 Diabetes Mellitus, following gestational diabetes; the Lifestyle InterVention IN Gestational Diabetes (LIVING) study

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Aims: To develop novel prediction models to identify women with gestational diabetes mellitus (GDM) who are at high risk of developing type 2 diabetes mellitus (T2DM) postpartum.

Methods: We used data from 1,299 women participating in the Lifestyle Intervention in Gestational Diabetes (LIVING) study from 19 urban hospitals located in India, Sri Lanka, and Bangladesh. Based on clinician input, statistical analyses, and relevant literature, two logistic regression models were developed: one for use during pregnancy and another for post-birth assessment. Predictors included antenatal and postnatal glucose test results, medical history, and biometric indicators. Model validation was performed through cross-validation and bootstrapping. Prediction performance was evaluated using discrimination, calibration, and decision curve analysis (DCA).

Results: Of the 1,299 women with recent GDM and no baseline T2DM, 124 (9.5%) developed T2DM within three years post-birth. The antenatal model included seven predictors (antenatal fasting plasma glucose [FPG] level, antenatal 2-hour glucose level post-oral glucose tolerance test [2h-OGTT], history of recurrent GDM, GDM insulin treatment, parity, history of irregular menstrual cycles, family history of diabetes mellitus) and demonstrated an area under the curve (AUC) of 0.76 (95% CI: 0.72 to 0.80). The postnatal model comprised four predictors (antenatal 2h-OGTT, postnatal FPG level, postnatal 2h-OGTT, postnatal body mass index) and showed an AUC of 0.85 (95% CI: 0.81 to 0.88). Both models demonstrated good calibration, with Brier Scores of 0.08 and 0.07, respectively. The models exhibited minimal optimism in predictive capability after rigorous internal validation processes. DCA showed the models to have superior clinical utility compared to ‘treat all’ and ‘treat none' scenarios.

Conclusions: The developed models effectively predicted T2DM risk among women with GDM, and could contribute to identifying high-risk women to initiate early interventions and reduce progression from GDM to T2DM. External validation in diverse settings is recommended before applying widely.

Keywords: Type 2 diabetes, Prognostic model, Predictive model, Gestational diabetes mellitus, Postpartum

Diabetes after Heart Transplantation is an increasingly Common issue

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Background & Aim: Heart transplantation (HTx) survival rates have improved with advances in immunosuppression and surgical techniques over the last 20 years. With these improvements there has been a greater focus on post-transplant care. Diabetes is common after transplantation and may be pre-existing (type 2 diabetes mellitus, T2DM) or develop after transplant (post-transplant diabetes mellitus, PTDM). In 2015 our institution introduced a dedicated endocrine clinic and registrar integrated into the heart and lung transplant unit. The aim of this study was to compare the incidence and prevalence of diabetes in HTx recipients in two cohorts separated by 20 years.

Methods: Retrospective audit comparing 88 consecutive HTx recipients in 1998 and 141 consecutive HTx recipients in 2018 at the same tertiary referral teaching hospital.

Results: The prevalence of T2DM at the time of HTx increased between 1998 and 2018, 6% (n=5) vs 18% (n=25) respectively, p=0.009. Similarly the incidence of PTDM increased from 15% (n=13) in 1998 to 32% (n=45) in 2018, p=0.005). HTx recipients with T2DM were older in 2018 (mean age 57 ± 9 years) vs 1998 (mean age 44 ± 9 years), p=0.006. The groups without diabetes and with PTDM were similar in age between the two cohorts. Body mass index in the subgroups was not different between the cohorts.

Conclusion: The incidence and prevalence of diabetes after HTx has increased over 20 years. With increasing HTx survival and rates of diabetes, endocrinologists should be incorporated into the care teams of transplant recipients. Further studies of diabetes therapies in this increasing cohort of patients with diabetes after transplantation is warranted.

Diabetes Alliance Program Plus: The Impact of the First year of enhanced funding built on a decade of achievements

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Background: The Diabetes Alliance Program (DAP) was jointly initiated in 2015 to address unmet healthcare needs in metropolitan, rural, and remote regions serviced by Hunter New England Local Health District, and the Hunter New England Central Coast Primary Health Network.

DAP provides GP practices with dedicated performance appraisals for diabetes standards of care; facilitates case conferences involving GPs, practice nurses, endocrinologists, diabetes educators, and people with diabetes as part of a capacity-building initiative; and conducts DAP Masterclasses. After assessing both clinical and economic outcomes, the pilot program transitioned into standard practice in 2017. In 2022, a philanthropic donation of $12.4 million led to the enhancement of program capabilities and the rebranding of DAP as DAP+. Here, we present the first-year impacts and cumulative outcomes since DAP's inception.

Outcomes: In 2023, 61 new GP practices received DAP+ intervention (bringing the cumulative total to 186 since 2017), and 1056 new case conferences with 231 GPs were conducted (a cumulative total of 6100). Fifteen percent of case conference participants identified as Aboriginal or Torres Strait Islanders. Since 2017, over 2,300 clinicians have participated in diabetes Masterclasses across 75 sessions. In 2013, a dedicated telephone advice line and virtual case conference clinics were introduced. "Yarn up" sessions, Indigenous branding, and an Aboriginal-specific reference group were established to co-design culturally appropriate models of care for Indigenous people with diabetes. Research activities included the development and evaluation of digital modules for physical activity, nutrition, and mental health, customized for patients with diabetes. Satisfaction surveys from consumers and clinicians, along with clinical and economic evaluations, confirm the cost-effectiveness of DAP.

Conclusion: DAP has proven to be an effective integrated model of care, and DAP+ further develops, implements, and evaluates additional components to enhance access to and outcomes of the program.

Diabetes and its risks among Australian Pasifika living in Greater Sydney: Baseline assessment from Pasifika Preventing Diabetes programme

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Aim: To assess the prevalence of diabetes and its risks among adult Pasifika residing in Sydney.

Method: Data were collected from April 2022 to May 2024 among Pasifika adults participating in the Pasifika Diabetes Preventing Programme (PPDP), a step wedge peer-support/community activation lifestyle cluster randomised control trial, through churches. Baseline data collection included sociodemographic, and lifestyle behaviours questionnaires (collected by a bespoke data collection platform, BTR), anthropometric measurements, blood pressure, random blood glucose (RBG), and HbA1c. Diabetes was defined by an HbA1c of ≥6.5% or a self-reported diabetes diagnosis. High blood pressure was defined as an average systolic blood pressure of two measurements ≥140 mmHg and/or an average diastolic blood pressure of two measurements ≥90 mmHg, with the two measurements taken 2-3 minutes apart.

Results: To date, baseline assessments occurred in 527 Pasifika adults (mean age 48.5 ± 15.7 years, 55% female). The prevalence of diabetes was 32.1% (95% CI: 28.1-36.2%), comprising of 19.6% with previously diagnosed diabetes (HbA1c 8.8±2.8% and RBG 11.7±6.6 mmol/L) and 12.5% with newly diagnosed diabetes (HbA1c 8.7±2.8% and RBG 10.3±4.6 mmol/L) with 36% had HbA1c 5.7-6.4%. Overweight or obesity was present in 94.8% including 26% with overweight. The prevalence of high blood pressure was 61%. Physical activity guidelines of at least 150 minutes per week were met in 27.2%, but 93% were either contemplating or actively making efforts to adopt healthier dietary habits and/or increase their physical activity levels.

Conclusions: The study identified a high prevalence of diabetes and its associated risk factors among a sample of Pasifika adults in Sydney, including high rates of undiagnosed diabetes and low rates of physical activity. The high intention to improve lifestyle highlights the importance of community-based lifestyle programs to mitigate the risk of diabetes.

Keywords: Australian Pasifika, Diabetes, behaviour change, community-based intervention

Diabetes Prevalence, Inpatient Glycaemic Control and Extent of Metabolic Monitoring in a large, multi-centre Cohort of Medical, Surgical and Psychiatry admissions.

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A bidirectional relationship exists between metabolic and psychiatric conditions. A psychiatry hospital admission may provide opportunities to holistically address this multimorbidity.

Aim: To determine diabetes prevalence, glycaemic control, and extent of metabolic monitoring of individuals with diabetes admitted under psychiatry.

Method: Retrospective, multi-centre, observational study of adult inpatients with length of stay >2 days between 1/1/2018 and 31/12/2021. Demographic and clinical information was extracted from electronic medical record and admissions database.
For a sub-cohort of 200 psychiatry admissions with diabetes, additional data was manually extracted.

Results: 82,693 medical/surgical admissions and 4751 psychiatry admissions were analysed. The psychiatry cohort was younger (41.3±15.5 vs. 65.1±19.8yrs, p<0.001) with less physical comorbidity. Diabetes diagnosis was recorded in 8.7% of psychiatry admissions and 21.0% of medical/surgical admissions (Table). Of those with diabetes, mean point-of-care capillary blood glucose (BGL) did not differ between psychiatry and medical/surgical admissions (9.1±3.1 vs. 9.1±2.8mmol/L, p=0.314). Fewer BGL checks were performed in psychiatry and half as many adverse glucose days recorded.

Of the subcohort of diabetes within psychiatry (n=200), Schizophrenia was the most prevalent mental health diagnosis (38%). 82.5% were treated with at least one antipsychotic. Use of agents with high risk of metabolic adverse effects was common (Olanzapine 25%, Clozapine 8.5%). Mean HbA1c was 7.7±2.0% with 55.6% ≥7.0%. 20% were not receiving glucose-lowering therapy. Diabetes was omitted from discharge summary in 55.5% of cases. Blood pressure (99.0%), BMI (89.5%) and eGFR (95.5%) were recorded in most patients. 34.5% had full lipid profile recorded and 10.5% uACR. Lipid-lowering and antihypertensive agents were prescribed to 57% and 38% respectively with majority achieving treatment targets (64.9% and 65.9%). 40% of the subcohort could be classified as at high atherosclerotic CVD risk.

Conclusion: In this large psychiatry cohort, we identify gaps and opportunities to provide metabolic management.

Table: Whole cohort data

	Psychiatry Admissions (n=4751)			Medical/Surgical Admissions (n=82,693)	
	Diabetes (n = 414)	**No Diabetes (n = 4337)**	***P-value*[%]**	**Diabetes (n=17,405)**	***P-value*[§]**
Age (years) (mean (SD))	53.4 (14.4)	40.2 (15.1)	*<0.001*	72.3 (14.0)	*<0.001*
Sex (n, %)			*0.538*		*0.349*
Male	220 (53.1)	2392 (55.2)		9867 (56.7)	
Female	194 (46.9)	1939 (44.7)		7537 (43.3)	
Weight (kg) (mean (SD))					
Male	80.1 (21.3)	78.6 (22.5)	*0.562*	78.0 (22.0)	*0.483*
Female	82.8 (21.5)	77.0 (21.5)	*0.029*	78.3 (22.2)	*0.070*
Diabetes total					*<0.001*
Type 1 (n, % of DM)	11 (2.6)	-		584 (3.4)	
Type 2 (n, % of DM)	341 (82.4)	-		15,680 (90.1)	
Other/Unknown (n, % of DM)	62 (15.0)	-		1141 (6.5)	
Mean BGL (mmol/L) (mean (SD))	9.1 (3.1)	6.2 (1.5)	*<0.001*	9.1 (2.8)	*0.314*
BGL checks per day of stay (SD)	0.5 (1.8)	0.1 (0.2)	*<0.001*	2.9 (3.0)	*<0.001*
At least one adverse glucose day (BGL<4.0 or >15mmol/L) (n, %)	129 (35.5)	78 (4.0)	*<0.001*	7127 (43.2)	*0.003*
Length of stay (days) (median, IQR)	14.8 (31.3)	8.4 (15.7)	*<0.001*	5.9 (7.7)	*<0.001*

[%] Psychiatry admissions with diabetes cf. psychiatry admissions without diabetes

[§] Psychiatry admissions with diabetes cf. medical/surgical admissions with diabetes

405

Diabetes remission following Bariatric Surgery in people with Young-onset vs Older onset Type 2 Diabetes: an Australian prospective cohort study

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Introduction and Aims: Young-onset T2DM (YT2DM) is a particularly aggressive form of diabetes characterised by rapid progression of micro- and macro-vascular complications and early manifestation of cardiometabolic risk factors, when compared with older-onset T2DM. Given the accelerated deterioration in *β*-cell function seen with YT2DM, we compared rates of diabetes remission following bariatric surgery in those with YT2DM (age of diagnosis < 40 years) vs older-onset T2DM (age of diagnosis 40 years or older).

Methods: This prospective cohort study included adults with T2DM and BMI ≥ 35 kg/m^2 who attended a multidisciplinary metabolic clinic and underwent bariatric surgery. The primary outcome was complete diabetes remission (defined as HbA1c < 6.0% and at least 3 months off glucose-lowering medications). Rates of partial diabetes remission (defined as HbA1c < 6.5% and at least 3 months off glucose-lowering medications) were also examined.

Results: Preliminary analyses showed that those with YT2DM (n=30) were significantly younger but were more likely to have had a duration of diabetes > 10 years compared to those with older-onset T2DM (n=24) ($p < 0.05$ for both). Those with YT2DM had a significantly lower rate of complete diabetes remission at 12 months following surgery compared to those with older-onset T2DM (40.0% vs 70.8%, p-value 0.031), though this was no longer significant on multivariate analysis after adjusting for baseline insulin use, duration of T2DM > 10 years, type of bariatric surgery, and weight loss (aOR 0.318, 95% CI 0.059 - 1.710). Rates of partial diabetes remission were similar between those with YT2DM versus those with older-onset T2DM.

Conclusions: This preliminary report included relatively small numbers of participants but the limited data available to date suggests that early and aggressive weight intervention needs to be prioritised in those with YT2DM in order to maximise the chances of complete diabetes remission in this cohort.

Diabetic Ketoacidosis Masked by Cannabis use: A wolf in sheep's clothing

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Introduction: Diabetic ketoacidosis (DKA) is characterised by hyperglycaemia, ketosis and high anion gap metabolic acidosis. Clinicians mostly rely on pH and bicarbonate to diagnose and classify DKA. Cannabis use has been associated with atypical acid-base profile in DKA which may lead to confusion in diagnosis.

Case: A 25-year-old man with type 1 diabetes mellitus presented with 2 days of nausea and vomiting. Emesis occurred 4 to 6 times a day. He reported good adherence to insulin therapy. Physical examination revealed dry mucous membranes and mild epigastric tenderness. Point-of-care investigations revealed a pH of 7.42 (7.30–7.43), bicarbonate of 26 mmol/L (22–30), glucose of 20.8 mmol/L, ketone of 3.2 mmol/L and anion gap of 18 (6–16), which did not meet the criteria for typical DKA. He was commenced on intravenous insulin infusion and fluid therapy. Infection, myocardial infarction, pancreatitis and medication non-adherence were excluded. A urine drug screen was positive for cannabinoids. Upon record review, the patient had a history of recreational cannabis use. He was transitioned to subcutaneous insulin following resolution of hyperglycaemia and ketosis 24 hours later.

Conclusion: The diagnosis of DKA in cannabis users may be missed due to its differing and conflicting acid-base profile compared with non-cannabis users. There is a higher pH than would be expected for the degree of symptoms and the extent of ketosis in those using cannabis. The underlying mechanism is hypothesised to be related to cannabis-related delayed gastric emptying and cyclic nausea and vomiting. Diabetic keto-alkalosis, rather than DKA, may be present as a consequence of recurrent vomiting that leads to gastric acid loss. This case demonstrates that cannabis use can mask DKA and highlights the importance of assessing for illicit drug use, particularly cannabis, in patients with clinical suspicion of DKA but with unexplained or unusual acid-base balance.

Diabetic Peripheral and Autonomic Neuropathy and Socioeconomic status in people with Type 2 diabetes in Bangladesh.

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Aim: Studies, from mostly Caucasian populations, have reported that diabetic peripheral neuropathy, the commonest diabetes-related complication, represents a substantial burden on the most socio-economically disadvantaged groups impacting diabetes care. This relationship, however, has not been optimally studied in countries such as Bangladesh. We evaluated the relationships between diabetic peripheral neuropathy and socio-economic parameters in a community setting in Bangladesh.

Methods: 448 unselected individuals (T2D: N = 227, female: 65.2%, mean age: 50.9±0.74 years, BMI: 24.6±0.22 Kg/m^2, waist circumference: 90.8±0.58 cm, duration of known diabetes: 6.3±0.34 years, random blood glucose: 13.0±0.54 mmol/L and non-diabetic 'controls': N = 221, females: 57.9%, mean age: 42.9±0.92 years, BMI: 23.9±0.23 Kg/m2, waist circumference: 87.6±0.60 cm, random blood glucose: 6.7±0.28 mmol/L) were recruited from the community in Bangladesh. Participants completed validated questionnaires for diabetic peripheral neuropathy (MNSI-Q) and autonomic neuropathy (COMPASS-31) to assess neuropathy, where score of ≥7 for MNSIQ and ≥16 for COMPASS-31 cutoff considered to indicate neuropathy respectively and compared with socio-economic parameters. P value ≤0.05 indicate statistical significance.

Results: Overall, individuals with T2D reported higher prevalence of peripheral (43.2% vs 9.5%, P<0.001) and autonomic (46.0% vs 11.6%, P<0.001) neuropathy compared to controls and this was higher across all categories of sociodemographic variables. The higher prevalence of neuropathy was observed across all categories of sociodemographic variables, except among urban dwellers, those were graduate and among single/divorced/widowed (Table 1). In both cohorts (T2D and non-diabetic controls) prevalence of peripheral and autonomic neuropathy was higher in female, rural dwellers and individuals with lower education. Rate of peripheral neuropathy was higher among those with longer duration of diabetes (>5 Yrs) and those were single/divorced/widowed (P<0.05), but autonomic neuropathy was not (P>005).

Conclusions: Diabetic neuropathy is common in T2D and associated with older age, female, rural areas, illiterate, divorced or widowed and obese.

Table 1: Comparison of peripheral and autonomic neuropathy between T2D and non-diabetic controls by socio-economic characteristics

	MNSIQ ≥7			COMPASS31 ≥16		
	Type 2 diabetes (n=227)	**Non-diabetic controls** (n=221)	**P**	**Type 2 diabetes** (n=227)	**Healthy control (n=221)**	**P**
Gender						
Female (n1=148, n2=128)	54.7%[a]	15.6%[a]	***	85.8%[a]	78.1%[a]	ns
Male (n1=79, n2=93)	21.5%[b]	1.1%[b]	***	67.1%[b]	36.6%[b]	ns
Area of residence						
Rural (n1=179, n2=158)	46.9%[a]	12.7.8%[a]	***	84.4%[a]	66.5%[a]	***
Urban (n1=48, n2=63)	29.2%[b]	1.6%[b]	***	60.4%[b]	46.0%[b]	ns
Education						
Up to Class five (n1=75, n2=97)	56.2%[a]	15.5%[a]	***	88.3.%[a]	70.1%[a]	***
Class twelve (n1=24, n2=86)	30.7%[b]	7.0%	***	72.0%[b]	52.3%[b]	*
Graduate (n1=128, n2=38)	12.5%[c]	0.0%[b]	***	54.2%[b]	55.3%	ns
Marital status						
Married (n1= 213, n2=197)	40.4%[a]	8.6%	***	78.4%	60.4%	***
Single/divorced/widowed (n1=14, n2=24)	85.7%[b]	16.7%	***	92.9%	62.5%	ns
Per capita annual income						
Lower (<2650 USD) (n1=73, n2=)	57.5%[a]	14.3%	***	86.3%	71.4%[a]	*
Upper (>2650 USD) (n1=154, n2=)	36.4%[b]	6.6%	***	76.0%	54.0%[b]	**

*: P<0.05; **:P<0.01; ***: P<0.001, ns: P>0.05 [each row in each category of sociodemographic characteristics with different superscript indicates significant difference (P<0.05); n1= total number in T2D, n2=total number in non-diabetic controls

Digital Interventions to Prevent Type 2 Diabetes: A Systematic Review

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Abstract title (max. 25 words) - Abstract (max. 300 words):

Aim: Digital health has transformed how health care is provided and experienced, leading to great health system efficiencies and clinical benefits. In the past ten years, advanced digital interventions have been applied to diabetes prevention studies. No study has systematically and comprehensively been undertaken to examine effectiveness of these cutting-edge digital interventions. Our aim was to systematically review the current literature to examine the effectiveness of digital interventions for type 2 diabetes prevention.

Method: The review was conducted and reported following PRISMA guidelines 2020 for the last 10 years. We searched four databases (PubMed, Embase, CINAHL and Web of Science) in the last 10 years and systematically reviewed 52 articles of effectiveness of digital interventions for type 2 diabetes prevention. Digital interventions were coded using WHO's digital intervention classification 2023 version.

Results: Our review covered a variety of digital interventions, categorised as untargeted client communication, targeted client communication, personal health tracking, telemedicine, health professional decision support and data management. The efficacious outcomes of digital interventions in prevention of type 2 diabetes were demonstrated, particularly within categories of targeted client communication, personal health tracking and telemedicine. The combination of diverse digital interventions displayed superior outcomes. Using digital interventions with human support was more effective than digital interventions alone. However, there is still lack of evidence of effective implementation of virtual reality, artificial intelligent or big data in type 2 diabetes prevention.

Conclusion: Digital interventions were effective tools for diabetes type 2 prevention. Health professionals should use different kinds of digital interventions and integrate them with clinical support to optimize the effectiveness.
Targeted client communication, personal health tracking and telemedicine were effective tools. Further research is needed to examine the effectiveness of virtual reality, artificial intelligent or big data for type 2 diabetes prevention.

DINGO Hypoglycaemia: Adherence to Hospital Policy and Efficacy for Preventing recurrent Inpatient Hypoglycaemia

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Aim: Hypoglycaemia is a common inpatient complication with potential for serious harm. While institutions typically mandate protocolised hypoglycaemia responses, systematic exploration of adherence to these is lacking. We aimed to characterise adherence to and efficacy of an institutional hypoglycaemia protocol and understand factors associated with recurrent hypoglycaemia.

Methods: This study explored a population subset from the Diabetes IN-hospital: Glucose and Outcomes (DINGO) prospective cohort study, which was a 26-week study involving inpatients from a quaternary hospital with ≥2 random capillary measurements (https://doi.org/10.1210/clinem/dgae051)[1]. Admissions with level 2 hypoglycaemia (blood glucose [BG] <3.0 mmol/L) formed the study population. Stratification was into groups experiencing 1 vs. >1 hypoglycaemia episodes; treatment efficacy and factors contributing to hypoglycaemia recurrence were assessed.

Results: Of 230 hypoglycaemia episodes, 3 (1%) demonstrated complete adherence to the hospital hypoglycaemia policy. Initial treatment with rapid acting carbohydrate was completed as per policy in 167/230 (73%), but long-acting carbohydrates were administered in only 89/230 (39%) cases. Early BG monitoring (within 15 minutes following hypoglycaemia treatment) occurred within the recommended timeframe in 204/230 (89%) cases, but hourly BG monitoring for 4 hours post treatment occurred in just 3/230 (1%) cases. Of note, glycaemic medication changes within 24 hours prior to the hypoglycaemic event were observed in only 23% of the single-episode population vs. 43% of the recurrent population. In people with documented altered conscious state during hypoglycaemia, a medical review was more likely to be performed in those with single episode (7/13 [54%]) vs. those with recurrent episodes (2/17 [12%]). Total daily insulin, time of hypoglycaemia, and specialist inpatient diabetes referrals were similar in both groups.

Conclusion: We identified high lack of adherence to an institutional hypoglycaemia protocol, with recent glycaemic medication changes and omission of mandatory medical reviews as associated iatrogenic factors for recurrent hypoglycaemia in the inpatient settin

Reference:

1. Hyperglycemia in Hospital: An Independent Marker of Infection, Acute Kidney Injury, and Stroke for Hospital Inpatients, *The Journal of Clinical Endocrinology & Metabolism*, 2024;, dgae051, https://doi.org/10.1210/clinem/dgae051

Does Flash Continuous Glucose Monitoring Improve dysglycaemia In Patients with T2D discharged from hospital – The FLASH-CGM Pilot RCT

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Background: Poor glycaemic control is common for patients discharged from hospital with type 2 diabetes, and can potentially contribute to further morbidity. Continuous glucose monitoring (CGM) is well established in the management of type 1 diabetes, and has also become the preferred tool for glycaemic monitoring in those with type 2 diabetes. This project was a small pilot randomized trial looking at providing CGM to patients with T2D who were discharged from Blacktown hospital.

Methods: Upon discharge, patients were randomized to either receive a Freestyle Libre CGM or to use traditional self-monitoring of blood glucose. We collected pathological data including HbA1c, as well as various CGM metrics for individuals in the intervention group. Patients were then followed-up at 3-4 months. Control patients were provided with a blinded CGM at follow-up to compare time-in-range and other CGM metrics.

Results: 32 patients were recruited and randomized to receive treatment. There was difficulty with recruitment due to the COVID-19 pandemic, and substantial loss to follow-up, leaving a final sample of 15 patients to analyze.
Due to the small sample size, there were no significant differences on any of the primary outcome measures. HbA1c was reduced in both groups from a baseline of 11.5% to 8.4% ($p<0.001$) but there was no difference in the change between groups ($p=0.29$). The intervention group had slightly lower GMI, with 7.7% in control vs 7.6% in intervention, but this was not statistically significant ($p=0.96$).

Conclusion: This study shows the challenges of conducting research using CGM during a pandemic. While the initial pilot aimed for 100 patients, the COVID-19 pandemic substantially limited recruitment in 2021 and 2022, and the trial was eventually ceased due to low retention of participants. We found suggestive benefits for CGM but the small sample size limits inferences.

Does Health Literacy level Affects Adherence to Anti-Diabetic Medication in patients from Ethno-Minority Background?- A systematic review.

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Aim: Optimal self-management and adherence to medical treatment are crucial for patients living with Type 2 Diabetes Mellitus (T2DM) to achieve desired health outcomes. Lower levels of health literacy are associated with poor medication adherence, but there is limited evidence on this association among ethnic minority groups with T2DM. The aim of this systematic review was to synthesise the evidence on the relation between health literacy and medication adherence among adults from ethnic minority backgrounds living with T2DM.

Method: Systematic searches were conducted in Medline (Ovid), The Cochrane Library, Embase (Ovid), PsycInfo (EBSCO), and Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCO) for eligible studies. Studies published in the English language with no restriction on the date of publication and design were included. Screening and selection of studies, assessment of methodological quality, and data extraction were conducted by two reviewers independently.

Results: The systematic search and related reference search yielded 6,318 records, which was reduced to 4,573 after removing duplicates. After screening the studies based on title and abstract, 51 studies were selected for full-text review out of the 4,267. The evaluation of 51 studies led to the inclusion of 13 articles representing 11 unique studies in the final review. Final assessment of the data from 11 studies showed only two studies support significant association between health literacy and medication adherence in people from an ethnic minority background.

Conclusion: Current evidence on the link between health literacy and medication adherence among ethnic minority adults with Type 2 Diabetes Mellitus (T2DM) is limited and inconclusive. There is variability in the findings, highlighting the need for further research into this association within ethnic minority populations. To address the disparities arising from cultural and linguistic differences, it is needed to conduct well designed studies that specifically target this demographic.

Drug Repurposing of an AP-1 inhibitor T-5224 for Diabetes Associated Atherosclerosis.

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Background. Atherosclerosis is a major contributor to cardiovascular disease (CVD) in diabetes. Residual increased risk of CVD remains even after treatment of standard risk factors specifically hyperglycaemia. Therefore, there is a huge potential for mechanism-based drug repurposing. Multiple anti-inflammatory drugs including those originally developed for rheumatoid arthritis have been assessed for efficacy in CVD clinical trials. A small molecule inhibitor of a transcription factor Activator Protein 1 (AP-1), T-5224 has been previously shown to prevent and resolve rheumatoid arthritis in mice. Although T-5224 has been advanced to a phase II clinical trial with an excellent safety profile, however, its role in CVD in diabetes is unknown.

Methods. *In vitro* studies involving cell culture models, mimicking diabetes-induced EndMT, microfluidics-based proatherogenic low shear stress conditions in human aortic endothelial cells (HAECs), and foam cell formation in human THP-1 monocytes, were conducted to investigate anti-atherogenic properties of T-5224. Moreover, atheroprone Apoe$^{-/-}$ mice made diabetic with streptozotocin, were treated with T-5224 in an intervention study.

Results. AP-1 inhibition with T-5224 attenuated *EndMT* and related gene expression changes as assessed by RNA sequencing. Several AP-1 target genes were identified including Col1A2, Col4A1, TGFB, THBD directly relevant to EndMT. Low shear stress ± high glucose mediated AP-1 activation in microfluidic experiments. T-5224 stimulation of HAECs not only blunted AP-1 activity but also reversed gene expression changes of *CAVIN2* and *TSC22D3* that are known for their role in endothelial function. Moreover, AP-1 members were also upregulated in the THP-1-based *in vitro* model of high glucose- and oxidised LDL-induced foam cell formation. THP-1 derived foam cells showed increased AP-1 activity and lipid uptake. Interestingly, T-5224 blunted *foam cell formation.* Critically, treatment with T-5224 attenuated atherosclerosis in diabetic *Apoe$^{-/-}$* mice.

Conclusion. This study implicate that T-5224 is a potential candidate for drug repurposing in diabetes associated atherosclerosis.

Duodenal Mucosal Re-Cellularization via Pulsed Electric Field Induced Electroporation (ReCET) in Type 2 Diabetes: First-In-Human Experience

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Background: ReCET utilizing an endoscope administered non-thermal pulsed electric field to stimulate duodenal cellular regeneration.may correct abnormal duodenal signaling in type 2 diabetes (T2D). We report updated results from a feasibility study of ReCET therapy in T2D.

Method: This multicenter, open-label, treatment-only study recruited 18-70 yr old; T2D <10 years; HbA1c 7.5%-11.0%; BMI 24 - 40 kg/m2; C-peptide > 333 pmol/l; and on 1-4 non-insulin glucose-lowering medications (GLMs) which were unchanged post-procedure.

Primary endpoint: Device/procedure-related serious adverse events (SAEs). Secondary endpoints: Changes in metabolic parameters at 24W.

Results: Participants received single energy application (Single Tx, n=12), double energy application (Double Tx, n=18), or the Gen 2 catheter (Gen 2, n=21). Procedure success was 100% with no related SAES. Common AEs were sore throat (25/51) and transient diarrhea (11/51), and mostly (76%) mild. Glycemia improved post procedure with trends suggesting an energy-dose response (Figure 1). Mean (SD) HbA1c at 24 wks vs baseline was 7.2 (1.2)% vs. 8.8 (0.9)% ($p<0.01$) in the Gen 2 group. Gen 2 group follow up is ongoing. Durability of glycemic improvement was observed in the Double Tx group at 48 wks.

Conclusions: ReCET therapy is feasible and safe. Glycemic observations support further research.

Early Inpatient Intervention with Electronic Specialist-led Model of Diabetes care Improves Glycaemia after Hospitalisation: Follow-up of STOIC-D Surgery RCT

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Aim: To assess the effect of an early, electronic specialist-led model of inpatient diabetes care on long term glycaemic outcomes following discharge.

Methods: The STOIC-D trial has demonstrated early, electronic specialist-led care by an inpatient diabetes service reduces inpatient hyperglycaemia. This follow-up study assessed glycaemic outcomes following discharge in a subgroup of 360 STOIC-D trial patients with admission HbA1c ≥ 7% and alive 1 year following hospitalisation. First HbA1c between 3-15 months following discharge was collected. Paired-sample t-test was used to compare baseline characteristics and mean absolute change in Hba1c between cohorts. Multivariable logistic regression identified predictors of clinically significant reduction in HbA1c, defined as ≥ 0.3%. Multivariable linear regression was used to assess correlation of baseline characteristics with change in HbA1c, with multicollinearity assessed in the final model.

Results: Baseline characteristics and admission HbA1c was similar between intervention and control arms (8.6% vs 8.5% [*p*=0.54*]*; 70.5 mmol/mol vs 69.5 mmol/mol [*p* = 0.54]). Average post-discharge HbA1c was lower in the intervention arm compared with control (8.2% vs 8.5%, [*p*= 0.095]; 67 mmol/mol vs 70 mmol/mol [*p*=0.095]). There was a greater reduction in HbA1c following discharge in intervention arm (-0.4% vs 0.04% [*p*= 0.041]; -3.9 mmol/mol vs 0.4 mmol/mol [*p*= 0.041]). A clinically significant reduction in HbA1c occurred more frequently in patients in the intervention arm (54% vs 36%, [*p*= 0.001], adjusted odds ratio 1.8 (95% confidence interval [CI]:1.1-2.70). Adjusted multivariable linear regression demonstrated inclusion in the intervention arm was correlated with reduction in discharge HbA1c (*p*=0.041).

Conclusion: Post hospitalisation, HbA1c improved following intervention with an early, electronic specialist-led consultation in hospital. Early intervention models of care could significantly improve medium-term glycaemia after hospitalisation.

Educational Interventions in the Management of Hyperglycaemia in Hospital inpatients at an Australian Teaching Hospital

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Background: Hyperglycaemia is a common issue affecting patients with Type 2 Diabetes who are hospital inpatients and can lead to increased morbidity and mortality as well as length of inpatient stay. There are many challenges to maintaining glycaemic control in this population of hospital inpatients and despite adherence to a patient's original insulin regimen, additional doses of rapid acting insulin are often administered. An Australia health service uses printed guidance to advise on supplemental insulin dosing for this population.

Objective: This study used educational interventions to inform on call doctors at an Australian teaching hospital about existing insulin prescribing guidelines to attempt to improve insulin prescribing to recommended guidelines and reduce the frequency of patient reviews for hyperglycaemia.

Method: A teaching hospital was audited over a weeklong period, the adherence to insulin guidelines as measured by comparing prescribed and recommended insulin units was determined for each patient with hyperglycaemia. Additionally, the number of reviews per patient due to hyperglycaemia was calculated. Two educational interventions were held for doctors working at the hospital with a subsequent reaudit after both interventions.

Results: There was no significant change in adherence to insulin prescribing guidelines following either intervention (3.29 $\pm$ 4.28 international units prior to intervention vs 2.65 $\pm$ 5.80 international units after both interventions). Additionally, there was no significant change in the frequency of review required for each patient with hyperglycaemia (1.75 $\pm$ 1.46 reviews prior to intervention vs 2 $\pm$ 1.15 after both interventions).

Conclusion: This study did not improve either adherence to recommended guidelines of insulin prescribing or reduce the frequency of doctor review required by patients with hyperglycaemia. This may be reflective of the complexity of causes of insulin prescribing and why no particular strategy of subcutaneous insulin therapy has been endorsed as superior.

Effect of a Digitally-enabled Diabetes prevention Peer Support Program on Weight over 6-months

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Aim: Scalable strategies to prevent type 2 diabetes in Australia, including in semi-rural/rural/remote areas, are limited. Face-to-face peer support shows great promise for improving lifestyles and preventing diabetes. Digital technologies offer platforms for scaling peer support, providing online structured support to assist peer support facilitators (PSFs) in delivering interventions. We explored feasibility and effect on weight of digital-enabled peer support in inner-regional Sydney.

Method: Participants were invited to participate through general practitioners(GP), community groups and workplaces and PSFs through local networks and students in a postgraduate Diabetes course. Participants received an online questionnaire to collect demographics. Weight was measured by a researcher/their general practitioner. Participants were provided with unlimited access to an online, individualised, behaviour change platform, incorporating self-monitoring and goal-setting relating to physical activity and healthy eating, for 6 months, plus PSF support calls monthly. Weight measurements were repeated after 6-months. Change in weight was explored (paired t-test).

Results: Participants were recruited via GPs(n=108), a Men's shed(n=4), local council(n=2), self-referral(n=1) and Facebook(n=1). PSFs were recruited through a community event (n=1), via GPs (n=2) and a local university (researcher (n=2), a postgraduate Diabetes course (n=15)). Twenty PSFs were trained,10 delivered the intervention (3 dropped-out, 7 not commenced).

116 participants completed baseline questionnaires, 80 (69.9%) of whom (43% male, aged=59(SD=10.8)yrs, weight=98.4(SD=19.7)kg) successfully onboarded the platform. 37 participants were active on the platform (logged achievements and weights for ≥1/24 weeks). Main reasons for dropping out were personal/family circumstances, unable to commit, unable to contact participants. Weight loss among the first 29 completers was -4.31(SD=3.44kg), $p<0.001$. Participants logged achievements on 8.6(SD=10.1) weeks/24 weeks.

Conclusion: Digital-enabled peer support reduced weight over 6-months. Recruitment via GP was the most successful method. Additional ways of supporting individuals to on-board and retain use in digital approaches to diabetes prevention need identified.

Effect of Baricitinib on growth in the BANDIT trial

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Baracitinib, a Janus kinase (JAK)1/JAK2 inhibitor, preserved β-cell function in the Baracitinib in New-onset Type 1 Diabetes Trial (BANDIT)[1]. JAK2 is part of the growth hormone signalling pathway. It has not been well-established whether JAK inhibitor use has a significant impact on growth in paediatric patients.

Aim: The primary objective of this study was to compare growth in paediatric patients taking 4mg baracitinib daily versus placebo.

Methods: In a post-hoc analysis, growth was analysed in participants in the BANDIT study aged 10-15 years. Height was measured at visits across the 2-year trial period, at 0, 6, 12 (on treatment) and 24 months (follow-up) and used to calculate normalised height (Z-score) according to CDC growth charts. Comparisons were made using linear mixed effects model with categorical time, comparing 12-month normalised height (thus removing the effect of sex and age) while adjusting for baseline values.

Results: Z-score (mean $\pm$ sd) at week 48 was .53 (.88) and .39 (1.04) in baricitinib (n=21) and placebo (n=13) groups respectively, p=.48. Similar results were also observed at 24 weeks (p=0.655). The mean change in Z-score over 24 weeks for the baracitinib group was -0.0010 [95% CI -0.10, 0.10] (p=0.986), while it was slightly higher for the placebo group at 0.08 [-0.05, 0.22](p=0.334). During follow-up these values were -0.07 [-0.16, 0.03] (baracitinib, p=0.913) and -0.14 [-0.27, -0.02](placebo, p=0.025).

Conclusion: There was no significant reduction in growth observed in participants taking Baricitinib during either the treatment or follow-up periods. Taking the drug in the morning would mean limited inhibition of JAK2 overnight, possibly explaining why no difference was observed. The very small differences observed make it unlikely that a larger trial would show significant growth reduction on this dose of baricitinib.

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Effect of Empagliflozin on all-cause Hospitalisation in EMPA-KIDNEY

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Aim: Chronic kidney disease (CKD) increases the risk of hospitalisation. In the randomised, phase III, EMPA-KIDNEY trial, empagliflozin significantly reduced the risk of all-cause hospitalisations ([ACH] first and recurrent) vs placebo. This post-hoc analysis of the EMPA-KIDNEY trial examines the burden of ACH in CKD and the effects of empagliflozin on ACH.

Methods: Participants with CKD (n=6609) were randomised to empagliflozin 10 mg or placebo. Reasons for hospitalisations were derived from adverse events (AEs) leading to hospitalisation, assessed by system organ class (SOC).

Results: 1995 participants had ≥1 ACH (1895 ACH in placebo and 1611 in the empagliflozin 10 mg groups). The mortality rate in participants with ≥1 hospitalisation was 12% after 1 year and 18% after 2 years and risk of death was ~10 times higher vs those without (hazard ratio [HR] 9.53; 95% CI 7.18, 12.64; p <0.0001). Most common reasons for ACH were infections and infestations, surgical and medical procedures, cardiac disorders, renal and urinary disorders, and investigations. Risk of ACH was significantly reduced for empagliflozin vs placebo (HR 0.86, 99.03% CI 0.75, 0.98, p=0.0025). This was consistent regardless of baseline diabetes status, estimated glomerular filtration rate or UACR. Mean cumulative incidence of ACH in empagliflozin and placebo groups diverged shortly after randomisation and continued to separate over time. Risk of hospital admissions attributed to cardiovascular (CV), renal or metabolic conditions was significantly lower with empagliflozin vs placebo (p<0.05).

Conclusion: Treatment with empagliflozin significantly reduced risk of all-cause hospitalisations, including those attributed to CV, renal or metabolic conditions.

Effect of Physical Activity intensity on Carotid Intima-media thickness in people with Type 2 diabetes Mellitus

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Objective To analyze the relationship between different levels of physical activity (PA) and Carotid intima-media thickening (CIMT) in T2DM.

Methods From 2019 to 2022, a total of 3,099 people with T2DM were selected from endocrinology clinics at two tertiary hospitals in Jiangsu Province, China. The IPAQ was used to assess their PA level, and they were categorized into mild-intensity, moderate-intensity, and high-intensity PA group. Restricted cubic splines were used to evaluate the dose-response relationship between PA and CIMT thickening. For the patients with sub-optimal HbA1c, stratified analyses were performed based on the status of BP and blood lipids.

Results There was a nonlinear relationship between PA and the risk of CIMT thickening ($P_{nonlinear}$=0.029). Moderate-intensity PA was negatively associated with the risk of CIMT thickening (*OR*=0.747, 95%CI:0.605,0.923, $P<0.05$). Stratified analyses of patients with sub-optimal HbA1c showed that, in the mild-intensity PA group, compared with the subjects that neither BP nor LDL-C reached the standard, reaching the standard for either index or both was negatively correlated with CIMT thickening (*P*<0.05). Compared with the subjects that only BP reached the standard, both indicators reached the standard and only LDL-C reached the standard was negatively correlated with CIMT thickening (*P*<0.05). Compared with the subjects that only LDL-C reached the standard, both indicators did not reach the standard and only BP reached the standard was positively associated with CIMT thickening (*P*<0.05). In the moderate-intensity PA group, there was no statistical correlation between the achievement of each indicator and CIMT thickening. In the high-intensity PA group, there was a negative correlation between the achievement of both indicators and CIMT thickening (*P*<0.05).

Conclusion There was a dose-response relationship between PA and CIMT thickening. Moderate-intensity PA was negatively associated with CIMT thickening, especially in patients with sub-optimal HbA1c, and, focusing on LDL-C compliance is particularly important to avoid CIMT thickening.

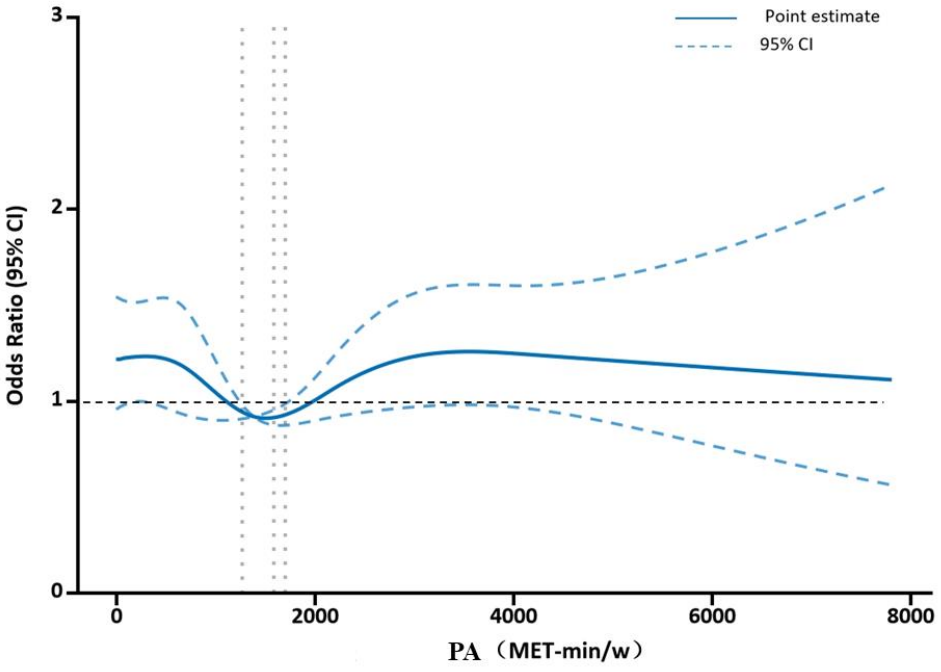

Figure1 Restricted cubic spline plot of PA with carotid intima-media thickening

Adjusted for patient sex, age, education, smoking, alcohol consumption, duration of T2DM, history of high blood pressure, history of hyperlipidemia, hypoglycemic agents, antihypertensive agents, lipid-lowering agents, BMI, HbA1c, TG, HDL-C, LDL-C
Abbreviations: BMI: body mass index, HbA1c: hemoglobin A1c, TG: triglycerides, LDL-C: low-density lipoprotein cholesterol, HDL-C: high-density lipoprotein cholesterol

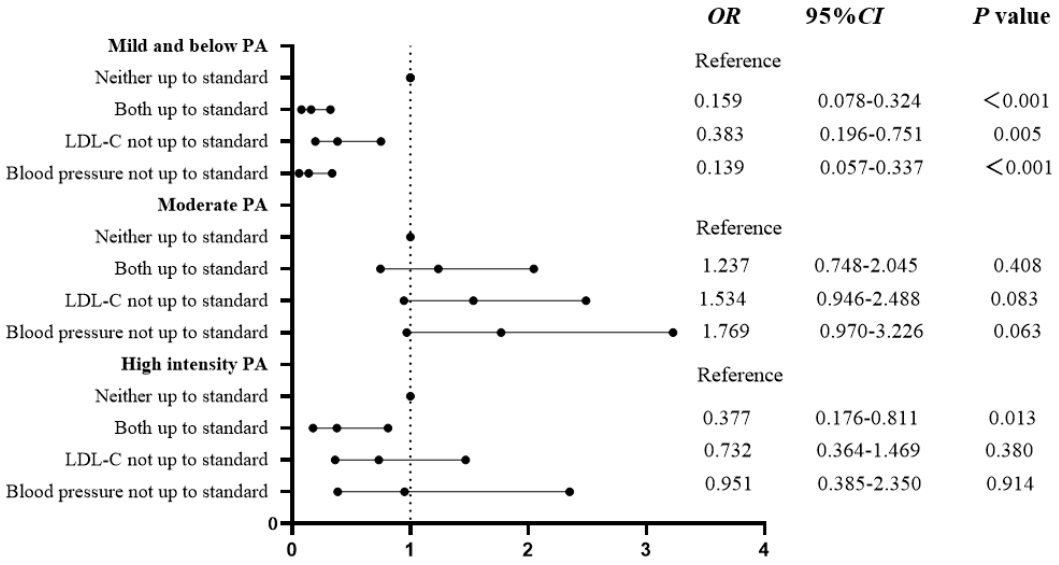

Figure 2(a) Relationship between PA and risk of CIMT thickening in different metabolic control attainment scenarios

Adjusted for sex, age, education, duration of T2DM, smoking, alcohol consumption, history of high blood pressure, history of hyperlipidemia, hypoglycemic agents, antihypertensive agents, lipid-lowering agents, BMI, HbA1c, HDL-C

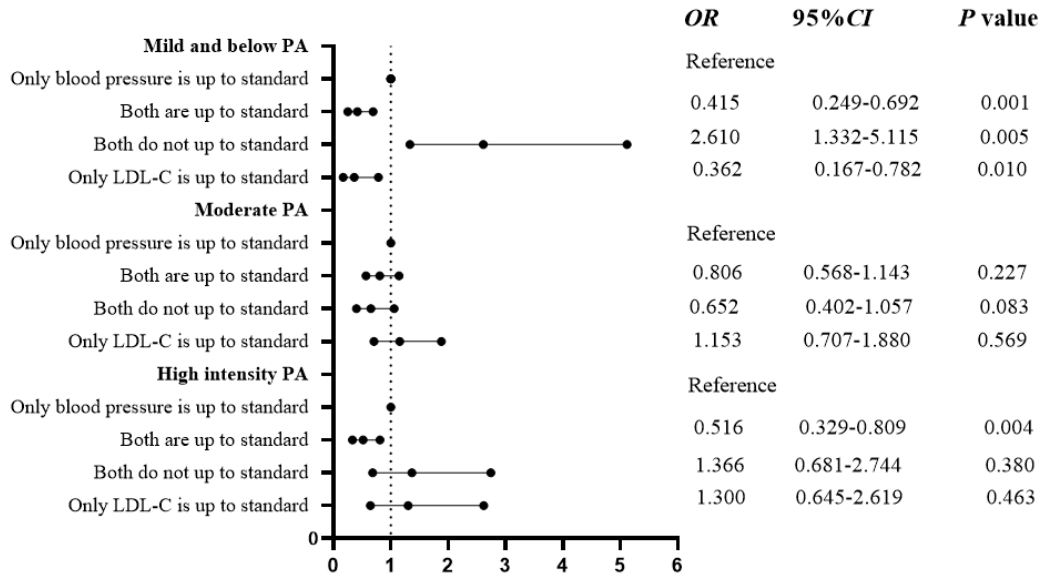

Figure 2(b) Association between PA and CIMT thickening risk for different metabolic control attainment scenarios

Adjusted for sex, age, education, duration of T2DM, smoking, alcohol consumption, history of high blood pressure, history of hyperlipidemia, hypoglycemic agents, antihypertensive agents, lipid-lowering agents, BMI, HbA1c, HDL-C

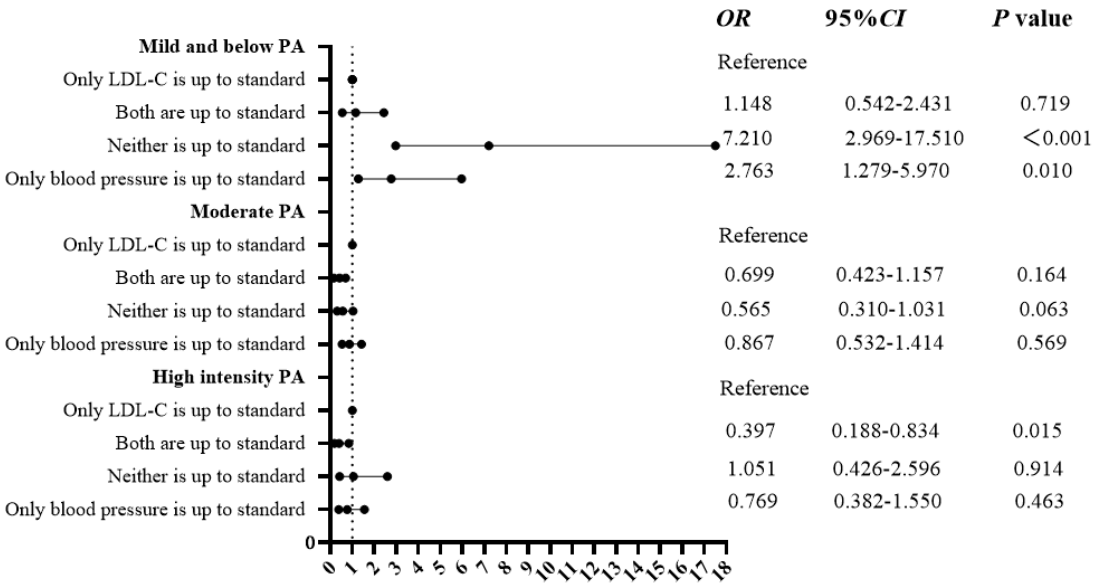

Figure 2(c) Relationship between PA and risk of CIMT thickening in different metabolic control attainment scenarios

Adjusted for sex, age, education, duration of T2DM, smoking, alcohol consumption, history of high blood pressure, history of hyperlipidemia, hypoglycemic agents, antihypertensive agents, lipid-lowering agents, BMI, HbA1c, HDL-C

Effect of Restoring Normoglycemia and Modification of Metabolic risk factors on Type 2 diabetes Risk Reduction in Prediabetic individuals; An individual-level meta-analysis

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Title: Effect of restoring normoglycemia and modification of metabolic risk factors on type 2 diabetes risk reduction in prediabetic individuals; An individual-level meta-analysis

Aim: To evaluate the reduction in type 2 diabetes (T2DM) incidence among individuals with prediabetes who achieve normoglycemia (NGR) and to assess the role of metabolic risk factor modifications.

Method: An individual-level meta-analysis was conducted using prospective cohort data from America, Australia, and Asia. Participants with prediabetes at baseline were categorised into NGR restoration and persistent prediabetes groups based on glucose status at the first follow-up. T2DM occurrence was assessed using hierarchical mixed-effect proportional hazards Weibull models, adjusting for age, sex, and metabolic risk factors.

Results: Individuals with prediabetes who achieved NGR had a 51% reduction in T2DM risk compared to those with persistent prediabetes. The model-adjusted hazard ratios (HRs) of prognostic factors indicated a significant reverse association between positive family history of T2DM and higher adiposity indices with future risk of T2DM. A negative family history of T2DM reduced the future risk of T2DM by 28% (HR 0.72, 95% CI 0.63–0.80, p<0.0001). When comparing normal weight with overweight and obesity, the future risk of T2DM was reduced by 25% (HR 0.75, 95% CI 0.64–0.86, p<0.0001) and 36% (HR 0.64, 95% CI 0.53–0.75, p<0.0001), respectively. A normal waist-to-height ratio reduced the future risk of T2DM by 29% (HR 0.71, 95% CI 0.57–0.81, p=0.01), and a normal waist-to-hip ratio reduced the risk by 31% (HR 0.69, 95% CI 0.57–0.81, p<0.001). A normal level of HDL-C decreased the future risk of T2DM by 20% (HR 0.80, 95% CI 0.70–0.90, p<0.0001). We also observed a greater reduction in T2DM risk when NGR restoration was combined with risk factor modification.

Conclusion: Restoring NGR and modifying metabolic risk factors in prediabetic individuals substantially reduces T2DM risk. These findings highlight the clinical and public health importance of targeted interventions during the prediabetes stage to mitigate the future burden of T2DM.

Effect of Tirzepatide on Kidney Parameters in People with Excess Body Weight and Type 2 Diabetes: A Post-Hoc Analysis of the SURMOUNT-2 Trial

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Aim: Tirzepatide (TZP), a glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist, has shown kidney protective effects in people with type 2 diabetes (T2D) at high risk for cardiovascular disease. In the SURMOUNT-2 (SM-2) trial in people with obesity or overweight with T2D, at 72 weeks TZP significantly reduced body weight by up to 15.7%, HbA1c by 2.22%, and systolic and diastolic blood pressure by 7.7mmHg and 2.9mmHg respectively. This post-hoc analysis assessed the potential impact of TZP vs PBO on kidney parameters in SM-2 trial participants.

Methods: Data from all participants randomly assigned to treatment were included (pooled TZP [10 and 15 mg], N = 623; PBO, N = 315). Assessments included CKD-EPI creatinine-cystatin-C-based eGFR (Cr-Cys-C-eGFR), and urine albumin-to-creatinine ratio (UACR). The change from baseline to week 72 was analyzed using mixed models for repeated measures with on-treatment data.

Results: Baseline mean Cr-Cys-C-eGFR was 91.3±19.5 mL/min/1.73m^2. The estimated treatment difference (ETD) between pooled TZP groups and PBO on the change from baseline in Cr-Cys-C-eGFR was 0.0 mL/min/1.73m^2 (95% confidence interval [CI] -1.7, 1.7; p=0.993). TZP compared to placebo did not change Cr-Cys-C-eGFR at week 72 in participants with baseline Cr-Cys-C-eGFR <60 ml/min/1.73m^2 (p=0.180) or ≥ 60 ml/min/1.73m2 (p=0.714). Baseline median UACR was 13.0 mg/g (interquartile range 6.0–35.0 mg/g). UACR significantly decreased with TZP vs. PBO (ETD -31.1 %, 95% CI -40.9, -19.7, p<0.001) and for those with baseline UACR ≥30 mg/g, the ETD was -55.2% (95% CI -68.5, -36.4; p<0.001).

Conclusion: In this post-hoc analysis SM-2 trial population of participants with obesity or overweight with T2D and preserved eGFR at baseline, TZP reduced albuminuria without adversely affecting eGFR.

Effect of Training program based on the guideline “Facilitating client centered learning” on Diabetes Specialist nurse’s Health education ability: A pilot randomized controlled trial

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Objective: To explore the effect of training program based on the guideline "Facilitating client centered learning" on health education ability training of diabetes specialist nurses.

Methods: The convenient sampling method was used to select 49 nurses who had received the theoretical training of diabetes specialist nurses from the Chinese Nursing Society and passed the examination as the research objects. According to the cluster random method, they were divided into the experimental group and the control group, with 26 cases in the experimental group and 23 cases in the control group. The control group adopts traditional health education teaching and practice. The experimental group adopted the "Guidelines for Facilitating Client Centered Learning" for teaching and practice, including: interpretation of the "Guidelines for Facilitating Client Centered Learning", structured problem education, diversified health education materials (such as education color pages, food models, videos, etc.), and the use of health education operation scoring tables for teaching guidance during the education process. Finally, the intervention effect within the group was evaluated using a health education operation scoring table, and the intervention effect between the groups was evaluated using a nurse's health education ability evaluation scale and a patient's disease knowledge questionnaire.

Results: Baseline knowledge scores were similar between the groups. A statistically significant increase in health education ability and diabetic patients knowledge score was evident immediately post intervention for the intervention group(t=7.947, P=0.000), (t=2.896, P=0.005).

Table 1 Demographics and baseline comparison between groups(N = 49)

Variable		Group, n (%)			
		Intervention (n = 26)	Control (n = 23)	t/x^2	P
Age, Mean ± SD		34.69±6.11	33.96±5.47	0.442	0.661
Working years	Working years	12.98±7.14	12.96±5.79	0.013	0.990
Gender, n (%)					
	Male	0	1	-	0.469
	Female	26	22		
Educational background				0.000	1.000
	junior college education	1	1		
	undergraduate course	25	22		
Title					
	nurse	1	0	1.380	0.710
	护师	12	10		
	nurse-in-charge	11	12		
	associate chief nurse	2	1		
Employment form				0.002	0.962
	contract system	16	14		
	Formal preparation	10	9		
Teaching experience				0.060	0.807

	not have	6	6		
	have	20	17		
Health education courses during school				0.127	0.721
	not have	10	10		
	have	16	13		
Health education and training at work				0.060	0.807
	not have	6	6		
	have	20	17		

Table 2 Health education ability between the two groups before intervention

Variable	Control Gruop	Intervention Gruop	t/x^2、Z	P
health education ability	121.00±23.87	131.04±12.47	-1.810	0.077
assessment	32.61±3.43	30.27±6.21	-1.601	0.116
planning	28.65±3.24	26.81±5.64	-1.378	0.175
implementation	42.91±4.39	39.96±8.33	-1.522	0.135
evaluation	26.87±2.36	23.96±4.52	-1.767	0.108

Table 3 Self-assessment of health education ability and patient knowledge questionnaire of nurses specialized in diabetes

Variable	Control Gruop	Intervention Gruop	t/x^2、Z	P
health education ability	144.43±12.11	172.54±12.57	7.94700	<0.001
assessment	36.09±3.00	43.12±3.18	7.931	<0.001
planning	32.13±2.82	38.31±2.92	7.509	<0.001
implementation	47.74±4.403	57.38±4.337	7.715	<0.001
evaluation	28.48±2.43	33.73±2.41	7.588	<0.001
Patient knowledge score	6.24±0.67	9.65±0.71	2.896	0.005

Conclusions: The health education training in diabetes specialist nurses based on the Guideline "Facilitating Client Centered Learning" is superior to the traditional health education training, which can improve the health education ability of diabetes specialist nurses and the degree of disease knowledge of diabetic patients.
Key words: Facilitating client centered learning, Diabetes Specialist nurse, Health education ability

Effectiveness of a 3-month mHealth Low-carbohydrate Dietary Intervention on Sleep Quality and Psychosocial outcomes in people living with Type 2 Diabetes.

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Aim: To examine the effectiveness of a mHealth low carbohydrate dietary application on sleep quality and psychosocial outcomes in people living with type 2 diabetes after 3 months of intervention.

Methods: The study recruited community-based people living with type 2 diabetes, with smartphone or internet access from around Australia. Participants were referred via a supporting registered general practitioner cohort, who were provided with medical guidelines and education through webinars pertaining to low carbohydrate dietary application. Following informed consent, participants were granted access to the online Defeat Diabetes Program, a digital app that provides education and resources on the low carbohydrate eating approach and support for ongoing management of type 2 diabetes.
Dietary intake of participants was assessed via a 3-day food record. Validated questionnaires were also used to assess: Sleep quality (B-PQSI), Quality of Life (QoL) (EQ-5D-5L), diabetes related distress (PAID-5) and diabetes self-efficacy (PDSMS) at baseline and after 3 months.

Results: The present study included 99 participants (mean age 59 ± 11 years, 55 female) with data at baseline and 3 months. Carbohydrate intake was reduced as a proportion of overall energy intake (-14%/kJ ± 1.4%/kJ, $p<0.001$).
Self-reported QoL (6.0± 2.5, $p=0.022$), self-efficacy (5.2±0.8, $p<0.001$) and diabetes related distress scores (-2.0±0.6, $p<0.001$) improved during the 3-month intervention. There was no significant difference in sleep quality. Subgroup analysis showed greater improvement in QoL for females. For those with additional preexisting medical conditions, there were greater improvements in self-efficacy and diabetes related distress.

Conclusion: People with type 2 diabetes who participated in the Defeat Diabetes Program for 3 months improved QoL, self-efficacy and diabetes related distress scores. This approach should be considered as a useful adjunct to current medical management of type 2 diabetes.

Effectiveness of a 3-month mHealth Low-Carbohydrate Dietary intervention on Weight status, Glycaemic profile and Blood pressure in people living with Type 2 Diabetes.

Kolivas D[1], Fraser L[2], Schweitzer R[3], Brukner P[1], Moschonis G[1]
[1]La Trobe University, [2]Watson General Practice, [3]East Bentleigh Medical Group

Aim: To examine the effectiveness of a mHealth low-carbohydrate dietary application on weight status, glycaemic profile, and blood pressure in people living with type 2 diabetes after 3 months of intervention.

Methods: The study recruited community-based people living with type 2 diabetes, with smartphone or internet access from around Australia. Participants were referred via a supporting registered general practitioner cohort, who were provided with medical guidelines and education through webinars pertaining to low carbohydrate dietary application. Following informed consent, participants were granted access to the online Defeat Diabetes Program, a digital app that provides education and resources on the low carbohydrate eating approach and support for ongoing management of type 2 diabetes.
Dietary intake of participants was assessed via a 3-day food record. Health data including HbA1c, anthropometry, blood pressure and medication use was obtained from GPs, recorded at baseline and after 3 months.

Results: The present study included 99 participants (mean age 59 ± 11 years, 55 female) with data at baseline and 3 months. Carbohydrate intake was reduced as a proportion of overall energy intake (-14%/kJ ± 1.4%/kJ, $p<0.001$).
HbA1c levels improved (-1.0% ± 0.2%, $p<0.001$) and were associated with percentage reduction of carbohydrate intake. Average systolic blood pressure improved (-6mmHg ± 2mmHg, $p=0.010$), but no significant changes in other health outcomes. Subgroup analysis showed greater improvement in HbA1c in males and in systolic blood pressure for people with preexisting medical conditions. Diabetes medications were reduced in 24% and increased in 3% of participants.

Conclusion: Participation in the Defeat Diabetes Program for 3 months resulted in improvements to the glycaemic profile of people with type 2 diabetes. Adherence to this approach is likely to help patients achieve improved glycaemic control, and should be considered a useful adjunct to current medical management of type 2 diabetes.

Effectiveness of Intermittently Scanned Continuous Glucose Monitoring in Improving Diabetes Management and Reducing Hospital Admissions: Insights from Association of British Clinical Diabetologists Study

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Introduction: This study aims to investigate the impact of intermittently scanned continuous glucose monitoring (isCGM) on glycemic control, diabetes-related distress, hypoglycaemia unawareness, and resource utilization, particularly in individuals with recurrent diabetes-related hospital admissions.

Methods: Utilizing data from the nationwide ABCD diabetes audit, this study analyzed information gathered from 107 NHS hospitals in the U.K. Clinicians submitted FreeStyle Libre (FSL) user data, collected during routine clinical care, to a secure web-based tool within the NHS N3 network. Baseline measurements included diabetes-related distress scores assessed using the two-item diabetes distress screening instrument (DDS2) and hypoglycaemia awareness evaluated using the Gold score. Recurrent hospital admissions were defined as individuals requiring two or more admissions related to diabetic ketoacidosis (DKA) or hypoglycaemia 1 year prior to FSL initiation.

Results: Among the 17,857 participants with Type 1 diabetes, 436 (2.5%) experienced recurrent hospital admissions, with follow-up data available for 155 individuals. The use of isCGM in this subgroup led to significant improvements: HbA1c levels decreased from 88.5 (±24.2) to 79.8 (±24.2) mmol/mol, DDS2 scores improved from 3.7 (±1.5) to 2.8 (±1.4) ($P<0.001$), although there was no significant change in Gold scores. Over the seven-month follow-up period (compared to one year of baseline data), there was a remarkable reduction in hospital admissions: a 100% decrease in hyperglycemia/DKA-related admissions, a 96% decrease in hypoglycemia-related admissions, and an 84% decrease in severe hypoglycemic episodes.

Conclusion: The findings suggest that the adoption of isCGM among individuals experiencing recurrent hospital admissions due to diabetes is associated with enhanced glycemic control, decreased diabetes-related distress, and a substantial reduction in hospital admissions.

Effectiveness of Low Intensity Mental Health Support via a Telehealth Enabled Network for adults with diabetes (LISTEN): Findings from a pragmatic randomised controlled trial

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Aim: Diabetes distress affects 20-55% of adults, varying by diabetes type, treatment and life stage. Our aim was to determine the effectiveness of LISTEN for reducing diabetes distress and improving mental health among adults with type 1 and type 2 diabetes.

Methods: A two-arm randomised controlled trial (ACTRN:ACTRN12622000168752). Participants, recruited primarily via the National Diabetes Services Scheme (NDSS), were eligible if they had elevated diabetes distress (PAID-20 score ≥25, or ≥2 on three or more items). They were randomised (1:1 ratio) to LISTEN (up to 4 sessions of evidence-based emotional support using a Problem-Solving Therapy framework with a diabetes educator from Diabetes Australia) or usual care (NDSS web-based factsheet about diabetes distress). Data were collected via online assessments at baseline (T0), 8 weeks (T1) and 6 months (T2). The primary endpoint was the between-group difference in diabetes distress (PAID-20 total) at T2. Secondary outcomes included the short (T1) and longer-term (T2) effects on emotional well-being (WHO-5) and psychological distress (K-10). Data were analysed on an intention-to-treat basis.

Results: Participants were N=428 adults (252 women, 172 men, 3 non-binary; mean±SD 54±21 years; 63% type 2 diabetes). There was a statistically significant and clinically meaningful between-group difference (favouring LISTEN) in diabetes distress at T2 (Mean diff: 7.20 (2.78,11.62); p<0.001), and emotional well-being at T1 and sustained at T2 (Mean diff: -7.55 (-12.62,-2.47) p=0.001). There was no significant between-group difference in psychological distress (T1 or T2). A statistically significant reduction in psychological distress at T1 was found among LISTEN participants with type 2 diabetes, but not type 1 diabetes, compared to usual care (Mean diff: 2.19 (0.25,4.13), p= 0.021).

Conclusions: LISTEN reduced diabetes distress and improved general emotional well-being. While further research is needed, e.g. in priority populations, LISTEN is ready for widespread implementation to address the unmet needs of adults with diabetes distress.

Effects of Endogenous and Exogenous GIP on Blood pressure, Heart rate, Gastric emptying and Blood glucose responses to Oral Glucose in Healthy older people

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Aims: Postprandial hypotension (PPH), a fall in blood pressure (BP) >20mmHg following a meal, occurs in ~15-20% of healthy people >65 years and ~35% of people with type 2 diabetes. Glucagon-like peptide-1 (GLP-1)/GLP-1 receptor agonists attenuate the postprandial fall in BP, in part by slowing gastric emptying, but the effects of glucose dependent insulinotropic polypeptide (GIP) on BP and gastric emptying are poorly defined. Using the specific GIP receptor antagonist, GIP(3-30)NH_2, we assessed the effect of GIP on the BP, heart rate (HR), gastric emptying and blood glucose responses to a glucose drink in healthy older people.

Methods: 18 healthy older participants (13F, 5M; mean age 67.7±0.7 years; BMI 28.1±0.9 kg/m^2) were studied on 3 occasions and received an intravenous infusion of (i) GIP (1.5 pmol/kg/min), (ii) GIP(3-30)NH_2 (800 pmol/kg/min) or (iii) 0.9% saline (placebo) in a randomised, double-blind, cross-over design. BP, mean arterial pressure (MAP) and HR were monitored using an automated device. Participants ingested a 75g glucose drink (300ml) radiolabelled with 20MBq 99mTc-calcium phytate to assess gastric emptying by scintigraphy. Data are means±SEM.

Results: There was a modest slowing of gastric emptying by exogenous GIP ($P<0.05$) with no effect of GIP(3-30)NH_2. Exogenous GIP and GIP(3-30)NH_2 had no effect on MAP, HR or blood glucose during the fasting period. Following the glucose drink, MAP fell ($P<0.01$) on all study days. The magnitude of the fall in MAP ($P=0.03$), and rise in HR ($P=0.01$) was less after GIP(3-30)NH_2 compared to placebo. Peak blood glucose was greater ($P<0.001$) after GIP(3-30)NH_2 (12.2±0.4 mmol/L), with no effect of GIP (10.6±0.4 mmol/L) when compared to placebo (10.6±0.5 mmol/L).

Conclusion: In healthy older people, the fall in BP and rise in HR after oral glucose are attenuated when GIP release is blocked. Accordingly, endogenous GIP, beyond its role in glucose metabolism, modulates postprandial cardiovascular responses.

Efficacy and Hypoglycaemia Outcomes of Once-Weekly Insulin Icodec Versus Once-Daily Basal Insulin in Type 2 Diabetes According to Baseline Glucagon-like Peptide-1 Receptor Agonist Use: ONWARDS 1–5

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****DATA UNDER EMBARGO FOR ADA – Table Watermarked****

Aim: To assess the treatment effects of once-weekly (OW) insulin icodec (icodec) vs once-daily (OD) basal insulin comparators ± concomitant glucagon-like peptide-1 receptor agonist (GLP-1 RA) use in ONWARDS 1–5.

Methods: A post hoc analysis by trial of insulin-naïve (ONWARDS 1, 3, 5) and insulin-experienced (ONWARDS 2, 4) adults with type 2 diabetes (T2D).

Results: Participants on icodec vs OD comparators had larger or similar A1C reductions from baseline (BL) to end of treatment (EOT) irrespective of GLP-1 RA use; there was no statistically significant treatment by subgroup interaction in A1C changes (Table). Overall rates of clinically significant or severe hypoglycemia were low (<1 event/patient-year of exposure) across arms among ONWARDS 1–3 and 5 subgroups, with numerically lower rates among GLP-1 RA users vs non-users; in ONWARDS 4 (basal-bolus trial), the hypoglycemia rate was similar among GLP-1 RA users vs non-users in the icodec arm (Table). There was no statistically significant treatment by subgroup interaction in any trial for the attainment of A1C <7% without clinically significant or severe hypoglycemia, nor body weight change from BL to EOT.

Conclusion: The efficacy and safety of icodec vs OD comparators was generally consistent among adults with T2D, irrespective of baseline GLP-1 RA use.

Table. Outcomes for icodec versus OD comparators according to baseline GLP-1 RA use in ONWARDS 1–5

Trial	Participants, n (with/without GLP-1 RA)	Outcome	With GLP-1 RA use at baseline			Without GLP-1 RA use at baseline			*p* value for test of subgroup interaction
			Icodec	OD comparator	ETD[a] (95% CI)	Icodec	OD comparator	ETD[a] (95% CI)	
ONWARDS 1[b] (insulin-naive)	Icodec: 83 / 409	LS mean change (SE) in A1C from BL to EOT, %-points	-1.57 (0.09)	-1.61 (0.09)	0.03 (-0.21, 0.27)	-1.55 (0.05)	-1.40 (0.04)	-0.14 (-0.27, -0.02)	*p* = 0.19
	OD comparator: 92 / 400	Clinically significant or severe hypoglycemia, events/PYE	0.17	0.09	-	0.32	0.17	-	-
ONWARDS 3[c] (insulin-naive)	Icodec: 64 / 230	LS mean change (SE) in A1C from BL to EOT, %-points	-1.63 (0.10)	-1.42 (0.12)	-0.21 (-0.5, 0.08)	-1.56 (0.05)	-1.35 (0.05)	-0.21 (-0.35, -0.06)	*p* = 0.98
	OD comparator: 48 / 246	Clinically significant or severe hypoglycemia, events/PYE	0.24	0.14	-	0.33	0.15	-	-
ONWARDS 5[d] (insulin-naive)	Icodec: 148 / 394	LS mean change (SE) in A1C from BL to EOT, %-points	-1.66 (0.11)	-1.33 (0.15)	-0.39 (-0.71, -0.07)	-1.69 (0.10)	-1.30 (0.13)	-0.33 (-0.69, 0.03)	*p* = 0.76
	OD comparator: 158 / 385	Clinically significant or severe hypoglycemia, events/PYE	0.11	0.07	-	0.22	0.17	-	-
ONWARDS 2[e] (basal switch; insulin-experienced)	Icodec: 68 / 195	LS mean change (SE) in A1C from BL to EOT, %-points	-1.12 (0.09)	-0.99 (0.09)	-0.13 (-0.38, 0.13)	-0.87 (0.06)	-0.61 (0.07)	-0.26 (-0.43, -0.09)	*p* = 0.39
	OD comparator: 69 / 194	Clinically significant or severe hypoglycemia, events/PYE	0.27	0.10	-	0.89	0.34	-	-
ONWARDS 4[f] (basal-bolus; insulin-experienced)	Icodec: 37 / 254	LS mean change (SE) in A1C from BL to EOT, %-points	-1.14 (0.14)	-1.04 (0.14)	-0.10 (-0.48, 0.28)	-1.16 (0.05)	-1.20 (0.05)	0.04 (-0.1, 0.18)	*p* = 0.50
	OD comparator: 34 / 257	Clinically significant or severe hypoglycemia, events/PYE	5.65	3.12	-	5.64	5.96	-	-

Individuals were not randomized according to their baseline medication. Change from baseline to EOT in A1C was analyzed using an ANCOVA, with treatment, region, treatment by subgroup interactions and, if applicable, additional relevant factors as fixed factors, and baseline response as a covariate. [a]Icodec – OD comparator. [b]78-week trial (52-week main phase + 26-week extension phase + 5-week follow-up), icodec vs glargine U100; EOT = week 78. [c]26-week-trial (+ 5-week follow-up), icodec + OD placebo vs degludec + OW placebo; EOT = week 26. [d]52-week trial (+ 5-week follow-up) with real-world elements, icodec with dosing guide app vs OD basal analogs (glargine U100, degludec, glargine U300); EOT = week 52. [e]26-week-trial (+ 5-week follow-up), icodec vs degludec; EOT = week 26. [f]26-week-trial (+ 5-week follow-up), icodec + aspart vs glargine U100 + aspart; EOT = week 26. [g]Blood glucose < 54 mg/dL (< 3.0 mmol/L), confirmed by blood glucose meter. [i]Severe cognitive impairment requiring external assistance. BL, baseline; EOT, end of treatment; ETD, estimated treatment difference; GLP-1 RA, glucagon-like peptide-1 receptor agonist; LS, least-squares; n, number of participants; OD, once-daily; OW, once-weekly; PYE, patient-year of exposure; SE, standard error of the mean.

Efficacy and safety study of Imeglimin as add on to multiple OADs and Insulin among Indians with Type 2 Diabetes – Real world evidence,Observational study

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Aim: Imeglimin as a novel therapy for type 2 diabetes has shown its efficacy as a monotherapy, add on to other oral anti diabetic drugs (oads) and insulin in TIMES 1,2 and 3 trials. However, there is a lack of real world evidence for effects of Imeglimin among Indians with Type 2 diabetes already on treatment. Hence this study is done to assess its efficacy and safety as add on to multiple oads and insulin among Indians with Type 2 diabetes.

Methodology: In this study individuals with Type 2 diabetes (n = 69) aged > 18 years with hba1c ≥ 6.3 % received Imeglimin (500mg and 1000mg) twice a day as add on to multiple oads and insulin. The oads used were (SGLT2 inhibittors,DPP4 inhibitors,Sulfonylurea,Metformin,GLP1 analogue).Fasting blood sugar (FBS) ,Post prandial blood sugar (PPBS) were measured on Day 0,Day 5 and Day 90.The hba1c and weight were measured on Day 0 and Day 90.The individuals were divided into Group A (n=36),Group B (n=42) and Group C (n=41).

Results: In Group A on Day 5 mean FBS,PPBS reduction was 50.25mg/dl and 101mg/dl.In Group B on Day 90 mean FBS and PPBS reduction was 31.0 mg/dl and 73.91 mg/dl.In Group C hba1c on Day 0 and Day 90 was 8.57% and 7.38%.There was mean weight reduction of 0.7 kgs by Day 90.3 individuals discontinued treatment due to gastrointestinal side effects.

Conclusion: The glycemic benefits of Imeglimin as an add on therapy to multiple oads and insulin is noticed as early as 5th day of treatment extending upto 90 days,with added benefits of weight loss and minimal side effects. This makes imeglimin an ideal a choice for early intensive treatment with sustainable glycemic benefits to prevent therapeutic inertia.

Efficacy of Tirzepatide in achieving the Composite Endpoints of Glycemic, Blood pressure and Lipid goals in SURMOUNT-2

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Aim: In the SURMOUNT-2 (SM-2) trial of adults with overweight/obesity and type 2 diabetes (T2D), tirzepatide (TZP), a once weekly GIP/GLP-1 receptor agonist, significantly reduced body weight (BW) in conjunction with a reduced calorie diet and increased physical activity. This post-hoc analysis assessed the proportion of participants achieving a triple end-point (TEP) composite of BP <130/80 mm Hg, non-HDL <130 mg/dl, and three HbA_{1c} thresholds of <7%, < 6.5% and <5.7% at 72 weeks.

Method: Logistic regression with missing value imputed by mixed model repeated measures, using the efficacy estimand, assessed participants who achieved the TEP goals from SM-2, in the 10mg (N=312) or 15mg (N=311) TZP groups, versus placebo (PBO) (N=315).

Results: Overall baseline mean BW was 100.7 kg, BMI 36.1kg/m^2, HbA_{1c} 8.02%, BP 130.5/79.8 mm Hg and non-HDL 132.5 mg/dl. For 15mg TZP, 33.8%, 32.8%, and 25.9% of participants achieved the TEP composite versus 7.5%, 3.9%, and 0.7% of PBO (HbA_{1c} <7%, <6.5% & <5.7% respectively) at 72 weeks. Findings for the TZP 10mg group were similar to those observed in the 15mg group.

Conclusion: In this post-hoc analysis in people with T2D and overweight/obesity, higher proportion of participants receiving TZP achieved the TEP composite, compared to PBO. This suggests that TZP can help people with obesity and T2D achieve multiple clinical goals, in addition to meaningful weight loss, important for improving cardiometabolic health.

Elucidating the Phenotype of Autoantibody negative Type 1 Diabetes

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Background: Autoantibody-negative type 1 diabetes (T1D) accounts for a minority of T1D cases. This group is excluded from all T1D intervention trials, assumed to be non-immune mediated and prone to misclassification. Prior studies have suggested that this cohort is older at diagnosis, with a higher body mass index (BMI) and slower beta-cell decline.

Methods: We recruited 3 groups of subjects (n=26 islet autoantibody-negative T1D, n=30 islet autoantibody-positive T1D and n=25 healthy controls without diabetes). Deep immunophenotyping was performed using a 28-colour flow cytometry panel. T1D genetic risk scores (T1DGRS) were undertaken in all subjects with diabetes.
Glucagon stimulation tests were performed on 15 autoantibody-negative and 19 autoantibody-positive T1D subjects. In these subjects, body composition was assessed using dual x-ray absorptiometry (DXA) scans and Fibroscans, to calculate liver controlled attenuation parameter (CAP) scores to assess liver steatosis.

Results: There were no differences in clinical or biochemical characteristics between autoantibody-negative and positive subjects (see table). There were no significant differences in the deep immunophenotype between groups.
Median glucagon-stimulated C-peptide was blunted in both groups (0.3 nmo/L in autoantibody-negative T1D, 0.4 nmol/L in autoantibody-positive T1D, p = 0.72). Rate of beta-cell decline did not differ at 9 month follow up (delta C-peptide -0.1 nmol/L in both groups). Body composition did not differ between groups.

Table: Clinical characteristics

	Ab- (n=26)	Ab+ (n=30)	HC (n=25)	p
Male, N (%)	18 (69%)	12 (46%)	11 (44%)	0.07
Ethnicity, N (% White European)	20 (77%)	23 (77%)	16 (64%)	0.30
BMI (kg/m2)	23.6 (22.0 - 25.3)	24.0 (21.8 - 25.7)	22.9 (20.8 – 24.5)	0.23
Diabetes duration (years)	3 (1 - 6)	3 (2 - 7)	-	0.88
Age at diagnosis (years)	34 (26 – 44)	29 (23 - 37)	-	0.18
1st degree relative with diabetes, N (%)	10 (38%)	7 (23%)	4 (16%)	0.46
Other autoimmune history, N (%)	5 (20%)	7 (23%)	2 (8%)	0.58

Values expressed as median (IQR), unless otherwise specified.

Conclusion: There was no difference in the clinical or immune phenotype of autoantibody-negative and positive T1D subjects. Beta-cell decline did not differ based on autoantibody positivity. Additional objective tools such as the T1DGRS and low stimulated C-peptide, should be used to facilitate accurate classification of adults presenting with islet autoantibody-negative T1D.

Empowering people living with Type 1 Diabetes to understand continuous glucose monitoring data – interim results

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Background: Education for people using diabetes technology is often device-specific and limited to sick day management and device troubleshooting. There is an absence of education focusing on interpreting CGM data in the context of insulin dosing and behavioural choices. *The Making Sense Program* has been co-designed to address this need.

Aim: To assess the feasibility of *The Making Sense Program*, a curriculum educating adults living with type 1 diabetes (T1D) to assess device generated data.

Method: Adult participants with T1D were recruited from Victorian Hospitals and enrolled in *The Making Sense Program* with Diabetes Victoria in groups of 7-10. The program consisted of three stages over two weeks; an introductory group session with a lived-experience facilitator and credentialled diabetes educator (CDE); three online training modules; and a final group session, virtual or face-to-face, with the same facilitator and CDE. Participants were followed over 26 weeks of routine care. The primary outcome was the proportion of participants who complete the study per protocol. Secondary glycaemic and patient-reported outcomes were assessed at baseline, mid-study and end of study.

Results: Sixty-eight participants were enrolled and 34 have completed the study. Eighty-five percent of participants strongly agree or agree they would recommend this program to others living with type 1 diabetes. There was a reduction in HbA1c and an improvement in CGM metrics, particularly less hyperglycaemia and less glucose variability. Interestingly, there was no change in diabetes management satisfaction but there was a reduction in diabetes distress and improved well-being.

Conclusion: Interim data suggests this program is feasible, and may improve glycaemic and patient-reported outcomes. Complete data will be presented in August.

	Baseline	End of Study	P-value
Gender, n (% males)	27 (38.5)		
Age, years	53.0 (15.7)		
Duration of diabetes, years	31.5 (13.4)		
CSII, n (%)	45 (64)		
HbA1c, %, mmol/mol	7.3 (0.7), 55.5 (8.1)	7.1 (0.8), 53.8 (8.6)	0.099
Mean total daily dose, units	45.0 (17.3)	45.7 (18.6)	0.619
% TIR 3.9-10 mmol/L	73.9 (12.2)	76.9 (12.6)	0.059
% TAR > 10 mmol/L	24.5 (12.5)	21.3 (13.2)	0.041
% TAR > 13.9 mmol/L	5.2 (5.2)	4.1 (6.0)	0.314
% TBR <3.9 mmol/L	1.5 (2.0)	1.7 (2.5)	0.540
% TBR <3.0 mmol/L	0.3 (0.5)	0.3 (0.5)	0.493
Mean SG, mmol/L	8.4 (1.0)	8.2 (1.1)	0.142
CV, %	32.4 (7.1)	30.0 (5.1)	0.021

PAID[a]	14.8 (12.2)	12.1 (11.1)	0.017
WBQ-28[b]	8.4 (2.6)	9.1 (2.6)	0.070
DME-Q Total Satisfaction[b]	3.7 (0.6)	3.8 (0.5)	0.150

Results presented as mean (SD)
[a]lower scores indicate more positive outcomes
[b]higher scores indicate more positive outcomes
PAID = Problem Areas in Diabetes scale. WBQ-28 = Well-being Questionnaire. DME-Q = Diabetes Management Experiences Questionnaire

Enhanced Gluconeogenesis in the Kidneys is Mediated by Angiotensin Converting Enzyme 2 (ACE2)

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Background: Overexpression of gluconeogenic enzymes, phosphoenol-pyruvate carboxykinase 1 (*PCK1*) and glucose-6-phosphatase (*G6Pase*), increases glucose production by the kidneys and contributes to fasting hyperglycaemia. The exact mechanisms remain poorly understood, with reduced insulin signalling, increased uptake of gluconeogenic substrates, and renin–angiotensin-aldosterone system activation implicated. We hypothesise that Angiotensin Converting Enzyme 2 (*ACE2*) also regulates renal gluconeogenesis.

Methods: *Ace2* knockout (KO) and wild-type C57bl6J (WT) mice (n=8/group) were placed on reduced carbohydrate diets with high-fat (HF) or high protein (HP), or standard diet (SD) as a control. *Ace2* KO mice were also treated with an ACE-inhibitor, perindopril (2mg/kg/day). Glucose and insulin tolerance, and calorimetry measurements were undertaken alongside the expression of key gluconeogenic enzymes in the kidney by RT-PCR.

Results: Following exposure of WT mice to a reduced carbohydrate diet, the expression of *Pkc1* and *G6pase* mRNA in the kidneys were increased ~3-4 fold, both with a HFD and HPD (p=0.002). The expression of *SGLT2* mRNA was similarly increased, reflecting the low carbohydrate state, while expression of *Ace2* mRNA was also increased 2-3-fold (p=0.003) when compared to SD. In contrast, there was no significant increase in gluconeogenic enzymes or *SGLT2* mRNA in *Ace2* KO mice receiving HF or HP diets compared to *Ace2* KO mice on a SD. Notably, the responsiveness of *Ace2* KO mice to a HF diet was not restored following treatment with perindopril, although perindopril improved peripheral glucose utilisation and fasting insulin concentrations in *Ace2* KO mice.

Conclusion: The rise in renal glucose release in diabetes contributes to hyperglycaemia. Independent of its angiotensinase activity, augmented ACE2 expression in the proximal tubule appears critical for increased renal gluconeogenesis. The progressive loss of ACE2 activity in chronic kidney disease and hypertension may contribute to greater susceptibility to hypoglycaemia, metabolic acidosis, and diabetes-associated tubular damage with a switch to increased glycolysis.

Enhancing Perioperative Care: A Novel Collaborative Approach by Pre-admission Clinic and Western Sydney Diabetes for pre-operative optimisation of glycaemic control

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Aim: Individuals with diabetes undergoing surgery face heightened perioperative risks, due to suboptimal glycaemic control, leading to surgery delays. Continuous Glucose monitoring (CGM) provides real-time insights into glycaemic control, addressing shortcomings related to HbA1c that measures glycaemic control over 2-3 months. A partnership between the Western Sydney outpatient diabetes service and Pre-admission Clinic (PAC), utilising CGM, aims to mitigate these risks by optimising pre-operative glycaemic control.

This study aims to: (1) outline the development of a novel service between PAC and the diabetes team and (2) evaluate its impact using CGM on reducing the duration from surgical decision to surgical clearance.

Method: We conducted a retrospective analysis of patients referred from December 2022 to February 2024 with suboptimal glycaemic control (HbA1c > 7.5% and/or new diabetes diagnosis). Referred patients received CGM devices from PAC. We extracted data from clinical records.

Results: 41 patients were referred from PAC to WSD for glycaemic optimisation, mostly for elective orthopaedic surgery (61%). The average HbA1c was 8.7% (SD = 2.7%). 34 patients accepted the service, with 27 (79%) achieving surgical clearance. Among 18 patients proceeding to surgery, 9 underwent procedures without delays. The average time from referral to specialist review was 3.25 weeks, with a mean wait time for surgical clearance of 6.1 weeks. Key interventions included discontinuing sulphonylureas, initiating insulin, and GLP-1 receptor analogues.

Conclusion: The average wait time in WSLHD during this period is roughly 9.28 weeks for semi-urgent surgeries and 43 weeks for non-urgent surgeries [2]. The collaboration between PAC and WSD streamlined the referral process expediting surgical clearance and potentially improving perioperative outcomes. Integrating services and advanced monitoring technologies in diabetes management demonstrates promising avenues for enhancing perioperative care protocols.

Epidemiology of Diabetic Ketoacidosis (DKA) and Evaluation of management at a major tertiary referral hospital in Australia

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Aim: This study describes the epidemiology, management, and outcomes of DKA episodes within Alfred Health (AH), a major tertiary referral hospital in Melbourne, Australia.

Methods: Retrospective audit of DKA episodes in AH between Jan 2019-Dec 2022 using pathology data extracted from the electronic medical record. Episodes were included where blood ketones >3 mmol/L, pH <7.3 or bicarbonate <15 mmol/L, and BGL >11 mmol/L (excluding recent sodium-glucose cotransporter-2 inhibitor [SGTL2i] use within 72 hours). Recurrent episodes of DKA were not included in this study.

Results: Total 235 episodes of DKA occurred (2019: n=17; 2020: n=56; 2021: n=77; 2022: n=85). Of these, 23 occurred ≥24 hours after admission (hospital-onset). Pre-existing T1DM was documented in 42% of cases, T2DM in 40% of cases, other types in 4% of cases, and no previous diagnosis in the remaining 14.5% of patients. Instances of DKA in those with T2DM increased across the study period (2019: n=5, 29%; 2020: n=21, 38%; 2021: n=31, 40%; 2022: n=36, 42%). A SGTL2i was used within 72 hours prior in 20% of DKA cases. On average, it took 2.8 hours to commence an insulin infusion, 11.6 hours to resolve acidosis and an overall DKA resolution time of 24.4 hours. The median length of stay was 4.19 days. Hypoglycaemia occurred in 5% and hypokalaemia in 17.9% of cases during treatment. There was a 4% diabetes-related readmission rate within 30 days, and 15 inpatient deaths.

Conclusions: There was an increase in DKA cases between 2019-2022. The higher-than-expected proportion of cases in T2DM has important implications for diabetes care across health settings. Variable-rate insulin infusion protocols, as used in this study, may result in a longer time to DKA resolution and length of stay, albeit with lower rates of hypoglycaemia and hypokalaemia. Future research should compare variable vs fixed-dose protocols on these outcomes.

Epidemiology of Metabolic Dysfunction-Associated Fatty Liver Disease in Type 2 Diabetes Mellitus and Effects of Antiglycaemic Therapy on Liver Fibrosis:

A Retrospective Study

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Aims: Our study aimed to analyse metabolic dysfunction associated fatty liver disease (MAFLD) prevalence, the impact of type 2 diabetes mellitus (T2DM) and other metabolic risk factors on liver stiffness measurement (LSM), the correlation of MAFLD with chronic kidney disease (CKD) and ischemic heart disease (IHD), and the influence of antiglycaemic medications on LSM utilising fibroscan data.

Methods: A retrospective analysis of electronic health records was conducted encompassing patients who underwent fibroscan at an Australian Hospital from January 2022 to March 2023. The inclusion criteria for MAFLD comprised a controlled attenuation parameter (CAP) score ≥ 248 dB along with metabolic dysfunction. Patients were stratified on the basis of presence or absence of T2DM while excluding patients with type 1 diabetes mellitus and other potential causes of hepatic steatosis. Linear regression analysis was employed to identify factors associated with LSM scores < 8 or > 8 kPa, indicative of clinically significant fibrosis.

Results: Among 1,129 participants, 437 (38.71%) individuals had MAFLD. Statistical evidence demonstrated significant association between T2DM and MAFLD ($P < 0.001$), revealing 4.81-fold increase in MAFLD odds, accompanied by 31% higher LSM ($P < 0.001$). Furthermore, a robust correlation was observed between MAFLD and CKD (3.38-fold increase in odds, $P < 0.001$), as well as IHD (2.10-fold increase in odds, $P < 0.001$). Of significance, individuals with T2DM using glucagon-like peptide-1 agonists (GLP-1a) and sodium-glucose co-transporter-2 inhibitors (SGLT-2i) manifested significantly lower LSM (-20.55% and -25.17%, respectively), while insulin use was associated with 101.38% higher LSM compared to non-insulin users.

Conclusions: MAFLD exhibits a notably high prevalence in this cohort, with T2DM leading to higher LSM. Concurrent CKD and IHD are common in individuals with MAFLD. The LSM reduction observed in SGLT-2i or GLP-1a users underscores the potential utility of clinical trials to assess their efficacy in attenuating MAFLD progression.

Epitope-specific autoantibody profiles after Pancreatic Islet Allotransplantation for impaired Hypoglycaemia awareness in Type 1 Diabetes

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Aim: Pancreatic Islet Allotransplantation is a treatment option for persons with Type 1 Diabetes Mellitus (T1DM) with impaired hypoglycaemia awareness and recurrent severe hypoglycaemia, with immunosuppression necessary to prevent immune-mediated rejection. This study explores profiles after islet allotransplantation of autoantibodies to the epitopes: insulin (INSAb); glutamic acid decarboxylase (GADAb); and, insulinoma-associated protein 2 (IA-2Ab). We previously reported a gradual decline in INSAb but others found, in small numbers of patients, elevated GADAb after transplantation. We aimed to investigate epitope-specific changes in islet autoantibodies after transplantation in a larger number of patients.

Method: Serial serum autoantibody (GADAb, IA-2Ab, INSAb) measurements were collated utilizing data from the Australian Islet Transplant Consortium (Westmead Hospital, Royal Adelaide Hospital, St Vincent's Hospital Melbourne (SVHM)). Nonparametric statistical analyses were used to identify trends up to 5 years post-transplantation.

Results: Fifty participants (median age: 53 years) with a median T1DM duration of 36.5 years demonstrated a pattern of gradual decrease in INSAb but initial increase in GADAb. We present here our analysis of the 19 SVHM patients, where we had the most detailed local clinical correlation data, with more complex analysis of the overall dataset in progress. Baseline autoantibody positivity was GADAb 53%, IA-2Ab 16%, and INSAb 90%. Notably, INSAb positivity decreased significantly to 47% (p=0.013), while GADAb and IA-2Ab showed no significant changes in positivity rates. GADAb notably increased by a mean of 6.2 U/mL (p=0.021) in the initial 300 days post-transplant. INSAb displayed a significant decline, averaging 3.2 U/mL (p=0.001) within the first 300 days and 0.6 U/mL (p=0.014) up to 1800 days post-transplantation.

Conclusion: Distinct responses were observed among GADAb, IA-2Ab, and INSAb autoantibodies following pancreatic islet transplantation despite immunosuppression. Further investigations could aim to clarify how the rise in GADAb relates to graft function and/or underlying T1D autoimmunity.

Evaluating Educational Exercise Resources to Improve Awareness and Knowledge of Type 1 Diabetes within Community sport settings

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Aim: A main challenge identified by youth during exercise and sport is the lack of knowledge and awareness around type 1 diabetes (T1D) particularly in community sport settings. Working with youth with T1D, parents and community sport coaches, our team have developed resources for the T1D and sporting community. This study was to evaluate the acceptability and usability of the resources.

Method: Participants completed an online evaluation survey consisting of a T1D quiz and ratings of subjective knowledge and confidence perception. The quiz on exercise and T1D management knowledge consisted of questions developed from the content of the resources and included: an understanding of T1D; signs and symptoms associated with T1D; identification and management of hypoglycaemic episodes. Participants were then provided access to the resources over a 4-week exposure period. After four weeks, participants completed the same online survey. Participants were interviewed to collect qualitative information relating to the usability and acceptability of the resources, which included concepts around confidence, trust, and frequency of use.

Results*:* 24 coaches, mean (range) age 38years (18-60years) participated. Prior to using the resources, coaches rated themselves low on knowledge on T1D during exercise (42%), confidence in supporting children with T1D during exercise (33%), knowledge on how to treat children with T1D during hypoglycaemic and hyperglycaemic events (50%), and confidence in managing T1D emergencies (severe hypoglycaemia and hyperglycaemia) (55%). After the four weeks, coaches self-rating was good 57%, 48%, 43%, 39% for the above subjective knowledge and confidence perception questions. Coaches indicated high trust in the resources, and feedback in interviews included adjustments to fonts and simplifying language to enable wide community engagement.

Conclusion*:* The resources developed were found to be informative, trustworthy, acceptable and easy to use. Following minor amendments, the resources will be implemented into community sport settings through a nationwide launch.

Evaluating the Clinical Efficacy of Reporting of Hypoglycaemia as a Hospital-acquired complication

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Aim: Inclusion of inpatient hypoglycaemia as a hospital-acquired complication (HAC) by the Australian Commission on Safety and Quality in Healthcare recognises its association with adverse health outcomes. However, clinical coding of HACs is dependent on the proficiency of clinical documentation. We have therefore reviewed the accuracy of HACs reporting methodology, which identified hospital-related hypoglycaemic episodes with particular focus on preventable clinical risk factors towards inpatient hypoglycaemia.

Method: We completed a retrospective review of 76 care episodes, coded as hypoglycaemic HACs, defined as measured capillary blood glucose level (BGL)< 4.0 mmol/L, which occurred between June 2022 and June 2023 in a tertiary hospital in New South Wales. The biochemical validity of reported hypoglycaemic episodes was examined in a context of clinical risk factors such as presence of diabetes mellitus (DM), receiving treatment with glucose-lowering medication, presence of malnourishment or critical illness.

Results: The mean age of examined subjects was 74 years (SD=17.5) with BMI of 27.4 kg/m^2 (SD=7.9). Nine subjects (12%) did not have a biochemically valid hypoglycaemic episode. The majority of valid episodes N=28 (42%) recorded BGL (mmol/L) between 3.5-3.9, followed by N=23 (34%) with BGL 3.0-3.4, and N=16 (24%) with BGL< 3.0. DM diagnosis was present in 42 (63%) subjects. Among valid cases, N=41(61%) were considered treatment-related with either insulin N=32 (48%) or sulphonylurea N=9 (13%) use. Total N=17 (25%) subjects had evidence of malnutrition while N=18 (27%) subjects were affected by critical illness.

Conclusion: Our data highlight the need to improve coding accuracy and delineation of pertinent risk factors for hospital-acquired hypoglycaemia with improved clinical validity. Inpatient hypoglycaemia associated with malnutrition or critical illness may not be reflective of medical management associated HACs. Finally, a deeper understanding of risk factors linked to inpatient hypoglycaemia is crucial for creating evidence-based interventions to prevent occurrence of hypoglycaemia during hospital admissions.

Evaluating the Impact of a Community delivered Lifestyle Management Program for people living with or at risk of Type 2 Diabetes – Logan Healthy Living

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Aim: Logan Healthy Living (LHL) is an interprofessional community-delivered healthcare service that delivers evidence-informed healthcare for people living with or at risk of type 2 diabetes in the Logan area, Queensland. The cornerstone of the service is an 8-week lifestyle management program (LMP). This study reports on the impact-to-date of the service's LMP on diabetes related distress (primary) and the three pillars targeted by the program: physical activity, nutrition, and social connection.

Method: Data were drawn from the services' data registry and include clients from inception of the service in July 2021 to May 2024. All clients participated in the LMP, that includes 1h of education and 1h of exercise per week for 8 weeks. Measures of diabetes related distress (Problem Areas in Diabetes), moderate-to-vigorous intensity physical activity (Active Australia Survey), fruit and vegetable consumption (meeting recommendations or not), and loneliness (UCLA loneliness scale as an indicator of social connection) were assessed using self-report surveys at intake and end of the 8-week LMP, with change assessed via paired t-test (continuous) or chi-squared (categorical).

Results: Change data were available on 144 participants (59.7% female; mean [SD] age = 63[11] years) to date. There was a significant reduction in diabetes related distress scores of -6.9 (95% CI -4.7 to -9.1, $p<0.001$) and significant increases in moderate-to-vigorous intensity activity of +139 (95% CI 83 to 194, $p<0.001$) minutes/week. The percentage of participants meeting fruit recommendations increased significantly from 44% at baseline to 63% at end-of-program ($p<0.001$), as did those meeting vegetable recommendations (9% to 12.5%, $p<0.001$). Changes in loneliness score were small and non-significant (0.02, 95%CI -0.22 to 0.27, $p=0.857$).

Conclusion: The LMP is showing promising findings on diabetes related distress and on the behaviours targeted by the program. Ongoing follow-up of participants will inform the sustainability of these changes.

Evaluating the Prevalence of Diabetes in Patients with Iron overload in an Australian Hospital setting

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Background: The prevalence of diabetes with iron overload is reported at 30-60%. The role of iron excess in diabetes pathophysiology is well described, especially in haemochromatosis. Despite the link between development of diabetes and iron excess, its prevalence in Australian healthcare settings has received less attention.

Aim: To investigate the prevalence of diabetes in patients diagnosed with iron overload and the temporal relationship between detection of diabetes in relation to iron overload.

Methods: Since the implementation of a hospital Electronic Medical Record (EMR) in 2020, patients documented with an 'iron overload' ICD diagnosis were assessed. These individuals were assessed for prevalence of diabetes based on diagnosis documentation in the EMR (including HbA1c ≥6.5%). In people with diabetes and iron overload absolute ferritin (ug/L), transferrin saturation (%), HFE gene mutation, islet autoantibody and insulin medication use were assessed.

Results: Of the 217 patients documented with iron overload (almost all hereditary haemochromatosis), 35 (16%) were documented with diabetes. Of the 35 people with diabetes, only 23 (66%) had the date of diagnosis for both diabetes and iron overload documented. Of these people with double diagnosis labels, in 7 (30%) diabetes was diagnosed after iron overload detection, 8 (35%) diabetes was diagnosed before iron overload and 8 (35%) had both conditions detected concurrently. Of those diagnosed with diabetes after iron overload, 3 of 7 (43%) were classified as type 2 diabetes and none were classified as type 3C diabetes (or secondary diabetes).

Conclusion: The prevalence of diabetes in patients diagnosed with iron overload in an Australian healthcare setting was less than previously reported at 16%, with the timing of diabetes diagnosis in relation to the detection of iron overload often unclear. This study highlights the need for documentation of diagnosis dates to determine the temporal relationship between iron overload and diabetes onset.

Evaluation of a Novel Medtronic Extended Wear Sensor (MEWS)

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Evaluation of a Novel Medtronic Extended Wear Sensor (MEWS)

Background: In a feasibility study we examined the use of low dose dexamethasone aimed at mitigating local inflammation thereby improving continuous glucose monitoring (CGM) sensor reliability and extending longevity.

Method: This single-center, open-label study included 69 participants >18 years old with type 1 diabetes (T1D) who wore control and extended-life sensors (with low dose dexamethasone).

Main outcome: Integrity of sensor stability, as calculated by a normalised BG/sensor signal, comparing control and extended life sensors.

Secondary outcomes: Sensor insertion site appearance on Day 17 of extended-life sensor; impact of site (arm vs abdomen) insertion on integrity; plasma dexamethasone levels post sensor insertion.

Results: Sixty-two control and 86 extended-life sensors were studied. The normalised sensor signal was more stable and had less sensor-to-sensor variation comparing extended-life sensors to the control sensors between days 7 to 17. Median (IQR) values at day 17 for the extended life sensors compared with control were for arm 0.88 (0.78-0.99) vs 2.02 (1.16, 3.04) respectively (Figure 1) and abdomen 1.16 (0.94-1.91) vs 4.92 (1.91,10.69) respectively (P<0.001 for both). There were no differences in site appearances. Plasma dexamethasone levels were undetectable for all sensors.

Conclusions: Use of low dose dexamethasone in CGM is feasible and safe. Data supports improvement in sensor integrity past the Day 7 mark, and up to Day 17.

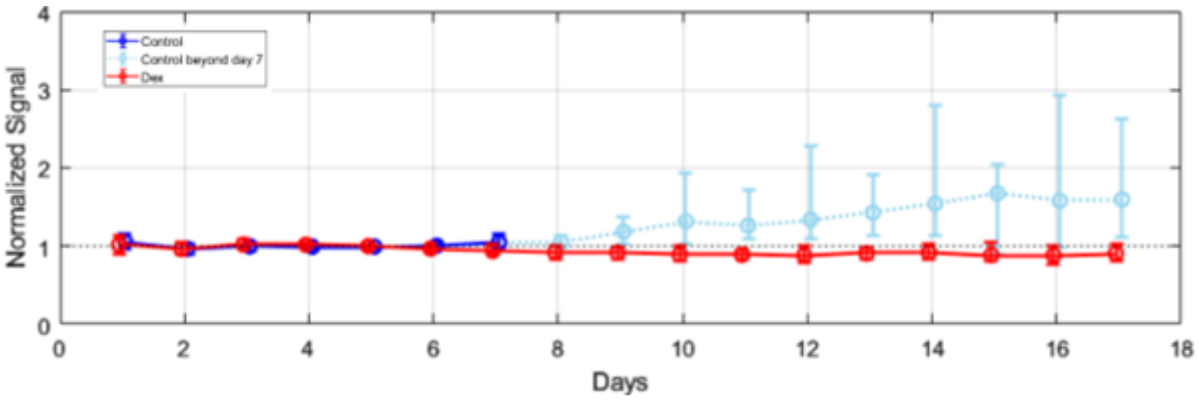

Figure 1: shows median (IQR) normalised signal for 63 extended-life sensors (Dexamethasone) vs 39 control inserted in the arms of 53 participants with type 1 diabetes.

Evaluation of a Specialist Telehealth model-of-care, Endocrinology Telehealth Rapid Access Clinical Services (Endo-TRACS), at a quaternary hospital: 2021- 2024

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Background: During the COVID pandemic, the Victorian Department of Health's 'Better-at-Home-Program' undertook several reforms to public hospital specialist clinics, developing clear pathways from referral to specialist service, greater use of telehealth for timely review of patients, and established arrangements for returning patients to primary care.

Aim: This study aimed to evaluate a new telehealth model of ambulatory care, Endo-TRACS, which delivers a rapid telehealth specialist response to patients referred to a quaternary hospital Endocrinology service. Endo-TRACS provides of a maximum of three specialist consultations along with specialist multi-disciplinary care for Diabetes management.

Method: From 2021 until 2024, administrative and clinical data were recorded for patients managed in Diabetes Endo-TRACS. This audit assessed administrative outcomes for all diabetes consultations and clinical outcomes in a subset (where data available).

Results: A total number of 1212 patients were included. Over 90% category 1 urgency cases were reviewed within the recommended 30 days. Of 990 individuals who completed Endo-TRACS care, 876 (89%) did so within three visits. Upon completion, 507 (58%) had care transferred to primary care, 50 (6%) were transferred to other services, while the remaining 319 (36%) patients were transferred to our mainstream Diabetes ambulatory care clinics, of whom 55% had type 1 diabetes.

A subgroup of 617 patients (mean age 55 years, 67% type 2 diabetes [T2D]) were assessed clinically. HbA1c decreased from mean 9.5±2.2% to 8.6±2.1% at third visit ($p < 0.001$). In T2D (n=414), sodium-glucose cotransporter-2 inhibitor and glucagon-like-peptide-1 receptor agonist use increased (23% to 35%, 13% to 34% respectively).

Conclusion: The Endo-TRACS model improved glycaemia and demonstrates how telehealth can be utilised effectively to deliver health outcomes for patients with diabetes referred to public hospitals. Endo-TRACS provides a rapid specialist response by optimising hospital resources and promoting better continuity of care between specialist Endocrine services and primary care.

Evaluation of an Obstetrics and Midwifery led pilot program for the Management of low risk women with Gestational Diabetes (GDM).

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Aim: In October 2021, a pilot program, aimed at shifting care of low risk women with diet controlled GDM into routine obstetric/midwifery led antenatal care was implemented at Pakenham Community health centre, a peripheral site at Monash Health. Prior to the pilot, all GDM care was delivered by specialist Endocrinologists. We aim to assess the maternal and foetal outcomes of women who were managed in the service before and after the pilot.

Method: Data were extracted from the Birth and Obstetric Services registry for all women with GDM who had antenatal care delivered at the Pakenham antenatal clinic during the 6 months prior to and following the implementation of the pilot. This included demographic information, medical history, maternal outcomes (diabetes treatment, hypertensive disorders of pregnancy, gestational age at delivery, method of delivery) and neonatal outcomes (including birth weight, APGAR scores and birth injuries) to 28 days post-partum.

Results: 370 and 407 women respectively were diagnosed with GDM in the 6 months prior to and following the introduction to the pilot. The demographic data were similar between the two groups. Rates of insulin use were similar before and after the pilot (33% and 35% respectively). 66 women (27%) had their entire diabetes care delivered in their routine obstetric/midwifery led antenatal clinic. Gestational age and mode of delivery were similar between the groups as were rates of maternal and neonatal complications. There were 3 neonatal deaths in the post implementation group, but all of these were unrelated to GDM.

Conclusion: An obstetric and midwifery led model of care for women with GDM and low maternal risk did not lead to an increase in adverse maternal or neonatal outcomes for women and their offspring. Ongoing referral to the Endocrine led service for women not commenced on insulin requires further exploration.

Evidence-Based practice of Exercise Rehabilitation Management in Patients with Diabetic Foot ulcers

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Background: Exercise rehabilitation is particularly important for patients with diabetic foot ulcers (DFUs).

Aims: To apply the best evidence based management of exercise rehabilitation in DFUs to clinical practice and to evaluate its effectiveness.

Methods: Evidence-based resources in the field of exercise rehabilitation related to DFU were searched according to the Knowledge-to-action framework. Twenty-one literatures were included through literature quality assessment. Thirty pieces of evidence were extracted and summarized from the literatures. The 30 pieces of evidence were evaluated through feasibility, appropriateness, and clinical significance, and were transformed into 12 clinical review indicators. Baseline data were collected using on-site inspections, reviewing records, and interviewing patients and healthcare professionals, and barriers were analyzed to construct a strategy for applying the best evidence. The implementation rates of the review indicators, patients' blood glucose levels, exercise knowledge, self-efficacy and behavioral scores, quality of life scores, and nurses' knowledge of exercise rehabilitation for diabetic foot ulcers were compared before and after evidence application.

Results: After best evidence application, DFUs (n=40) performed significantly better (P<0.05) on all 5 review metrics compared to baseline (n=40), with fasting glucose level (7.05±1.01) vs (6.16±0.72), postprandial glucose level (9.91±1.33) vs (8.13±1.42), exercise knowledge, self-efficacy, and behavioral levels (28.25±8.52) vs (35.83±6.24), and quality of life (48.25±10.15) vs (65.82±15.36). The nurses' implementation of all four review indicators increased significantly from baseline (P<0.05), and the nurses' score on the level of knowledge of exercise rehabilitation for diabetic foot ulcers increased from (26.51±8.81) points to (39.45± 9.57) points (P<0.05). The implementation rate of the three review indicators at the system level was 100%, which was a significant increase from baseline (P<0.05).

Conclusions: Applying the best evidence for the management of exercise rehabilitation in DFUs can standardize nursing practice, improve the overall health of patients, and enhance nursing practice.

Exercise for People with Diabetes-Related Foot Ulcers – an Update from the DFUEx Study

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Introduction & aims: Current treatments for people with diabetes-related foot ulcers (DFUs) focus on foot outcomes - potentially at the expense of broader health and wellbeing considerations. There are barriers to exercise for people with DFU and hesitancy in promoting physical activity by clinicians. The aim of this study was to examine the impact of supervised exercise intervention on cardiorespiratory fitness, health and wound healing in adults with DFU.

Methods: Using a randomised control trial design (ANZTR registration: 12622000885796p) adults aged 18 to 70 years (n=32) with active DFU are being recruited from an interdisciplinary High-Risk Foot Service (iHRFS) at Royal Prince Alfred Hospital Sydney Australia, and randomised to receive 12 weeks of supervised exercise (aerobic and resistance) training (Exercise) with usual care or usual care only (Control). Measurements including fitness, metabolic and wound outcomes are acquired at baseline and post intervention.

Results: The study is ongoing. Between February 2023 and March 2024, 34 potential participants were assessed for eligibility and 11 participants entered the study. Participants (n=10) had T2DM, mean age of 59.4 years (range:48-88), diabetes duration 11.4 years (SD: 4.7), and VO_2peak 11.2ml/kg/min (SD:2.2). To date there have been no adverse events. Key considerations relating to implementation of exercise therapy for people with DFU relate to managing weight bearing restrictions, comorbid disease, exercise-medication interactions, and access to transport. There is a need for robust evidence concerning the efficacy and safety of exercise intervention, and a need for strategies to engage exercise specialists into the multidisciplinary care of people with DFUs.
Supported by the 2022 Exercise and Sports Science Australia Research Grant.

Exploration of Gene expression profiling showed Local Peroxisome Proliferator-activated Receptor expression levels were critical in Diabetes-related Foot ulcers

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Aim: The exact pathogenesis and difficult healing mechanisms of Diabetes-related Foot Ulcer (DFU) have not been fully elucidated, and conventional therapeutic effects remain unsatisfactory. Peroxisome proliferators-activated receptors (PPARs) are reported to be excellent in regulating inflammation and immune responses and promoting angiogenesis. We aim to identify if PPARs are predictive and prognostic biomarkers and therapeutic targets of DFU.

Method: Full-thickness foot skin tissues gathered from individuals with diabetes with or without foot ulcers were subject to RNA sequencing. The differentially expressed genes (DEGs) landscape, their functions, and enriched signaling pathways were analysed by bioinformatic strategies (GO, KEGG). qRT-PCR and WB of the origin tissues and high-glucose-induced human immortal keratinocyte line (HACAT) were used to verify the expression of pivotal PPARs.

Results: Six samples in each group were completely sequenced, while the clinical characteristics of the individuals corresponding to these samples were completely matched. The results showed that 2443 genes differed between the two groups. Compared to diabetic non-foot ulcer tissues, there were 812 up- and 1631 downregulated genes in DFU tissues. The expression of PPARD and PPARG reduced, while the PPARA expression was not conspicuously different. GO/KEGG enrichment analysis illustrated that DEGs enriched significantly in the PPAR signaling pathway, neuroactive ligand-receptor interaction, cAMP signaling pathway, etc. High-glucose (45mM) induced HACAT were successfully cultured with inhibited proliferation and migration abilities and increased apoptosis which mimicked the damaged healing of DFU *in vivo*. The expression of PPARs (PPARA, PPARD, PPARG) in skin tissues and cell models were verified by qRT-PCR and WB and were basically consistent with the sequencing results.

Conclusion: Healing disorders of DFU are associated with underlying histological and anatomical changes. These changes may relate to the expression of PPARs and the PPAR signaling pathway, suggesting that the above genes and pathways may be pivotal targets in promoting DFU healing.

Exploring Biological Diversity in Dietary Responses for Type 2 Diabetes Prevention

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Aim: Type 2 diabetes (T2D) remains a significant public health challenge, with dietary management being a cornerstone of effective intervention in both the treatment and prevention of the disease. However, emerging evidence in the field of precision nutrition indicates that a one-size-fits-all dietary approach is ineffective. The aim of our study is to examine individual responses to different diets promoted in the management or prevention of T2DM.

Method: In our study, we investigated the biological diversity in response to the same dietary inputs among 23 participants at risk of T2D over a two-week period. All participants completed four days on three dietary interventions (Mediterranean, Australian and low carbohydrate diets). Urine, serum, plasma, and faecal samples were collected, alongside the use of continuous glucose monitoring data, to explore the metabolic and glycaemic responses.

Results: Our findings reveal significant individual differences in blood glucose levels and metabolic outcomes. When examining fasting blood glucose levels, the low carbohydrate and Australian diets were optimal for 8 participants each, while the Mediterranean diet was optimal for 7 participants. However, this did not always correlate with post prandial blood glucose level optimisation. While blood, urine and faecal samples are yet to be analysed, these are expected to provide further understanding of individual biological responses.

Conclusions: These results underscore the limitations of a universal dietary approach for optimizing glycaemic control and highlight the necessity of personalised dietary recommendations that consider individual metabolic profiles. Our study provides crucial insights for future advances in precision nutrition, suggesting that personalised nutrition plans could lead to more effective management and prevention of T2D.

Eyes as a Window to Pre-clinical Detection of Microvascular Complications in People with Diabetes Mellitus – A scoping review.

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With increasing diabetes mellitus prevalence, and people living longer with this condition, microvascular complications such as retinopathy, neuropathy, and nephropathy are increasingly affecting lives. Previous literature has demonstrated vascular and neural architectural changes caused by diabetes develop well before the occurrence of symptoms, but also prior to standard diagnostic techniques showing changes. The detection of microvascular complications earlier should allow initiation and monitoring of interventions to prevent progression to symptomatic disease. Advanced ocular examination modalities including optical coherence tomography (OCT), corneal confocal microscopy (CCM), and multifocal pupillographic objective perimetry (mf-POP), have been shown to be sensitive to pre-clinical microvascular disease changes in people with diabetes mellitus (PwDM). We conducted a scoping review of the literature to characterise the utility of advanced ocular examination modalities for pre-clinical detection of microvascular complications in PwDM. We included 159 studies of both cross-sectional and longitudinal design from a search of PubMed/Medline, Scopus, TRIP, EMBASE and Cochrane library. Initial analysis of the results demonstrated CCM to be proficient for pre-clinical detection of diabetic neuropathy. OCT parameters including foveal avascular area demonstrated moderate effect sizes for detecting diabetic retinopathy, though a high level of heterogeneity in examination methodologies was observed. We found there was limited investigation of mf-POP for PwDM without diagnosed microvascular disease. Ongoing optimisation of these modalities will enable comprehensive investigation of disease progression and earlier interventions to reduce the burden of microvascular complications for PwDM.

Factors predicting persistently High HbA1c Levels in Adults with Type 1 Diabetes

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Aims: The aim of this study was to identify factors that may predict adults with type 1 diabetes (T1D) that have a HbA1c ≥ 80 mmol/mol (≥ 9.5%) for at least 12 months.

Methods: We performed a retrospective case-control study of adults with T1D attending the Northern Adelaide Local Health Network Diabetes Service between July 2015 and January 2023 who had at least two HbA1c measurements 12 months apart. We compared the demographic and clinical data parameters for those with a HbA1c of ≥80 mmol/mol (≥9.5%) for at least 12 months, and those who did not, and analysed for univariate associations. Associated factors were then analysed using multivariable logistic regression with backwards elimination.

Results: Of 818 participants, 143 (17.5%) had a persistently high HbA1c, and 675 (82.5%) did not. Persistently high HbA1c was associated with younger age ($p<0.001$), active smoking ($p<0.001$), former or current recreational drug use ($p<0.001$), administering insulin via injection compared to continuous subcutaneous insulin infusion (CSII) ($p<0.001$), not counting carbohydrates ($p<0.001$), not using continuous glucose monitoring ($p<0.001$), history of depression ($p<0.001$), anxiety ($p=0.009$), socioeconomic disadvantage ($p=0.005$), low or normal body mass index ($p<0.001$), lower systolic blood pressure ($p=0.009$) and previous diabetic ketoacidosis ($p<0.001$). Multivariate analysis showed that potential predictors of persistently high HbA1c were socioeconomic disadvantage (lowest index of relative socioeconomic disadvantage quartile vs highest quartile within the state, odds ratio [OR]=3.03, $p=0.033$), depression (OR=2.90, $p<0.001$), administration of insulin via injection as opposed to CSII (OR=3.81, $p=0.002$), and current or former recreational drug use (OR=2.83, $p=0.002$).

Conclusion: Our study showed that potential predictors of persistently high HbA1c levels in adults with T1D include socioeconomic disadvantage, depression, not using CSII therapy, and current or former recreational drug use. Strategies focusing on addressing these factors may help to improve diabetes management in these individuals.

Feasibility and Validity of In-Home Self-Collected Capillary Blood Spot Screening for Type 1 Diabetes Risk

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Aims: Self-collection of a blood sample for autoantibody testing has potential to facilitate screening for type 1 diabetes risk. We sought to determine the feasibility and acceptability of this approach and the performance of downstream antibody assays.

Methods: People living with type 1 diabetes and their family members (N = 97) provided paired capillary blood spot and serum samples collected, respectively, by themselves and a health worker. They provided feedback on the ease, convenience, and painfulness of blood spot collection. Islet antibodies were measured in blood spots by antibody detection by agglutination PCR (ADAP) or multiplex enzyme-linked immunoassay (ELISA), and in serum by radioimmunoassay (RIA) or ELISA.

Results: Using serum RIA and ELISA to define antibody status, 50 antibody-negative (Abneg) and 47 antibody- positive (Abpos) participants enrolled, of whom 43 and 47, respectively, returned testable blood spot samples. The majority indicated that self-collection was easier, more convenient, and less painful than formal vene- section. The sensitivity and specificity for detection of Abpos by blood spot were, respectively, 85% and 98% for ADAP and 87% and 100% for multiplex ELISA. The specificities by ADAP for each of the four antigen specificities ranged from 98% to 100% and areas under the receiver operator curve from 0.841 to 0.986.

Conclusions: Self-collected blood spot sampling is preferred over venesection by research participants. ADAP and multiplex ELISA are highly specific assays for islet antibodies in blood spots with acceptable performance for use alone or in combination to facilitate screening for type 1 diabetes risk.

Clinical Trial Registration: ACTRN12620000510943.

Feasibility of a Combined Electrochemical Continuous Glucose Monitor with an Insulin Delivery Cannula (CGM-IS) in People with Type 1 Diabetes (T1D)

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Aim: Combining a single-needle insertion site continuous glucose monitor (CGM) with an insulin delivery system could help reduce the burden of care in people living with T1D. Our aim was to assess glucose sensor accuracy, infusion site patency and user tolerability of an experimental CGM-IS over 4 days.

Method: 12 adults with T1D underwent 48 hours of run-in with the Medtronic MiniMed 780G connected to a commercial cannula infusion set. Subsequently, the commercial infusion set was replaced with the trocar-free SynerG™ CGM-IS system. Participants consumed a standardised 80 g carbohydrate meal on day 1 and 4, with venous blood samples collected for glucose YSI and fingerstick test strips 10-minutely for 1 hour before, and 15-minutely for 4 hours after the meal. SynerG™ was used to deliver an insulin bolus prior to the meal. Participants performed fingerstick glucose monitoring and continued insulin delivery via SynerG™ at home between meal tests. A Dexcom G6 CGM was worn during run-in and throughout the study.

Results: MARD for SynerG™ against glucose YSI during the two meal tests was 9.0% (484 datapoints). Consensus error grid for SynerG™ against YSI showed 88.6% of values within Zone A and 100% within Zone A+B. Mean (SD) % bias was 3.5 (11.6) %. There were 35 paired YSI readings <5.6 mmol/L and 449 ≥5.6 mmol/L with 81.4% within 0.8 mmol/L or ±15%, and 89.9% within 1.1 mmol/L or ±20%. No artifact sensor spikes were observed. Two cannula occlusions occurred requiring discontinuation of insulin delivery. Mean glucose (9.0 ± 1.5 mmol/L vs 8.8 ± 1.4 mmol/L; p=0.39) and mean total daily insulin dose via pump (58.0 ± 25.4 units vs 57.1 ± 28.8 units; p=0.47) during run-in and between meal tests did not differ. The device was well tolerated.

Conclusion: This study supports the feasibility and tolerability of the SynerG™ CGM-IS over 4 days.

Fibrosis-4 Index (Fib-4) screening suggests Elevated Liver Fibrosis risk in Type 1 Diabetes: Implications for diabetes clinics

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Background: Guidelines recommend liver fibrosis screening using the Fib-4 calculator in all adults with type 2 diabetes (T2D) due to elevated risk of metabolic dysfunction-associated steatotic liver disease (MASLD) and fibrosis progression. Guidelines in type 1 diabetes (T1D) are lacking. Whether T1D are at increased fibrosis risk, and their identifying features is unknown.

Aim: evaluate the proportion of T1D and T2D needing referral for suspected liver fibrosis based on Fib-4 scores and identify the metabolic characteristics of at-risk T1D patients.

Methods: We included adults (>18 years) with T1D or T2D attending St.Vincent's Hospital Sydney diabetes clinics in 2023 (established cirrhosis excluded). We compared demographic, metabolic, and anthropometric characteristics by diabetes type and Fib-4 risk category (<1.3 low risk, 1.3-2.67 indeterminate risk warranting further investigation, >2.67 high probability advanced fibrosis). T-test and chi-square tests were used.

Results: We screened 362 adults including n=285 with T2D (age 70±11.2 years, BMI 30.0±6.7kg/m^2 HbA1c 8.0±1.8%, male 73%) and n=77 with T1D (age 57.3±14.4 years, BMI 27.6±4.57kg/m^2, HbA1c 7.5±1.3%, male 60%). Fib-4≥1.3 was present in 47% (n=36) of T1D and 64% (n=183) of T2D. Compared to indeterminate risk T2D, indeterminate risk T1D were younger (age 65.7±8.9 vs 72.6±9.0 years, p<0.001), had longer duration diabetes (37.4±14.9 vs 17.8 ±11.3 years, p<0.001) and a lower BMI (26.3±4.2 vs 30.2±6.4 kg/m^2, p=0.002). Compared to low risk T1D, indeterminate risk T1D were older (65.7±8.9 vs 49.4±13.5 years, p<0.001) and had a lower BMI (26.3±4.2kg/m^2 vs 28.6±4.6kg/m^2, p=0.045). Most (83%) of T1D with Fib-4≥1.3 had BMI<30kg/m^2 and 52% BMI<25kg/m^2.

Conclusion: This study suggests 1) both T1D and T2D are at increased risk of liver fibrosis, 2) normal BMI should not preclude Fib4 screening in T1D, and 3) transient elastography referral pathways are needed in all diabetes clinics. Validation of the Fib-4 index in T1D is required.

Financial impact of Inpatient Hypoglycaemia: Analysis of Direct costs and Hospital acquired Complication Penalties

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Aim: With the negative health outcomes of hypoglycaemia well-established in the literature, inpatient hypoglycaemia has been listed as an hospital acquired complication (HAC). We aimed to investigate the financial impacts of inpatient hypoglycaemia from the viewpoints of patient morbidity, associated hypoglycaemia treatments, and HAC penalties.

Methods: The study was completed in two separate segments. The first part involved liaising with a quaternary hospital's Clinical Coding Department to understand the process of detecting hypoglycaemia as a HAC. This was followed by consulting the hospital's Clinical Costing Department, where the direct costs of inpatient hypoglycaemia (patient morbidity and treatment of hypoglycaemia) and the HAC penalties were sought to be identified. The direct costs were estimated by hypothesising complete adherence to the inpatient hypoglycaemia treatment protocol. As the financial year is yet to be complete, data collection regarding HAC penalties remains ongoing with a projected completion at the end of the 2023-24 financial year.

Results: The minimum direct cost of inpatient hypoglycaemia (with complete adherence to the inpatient hypoglycaemia protocol) includes the provision of food and 60 minutes of nursing time (total 6 uses of glucometer, 20 minutes of carbohydrate administration) incurring a total of $50. This is amplified if medical reviews are involved, which will lead to 20 minutes of resident's work hours or potentially 60 minutes of on-call registrar pay. If the MET team is activated, the tally may increase by an additional $200. Overnight bed cost of $350-$580 may be required for patients extending their hospital stay.
The HAC funding deficits as a result of inpatient hypoglycaemia continues to be investigated.

Conclusion: Depending on the disease severity, the direct costs of inpatient hypoglycaemia alone may cause a substantial financial impact to the hospital. The associated HAC costs of inpatient hypoglycaemia remain to be calculated.

Formation Mechanism of α Particles in Glycogen: Testing the budding hypothesis by Monte-Carlo simulation

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Glycogen, a complex branched glucose polymer and a blood-sugar reservoir in animals, comprises small β particles joined together into composite α particles. In diabetic animals, α particles fragment more easily than those in healthy animals. Finding evidence for or against postulated mechanisms for α -particle formation is thus important for diabetes research. Insight into this is obtained here using Monte-Carlo simulations, including addition and loss of glucose monomer, branching and debranching, based on earlier simulations which were in acceptable agreement with experiment [Zhang et al., Int J Biol Macromolecules 2018, 116, 264]. One postulated
mechanism for α -particle formation is “budding”: occasionally a glucan chain temporarily protrudes from the particle, and if its growing end is sufficiently far from its parent particle, it propagates to a new linked particle. We tested this by simulations in which an “artificial” bud (a chain extending well outside the average particle radius) is added to a glycogen molecule in a dynamic steady state, and the system allowed to evolve. In some simulations, the particle reached a new steady state having an irregular dumbbell shape: a rudimentary α particle. Thus ‘budding’ is a possible mechanism for α particles to form. If no simulations had shown this behaviour, it would have refuted the postulate.

GIRFT Diabetes (Getting It Right First Time): Leading the way in quality improvement for the future of diabetes care in Queensland

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Aim: Getting It Right First Time (GIRFT) quality improvement program originated in the UK and has been adopted by Queensland Health to reduce unwarranted variation and improve patient outcomes through peer-reviewed, clinician-led data discussion.

Method: Clinical Excellence Queensland (CEQ), through stakeholder consultation, including clinical reference group and data analysts, developed key indicators identifying unwarranted variation across Queensland with a diabetes focus.
An interactive, quarterly refreshing dashboard was developed and shared across 20 participating sites. With support from program clinical-lead, site visits were held with focus on peer-to-peer, deep-dive review of data, identifying opportunities to improve patient outcomes and exemplar service models of care.

Results: The chosen, data driven indicators suitable for the large breadth of sites across Queensland include:

- Patient demographics including casemix, complexity, first nation status, disease prevalence.
- Priority Area 1: Type I diabetes (eg. DKA admission and re-admission rates)
- Priority Area 2: Inpatient care (eg. Medication errors, control for episodes of hypoglycaemia, clinical coding, length of stay for person with and without diabetes, surgical intervention differences including infections, in-scope hospital acquired complications, patient reported experience survey)
- Priority Area 3: High Risk Diabetic Foot (eg. Foot amputation rates, length of stay and readmission)

Desire for further data related to outpatients, workforce, models of care and service delivery was not able to be accessed within the existing systems available in Queensland, however discussion around these key indicators is currently included.

Conclusion: GIRFT Diabetes Queensland methodology identified gaps in data, however, has also begun meaningful engagement and local conversations within facilities to identify opportunities for quality improvement. The systemic support including regular site visits, tailored site reports and suggested action plans facilitates continuous, supported quality improvement over time as business as usual.
Sharing the insights behind the application of these particular data sets to the broader diabetes clinical community is vital.

Glucocorticoid-induced Hyperosmolar Hyperglycaemic state: A case report and literature review

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Introduction: Hyperosmolar hyperglycaemic state (HHS) is serious complication of diabetes. Glucocorticoids are associated with many adverse effects including hyperglycaemia. We report a case of HHS associated with the use of high-dose prednisolone for treatment of acute interstitial nephritis in a patient with type 2 diabetes mellitus.

Case: A 73-year-old woman with a history of type 2 diabetes mellitus (HbA1c 7.0 – 8.0%) on treatment with metformin and vildagliptin was investigated for declining kidney function. She was diagnosed with acute interstitial nephritis and was commenced on high-dose prednisolone. Due to her kidney disease, metformin and vildagliptin were substituted with gliclazide and linagliptin. Insulin therapy was subsequently commenced for treatment of glucocorticoid-induced hyperglycaemia. However, she started to have increasing blood glucose levels associated with worsening symptoms of hyperglycaemia and had to present the hospital. Investigations demonstrated serum glucose of 39 mmol/L with serum osmolality of 323 mOsmol/kg (reference range: 275 – 300), in keeping with HHS. Infection and myocardial infarction were excluded. She was treated with intravenous fluid therapy which resulted in gradual improvement of blood glucose. Following resolution of HHS, she was able to achieve and maintain good glycaemic control with the use of pre-mixed insulin, dulaglutide and gliclazide. Prednisolone was tapered over the subsequent two months. Her renal function remained stable following discontinuation of prednisolone.

Conclusion: This case highlights the importance of regular blood glucose monitoring in patients on high-dose glucocorticoid therapy and demonstrates that high-dose glucocorticoids can precipitate HHS.

Glucoregulatory Impact of Whey Protein Ingestion in adults with Type 1 Diabetes

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Aim: This study aims to characterise the magnitude, timing, and dose effect of glucoregulatory responses to whey protein ingestion in adults with type 1 diabetes (T1D).

Method: This preliminary analysis of 2 adults with T1D (average, Age: 51y; Weight: 67.5kg; Duration of diabetes: 19y; HbA1c: 6.3%) using insulin pumps, involved four interventions in random order following an overnight fast; i) Water (Con), ii) low-dose whey protein (LP; 0.25g/kg), iii) high-dose whey protein (HP; 0.5g/kg), and iv) carbohydrate (CHO; 0.25g/kg). Participants' insulin infusion was replaced by IV insulin, and after allowing 4h for subcutaneous insulin wash-out, blood samples were taken every 10min for 3h post-ingestion under stable IV insulin infusion. All values are calculated as change from time=0min.

Results: Peak change in blood glucose was highest for CHO (+4.7mmol/l), compared to HP (+3.3mmol/l) and LP (+1.6mmol/l). Glucose AUC was similar for CHO and HP (398 mmol/l x min vs 374 mmol/l x min), albeit a different time-course (time-to-peak; 55min vs 130min), but higher than LP (127 mmol/l x min) which had time-to-peak between CHO and HP (85min)(Figure 1A). Blood glucose decreased steadily for the sampling duration for Con. HP compared to LP had higher peak change in glucagon and glucagon AUC, while glucagon was suppressed throughout the sampling period for CHO and Con (Figure 1B).

Conclusion: Whey protein ingestion rapidly stimulates glucagon secretion and significantly increases blood glucose, in a dose-dependent manner, albeit with a delayed response compared to carbohydrate. Further metabolic analysis will elucidate the physiological mechanisms of this response. This highlights the possibility for whey protein ingestion as an intervention to manage hypoglycaemia in people with T1D.

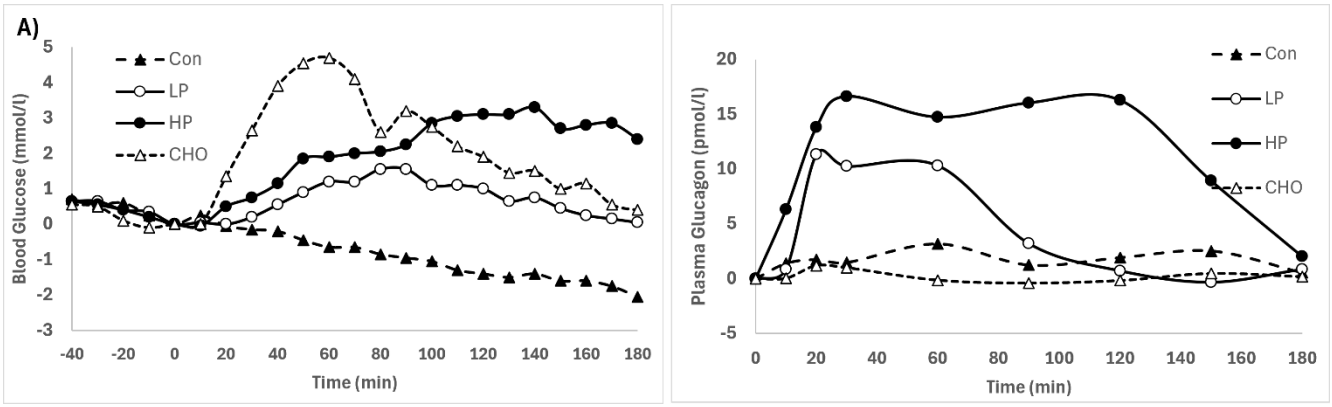

Figure 1: Average blood glucose (A) and plasma glucagon (B) responses to water (Con), low-dose protein (LP), high-dose protein (HP) and carbohydrate (CHO). Values are change from time=0min.

Glucose lowering Drug Utilisation and Expenditure in Australia 2003-2023.

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Aim: To explore changes in utilisation and expenditure of insulin from 2003 to 2023 and non-insulin glucose lowering drugs (GLDs) from 2013 to 2023 in Australia.

Method: Pharmaceutical Benefits Scheme GLD dispensing data were obtained from Services Australia. Units of insulin and Defined Daily Doses (DDD) were calculated and adjusted for diabetes prevalence. The proportion of people with insulin-treated type 2 diabetes was obtained from National Diabetes Services Scheme data. Inflation adjusted expenditure was calculated. Utilisation changes were assessed by Joinpoint analysis and insulin changes by interrupted time series analysis.

Results: Insulin utilisation increased by an average of 2.7% per annum (95% CI 2.0%, 3.7%) from 2003 to 2015, then fell by 2.7% p.a. (-4.6%, -1.4%) from 2015 to 2023. The proportion of people with type 2 diabetes who were insulin-treated increased by 1.0% p.a. (0.8%, 1.3%) from 2013 to 2020, then fell by 0.7% p.a. (-1.6%, -0.04%) between 2020 and 2023. Interrupted time series analysis of the slopes of insulin utilisation before and after 2015 demonstrated significant differences for total insulin, basal insulin and quick acting insulin, but not premixed insulin. SGLT2i DDD increased by 59.2% p.a. (51.4%, 68.1%) from 2014 and GLP-1 RA DDD by 29.3% p.a. (26.1%, 32.6%) between 2013 and 2023. DPP4i DDD increased by 11% p.a. (8.2%, 13.8%) and metformin DDD by 3.4% p.a. (2.0%, 4.8%). Sulphonylureas, acarbose and glitazone DDD all fell. SGLT2i and GLP-1RA expenditure increased by 50.8% p.a. and 28.1% p.a. respectively whilst insulin expenditure decreased by 43% between 2015 and 2023, due to reduced utilisation and a substantial price reduction of insulin glargine.

Conclusion: Non-insulin GLD utilisation doubled, and expenditure tripled over the last 11 years, mainly due to increased GLP-1 RA and SGLT2i use. Insulin utilisation and expenditure peaked in 2015 and thereafter declined, partially offsetting increased non-insulin GLD expenditure.

Glucose-Dependent Insulin Granule Fusion in Pancreatic β cells is regulated by Dynamic Microdomain Protein complexes containing liprin-α1

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Exocytotic release of hormones from endocrine cells must include mechanisms that direct the hormone into the blood stream. In pancreatic β cells, insulin secretion is targeted to the region of the cell contacting the islet capillaries to accomplish direct secretion into the vasculature. However, the mechanisms that control this targeting remain unclear. Using global liberation of caged Ca^{2+} (Ca^{2+}-NP-EGTA), we show that insulin secretion is still targeted in the absence of localised Ca^{2+} entry, indicating a specific mechanism of granule positioning to the capillary interface. Knockdown of liprin-α1, a presynaptic scaffold protein known to organise vesicle docking and exocytosis at the neuronal presynaptic active zone, reduces glucose-stimulated insulin secretion and impairs granule targeting. Moreover, liprin-α1 assembles in dynamic glucose-dependent microdomain clusters at the β cell vascular face that spatially constrain insulin granule fusion. Finally, co-immunoprecipitation of liprin-α1 followed by mass spectrometry analysis identified protein-protein interactions indicative of a broader β cell presynaptic-like complex and an association with insulin granules via β-syntrophin. Together, we conclude that liprin-α1 regulates insulin secretion in pancreatic β cells by assembling in a presynaptic-like complex that controls insulin granule fusion at the β cell vascular face.

Glycaemic outcomes in Children with Type 1 Diabetes on Advanced Hybrid Closed Loop Therapy: the impact of clinical and socioeconomic characteristics.

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Aim: To evaluate real-world Advanced Hybrid Closed Loop (aHCL) outcomes based on clinical and socioeconomic characteristics in a population-based, Western Australian cohort of youth with type 1 diabetes (T1D).

Methods: A population-based retrospective study was conducted of youth in Western Australia commencing aHCL between December 2021 and June 2023. Youth with 2-weeks CGM pre-aHCL were included. CGM metrics were analysed in those with ≥70% use and data at baseline and 6 months post aHCL . Change in time in range (TIR) was analysed based on age at aHCL start (<12 years, ³12 years), baseline % TIR (<40%, 40-49%, 50-59%, 60-69%, ³70%) and Socio-Economic Indexes for Areas (SEIFA) Index of Relative Socioeconomic Disadvantage (IRSD) of residential postcode.

Results: 245 youth (53% male, age 12.4 [3.1] years, diabetes duration 5.0 [3.3] years,95% self-funded pumps, 5% subsidised pumps) commenced aHCL. aHCL improved glycaemic outcomes with a mean change in TIR from baseline of +8% (p<0.001) at 6-months. Children with the lowest TIR at baseline experienced the greatest increases in TIR with aHCL therapy (+20.9% vs -0.2%; p<0.001) for baseline TIR < 40% vs > 70%. Children <12 years had a +9% change in TIR vs +10% in those ³12 years (p=0.07). When stratified by SEIFA IRSD Quintile, there was no difference in TIR gain post-aHCL start across the quintiles, with those from the most socioeconomic disadvantaged areas (quintile 1) showing +9% change in TIR compared to +6% in those from the least disadvantaged areas (quintile 5) (p= 0.3).

Conclusion: In real-world clinical use across a state-wide cohort of youth with type 1 diabetes, aHCL therapy improves glycemia, irrespective of age and socioeconomic characteristics, with the greatest changes seen in those with lowest baseline TIR.

Glycaemic outcomes in young adults with Type 1 Diabetes before and after universal subsidised Continuous Glucose Monitoring funding

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Background: In July 2022, fully-subsidised access to continuous glucose monitoring (CGM) was broadened to all >21 years with type 1 diabetes mellitus (T1D). Previous paediatric studies have established benefits of subsidised CGM benefits in this cohort. Given poorer glycaemic outcomes, disproportionate hospital admissions for diabetic ketoacidosis and less health care engagement, we hypothesised that increased CGM uptake would result in improvement in these parameters amongst young adults.

Method: 166 individuals with T1D (707 clinic visits) aged 20-26 years from the Westmead Young Adult Diabetes Clinic were reviewed between 2021– 2023. Three groups were identified – those starting CGM after July 2022, those who never used CGM and those who used CGM continuously through the study period. Primary outcome was the improvement in HbA1c following CGM commencement age >21. Secondary outcomes include percentage use of CGM, clinic visit frequency, socio-economic status (IRSAD quintiles), and rates of glycaemic emergencies.

Results: Following the introduction of CGM, mean HbA1c improved from 9.1% to 8.7% (p=0.004), improving further in those using CGM >50% of the time (mean HbA1c decrease -0.52%). 20% of new CGM users achieved an HbA1c target of 7% or less, compared to 5% prior to use.
In all users, mean HbA1c improved with increasing CGM use. When CGM was used >75% of the time, mean Hba1c was 7.9% (+/- 1.3%). CGM-users attended follow up more frequently than CGM non-users (interval 135 vs 174 days). When adjusted for effect of COVID pandemic, median frequency of visits was 105 days. Glycaemic emergencies were rare (2 per 100 patient years), across groups. Despite wide availability of CGM, uptake is still higher in those from higher socio-economic backgrounds.

Conclusion: The use of CGM in young adults over the age of 21 was associated with a small but significant improvement in glycaemic control and improved attendance frequency.

Grouping Ethnicity by Region significantly underestimates Variation in Diabetes risk

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Aim: Ethnicity is a major risk factor for diabetes. We aimed to determine if using large geographic region as a proxy for ethnicity masks important variation in diabetes risk within regions.

Methods: We performed a cross-sectional analysis of the 2021 Australian census, which for the first time included health data. Diabetes prevalence was age- and sex-standardised to a reference population of all adult respondents to the census.

Results: More than 17.7 million adults who had diabetes status data available were included. There was significant heterogeneity in age- and sex-standardised diabetes prevalence between and within geographic regions (Table 1). For South/Central Asia, among those reporting a sole ancestry, diabetes prevalence ranged from 9.0% (95%CI 8.7-9.3%) in Punjabi people to 18.7% (95%CI 18.3-19.1%) in Bangladeshi people. The prevalence of diabetes among sole East Asian ancestries ranged from less than the Australian prevalence (Japanese 4.1% (95%CI 3.9-4.3%), Thai 5.8% (95%CI 5.6-6.0%)) to almost twice the Australian prevalence (Filipino 12.0% (95%CI 11.9-12.1%)). Sole Middle Eastern/North African ancestries had diabetes prevalences ranging from 7.3% (95%CI 7.1-7.5%) in Iranian people to 12.0% (95%CI 11.6-12.4%) in Egyptian/Iraqi people. In Oceania, Australian Aboriginal, Maori and Samoan people all had diabetes prevalences much greater than the Australian prevalence (17.0% (95%CI 16.8-17.2%), 9.8% (95%CI 9.5-10.1%), 15.7% (95%CI 15.3-16.1%) respectively vs 6.1% (95%CI 6.1-6.1%)). Considering those reporting dual ancestries further widened the already large range of diabetes prevalences.

Conclusions: In nearly 18 million adults, there was a 2 to 3-fold variation in diabetes prevalence within each of four geographical regions. This indicates that aggregating ethnicity into regional groups is overly simplistic, thereby potentially leading to incorrect conclusions regarding diabetes risk. As Australia becomes more ethnically diverse, clarity on the definition and composition of ethnic origin will influence understanding of diabetes in specific populations and help design more effective health policy.

Table 1. Crude and age- and sex-standardised diabetes prevalence for people in the Australian census by geographic region and ancestry. Only single ancestries of non-European origin with greater than 25,000 people with self-report diabetes status data available were included. For people reporting dual ancestries with a matching single ancestry meeting selection criteria and at least one non-European ancestry, groups with greater than 10,000 people with self-report diabetes status data available were included.

Geographic region	Ancestry		Crude prevalence % (95% CI)	Age- and sex-standardised prevalence % (95% CI)
Oceania	Australian		6.4 (6.4-6.4)	6.1 (6.1-6.1)
	Australian Aboriginal	Sole ancestry	13.4 (13.2-13.6)	17.0 (16.8-17.2)
		& Australian	7.7 (7.6-7.8)	12.6 (12.4-12.8)
		& British/Irish	8.6 (8.4-8.8)	11.0 (10.8-11.2)
			10.7 (10.2-11.2)	16.8 (16.2-17.4)

		& Torres Strait Islander		
	Maori	Sole ancestry & British/Irish	7.8 (7.5-8.1) 5.1 (4.9-5.3)	9.8 (9.5-10.1) 6.8 (6.6-7.0)
	Samoan		11.0 (10.7-11.3)	15.7 (15.3-16.1)
East Asia	Chinese	Sole ancestry & Australian & British/Irish & Indonesian & Vietnamese	4.8 (4.8-4.8) 3.4 (3.2-3.6) 3.9 (3.7-4.1) 3.5 (3.2-3.8) 5.6 (5.3-5.9)	6.2 (6.2-6.2) 6.5 (6.2-6.8) 6.0 (5.8-6.2) 7.1 (6.7-7.5) 8.6 (8.2-9.0)
	Filipino	Sole ancestry & Australian & British/Irish & Spanish	8.3 (8.2-8.4) 2.3 (2.1-2.5) 1.7 (1.5-1.9) 9.0 (8.5-9.5)	12.0 (11.9-12.1) 10.5 (10.0-11.0) 6.8 (6.4-7.2) 11.1 (10.6-11.6)
	Indonesian		4.2 (4.0-4.4)	7.6 (7.3-7.9)
	Japanese		2.1 (2.0-2.2)	4.1 (3.9-4.3)
	Khmer (Cambodian)		6.1 (5.8-6.4)	8.8 (8.5-9.1)
	Korean		3.7 (3.6-3.8)	6.6 (6.4-6.8)
	Nepalese		1.5 (1.4-1.6)	9.8 (9.6-10.0)
	Thai		2.6 (2.5-2.7)	5.8 (5.6-6.0)
	Vietnamese		5.8 (5.7-5.9)	8.0 (7.9-8.1)
South and Central Asia	Afghan		6.3 (6.0-6.6)	11.8 (11.4-12.2)
	Bangladeshi		9.3 (9.0-9.6)	18.7 (18.3-19.1)
	Indian	Sole ancestry & Australian & British/Irish & Punjabi	6.9 (6.8-7.0) 4.1 (3.7-4.5) 6.7 (6.4-7.0) 2.3 (2.1-2.5)	12.9 (12.8-13.0) 10.1 (9.6-10.6) 8.3 (7.9-8.7) 6.0 (5.6-6.4)
	Nepalese		1.5 (1.4-1.6)	9.8 (9.6-10.0)
	Pakistani		5.5 (5.3-5.7)	15.3 (15.0-15.6)
	Punjabi	Sole ancestry & Sikh	3.0 (2.8-3.2) 3.0 (2.8-3.2)	9.0 (8.7-9.3) 8.3 (8.0-8.6)
	Sinhalese		9.6 (9.3-9.9)	13.8 (13.5-14.1)
	Sri Lankan		10.4 (10.1-10.7)	13.6 (13.3-13.9)

Middle East & North Africa	Assyrian		9.5 (9.1-9.9)	10.6 (10.2-11.0)
	Egyptian		11.3 (10.9-11.7)	12.0 (11.6-12.4)
	Iranian		4.4 (4.2-4.6)	7.3 (7.1-7.5)
	Iraqi		8.2 (7.9-8.5)	12.0 (11.6-12.4)
	Lebanese	Sole ancestry & Australian & British/Irish	9.2 (9.0-9.4) 4.6 (4.3-4.9) 2.0 (1.7-2.3)	10.8 (10.6-11.0) 10.0 (9.5-10.5) 3.0 (2.7-3.3)
	Turkish		9.4 (9.1-9.7)	11.1 (10.8-11.4)

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Haptoglobin (Hp) Levels and Phenotype are not related to Retinopathy in Type 2 Diabetes, but Hp response to Fenofibrate is associated with Retinopathy Benefit

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Background: Haptoglobin (Hp) has anti-oxidant and anti-inflammatory effects. Hp genotype/phenotype modulates chronic diabetes complication risk and fenofibrate benefit on coronary artery and kidney disease in type 2 diabetes (T2D). It is unknown whether Hp phenotype and level are associated with risk of sight-threatening diabetic retinopathy (STDR) and fenofibrate benefit. Fenofibrate reduced STDR by 31% overall in the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) trial.

Aim: To determine if Hp phenotype and levels are associated with new on-trial STRD in T2D and fenofibrate benefit over 5-years.

Methods: Hp phenotype (ELISA) and level (immunoturbidimetric assays) were measured in 8047 FIELD subjects at baseline and randomisation (after a run-in, including 6-weeks fenofibrate).

Results: There were 307 new STDR events on-trial. Hp phenotype and baseline levels were not related to STDR risk. Fenofibrate benefit on STDR risk tended to be greater for Hp 2-2 phenotypes, but was not statistically significant (HR [95% CI] = 0.68 [0.35-1.34], 0.80 [0.58-1.10] and 0.55 [0.37-0.82] for Hp 1-1, 2-1 and 2-2 phenotypes respectively, p for trend = 0.50). During run-in fenofibrate reduced Hp levels by 20.7% (p<0.001). Fenofibrate benefit, compared with placebo, was greatest in those with the lowest tertile of baseline Hp levels (HR [95% CI] = 0.40 [0.25-0.64], 0.84 [0.57-1.23], and 0.84 [0.55-1.26] for tertiles 1, 2 and 3 respectively, p for trend = 0.047) and among those in whom Hp levels showed least change during active run-in (HR [95% CI] = 0.47 [0.31-0.72], 0.74 [0.49-1.12], and 0.90 [0.61-1.33] for tertiles 1, 2 and 3 of Hp change respectively, p for trend = 0.021).

Conclusion: Neither Hp level or phenotype is strongly related to STDR risk in T2D, but benefits of fenofibrate vary by Hp level and extent of changes during 6-weeks fenofibrate.

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Health Care Provider Perspective on the Use of Smart Insulin Pens for Diabetes Mellitus

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Aim: This study aimed to assess the satisfaction of heath care providers (HCPs) upon prescribing smart insulin pens to ascertain real-world HCP opinions.

Methods: Twenty-minute online quantitative interviews were conducted with HCPs responsible for prescribing or interacting with NovoPen® 6 or NovoPen EchoPlus® users.

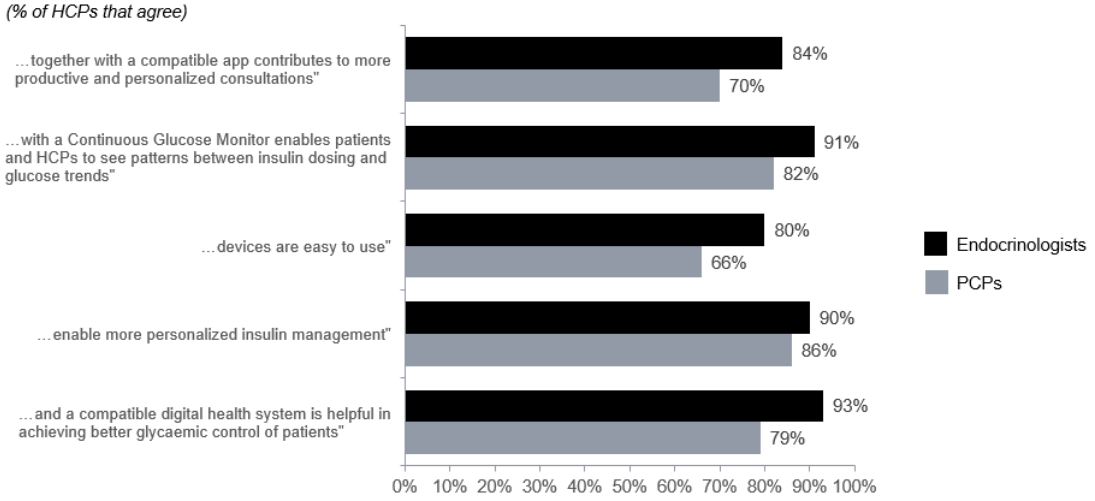
Results: Among 302 HCPs, median specialty duration was 18 years, median time in direct patient care was 90%, and median caseload was 40 and 100 patients/month with type 1 (T1DM) and 2 diabetes mellitus (T2DM), respectively. Of total T1DM or T2DM caseload, HCPs prescribed smart pens similarly to patients with T1DM (22%) and T2DM (20%). HCPs most frequently cited medical (uncontrolled hypoglycemia [65% of HCPs]; glycemic fluctuations [62%]) and technical (ability to learn smart pen use [64%]; high motivation to manage diabetes [63%]) reasons for prescribing smart pens. HCPs agreed (data in **Figure**) that connected (i.e., compatible app, continuous glucose monitor, or compatible digital health system) smart pens are easy to use and provide benefits, including enabling more productive and personalized consultations, showing patterns between insulin dosing and glucose, and helping patients achieve better glycemic control. Pen access (47%), need to sync pen with an app (34%), and insulin compatibility (31%) were disliked by HCPs.

Conclusions: HCPs found smart insulin pens easy to use and believed they were suited to patients with T1DM and T2DM. Poor glycemic control, patient ability to learn, and patient motivation most frequently prompted HCPs to prescribe smart pens. HCPs agreed that connected pens enable personalized insulin management and help achieve better glycemic control.

Figure. Proportion of HCPs that agree with select survey questions.

"Connected Novo pens…

(% of HCPs that agree)



Health Professionals' unmet needs for Supporting Adults with Type 1 Diabetes and fear of Hypoglycaemia: Findings from HypoPAST (Hypoglycaemia Prevention, Awareness of Symptoms, and Treatment)

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Aim: To explore diabetes health professionals' (DHPs) experiences of, and unmet needs for, supporting adults with type 1 diabetes (T1D) and fear of hypoglycaemia (FoH).

Method: A brief (10-minute) online survey explored DHPs perceived capability, opportunity, motivation and behaviours related to supporting adults with T1D and FoH in Australia. Participants were recruited via online methods, mailing lists, and at the Australasian Diabetes Congress 2023. Data were analysed using descriptive statistics.

Results: The survey was completed by 106 eligible DHPs (83% credentialled diabetes educators, 92% women, mean(SD) age 49(11) years) representing all states/territories. DHPs estimated a median (IQR) of 62% (30-80) of adults with T1D they consult with experience FoH. Most DHPs feel confident to ask adults with T1D about FoH (86%), and 74% do so 'most' or 'all' of the time. Yet only 24% have access to, and 28% know how to use, a validated tool to assess for FoH. Few perceive that mental health care for FoH is affordable for adults with T1D (8%) or that financial remuneration is available to DHPs to address FoH (9%). The NDSS 'fear of hypoglycaemia' factsheet for people with diabetes is known to 58% of participants, and this group would recommend it 'sometimes' (52%) or 'often' (34%). If an effective online self-help program were available to reduce FoH, most DHPs would be 'likely' (29%) or 'very likely' (53%) to recommend it to adults with T1D.

Conclusion: DHPs report that FoH is common among adults with T1D in Australia, and many DHPs feel motivated and capable to talk about, and address FoH in clinical consultations. However, opportunity to do so is limited by inadequate access to screening tools, remuneration, and affordable mental health care. There is unmet need for affordable and accessible interventions for people experiencing FoH, such as an effective, online self-help program.

Hepatocyte-specific CCN2/CTGF Gene deletion prevents NASH Fibrosis in a mouse model of high fat feeding and diabetes: Exploring potential mechanistic pathways

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Introduction: Cellular communication network factor 2 (CCN2/CTGF) is a pro-fibrotic protein that is implicated in the progression of non-alcoholic steatohepatitis (NASH) fibrosis.
Aim: To examine whether hepatocyte-specific gene deletion of CCN2 leads to less severe liver fibrosis in high-fat-fed mice with or without diabetes, and to explore potential related signaling pathways.

Methods: Male control mice (B6.Cg-Tg(AlbCre)21Mgn/J (AlbCre) and floxed CCN2 ($CCN2^{fl/fl}$), and hepatocyte-specific CCN2 knockout mice (CCN2flxB6.Cg-Tg(AlbCre)21Mgn/J (CCN2-KO)), were fed either standard Chow or high-fat-diet (HFD). Half of the HFD mice were rendered diabetic (HFD+DM) after 16wks with low dose streptozotocin. Mice were then maintained for a further 10wks. Liver fibrosis was histologically assessed with Picro Sirius Red (PSR) staining; mRNA and protein levels of key fibrosis markers were measured by RT-qPCR and Western immunoblot.

Results: In CCN2-KO HFD+DM mice, there was a ~50% reduction in liver fibrosis examined by PSR staining compared with AlbCre HFD+DM ($p<0.001$) and $CCN2^{fl/fl}$ HFD+DM ($p=0.002$) mice. There were also significant reductions in mRNA levels of collagen-1 (vs $CCN2^{fl/fl}$, $p=0.049$), collagen-6 (vs $CCN2^{fl/fl}$, $p=0.022$), TGFβ-1 (vs AlbCre, $p=0.002$) and fibronectin-1 (vs $CCN2^{fl/fl}$, $p=0.015$). At the protein level, collagen-1 (vs AlbCre, $p<0.001$; vs $CCN2^{fl/fl}$, $p=0.022$) and TGFβ-1 (vs AlbCre, $p=0.017$; vs $CCN2^{fl/fl}$ $p<0.001$) showed reduced expression in CCN2-KO HFD+DM mice by Western immunoblot compared with control HFD+DM mice, but no changes were identified in active YAP-1 levels. There was no significant change in fibrosis outcomes in CCN2-KO HFD mice compared with control HFD mice. Reduction of liver CCN2 mRNA and protein was confirmed in CCN2-KO HFD+DM mice but not in CCN2-KO HFD mice.

Conclusion: In the high fat feeding and diabetes murine model, attenuation of liver fibrosis in hepatocyte-specific CCN2 gene knockouts is diabetes-dependent. The reduction of liver fibrosis in CCN2-KO HFD+DM mice may be due to the regulation of TGFβ-1 by CCN2.

High Diabetes prevalence among Inpatients at Alice Springs Hospital – Comparison between Hospital-wide audit and ICD-10 coding data

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Aim: There is a diabetes epidemic affecting Aboriginal people in Central Australia, and reported prevalence of diabetes in hospitalised inpatients from ICD-10 data may be an underestimate. An audit of inpatients at Alice Springs Hospital, with comparison to ICD-10 data, could provide useful information on the prevalence of diabetes.

Method: A hospital-wide snapshot audit of all admitted adult inpatients at Alice Springs Hospital was performed on September 9th, 2022. Data were obtained by review of medical records and pathology systems and included demographic data, prevalence, complications and management of diabetes. This was compared to ICD-10 coding data for the same group of inpatients.

Results: Hospital-wide audit identified 51.9% (95/183) adult inpatients had diabetes. Majority were Indigenous and 61.8% (84/136) had diabetes, compared to 23.4% (11/47) non-Indigenous inpatients. 93.7% (89/95) had type 2 diabetes, while 2.1% (2/95) had gestational diabetes, 2.1% (2/95) had type 3c diabetes and 2.1% (2/95) had both type 2 and type 3c diabetes.

ICD-10 coding data obtained similar results with a diabetes prevalence of 53.6% (96/179) with coding data missing for four individuals. There were also discrepancies, with five recorded as having diabetes in the ICD-10 data but not in the audit, and two recorded as having diabetes in the audit and not in ICD-10 data.

ICD-10 data for prevalence of diabetes in adult inpatient Alice Springs Hospital in 2021 was much lower, at 31.2% (6,985/22,373), of which there was a 43.4% prevalence in Indigenous Australians (6,015/13843) and 11.4% (970/8,530) in non-Indigenous Australians.

Conclusion: The very high burden of diabetes in Indigenous Australians admitted to Alice Springs Hospital is reflective of an increasing epidemic. There were differences between ICD data and hospital audit data which need to be further investigated, as ICD data may not accurately reflect the extent of the problem.

Host or the Hosted. Effects of non-nutritive Sweeteners on Intestinal and Microbial Mechanisms of Glycaemic control

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Objectives: High-habitual consumption of non-nutritive sweeteners (NNS) is linked to increased incident type 2 diabetes, with clinical evidence indicating that NNS effects on the gut microbiome may, in part, drive this risk. The precise contribution of NNS-dependent microbiome disruption to NNS effects on host glycaemia, however, remains unclear. Therefore, we aimed to determine effects of combined NNS (sucralose-acesulfame-K) supplementation on glycaemic responses in C57BL/6 mice in the presence and absence of an intact gut microbiome.

Methods: Ten-week-old male C57BL/6 mice were randomised to drinking water with or without combined NNS (sucralose 1.5 mg/mL plus acesulfame-K 2.5 mg/mL) over two weeks, and with or without concurrent antibiotic administration (ABX, ampicillin plus neomycin, both 1 mg/mL) (N = 10 per group). Oral glucose tolerance tests (OGTT, 2 g/kg) were conducted before and during supplementation (day -1, 12). On day 14, glucose was infused into the jejunum (300 mg/1.5mL, plus 30 mg of 3-O-methyl glucose, 3-OMG, a glucose absorption marker) for 30 min followed by blood collection and bioassays. Data were analysed using ANOVA with NNS and ABX as factors.

Results: Jejunal glucose absorption was augmented in NNS-supplemented mice relative to water (31%; 3-OMG T_{30}; $P \leq 0.05$), a change unaffected by ABX administration. ABX markedly attenuated OGTT glycaemic responses independent of NNS supplementation (-35%; incremental AUC, $P \leq 0.001$). NNS+ ABX+ mice had markedly augmented GLP-1 responses to intrajejunal glucose relative to other groups (69 - 108%, $P < 0.05$), while glucagon responses were 98% higher in ABX+ compared to ABX− mice ($P < 0.001$).

Conclusion: Effects of NNS supplementation to augment glucose absorption are host-related and independent of gut microbiota in mice; this increase, however, is compensated for in glycaemic responses. Antibiotic depletion of gut microbiota markedly increased glucose tolerance in mice, which may involve actions of GLP-1.

Hybrid closed Loop Therapy is associated with reduced Hospital admissions for Acute Diabetes complications and lower Hospital costs in Youth with Type 1 Diabetes.

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Aim: To evaluate the association between insulin regimen and hospitalisation for acute diabetes complications in youth with type 1 diabetes (T1D), and to estimate associated health care costs in a statewide population-based diabetes service where >98% of youth receive their care.

Method: Admissions to Perth Children's Hospital with a discharge diagnosis code of DKA or hypoglycaemia between 05/01/2022 and 30/04/2024 were retrieved and merged with the Western Australia Children's Diabetes Database. Treatment regimen at time of admission was classified as hybrid closed loop (HCL), insulin pump (non-HCL pump therapy inclusive of predictive low glucose suspend) or multiple daily injections (MDI). Admissions for a new diagnosis of T1D were excluded. A mixed-effects Poisson model was used to compare rates of hospitalisation across regimen adjusting for age and diabetes duration. Costs were derived from Australian hospital admission data and reflect 2023-34 values.

Results: A total of 1440 patients comprising 2674 patient years were included: 47% female, mean age 11.7(4.1) years, median (IQR) duration of T1D 2.9(5.7) years, mean HbA1c 7.8(1.5) %.

Table 1: Unadjusted acute diabetes complication admission rates by insulin regimen

Regimen	Hypo admissions	DKA admissions	Patient Years	Hypo Rate	DKA Rate	Admission Rate (/100 patient years)	Cost (/100 patient years)
HCL	2	10	606.48	0.33	1.65	1.98	$20,132
Pump	10	23	957.40	1.04	2.40	3.45	$35,070
MDI	16	49	1110.13	1.44	4.41	5.86	$59,574

Hospitalisation rate ratios were 2.62 [95% CI; 1.06, 6.48]; p = 0.038 for MDI vs HCL and 1.40 [95% CI; 0.61, 3.16]; p = 0.424 for Pump vs HCL. Associated costs, reported per 100 patient years, were $20,132 for those on HCL, $35,070 for non-HCL pump, and $59,574 for MDI.

Conclusion: HCL is associated with fewer acute diabetes complication admissions in youth with T1D, with corresponding savings of ~$40,000 per 100 patient years compared to MDI. Acute hospitalisation rates and associated health system costs are important components of a broad evaluation of the benefits and costs of HCL therapy. Improving access to HCL is likely to result in longer-term health and economic benefits beyond those measured in this study.

Hypertriglyceridemia in the setting of Pregnancy and Gestational Diabetes

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A 36 year old female of gravida two, para 1 (G2P1) with a past history of diet controlled gestational diabetes was admitted for an induction of labour. On testing, due to a grossly lipemic blood sample, she was found to have elevated triglycerides of 42.1mmol/L. She had no notable family or personal history of lipid or cardiometabolic disorders. Her body mass index prior to pregnancy was 20.8kg/m2 compared to 24.6kg/m2 post-partum. Her examination was unremarkable with no tendon xanthomata or xanthelasma. She remained asymptomatic throughout her admission. The patient was commenced on an insulin and dextrose infusion as well as 15,000mg daily of fish oil. Ongoing management was limited due to the patient's wishes to continue breastfeeding and the limited safety data around commonly used medications. On the day of discharge her triglycerides were 13.1mmol/L and she remained on fish oil 15,000mg daily.

Aims:

1. To review in the pregnant and breastfeeding population:
    a. gestational and pre-existing diabetes as risk factors for hypertriglyceridemia
    b. Thresholds for treatment
    c. The management of hypertriglyceridemia
    d. Risk of pancreatitis
    e. Should screening of women with gestational diabetes and pre-existing diabetes in pregnancy with cholesterol levels become routine practice?

Method: Systematic literature review

Results/Conclusion: Hypertriglyceridemia is a known cause of pancreatitis and is associated with myocardial infarction and stroke. It is known that certain increases in LDL cholesterol and triglycerides in pregnancy, particularly in the third trimester is physiological. However the extent of this rise is less clear. With regards to women with gestational diabetes it is thought that the combination of increased insulin resistance, leading to increased free fatty acid delivery to the liver and therefore overproduction of triglycerides, and decreased oestrogens may be responsible for dyslipidaemia seen. Current guidelines for the treatment and screening in this patient group and safety data is lacking.

Hypoglycaemia in Inpatients receiving Sulfonylureas.

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Background: Hypoglycaemia is reported in up to 30% of hospital inpatients administered sulfonylureas and has been associated with increased morbidity, mortality and length of hospital stay (LOS). It is monitored as a Healthcare Acquired Complication (HAC).

Aims*:* To assess the prevalence of hypoglycaemia in hospital inpatients administered a sulfonylurea and review potential contributing factors. To review the accuracy of hypoglycaemia data capture in the local HAC database.

Methods: A retrospective review of 100 inpatients administered > 2doses of a sulfonylurea, identified using electronic medication administration records, was conducted in 2022. Routine demographics, clinical data, and occurrence of hypoglycaemia (blood glucose<4mmol/L) were obtained from healthcare records. Data were analysed descriptively using IBM SPSS 29®. Identified episodes of care which included hypoglycaemia were compared to those reported in the local HAC database. Institutional ethics approval was obtained.

Results: In this cohort 34/100 patients (34%) experienced hypoglycaemia. The mean patient age was 73 (SD 11) years, 67% were male, gliclazide was administered in 30/34 (88%) of these patients. The mean number of hypoglycaemic events was 4 events/patient (range 1-10) and 11 patients had an episode with glucose <3mmol/L. The median LOS was increased in patients who experienced hypoglycaemia, 16 days vs 8.5 days (p=0.004). Insulin was co-administered to 16/34 patients (47%). Documented cognitive impairment was more prevalent in patients with hypoglycaemia (RR 1.64, 95% CI 0.77-3.5). The endocrinology team was involved in the care of 18/34 patients (53%). Of the healthcare record identified episodes of care including hypoglycaemia, 10/34 (29%) were included in the HAC database.

Conclusion*:* Despite the recognised risk of hypoglycaemia with administration of sulphonylureas, one third of this inpatient cohort experienced multiple episodes of hypoglycaemia associated with increased LOS. Prospective review of patients prescribed sulfonylureas on admission may mitigate this risk. Documentation of hypoglycaemia in the HAC database requires improvement.

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Hypoglycaemic events in inpatients at Eastern Health, Melbourne, 2023

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Objective : Hypoglycaemia coded as Hospital Acquired Complications (HACs) at Eastern Health (EH) were reported as a statistical outlier in the excess. We undertook to review inpatient hypoglycaemic events at EH over the 2023 calendar year, aiming to identify and address contributors, and to reduce incidence, then compare to the actual incidence based on blood glucose measurements recorded in the Electronic Medical Record (EMR).

Method: An audit of electronic medical records across three EH hospitals was performed. Episodes of hypoglycaemia were identified through the HACs reporting system which identifies coded hypoglycaemic events. Only the index event was included. For the same time period we generated a report of EMR blood glucose readings ≤4 and ≤3.5mmmol/L.

Results: There were 192 admissions with coded hypoglycaemia events between 1st January 2023 and 31st December 2023. We report only 32 patients included in preliminary analysis full data will be available at the time of presentation. Median age was 71 years, IQR (58.5, 78.5) and 18 (56.3%) were female. The median level of hypoglycaemia was 3.45 IQR (3.25, 3.80), with 84.4% having Level 1 hypoglycaemia (≤3.9mmol/L), 15.6% having Level 2 (≤3.0mmol/L) and none with Level 3 hypoglycaemia. At time of hypoglycaemia 24 (75%) were on insulin, 3 (9.4%) were on insulin infusion and 6 (18.8%) were on a sulphonylurea. Six patients (18.8%) had an acute kidney injury. Seventeen (17/24, 70.8%) patients on insulin had a change in regimen after hypoglycaemia. Eleven of 32 (34.4%) patients were referred to endocrinology after hypoglycaemia.

Conclusion: Preliminary key findings indicate that the majority of inpatient hypoglycaemic events at EH are level 1, occurring in patients on insulin. The extent to which hypoglycaemia is under reported will become evident after comparison with the EMR data.

HypoHACs: Exploring the Utility of Hospital Recorded Data to Identify Patients with Diabetes Mellitus most at risk of Hospital acquired Hypoglycaemia.

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Background: Hospital acquired complications (HACs) present a serious risk to patients and a significant cost to healthcare facilities. Data stored in electronic medical records (eMR) can be accessed by clinicians for audit level analysis to complete internal reviews, however this data is not currently used for risk evaluation. One such complication for inpatients with diabetes is hypoglycaemia (BGL level <4 mmol/L). Inpatient hypoglycaemia is associated with decreased patient survival as well as other significant negative patient outcomes.

Aim: To identify if data recorded during hospital stays has utility for developing a model to predict hospital acquired hypoglycaemia in patients with diabetes mellitus.

Method: A retrospective audit of hypoglycaemia reports between January 2023 – January 2024 within the Northern Sydney Local Health District (NSLHD) was done to generate historically recorded blood glucose records (BGL). Patients were included if they were in-hospital patients with diabetes, > 18 years old, and had a BGL result captured during the inclusion period.

Results: Approximately 500,000 BGL results were obtained from approximately 10,000 patient records. Patients were grouped based on normoglycaemia only (BGL: 4.0 mmol/L-15 mmol/L), incidence of hypoglycaemia (BGL < 4.0 mmol/L), incidence of hyperglycaemia (BGL > 15 mmol/L), or incidence of both hypo- and hyperglycaemia. The data included 44 unique factors including BGL result, age, gender, nationality, length of stay, and facility. It is expected that there will be significant demographic differences between patient groups.

Conclusion: These findings suggest that eMR audit reports could have value in the development of a tool for identifying patients at risk of hospital acquired hypoglycaemia. This could provide an evidence base for incorporating this patient data into an eMR alert system for at risk patients. Future studies should aim to utilise this patient data to develop and train a risk stratification model for use by clinicians at triage.

Identification of Proteomics Signature for Vascular Complications in Type 2 Diabetes

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Aim: To identify robust predictive measures for Type 2 diabetes (T2D) vascular complications to facilitate early intervention strategies.

Methods: Fasting plasma samples from 363 Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) trial participants [(mean±SD) age: 61.3±6.4 yrs, 5.6±5.4 yrs T2D, HbA1c: 6.7±1.2% (49.7±13.4 mmol/mol)], were collected at baseline and subjected to quantitative proteomics analysis of tryptic peptides using liquid-chromatography mass spectrometry. Protein signatures associated with future micro- (n=100) or macrovascular (n=54) complications were identified using a random forest approach, adjusted for treatment allocation. Exhaustive search using logistic regression was then applied to optimise predictive models.
Pathway analysis was carried out using the NIH functional annotation tool, DAVID Bioinformatics.

Results: Fifty targets were selected: 14 were uniquely associated with microvascular, 13 with macrovascular complications and 23 were common for both. Pathway analysis revealed six main pathways: cholesterol metabolism, platelet activation, complement and coagulation, focal cell adhesion, actin cytoskeleton and hypertrophic cardiomyopathy. In logistic regression, the optimal model for prediction of microvascular complications with overall $p<0.0001$, AUC=0.74 contained Cadherin-5, Clusterin, Ceruloplasmin, Glutathione peroxidase 3 and Inter-alpha-trypsin inhibitor heavy chain H3. For macrovascular complications the model contained Zinc-alpha-2-glycoprotein and Coagulation factor V ($p<0.0001$, AUC=0.72). For any micro- or macro-vascular complications, the model contained Cholinesterase, Ceruloplasmin, Mannose-binding protein C and Coagulation factor V ($p<0.0001$, AUC=0.70).

Conclusion: Our novel proteomic findings represent a promising first step towards identifying protein signatures associated with T2D complications. Future research will aim at finding therapeutic targets in the metabolic pathways identified by those proteins.

Impact of early Post-transplant Hyperglycaemia and Post-transplant Diabetes Mellitus following Heart Transplantation: A single-centre retrospective cohort study

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Aim: Early post-transplant hyperglycaemia (EPTH) and post-transplant diabetes mellitus (PTDM) occur following heart transplantation (HTx). We evaluated the incidence of EPTH and PTDM and their impact on transplant-related outcomes in HTx recipients at our hospital.

Method: Patients without pre-existing diabetes who underwent HTx between 2015 and 2018 were included. EPTH was defined as fasting blood glucose ≥7.0mmol/L or random blood glucose ≥11.1mmol/L on two occasions within the first 45 days after transplant. PTDM was diagnosed when hyperglycaemia persisted (or developed) more than 45 days after HTx. The primary outcome was prevalence of EPTH and PTDM. Secondary outcomes included the association of baseline characteristics with EPTH and PTDM development, and the effect of EPTH and PTDM on transplant-related outcomes like graft rejection and all-cause mortality.

Results: 116 patients met inclusion criteria. EPTH developed in 88 (76%) patients, and 41 (35%) progressed to PTDM within one year. Although the majority of patients that developed PTDM did so within the first 12-months post-transplant, prevalence continued to increase during follow-up (5-year cumulative prevalence 39%). Recipient age, female sex, and higher BMI were independently associated with EPTH development. EPTH was the strongest predictor of PTDM development, as all patients diagnosed with PTDM also experienced prior EPTH ($p<0.01$). EPTH was associated with an increased likelihood of graft rejection compared to euglycaemic patients (OR=3.83, 95% CI=1.34-11.00). Five-year mortality was highest in patients with EPTH and PTDM (22.7%), intermediate in patients with EPTH that resolved (9.1%), and lowest in euglycaemic patients (0%).

Conclusion: EPTH and PTDM are prevalent following HTx. EPTH is strongly associated with future development of PTDM. Both EPTH and PTDM were associated with increased graft rejection and mortality compared to euglycaemic patients, suggesting that dysglycaemia in HTx recipients has important prognostic implications and effective management could potentially improve transplant outcomes.

Impact of once-weekly Subcutaneous Semaglutide 2.4 mg on Metabolic Syndrome in the 2-year, randomised controlled STEP 5 trial

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Background and aims: Obesity can drive metabolic syndrome (MetS), which is associated with increased risk of cardiovascular disease (CVD) and type 2 diabetes (T2D). The STEP 5 trial demonstrated increased weight loss in semaglutide-treated versus placebo-treated patients; this *post hoc* analysis investigated the impact on MetS.

Materials and methods: 304 adults with BMI ≥30 kg/m^2, or ≥27 kg/m^2 with ≥1 weight-related comorbidity, without diabetes, were randomised 1:1 to once-weekly subcutaneous semaglutide 2.4 mg or placebo (both plus diet and physical activity), for 104 weeks. We assessed MetS (defined as ≥3 National Cholesterol Education Program Adult Treatment Panel III criteria) prevalence and weight loss (<10%/≥10%) over the treatment period. *P*-values were from chi-square test of proportions (analyses not adjusted for multiplicity).

Results: At baseline, 89 and 79 participants had MetS in the semaglutide and placebo groups, respectively. The proportions of participants with remission of MetS at weeks 52 and 104 were significantly greater with semaglutide vs placebo (59% vs 27% and 57% vs 22%, respectively; $p<0.01$). Similarly, the incidence of MetS by weeks 52 and 104 were significantly lower with semaglutide vs placebo (2% vs 23%, and 7% vs 26%, respectively; $p<0.01$). MetS remission rate was higher in semaglutide-treated participants with <10% weight loss than placebo at 52 (57.9% vs 25.0%) and 104 weeks (39.5% vs 15.3%). Weight loss of ≥10% led to higher remission rates, which were similar in semaglutide- and placebo-treated participants (63.0% vs 66.7%, respectively, at 52 weeks; 71.1% vs 83.3% at 104 weeks).

Conclusion: Over 2 years, more participants treated with once-weekly subcutaneous semaglutide 2.4 mg achieved remission of MetS, and fewer developed incident MetS, versus placebo. These results suggest that semaglutide could impact the progression of MetS to T2D and CVD; however, they should be interpreted with caution due to small participant numbers.

Impact of Perioperative Dexamethasone in Patients with Diabetes Mellitus: Audit at a Tertiary referral Teaching Hospital

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Aim: Inpatient hyperglycaemia is associated with increased mortality and length of hospital stay (LOS). Therapeutic glucocorticoids increase risk of hyperglycaemia. Dexamethasone, a potent synthetic glucocorticoid, is commonly used at supraphysiological doses as prophylaxis for perioperative nausea and vomiting. We aimed to understand the glycaemic impact of perioperative dexamethasone in patients with diabetes mellitus (DM).

Method: An audit of perioperative dexamethasone use in patients with DM was performed between January 2022 and February 2024 at a tertiary referral teaching hospital. Blood glucose (BGL) and ketones were measured 24 hours prior to 72 hours following dexamethasone administration. Primary outcomes were prevalence of hyperglycaemia (maximum BGL >10mmol/L), significant ketosis (>=1.5mmol/L) and hyperglycaemic emergencies. Patients treated with pre-existing glucocorticoids were excluded.

Results: 208 patients with DM were treated with perioperative dexamethasone. The dose of dexamethasone used was 4mg in 47.1% (n=98), 6mg in 1.0% (n=2) and 8mg in 51.9% (n=108) of patients respectively. 44.6% (83 of 186) of DM patients had BGL >10mmol/L in the day prior to receiving dexamethasone. For DM patients without pre-existing BGL >10mmol/L, 71.8% (74 of 103) experienced new BGL >10mmol/L post dexamethasone. The rate of new BGL >10mmol/L post dexamethasone was 77.3% (34 of 44) in DM patients who received 4mg or 6mg dexamethasone compared to 67.8% (40 of 59) in DM patients who received 8mg dexamethasone (odds ratio 0.62 [0.25 – 1.50]). The rate of ketosis >=1.5mmol/L was 8.1% (9 of 111) whilst the rate of hyperglycaemic emergencies was 1.0% (2 of 208).

Conclusion: Hyperglycaemia commonly occurs following administration of peri-operative dexamethasone in patients with DM. The dose of dexamethasone does not affect the rate of hyperglycaemia. Further research is needed on the impact of perioperative dexamethasone-induced hyperglycaemia on inpatient morbidity, mortality and LOS, and the suitability of non-glucocorticoid treatments for perioperative nausea and vomiting.

Improved Insulin Sensitivity Post-phaeochromocytoma Resection: case report

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Phaeochromocytoma is associated with dysglycaemia, impaired fasting glucose and reduced insulin sensitivity with a prevalence of secondary diabetes occurring in 21-37% of cases. Glucose intolerance is mainly attributed to high circulating levels of catecholamines, causing a hypermetabolic state, which compromises the early phase of insulin secretion and impairs glucose uptake in peripheral tissues. Secondary diabetes from catecholamine excess improves substantially post-surgery, with an up to 80% remission rate. Here, we present a case outlining improved glycaemic control and insulin sensitivity following surgical resection of a phaeochromocytoma in a 65-year-old female with long-standing type 2 diabetes mellitus on basal-bolus insulin with previous total daily dose of 160 units, who was able to discontinue regular insulin administration post-operatively and able to lose a significant amount of weight.

The patient initially presented with abdominal sepsis and symptoms of catecholamine excess with intermittent palpitations and nausea. An abdominal CT scan identified a smooth homogenous 27mm x 25mm nodule in the right adrenal (80 Hounsfield units). Plasma metanephrine levels were markedly elevated: normetanephrine 9458 pmol/L (RR <1080 pmol/L), metanephrine 1873 pmol/L (RR <447 pmol/L), and 3-methoxytyramine at 313 pmol/L (RR <100 pmol/L). Perioperative uptitration of alpha-blockade was complicated by significant postural hypotension and dizziness, but she was able to proceed to laparoscopic adrenalectomy. Immediately following surgery, she was able to discontinue all insulin therapy. Her glycaemic control was maintained with dietary adjustments and gliclazide 60mg modified release daily. Her HbA1c level was 7.7% prior to surgery and improved to 7.2% in the month following surgery. She has subsequently required supplemental NovoRapid doses with meals at substantially reduced doses.

This case highlights the potential impact of phaeochromocytoma on glucose metabolism and the substantial metabolic benefits achievable with treatment. Normalisation of catecholamine levels following tumour resection likely contributed to the observed improvements in weight and insulin requirements.

Improving Diabetes care to people in Unstable Housing through Proactive Community Outreach and Engagement

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Aim: Patients with diabetes mellitus (DM) who live in unstable housing face significant barriers to effective diabetes care contributing to adverse clinical outcomes. Numerous personal and systemic factors play a role such as financial constraints, psychiatric co-morbidities, reduced access to transport and communication, fragmented care and care avoidance behaviours. This paper describes examples of proactive community outreach and engagement strategies to facilitate better access to health care for patients with DM in unstable housing.

Method: The Diabetes Street Hub (DSH) is an integrated, community-based service to improve diabetes outcomes for people in unstable housing and was established as a partnership between Metro South Health and Hospital Service and Micah Projects, a not-for-profit organisation providing services and opportunities for people in need. A key priority of the service is proactive community outreach, engagement, education and advocacy.

Results: Since its launch in February 2023, the DSH has engaged with relevant networks with a wide community reach. We are a regular participant in the annual Brisbane City Council event “Homeless Connect” where organisations and services present themselves to the broader community. Attendance at these events have not only facilitated conversations with individual members of the public but has also helped raise awareness about the existence of our service and establish relationships with relevant organisations and services. In addition to this, the DSH Nurse Navigator runs a community outreach program with regular visits to an expanding number of residential facilities to support existing clients and provide opportunistic pathways for other people to link with our service. Collaboration with community partners such as food relief organisations to seek opportunities for community engagement are also being explored.

Conclusion: Proactive community outreach, engagement and partnerships are essential to achieve better case detection, health care access and clinical outcomes for patients with DM in unstable housing.

Improving Prediction of Gestational Diabetes Mellitus From Early in Pregnancy

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Background and Aims: GDM is a leading cause of perinatal mortality and morbidity for both mother and baby worldwide. More than ever, clinicians desperately require improved methods to identify women at risk of GDM, institute preventative strategies, and reduce the burden of diabetes and its associated complications. The overall objective of this project, made possible by the ADS Skip-Martin Fellowship 2023, is to discover whether the prediction of GDM can be enhanced by incorporating biomarkers together with clinical risk factors. This project aimed to identify gestational proteomic profiles that correlate with high risk of developing GDM.

Methods: We recruited 113 pregnant women, gestational age 12-18 weeks, who had at least one clinical risk factor for GDM (e.g., advanced maternal age, high BMI, ethnicity with high risk of GDM, family history of type 2 diabetes). Anthropometric parameters and a blood test were collected at 12-18 weeks gestation, and then an oral glucose tolerance test performed at 26-28 weeks gestation. 5uL of whole blood was used to undertake proteomic analysis which was performed by data dependent acquisition (DDA) mass spectrometry.

Results: 29% (33/113) women developed GDM. There were 234 proteins identified by DDA mass spectrometry, and 37 were differentially expressed between the two groups. Utilising Gene Ontology pathway analysis, our results showed that the relevant proteins differentially expressed in GDM are related to immune system function, specifically mononuclear cell differentiation, chemotaxis, regulation of innate immune response and lymphocyte differentiation, key regulators of inflammation.

Conclusion: Our results suggest that proteins implicated in immune system function are differentially expressed in early pregnancy and predict the development of GDM. This aligns with previous research that has established GDM as a state of chronic low-grade inflammation, often associated with maternal adiposity. Once validated in a separate cohort, we intend to utilise our novel biomarkers together with clinical risk factors, to predict GDM and offer s tailored intervention strategy to mitigate the risk of GDM development and adverse perinatal outcomes.

Improving The Experience of Women with Diabetes in Pre-pregnancy, Antenatal and Postpartum Period: a qualitative study in Australia

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Aim: To understand the experiences of women with T1D during the pre-pregnancy, antenatal and postpartum periods, in comparison to women with gestational diabetes mellitus (GDM) undergoing a similar high-risk model of care, versus women without diabetes.

Method: Participants who attended the antenatal clinic at the Royal North Shore Hospital were contacted via email. The interviews were semi-structured, one-on-one via telephone conducted by the first author. The interviews were audio-recorded and transcribed into text. The data was analysed via inductive and descriptive coding approach. The codes were then categorized into main themes and sub-themes.

Results: 17 women (6 T1D, 8 GDM, and 3 control) were interviewed. 5 main themes were identified: (1) Pre-pregnancy planning, (2) Antenatal diabetes management, (3) Experience in postpartum period, (4) Experience with healthcare system, and (5) Family support. Women without diabetes did not have any concerns about antenatal care prior to conception. Women with GDM in their previous pregnancies and those with T1D were concerned about poor blood glucose control before and during their pregnancy and its impact on foetal health. Long waiting times was a common issue for women attending the antenatal clinic. Women with GDM found antenatal diabetes management more stressful and challenging than those with T1D. The support received during recovery in hospital after birth was generally poor due to lack of healthcare staff. Family members of participants were generally supportive throughout their pregnancy journey.

Conclusion: Healthcare models should provide more emotional support upon antenatal diabetes management and recovery after birth to enhance the pregnancy of experiences for women with and without diabetes.

Increasing Prevalence of Continuous Glucose monitoring Data availability in Adults with Type 1 Diabetes admitted to Hospital

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Aim: Continuous glucose monitoring (CGM) has increased following introduction of the NDSS subsidy in 2017 for people living with type 1 diabetes (T1D). Given the increasing prevalence of diabetes amongst inpatients and known risk of acute dysglycaemia, we aimed to determine the proportion of patients with T1D admitted to hospital over the last three years, with software-linked CGM data available for assessment during their hospital stay.

Methods: In this multi-centre retrospective observational study, we screened adult patients with T1D who required multi-day acute hospital admissions during 2021-2023 across three health services in metropolitan Melbourne, Australia. Patients using a CGM linked to their respective health service's Libreview, Carelink and Clarity web-based software accounts, respectively, were included and examined for availability of CGM data during their admission. Patients admitted under paediatric, obstetric, palliative care, and psychiatry units were excluded.

Results: A total of 1763 people with T1DM who had multi-day acute admissions were assessed. The proportion of patients in each year with hospital-linked inpatient CGM glucose data recorded during their admission increased over time: 3.2% in 2021; 10.4% in 2022; 20.5% in 2023 (Figure 1A). For people with T1D, the rise in inpatient CGM data availability parallels the rise in outpatient CGM use evident in serial ANDA/ADCQR national audits (Figure 1B).

Conclusion: In a real-world cohort of inpatients with T1D, the availability of CGM data linked to health services' web-based software accounts during hospital admissions significantly increased between 2021 and 2023. The increasing use of CGM by patients with T1D admitted to hospital provides an opportunity to better understand glycaemia and utility of CGM during acute illness.

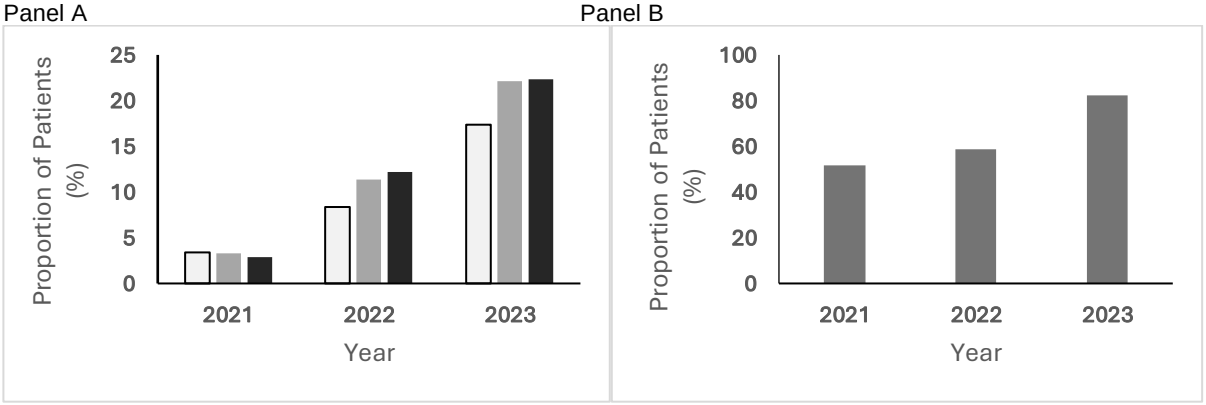

Figure 1. A: Percentage of people with T1D and CGM data linked to health services' web-based software accounts during hospital admission, by year and health service (white: health service A; grey: health service B; black: health service C). B: Comparison with CGM use according to ANDA/ADCQR 2021-2023 annual report data

Inpatient accuracy of Continuous Glucose monitors: Metrics and medical record pitfalls

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Aim: Continuous glucose monitoring (CGM) is increasingly used in Australia following the NDSS subsidy for people with type 1 diabetes (T1D) in 2017. However, routine in-hospital use is not recommended due to accuracy concerns. We aimed to determine CGM accuracy amongst individuals with T1D admitted to hospital.

Methods: In this multi-centre retrospective observational study, we compared interstitial fluid CGM with reference blood glucose (capillary point-of-care [POC], blood gas [GAS], plasma) in patients with T1D and multi-day admissions during 2020-2023 across three Melbourne health services. Patients requiring dialysis or admitted under paediatric/obstetric/palliative care/psychiatry units were excluded. Absolute difference between time-matched pairs (within 7 minutes) of CGM and reference blood glucose, divided by reference glucose, was calculated. The mean of these results determined overall mean absolute relative difference (MARD).

Results: 7,631 glucose pairs from 211 patients (326 admissions) were analysed. A majority were men (55%), median age 48 years (IQR 31-65), median Charlson comorbidity index 3 (IQR 1-5), mean HbA1c 9.0% (SD 2.1), and median length of stay 2.9 days (IQR 1.5-5.8). Initial aggregate MARD was 11.6%. Given ward nurses could have manually documented CGM measures as substitutes instead of POC glucose in the hospital record, 6,166 manually entered POC measures were then excluded. Also, given potential date/time inaccuracy on CGM readers/receivers, an additional 184 measures were excluded. When evaluating the remaining direct electronically uploaded glucose measures, MARD was higher at 14.4% (1,281 glucose pairs). The accuracy of different CGM devices is presented in Table 1.

Conclusion: Amongst inpatients with T1DM, CGM agreed relatively well with blood glucose (MARD 11.6-14.4%). Substitution of POC with CGM glucose measures in hospital records is likely to be occurring. Accurate assessment of inpatient CGM MARD requires accurate glucose data entry. National consensus guidelines on the inpatient use and documentation of CGM and blood glucose are required.

Table 1: CGM accuracy by CGM device and reference glucose source

	Libre 2	**Guardian 3**	**Dexcom G6**
MARD % (CGM-POC glucose pairs)			
Overall	13.7% (238)	10.9% (57)	16.8% (364)
Blood glucose (mmol/L)			
<3.9	*	*	21.2% (32)
3.9-10	15.2% (115)	16.5% (15)	17.2% (184)
>10.0	12.0% (116)	7.7% (39)	15.4% (148)
MARD % (CGM-GAS glucose pairs)			
Overall	11.3% (297)	17.3% (52)	16.6% (221)
Blood glucose (mmol/L)			
<3.9	*	*	*
3.9-10.0	11.3% (116)	20.2% (20)	16.7% (119)
>10.0	11.4% (172)	15.4% (32)	13.9% (90)

* Insufficient glucose pairs were available to report MARD

Inpatient Hypoglycaemia Prevention and Management: A quality Improvement Study

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Hospital acquired hypoglycaemia is considered a preventable complication. Identifying potential causes and developing interventions may help lower the incidence

Aim: We aim to reduced the number and severity of inpatient hypoglycaemic events by improving the knowledge and prevention strategies of nurses providing inpatient care.

Method: This is a qualitative study that consists of two parts. Ethics approval has been granted.
Initially a retrospective audit will be conducted to identify the number and severity of hypoglycaemic events over a 4-week period. We aim to identify any contributing factors including potential errors by nursing staff. We will also conduct same data collection over 4 weeks period
We then will deliver a targeted education program to the nursing staff on a medical ward. We will conduct a knowledge questionnaire pre and post the education to measure improvements in nurses' knowledge around hospital procedures on insulin administration, recognition of hypoglycaemia and prevention strategies.
Questionnaires are de-identified to remove anxiety for nurses participating in the study.
After staff education, we will conduct another hypoglycaemia incident data collection over 4 weeks by using the same data collection tool.

Discussion: Analysis of the questionnaires pre and post education will identify knowledge gaps and whether those gaps have been addressed by the education provided. Any unmet needs can be addressed with follow-up education sessions.
If the education is successful the number and severity of hypoglycaemia on the ward will be reduced as evidence by pre- and post-staff education hypoglycaemia incidents data.

Conclusion: Education of nursing staff to recognise the risk factors, symptoms and treatment of hypoglycaemia is an effective way to prevent and manage inpatient hypoglycaemia.

IRiS: Improving Retinal Screening in people with Diabetes-related Foot Ulcers

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Aim: The "IRiS" project aimed to identify and address barriers to timely diabetic retinopathy screening and monitoring among patients with diabetes-related foot ulcers (DFU). The project aimed to enhance awareness and streamline referral pathways for appropriate ophthalmic care for this high-risk patient cohort.

Method: This retrospective observational study included Multidisciplinary Diabetes Foot Unit (MDFU) outpatients aged ≥18 years with diabetes (n=50) attending podiatry and/ or MDFU clinics at Fiona Stanley Hospital in October 2022. Governance, Evidence, Knowledge and Outcome (GEKO) quality improvement project approval was obtained from the South Metropolitan Health Service. A questionnaire was used to ascertain retinal screening rates, screening location, pre-existing retinopathy and perceived barriers to care. Electronic medical records were reviewed to detect unreported retinopathy. Key stakeholders from Fiona Stanley Hospital Endocrinology, Podiatry and Fremantle Ophthalmology services participated in process mapping to identify challenges in referral pathways for retinal screening and monitoring.

Results: Retinal screening or monitoring within 2 years was reported in 39 (78%). Of those overdue (11), 2 reported recent visual deterioration and 4 had known retinopathy. Of the 26 patients who self-reported no eye disease, 13 (50%) had evidence of prior documented retinopathy on electronic record review. Fremantle Eye Clinic referral pathways were strained due to high demand, resulting in an average wait time of 173 days. Referrals to private optometrists were limited, partly due to unclear referral criteria and patient concerns about cost.

Conclusions: There are gaps in retinopathy screening among patients with DFU, with inadequate eye health awareness and strained public healthcare services. Improving patient education and pathways to accessing community diagnostic services is critical for early detection and intervention in diabetic retinopathy, thereby mitigating the risk of progressive vision loss among DFU patients.

Is a National Screening Program for type 1 diabetes in children feasible and acceptable to Australian families?

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Aim: Routine general population screening for type 1 diabetes (T1D) is recommended internationally to reduce the risk of diabetic ketoacidosis at diagnosis, however the feasibility and acceptability to Australian families is unclear.

Method: Three potential national T1D screening models were compared in catchment areas across 5 states of Australia: M1) genetic risk-stratified screening using a heel-prick dried bloodspot in newborns (NSW, SA); or M2) genetic risk-stratified screening using a saliva swab in infants (NSW, QLD), both with subsequent autoantibody screening for at-risk children; or M3) autoantibody screening using a finger-prick dried bloodspot in children aged either 2, 6 or 10 years (VIC, WA, NSW). Demographics, parental anxiety (state anxiety inventory; SAI modified to be specific T1D screening) and acceptability were assessed using self-administered online surveys at screening.

Results: In total, 6,701 children were registered for screening (M1: n=2,287, M2: n=2,159 and M3: n=2,255 children). Screening samples were collected from 91%, 74% and 57% of consented children in each model, respectively. Demographics did not differ substantially, with equal males to females, 31-45% of children of non-European or Oceanian ethnicity and ~1% with a family history of T1D. Parental anxiety related to T1D screening was low and similar between groups (M1: 33 ± 10, M2: 32 ± 10, M3: 33 ± 10). The top reasons for opting into screening their child were: the potential benefit to their child (26%) or to other families (16%), and the ease of screening (14%). Twenty-eight percent reported no barriers. For others, the top barriers were: being too busy (15%) or concern about the test, e.g., pain (12%).

Conclusion: These finding suggest that screening for T1D is both feasible and acceptable to Australian parents.

Islet Transplantation for Severe recurrent Hypoglycaemia in Type 1 Diabetes comparing Clinical and Neuropathy complication parameters pre- and post-transplant.

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Aim: To evaluate changes in diabetes related complications following islet cell transplantation (ICT) for recurrent severe hypoglycaemia.

Method: People with recurrent severe hypoglycaemia were referred to Westmead hospital between 2006 and 2017 and met criteria for ICT without renal disease. They were evaluated at baseline and following ICT with graft function marginal or greater(IGLS) including: BMI, stimulated C-peptide, insulin dose (IU/kg/day), HbA1c, Edmonton HYPO score, random albumin/creatinine ratio and CGM (72 hours blinded). Peripheral nerve function was assessed with thermal threshold testing at the left foot, and vibration threshold testing at the medial malleolus and great toe. Autonomic nerve function was assessed as pupillary reflexes and heart rate variability (HRV).

Results: Thirteen people with ICT were evaluated (1-3 grafts) at a median interval of 3.9 [IQR; 2.1-5.4 years] (Table). Graft function was optimal in 5, good in 3 and marginal in 5. At baseline 4 people had at least one peripheral nerve abnormality and 2 people had at least one autonomic function abnormality. At follow-up these abnormalities were present in 3 and 2, respectively.

Table. Characteristics pre-transplant and post-transplant.

	Pre-Transplant	Post-Transplant	p-value
Age(years)	49.7±9.7	53.9±11.0	<0.0001
Duration of Diabetes (years)	34.0±7.0	38.7±8.5	<0.0001
Female/Male	8/5	8/5	
BMI	24.1±3.7	22.2±3.8	0.0016
Stimulated C-peptide	0.0±0.0	0.79±0.54	0.0002
Insulin Dose (Units/Kg/day)	0.4±0.2	0.1±0.2	0.0004
HbA1c (%)	8.0 ±1.4	6.8±1.3	ns
HYPO Score	2060±1441	207±345	0.0010
CGM (% TIR)	42.5±13.7	69.5±24.7	0.0268
CGM (% time <3.9)	4.8±4.5	1.6±2.5	ns
CGM (% time Hypo<3)	1.4±2.2	0.1±0.3	ns
Mode of Insulin Delivery			
CSII	10	8	
MDI	3	0	
Nil	0	5	
Random Albumin Creatinine Ratio (mg/mmol)	4.7±9.8	7.0±16.1	ns
Left Foot cold (°C)	9.5±9.0	7.9±7.5	ns
Left foot warm (°C)	10.8±3.4	10.7±4.4	ns
Left Toe (°C)	8.7±6.7	10.2±15.6	ns
Left malleolus (°C)	19.1±14.1	10.7±11.8	ns
Average Heart Rate (bpm)	75.5±9.8	73.9±11.3	ns
SDNN (ms)	30.2±15.4	27.2±15.5	ns
RMSDD (ms)	18.8±14.7	19.1±16.5	ns
Power in LF range (ms^2)	458±532	228±371	ns
Power in HF range (ms^2)	136±183	121±185	ns
LF: HF	6.2±4.4	3.0±3.1	ns
Initial Pupil Diameter (mm)	4.8±0.9	4.7±0.6	ns
Reflex amplitude (mm)	1.0±0.3	1.3±0.4	ns
Max constriction Velocity (mm/s)	3.5±1.1	3.9±1.4	ns

Conclusions: Persons who received 1-3 ICT had significant reduction in hypoglycaemia. C-peptide, BMI, Insulin requirements and CGM (%TIR) were all found to have improved. Sensory and autonomic abnormalities remained unchanged post ICT consistent with no progression of existing complications.

Isolation and Proteomics of the Insulin Secretory Granule

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Background & Aim: Pancreatic beta-cells store insulin in vesicles termed insulin secretory granules (ISGs). Following glucose stimulus, ISGs are initiated for exocytosis to release insulin. Previously, insulin granules were regarded as inert carriers of the insulin hormone. However, more recently, ISGs have been defined as regulatory structures on their own; ISG turnover is controlled by processes from biogenesis and trafficking to degradation that is regulated both by proteins in and on the ISG. Only 4 studies have previously looked at ISG proteins in beta-cells with 5 consensus proteins. We aim to identify potential ISG proteins that affect their function within the ISG of mouse MIN6 beta-cells, using subcellular fractionation techniques, LC-MS/MS analyses and computational analysis of these ISG enrichments.

Methods & Results: To identify potential ISG proteins, MIN6 cell lysates were subject to two subsequent subcellular fractionations to obtain ISG enriched samples. Western blot analysis validates the enrichment of both immature and mature ISGs. Further enrichment processes enrich the mature insulin granule fraction and the exclusion of contaminant proteins. LC-MS/MS analysis was performed on all enriched insulin granule fractions from the MIN6 cells. Using unbiased protein correlation profiling, we identify a 431 ISG proteins, with many potential novel proteins identified. Moreover, using marker proteins and pRoloc analysis of this ISG enrichment we further identify a list of 211 proteins of “high potential” association with the ISG.

Conclusion: These results provide an efficient and transferrable method of ISG isolation from beta-cells (~7 h) and the first identification of an ISG proteome of the mouse insulinoma beta-cell.

Joint ADS/ANZSNM procedure guideline for FDG PET/CT imaging in type 1 and Type 2 Diabetes.

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Background: FDG-PET/CT is an established imaging technique for tumour diagnosis and staging. In diabetes, the quality of images is dependent on the blood glucose concentration at the time of FDG injection. Adequate preparation to ensure appropriate blood glucose concentrations are critical for precise interpretation of PET/CT findings. However, protocols for preparing patients with diabetes vary among institutions and are influenced by resource availability and staff expertise.

Aim: We have proposed a de novo guideline, collectively endorsed by the Australian Diabetes Society (ADS) and the Australian and New Zealand Society of Nuclear Medicine (ANZSNM). The guideline aims to support medical, nursing and nuclear medicine staff with the preparation and management of people with diabetes undergoing an FDG PET/CT scan.

Method: Tailored protocols are provided based on the type of diabetes and insulin requirement. For individuals with Type 2 diabetes not on insulin, the guideline recommends discontinuing certain diabetes medication, and following specific dietary guidelines. For patients requiring insulin therapy, including those with Type 2 and Type 1 diabetes, the guideline offers preparation recommendations for either fasting from midnight, or following an early breakfast. Patients with Type 1 diabetes utilising multiple daily injections or insulin pumps are provided with additional instructions for continuous glucose monitoring and the timing of insulin pump removal. Collaboration with endocrinology specialists is emphasised for complex cases. Post-scan instructions highlight the importance of checking the blood glucose concentration prior to patient departure.

Results: Implementing these guidelines in clinical practice has the capacity to standardize care, streamline patient management procedures, and improve FDG PET scan quality for individuals with diabetes nationwide in Australia.

Conclusion: The guideline endorsed by both societies is intended to assist nuclear medicine centres in the preparation of patients with diabetes for their FDG PET/CT scans. They provide a structured, yet personalised, approach that can be easily implemented to optimise FDG PET/CT images, while prioritising patient safety.

LIFTS (Logan Inpatient Foot Treatment Service) and LOFTS (Logan Outpatient Foot Treatment Service) model implementation: an integrated approach to improving diabetic foot amputation patient recovery.

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Aim: LIFTS/LOFTS model deployment was driven by a multi-faceted aim: to reduce diabetic foot patient length of stay (LOS), decrease foot amputation-related readmissions, alleviate diabetic foot disease burden on Logan Hospital, and improve patient outcomes in a region grappling with significant socio-economic disadvantage.

Method: LEADS Podiatry team partnered with local stakeholders ascertaining clinical need, capacity, and mutual investment required to address the acute diabetic foot disease burden at Logan Hospital, informing the co-designed comprehensive care model. To quantify the anecdotal needs expressed by clinicians and assess effectiveness of the implemented service data was collated from the statewide diabetic foot form platform, *Getting It Right First-Time* dashboard and electronic medical record databases. Additionally, patient-reported outcome measures were evaluated upon patient entry and discharge from the service.

Results: Core data points assessing service effectiveness demonstrated:

- Patient demographics: Logan patients average 0.94 on the Charlson Comorbidity Index where 56% of patients were in the most disadvantaged IRSAD Deprivation Quintile, exceeding the statewide average by 23%.
- LOS: Pre-LEADS, Logan Hospital demonstrated higher mean diabetic foot related LOS (12.15-days) than the statewide mean (11.88-days). LIFTS/LOFTS service implementation evidenced a 3.82-day LOS reduction within 1-year of service launch.
- Foot amputation rates: A 3-fold rise at Logan Hospital post-LIFTS/LOFTS implementation was seen (pre-LEADS: 0.13%, post-LEADS: 0.39%), surpassing the statewide increase within the same timeframe (0.06% increase).
- Foot Amputation Readmission rates within 7-days: Post-LIFTS/LOFTS implementation a 0.02 readmission reduction was seen (pre-LEADS: 0.39/1000 admits, post-LEADS: 0.37/1000 admits).

Conclusion: A significant impact on diabetic foot disease burden is apparent post-implementation of the LIFTS/LOFTS integrated model of care. This pull model demonstrates the magnetism of care closer to home with the increase of local amputation rates where patients would previously have attended city centre hospitals for access to specialised care and rehabilitation. Findings support the need for cohesive inter-disciplinary care to improve patient outcomes and fortify services against projected long-term increase in diabetic foot disease.

Listening to Young People with Type 1 Diabetes, Parents, Clinicians, and Researchers: Co-Designing a Digital Diabetes Platform (DiabHQ)

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Aim: This study aimed to engage young people with Type 1 Diabetes (T1D) and parents/carers, clinicians, and researchers in a collaborative process to identify their needs and priorities for a digital diabetes platform.

Method: Structured consultation sessions were conducted between March and December 2023 by the Children's Diabetes Centre, based in Perth, Western Australia. Participants included young people with T1D and parents/carers, clinicians (endocrinologists, diabetes educators, dietitians, social workers) and researchers. Sessions were in-person and online and included interviews, focus groups and participatory design workshops. Data were analysed to identify common themes, preferences and priorities.

Results: More than 100 stakeholders participated in the consultation sessions, including approximately 25 young people with T1D/parents, 50 clinicians, and 40 researchers. Participants resided in Western Australia (90%), other parts of Australia (8%) and overseas (2%). Analysis of the qualitative data revealed several key themes and preferences regarding the desired features and functionalities of the digital diabetes platform:

- Young people with T1D/parents: "one-stop-shop" incorporating personal data tracking, individualised education, access to resources, access to support, communication with care team, enrolment to research trials, alerts and reminders, research updates; data security; use of data to drive improvements.
- Clinicians: simplified access to data and patient resources; patient prioritisation tools and alerts; patient monitoring; collection of PROMs and PREMs; connectivity with patients; equitable care.
- Researchers: identification of patients eligible for trials and rapid recruitment; collection of research data; dissemination of research findings; community engagement.

Conclusion: This collaborative process provides crucial insights to inform the next phase of the DiabHQ development. Understanding diverse user requirements and maintaining engagement will ensure that the ongoing co-design process delivers a platform that meets the needs of the different user groups and can be scaled to other centres.

Looking for an Association between Keeping a Food record and CGM outcomes in Patients with Type 2 Diabetes referred to a Specialty service?

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Introduction - Patients with type 2 diabetes attending the Western Sydney Diabetes (WSD) Clinics undergo an assessment that includes 14-day Continuous Glucose Monitoring (CGM) using the Abbott Freestyle Libre system. Patients were requested to keep a food diary to facilitate meaningful discussions with dietitians about their dietary intake relative to glucose measurements. This study aimed to determine if patients who kept a diary had different Ambulatory Glucose Profiles (AGP) on CGM than those who did not.

Methods - This is a retrospective cohort study of 97 patients attending the clinics between January and February 2024, of whom 29 completed a food diary. A food diary was classified as complete if it included more than two food entries with meal descriptions over a minimum of two days. Food diary records and CGM outcomes were analyzed descriptively and comparatively using Stata.

Results - The average Glucose Management Indicator (GMI) was 8.17% in the non-diary group and 8.05% in the diary group (p=0.777). The average time in range was 47% for the diary group and 49% for the non-diary group. Neither metric showed statistically significant differences.

Conclusion - The use of CGM provides real-time feedback to users on various aspects of glycaemic control, including how oral intake impacts glucose levels. This study did show slight benefits for keeping a food diary, but these differences were not statistically significant. The WSD speciality team, including a dietitian use the AGP report alongside the food diary to provide education and implement a tailored management plan, involving medication and lifestyle adjustments. Therefore, the benefit of keeping a food diary may be too early to observe in this patient journey.

Losing Sight of my Sugars – A Case of Acute Vision Impairment in Diabetic Ketoacidosis

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We report a case of a 42-year-old man with a 12-year history of type 1 diabetes mellitus and suboptimal control, who presented with complete and bilateral visual loss developing over 24 hours in conjunction with a short history of vomiting, malaise, and feeling generally unwell. He was confirmed to have severe diabetic ketoacidosis (DKA) with glucose 41 mmol/L, ketones 4.6 mmol/L and pH 6.69. The diagnostic work-up excluded cerebral and ocular causes of blindness. He was treated with the standard DKA management protocol and his vision returned to normal 3 days after his presentation.

Uncontrolled type 1 diabetes is associated with symptoms of insulinopaenia, such as weight loss and fatigue, and of hyperglycaemia, including polyuria, polydipsia, infections, and reduced visual acuity. Acute severe visual loss, leading to self-limiting blindness, has been described in case reports in the setting of acidosis secondary to DKA in addition to various other aetiologies of metabolic acidosis. All case reports describe prompt return of vision to baseline following the treatment and resolution of acidosis. We propose that this acute vision loss is related to a combination of severely low serum pH and low serum bicarbonate, which have both been described in animal studies as factors necessary for retinal photoconduction.

This case underscores the importance of optimal control of diabetes to prevent such severe complications. It also emphasises the need for further research to understand the exact pathophysiology behind this phenomenon and potentially develop preventive strategies.

Low Carbohydrate Diets and Intermittent Fasting in Adults with Type 1 Diabetes and overweight/obesity: preliminary results from a systematic review

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Background and Aims: The rates of overweight and obesity are rising amongst people affected by type 1 diabetes mellitus (T1DM). Low carbohydrate diets and intermittent fasting are popular for weight loss in the general population but there is a relative lack of trial data on the safety and efficacy of these diets in people with T1DM.

Aim and Methods: The aim was to review the safety and efficacy of low carbohydrate diets and intermittent fasting in people with T1DM and overweight/obesity. This systematic review synthesised data from randomised and non-randomised interventional studies. Electronic searches were run (inception to 31 July 2023) on MEDLINE, CENTRAL, Embase, Scopus, clinicaltrials.gov, and ICTRP. Primary outcomes included body weight/BMI, glycaemia, and quality of life measures. Studies had to include at least some participants with a BMI belonging to the categories of overweight or obesity as per WHO recommendations or other established national/international guidelines. This systematic review was conducted according to recommendations from the "PRISMA 2020 statement: an updated guideline for reporting systematic reviews" and the "Cochrane Handbook for Systematic Reviews of Interventions".

Results: The search yielded 3357 results, and 8 individual study populations (13 papers) were included. Hypocaloric low carbohydrate diets were associated with significant reductions to body weight and fat mass, but no significant change to HbA1c. Studies involving eucaloric low carbohydrate diets reported inconsistent results with regard to changes to body weight and HbA1c. None of the studies involving hypocaloric low carbohydrate diets reported quality-of-life measures whereas studies involving eucaloric low carbohydrate diets reported inconsistent changes to quality-of-life measures when compared to baseline/comparator diets.

Conclusions: The limited evidence available suggests that hypocaloric low carbohydrate diets result in significant reduction to body weight. Further high-quality, large-scale RCTs are required to confirm and elaborate on the findings of this systematic review.

Low Prescription Rates of SGLT2 Inhibitors on Admission and Discharge in people with Type 2 diabetes and Heart Failure

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Background: Sodium-glucose co-transporter 2 inhibitors (SGLT2i) are recommended in the management of heart failure in people with type 2 diabetes, but there are no real-world studies in the Australian setting describing their use. We aimed to describe the prescribing rates of SGLT2i pre-admission and upon-discharge in those with a history of type 2 diabetes and heart failure who were hospitalised.

Methods: We performed an analysis of inpatient admission data. All admissions for any reason to Austin Health (a tertiary referral hospital) of more than 24 hours between 1st January 2021 and 31st December 2023 were included. Data was extracted from the Cerner electronic medical record. Diagnosis of type 2 diabetes and heart failure was defined through ICD-10 coding. Pre-admission and discharge medications were determined through automated extract of medical and pharmacy records.

Results: There were 21,335 admissions in people with type 2 diabetes and 3,353 (16%; 95% CI, 15-16) of these people had a history of heart failure. Pre-admission SGLT2i were used in 14% (95% CI, 13-15) of patients with type 2 diabetes and history of heart failure and in 13% (95% CI, 12-13) of patients with type 2 diabetes who did not have a history of heart failure. Of those prescribed SGLT2i pre-admission, 49% (95% CI, 47-50) did not have the SGLT2i prescribed upon discharge. For the subset of admissions where the principal diagnosis was heart failure, 16% (95% CI, 13-18) were prescribed an SGLT2i on discharge.

Conclusion: SGLT2i prescription rates were low among those with type 2 diabetes and heart failure both pre-admission and on-discharge. Discharge prescriptions did not include SGLT2i in many patients taking them prior to admission. Our findings highlight a need for enhanced awareness to ensure patients are prescribed these medications consistent with guidelines in order to optimise clinical outcomes.

Low-density Lipoprotein Cholesterol goal attainment in Patients with Diabetes-related Foot Ulceration

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Aim: Atherosclerotic cardiovascular disease (ASCVD) is a leading cause of morbidity and mortality in patients with diabetes-related foot ulceration (DFU), highlighting the importance of intensive risk factor modification. Low-density lipoprotein cholesterol (LDL-C)-lowering reduces cardiovascular risk. We aimed to evaluate whether patients with DFU are attaining LDL-C goals.

Method: A cross-sectional study of 551 patients attending the Fiona Stanley Hospital multidisciplinary DFU service (Western Australia) between January 2022 and May 2024 was conducted. Data was extracted retrospectively from medical records and an existing database. Patients with ASCVD, microvascular complications in 3 different sites (neuropathy, nephropathy, and retinopathy), estimated glomerular filtration rate (eGFR) <45 ml/min/1.73m2 or >1 other ASCVD risk factor (dyslipidaemia, hypertension, or smoking) were considered “very high-risk”. Patients with a microvascular complication, one other ASCVD risk factor, eGFR 45-59 ml/min/1.73m2 or diabetes duration >10 years were considered “high-risk”. LDL-C goal was defined as <1.4 and <1.8 mmol/L for very high-risk and high-risk patients, respectively.

Results: 351 patients had LDL-C results available: the mean age was 63.7±12.8 years, 265 (75.5%) were men, mean HbA1c was 8.9±2.1%, 330 (94.0%) had peripheral neuropathy, 157 (44.7%) had peripheral arterial disease and 123 (35.0%) had ischaemic heart disease. Statins were prescribed in 259 (73.8%) patients, ezetimibe in 37 (10.5%) and proprotein convertase subtilisin/kexin type 9-directed therapies in 2 (0.6%). In 206 (58.7%) patients with ASCVD, 117 (56.8%) were prescribed high-intensity statins. Of 269 (76.6%) very high-risk patients, LDL-C <1.4 mmol/L was attained in 86 (32.0%). Of 78 (22.2%) high-risk patients, LDL-C <1.8 mmol/L was attained in 24 (30.8%).

Conclusion: Three-quarters of patients with DFU were at very high-risk and over half had prevalent ASCVD. Despite this, only three-quarters were prescribed statins, and the use of additional LDL-C-lowering therapies was limited. LDL-C goal was attained in only one-third of patients, indicating scope for improved management.

Management Implications of Monogenic Diabetes in Non-Caucasian patients with the Rare genetic variants of APPL1 and INS

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A number of genetic mutations are established causes of monogenic diabetes. Phenotypes and implications of rarer genetic variants are lesser known, especially amongst non-Caucasian individuals who are not well represented in genetic databases (1, 2).
We present two patients with Asian ethnicity, both with a positive family history of diabetes mellitus and phenotypes consistent with monogenic diabetes, however with rare genetic variants. Our first patient is a 24-year-old Filipino woman with a Body Mass Index (BMI) of 23.3 kg/m2. She was diagnosed with presumed type 1 diabetes mellitus and had an HbA1c of 9.2% (77 mmol/L), detectable c-peptide and was treated with basal insulin alone. Autoantibodies were negative and genetic testing revealed a variant in the *APPL1* gene. *APPL1* is associated with diabetes via its role in insulin metabolism (3), but given its rarity, its pathogenicity was unclear in a non-Caucasian patient. Metformin and gliclazide were commenced, and insulin was eventually ceased.
Our second case is a 63-year-old Iranian woman with a BMI of 24 kg/m2, diagnosed with type 2 diabetes at the age of 50. She required Ryzodeg insulin in addition to metformin and dapagliflozin soon after diagnosis. 10 years after diagnosis, she was screened for monogenic diabetes given post-prandial hyperglycaemia with detectable c-peptide and negative diabetes autoantibodies. Testing revealed a variant of unknown significance in the *INS* gene, a mutation associated with structurally abnormal insulin (4). Gliclazide was added and her insulin dose was halved. Her HbA1c remains over 7.5% (58 mmol/L).
These clinical cases demonstrate possible phenotypes for *INS*- and *APPL1*-diabetes with variable glycaemic outcomes following treatment changes. Clinical implications and interpretation of such variants, especially in non-Caucasian patients, proves challenging. Increased access to genetic testing may improve detection of rare variants, establish clinical phenotypes and improve targeted treatment for these patients.

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Management of Blood Glucose Concentration in Adults with Type one Diabetes Mellitus while at the Beach

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Aims: A severe episode of hypoglycaemia while at the beach can increase the risk of drowning in people with type one diabetes mellitus (T1DM). This study tests the hypothesis that individuals who rarely experience hypoglycaemia avoid moderate to high-intensity activity, and those who do are more likely to adhere to diabetes management guidelines.

Methods: In a retrospective cross-sectional study, 44 participants with T1DM completed a 55-item survey about their physical activity and glucose management patterns at the beach.

Results: Only 9% frequently experienced severe hypoglycaemia while in the water, and 64% engaged in moderate or high-intensity activity. Participants who experienced hypoglycaemia in less than 5% of beach visits were more likely to measure their blood glucose before or after going into the water ($p < 0.05$) and considered a higher glucose concentration safe before entering (6.8 (1.69) vs. 4.5 (1.07) mmol/l, $p < 0.05$). There was no difference in carbohydrate intake or insulin doses between those with low or high rates of hypoglycaemia ($p > 0.05$). More participants involved in moderate to high-intensity activity decreased their bolus insulin dose before beach activity than those in light activity ($p < 0.05$), but did not adhere more to other diabetes management guidelines ($p < 0.05$).

Conclusion: Most participants with T1DM did not experience severe hypoglycaemia at the beach despite engaging in moderate to high-intensity activity. Those who rarely experienced hypoglycaemia monitored their blood glucose more frequently and ensured their glucose was at least 6.8 mmol/l before entering the water. There was no general association between activity intensity and adherence to diabetes management guidelines, however those who engaged in moderate to high-intensity activity were more likely to decrease their dose of bolus insulin prior to beach activity.

Management of Diabetic Ketoacidosis in Adult Inpatients: A retrospective analysis of Rates of Hypoglycaemia with variable-rate and fixed-rate Intravenous Insulin Infusion protocols

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Background: Diabetic ketoacidosis (DKA) is a potentially life threatening complication of diabetes mellitus. Insulin is the mainstay of DKA treatment, in addition to intravenous fluids, electrolyte replacement, and correction of underlying precipitants. There is a lack of evidence supporting the ideal administration rate of intravenous insulin.

Aim: To compare variable-rate intravenous insulin infusion (VRIII) to fixed-rate intravenous insulin infusion (FRIII) on the incidence of hypoglycaemia during DKA management. Secondary outcomes were time to resolution of ketosis (defined as ketone <1 mmol/L) and hospital length of stay.

Method: Single centre retrospective cohort study of adults with DKA managed with insulin dextrose infusion using a VRIII protocol (2021) and FRIII protocol (2022).

Results: Eighty patients were included, 45 treated with VRIII and 35 treated with FRIII. There was no difference in hypoglycaemia incidence, n=7 (16%) in VRIII and n=8 (23%) in FRIII (p = 0.56). Of those who developed early hypoglycaemic events (<12 hours) 88% were in the FRIII cohort versus 2% in VRIII (p=0.04). Time to resolution of ketosis was no different between groups (VRIII median 11 [IQR 5-24] vs FRIII median 9 [IQR 14-28], p = 0.21). The VRIII cohort had both longer hospital length of stay (VRII median 3 days [IQR 1-7] vs FRIII median 2 days [IQR 1-4], p = 0.048) and longer time on insulin infusion (VRIII median 25 hours [IQR 18-41] vs FRIII median 18 hours [IQR 14-28], p=0.02).

Conclusion: Hypoglycaemia incidence did not differ between VRIII and FRIII treatments, although the FRIII cohort had higher incidence of early hypoglycaemia. The longer hospital length of stay and time on insulin infusion in the VRIII cohort does not appear to be related to time to resolution of ketosis as this did not differ between groups. Further research is needed to determine the optimal insulin infusion regimen.

Management of Hyperosmolar Hyperglycaemic State after Implementation of a Standardised Protocol in a regional tertiary hospital – Retrospective Audit.

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Aim: A standardised hospital protocol for Hyperosmolar Hyperglycaemic State (HHS) was introduced in our regional tertiary hospital in 2019. This study aims to evaluate the management of HHS following implementation of this protocol.

Method: A retrospective audit was conducted on patients identified using ICD-10 coding between 01/01/2012 to 01/03/2022. HHS was defined as serum osmolality>320mOsm/kg and BGL>30mmol/L. Mixed diabetic ketoacidosis(DKA)/HHS was specified when serum ketones>3mmol/L or positive ketonuria, and pH<7.3. Statistical analyses were performed to assess the rate of osmolality correction and complications comparing pre-protocol (01/01/2012 to 31/12/2018) and post-protocol (01/01/2019 to 01/03/2022) implementation.

Results: 81 patients were admitted with HHS or mixed DKA/HHS, of which 41 were managed pre-protocol and 40 post-protocol. 33(40.7%) had type 2 diabetes, 47(58.0%) type 1 diabetes, and 11(13.6%) were new diagnoses. The average age was 49.8±20.2years and mean HbA1c 104±7mmol/mol (11.7±2.78%). The most common precipitant was insulin omission (32.1%). Higher initial osmolality and slower osmolality reduction had significantly higher rates of complications (p=0.004 and p=0.042 respectively).
Post-protocol implementation, there were no significant differences in average initial osmolality (pre- 343.4±17.3 vs post- 346.7±26.13mmol/L, p=0.545), initial BGL (56.3±16.9 vs 63.0±23.4mmol/L, p=0.197), average time to resolution (38.4±44.8hours vs 32.3±35.7hours, p=0.495) and average rate of osmolality reduction [6-hours (pre- 13.9±12.7mOsm/kg vs post- 12.1±9.1mOsm/kg, p=0.453), 12-hours (20.9±15.8mOsm/kg vs 18.4±12.3 mOsm/kg, p=0.457) and 24-hours (29.5±12.9mOsm/kg vs 32.3±35.7mOsm/kg, p=0.799)].
Complications of mild hypokalaemia was increased post-protocol (pre- 14.6% vs post- 42.5%, p=0.005), albeit less fluid overload (36.6% vs 10%, p=0.005), cardiovascular events (31.7% vs 5%, p=0.002), and death (9.8% vs 0%, p=0.0043).
Uptake of the HHS protocol was poor at 12.5% (5/40).

Conclusion: The average rates of osmolality reduction were slower than recommended despite protocol implementation, which can prolong hospital stay and lead to more complications. Further education of standardised management of HHS may facilitate timely resolution and reduce adverse outcomes.

Management of Insulin Pump therapy in the Peripartum period in Type 1 Diabetes: A case report and review of literature

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Aim: The use of insulin pump therapy is becoming more widespread, including during pregnancy in type 1 diabetes, a period of drastic shifts in physiology. This presentation aims to evaluate the safety and efficacy of pump therapy during labour, delivery and the immediate postpartum period and develop a framework for management using a case-based example.

Case: A 25 year old primigravida with type 1 diabetes presented at 32 weeks' gestation with pre-eclampsia and spontaneous rupture of membranes. She was using a hybrid closed loop MedTronic insulin pump and sensor system, with a plan for modified pump settings during planned delivery. However, as she proceeded to an emergency Caesarean section, she was transitioned onto an insulin infusion intraoperatively, and transitioned back to insulin pump with new manual settings after delivery. Aspects of how to manage the transition with pump therapy in this case were examined, and a literature search was performed to determine the optimal management of such a situation.

Results: Randomised data for insulin pump use in pregnancy, labour and delivery are lacking and very few studies examine closed loop systems. Observational studies show that insulin pump therapy in general is safe and effective in maintaining adequate glycaemic control during labour and delivery, even during operative or emergency cases. Some studies report an association between insulin pump use and superior intrapartum glycaemic control, although this does not appear to affect neonatal outcomes. Reduced basal rates are required during active labour due to the physiologic reduction in insulin requirements. In the immediate postpartum period, a reduction in total insulin dosing of 50-60% of the pre-pregnancy dose results in the lowest rate of hypoglycaemia and glucose excursions.

Conclusion: Insulin pump therapy appears to be safe and effective during labour, delivery and postpartum. Basal rates should be reduced by at least 50% during active labour, with an immediate postpartum rate of 50-60% of the pre-pregnancy rate. Further research is required to determine whether insulin pump therapy and hybrid closed loop therapy during the peripartum period is superior to intravenous insulin infusion with regards to maternal and neonatal outcomes.

Measuring the Effectiveness of Digital Innovative tools that Promote Healthy Lifestyle behaviours and prevent Diabetes in the Pacific.

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Aim: To evaluate the effectiveness of digital innovative tools that promote healthy lifestyle behaviour among children, as part of the strategy to prevent type 2 diabetes in the Pacific.

Method: Formal evaluation using a standardised methodology was conducted in 2023 in the Island state of Wallis and Futuna. The digital innovative tools include child-friendly health promotion resources such as interactive games and educational videos on healthy diet and physical activity, as well as training kits and curricula for teachers.

Results: The evaluation revealed that the integration of digital tools significantly enhanced children's knowledge and understanding of the healthy lifestyle behaviours. Notably, there was an improvement in children's participation and knowledge assimilation. The findings showed the improvement in engagement of physical activity program among students. In addition, there has been a significant change in children's food choices for healthier lunches with increased consumption of fruits and vegetables prepared by their parents. Moreover, teachers and school principals widely acknowledged the digital tools as valuable educational assets that facilitated and enhanced teaching and learning.

Conclusion: These positive outcomes will contribute to the reduction of childhood obesity, prevention of type 2 diabetes and the long-term goal of reducing premature mortality from non-communicable diseases. The nation of Wallis and Futuna serves as a role model in introducing and utilisation digital tools for behaviour change, setting an example for other Pacific Island nations to adopt or adapt these tools to tackle childhood obesity and type 2 diabetes in their respective countries.

Mechanism for Cross-reactivity of T-cell-receptors with InsC-peptide and Hybrid-insulin peptides presented by HLA-DQ8

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Type 1 diabetes (T1D) is a T cell-mediated autoimmune disease that has a strong HLA association, where a number of self-epitopes have been implicated in disease pathogenesis. It has been shown that fusion of self-peptides by post-translational modifications (PTMs) may play a role in the T1D pathogenesis. Hybrid insulin peptides (HIPs) are formed by the splicing of insulin peptides with other abundant peptides from highly expressed islet proteins. We previously observed that human pancreatic islet-infiltrating $CD4^+$ T cell clones not only respond to proinsulin C-peptide ($InsC_{8-22}$) but also cross-react with a hybrid insulin peptide (HIP; $InsC_{8-15}$-$IAPP_{74-80}$) presented by HLA-DQ8. How T cell receptors recognise self-peptide and cross-react to HIPs is unclear. Here, we performed functional studies on TCR transduced SKW3 T-cell lines and observed that five out of the selected seven SKW3 T-cell clones expressing TCRs, isolated from $CD4^+$ T cells of people with T1D, responded to native $InsC_{8-22}$ and cross-reacted to multiple HIPs containing N-terminal $InsC_{8-15}$ fused at the C-terminus to other degradation products, Neuropeptide Y (NPY) and another $IAPP_{23-29}$ peptide. Crystal structures of selected TRAV26-1^+/TRBV5^+ TCRs in complex with $InsC_{8-22}$ or HIPs bound HLA-DQ8 exhibited distinct mechanisms in recognition. Alanine scanning mutagenesis of the C-terminus of the $InsC_{8-22}$ and HIPs showed that the P7 and P8 residues in these epitopes were key determinants of TCR specificity.

These findings fill knowledge gaps in our understanding of the immune response to HLA-DQ8-HIPs in T1D patients. Analysis of these structures that will be presented here will provide key insights into the mechanisms responsible for the selection of HLA-DQ8-$InsC_{8-22}$/-HIP restricted autoreactive CD4+ T cells that are associated with T1D pathogenesis. This may help to gain a better understanding of the progression of the disease and better diagnostic tools for early screening to allow potential interventions before the disease develops.

Mental Health and Medical Trauma of Young people living with Type 1 Diabetes; A parent's perspective.

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Aim: Parents of children living with Type 1 Diabetes (T1D) are instrumental in its management, facing the brunt of the diagnostic shock, and the transition of care through developmental stages. There is a paucity of research on parents' perceptions of their child's wellbeing and experience. This study aims to explore these using a trauma-sensitive lens.

Method: A descriptive qualitative design was implemented. Online focus groups were held via Microsoft Teams with parents of young people (aged 17 years and under) with T1D. Focus groups aimed to investigate parents' perceptions of their child's experience and explored coping strategies and gaps in psychosocial care. Audio recordings were transcribed verbatim and analysed using Reflexive Thematic Analysis.

Results: Three themes were identified pertaining to the parent-child experience of living with T1D. First, the overwhelming presence of grief and shock at diagnosis saw coping in the early stages fueled by adrenaline, the desire to keep one's child alive and protecting them from emotional burden. Second, the relentless nature of T1D management required an adaptation to a 'new normal,' and the importance of peer support. Finally, the transition of care from parent to child was characterised by parental worry, and varying levels of willingness to relinquish control. Parents identified a lack of psychosocial support accounting for the child's needs; both developmentally and in their trajectory of T1D management. In generating these themes, we will explore the inclusion of facets of acceptance, adaptation, resilience, and self-efficacy in the development of a prototype intervention.

Conclusion: The strict regime, unpredictability, and invasiveness of care in T1D sees young people confronted with psychological and physical burden. Resultant medical trauma is associated with poorer health outcomes. Findings will inform the design of a brief, medical trauma-focused psychosocial intervention, aimed at promoting wellbeing and mental health recovery in children with T1D.

Metformin reduces Insulin dose independent of changes in Insulin resistance in Adults with Type 1 Diabetes: results from INTIMET, a 26-week, randomised, double-blind placebo-controlled trial

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Background: Insulin resistance is a cardiovascular (CV) risk factor in type 1 diabetes (T1D). The effect of metformin on liver and muscle insulin resistance has not been studied in adults with T1D. The mechanisms of action of metformin in T1D remain unknown. Growth differentiation factor 15 (GDF15), a novel molecule associated with weight balance and insulin sensitivity, is a possible mediator of metformin's effects.

Methods: Forty adults with T1D (HbA1c 7.5±0.9%, age 37.4±8.8 years, diabetes duration 22.9±8.9 years, 60% male, BMI 26.4±3.8 kg/m^2) were randomised to metformin XR 1500mg daily or placebo for 26 weeks. Twenty age-, gender- and BMI-matched controls without diabetes were studied at baseline only. Two-step hyperinsulinaemic-euglycaemic clamps with 6,6-$^2H_2$glucose were undertaken at baseline and 26 weeks. Primary outcome was liver insulin resistance (endogenous glucose production [EGP]). Secondary outcome measures were muscle (glucose infusion rate [GIR]) and adipose (non-esterified fatty acids [NEFA]) insulin resistance, body composition (DXA, MRI), metabolites, arterial stiffness (augmentation index [AIx]), continuous glucose monitoring (CGM) and serum GDF15.

Results: Adults with T1D displayed insulin resistance at the liver (EGP 64% higher), muscle (GIR 29% lower) and adipose tissue. After 26 weeks, metformin did not reduce EGP, GIR, NEFA, AIx, body composition, HbA1c or CGM time in range vs placebo. Metformin significantly reduced total daily insulin dose (estimated treatment difference [ETD] -0.10 units/kg/day [95% CI -0.15 to -0.04]; p<0.001) and visceral fat (p=0.04, NS after adjustment for multiple comparisons), and increased serum GDF15 levels (ETD 382 pg/mL [59 to 704]; p<0.001), relative to placebo.

Conclusion: Metformin reduced insulin dose and increased GDF15 compared to placebo, without improving insulin resistance. This study: 1) Highlights that metformin may have metabolic benefits in T1D; 2) Implicates insulin resistance-independent actions of metformin; and 3) Raises new hypotheses that metformin's effects in adults with T1D may involve GDF15. ACTRN12619001440112

Moderate Resistance Training Reduces Intermuscular Adipose Tissue and Risk Factors of ASCVD for Elderly Patients with type 2 Diabetes

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Aims: This study aimed to assess the impact of moderate resistance training on intermuscular adipose tissue (IMAT) in elderly patients with type 2 diabetes and the independent effect of IMAT reduction on metabolic outcomes.
Methods: In this randomized controlled trial , 85 type 2 diabetes patients were assigned to either the resistance training group (42 participants) or the control group (43 participants) for a 6-month intervention. The primary outcome was changes in IMAT measured by computed tomography scan and magnetic resonance imaging using the interactive decomposition of water and fat with echo asymmetry and least squares qualification sequence. Secondary outcomes included changes in metabolic parameters.

Results: Thirty-seven participants in each group completed the study. IMAT area in the resistance group decreased from 5.176±1.249 cm^2 to 4.660±1.147 cm^2, a change of -0.512±0.115 cm^2, representing a 9.89% decrease from the least-squares adjusted mean at baseline, which was significantly different from that of the control group (a change of 0.587±0.115 cm^2, a 10.34% increase). NAMA area (representing normal muscle density) in the resistance group increased from 82.113±8.776 cm^2 to 83.054±8.761 cm^2, a change of 1.049±0.416 cm^2, a 1.3% increase, which was significantly different from that of the control group (a change of -1.113±0.416 cm^2, a 1.41% decrease). HOMA2-β (increased from 52.291±24.765 to 56.368±21.630, a change of 4.135±1.910, a 7.91% increase from baseline) and ΔI30/ΔG30 (increased from 4.616±1.653 to 5.302±2.264, a change of 0.715±0.262, a 15.49% increase) in the resistance group were significantly improved compared to those in the control group, which had a change of -3.457±1.910, a 6.05% decrease in HOMA2-β, and a change of -0.195±0.262, a 3.87% decrease in ΔI30/ΔG30, respectively. Linear regression showed that the change in IMAT area was significantly related to the changes in ΔI30/ΔG30 (β=-0.439, p=0.047), 2-h postprandial glucose (β=1.321, p=0.026), diastolic blood pressure (β=2.425, p=0.018), NAMA (β=-0.907, p=0.019), and 10-year risk of atherosclerotic cardiovascular disease (ASCVD) (β=0.976, p=0.002).

Conclusion: Low-level moderate resistance training reduces IMAT content. Even a small reduction in IMAT may be related to a decrease in risk factors for ASCVD, but this small reduction may not be sufficient to reduce insulin resistance.

Table 1. Outcomes comparison between two groups with classification and regression trees imputation (n=85).

Index	Resistance (n=42)	Control (n=43)	P-Value	
			Group–Time	Resistance VS
IMAT (cm^2)				
Baseline	5.145±1.206	5.732±1.339		
Change at 6 months#	-0.407±0.124*	0.668±0.123*	<0.001	<0.001
NAMA (cm^2)				
Baseline	82.011±8.548	78.854±6.573		
Change at 6 months#	0.686±0.429	-1.018±0.424*	0.007	<0.001
LAMA (cm^2)				
Baseline	23.358±6.003	23.410±6.936		
Change at 6 months#	0.960±0.527	0.043±0.521	0.229	0.220
FF				
Baseline	4.377±2.204	4.832±2.294		
Change at 6 months#	-0.033±0.126	0.230±0.125	0.150	0.121
ΔI30/ΔG30				
Baseline	4.565±1.606	5.025±1.292		
Change at 6 months#	0.634±0.234*	-0.152±0.231	0.021	0.016
HOMA2-β				
Baseline	51.991±24.900	55.140±23.69		
Change at 6 months#	4.727±2.191*	-2.897±2.165	0.017	0.005
HOMA2-IR				
Baseline	2.773±1.422	2.796±1.332		
Change at 6 months#	0.671±0.302*	0.327±0.298	0.429	0.991
FPG (mmol/L)				
Baseline	7.304±2.881	7.673±2.144		
Change at 6 months#	0.298±0.555	-0.157±0.549	0.569	0.271
2hPG (mmol/L)				
Baseline	13.024±3.832	12.697±4.801		
Change at 6 months#	-0.527±0.703	2.101±0.695*	0.011	0.008
HbA1c (%)				
Baseline	7.645±2.565	7.970±1.682		
Change at 6 months#	-0.367±0.460	0.007±0.455	0.573	0.339
BMI (kg/m^2)				
Baseline	23.823±3.397	24.525±3.247		
Change at 6 months#	-0.295±0.109	0.032±0.108	0.014	0.041
TG (mmol/dL)				
Baseline	2.197±0.598	2.147±0.685		
Change at 6 months#	-0.351±0.118*	-0.231±0.117	0.481	0.855
HDL-C (mmol/dL)				
Baseline	1.481±0.410	1.437±0.319		
Change at 6 months#	-0.028±0.082	0.206±0.081*	0.051	0.359
LDL-C (mmol/dL)				
Baseline	3.313±1.060	3.260±1.159		
Change at 6 months#	-0.815±0.181*	-0.337±0.179	0.069	0.112
SBP (mmHg)				
Baseline	129.286±14.826	132.023±11.9		
Change at 6 months	4.622±1.624*	1.671±1.604	0.208	0.216

DBP (mmHg)				
Baseline	79.405±9.776	76.256±8.392		
Change at 6 months[#]	-2.377±1.594	3.740±1.575[*]	0.009	0.043
ASCVD 10-year risk				
Baseline	7.181±2.668	8.547±4.299		
Change at 6 months[#]	-0.399±0.442	0.323±0.436	0.257	<0.001

Notes: #: Change values represent the least-squares adjusted means ± SE from repeated-measures analyses of variance (adjusted for baseline values, sex, age, and duration of diabetes); *: P<0.05 for within-group comparisons of the value at 6 months with the baseline value, using mixed-model repeated-measures analysis of variance (adjusted for sex, age, and duration of diabetes).
Resistance = Resistance training group, Control = control group, IMAT = intermuscular adipose tissue, NAMA= Normal Attenuation Muscle Area, LAMA=Low Attenuation Muscle Area, FF=Fat Fraction, ΔI30/ΔG30=Early Insulin Secretion Index, HOMA2-β=Homeostasis model assessment of Beta Cell Function, HOMA2-IR= Homeostasis model assessment of insulin resistanc, FPG=Fasting Plasma Glucose, 2hPG=2-h Postprandial Glucose, HbA1c=Hemoglobin A1c, BMI=Body Mass Index, TG=Triglycerides, HDL-c=High-density-lipoprotein Cholesterol, LDL-c= Low-density-lipoprotein Cholesterol, SBP=Systolic Blood Press, DBP=Diastolic Blood Press, and ASCVD=Atherosclerotic cardiovascular disease.

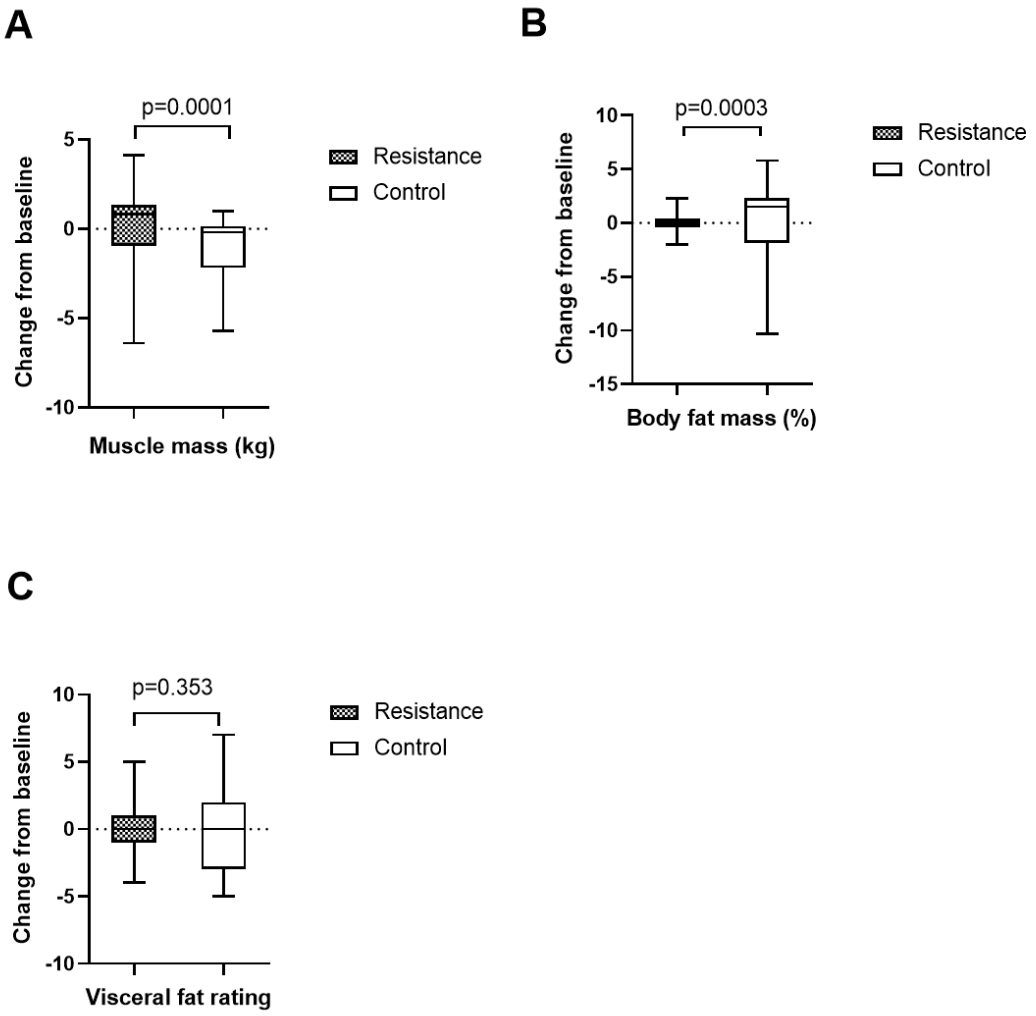

Figure 1. Comparison of changes in body composition (Muscle mass, Body fat mass and Visceral fat rating) from baseline to 6 months between the Resistance and Control groups.

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Nanoformulations of Low dose Oral-liraglutide to Improve Metabolic Health in aging mice.

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Introduction. Reformulation of injectable medications to make them orally bioavailable is a critical area of research with the aim to improve patient compliance and quality of life. Glucagon-like peptide 1 (GLP-1) agonists are anti-diabetic medication used to treat type 2 diabetes, obesity, and chronic weight management. Currently liraglutide is not orally bioavailable and must be given via subcutaneous injection. In elderly patients, GLP-1 agonists may improve metabolic parameters, but weight loss can be detrimental if associated with loss of muscle mass and bone density.

Aims. This study aimed to develop and demonstrate a nanoformulations of liraglutide for oral delivery and evaluate the effects of low dose oral and injected liraglutide in 2-year aged mice.

Results. Pharmacokinetic data demonstrated oral liraglutide localization to the pancreas at similar concentrations to injected liraglutide. Oral formulations had minimal expression in the blood and gut compared to injected. Pharmacodynamics studies in young mice highlighted that both injected and oral liraglutide were effective at reducing blood glucose in a dose dependent manner in oral glucose tolerance tests. In aged (2 years) mice, 4-week treatment with low dose oral liraglutide improved metabolic parameters (insulin resistance, fasting insulin, free and total cholesterol and glucose regulation) without promoting weight loss or reduction in food intake. Injected liraglutide showed improved glucose regulation only. Oral liraglutide also promoted greater upregulation of fibroblast growth factor 21 (FGF-21) and reduced insulin growth factor 1 (IGF-1).

Discussion. These studies demonstrate the broad application of our nanotechnology for non-liver acting medications and highlight an organic platform for oral drug delivery. Given the FGF-21 and IGF-1 effects we will investigate if oral-liraglutide can increase longevity.

Novel risk factors for incident heart failure in type 2 diabetes: The Fremantle Diabetes Study Phase II

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Aim: To determine whether N-terminal prohormone of brain natriuretic peptide (NT-proBNP), high-sensitivity C-reactive protein (hsCRP), thyroid-stimulating hormone (TSH), and liver disease biomarkers are independently associated with incident heart failure (HF) in type 2 diabetes after adjusting for conventional risk factors.

Methods: 1493 participants with clinically-defined type 2 diabetes from the Fremantle Diabetes Study Phase II were followed from entry (2008-11) to end-2021 for first hospitalisation for/with HF or death from/with HF. Cox regression was used to identify independent determinants of incident HF.

Results: At baseline, 97 (6.5%) participants had a prior hospitalisation for/with HF and were excluded. The remaining 1396 had a mean±SD age of 65.0±11.5 years, 52% were males, and their diabetes duration was a median [inter-quartile range] 8.0 [2.1-15.0] years. During 13,883 person-years (9.9±3.7 years) of follow-up, 297 (21.3%) had incident HF (crude incidence rate 2.14 (95% CI: 1.90, 2.40) /100 person-years or 2.1%/year). The most parsimonious Cox regression model of independent conventional risk factors for incident HF included age, current smoking, abdominal obesity, diabetes duration, HbA_{1c}, beta-blocker use, urinary albumin:creatinine ratio, estimated glomerular filtration rate, peripheral arterial disease, ischaemic heart disease, and Charlson's Comorbidity Index (CCI) (log likelihood (LL) -1846, likelihood ratio (LR) Chi-squared 319.9, df=12). Of NT-proBNP, hsCRP, AST/ALT, serum albumin, hyaluronic acid, haptoglobulin, alpha-2 macroglobulin and anaemia, only NT-proBNP, serum albumin (negatively), and alpha-2 macroglobulin added significantly to the most parsimonious model, displacing diabetes duration, beta-blocker use, and CCI (LL -1802, LR Chi-squared 403.3, df=13). The LR test comparing the two models was highly significant ($P<0.00001$) indicating that the model including NT pro-BNP and liver disease biomarkers was superior to the conventional model.

Conclusions: NT-proBNP is an important prognostic predictor of HF in addition to its diagnostic role. Raised alpha-2 macroglobulin and low serum albumin levels are also prognostic of future heart failure.

Octreotide for the Treatment of Sulfonylurea induced Hypoglycaemia

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Background: Sulfonylurea induced hypoglycaemia is often refractory to conventional management, particularly in the setting of renal impairment.

We present a case of sulfonylurea induced hypoglycaemia in a patient with chronic kidney disease and severe tricuspid regurgitation who was successfully treated with subcutaneous octreotide.

Case summary: A 76-year-old female presented to a tertiary centre with symptoms of hypoglycaemia secondary to unintentional sulfonylurea ingestion after inadvertently consuming her partner's webster pack contents including gliclazide 120 mg mane. Her background history was significant for cognitive impairment, chronic kidney disease (eGFR 27), atrial fibrillation, hypertension and severe tricuspid regurgitation.

On presentation to the emergency department, her capillary BGL was 2.3 mmol/L. She was treated with repeat boluses of 50 ml of 50% dextrose and a continuous 10% dextrose infusion at 100 ml/h. The rate of 10% dextrose was increased to 150 ml/h with only brief periods of normoglycaemia followed by recurrent hypoglycaemic episodes.

Investigations were consistent with sulfonylurea use with a c-peptide of 4402 pmol/L, insulin level 290 pmol/L, and glucose of 8.9 mmol/L. Proinsulin is pending. A sulfonylurea screen returned positive for gliclazide confirming our provisional diagnosis.

Given the history of severe tricuspid regurgitation and concerns regarding volume overload and refractory hypoglycaemia, a decision was made to trial octreotide 50 mcg. Two doses, 12 hours apart resulted in resolution of hypoglycaemia and maintenance of euglycaemia.

Investigations following administration of octreotide revealed a glucose of 8.4 mmoll/L, insulin level 22 pmol/L, c-peptide 1000 pmol/L.

Octreotide is an effective treatment for sulfonylurea induced hypoglycaemia.

Once-weekly semaglutide in heart failure with preserved ejection fraction and obesity: main results from the STEP-HFpEF Trial

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Aim: Obesity is a major risk factor for heart failure (HF) with preserved ejection fraction (HFpEF). To date, no approved therapies targeting the obesity phenotype of HFpEF exist. STEP-HFpEF (NCT04788511) was a phase 3a trial investigating the effects of semaglutide 2.4 mg on symptoms, physical limitations and exercise function in people with HFpEF and obesity.

Methods: In this 52-week double-blind trial, adults with HFpEF and body mass index (BMI) ≥30 kg/m^2 were randomised 1:1 to once-weekly subcutaneous semaglutide 2.4 mg or placebo. Eligible participants had left ventricular ejection fraction (LVEF) ≥45%, New York Heart Association functional (NYHA) class II–IV, Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS) <90 points and ≥1 of the following: elevated filling pressures; elevated natriuretic peptide levels plus structural echocardiographic abnormalities; or HF hospitalisation (within past year) plus ongoing diuretic use and/or structural echocardiographic abnormalities. Key exclusion criteria were prior/planned bariatric surgery; recent >5 kg change in body weight; recent cardiovascular event or HF hospitalisation; systolic blood pressure >160 mmHg; and diabetes history. Dual primary endpoints were change from baseline to week 52 in KCCQ-CSS and body weight.

Results: 529 participants (56.1% female, 95.8% White, median age 69 years) were randomised (83 sites, 13 countries). Median body weight was 105.1 kg and BMI 37.0 kg/m^2; 66.0% (n=349) of participants had BMI ≥35 kg/m^2. Median baseline measurements were KCCQ-CSS 58.9 points, 6-minute walk distance 320 meters, high-sensitivity C-reactive protein 3.8 mg/L and LVEF 57%. Overall, 52% had a history of atrial fibrillation, 15.3% were hospitalised for HF, and 66.2% and 33.8% were in NYHA class II and III–IV, respectively. Data for the primary endpoints will be presented.

Conclusions: STEP-HFpEF will determine whether semaglutide 2.4 mg can improve symptoms, physical limitations and exercise function, plus weight loss, in patients with unmet needs for additional therapies.

Once-weekly semaglutide in patients with heart failure with preserved ejection fraction, obesity and type 2 diabetes: main results from the STEP-HFpEF DM trial

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Aim: Obesity and type 2 diabetes (T2D) are highly prevalent in patients who have heart failure with preserved ejection fraction (HFpEF) and associated with an especially high burden of symptoms and functional impairment. No approved therapies specifically target obesity-related HFpEF in patients with T2D. The STEP-HFpEF DM trial tested the efficacy and safety of once-weekly semaglutide 2.4 mg compared with placebo in patients with obesity-related HFpEF and T2D.

Methods: In this double-blind trial, we randomised 616 patients across 108 sites in 16 countries with HFpEF, body mass index (BMI) of ≥30 kg/m^2 and T2D to once-weekly semaglutide 2.4 mg or placebo for 52 weeks. Dual primary endpoints were change in the Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS) and body weight. Confirmatory secondary endpoints were change in 6-minute walk distance (6MWD), hierarchical composite (death, HF events, and change in KCCQ-CSS and 6MWD) and change in C-reactive protein. Exploratory endpoints included NTproBNP and adjudicated HF events.

Results: Median age was 69 years, 44% were women, median BMI was 36.9 kg/m^2, KCCQ-CSS 59.4 points, 6MWD 280 meters, NTproBNP 493 pg/mL, LVEF 56% and 29.4% were in New York Heart Association functional (NYHA) class II–IV. Most patients were treated with diuretics (80.8%); 32.5% received MRAs and 32.8% SGLT-2 inhibitors. Main results will be presented.

Conclusion: STEP-HFpEF DM randomised patients with obesity-related HFpEF and T2D who have marked symptomatic and functional impairment and will determine whether semaglutide can improve symptoms, physical limitations and exercise function in this group with a large need for additional therapies.

Once-weekly Subcutaneous Semaglutide 2.4 mg in Adolescents with Overweight or Obesity

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Background: STEP TEENS (NCT04102189) was the first phase 3a trial to examine efficacy and safety of once-weekly subcutaneous semaglutide 2.4 mg (sema) + lifestyle intervention in adolescents (12–<18 yrs) with obesity (BMI ≥95th percentile), or overweight (BMI ≥85th percentile) with ≥1 weight-related comorbidity.

Methods: Participants were randomised 2:1 to sema (n=134) or matching placebo (PBO; n=67). Endpoints (baseline [BL]–wk 68) were %-change in BMI (primary); ≥5% weight loss (WL; confirmatory secondary); and ≥10, ≥15 and ≥20% WL, change in cardiometabolic risk factors and quality of life (QoL; secondary), assessed by the treatment policy estimand. Primary and confirmatory secondary endpoints were controlled for multiplicity.

Results: Of 201 adolescents (62.2% female; mean age 15.4 yrs, body weight 107.5 kg, BMI 37.0 kg/m^2) randomised, 89.6% completed treatment. Mean BMI change (BL–wk 68) was –16.1% (sema) vs 0.6% (PBO; estimated treatment difference [ETD]: –16.7%-points; 95% CI: −20.3;−13.2; p<0.0001). ETD in body weight %-change (BL–wk 68) for sema vs PBO was –17.4%-points (95% CI: –21.1;–13.7; p<0.0001). More participants achieved ≥5, ≥10, ≥15 and ≥20% WL with sema vs PBO (72.5 vs 17.7%, 61.8 vs 8.1%, 53.4 vs 4.8%, 37.4 vs 3.2%; p<0.0001). Waist circumference, HbA_{1c} and lipids (except HDL) were reduced with sema (p<0.05). Sema improved overall weight-related QoL (p=0.038) and physical comfort (p=0.005). Adverse events (AEs) were reported by 78.9% (sema) and 82.1% (PBO) of participants. Serious AEs were reported by 11.3% (sema) and 9.0% (PBO) of participants. More participants reported gastrointestinal AEs with sema (61.7%) vs PBO (41.8%). In each group, 4.5% of participants stopped treatment due to AEs.

Conclusions: In adolescents with overweight/obesity, sema resulted in significant BMI, body weight and waist circumference reductions, and improvements in cardiometabolic risk factors and QoL. Sema was generally well tolerated with a safety profile consistent with the GLP-1 RA class.

Only 50% of Parents confident in managing their Child's type 1 Diabetes: Need for greater involvement of families with clinical teams, education, tools and supports

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Introduction: Type 1 diabetes (T1D) requires constant monitoring and insulin dose adjustment to achieve and maintain safe blood glucose levels. Families of children with T1D rely on consistent, high-quality support from healthcare professionals and educational resources to help them navigate the constant demands of managing T1D. To what extent Australian families of children living with T1D are integrated with their clinical teams has not been studied before.

Aim: To map the current experiences of accessing health services among Australian families.

Methods: A mixed methods study design, using surveys and interviews, was used to collect data from Australian families of children living with T1D. Survey data were analysed using descriptive statistics and interviews were thematically analysed.

Results: A total of 525 survey responses and 17 interviews were completed by parents of children with T1D across all Australian states. The majority of families were scheduled for clinic visits every 3 months (378, 76%) and received care in a paediatric hospital (393, 75%). Most families felt very involved in discussions about T1D with their healthcare professionals (376, 77%) and reported being offered a range of sources of information, such as support groups and apps. However, only 51% (n=248) of parents reported feeling confident about their knowledge and management of T1D. Parents expressed a need for additional support in T1D-specific areas such as psychological support for both their children and families, better support with major transitions of care (e.g., from paediatric to adult health services), improved access to educational resources (e.g., nutrition) and increased access to care (e.g., after hours).

Conclusions: Parents reported being satisfied with their overall experience with T1D services. However, they strongly expressed the need for additional support in specific areas such as psychological support, educational resources and better access to care and support.

OPERATION GLUCOSE: The role of Continuous Glucose monitoring in Hospitalised individuals with Insulin-requiring type 2 Diabetes undergoing an operation

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Background: People with diabetes, undergoing surgery, have a high rate of adverse perioperative outcomes, including surgical site infection (SSI), re-operation, greater length of stay (LOS) and death. Perioperative hypo- and hyperglycaemic greatly increases adverse outcomes. Our previous retrospective audit showed that people with type 2 diabetes (T2D) on insulin therapy, with HbA1c ≥ 7.5% are a high-risk group. Continuous glucose monitoring (CGM) may aid in optimising glycaemic metrics and reduce adverse perioperative outcomes.

Aim: This multi-site open-label randomised controlled trial aims to determine if real-time CGM, alongside standard point of care monitoring (POC), facilitates improved glycaemic control in people with insulin-requiring T2D, with HbA1c ≥ 7.5%, undergoing an operation compared to standard care.

Method: Adults with insulin-requiring T2D intending to undergo an operation with expected admission > 24hours are recruited 1-7 days prior to the operation. Participants in the CGM group will receive a FreeStyle Libre 2 device and instructed on its use. Participants in the control group will received a Libre ProIQ, providing blinded CGM data for research purposes only. Both groups receive POC monitoring 4 times daily whilst in hospital, per standard of care. Clinical decisions can be made using either CGM or POC readings in the CGM group, or POC testing only in the control group. Differences in percent time in range (4.0–10.0 mmol/L), time below or above range and glucose variability by CGM will be compared. POC-derived metrics (percent days with hypoglycaemia, percent days with hyperglycaemia,) and discordance between POC and CGM will be compared between groups. Clinical outcomes including hospital and ICU length of stay, 28-day hospital readmission rate and post-operative complications will be compared. Patient-reported experiences of glucose management with or without self-monitoring with CGM will be studied.

Results & Conclusion: This trial is ongoing, and expects to fully recruit by December 2025.

Optimal R&D Spending on Treatments and Therapies for Type 1 Diabetes

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Introduction: Type 1 Diabetes (T1D) has a substantial global disease burden and optimal therapeutic goals are often not achieved. There is considerable interest in developing new models of care and more effective therapies. However, it is unclear how much to spend on this endeavour.

Aim: To estimate optimal research and development (R&D) spending on novel therapies for prevention, delaying progression, management, and cure of T1D.

Methods: We develop a mathematical model to calculate the optimal level of T1D R&D. We take a global, societal perspective. Our model parameters are: total economic T1D harm, the probability a T1D R&D project will result in an approved product, development costs of a successful product, fraction of T1D harm reduced by a successful product, and the number of available approaches to address T1D harm. We calibrate these parameters using medical and economic literature, and expert opinion.

Results: Total cumulative optimal spending on T1D R&D is USD 246 billion. This level of spending funds 438 projects to address T1D harm. Social surplus is USD 2.4 trillion, resulting in a benefit-cost ratio equivalent to an 11.5% rate of return (RoR) annually for thirty years. Actual R&D is substantially below our estimated amount. Sensitivity analysis indicates a range for the optimal number of projects (438-791), spending (111-445 billion), social surplus (2.1-11.9 trillion) and RoR (8-19.5%).

Conclusions: Investment in R&D for developing new T1D preventatives, treatments, and methods of care management is far below the optimal level. Our results support more direct government investment in T1D R&D. They also support government efforts to de-risk private investment in R&D and to streamline the regulatory approval pathway. Promoting international co-operation in health R&D and public-private partnerships to address needs in low income countries can help reduce the gap between actual and optimal T1D R&D.

Optimising Diabetes Detection: A comparison of linked administrative data, National Diabetes Services Scheme, and self-report methods.

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Aim: To compare diabetes case detection determined using National Diabetes Services Scheme (NDSS) data or self-report, with an algorithm using linked administrative health datasets.

Methods: This prospective cohort study linked baseline survey data for 266 414 individuals aged ≥ 45 years from the 45 and Up Study, Australia, to administrative health records. An algorithm for detecting diabetes cases was developed using a combination of diabetes-specific Medicare Benefit Schedule (MBS) claims, Pharmaceutical Benefit Scheme (PBS) claims for dispensed insulin and glucose lowering medications, and diabetes-related hospital admissions (Admitted Patient Data Collection, APDC). Using the algorithm, participants considered to have certain diabetes were classified as type 1, type 2, or unclear type. The number of diabetes cases detected using the algorithm was compared with NDSS registrations up to 31 Dec 2019, and with self-reported prevalence at baseline survey.

Results: A total of 53 669 diabetes cases were detected using the algorithm, with 81% of cases identified in at least two administrative datasets (MBS, PBS and/or APDC). The NDSS contained 35 990 registrants, 97% of whom were also detected using the algorithm. The algorithm detected an additional 18 835 diabetes cases not registered with the NDSS. At baseline, 23 884 participants self-reported diabetes; 85% of these were detected using the algorithm. The algorithm detected an additional 4 367 cases who did not self-report diabetes at baseline. Preliminary results for diabetes type highlight the complexities in using administrative data to distinguish type 1 and type 2 diabetes. The NDSS will be used to further refine the diabetes algorithm by type.

Conclusions: This study demonstrates the value in using an administrative linked data algorithm to identify diabetes cases. National estimates of diabetes using the NDSS or self-report may underestimate the burden by up to 35%.

Optimising Glucose-lowering Medication Treatment following Cardiothoracic Surgery: Implementation of a pharmacist-led guideline

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Background: In people with type 2 diabetes (T2D) and established cardiovascular disease, treatment with sodium-glucose cotransporter-2 inhibitors (SGLT2i) and glucagon-like peptide-1 receptor agonists (GLP1RA) are preferred due to their cardio-protective properties. Following cardiothoracic surgery, there is potential to optimise treatment with these glucose-lowering medicines (GLM) in this population.

Aim: To determine if a pharmacist-led glycaemia management guideline for inpatients with T2D following coronary artery bypass graft (CABG) or valve replacement surgery improves cardio-protective GLM prescription.

Method: We developed and implemented a pharmacist-led guideline at our quaternary hospital to optimise inpatient glycaemia, and to prioritise prescription of SGLT2i/GLP1RA following CABG or valve surgeries. A sample of 100 consecutive patients who underwent these procedures, before and after guideline implementation were identified. Patients without a diagnosis of T2D were excluded. GLM at admission and discharge were compared to ascertain whether the guideline increased treatment with SGLT2i/GLP1RA.

Results: We included 69 individuals in the pre-implementation and 37 individuals in the post-implementation groups. The cohort's characteristics (mean age 66 years, median [IQR] HbA1c 7.1 [6.5, 8.0]%, and 28% insulin-requiring at admission) were well matched, except the post-implementation group had lower median weight (88 vs 78 kg, p=0.016). At discharge, the proportion of individuals treated with SGLT2i/GLP1RA was not different (49% vs 49%, p=0.9). When both groups were combined, inpatient diabetes team consultation increased the likelihood of SGLT2i/GLP1RA prescription at discharge when adjusted for age and admission HbA1c (adjusted OR 2.9, p=0.017).

Conclusion: In patients with T2D undergoing CABG and valve surgery, prescription of SGLT2i and/or GLP1RA at the time of discharge was evident for half the cohort but did not increase following implementation of a pharmacist-led guideline. Strategies including education on safety of initiating SGLT2i/GLP1RA, or increased inpatient diabetes team involvement should be explored to increase uptake of cardio-protective GLM following cardiac surgery.

Optimum Diagnostic testing for Glucocorticoid-induced Hyperglycaemia: A cross-sectional study

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Background: Glucocorticoid hormones (e.g prednisolone) predominantly increase postprandial more than fasting glucose and it is recommended that patients prescribed chronic prednisolone are screened for diabetes with an oral glucose tolerance test (OGTT). However, an OGTT entails greater cost and patient commitment than other screening methods. We have investigated the efficacy of a random afternoon glucose to screen for diabetes in outpatients prescribed long-term prednisolone.

Methods. In a cross-sectional study of subjects with inflammatory disease but without known diabetes, 65 subjects [age = 62±12 years, 63% female] who were receiving chronic (>3 months) prednisolone [7 (IQR 5,10) mg/day] therapy underwent an OGTT, glycated haemoglobin (HbA1c) and random afternoon glucose measurement between 14:00 and 17:00 hours at least 48 hours post OGTT. Areas under the receiver operator characteristic (ROC) curves with 95% confidence intervals were calculated to compare the screening modalities.

Results. 11 of 65 (17%) subjects were identified with diabetes. Fasting glucose (5.8±0.3 mmol/L vs 4.7±0.1 mmol/L, P<0.001), two-hour glucose (14.9±1.1 mmol/L vs 6.7±0.2 mmol/L, P <0.001), HbA1c (6.6±0.2% vs 5.6±0.1%, P<0.001), and random afternoon glucose (8.4±0.8 vs 6.2±0.2 mmol/L, P<0.001) were higher in patients with diabetes. The area under the ROC curve for fasting glucose [0.86 (0.70, 1.01) P<0.001], HbA1c [0.91 (0.82, 1.03) P<0.001] and random afternoon glucose [0.76 (0.59, 0.94) P=0.003] were significantly greater than 0.5. A HbA1c ≥6.2% had 91% sensitivity and 87% specificity to diagnose diabetes. To achieve the same sensitivity, fasting glucose and random afternoon glucose had lower specificities of 66% and 30% respectively.

Conclusion. A random afternoon glucose has low specificity to screen for diabetes in outpatients prescribed long-term prednisolone. A HbA1c threshold of ≥6.2% may allow determination of which patients prescribed prednisolone require confirmatory testing with an OGTT.

Orforglipron Improves Markers of Beta-Cell Function and Insulin Sensitivity in Type 2 Diabetes

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Aim: Orforglipron (OFG), an oral, non-peptide GLP-1 receptor agonist, demonstrated significantly greater glycemic control and weight loss at doses ≥12 mg vs placebo (PBO) or dulaglutide (DU) 1.5 mg in a 26-week phase 2 study of adults with type 2 diabetes (T2D). These exploratory analyses investigated mechanisms by which OFG improved glycemic control in T2D by analyzing exploratory biomarkers.

Method: Participants with T2D (mean age, 58.9 years; baseline HbA_{1c}, 8.1%; weight, 100.3 kg) treated with diet and exercise, with/without metformin, were randomized to PBO, DU 1.5 mg, or once-daily OFG 3, 12, 24, 36, or 45 mg. Biomarkers of β-cell function and insulin sensitivity were analyzed by mixed model repeated measures, excluding data after study drug discontinuation or rescue drug initiation.

Results: Biomarkers of β-cell function were improved by OFG at 26-weeks from baseline. HOMA-B significantly increased with OFG at doses ≥12 mg vs PBO [HOMA-B (computed with insulin) for OFG 12, 24, 36, 45 mg % change from baseline (CFB) was 111%, 90%, 104%, 90% vs PBO 6% and DU 1.5 mg 42%; HOMA-B (computed with C-peptide) CFB for OFG 12, 24, 36, 45 mg was 118%, 92%, 114%, 113% vs PBO 14% and DU 46%]. HOMA-IR (computed with insulin) significantly decreased from baseline with OFG at doses ≥24 mg (OFG 24, 36, 45 mg CFB was 19%, 14%, 23%) but was not significantly different vs PBO (12%) and DU (13%). Fasting glucose-adjusted glucagon significantly decreased with OFG at doses ≥12 mg vs PBO (30%) and with OFG 12 mg (58%), 24 mg (59%), and 45 mg (60%) vs DU (44%).

Conclusion: These analyses suggest improved glycemic control with OFG vs DU may be partly explained by improved β-cell function and insulin sensitivity. Additional studies are ongoing to understand these mechanisms.
Previously accepted at ADA 2024.

Outcomes of CRUSADES: Charcot Foot Quantitative Ultrasound and Denosumab Study

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Aim: We aimed to investigate the effect of denosumab on pedal bone health and clinical resolution in active Charcot foot (CN).

Method: This multicentre open-label phase 2 randomised controlled trial recruited adults with diabetes mellitus and active CN within 3 months of onset. Participants were randomised to standard care alone, or with denosumab 60mg subcutaneously. Denosumab was administered at baseline and again at 6 months, unless foot temperature had normalised (i.e. <2^{o}C compared to contralateral foot). Co-primary outcomes were change in calcaneal Stiffness Index and foot temperature normalisation over 18 months.

Results: Twelve participants per group were analysed; mean age 58 (SD 11) years, 83% male and 92% had type 2 diabetes. Active CN duration was median 8 (IQR 7-12) weeks. Ninety-two percent were Eichenholtz stage 1 and 96% involved the midfoot. After 1-month, median decline in Stiffness Index was less in the denosumab verses standard care group (0.5 [IQR -1.0 to 3.9] vs -2.8 [-8.5 to -1.0], p=0.008). At 18-months, 92% of the denosumab group attained foot temperature normalisation versus 67% of the standard care group (p=0.13).

Conclusion: Denosumab ameliorated the early decline in calcaneal Stiffness Index associated with active CN. However, no difference in normalisation of foot temperature was observed.

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Overweight yet undernourished: A common Juxtaposition in the Diabetes High Risk Foot Service

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Introduction: Adequate nutrition is important for wound healing, however the optimal approach to assessing and managing nutrition in interdisciplinary High Risk Foot Services (HRFS) remains uncertain.

Aim: To describe the nutritional status of people attending a diabetes HRFS, encompassing dietary intake and biochemical measures.

Method: Participants were attendees of the St Vincent's Hospital Sydney HRFS who had diabetes mellitus and an active foot complication. Inclusion required completion of a standardised dietary questionnaire administered by an Accredited Practicing Dietitian between 2021-2023. Adequacy of fruit and vegetable intake was assessed against the Australian Guide to Healthy Eating. Recommended daily intake (RDI) of protein was defined as 1.25 g/kg/day. Supplement use was recorded. Biochemical measures were reported if available within 3 months of the questionnaire. Ethics approval: 2022/ETH00717.

Results: Included were 102 participants, mean age 68 (SD 12), predominantly men (83%), and mean body mass index 28.6 (SD 6.1) kg/m^2. Diabetes was median duration 16 (IQR 9-23) years, mostly type 2 (86%), and mean HbA1c was 8.1 (SD 1.8) %. Collectively, participants had 154 active ulcerations and 7 active Charcot feet at time of dietary assessment. Ulcerations were typically neuropathic (65%) or neuroischaemic (22%), and 36% were severe (SINBAD score $\geq$3).
Protein intake was mean 0.9 (SD 0.3) g/kg/day with 17% meeting the RDI. A mean of 3.4 (SD 1.9) serves of vegetables and 2.0 (SD 1.8) serves of fruit were consumed daily, with the RDI met by 14% and 53%, respectively. Two-thirds reported supplement use, most commonly vitamin D (43%), vitamin C (23%) and multivitamins (18%). Prevalent biochemical micronutrient insufficiencies were 25-OH vitamin D (n=35/88, 40%), zinc (n=18/66, 27%), iron (n=19/82, 23%) and vitamin C (15/70, 21%).

Conclusion: Nutritional inadequacies are common in people with diabetes-related foot complications. Further study will investigate associations with ulceration healing and effectiveness of dietary intervention.

Patient and Family Perspectives on Optimal Timing of Hybrid Closed Loop Commencement After Diagnosis of Type 1 Diabetes.

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Aim: Increasing availability of hybrid closed loop (HCL) systems results in opportunities to commence HCL therapy soon after diagnosis of type 1 diabetes (T1D). Models of care incorporating early HCL commencement should be designed and evaluated with stakeholder perspectives considered.
At Perth Children's Hospital (PCH), youth commenced on insulin pump therapy are followed in a nurse specialist driven model of care for 6 weeks.
The purpose of this study was to evaluate patient and family perspectives on the optimal timing of HCL therapy after a T1D diagnosis in a statewide diabetes service.

Method: A survey evaluating first awareness of HCL systems, preferred timing of initiation and reasons for this timing was developed. Parents of children with T1D and/or adolescents were approached ad hoc at 6 weeks post initiation of HCL. Patient Characteristics were summarised using mean and standard deviation (SD) for continuous measures and count (percentage) for categorical measures. Common themes that emerged regarding opinion for reason of timing of HCL start is described.

Results: There were 54 survey respondents, mean (SD) age 11.3 (4.3) years, mean duration of diabetes 15 (22.6) months, mean HbA1c 7.2 (1.2)%. Nearly all (45) respondents answered that their preferred time for HCL start would have been within four months from diagnosis. Of these, 25 said their preferred time to start HCL would have been less than two months from diagnosis. Common themes families stated for these time frames were; enough time to consolidate basic diabetes knowledge and skills, increased flexibility with HCL and decrease in diabetes-related burden.

Conclusion: Majority of individuals with T1D and their families commencing HCL at PCH reported a preference for early initiation of HCL, within four months of diagnosis. It was reported that HCL initiation in this period was preferable while allowing for consolidation of basic diabetes skills.

Patient Experience with the Use of Smart Pens for the Management of Diabetes Mellitus

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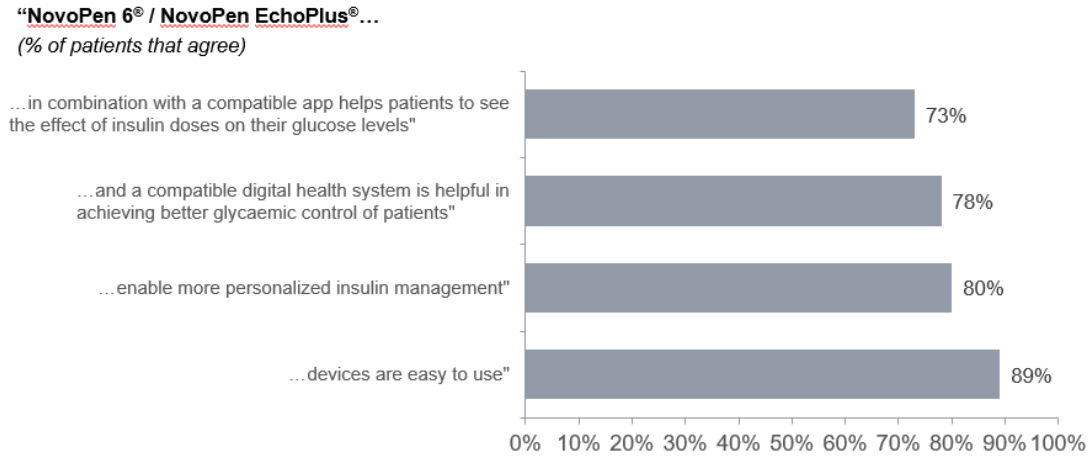
Aim: This study aimed to assess the real-world experience and attitudes of patients who used smart insulin pens.

Methods: Twenty-minute online quantitative interviews were conducted with patients, or the parents of a child, diagnosed with type 1 or 2 diabetes mellitus who had used a NovoPen® 6 or NovoPen EchoPlus®.

Results: Of 45 patients who used a smart pen to manage diabetes (type 1: 51%; type 2: 49%), the median time since diagnosis was 13 years, the median duration of smart pen use was 11 months, and 73% were male. Smart pen users (n=45) were highly satisfied with their pens (71%) and highly rated the “ease of injection” (87%), “ease of changing the tip” (78%), and “impact on glucose levels” (78%). Patients agreed (data in **Figure**) that smart insulin pens enabled more personalized insulin management and that a smart pen together with a compatible digital health system is helpful in achieving better glycemic control. Twenty-four percent of patients reported requesting a smart pen, and 53% reported that it was a joint decision with their health care provider. Online information about smart pens (31%), demonstrations (31%), and training on how to use compatible apps (29%) were the most commonly reported support needs for smart pen users.

Conclusions: Ease of use and improved glucose levels were the attributes that patients rated highly. Patients were frequently involved in the decision to use the device. Although some patients desired more training about smart pens, most were satisfied with their glycemic control when using a smart pen.

Figure. Proportion of patients who agreed with select survey questions.



People with established Diabetes-related Foot disease experience a high burden of Autonomic neuropathy

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Aims: While the role of autonomic neuropathy in the pathogenesis of diabetic foot ulcer (DFU) is well-recognised, there is limited information about the association of cardiovascular autonomic neuropathy (CAN) with the healing of foot ulcers and longer-term outcomes. Furthermore, no study has hitherto evaluated the myriad of manifestations of diabetic autonomic neuropathy (DAN) in people with diabetes-related foot disease (DFD). Our study aimed to comprehensively assess for DAN in people with established DFD.

Methods: This prospective cohort study recruited people presenting for management of DFU at two high-risk foot clinics (Royal Adelaide and The Queen Elizabeth Hospitals) in Adelaide, Australia. Assessment of DAN included standardised cardiovascular autonomic reflex tests (CARTs), validated questionnaires for autonomic neuropathy (COMPASS31), gastrointestinal symptoms (PAGISYM), prostate (IPSS) and sexual (IIEF for male and FSFI for female) function. Cut-off of ≥16 was considered abnormal for COMPASS31, as were scores ≥1, ≥20, <16 and <27.5, for gastrointestinal symptoms, abnormal prostatic function (IPSS), male erectile dysfunction and female sexual dysfunction respectively. Participants with ≥2 abnormal CARTs were considered to have definite CAN.

Results: We recruited 72 consecutive individuals with established DFU (mean age: 68.5±1.4yrs; male: 84.9%; BMI: 30.4±0.9 kg/m^2; duration of known diabetes: 21±2 years, HbA1c: 8.5±0.3%, Wound, Ischaemia, Foot Infection (WIFI) Score: 1.9±0.2). DFU types were as follows: 37 (51%) neuropathic, 32 (45%) neuroischaemic and 3 (4%) ischaemic. Thirty-three (46%) participants had definite CAN, 44 (62%) autonomic neuropathy, 13 (18%) had significant gastrointestinal symptoms and 7 (10%) had abnormal prostate function. Sixty-two (86%) males and 64 (89%) females reported sexual dysfunction.

Conclusions: There is very high burden of autonomic neuropathy in people with established DFU attending high-risk foot clinics which is under-recognised. Management of the manifestations of DAN should be considered alongside standard diabetes-related foot care.

Table 1: Prevalence of various manifestations of diabetic autonomic neuropathy in people with established foot disease

	DFU (n=72) % or (mean±SEM)
CAN+ (≥2 out of 5) (N=69)	46.4%
Autonomic neuropathy (COMPASS31 ≥16)	61.7%
Gastrointestinal symptoms (PAGISYM ≥1)	18.3%
Prostate symptoms (IPSS ≥20)	10.0%
Male erectile dysfunction (IEEF ≤16)	86.3%
Female sexual function (FSFI ≤27.5)	88.9%

DFU: Diabetic Foot Ulcer,

Performance of the CKD-EPI Equation in estimating Glomerular Filtration rate change over time in people with Diabetes

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Aims: To evaluate the performance of CKD-EPI glomerular filtration rate (GFR) estimation equations (2009 and the race free 2021) compared to direct measures of GFR over time in people with diabetes.

Methods: A total of 786 patients with type 1 and type 2 diabetes attending Austin Health who had two or more direct GFR measurements were studied. Measured GFR (mGFR) was calculated using the plasma disappearance rate of diethylene-triamine-penta-acetic acid. Estimated GFR was calculated using the 2009 and 2021 CKD-EPI equations. Absolute GFR slopes for mGFR, CKD-EPI 2009 and CKD-EPI 2021 were calculated for the overall population and stratified by clinically relevant mGFR categories using mixed-effects linear regression models.

Results: Patients had a median of 3 (IQR: 2-4) repeated mGFR measurements over a median follow-up of 5.1 (IQR: 2.5-8.5) years. The median baseline mGFR, CKD-EPI 2009 eGFR, and CKD-EPI 2021 eGFR were 68, 78, and 83 ml/min per 1.73m^2, respectively. Both CKD-EPI equations consistently underestimated the mGFR slope in the overall population (Table). When considering clinically relevant mGFR categories, both the 2009 and 2021 CKD-EPI equations tended to overestimate GFR slopes at lower mGFR values and underestimate at higher GFR values.

Conclusion: The CKD-EPI equation underestimates the rate of GFR decline over time in people with diabetes overall and overestimates at lower GFR values.

Table: Rate of GFR decline (ml/min/1.73m^2 per year) overall and by mGFR categories at baseline

mGFR categories at baseline (ml/min/1.73m^2)	mGFR	CKD-EPI 2009	CKD-EPI 2021
Overall	-1.67 (-1.80, -1.54)	-1.21 (-1.32, -1.10)	-1.21 (-1.34, -1.07)
0-29	-0.01 (-0.92, 0.90)	-1.23 (-2.01, -0.45)	-1.29 (-2.11, -0.47)
30-59	-1.29 (-1.49, -1.09)	-1.54 (-1.75, -1.33)	-1.60 (-1.82, -1.37)
60-89	-1.72 (-1.90, -1.54)	-1.34 (-1.51, -1.18)	-1.36 (-1.54, -1.17)
90-119	-1.98 (-2.30, -1.66)	-0.93 (-1.14, -0.73)	-1.06 (-1.37, -0.74)
≥120	-2.52 (-3.18, -1.87)	-0.35 (-0.70, 0.01)	0.25 (-0.59, 1.09)

Peri-operative and Endocrine Medicine Service (POEMS) - A pilot program for efficient and collaborative care of the surgical inpatient

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Aim: The Peri-operative and Endocrine Medicine Service (POEMS) was established in 2024 at Footscray Hospital, Western Health in Melbourne, Victoria. It has been designed as a quality assurance project. Our aim is to institute a peri-operative and endocrine medicine service at a large secondary hospital to improve peri-operative outcomes.

Methods: Surgical inpatients admitted under the urology and vascular surgery units undergoing an operative with a high-risk of physiological disturbance and an expected length of stay longer than 48 hours will undergo direct medical reviews to optimise existing medical co-morbidities in preparation for surgery, as well as assess for and prevent complications post-operatively.
The POEMS unit consists of a general medicine and endocrinology physician, a geriatrician and a general medicine and endocrinology advanced trainee working in collaboration with the surgical inpatient units to provide holistic patient care.
The primary composite outcome is rates of inpatient mortality and post-operative complications including hospital acquired infections, acute kidney injury, cardiac complications, stroke and transient ischaemic attacks. Key secondary outcomes include indicators of glycaemic control and total length of stay.

Results: Data collection is ongoing. As of the writing of this abstract the service has been involved in the care of 47 patients. Clinical characteristics of the study population include a mean age of 69, 60% male population, and 24% and 76% urology and vascular surgery unit distribution respectively.

Conclusions: The program is going well to date with outcomes analysis to be performed in 2025 following accumulation of one year of program data.

Pharmacy Approach to Early Detection of Diabetes through Opportunistic Screening in Rural Australia

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Background: The global rise in diabetes prevalence, with approximately 1.3 million people diagnosed in Australia in 2021, poses a significant public health challenge. Rural communities are disproportionately affected. This study aimed to identify undiagnosed diabetes and prediabetes and assess the uptake of diabetes screening by pharmacies.

Methods: Over a 5-month period, pharmacy representatives were trained in consent procedures, data recording on Qualtrics, and testing using HbA1c and Random Blood Glucose (RBG) machines. Participants with intermediate (AUSDRISK score of 6-11) or high (11 or greater) risk scores underwent further screening using HbA1c and/or RBG. Those with above-threshold readings (RBG ≥5.5 mmol/l and/or HbA1c ≥5.7%, 39 mmol/mol) were referred to their GPs for additional testing. Data on blood pressure (DBP, SBP), body mass index (BMI), and lifestyle factors were collected and analyzed using descriptive statistics.

Results: Nine of 17 pharmacies (52.9%) completed the project, enrolling 119 participants. Participants were mostly female (n=67, 56%), aged 57 years (SD 17.5), with a high BMI (30.4±6.9 kg/m2) and blood pressure readings of 139±18 mmHg (SBP) and 82±11 mmHg (DBP). AUSDRISK assessments of 116 participants revealed 85% had an intermediate or high risk of T2DM, with 44% having a positive family history of diabetes, 39% on hypertension medication, and 10% using tobacco. Of those screened with HbA1c (n=84) and RBG (n=49), 33% and 76% had above-threshold readings, respectively. Forty participants were referred to GPs, with nine (23%) undergoing oral glucose tolerance tests, of whom four (44%) were diagnosed with diabetes.

Conclusions: In this rural community of Western NSW, a significant proportion were at risk for developing T2DM, with the rate of undiagnosed diabetes twice as high as previous reports from rural NSW (44% vs. 23%). The study highlights the potential role of pharmacies in expanding diabetes screening efforts and underscores the need for targeted interventions to combat the growing burden of diabetes in rural settings

Porous Hydrogel Microcarriers with Human Islet Organoids for Diabetes modeling

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Background and aims: Islet transplantation has emerged as a long-term treatment option for Type 1 diabetes. However, its therapeutic utility is limited by the shortage of donors and the necessity for immunosuppressive drugs. An attractive alternative to traditional islet transplantation is the development of islet organoids derived from human stem cells. Encapsulating islet organoids with hydrogel microcarriers endows the cells with protective layer, shielding them from the host immune attack.

Materials and methods: Human induced pluripotent stem cells (hiPSCs) were cultured and enriched within porous microcarriers composed of a photoresponsive hydrogel. Using a chemical small molecule induction method, these hiPSCs were differentiated and matured into islet organoids (IOs). The viability of the cells within the microcarriers was assessed using CCK8 assays. The glucose responsiveness of the islet organoids was evaluated through glucose-responsive insulin secretion assays. Subsequently, the porous hydrogel microcarriers containing islet organoids (p-MCs@IOs) were subjected to treatment with anti-diabetic drugs under conditions of high glucose.

Results: The homogeneous porous microcarriers were fabricated using a microfluidic system. Then near-infrared radiation exposures enriched these microcarriers with hiPSCs. The hiPSCs-derived human islet organoids displayed the expression of insulin, glucagon, polypeptide, and somatostatin, indicating their multi-hormonal functionality. The engineered p-MCs@IOs exhibited enhanced cell viability and glucose responsiveness. When exposed to high glucose conditions, the p-MCs@IOs showed mitochondrial dysfunction. This dysfunction was mitigated when treated with a glucagon-like peptide-1 receptor agonist (GLP-1Ra), indicating the therapeutic benefit observed in such diabetic model based on p-MCs@IOs.

Conclusion: This study demonstrated that these fabricated microcarriers loaded with human islet organoids held the capacity of insulin secretion. This approach can recapitulate human islet under both physiological and pathological conditions, providing a unique platform for future T2DM research and drug development.

Post-menopausal Virilisation due to Ovarian Hyperthecosis with improved Glycaemic control Post-resection: case report

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Post-menopausal virilisation accompanied by insulin resistance is rare and presents a diagnostic challenge. Ovarian hyperthecosis is characterised by ovarian stromal cell proliferation, leading to androgen excess and insulin resistance due to impairment of insulin signalling pathways. Here, we present a case of a 58-year-old post-menopausal woman with new onset virilisation, type 2 diabetes and metabolic syndrome due to ovarian hyperthecosis, who was successfully treated with bilateral oophorectomy resulting in normalisation of hyperandrogenism and improvement in glycaemic control.

The patient presented with a one-year history of virilisation with coarse facial hair growth, male pattern baldness and hair thinning. She was not Cushingoid. Her background was significant for suboptimally controlled type 2 diabetes (HbA1c 9.2%), hypertension, hypercholestoleraemia and obesity (BMI 35.9 kg/m2). Androgen levels were markedly elevated: total testosterone 9.9 nmol/L (RR 0.2-1.1nmol/L), androstenedione 18.4 nmol/L (1-13nmol/L) and free testosterone 135pmol/L (1-22pmol/L). SHBG 57 nmol/L (16-120nmol/L) and DHEAS 4.6umol/L (1-7umol/L) were normal. Gonadotrophins were not suppressed: LH 16.3IU/L and FSH 21.7IU/L. Oestradiol (<88 pmol/L) and progesterone (<1.6nmol/L) were within post-menopausal levels. Her 24-hour urinary free cortisol and late-night salivary cortisol were not elevated, excluding Cushing syndrome. Abdominal CT and MRI imaging revealed a bulky uterus, normal adrenals and no pelvic lesion. Pelvic ultrasound revealed fibroids with endometrial thickening and her ovaries were unable to be visualised. She underwent laparoscopic hysterectomy and bilateral oophorectomy. Histopathology confirmed ovarian hyperthecosis. Post-operatively, androgen levels normalised and glycaemic control improved (Hba1c 6.8%) with metformin.

This case highlights the importance of considering ovarian pathology in the evaluation of post-menopausal virilisation and insulin resistance. Normalisation of androgen levels following resection likely contributed to the observed glycaemic improvements.

Post-prandial performance of Fiasp versus Insulin aspart in Automated Insulin Delivery Systems following Ingestion of various meal compositions

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Note: Preliminary data are included here but are subject to change. Data analysis to be completed prior to ADC conference.

Background: In people with type 1 diabetes (T1D), meals may be characterized by rapid increases in blood glucose even when using automated insulin delivery (AID) systems. The pharmacokinetics of subcutaneous insulin administration, with delayed onset and offset in action limit the ability of AID to respond to rapid changes in insulin requirements. Faster-acting insulin aspart (FiAsp) may improve postprandial glycemic outcomes.

Methods: Twelve adults with T1D (7 male; age, mean [SD] 48 [13] yrs; BMI, 29.1 [5.6] kg/m^2; duration T1D 28.3 [16.1] yrs; total daily insulin dose, 0.54 [0.15] U/kg/day) using the Medtronic 780g underwent two 11wk study phases. Study participants used insulin aspart (Asp) or FiAsp during each stage. Sixteen standardized meals were eaten during each phase, separated by at least 48hrs. Meal challenges all contained 60g carbohydrate with the following characteristics:

(a) High GI
(b) High fat
(c) High protein/ high fat
(d) Mixed meal

Each meal type was eaten four times: twice each for breakfast and dinner with either a full or 50% reduction in insulin bolus. The primary outcome of interest was time in range (TIR; 3.9-10.0mmol/L) using a continuous glucose monitor (Medtronic™ Guardian Sensor 3) for ~4h post meal ingestion.

Results: FiAsp compared to Asp did not differ regarding TIR for any meal composition, bolusing strategy or meal time. However, for high-GI meals at breakfast, with reduced boluses, FiAsp improved time in tighter range (3.9-7.8mmol/L; median difference 25.60 (-8.33, 45.95), p=0.014).

Conclusions: Across a spectrum of meal conditions, FiAsp compared to Asp at best only moderately improves glycemic outcomes. Further exploration of meal timing, composition and bolus strategies is necessary.

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Predicting Chronic Complications in 1100 adults with Type 1 diabetes: High Risk Rates and Concordance between Type 1 Diabetes-specific risk calculators.

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Background and aims: People with Type 1 diabetes (T1D) are at risk of chronic complications. T1D-specific calculators are more accurate than those developed for people with T2D. We aimed to determine (i) rates of high risk; (ii) concordance between risk of cardiovascular disease (CVD), end-stage kidney disease (ESKD) and sight threatening diabetic retinopathy (STDR) and (iii) major modulating factors.

Methods: An ethics-approval audit of data from adults with T1D attending the Baker Heart and Diabetes Institute Diabetes Clinics (Melbourne) in the last decade was conducted. Risk calculators used were: (i) Steno T1 (CVD) Risk Engine (5- and 10-yr), (ii) MSD Cardiovascular Risk Assessment in T1D (5-yr), (iii) QRisk3 for CVD (10-yr), (iv) Steno ESKD (5-yr) and (v) RetinaRisk STDR (5-yr). Concordance (Spearman correlation coefficient) and difference between groups (Kruskal-Wallis or Mann-Whitney test) were assessed.

Results: After excluding patients with missing data or prior CVD, outputs were available for n=1100/1480 (74%); mean±SD age 50±16.2yrs, 24.3±13.5 yrs T1D, HbA1c 7.7±1.35%. 'High' CVD risk differed by calculator: 41.7% Steno-10 yr; 16.2% MSD; 66.5% QRisk3. For STDR 2.4% were high. Concordance was strong between CVD risk calculators (r=0.86-0.93, p<0.0001); modest between CVD and microvascular complications (r=0.25-0.65, p<0.0001), and between ESKD and STDR risk (r=0.37, p<0.0001; Figure 1).
Risk increased with age (<40, 40-60, >60 yr) for CVD (p<0.0001) and STDR (p<0.001), but not for ESKD. CVD (except MSD) and ESKD risks were higher in males vs. females (p<0.01-0.001). Insulin pump vs. injection use associated with lower CVD (p<0.0001) and ESKD (p<0.05) risk. CGM-use lowers CVD risk (p<0.01-0.001; except MSD).

Conclusions: There is good concordance between risk calculators for CVD and microvascular complications. Risks increase with age (CVD and STDR) and being male (CVD and ESKD), and are lower with pump- (CVD and ESKD) and CGM-use (CVD risk).

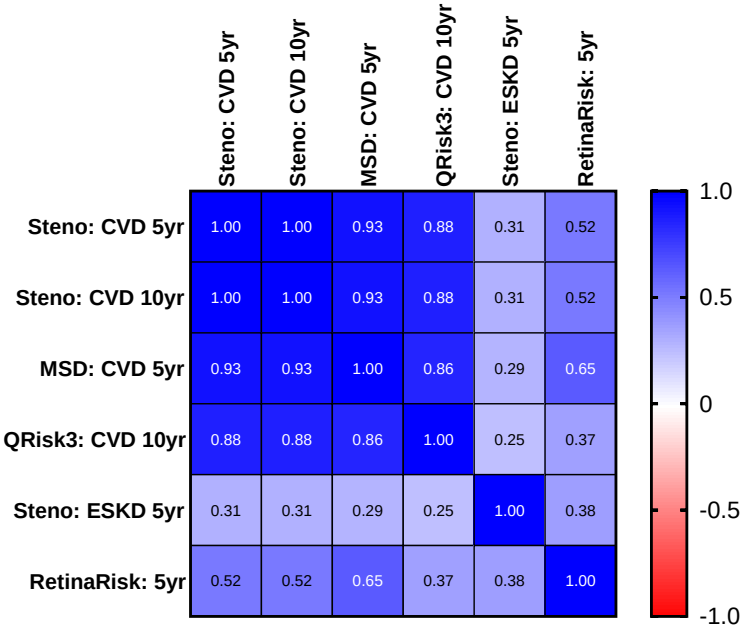

Figure. Correlation matrix of risk calculators (Spearman correlation coefficient).

Preliminary Implementation outcomes of a Virtual multidisciplinary foot hub model of care across Central Queensland

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Introduction: Diabetes-related foot disease (DFD) contributes significantly to hospitalisation, amputation, disability and healthcare expenditure. DFD costs Queensland Health approximately $21M annually. The Community Foot Care Hub is an innovative model of care (MOC) aimed at improving clinical outcomes for DFD by closing geographic gaps that exist in Queensland through healthcare partnerships. The central foot hub multidisciplinary team (MDT) at the Royal Brisbane and Women's Hospital commenced in February 2024. The aim of this study was to evaluate preliminary MOC implementation at three spoke sites prior to broader roll-out across central Queensland.

Methods: This was a quality improvement project. A mixed-methods approach combining both qualitative and quantitative methods were used to deliver on 14-week (13/2/2024 – 14/5/2024) PIPE Impact Metric (Penetration, Implementation, Participation and Effectiveness) of the MOC from an endocrinology viewpoint. Data was sourced from administrative databases and electronic health records. Outcomes included:

- **P**enetration: Percentage of patients with confirmed diabetes and suboptimal glycaemic control (HbA1c ≥7%) referred
- **I**mplementation: Percentage with confirmed diabetes and suboptimal glycaemia consenting to diabetes support
- **P**articipation: Barriers to diabetes telehealth consultation
- **E**ffectiveness: change in HbA1c pre/post endocrinology support over a 3-month period

Results: A total of 50 adults with DFD were referred to the virtual MDT of whom 84% had confirmed diabetes and majority (83%, n=35) demonstrated sub-optimal diabetes control *(Penetration)*. 70% consented to telehealth endocrinology consultations *(Implementation)*. Key barriers to *participation* included patient preference to initially engage with local diabetes educator, housing/location instability and inability of workforce at spoke site to facilitate appointments. The majority of telehealth appointments were co-consultations with the hub endocrinologist and local diabetes educators. Median HbA1c for those referred was 8.2% (IQR 7.1-9.9%) and 3-month change in HbA1c is still being analysed *(Effectiveness).*

Conclusion: The central foot hub virtual MDT showed high-level engagement in the preliminary roll-out across central Queensland.

Preliminary Study on the Fragility of Liver Glycogen Alpha Particles in Type 2 Diabetes

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Aim: Liver glycogen is composed of highly branched polymers, including smaller beta particles and much larger alpha particles, which are aggregates of beta particles. This study aims to investigate the structural differences in liver glycogen alpha particles in mice and humans with type 2 diabetes, focusing on their fragility when treated with hydrogen bond disruptors.

Method: We employed Size-Exclusion Chromatography (SEC) and Fluorophore-Assisted Carbohydrate Electrophoresis (FACE) to analyze the molecular size distributions and chain length distributions of glycogen. Additionally, we utilized proteomics to identify overlapping proteins between human and mouse liver samples, aiming to uncover key proteins that may influence the structural differences between fragile and stable alpha particles.

Results: Our results demonstrated that liver glycogen alpha particles from diabetic mice and humans exhibit fragility upon treatment with hydrogen bond disruptors. Morphological analysis revealed significantly smaller particles in the DMSO-treated samples compared to the control groups. Proteomic analysis identified some proteins (i.e. ppp1r3g) as a potentially significant proteins associated with the stability of glycogen structure, consistently found in both human and mouse liver samples.

Conclusion: The fragility of liver glycogen alpha particles appears to be a widespread phenomenon in diabetic mammals. The identification of proteins potentially involved in glycogen stability suggests a new avenue for understanding and potentially mitigating the structural vulnerabilities of glycogen in diabetes.

Preparing Primary Care for Precision Diabetes: A systematic review

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Background: As of 31 December 2023, there were 1,270,865 people with type 2 diabetes (T2D) registered with the National Diabetes Services Scheme, and this number is expected to increase. A growing body of evidence supports the idea that there is variability in T2D presentation and progression, as well as individual responses to therapy. This suggests that a one-size-fits-all approach to diabetes management is inappropriate and will have an adverse impact on provision of health services, expenditure and health outcomes as the population with diabetes increases. Precision diabetes evolves the one-size-fits-all approach into one in which data personalises and enhances clinical decisions.

Aim: The aim of this systematic review was to identify, appraise and synthesise the international evidence base for precision diabetes.

Methods: The systematic review protocol was pre-registered on PROSPERO. Multiple databases were searched using a prespecified strategy. Two review authors independently screened titles, abstracts and full texts, and a third reviewer resolved conflicts, using Covidence software. Two reviewers undertook risk of bias assessment using checklists appropriate to study design. The primary outcome was glycaemia as measured by glycated haemoglobin (HbA1c). Secondary outcomes were response to glucose-lowering therapies and onset of cardio-renal complications. A narrative synthesis and meta-analysis were conducted. Results (in progress) will be presented using the Preferred Reporting Items of Systematic Reviews and Meta-Analysis checklist.

Results and Conclusion: The systematic review will underpin future research to explore how precision medicine can enhance the prevention and management of T2D. Findings will include insights for clinical and research practice and policy, considering the varying availability, quality and utility of data across clinical and research settings; and the careful interpretation of data to avoid digital overdiagnosis, and to support inclusivity and equity.

Prevalence of Autoimmune Diabetes among Aboriginal Australians: The Fremantle Diabetes Study Phase II

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Aims: There are few and inconsistent data relating to the frequency of autoimmune diabetes in Australian Indigenous communities. Our aim was to determine the relative prevalence of type 1 diabetes and latent autoimmune diabetes of adults (LADA) in Aboriginal participants in the community-based Fremantle Diabetes Study Phase II (FDS2).

Methods: Baseline sera were assayed for glutamic acid decarboxylase (GAD) and tyrosine phosphatase-related islet antigen 2 (IA2) autoantibodies by radioimmunoassay and enzyme-linked immunosorbent assay (ELISA), respectively. A second-generation ELISA was used subsequently to confirm all first-generation GAD antibody positive and a random sample of antibody negative results.

Results: There were 113 Indigenous FDS2 participants (mean age 53.7 years, 36.3% males) of whom 4 (3.5%) had been diagnosed clinically with type 1 diabetes (on insulin from diagnosis), 108 (95.6%) with type 2 diabetes and 1 (0.9%) with type 3C diabetes. Using the first-generation GAD antibody assay and baseline sera from 103 Indigenous participants with clinically-diagnosed type 2 diabetes, 7 were GAD antibody positive and thus were considered to have LADA, but this reduced to 1 (1.0%) using the second-generation assay. Six (5.8%) were positive for IA2 but negative for GAD antibodies; if these had LADA, the prevalence increased to 6.8%. Of 1,553 non-Indigenous FDS2 participants, 127 (8.2%) had type 1 diabetes (*P*=0.136 vs Indigenous sample) and 80 (5.2%) had LADA based on the second-generation GAD antibody assay (*P*=0.039 vs Indigenous sample, excluding type 1/3C diabetes and monogenic diabetes).

Conclusions: These data suggest that rates of autoimmune diabetes are relatively low among Indigenous Australians with diabetes. A greater prevalence of isolated IA2 versus GAD antibody positivity has been described in people from other non-White Caucasian racial groups who have adult-onset diabetes, and this may have implications for screening and management of Indigenous Australians.

Prevalence of Food and Nutrition Insecurity in Gestational Diabetes: QR Survey results from a tertiary centre

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Background: Dietary management remains the cornerstone of Gestational Diabetes Mellitus (GDM) management. In GDM, the presence of food and nutritional insecurity, affecting food availability and quality, may result in the consumption of energy-dense, nutrient-poor foods contributing to excessive weight- gain, poor glucose control and nutritional deficiencies. Food and nutritional insecurity may critically affect GDM management, yet the true prevalence in Australian populations is unclear.

Aim: We audited the prevalence of food and nutritional insecurity in an Australian GDM cohort and examined the feasibility of administering validated screening inventories by QR code at the point-of-care, capitalising on their widespread adoption in the post-pandemic era.

Methods: Women with GDM attending the RPAH Antenatal Diabetes in Pregnancy service were invited to self-administer i) The US Adult Food Security Survey Module and, ii) Two Question Nutrition Insecurity Screener, by scanning a QR-code linked to a REDcap database.

Results: To-date 49 women have completed screening. Food insecurity was present. While 4.3% (n=2) 'often' worried about food running out, an additional 8.5% (n=4) reported it 'sometimes'. Similarly, 4.3% (n=2) 'often' cut meal sizes/skipped meals due to financial limitations, with an additional 8.5% (n=4) experiencing this 'sometimes'. Nutritional challenges were also evident. Over 18% (n=9) found it 'somewhat difficult', and 4.1% (n=2) found it 'very difficult' to obtain and consume healthy foods regularly. The most common barriers to healthy eating included cost (44.9%, n=22), lack of time for shopping (18.4%, n=9) or cooking (28.6%, n=14), traditional foods lacking nutritional value (20.4%, n=10), and limited transportation access to healthy foods (6.1%, n=3).

Conclusion: These preliminary data highlight that the presence of food and nutritional insecurity may be prevalent in Australian GDM cohorts and support the feasibility of point-of care screening via QR code. This methodology would facilitate a future broader study of food and nutritional insecurity nationally.

Prevalence of Type 2 Diabetes Mellitus and Micro-vascular Complications in Sri Lanka: A Systematic Review and Meta-Analysis

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Aim: The prevalence of type II diabetes and its complications is increasing around the globe, especially in low- and middle-income countries. Current estimates of these complications are necessary for resource allocation. According to the International Diabetes Federation, in 2021, about 1.4 million people were estimated to have diabetes in Sri Lanka, and this figure is projected to increase to 1.7 million by 2045. The aim of this study was to conduct a systematic review and meta-analysis to estimate the prevalence of type II diabetes and its complications in Sri Lanka.

Methods: A comprehensive literature search was conducted using PubMed database. Studies that had reported type II diabetes or its related complications among the Sri Lanka adults (>18 years) were included. Prevalence of type II diabetes, diabetic retinopathy and neuropathy were presented using a forest plot. Due to limited number of publications, we only conducted a narrative synthesis on nephropathy.

Results: In this study we included 24 (1.6%) articles from 57 (3·8%) eligible articles of 1491 assessed. 41340 people with Type II diabetes (mean sample size n=2584 [SD 2288], with mean age of 48.6 years [SD 4.94]) were included. The forest plot highlighted an increasing trend in diabetic retinopathy in Sri Lanka.

Conclusions: This study shows that the prevalence of type II diabetes in Sri Lanka and its complications have increased over the years, highlighting the need to strengthen screening for early identification and prompt treatment of all complications.

Proactive Optimisation of Glycaemia following Cardiothoracic Surgery using a Pharmacist-led management guideline

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Background: In people undergoing cardiothoracic surgery, optimising perioperative and postoperative blood glucose (BG) is critical to decrease the risk of sternal and surgical site infections. Although glycaemic control in the immediate perioperative period is usually standardised, there is variability in treatment practice and glycaemic control once patients are transferred from the intensive care unit (ICU) to the general ward.

Aim: To determine if a pharmacist-led glycaemia management guideline for inpatients with diabetes or stress-hyperglycaemia following coronary artery bypass graft (CABG) or valve surgery improves inpatient glycaemia.

Method: A ward-based glycaemia management algorithm was developed by endocrinologists and pharmacists for use in patients following CABG or valve surgery. A sample of 100 consecutive patients who underwent these procedures, before and after implementation of the algorithm were identified. We included individuals with type 2 diabetes (T2D) and/or stress-hyperglycaemia but excluded individuals with type-1 diabetes and those managed at another institution's ICU. We analysed capillary BG data from the day of ICU transfer to ward until day of hospital discharge. Patient-day mean glucose (PDMG) and patient-days with hyperglycaemia and hypoglycaemia were analysed.

Results: We included 60 and 88 individuals in the pre- and post-implementation groups respectively. The post-implementation group had lower median weight (76 vs. 88 kg, p=0.01), and a higher proportion of individuals with stress-hyperglycaemia (62% vs. 42%, p=0.013). The post-implementation group had a lower mean PDMG (8.4 vs. 8.8 mmol/L, p=0.006), patient-days with BG>15 mmol/L (6.3% vs. 13.6%, p=0.05) and patient-days with BG >10 mmol/L (45% vs. 53%, p=0.03).

Conclusion: In patients with T2D or stress-hyperglycaemia following cardiothoracic surgery, there was lower mean glucose and lower rates of hyperglycaemia following implementation of a pharmacist-led glycaemia management guideline. This suggests there is a positive role of a proactive multidisciplinary approach in improving guideline-directed hospital care for people with diabetes.

Proactive Review of Hospitalised Patients with High HbA1c by an Inpatient Diabetes Team Leads to Increased Medication Changes

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Background: There is a high burden of hospitalized patients with diabetes in Australia [1]. Patients with high HbA1c are at risk of multiple adverse outcomes [2,3]. We developed the Diabetes Discovery Initiative (DDI), an early identification and intervention model to identify patients that benefitted rapid diabetes review.

Aim: To determine if diabetes therapy changed in those who were reviewed compared to those who were not in 2023 as part of the DDI.

Methods: The DDI utilized the electronic medical record CERNER™ at The Austin Hospital, Melbourne, and generated an automatic HbA1c measurement for patients aged >54 years who did not have a preceding HbA1c reading within 3 months of admission. Patients with elevated HbA1c results ≥8.3% were automatically referred to the DDI team for diabetes management. Patients that were proactively reviewed by the DDI team were compared to those that were not reviewed. Analysis of parameters include change of diabetes medication and more specifically, the medications that were adjusted.

Results: In 2023, there were 271 hospitalised patients identified by the DDI to have an HbA1c ≥8.3%. 197/271 (72.7%) were reviewed by the inpatient diabetes team. Almost all patients had type 2 diabetes (99.2%) and the average HbA1c was 9.6%±1.4. Patients reviewed by the DDI team compared to those that were not reviewed were more likely to have their diabetes medications adjusted (65.5 ± 5.7% vs 50.0 ± 6.0%, p=0.02). The inpatient diabetes team review resulted in higher rates of metformin adjustments (34.0 ± 5.6% vs 20.3 ± 4.8%, p=0.03) and DPP4 inhibitor adjustments (27.9 ± 5.3% vs 14.9 ± 4.2%, p=0.03).

Conclusion: Opportunistically reviewing hospitalised patients with suboptimal diabetes control by an inpatient diabetes team leads to more adjustments to their medications compared to those that were not reviewed. This is likely to result in improved glycaemic control in hospital and in the community [4].

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Progression to postpartum type 2 diabetes after gestational diabetes in Far North Queensland

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Aim: Gestational diabetes (GDM) is a strong risk factor of type 2 diabetes however, frequency of postpartum screening was shown to be low in the previous studies. This study was to determine (i) postpartum diabetes screening rates; and (ii) the incidence of dysglycaemia (diabetes or prediabetes), in women with recent GDM in Far North Queensland (FNQ).

Method: A retrospective cohort study of all pregnant women on the FNQ Diabetes in Pregnancy Clinical Register with GDM who gave birth 2017-2019. Women with pre-existing (type 1 or type 2) diabetes or who declined register enrolment were excluded. Results for haemoglobin A1c (HbA1c) and 75g oral glucose tolerance test (OGTT) within 12 months postpartum were collected. Australian Diabetes Society criteria were used for prediabetes and diabetes. We determined rates of screening, and incidence of prediabetes and diabetes among those who had been screened. Characteristics of those with and without a positive test were compared using $\chi 2$ test and logistic regression analysis was used to determine odds ratios.

Results: Of 1317 women with GDM, 584 (44%) had either OGTT (197 women) or HbA1c (396 women) within 12 months postpartum. The diagnostic threshold for diabetes was met in 9 women (1.5%), 7 by HbA1c and 2 by OGTT. Prediabetes diagnostic thresholds were met in 38 women (6.5%), 14 by HbA1c (6.0% to 6.5%) and 24 by OGTT (fasting glucose 6.0-6.9mmol/L or 2 hour glucose 7.8-11.0 mmol/L). Overall 47 (8.0%) women who were tested had dysglycaemia in the first 12 months post-partum. The rate of dysglycaemia was 14% in Aboriginal and Torres Strait Islander women (OR 3.8, p<0.01), 9% for women with 'Other' ethnicities (OR 2.5, p=0.03), compared to 4% in Caucasian women.

Conclusion: Rates of postpartum screening need to be improved, particularly for women at high risk of developing prediabetes and type 2 diabetes.

Psychosocial complexity and limited preparation for Transition to Adult services for Young people living with Type-1 Diabetes results in care fragmentation: a multi-method study

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Introduction: Type 1 diabetes (T1D) is a chronic, incurable autoimmune condition, typically diagnosed in childhood and managed in paediatric services until ages 16–18 years, when young people (YP) transition to adult services. YP may encounter barriers to accessing adult healthcare services, including a lack of age-appropriate health information and limited referral pathways. International guidelines suggest that YP and their clinical teams need to prepare and plan for transition while supporting YP to maintain glycaemic control during this vulnerable life stage.

Aim: We conducted a multi-methods study to understand the level of care continuity at transition to adult services for Australian YP living with T1D.

Methods: Interviews and surveys were conducted with YP living with T1D along with a survey of service leaders across Australia in 2023. The surveys were made available online and participants were recruited via diabetes related organisations and networks.

Results: YP aged 14 – 25 years (n=226) from across Australia completed the survey. Approximately half (111, 49%) had transitioned to adult services and of these, only 21(23%) felt that they had been well prepared for transition, 9(8%) said transition had never been mentioned, and only 22(24%) had a written transition plan. YP reported significant psychosocial complexity in addition to their T1D. Many had been referred to psychological services for depression (45%) and anxiety (37%). The survey of 32 service leaders confirmed a lack of comprehensive preparation for transition: only 8(25%) services provided structured transition preparation programs, and only 3(9%) followed up on the YP and their retention in the adult service.

Conclusions: Preparation and planning for YP transitioning to adult services are sub-optimal and inconsistent in Australia, putting young people at risk of hypoglycaemia and disengagement with health services. Improving care continuity and enhancing psychosocial support requires further research to inform new interdisciplinary models of care.

Real-world performance Characteristics of Glucose Meters compared with Blood Gas and Laboratory Glucose methods in a Quaternary Australian Hospital Inpatient Population and the MIMIC-IV dataset

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Aim: This study aims to correlate and characterise the performance of glucose meters against laboratory and blood gas glucose results in the inpatient setting in an Australian and US hospital.

Methods: We obtained all glucose results from 2021-2022 for patients at a quaternary Australian hospital and all data from the publicly available MIMIC-IV dataset. Glucose meter (Australia: StatStrip®, MIMIC-IV: various), blood gas and laboratory glucose measures were matched to coincident measures of an alternative collection type occurring within 15 minutes, obtaining between 566 and 31233 pairs dependant on collection types. Glucose pairs of each type were analysed to assess accuracy and precision by robust linear modelling, and calculation of bias and mean absolute relative difference (MARD), both overall and within glucose brackets.

Results: In the Australian dataset, when compared with laboratory glucose, the MARD of blood gas glucose was within the 8% performance specification of the blood gas device. For the same comparison in the MIMIC-IV dataset, MARD was within 8% only between 50-400 mg/dL. For all further analysis, only blood gas and glucose meter glucose was compared. In both datasets, glucose meters showed increased variability at extreme glucose values, with a positive bias at low values and a negative bias at high glucose values. Despite this variation, >98% of glucose pairs fell within categories A or B (no or slight clinical risk) on the Parkes and surveillance error grids in both datasets. Performance did not vary significantly with pO2 in either dataset. However, haemoglobin <80 g/L was associated with increased negative bias for the blood gas-glucose meter comparison in both datasets.

Conclusion: This study demonstrates excellent correlation between glucose meters and blood gas glucose in real-world hospital inpatient settings and provides guidance for scenarios where results should be interpreted with caution. This study provides a framework for other centres to interrogate glucose meter performance.

Recurrence Rates of Diabetes-related Foot Ulcers in Patients attending an Australian interdisciplinary High Risk Foot Clinic.

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Background: Diabetes-related foot ulcers (DFUs) are a common and burdensome diabetes complication. Factors contributing to the development of DFU such as microvascular disease and foot deformity persist after healing leading to high DFU recurrence rates. 40% of patients are reported to have a recurrence of DFU within 1 year and 60% within 3 years, however information regarding contemporary Australian DFU recurrence rates is lacking.

Aims: To determine the rate of DFU recurrence in patients attending an Australian interdisciplinary High Risk Foot (iHRF) Clinic.

Methods: We conducted a retrospective observational study of 337 patients who first attended Fiona Stanley Hospital Multidisciplinary Diabetes Foot Ulcer clinic between 1/4/2015 to 13/12/2017.

Results: The mean patient age (±SD) was 61.4 (±13.7) years. 73% were male, median HbA1c [IQR] was 8.3% [7.1-9.9%]. 77.2% (260) had one or more DFUs at presentation, with index DFU located on the forefoot in 69.2% (180) midfoot in 13.5% (35) and hindfoot in 17.3% (45). 51.5% (134) healed, 8.5% (22) did not heal, 17.7% (46) resulted in a minor or major amputation, 22.3% (58) were lost/discharged. Of the 134 patients that healed, 14.2% (19) remained in remission and 64.9% (87) relapsed. 44.0% (59) relapsed within 1 year of healing and 58.2% (78) within 3 years. 26.4% (23) relapsed in the same foot location, 67.8% (59) recurred in a different foot location, 5.7% (5) relapsed in both the same and a different location. 20.1% (28) were discharged/lost from the service with 39.3% (11) deceased within 3 years since index ulceration.

Conclusions: DFU recurrence rates in patients attending an Australian iHRF clinic are consistent with international reports. DFU is a persistent recurrent complication which requires investment in services not only to support patients to achieve DFU healing but also to remain healed in the longer term.

REducing Cardiometabolic risk with SEmaglutide in Type 1 Diabetes (RESET1): Study Protocol of a Double-blinded randomised Placebo-controlled trial

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Background: New approaches are needed to improve cardiovascular risk in type 1 diabetes. Semaglutide, a glucagon-like peptide-1 receptor agonist, has been shown to reduce cardiovascular events in type 2 diabetes and obesity, and may also offer cardiometabolic protection in type 1 diabetes. The REducing cardiometabolic risk with SEmaglutide in Type 1 diabetes (RESET1) study is a double-blind randomized, placebo-controlled trial of semaglutide in T1D.

Methods: We will study 60 adults aged 25-70 years with type 1 diabetes (duration >2 years), body mass index ≥25 kg/m^2, HbA1c ≥ 7% and at least one cardiovascular risk factor (microalbuminuria, hypertension or anti-hypertensive treatment, hyperlipidemia or lipid lowering therapy, current smoking). Subjects will be randomized to semaglutide, titrated to 1.0mg weekly or matched placebo for 26 weeks (supplied by Novo Nordisk). The primary endpoint is arterial stiffness measured using carotid femoral pulse wave velocity, a surrogate marker for cardiovascular risk validated in a type 1 diabetes population. Potential mechanisms of response will also be explored including change in insulin sensitivity determined by hyperinsulinaemic-euglycaemic clamp, and incretin and pancreatic hormone action measured during mixed meal tolerance test. The trial is registered (Australian New Zealand Clinical Trial Registry, ACTRN12623001277639) and will be conducted in Sydney, Australia.

Conclusion: The RESET1 study will establish the effect of semaglutide on measures of cardiometabolic health in adults with type 1 diabetes.

Reducing the use of Disposable Insulin Pens: Results of an 8-week diabetes department campaign

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Aim: The use of disposable insulin pens creates more plastic waste than permanent pens. We evaluated the results of an 8-week campaign offering patients a choice to change to permanent pens.

Methods: After creating advertising posters and acquiring permanent insulin pens and instruction leaflets from insulin companies, Endocrinologists and DEs in our department evaluated the types of insulin formulations used during routine clinics. Patients using disposable insulin pens were offered the option to change to insulin penfills, together with a free permanent pen and relevant prescription. We evaluated the proportion of patients eligible, offered, and agreeing to the change, respectively. We did not change their insulin brands.

Results: Ninety patients were identified to be on insulin with 64% having type 1 diabetes. The three most frequent insulins used were Novorapid Flexpens (51%), Optisulin Solostar (46%) and Toujeo Solostar (19%). Seventeen patients had no option to change to penfills, either already using penfills or using Toujeo Solostar. Of the remaining 73 patients, 21 (29%) were not offered the choice to change to insulin penfills, 37 (51%) agreed to change, and 15 (21%) declined making a change. The most common reason for not offering a change was the clinician being too busy (38% of reasons). The most common reason for patient declining to change was ongoing preference of disposable pens (27%) and patient not coping with changes (27%). The total dose of insulins changed to penfills was 1725 units per day. This equates to a reduction of 2099 disposable insulin pens used per year from an 8-week campaign.

Conclusions: This campaign highlights the challenges and rewards of attempting to change patients over to permanent insulin pens. Busy clinics, familiarity to disposable pens and lack of a penfill option for Toujeo were barriers to more patients converting to a more environmentally friendly insulin formulation.

Regulation of Anti-Inflammatory CD163+ Macrophages in Sex Specific Models of Non-Alcoholic Steatohepatitis in Type 2 Diabetes

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Non-alcoholic steatohepatitis (NASH), a chronic inflammatory form of fatty liver disease, is strongly linked with type 2 diabetes (T2DM). Macrophages play a significant role in both inflammatory and fibrotic changes in NASH. We reported that sCD163, a cleavage form of the anti-inflammatory monocyte/macrophage-specific cell surface marker CD163, is systematically increased in people with advanced NASH fibrosis and T2DM. However, changes to CD163+ macrophages in liver tissue in NASH and diabetes have not been described.

Aim: To study liver CD163 and associated cleavage enzymes in our established Fat and Diabetes (FaD) mouse model and to identify sex differences in NASH.

Methods: Our lab-developed FaD mouse model of NASH fibrosis in T2DM was utilized in this study. C57BL/6 mice were either fed a high fat diet and received low-dose streptozotocin injections (65mg/kgbw)(FaD, n=8/sex) or fed normal chow (controls, n=6/sex), before euthanasia at 18 weeks. Liver fibrosis was assessed histologically by PSR staining. The mRNA levels of fibrosis markers (collagens-1 and -3), CD163, and genes involved in its cleavage (MMPs/TIMPs, TACE, and elastase), were measured by qRT-PCR.

Results: In male mice, FaD exhibited higher blood glucose levels (BGL)($p<0.0001$) and greater liver fibrosis than controls (PSR staining, collagens-1 and -3, $p<0.05$, $p<0.01$ and $p<0.05$, respectively); in female mice, BGL increased slightly, and fibrosis was attenuated or absent in FaD. In male FaD, the CD163 mRNA level remained unchanged, although the expression of enzymes responsible for CD163 cleavage was upregulated, when compared to controls ($p<0.05$). These changes were not observed in female mice.

This study indicates that liver fibrosis reliably developed in male mice, but not female mice. Furthermore, the upregulated liver CD163 cleavage enzymes in NASH suggests they may reduce surface expression of CD163 in liver. Further research will investigate regulation of CD163 surface expression and its potential impact on NASH fibrosis.

Relationship between Age, Sex and Glycaemia in older individuals: STAtins in Reducing Events in the Elderly (STAREE) trial

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Aim: Ageing is associated with increasing blood glucose through unclear mechanisms that may include age-related changes in diet, physical activity, body composition and insulin secretion and sensitivity. Such changes may explain why older age is a major risk factor for diabetes development. This study examines factors affecting glycaemia in community dwelling older adults (aged ≥ 70 years) without diabetes.

Method: Baseline data from participants randomised into the STAtins in Reducing Events in the Elderly (STAREE) trial was analysed. The associations between age and body habitus (body mass index [BMI], waist-to-hip ratio) with HbA1c and fasting blood glucose were estimated using linear regression stratified by sex. Linear regression models were extended to include living arrangements (living alone, with spouse, with family, other).

Results: A total of 9971 participants, 51.9% female, median±IQR age 73±6 years, median±IQR BMI 27±6kg/m^2 were included. 24.1% and 3.6% of participants met criteria for pre-diabetes according to American Diabetes Association and Australian Diabetes Society HbA1c criteria, respectively. Older age was correlated with increased HbA1c (female: R^2=0.004, p<0.001; male: R^2=0.007, p<0.001) but not fasting plasma glucose. BMI was associated with both HbA1c (female: R^2=0.024, p<0.001; male: R^2=0.011, p<0.001) and fasting plasma glucose (female: R^2=0.061, p<0.001; male: R^2=0.044, p<0.001). Similarly, waist-to-hip ratio was associated with both HbA1c (female: R^2=0.012, p<0.001; male: R^2=0.008, p<0.001) and fasting plasma glucose (female: R^2=0.023, p<0.001; male: R^2=0.026, p<0.001). There was no statistically significant difference in mean HbA1c or fasting blood glucose levels between participants with different living arrangements.

Conclusion: Ageing is associated with an increase in HbA1c among community dwelling older adults without diabetes in Australia. Glycaemia is significantly correlated with body habitus in this cohort. The targeting of modifiable risk factors for diabetes should form a key component in the healthcare of older adults, particularly those with pre-diabetes.

Relationship between Psychological Stress, Diabetes Distress and Glycaemia among Young Adults with Diabetes

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Background and Aim: Transitioning from adolescent to adult life can be challenging for young adults with diabetes, potentially adversely affecting their mental health (MH) and diabetes self-management. The APHLID-M (Apps and Peer support for a Healthy future and Living Well with Diabetes – MH) trial is testing whether a new digital platform ("app") can improve MH among young adults with diabetes. This analysis compared the association between glycaemia and either diabetes distress or psychological stress.

Method: Consecutive young adults aged 16-30 years, with diabetes were recruited into APHLID-M from eight hospital services, completing questionnaires including Kessler Psychological Distress Scale (K10) and Problem Areas in Diabetes Scale (PAID) and providing blood for HbA1c. Participants were classified as having MH if K10≥20 (HiK10) and/or PAID≥40 (HiPAID). Receiver Operator curves (ROCs with 95% confidence interval) were used to assess prediction of an HbA1c≥10.0%, HiK10 or HiPAID.

Results: Of 233 recruited, 126 (54.1%) identified as male, 144 (61.8%) of European descent, 217 (93.1%) had T1DM; age: 22±4 years; body mass index 27.4±6.0 kg/m^2; HbA1c 8.5±2.2%, Mean K10 22±8 (51.9% HiK10); mean PAID 22±17 (26.2% HiPAID). HiK10 and HiPAID were concordant in 69.1%; 28.3% had HiK10 but not HiPAID and 2.6% had HiPAID but not HiK10. The HbA1c was 8.7±2.1% vs 8.2±2.2% in those with a HiK10 (vs not: p=0.108) and 9.1±2.5 vs 8.2±2.0% in those with a HiPAID (vs not p=0.006). Neither K10 (ROC=0.50) nor PAID (ROC=0.55) predicted HbA1c≥10.0%. HbA1c predicted HiK10 (ROC 0.59(95%CI 0.52-0.67)) and HiPAID 0.61(95%CI 0.53-0.69) overall, among males (HiK10: 0.60(95%CI 0.50-0.70), HiPAID: 0.66(95%CI 0.54-0.77) but not among females.

Conclusion: Among young adults with diabetes, diabetes distress, but not psychological distress, was significantly associated with a higher HbA1c. Increasing HbA1c predicted diabetes distress and psychological stress among males but not females. MH interventions may have a different impact among males vs females.

Relationship of Haptoglobin Phenotype and level with Cardiovascular Disease in Type 2 Diabetes: A Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) Sub-Study

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Background: Haptoglobin (Hp) 2-2 phenotype has been reported to show a higher cardiovascular disease (CVD) risk and modulate fenofibrate benefit on CVD in type 2 diabetes (T2D). However, little is known as to whether Hp levels could also play a role in identifying these risks and treatment benefits.
Aim: To determine associations of Hp phenotype and levels with on-trial total CVD events CVD events in adults with T2D over 5 years.

Methods: Hp phenotype (ELISA) and levels (immunoturbidimetric assays) were measured in 8047 FIELD trial participants at baseline and randomisation (after 6-week fenofibrate).

Results: Baseline Hp level, but not Hp phenotype, was associated with risk for total CVD events among placebo group (n=4030) after adjustment for confounding factors (adjusted HR [95% CI] = 1.31 [1.02-1.67] for Hp level tertile 3 vs. tertile 1, P=0.033). A significant interaction existed between Hp phenotype and levels (P=0.014). Higher Hp level was associated with risk of total CVD events in participants with Hp 1-1 phenotype only (HR [95% CI] = 1.39 [0.39-4.92] and 2.68 [0.86-9.51] for tertile 2 and 3 respectively vs. tertile 1, P for trend=0.010). Participants with both highest Hp level tertile and Hp 1-1 phenotype had similar risk to participants with Hp 2-2 phenotype, regardless of Hp levels. During active run-in fenofibrate reduced Hp levels on average by 20.7%, but its beneficial effect on total CVD events did not differ significantly across different Hp phenotypes, baseline Hp levels or changes in Hp level during the run-in phase.

Conclusion: Hp level is a better CVD risk predictor than Hp phenotype. Not all subjects with Hp 1-1 phenotype are at low CVD risk, including those with higher Hp levels with similar high risk to those with Hp 2-2 phenotype. Benefits of fenofibrate did not differ by Hp level or phenotype.

Remission of diabetes with Cystic Fibrosis Modulator Therapies

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Aims: Cystic fibrosis (CF)-related diabetes includes a complex spectrum of glucose abnormalities, and diagnosis requires an oral glucose tolerance test (OGTT). Annual screening for CF-related diabetes is recommended after age 10 due to its association with higher morbidity and mortality. Emerging evidence suggests that Elexacaftor/Tezacaftor/Ivacaftor (ETI), a highly effective CF modulator therapy may improve glycaemic profiles. This study aimed to evaluate the remission of diabetes associated with the initiation of ETI in our CF centre cohort.

Methods: Diabetes remission was defined as achievement of a plasma HbA1c or continuous glucose monitoring (CGM) glycaemic indicator of ≤6.0% at least 3-months after insulin cessation. Using a prospective clinical CF database, we:
a) identified individuals with a confirmed diagnosis of CF-related diabetes,
b) delineated those who had ceased insulin following ETI initiation, and
c) comprehensively evaluated clinical, biochemical, and CGM data to corroborate diabetes remission.

Results: We identified four adults (one female) who met the OGTT criteria for CF-related diabetes more than 12 months prior and had been on basal insulin (median dose 6 units, range 2-15) for glycaemic optimisation. Their ages ranged between 17 to 22 years, all were homozygous for F508del, and had commenced ETI in mid-2022. Their weight ranged from 43 to 63.7 kg. Since starting ETI, none required hospitalization for pulmonary exacerbations. Indication for insulin cessation was new onset hypoglycemia following ETI initiation and mean HbA1c at least 3 months following insulin cessation was 5.6% (range 5.3 – 6.0%).

Conclusion: Our database identified four adults with CF who ceased insulin for previously diagnosed CF-related diabetes due to new onset hypoglycemia following ETI initiation. The underlying pathophysiological mechanisms are not yet clear, but we hypothesize that reduced inflammation leading to decreased insulin resistance and direct effects of CFTR modulation at the pancreas may be involved.

REMOVAL Substudy: Relationship between Peripheral Augmentation Index and Renal Function Decline in Adults with Type 1 Diabetes

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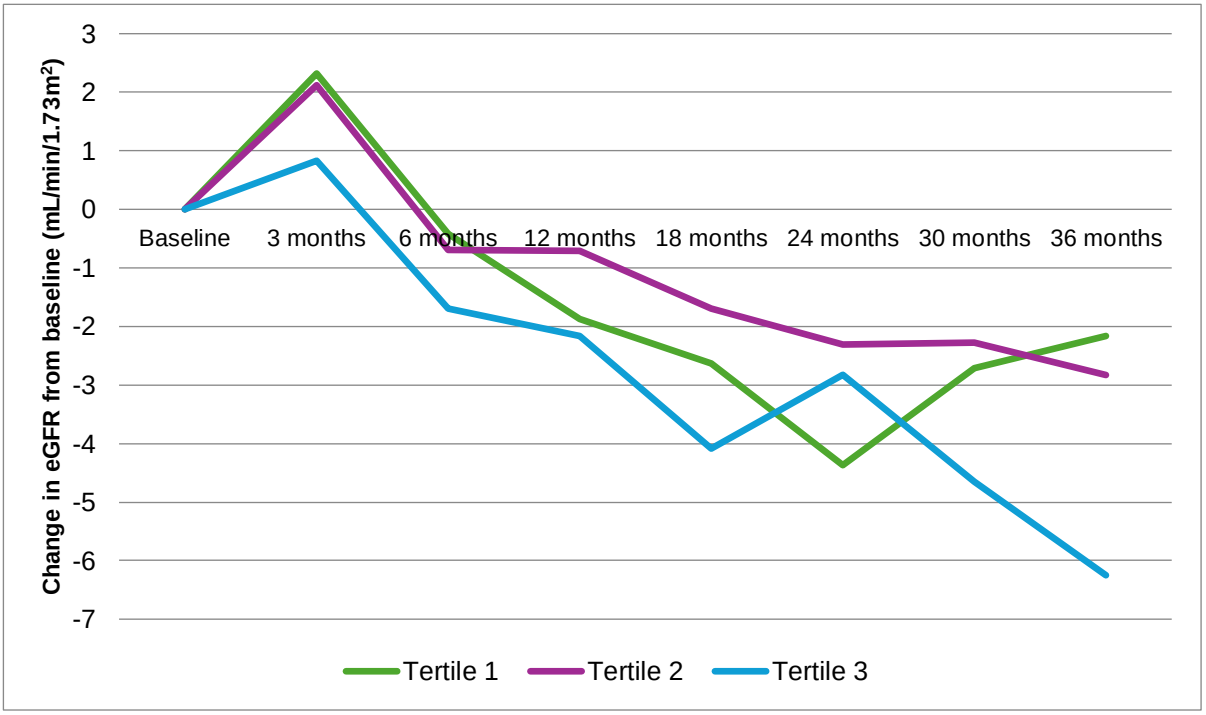
Aim: In the REMOVAL Trial of 428 high cardiovascular risk adults with type 1 diabetes (T1D), adjunct metformin therapy was nephroprotective. Early biomarkers that predict subsequent complications in people with diabetes are desirable. Increased vascular stiffness is an independent predictor of cardiovascular disease and renal dysfunction in people with type 2 diabetes but T1D literature is limited. The EndoPAT peripheral arterial tonometry system measures augmentation index (AI), an integrative marker of vascular dysfunction reflecting higher vascular stiffness. We examined if baseline AI predicts renal dysfunction.

Methods: Arterial tonometry (EndoPAT) was performed in 85% of REMOVAL Trial subjects. We report post-hoc analyses of associations between baseline AI tertiles and renal function over 3-years. Univariable and multivariable analyses were performed (significance at $p<0.05$).

Results: In 364 adults (mean±SD age 55.2±8.5 years, 34.0±10.6 years T1D and HbA1c 8.1±0.8% or 64.5±9.0 mmol/mol), mean±SD eGFR was 93.3±21.7mL/min/1.73m^2 and AI was 15.9±19.2 arbitrary units. On average over 3-years, mean eGFR (change from baseline) was improved in the metformin group compared to placebo by 2.5±1.0mL/min/1.73m^2 ($p=0.02$). Baseline AI inversely correlated with baseline eGFR ($r=-0.16$, $p=0.002$). Following adjustment for trial treatment arm, eGFR decline was significantly greater in the highest vs. lowest baseline AI tertiles (-9.5±2.3 mL/min/1.73m^2, $p<0.0001$) (Figure 1). eGFR decline in the lowest and middle AI tertiles were similar. Baseline AI tertiles did not predict eGFR loss following further adjustment for age and sex or for other cardiovascular risk factors (including blood pressure and use of antihypertensive drugs).

Conclusion: In high cardiovascular risk adults with T1D, baseline AI levels were inversely associated with baseline eGFR and on trial eGFR loss, but this was not independent of covariates. These analyses suggest that the measurement of arterial tonometry using EndoPAT does not add value to the prediction of future renal dysfunction above routinely available measurements.

Figure 1. Change in eGFR over Time According to Baseline AI Tertiles (Unadjusted Data)


3
2
1
0
-1
-2
-3
-4
-5
-6
-7
Change in eGFR from baseline (mL/min/1.73m²)
Baseline
3 months
6 months
12 months
18 months
24 months
30 months
36 months
Tertile 1
Tertile 2
Tertile 3

Renal outcomes in Heart Transplant recipients with Diabetes treated with Sodium Glucose co-transporter 2 Inhibitors

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Abstract: Background & Aim: Sodium glucose co-transporter 2 inhibitors (SGLT2i) have glycaemic, cardiac and renal benefits. Heart transplant (HTx) recipients are at increased risk for diabetes and progressive renal impairment. The impact of SGLT2i use in HTx patients is understudied. Therefore, we assessed the renal effects of SGLT2i use following HTx.

Methods: Observational study of patients who underwent HTx at our institution between 1 January 2015 and 31 December 2018. Change in estimated glomerular filtration rate (eGFR) over time was assessed in patients exposed to SGLT2i for >6 months.

Results: Of 71 patients with diabetes, 26 (37%) were commenced on SGLT2i. Most patients (n=16, 62%) were commenced on SGLT2i within the first 12 months after HTx, including 9 (35%) within 3 months. Median exposure to SGLT2i was 51 months (IQR 16-63). At commencement of SGLT2i, the median eGFR was 65 mL/min/1.73m^2 (IQR 55-88). Compared to baseline, SGLT2i use was associated with a median decline in eGFR of 5 mL/min/1.73m^2 at 1 month (p=0.03) and 10 mL/min/1.73m^2 at 6 months (p=0.01). However, after 12 months of SGLT2i use, eGFR improved and was not different to baseline (p=0.39). This rebound was maintained to 3 years of follow-up (p=0.56). Seven patients (39%) experienced a dip in eGFR of >10 mL/min/1.73m^2 after 1 month of SGLT2i use. Compared to 11 (61%) patients that did not experience an eGFR dip, there was no difference in eGFR at 1 year or 3 years of follow-up. SGLT2i were discontinued in 8 patients, with no serious adverse events recorded.

Conclusion: SGLT2i may protect against renal decline in HTx recipients independent of whether they experience a dip in eGFR in the first month after initiation. SGLT2i appear to be underutilised in our HTx patients and prospective studies are required to further assess potential glycaemic and renal benefits in transplant recipients.

RenoTrue®: A Machine Learning Model to better estimate Glomerular Filtration rate for people with Diabetes

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Aim: To develop and validate an artificial neural network (ANN) machine learning algorithm – RenoTrue® – in estimating kidney function for people with diabetes using an international cohort.

Method: Data were collated from five collaborating cohorts (N = 6,774) from people with type 1 and type 2 diabetes with direct measurements of kidney function and split into training (70%), validation (10%) and test (20%) datasets. RenoTrue® was developed to estimate glomerular filtration rate (GFR) using age, sex, and serum creatinine as input variables into the ANN model. We evaluated the performance of RenoTrue® by estimating a concordance correlation coefficient (CCC), bias (median difference) and accuracy (p10, p15 & p30) between measured GFR measurements and RenoTrue® estimates in the test dataset and compared to the CKD-EPI estimates performance.

Results: People with type 1 diabetes (n = 1769, median age: 32 years (IQR: 12), median mGFR: 104 ml/min per 1.73m^2 (IQR: 27)) and people with type 2 diabetes (n = 3578, median age: 65 years (IQR: 15.3), median mGFR: 60 ml/min/1.73m^2 (IQR: 41)) were included in the analysis. In the test dataset, RenoTrue® indicated high agreement (CCC: 0.87) and low bias with a median difference of 0.39 ml/min per 1.73m^2 when compared to mGFR measurements. In terms of accuracy, 39%, 55% and 82% of RenoTrue estimates were within 10%, 15% and 30% of their respective mGFR measurements. This compares to the 2009 CKD-EPI equation that had a CCC of 0.85, median difference of 4.12 ml/min per 1.73m^2 and 33%, 49%, 74% of estimates within 10%, 15% and 30% of their respective mGFR measurements.

Conclusion: RenoTrue indicated better agreement, lower bias (median difference), higher accuracy against mGFR measurements when compared to the 2009 CKD-EPI equation in people with diabetes.

Retatrutide, an Agonist of GIP, GLP-1, and Glucagon Receptors, Improves Markers of Pancreatic Beta Cell Function and Insulin Sensitivity

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Aim: Retatrutide (RETA), an agonist of GIP, GLP-1 and glucagon receptors, significantly reduced HbA1c up to 2.2% in T2D and body weight up to 17% in T2D at wk 36 and 24% in obesity without T2D (OB) at wk 48 in phase 2 trials. To explore mechanisms by which RETA improved glycemic control, we assessed markers of beta-cell function and insulin sensitivity.

Method: Mixed models for repeated measures evaluated fasting biomarkers from two Phase 2 double-blind randomized placebo-controlled trials in T2D (281 subjects, 36-wks) and in OB (338 subjects, 48-wks).

Results: Homeostatic model assessment (HOMA2)-IR index (insulin), a measure of insulin resistance, decreased over time from baseline with RETA 12 mg reaching reductions of 39% in T2D at 36 wks and 52% in OB at 48 wks. Adiponectin, a marker of insulin sensitivity, increased with RETA from baseline up to 52% in T2D and up to 70% in OB, ($p<0.001$). HOMA2-B index (C-peptide), a marker of beta-cell function, rapidly increased with RETA up to 88% from baseline in T2D but did not significantly increase in OB. Proinsulin and proinsulin/C-peptide ratios, measures of beta-cell stress and dysfunction, decreased from baseline with RETA, by up to 71% and 62%, respectively, in T2D ($p<0.001$).

Conclusion: In conclusion, RETA improved markers of beta-cell function in T2D and markers of insulin sensitivity in T2D and OB.

Retrospective Audit of an Insulin Stabilisation Program at a Single Tertiary Centre

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An insulin stabilisation program (ISP) is run jointly by diabetes educators and endocrinologists at a regional hospital in NSW. This involves twice weekly contact with patients to titrate insulin doses, for up to 4 weeks.

Aims: To determine the efficacy of an insulin stabilisation program in improving glycaemic control.

Methods: We performed a retrospective audit of an ISP. Data was collected from patients enrolled into the ISP during 2022. Data included baseline characteristics, HbA1c, glycaemia as determined by continuous glucose monitoring or finger-prick glucose levels, medication regimens, and hospitalisations.

Results: 297 patients were included in the study. Mean age was 60.4 ± 17.1 years and 56% were male. Diabetes subtypes included T2DM (78%), T1DM (20%), and others (2%). 88% of patients were new to ISP. 54% of patients were new to insulin. 72% of patients engaged with twice weekly ISP contact. The median (IQR) duration of insulin stabilisation was 2.6 (1.3 to 3.9) weeks. 80% had a change to insulin dose/type. The average blood glucose level was 10.3 ± 3.2 mmol/L, and average time in range was 55.1 ± 28.2%. The average time below and above range was 1.4 ± 4.8% and 40.7 ± 29%, respectively. The median (IQR) number of hypoglycaemic episodes per patient was 0 (-0.5 to 0.5). There was a statistically significant reduction in HbA1c following completion of ISP (post-ISP HbA1c 8.20 ± 2.0% [66.2 ± 21.7 mmol/mol] versus pre-ISP HbA1c 10.52 ± 2.6% [90.20 ± 28.5 mmol/mol], p-value <0.001). 61% presented to hospital following ISP, of which 63% and 15% presented within 3 and 12 months of completion, respectively. Of these hospitalisations, 8% were for hypoglycaemia or hyperglycaemia, and 3% were for diabetes emergencies.

Conclusion: The ISP is an effective and safe intervention to improve glycaemia, especially in patients newly commenced on insulin.

Retrospective Audit of the Frequency of Autoimmune Diabetes in the COVID-19 era

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Aims: To determine the frequency of autoimmune diabetes mellitus (DM) in the COVID-19 era.

Methods: A retrospective audit was conducted on cases of autoimmune DM diagnosed during pre-COVID-19 (2016-2018) and COVID-19 (2019-2023) eras. Australian data from the National Diabetes Services Scheme (NDSS) (2016-2022) was reviewed.

Results: From 2016-2023, there were 121 newly diagnosed autoimmune DM at our centre, with 83 from the COVID-19 era. The median age was 35 versus 26.5 years (p-value=0.020) in the COVID-19 era compared to pre-COVID-19. There were 59% versus 45% males in the COVID-19 era compared to pre-COVID-19. Type 1 DM, slowly evolving immune-mediated DM, and checkpoint inhibitor-associated DM comprised 40%, 57%, and 4% of cases in the COVID-19 era compared to 55%, 42%, and 3% in the pre-COVID-19 era. There was a trend towards increased frequency of autoimmune DM in the COVID-19 era (16.60±3.1 cases/year versus 12.67±4.7 cases/year, p-value=0.287) compared to the pre-COVID era. Higher anti-IA2 antibody titres occurred in the COVID-19 era (465.62 kIU/L versus 95.09 kIU/L, p-value=0.008) compared to pre-COVID-19. The median C-peptide level was 163pmol/L versus 217pmol/L (p-value=0.845) in the COVID-19 era compared to pre-COVID-19. In the COVID-19 era, 33% patients were vaccinated against COVID-19 prior to diagnosis. Median onset of autoimmune DM following vaccination was 10 months. Median onset of autoimmune DM after COVID-19 exposure was 3 months. There was an increased frequency of autoimmune DM reported to the NDSS in the COVID era compared to pre-COVID, which was statistically significant (11772±430.1 cases/year versus 10633.33±388.0 cases/year, p-value=0.02).

Conclusion: The frequency of autoimmune DM may have increased in the COVID-19 era, possibly due to a rise in anti-IA2 antibody titres. The relationship with rising antibody titres, COVID-19, and development of autoimmune DM is unclear. Further research is required to evaluate the increasing frequency of autoimmune DM in the COVID-19 era.

Retrospective Case Series of Postprandial Insulin Secretion and Blood Glucose Profile Following Mixed Meal Testing in Non-Diabetes Postprandial Hypoglycaemia.

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Aim: To evaluate the diagnostic utility of postprandial insulin secretion and blood glucose patterns in non-diabetes postprandial hypoglycaemia.
The secondary endpoint is to evaluate the adjunctive diagnostic utility of the insulin resistance index in non-diabetes postprandial hypoglycaemia.

Method: Demographic and clinical data of individuals undergoing a mixed meal test (MMT) over 61 months were collected from the electronic medical records. Data of interest included blood glucose, insulin levels, and C-peptide concentrations at each testing interval of the MMT were collected and analysed to determine trends, patterns and statistical significance. Insulin resistance indexes were calculated using the official Matsuda Index (MI) online calculator.

Results: Twenty MMTs were performed, and data were group into those with post-bariatric surgery hypoglycaemia (PBH) versus postprandial syndrome due to insulin resistance (PPS-IR). The cohort with PBH exhibited earlier postprandial insulin spikes (30 vs ≥60 minutes) and lower postprandial insulin AUC ($p=0.028$). MI scores were higher in PBH compared to PPS-IR ($p < 0.01$). The difference in timing of glucose peaks and trough and HOMA-IR score did not reach statistical significance.

Conclusion: Individuals with PBH and PPS-IR demonstrated distinct postprandial insulin and glucose patterns. Insulin resistance index incorporating postprandial insulin and glucose may be of value in establishing a diagnosis of PBH or PPS-IR.

Rhabdomyolysis Associated with Concomitant use of Sitagliptin and Atorvastatin: A case report and review of the literature

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Introduction: Rhabdomyolysis is a clinical syndrome characterised by muscle injury leading to the disintegration of muscle constituents into the extracellular fluid and systemic circulation. Rhabdomyolysis has a wide range of causes and can be caused by medications. A case of rhabdomyolysis in the context of concomitant use of sitagliptin and atorvastatin is reported here.

Results: This case describes a 70-year-old woman who presented to the hospital with 5 days of generalised weakness and myalgia after she was started on sitagliptin a few weeks prior as an adjunct to metformin for treatment of type 2 diabetes mellitus while on chronic atorvastatin therapy. Blood tests demonstrated elevation of creatine kinase level greater than five times the upper limit of normal, in keeping with rhabdomyolysis. In view of the plausible temporal relationship, sitagliptin was thought to be the most probable culprit in the development of rhabdomyolysis, on background of long-term atorvastatin use. There was no acute kidney injury. Sitagliptin and atorvastatin were discontinued during her hospital admission. She was treated with intravenous fluid therapy which led to resolution of rhabdomyolysis. She had significant symptomatic improvement following normalisation of creatine kinase level. Atorvastatin was restarted at a low dose and gradually uptitrated to the pre-admission dose. Sitagliptin was replaced with empagliflozin which she tolerated well. There was no recurrence of rhabdomyolysis. A literature review revealed eight previous reports of rhabdomyolysis due to drug interaction between sitagliptin and statin therapy. Of these eight cases, only three developed rhabdomyolysis-associated acute kidney injury and one required dialysis.

Conclusion: As the co-prescription of dipeptidyl peptidase-4 (DPP-4) inhibitors and statins is becoming common in patients with type 2 diabetes and dyslipidaemia, it would be crucial to monitor the drug interaction between these agents. Studies regarding the long-term safety of the concurrent use of DPP4-inhibitors and statins may be warranted.

Risk of Gestational Diabetes and Gestational Diabetes-Related Morbidity: A Stratification Model

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Aim: Pregnant women are a heterogeneous group with varying risks of gestational diabetes (GDM) and GDM-related morbidity. We aimed to develop a clinically practical approach to early risk stratification to guide models of care.

Method: Multicentre, retrospective analyses of all women without pregestational diabetes receiving antenatal care for singleton pregnancy in the Western Sydney Local Health District (comprising three hospitals including a tertiary referral centre) between 2018-2022. Routinely collected booking data and pregnancy outcomes were extracted. Decision tree analysis was performed to determine the hierarchy of variables for risk of GDM to inform risk groupings. Incidence of GDM and GDM-related morbidity were compared between the groups.

Results: Of 43012 women, 7485 (17%) had GDM. Median age was 31.3±5.1 years, booking BMI was 25.8±5.8 kg/m^2 and 81% were of non-Caucasian ethnicity. Decision tree analysis revealed prior history of GDM as the most important factor followed by Asian ethnicity, leading to six groupings: Group 1 (primiparous, Asian) with 22% GDM, Group 2 (primiparous, non-Asian) with 14% GDM, Group 3 (no prior GDM, Asian) with 17% GDM, Group 4 (no prior GDM, non-Asian) with 10% GDM, Group 5 (prior GDM, Asian) with 59% GDM, and Group 6 (prior GDM, non-Asian) with 47% GDM. Amongst women with GDM, GDM-related morbidity significantly differed between groups, non-Asian women with prior GDM (Group 6) having highest rates of large for gestational age (17% vs 2.0% in Group 1 with lowest risk) and neonatal hypoglycaemia (18% vs 11% in Group 3). Primiparous Asian women (Group 1) were at highest risk of having small for gestational age births (16% vs 3.6% in Group 6).

Conclusion: Decision tree analysis identified six groups with distinct risks of GDM and GDM-related morbidity, suggesting utility of this clinically practical approach for early identification of women to consider for higher-risk models of care.

Role of Histone Methyltransferase EZH2 in Foam cell formation in Diabetes-associated Atherosclerosis.

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Background: Atherosclerosis is a chronic inflammatory disease and is characterised by plaque build-up in arteries leading to cardiovascular disease. Atherosclerosis is significantly accelerated in diabetes. Macrophages are key immune cells in inflammation which upon oxidized low-density lipoprotein(oxLDL) uptake transform into foam cells. Recent studies have highlighted significance of epigenetic mechanisms in modulating macrophage inflammation. Studies have shown deficiency of Enhancer of zest homolog 2(EZH2) results in reduced foam cell formation. However, role of EZH2 in foam cell formation in diabetes associated atherosclerosis is not known.

Methods: In an *in-vitro* model, THP-1 derived macrophages were stimulated with ox-LDL and ox-LDL+High glucose(HG) for 24hrs to induce foam cell formation. EZH2 mediated trimethylation of lysine 27 on histone 3(H3K27me3) was inhibited using a specific EZH2 inhibitor, GSK126. Genetic knockdown of EZH2 in THP-1 monocytes was also performed. EZH2 mediated H3K27me3 and foam cell formation was assessed in atheroprone diabetic mice by performing immunofluorescence and Oil Red O(ORO) staining. H3K27me3 levels were measured in human carotid plaque samples by immunohistochemistry.

Results: Foam cell formation was significantly reduced with GSK-126 in ox-LDL and ox-LDL+HG stimulated THP-1 cells as assessed by ORO staining. Western blot analysis confirmed EZH2 knockdown in THP-1 monocytes, which also showed reduced foam cell formation in stimulated cells. In the *in-vivo* model, plaque formation was significantly reduced in the aorta of diabetic mice treated with GSK-126. Immunofluorescence staining showed reduced EZH2 mediated H3K27me3 in GSK-126 treated diabetic mice. Immunohistochemistry staining showed expression of foam cell markers and necrotic core area was significantly decreased with GSK-126 in diabetic mice. Human carotid plaque samples also presented higher H3K27me3 levels in samples from individuals with diabetes when compared to a non-diabetic group.

Conclusion: Our study identified that inhibiting EZH2 with GSK-126 is important strategy to inhibit diabetes associated atherosclerosis due to its impact on macrophages and epigenetic regulation.

Secretory Carrier Membrane Protein 3 (SCAMP3) is a novel regulator of the insulin secretory pathway in pancreatic β-cells

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Background: The insulin secretory granule (ISG) plays an important role in insulin biogenesis and secretion in pancreatic β-cells, however many aspects of its properties are still unknown. Recently, the Kebede Lab purified ISGs from mouse MIN6 cells and performed proteomics to uncovered 211 ISG-associated proteins. Secretory Carrier Membrane Protein 3 (SCAMP3) was identified as a novel protein expressed on the membrane of ISGs. The **aim** of this study was to investigate the function of SCAMP3 along the insulin secretory pathway.

Method: In this study, we knocked down SCAMP3 in rat INS-1 cells using short interfering RNAs (siRNAs) or a non-targeting control (siNTC). Through SDS-page analysis we measured the effect on insulin content. We then performed a glucose-stimulated insulin secretion (GSIS) assay to measure the effect on insulin secretion. Furthermore, we underwent immunofluorescent staining of SCAMP3 and various markers in INS-1 cells, MIN6 cells and human pancreatic islets, then performed co-localisation analysis on confocal images.

Results: Cells with about an 80% reduction in SCAMP3 expression exhibited decreased insulin expression. Knocking down SCAMP3 also caused a significant decrease in the fold change in insulin secretion under basal (2.8mM) glucose compared to stimulated (16.7mM) glucose conditions. Confocal images revealed SCAMP3 has a predominantly perinuclear distribution with diffuse cytoplasmic staining. SCAMP3 showed high colocalization with insulin in human islets and mouse MIN6 cells, and partial colocalization in rat INS-1 cells. Furthermore, SCAMP3 highly colocalised with TGN38, a *trans*-Golgi Network marker. These data could represent an interaction between SCAMP3 and insulin early on in the secretory pathway.

Conclusion: Together this data demonstrates that SCAMP3 is present on ISG membranes and regulates insulin secretion and content.

Semaglutide and cardiovascular outcomes in patients with overweight or obesity who do not have diabetes

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Aim: Semaglutide, a long-acting agonist of the glucagon-like peptide-1 receptor, is approved for use in people with type 2 diabetes and overweight or obesity. It has been shown to reduce the risk of adverse cardiac events in those with type 2 diabetes. Whether semaglutide can reduce cardiovascular risk associated with overweight and obesity in the absence of diabetes is unknown.

Methods: In a multicentre, randomised, double-blind, placebo-controlled, event-driven superiority trial, we enrolled 17,604 patients aged 45 years or older with pre-existing cardiovascular disease and a body mass index of ≥27 kg/m^2 who did not have diabetes. Patients were randomly assigned to receive once-weekly subcutaneous semaglutide 2.4 mg or placebo. The primary cardiovascular efficacy endpoint was any component of the composite of death from cardiovascular causes, non-fatal myocardial infarction or non-fatal stroke in a time-to-first-event analysis. Confirmatory secondary endpoints, assessed in a time-to-first-event analyses and tested in hierarchical order, were death from cardiovascular causes, a heart failure composite of death from cardiovascular causes or hospitalisation or urgent medical visit for heart failure, and any-cause death. Supportive secondary endpoints, also assessed in a time-to-first-event analyses but without control for multiplicity, included expanded cardiovascular composite endpoints, individual components of cardiovascular composite endpoints, a composite nephropathy endpoint, progression to diabetes or progression to prediabetes as diagnosed by glycated haemoglobin levels. Changes from randomisation to week 104 in body weight, glycated haemoglobin concentrations and other cardiovascular risk factors were measured.

Results: The trial met its primary objective, with a 20% reduction in the primary endpoint by semaglutide versus placebo. Details of primary and secondary efficacy endpoints and safety findings will be presented.

Conclusions: In patients with pre-existing cardiovascular disease and overweight or obesity, but without diabetes, weekly subcutaneous semaglutide 2.4 mg was superior to placebo in reducing the incidence of major adverse cardiovascular events.

Semaglutide improves Cardiovascular outcomes in Patients with high risk for Metabolic Dysfunction-associated Steatohepatitis – A subgroup analysis from the SELECT trial

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Aim: Cardiovascular (CV) risk is increased in people living with metabolic dysfunction-associated steatohepatitis (MASH). Non-invasive tests, such as Fibrosis-4 score (FIB-4), help stage patients with fibrotic MASH and predict overall CV- and liver-related mortality. In the SELECT CV outcome trial, patients treated with semaglutide had a 20% CV risk reduction versus placebo. We examined the CV benefits of semaglutide in a subgroup of participants at high risk of MASH.

Methods: In SELECT, 17,604 patients (≥45 years, BMI ≥27.0 kg/m^2, with established CV disease, without diabetes) were enrolled. Patients were randomised 1:1 to once-weekly subcutaneous semaglutide 2.4 mg or placebo, plus standard-of-care recommendations for CV disease prevention. This subgroup analysis for 3-point major adverse CV event (MACE; non-fatal myocardial infarction, non-fatal stroke, CV death) was performed for patients with increased MASH risk (FIB-4 ≥1.3 for patients aged <65 years and FIB-4 ≥2.0 for patients ≥65 years), and for a second subgroup of patients of any age with advanced fibrosis (FIB-4 >2.67) and suspected MASH, respectively. Patients with medical history or co-medication for any non-MASH liver disease were excluded.

Results: Of the SELECT cohort, 3665 patients (20.8%) aged <65 years with FIB-4 ≥1.3 and aged ≥65 years with FIB-4 ≥2.0 were included in this analysis. A MACE occurred in 7.6% (n=140/1834) of semaglutide-treated patients (140/1834) and 9.6% (n=176/1831) of placebo-treated patients (hazard ratio [HR] 0.79; 95% confidence interval [CI]: 0.63;0.98; p<0.03). In the advanced fibrosis subgroup (n=475), 22 CV events occurred in 235 patients treated with semaglutide compared with 35 events in 240 placebo-treated patients (HR 0.64; 95% CI: 0.37;1.08; p=0.10).

Conclusions: Aligned with the SELECT trial primary analysis, use of semaglutide 2.4 mg in a subgroup of patients at high risk of fibrotic MASH as defined by FIB-4 produced a 21% reduction in MACE outcomes.

Severe Hypertriglyceridemia with length related small fibre Sensory Neuropathy as a complication of previous Gestational Diabetes Mellitus

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Background: Gestational diabetes mellitus is a risk factor of dyslipidaemias. Hypertriglyceridemia is rarely known to be associated with neurologic disorders.

Case presentation: A 38-year-old lady was referred to an endocrinologist with 4-week history of paraesthesias along with an incidental finding of significantly elevated triglycerides 78.4 mmol/L with total cholesterol 14.7mmol/L on bloods done a week prior to the appointment. The numbness started in the left first toe and subsequently spread to the other toes on the left side, and then to the right side. She also developed hyperalgesia on her fifth finger bilaterally. There was no history of trauma or back injuries. Her history included insulin dependent gestational diabetes and HELLP syndrome 4 years prior, and endometriosis with adenomyosis. She did not have pertinent family history nor history of type 2 diabetes, hypothyroidism, alcohol use, kidney or liver disease, obesity, physical inactivity, or any regular medications. Her repeat bloods in a small general hospital showed total cholesterol of 12.1mmol/L and triglycerides of 18.5 mmol/L. Given the elevated triglycerides, she was admitted to ICU to quickly reduce her lipid levels to try and prevent further complications. She was fasted and started on an insulin-dextrose infusion as per local pancreatitis protocol which she couldn't tolerate due to multiple hypoglycaemic episodes down to 2.8mmol/L despite boluses of glucose. Thus, the infusion was ceased after 12 hours. Her repeat bloods showed total cholesterol 12.1mmol/L and triglycerides 13.1 mmol/L. She was seen by a neurologist who diagnosed her with small fibre sensory neuropathy secondary to hypertriglyceridemia. She was discharged on fenofibrate, high-dose fish oil and low-fat low-carbohydrate diet with the plan of referral for genetic testing and following up on lipid electrophoresis.

Conclusion: Hypertriglyceridemia has many health impacts including pancreatitis, coronary artery disease and strokes. Early optimisation of lipid levels is important to prevent these adverse outcomes.

Severe Hypomagnesaemia and Hypocalcaemia in a Patient with type 2 Diabetes treated with Semaglutide

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A 78 year old woman with a 15-year history of type 2 diabetes was referred because of suboptimal glycaemic control. Her HbA1c was 8.7% (72 mmol/mol) despite treatment with metformin, gliclazide, sitagliptin, dapagliflozin and acarbose. Because of reluctance to consider insulin, semaglutide 0.25 mg s.c. weekly was started and the sitagliptin was stopped. She increased the semaglutide to 0.5 mg weekly after 4 doses but developed nausea/vomiting and so discontinued therapy. Because she had acceptable side-effects on 0.25 mg weekly and her glycaemic control had improved, she restarted this dose but redeveloped upper gastrointestinal symptoms and discontinued again. Two weeks after her last semaglutide dose, she collapsed. She was hospitalised with an undetectable serum magnesium (<0.3 mmol/L) and a low total corrected serum calcium (1.90 mmol/L). Her admission serum glucose was 11.5 mmol/L, lactate 2.2 mmol/L and eGFR 56 mL/min. She responded to intravenous replacement and was discharged on oral magnesium/calcium. Her serum magnesium and calcium concentrations had normalised by 3 weeks post-discharge and her supplemental doses were reduced. Her longstanding muscle cramps had resolved. Her metformin was stopped but her home blood glucose tests were consistently ≥9 mmol/L and she was subsequently started on insulin. Metformin, but also renin-angiotensin system blockers and proton pump inhibitors (the patient was taking irbesartan/esomeprazole) and alcohol (she consumed 1-2 standard drinks most days), have been associated with hypomagnesaemia which is found in 10-30% of people with type 2 diabetes and can induce secondary hypocalcaemia. There have been isolated case reports of hypomagnesaemia complicating GLP1 agonist therapy but SGLT2 inhibitors may be protective. The patient may have had unrecognised longstanding polypharmacy-induced hypomagnesaemia but the temporal relationship between semaglutide therapy and hospitalisation suggests a significant contribution to its severity. We recommend serum magnesium monitoring when patients are taking several medications that can provoke hypomagnesaemia.

Severe Osteoporosis in a Female with Type 1 Diabetes and Pancreatic Exocrinopathy with Chronic Malabsorption and Vitamin D deficiency

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The prevalence and severity of osteoporosis in patients with type 1 diabetes (T1DM) is increased compared to non-diabetic patients, attributed mainly to insulin deficiency and its positive effects on osteoblast proliferation. The association of T1DM with other autoimmune malabsorptive conditions, such as coeliac disease, predisposing to osteoporosis is not uncommon. However, the co-existence of pancreatic exocrinopathy and T1DM leading to osteoporosis is exceptionally rare. Here we present a case of a 29-year-old female with a 10-year history of suboptimally controlled T1DM presenting with significant weight loss and osteofragility fractures who was found to have chronic malabsorption, prolonged vitamin D deficiency and probable osteoporosis/osteomalacia due to severe pancreatic exocrinopathy.

The patient initially presented with an atraumatic left tibial fracture. The patient had suboptimally controlled T1DM with an elevated HbA1c (10.1-14.7%), proliferative retinopathy, polyneuropathy, nephropathy and autonomic neuropathy. Physical examination revealed reduced muscle strength and body composition confirmed very low skeletal muscle mass (19.2kg) but an elevated fat mass (25.5kg). She had a 4-year history of amenorrhea due to weight-related hypothalamic hypogonadism (low FSH <0.1mu/L and estradiol <70pmol/L). Spinal x-rays demonstrated osteofragility fractures. DXA confirmed a low peak bone mass/osteoporosis with significantly reduced total hip BMD of 0.60g/cm² (t-score of -3.4). Malabsorption was documented with low serum 25-vitamin D (50nmol/L), ferritin (8µmol/L), vitamin B12 (12pmol/L) and faecal elastase (42mcg/G). Coeliac serology was negative.

Therapy was initiated with oral cholecalciferol 5000IU daily, calcium citrate 500mg TDS and Creon pancreatic enzyme capsules 75,000IU TDS. Intensive diabetic management was achieved using a Medtronic-770G Smartguard insulin pump and dietary adjustments. The benefits of parenteral bisphosphonates were considered.

This case highlights the complex nature of osteofragility fractures in a young individual with T1DM and highlights the need for a comprehensive investigation of potential contributing factors. A multifactorial approach to management is vital to ensure overall long-term well-being.

Severe Palmoplantar Keratoderma – A Cutaneous complication from Subobtimally controlled Type 2 Diabetes

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Background: Palmoplantar keratoderma is a group of hereditary or acquired disorders defined as the excessive epidermal thickening of skin on the palms of the hand and/or the plantar aspect of feet. The incidence is 4.4 in 100,000. It is one of the cutaneous manifestations of suboptimally controlled diabetes mellitus. The exact mechanism is unknown.

Case presentation: A 53-year-old lady presented to a large tertiary hospital with fevers and reduced GCS. She was found to be in diabetic ketoacidosis (DKA) with blood glucose level of 40 and ketones of 7 in the context of MSSA necrotising soft tissue infection of her back. She had known history of diabetes on insulin and did not have regular follow up with an endocrinologist or allied health. On examination, she had an infected right back wound that required debridement and a course of broad-spectrum IV antibiotics. She also had significant skin thickening of the plantar aspects of both feet with very long toenails which she reported to having for the past few years (pictures below). The dermatology team was consulted and diagnosed her with acquired palmoplantar keratoderma likely due to suboptimally controlled diabetes. She was prescribed 40% urea cream that was applied twice a day which aided in softening the thickened skin that sloughed off after a few weeks. On bloods, she was found to have a HbA1c of 10.4% along with negative diabetes antibodies, making her likely type 2 diabetes. She was treated with an insulin-dextrose infusion until her DKA resolved. She was subsequently transitioned to twice daily Ryzodeg 12 units in the morning and 10 units in the evening along with metformin 1000mg twice daily.

Conclusion: Optimal diabetes control is crucial to prevent complications from arising. Regular follow-up with an endocrinologist, diabetes nurse educators and allied health professionals such as podiatry is recommended.

Initial presentation 2 weeks after using urea A month after urea use

Severe Starvation Ketoacidosis Mimicking Diabetic Ketoacidosis

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Background: Fad diets such as carbohydrate-restricted diets have been popularised in the press and social media lately. A case of severe starvation ketoacidosis mimicking diabetic ketoacidosis in a patient on a very low-carbohydrate ketogenic diet (VLCKD) is described here.

Case: A 40-year-old man with overweight (body mass index of 29 kg/m^2) presented with nausea and vomiting. He also reported weight loss of 6 kg over 2 weeks. Point-of-care investigations revealed severe ketoacidosis: pH, 7.06; bicarbonate, 5mmol/L; ketone, 6.8mmol/L; glucose, 22.5mmol/L; anion gap 37mmol/L; and lactate, 3.5mmol/L. He was treated for presumed diabetic ketoacidosis with an insulin-glucose infusion. Apart from overweight, he had no significant medical history and took no regular medications. He reported no history of diabetes, or a family history of diabetes or autoimmune disorder. After excluding excessive alcohol consumption, toxin ingestion and pancreatitis, he was investigated for latent autoimmune diabetes of adults. He achieved biochemical and symptom resolution 24 hours later and was transitioned from intravenous to subcutaneous insulin. Blood tests showed an HbA1c of 5.5% and C-peptide in the mid-normal range. He later revealed that 2 weeks prior to his hospital presentation, he had started on a VLCKD with a carbohydrate intake of <20grams/day. His weight loss was due to this diet plan. Insulin therapy was discontinued following a single dose of insulin glargine. He remained euglycaemic without glucose-lowering therapy. Diabetes-related autoantibodies subsequently returned negative. He was discharged with dietary advice to avoid carbohydrate-restricted diets in the future.

Conclusion: Severe carbohydrate-restricted diets may induce ketoacidosis with hyperglycaemia in predisposed individuals. This case illustrates the importance of taking a detailed dietary history during an atypical presentation of what is thought to be diabetic ketoacidosis. It also highlights the need for clinicians to remain open-minded in revising the working diagnosis as further information is obtained in the diagnostic process.

Sex differences in early uptake of Medicare-funded Chronic Disease Management Services: A linked data study among 12 875 people with newly diagnosed diabetes

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Aim: To investigate sex differences in the use of Medicare-funded chronic disease management (CDM) services in people with newly diagnosed diabetes.

Methods: This cohort study linked data from the 45 and Up Study, Australia, to administrative health records. The study sample included 12 875 individuals (52% men), aged ≥ 45 years (mean age 66 years), with newly diagnosed diabetes. Diabetes cases were ascertained using a combination of medical and pharmaceutical claims, hospitalisation data and National Diabetes Services Scheme (NDSS) registrations from 2011 until 2017. Medicare Benefits Schedule (MBS) data were used to identify claims for CDM services up to 24-months post-diagnosis. MBS items included: General Practitioner Management Plans (GPMP), Team Care Arrangements (TCA), GPMP and/or TCA reviews, diabetes-related allied health services (dietitians, diabetes educators, exercise physiologists and podiatrists), and type 2 diabetes group education. Descriptive statistics were used to compare service use by sex.

Results: Close to 70% of individuals with newly diagnosed diabetes had a claim for a GPMP, 60% had a claim for both a GPMP and TCA, and 45% had a claim for a GPMP/TCA review during the first 24-months post diagnosis. Approximately 50% of participants had a claim for any allied health service; uptake was highest for podiatrists (28%) and dietitians (19%), and lowest for diabetes educators (6%) and exercise physiologists (7%). Group education was poorly utilised overall (2%). The proportion of women claiming for services was higher than men for all CDM items. Amongst eligible participants with a TCA, women were more likely to access the 5 allied health services to which they are entitled (37% in men vs. 48% in women, $p<0.001$).

Conclusion: Although a higher proportion of women utilised Medicare-funded CDM services compared with men, early uptake of services such as group education and diabetes educator consults are suboptimal for both sexes.

SGLT1/2 Inhibition improves Glycemic control and Multi-organ Protection in Type 1 Diabetes.

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Introduction: Sodium Glucose Co-transporters (SGLT's) are transport proteins that are expressed throughout the body. Inhibition of SGLTs is a relatively novel therapeutic strategy to improve glycaemic control and has been shown to promote cardiorenal benefits. Dual SGLT1/2 inhibitors (SGLT1/2i) such as Sotagliflozin target both SGLT1 and 2 proteins. We have reproducibly shown that, in diabetic Akimba mice, SGLT2i with Dapagliflozin or Empagliflozin promotes upregulation of SGLT1 in the retina or kidney. This finding highlights the critical requirement for dual SGLT1+2i to fully understand the benefits and the mechanism of action of this drug class.

Aim: To conduct investigations utlizing our well-established T1D Akimba mouse model to determine the effects of dual SGLT1+2i on relevant target organs in T1D.

Method: Sotagliflozin (SOTAG) or vehicle was administered to diabetic Akimba mice for 8 weeks at a dose of 25 mg/kg/day in drinking water. Urine glucose levels, water consumption and body weight were measured weekly. Serum, kidney, pancreas and brain tissue were harvested under terminal anaesthesia. Tissues were assessed using immunohistochemistry or ELISA techniques.

Results: Treatment with Sotagliflozin promoted multiple metabolic benefits in diabetic Akimba mice resulting in decreased blood glucose and improved polydipsia. Our studies are the first to demonstrate that SOTAG treatment in type 1 diabetic mice promoted a significant increase in glucagon expression. Sotagliflozin also prevented mortalities associated with diabetes. There were 2 cases of mortality (14.3%), both due to possible dehydration. As both mice were on vehicle, it highlights the possible protective effects associated with SOTAG. We demonstrated that combined SGLT1/2i with SOTAG also results in reduced norepinephrine content in renal tissue lysate.

Conclusion: Our data suggests that there is the possibility that combined SGLT1/2i may be superior to SGLT2i in controlling glucose homeostasis and provides protection of multiple organs affected by diabetes.

Short-acting GLP-1RA Therapy attenuates the Counter-regulatory acceleration of Gastric emptying during Insulin-induced Hypoglycaemia in Type 2 Diabetes

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Aims: Insulin-induced hypoglycaemia accelerates gastric emptying (GE) substantially. In contrast, glucagon-like peptide-1 receptor agonists (GLP-1RAs) may delay GE markedly. The aim of this double-blind, placebo-controlled, randomised, cross-over study is to evaluate if the GLP-1RA exenatide twice daily (BD) attenuates the acceleration of GE during insulin-induced hypoglycaemia in adults with type 2 diabetes (T2D).

Methods: Seven adults with T2D managed with diet and/or metformin [age 62.7±1.6 years, 4M, 3F, HbA1c 6.8±0.1% (50.8±1.3 mmol/mol), BMI 31.7±0.9 kg/m2, median duration of T2D 5 years (IQR 4.3-10 years)] each participated in 4 study visits. They were initially randomised to either placebo (saline) or exenatide 10microgram subcutaneously BD for 4 weeks and then randomised to either a euglycaemic (6 mmol/L) or hypoglycaemic (2.6 mmol/L) clamp. After 60 min at the target blood glucose concentration, they consumed a beef patty labelled with 20MBq 99mTc sulphur colloid and 150ml unlabelled water. GE was monitored by scintigraphy for over 3 hours. After 3 days, the alternate clamp study was performed. Following this, participants crossed over treatment arms and the protocol was repeated. Data, analysed using a two-tailed, paired t-test, are presented as mean±SEM. As a secondary outcome, the areas under curve (AUCs) of GE were assessed with a two-way ANOVA.

Results: Exenatide BD delayed GE during both euglycaemia (placebo 48.8±12.9% percentage food retained at 100 mins vs exenatide 90.7±6.0%, P=0.01) and hypoglycaemia (placebo 34.8±14.6% vs exenatide 78.7±12.1%, P=0.02). During hypoglycaemia, the intragastric retention of food at 100 min was reduced by 17.8±7.1% with placebo and 14.1±8.1% with exenatide (P=0.77). There was a difference in the AUCs for the four conditions (P<0.0001) and a treatment x time effect for total GE (P<0.0001).

Conclusion: In adults with T2D, exenatide BD delays GE markedly during both euglycaemia and hypoglycaemia, but the magnitude of acceleration of GE by insulin-induced hypoglycaemia is comparable.

Six month snapshot audit of admission, Clinical and Glycaemic characteristics of In-patients with Diabetes Mellitus in Liverpool Hospital.

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Aim: To examine, in a quaternary level hospital, in-patient characteristics and Diabetes Mellitus (DM) management of inpatients to high risk wards so to determine patterns and areas to improve patient care.

Methods: For 6 months from March 2024, monthly snapshot audit across the Cardiology and Neurology (medical) and Cardiothoracic and Vascular (surgery) wards was conducted: demographics, DM characteristics, admission data and from 72 hours before audit day, blood glucose (BGL) monitoring and clinical actions, will be collected.

Results: Interim analyses (March and April) for Cardiology and Cardiothoracic wards are presented. % DM occupancy rates were 67.9% and 41.1% in Cardiology and Cardiothoracic wards respectively; (p=0.001). Prevalence of T2DM was >96% across both wards; length of stay (LoS) was 23.3 days (Cardiology) and 15.5 days (Cardiothoracic) . Of DM meds: SGLT2i were used in 26.3% vs 39.1% (Cardiology versus Cardiothoracic; p=0.04); GLP1-RA was only used ~5% across both. Mean HbA1c was 7.5% (both); BGLs were checked ~10 times over the 72hrs; 11% & 13% had at least one hypo reading (none were severe); BGLs >10 occurred 74% vs 43% (p<0.0001) while BGLs > 14 32% vs 48% (p<0.01) across Cardiology and Cardiothoracic wards respectively.

Conclusion: People with DM made up at least 40% of beds; were predominately T2DM, had fair pre-admission control but very frequent hyperglycaemia and some hypoglycaemia. Interestingly use of SGLT2inhibitors were not as prevalent as expected. More detailed results from 6 months of audit will enlighten these preliminary trends and may provide potential areas where inpatient glycaemic management can be improved.

Snapshot of Pre-diabetes in Western Sydney

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Background: Pre-diabetes is under-recognised and remains an ongoing global issue that is on the rise. Previous survey data has indicated a rate of 16.4% in Australian adults (AusDiab). In Australia, there is a data on the impact of country of birth and ethnicity on the risk of diabetes, but a paucity of information on how these factors impact pre-diabetes risk. This data is useful to understand the future burden of diabetes in disadvantaged populations. We reviewed data from a large database of glycated haemoglobin A1c (HbA1c) tests undertaken in western Sydney to identify changes in the rates of pre-diabetes between 2017 and 2019 as a group and in different ethnic populations.

Methods: Approximately 35,000 opportunistic HbA1c tests were undertaken through the Emergency Departments in both 2017 and 2019. Pre-diabetes was defined according to the American Diabetes Association's criteria (HbA1c 5.7%-6.4%). Patient reported Country of birth was used to define ethnicity. This was grouped into nine regions: Aus/NZ/UK, Subcontinent, Africa, Asia, Europe, Middle East, Pacific Island, North America and South America.

Results: The total rate of pre-diabetes increased from 30.5% to 32.5% in this period ($p<0.001$). Excluding groups with less than 500 people, the region with the highest rates of pre-diabetes was Asia across the period analysed, however other regions also changed. In particular, the rate of pre-diabetes in Europeans increased from 38% to 41%. Aus/NZ/UK, Subcontinent, Africa and Asia ethnicities had the greatest proportions of pre-diabetes to diabetes.

Conclusion: Understanding the epidemiology of pre-diabetes is key to the prevention of Type 2 diabetes. The different proportions and rate of change of pre-diabetes in the different ethnic groups facilitates the tailoring of targeted intervention.

Sodium-glucose Cotransporter-2 inhibitor discharge prescribing trends in patients with Type 2 Diabetes Mellitus, Heart Failure and Chronic Kidney Disease

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Introduction: Sodium-glucose cotransporter-2 (SGLT2) inhibitors have favourable metabolic effects in type 2 diabetes mellitus (T2DM). More recently, evidence also supports a role in optimising heart failure (HF) and chronic kidney disease (CKD) management in patients with and without T2DM.

Aim: To identify discharge-prescribing trends of SGLT2 inhibitors from a tertiary metropolitan hospital in patients with T2DM, HF and CKD, particularly exploring uptake for the newer HF and CKD indications.

Methods: Patient admission data between 2017 and 2023 with ICD-10 codes for T2DM, HF and CKD in addition to pharmacy discharge prescribing data for empagliflozin or dapagliflozin was collected. Trends in prescribing rates were analysed for statistical significance with Joinpoint regression. An audit was also performed on SGLT2 inhibitor-prescribing patterns in patients admitted with HF and CKD (with and without T2DM) in the final quarter of 2023.

Results: Prescribing of SLGT2 inhibitors on discharge increased for all indications, represented by an Average Annual Percentage Change of 23.21%, $p < 0.05$ (including 49.77% in HF, 89.80% in CKD and 19.45% in T2DM). Despite the above, an audit of the final quarter of 2023 highlighted a gap in prescribing in potentially eligible patients, with only 9% of non-diabetic HF patients and 1% of non-diabetic CKD patients receiving an SGLT2 inhibitor on discharge.

Conclusion: SGLT2 inhibitor prescribing on discharge has increased over time for all indications. However, our data suggests that there is still a large gap in prescribing for patients within the newer HF and CKD indications.

Substantial Cardiovascular benefit from Icosapent Ethyl in Patients with established CVD and Diabetes: REDUCE-IT eCVD with diabetes

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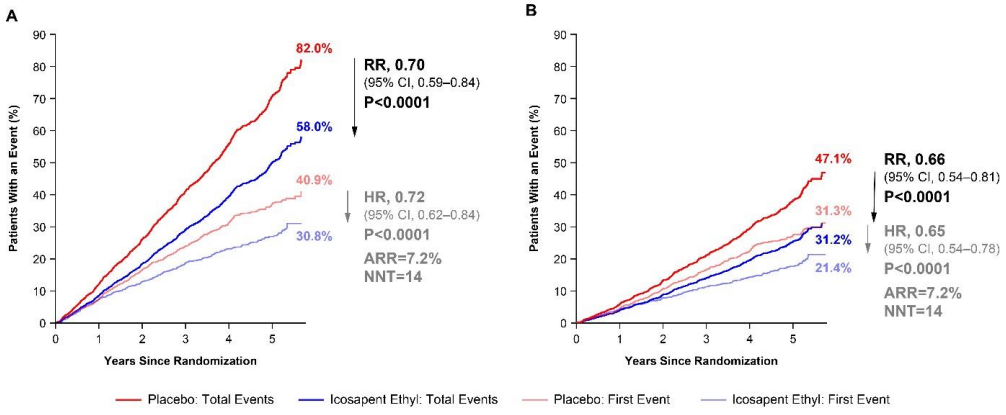
Aim: Statin-treated patients with established cardiovascular disease (eCVD) and diabetes mellitus (DM) are at high CV risk. REDUCE-IT was a multinational, double-blind trial that randomized 8179 statin-treated patients with controlled LDL-C and elevated triglycerides to icosapent ethyl (IPE) 4 g/day or placebo. In the overall trial, IPE reduced CV risk in statin-treated patients with either eCVD or with DM plus CV risk factors. Here we examined the effect of IPE on the primary and key secondary endpoints and on total (first and subsequent) events in REDUCE-IT eCVD patients (secondary prevention) with DM at baseline.

Methods: The primary endpoint was a composite of CV death, myocardial infarction (MI), stroke, coronary revascularization, or unstable angina. The key secondary endpoint was a composite of CV death, MI, or stroke. Endpoint analyses in patients with DM at baseline were prespecified using approaches consistent with the ITT population.

Results: In REDUCE-IT, 41.5% of participants with eCVD had diagnosis of DM at baseline. In these participants, IPE compared with placebo showed a 28% relative risk reduction (RRR) for the primary endpoint (hazard ratio [HR] 0.72 (95% CI 0.62-0.84), P<0.0001; absolute risk reduction [ARR]=7.2%; number needed to treat [NNT]=14); and 30% reduction in total events (rate ratio [RR] 0.70 (95% CI 0.59-0.84), P<0.0001). For the key secondary endpoint, there was a 35% RRR (HR 0.65 (95% CI 0.54-0.78), P <0.0001; ARR=7.2%; NNT=14); and 34% reduction in total events (RR 0.66 (95% CI 0.54-0.81), P <0.0001) (Figure). IPE also significantly reduced risk of the secondary endpoint composites of CV death or nonfatal MI, fatal or nonfatal MI, urgent or emergent revascularization, and total mortality or nonfatal MI or nonfatal stroke in this secondary prevention subgroup.

Conclusion: In statin-treated patients with eCVD and DM, IPE 4 g/day provides robust reductions of first and total ischemic events compared with placebo.

FIGURE. Total Events (First plus Subsequent) and Time to First Primary and Key Secondary Composite Endpoints in Patients With Established Cardiovascular Disease With Diabetes. (**A**) Primary Composite Endpoint, (**B**) Key Secondary Composite Endpoint.



Substantial variation in Perioperative Insulin treatment at a Quaternary Hospital

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Aim: Inpatients undergoing surgery experience variation in diabetes medication treatment. Insulin-requiring patients may require less insulin on day of surgery due to fasting. Types of variation in perioperative insulin treatment and contributors, are relatively understudied. We aim to investigate perioperative insulin treatment and subsequently explore contributors to insulin changes and glycaemic outcomes.

Methods: This was a retrospective analysis of the STOIC-D Surgery trial[1] including surgical inpatients with a diagnosis of diabetes or newly-detected hyperglycaemia, admitted February-December 2021. 518 patients who underwent surgery were included. Data from day prior to surgery, day of surgery and day after surgery was collected, including hypoglycaemic agents, glucocorticoids, parenteral and enteral nutrition, fasting status, and inflammatory markers. Insulin trends were categorised as an increase or reduction in total daily insulin. Collected blood glucose data is currently pending analysis.

Results: Of 518 patients, 294 (57%) received insulin during the three peri-operative days. From day prior to surgery, to day of surgery, 47% of these patients had an increase in total daily insulin, while 34% had a reduction in total daily insulin. From day of surgery, to day after surgery, 63% of insulin-receiving patients had an increase and 27% had a reduction in total daily insulin. Only 1.4% of insulin-receiving patients did not have any changes to their total daily insulin.

Conclusion: High variation in perioperative insulin treatment was evident with a substantial proportion of patients receiving increased total daily insulin on day of surgery, compared to day prior to surgery. We speculate that perioperative glucocorticoid use, cessation of non-insulin diabetes medications, and acute dysglycaemia may result in higher than expected insulin need on day of surgery. We intend to investigate the contributors to increased insulin treatment on day of surgery and the glycaemic outcomes.

[1] *Diabetes Care*, 18 Jan 2024, dc231905

Survival of a 62 year old Non-diabetic woman with Enfortumab Vedotin associated Diabetic Ketoacidosis

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Enfortumab vedotin (EV) is a novel antibody-drug conjugate approved to treat urothelial carcinoma. One rarely reported adverse effect has been life-threatening diabetic ketoacidosis (DKA) driven by profound insulin resistance. We report a case of a 62-year-old woman diagnosed with metastatic urothelial carcinoma who experienced DKA following her third dose of EV, leading to extreme insulin requirements of >1000 units daily, with full resolution of insulin requirement by day seven of admission. Including this case, four of nine reported patients with EV-associated diabetic ketoacidosis have survived. Monomethyl auristatin E (MMAE), the cytotoxic component of EV, is the likely cause, although the exact mechanism remains unclear. This rare clinical event challenges the usual protocols and practice surrounding insulin infusion administration and this case provides evidence to assist in understanding the mechanism by which EV causes ketoacidosis.

Systematic Literature Review of Economic Evaluations of Overweight and Obesity Models of Care in Australia

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Aims: The aim of this systematic literature review was to synthesise and evaluate the economic evidence reporting interventions for people with overweight and obesity in Australia.

Methods: A systematic review of economic evaluations of interventions for overweight and obesity in Australia was undertaken. Medline, Embase, PsycINFO, EconLit, Cochrane Clinical Answers and the Cost-Effectiveness Analysis Registry were searched and publications from January 2013-October 2023 were screened. Economic evaluations of lifestyle or medical interventions for adults with overweight and/or obesity were included. Study characteristics including the intervention, study population, outcome measures, time horizon and cost-effectiveness thresholds were extracted.

Results: Nine eligible records were identified from 493 unique records. Six studies concluded that one or more interventions were cost-effective. For studies with overweight and obesity cohorts (n=5), weight watchers (n=3) and a telehealth diet and exercise program (n=1) were reported as cost-effective, while a lifestyle modification program (n=1) was not. In studies of patients with obesity only (n=4), bariatric surgery was seen as cost-effective at a high willingness to pay threshold (n=2). Time horizons of less than one year were used in four studies. Effectiveness measures used included quality-, healthy- or disability-adjusted life-years (QALYs, HALYs or DALYs), and life-years gained.

Conclusion: Economic evaluations of interventions for overweight and obesity in Australian adults are scarce. The variability in time horizons and effectiveness measures across studies limits comparability. Disaggregation of results is recommended to enable identification of cost-effective interventions for obesity and overweight cohorts. Future economic evaluations of these interventions should utilise longer time horizons, realistic willingness to pay thresholds, use QALYs as outcome measures, and present results separately for populations living with overweight and obesity. To address the serious health challenges posed by overweight and obesity, it is necessary to improve evidence available to policymakers.

The Apolipoprotein Mimetic Peptide C-II-a increases Pancreatic Insulin content and improves Glucose tolerance in mice with β-cell loss.

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Aims: C-II-a is an apolipoprotein mimetic peptide that mimics the anti-diabetic properties of apolipoprotein A-I. We have previously shown that apoA-I increases glucose stimulated insulin secretion and pancreatic duodenal homeobox 1 (*Pdx1)* expression. This study asks whether C-II-a is a viable treatment option for T1DM.

Methods: 12-week-old-C57BL/6J mice were rendered diabetic with streptozotocin (STZ) (55 mg/kg ip) then randomised to twice-weekly C-II-a (40 mg/kg ip) or PBS treatment for 4 weeks (n=10/group). Mice were subjected to an intraperitoneal glucose tolerance test (1g/kg). Pancreata were excised for histological analysis. Spatial transcriptomics was performed using the Visium Spatial Platform (10x Genomics). Islet specific genes were identified via colocalization with insulin genes. Spatially upregulated genes were identified using Moran's I ≥ 0.05 and adjusted p-value < 0.05.

Results: C-II-a treatment decreased fasting blood glucose levels (10.3±0.4 vs 9.2±0.2 mM, $p<0.05$) and improved glucose tolerance (1200±86 vs 650±120 AUC, $p<0.01$) in diabetic mice. C-II-a treatment increased insulin from 0.4±0.2 to 1.3±0.4% of the total pancreatic area ($p<0.05$) despite similar islet area (10,464±6845 vs 10,890±3903 μM^2). It also generated cells that stained positive for insulin in the exocrine pancreas. In the spatial transcriptome of the endocrine pancreas, protease, serine 3 (PRSS3) was significantly upregulated in C-II-a treated mice compared to healthy control (0.229±0.100 vs 2.762±1.064 $\log_2$ fold-change, $p<0.01$). PRSS3 protein expression was significantly increased in the peri-islet acinar space of C-II-a treated mice (0.0296±0.0329% vs 0.087±0.0485%, $p<0.05$). Wider analysis of the pancreatic transcriptome highlighted three regenerating islet-derived protein (Reg) genes with significantly upregulated spatial correlation (Reg3α, Reg3β and Reg3γ, Moran's I≥0.05 and $p<0.05$).

Conclusion: C-II-a increases pancreatic insulin content in mice with STZ-induced diabetes. C-II-a treated STZ-mice also have spatially upregulated PRSS3, Reg3α, Reg3β and Reg3γ in the endocrine and exocrine pancreas which are potentially associated with islet remodelling and the anti-diabetic properties of C-II-a.

The Association between Diabetes and Frailty in Older adults Hospitalised in an Australian Frailty registry.

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Background: Frailty is an important aspect of the management of older people in the acute hospital setting. Frailty is predictive of worse outcomes across a range of health measures, including mortality, rehospitalisation and adverse events. Understanding frailty and how it interacts with diabetes is an important aspect of care in this population.

Aim: to examine the relationship between frailty and diabetes in hospitalised older adults.

Methods: In 2020, Blacktown and Mount Druitt Hospitals in Western Sydney, Australia, launched the Western Sydney Clinical Frailty Registry, Australia's first and only frailty clinical quality registry. We linked this registry with HbA1c and hospitalisation data to compare frailty scores with the risk of diabetes in this group. We used HbA1c data from the Blacktown ED testing database, which records 35,000 HbA1c tests a year in ED.

Results: A total of 1,028 individual records were linked, mean age 82 years, 60% were female (n=603), the mean total number of prescription medicines taken by this cohort was 9.9. 25% (n=255) had a history of stroke, 22% (219) had a history of chronic pulmonary disease and 20% (n=204) had dementia with chronic cognitive deficit. The mean Charlson comorbidity index score for this cohort was 2.2. Frailty was assessed using the Clinical Frailty Scale with 19% (n=192) classified as severely frail, 57% (n=582) classified as mild-moderately frail and 25% (n=254) classified as non-frail.
Correcting for age and sex, the rate of diabetes increased from 34% at a clinical frailty scale category of 0 to 49% at the highest category of clinical frailty ($p<0.001$).

Conclusion: Diabetes is common in geriatric syndrome seen in hospitalised older adults. There is a strong association between diabetes and frailty. In addition, some frail individuals have undiagnosed diabetes. It is important to screen for diabetes in this group, to optimise patient outcomes.

The Association between the presence of Comorbidities/Risk factors and Acute Glycaemic Emergencies in Patients with Diabetes; A cross-sectional study from the Australian National Diabetes Audit

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Background: Acute glycaemic emergencies account for significant morbidity and mortality in patients with diabetes. The presence of comorbidities contributes to worse outcomes; however, its association with acute glycaemic emergencies remains undefined.

Aim: We investigated the association of comorbidities/risk factors with acute glycaemic emergencies in individuals with type 1 (T1DM) and type 2 diabetes (T2DM).

Methods: This cross-sectional analysis includes 7,068 adult patients with T1DM and 17,424 with T2DM from the Australian National Diabetes Audit between 2015-2022. A mixed effect logistic regression model, adjusted for age, sex, diabetes duration and year of visit was used to analyse the relationship between presence of comorbidities/risk factors ('none', 'risk factors only', 'comorbidities only', and 'both') and acute glycaemic emergencies in patients with T1DM and T2DM. Risk factors included hypertension, dyslipidaemia, overweight/obesity and current smoking. Comorbidities were dementia, depression, malignancy and liver disease. Acute hyperglycaemic emergencies, presented in the past 12 months, included diabetic ketoacidosis, hyperosmolar hyperglycaemia syndrome and/or severe hypoglycaemia.

Results: The prevalence of acute glycaemic emergencies was 15.1% and 3.9% in those with T1DM and T2DM, respectively. Among people with T1DM, 14.6% had no comorbidities/risk factors, 73.6% risk factors only, 1.3% comorbidities only, and 10.5% had both. For those with T2DM, 4.5% had no comorbidities/risk factors, 71.7% risk factors only, 1.4% comorbidities only, and 22.4% had both. After adjustment for putative confounders, odds of acute glycaemic emergencies were higher in individuals with 'comorbidities only' compared to those without any comorbidities/risk factors in both people with T1DM (OR 2.68, 95%CI 1.59-4.52, p<0.001) and T2DM (OR 2.03, 95%CI 1.06-3.89, p=0.03).

Conclusion: Patients with T1DM and T2DM with comorbidities have higher odds of acute glycaemic emergencies. These findings may assist clinicians in identifying patients who may benefit from targeted education to prevent acute glycaemic emergencies, in order to mitigate the adverse consequences including need for hospitalisation.

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The Broad Health, Social, and Economic burden of Type 1 Diabetes: A value taxonomy

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Introduction: The burden of Type 1 diabetes (T1D) and the potential benefits of novel technologies have been underestimated mainly because traditional health technology assessment (HTA) has focused on a narrow list of health-related outcomes (i.e., direct mortality and morbidity and healthcare cost savings) and failed to consider the broad health, social, and economic burdens of T1D. Examples of broad impacts include labour force participation and productivity, educational attainment, mental health, and stigma.

Aim: To develop a conceptual framework capturing the broad health, economic, and social impacts of T1D and to assess the extent to which these impacts have been overlooked in traditional HTA.

Methods: We conducted a targeted literature review on the nature and magnitude of the broad impacts of T1D on patients, caregivers/family, the health sector and society. We also elicited the opinions of T1D experts and those with lived experience of T1D on the broad impacts.

Results: Our conceptual framework includes 19 value elements related to the impacts of T1D on physical and mental health, labour market outcomes, healthcare and non-health costs, education, public finances, and social outcomes. We found significant gaps in the evidence that considers the broad benefits of T1D-related technologies. Some studies reviewed incorporate certain labour market impacts of T1D in assessing the value of alternative technologies. Other impacts (e.g., education, caregiver productivity) have been substantially neglected so far.

Conclusions: Since T1D is a lifelong condition with sizable health, social, and economic impacts, failure to account for those broad impacts may lead to biased decisions concerning the funding, development, approval, and reimbursement of novel therapies. Accurate assessment of the full societal burdens of T1D would likely support further investment in approaches to delay T1D onset and improve T1D management.

The Challenges of Using Diabetes Technology in Individuals with Vision Impairment

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Case: A 32M with type 1 diabetes presented with severe diabetic ketoacidosis precipitated by severe recurrent idiopathic pancreatitis. He has multiple complications including severe diabetic retinopathy rendering him legally blind. He utilizes a Dexcom G6 for glucose monitoring, but struggles even when using the largest font size on his phone to read glucose results. Insulin is administered four times a day by using larger sized needles with dosing requirements dependent on click counts.
His visual impairment creates a barrier in accessing health care or seeking Disability Insurance Scheme (NDIS) support due to inability to read letters, or information along with challenges in navigating unfamiliar surroundings; and indirectly through social isolation.

Discussion: The most common causes for visual impairment in diabetes are age-related macular degeneration, glaucoma and microvascular complications such as diabetic retinopathy and macular oedema [1]. This case highlights some of the challenges clinicians should consider in patients with diabetes and vision impairment, including glucose monitoring that is so often taken for granted. Inability to do so leads to suboptimal management, with hyperglycaemia and its associated complications along with hypoglycaemia which carries high morbidity [2].

There has been a rapid evolution of diabetes care technology, however sufficient visual acuity tends to be a pre-requisite to facilitate these tasks. Nonetheless, due to recent advances, there is now a growing role for diabetes devices that have helped bridge the gap of accessibility of technology to those with impaired vision.

Diabetes care in patients with low vision is not a new issue, but it is certainly challenging to keep up to date with the constantly evolving technology [3]. Newer features designed to support patients with impaired vision are vital to maintain one’s autonomy and ability to manage their own diabetes care.

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The Diabetes Regional Education, Access and Management (DREAM) Initiative: A pilot study of regional diabetes control and impact of a mobile service on clinical outcomes

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Background: People living with diabetes are recognised as a vulnerable at-risk group. Regional and remote patient care is impacted by limited access to specialist level healthcare. St Vincent's Hospital Sydney (SVHS) has initiated a rural and remote General Practice case conferencing diabetes management service in the Murrumbidgee region in partnership with the Primary Health Network. The DREAM program comprised an initial case-conferencing consultation with the patient, their General Practitioner, a SVHS Endocrinologist and Diabetes Educator and a 6-month telehealth follow up.

Aim: To evaluate characteristics of patients living with diabetes in a rural and regional settings compared with a matched cohort from a public tertiary hospital diabetes centre.

Methods: A prospective pilot cohort study including patients with type 2 diabetes aged over 18 years old. Rural patients seen by the DREAM team were compared to metropolitan patients managed at SVHS, with groups matched for age, gender and duration of diabetes.

Results: Forty-seven type 2 diabetes patients were included in the pilot DREAM baseline evaluation, matched with 47 SVHS patients. Within each cohort, there were 22 women, median age 63 years [IQR 50-72] and median diabetes duration 10 years [IQR 4-19]. There was a trend towards increased Aboriginal and Torres Strait Island patients within the DREAM cohort (7/47 vs 1/47, p = 0.072). HbA1c was higher in the DREAM cohort compared to the SVHS group (8.2 [7.5-9.9] v 7.2 [IQR 6.5-9.1] %, p = 0.008). Body Mass Index was similar in the DREAM and SVHS cohorts (33.5 [IQR 29.5 – 40.2] v 31.4 [25.9-37.0] kg/m2, p = 0.158).

Conclusions: When compared with a sex-, age- and duration of diabetes-matched metropolitan cohort, rural and regional patients had higher HbA1c and trend towards higher levels of obesity. Aboriginal and Torres Strait Island patients were more highly represented within a rural and regional diabetes population.

The different effect of Ethnicity and Country of residence of Women with Gestational Diabetes on Pregnancy outcome

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Aim: Women from South Asian ethnicity are known to have a higher rate of gestational diabetes (GDM) than Caucasian women, yet the impact of ethnicity on GDM outcomes, specifically adverse maternal and neonatal outcomes, has not been explicitly determined. Therefore, the aim of this study was to assess the differences in GDM pregnancy outcomes in South Asians living in South Asia, South Asians living in Australia, and Caucasian women living in Australia.

Method: After ethics approval was achieved, this retrospective study included 88 Sri Lankan women with GDM living in Sri Lanka (SL_SL), 57 Sri Lankan women with GDM living in Australia (SL_AUS), propensity matched by maternal age and BMI to 138 Caucasian women with GDM born in Australian (AUS_AUS). A diagnosis of GDM was made by 75g oral glucose tolerance test performed at 26-28 weeks, with the same WHO diagnostic criteria for GDM applied.

Results: 12.2% of the SL_SL group had had pre-pregnancy BMI >= 30kg/m2, compared to 15.8% in the SL_AUS group, and 17.4% in the AUS_AUS group. The mean birth weight was 2743g, 3132g, and 3312g in the SL_SL, SL_AUS, and AUS_AUS groups respectively (p<0.001), and between group comparisons were significant between SL-SL and SL-AUS (p=<0.001), and SL-SL and AUS_AUS (p=<0.001). The odds of caesarean delivery were 6.52 times more likely in SL_SL compared to AUS_AUS (p=<0.001). The mean gestational week at delivery was lower in the SL-SL being 37.79 versus SL-AUS group being 38.74 (p=0.009), and lower in the SL-SL versus AUS_AUS group being 38.73 (p=<0.001). Neonatal hypoglycaemia was more common in the AUS_AUS versus SL_SL group (OR 2.93, p=0.03).

Conclusion: The population characteristics and pregnancy outcomes of Sri Lankan women with GDM living in Australia more closely aligns to the outcomes experienced by Caucasian Australians, rather than Sri Lankans living in Sri Lanka. The country of residence has a significant impact on GDM pregnancy outcomes independent of ethnicity.

The effect of Weight loss, before or during Pregnancy, in mothers with obesity, on structural and metabolic changes of offspring adipose tissue.

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Background and Aims: Maternal obesity affects 1 in 5 women of reproductive age, having detrimental effects on maternal and offspring health outcomes. Offspring born to mothers with obesity have an increased risk of foetal overgrowth, rendering them more susceptible to developing metabolic diseases like type 2 diabetes, cardiovascular and liver diseases. Maternal weight loss interventions improve maternal outcomes, however, the effect on offspring outcomes remains largely unexplored. We aimed to determine whether maternal perinatal weight interventions, with either diet or pharmacology, improves offspring adipose tissue metabolic outcomes.

Methods: A diet-induced obesity mouse model was used; female C57BL/6 mice were fed either a high fat diet (HFD) or chow diet for 8 weeks. Then, the HFD-fed dams were allocated to 3 groups: HFD+liraglutide (0.3mg/kg), HFD switch to chow, or continuation of HFD for 4 weeks before pregnancy. After conception, a further group of HFD-fed dams were switched to chow. All male offspring were weaned to HFD, and at postnatal week 12, offspring epididymal white adipose tissue (eWAT) were collected. Real-time PCR, immunohistochemistry and western blot were used to investigate changes in inflammatory, oxidative stress, lipid, and fibrotic markers.

Results: Male offspring born to HFD-fed dams and HFD+liraglutide dams had significantly higher body weight and eWAT mass compared to offspring born to chow-fed dams. Offspring from HFD-fed dams also had elevated oxidative stress and fibrosis gene markers, compared to offspring born to chow-fed dams. Pre-pregnancy liraglutide treatment significantly reduced gene expression in lipid metabolism, oxidative stress, and fibrotic markers. Pre-conception diet modification also decreased offspring body weight, serum insulin, and metabolic markers.

Conclusion: Maternal weight intervention with either liraglutide or diet modification before pregnancy effectively ameliorates dysfunctional adipose tissue in offsprings, supporting ongoing public health messages for women with obesity to undergo weight interventions before pregnancy and interpregnancy for improved offspring outcomes.

The Effectiveness of The Glucose Control Team In Improving Inpatient Glycaemic Control In Surgical Patients With Diabetes

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Background: Dysglycaemia is a main contributor to poor outcomes for surgical patients with diabetes including surgical site infection and longer length of stay (LOS).[1-5] In 2020, Royal North Shore Hospital introduced the Glucose Control Team (GCT), aiming to improve outcomes in this population. The multidisciplinary team identified surgical patients with inpatient dysglycaemia and provided proactive diabetic management by automatic referral, circumventing the usual routes of medical referral.

Aims: This audit assessed the effectiveness of the GCT in improving the glycaemic control of surgical patients with diabetes and identified characteristics of high-risk patients.

Methods: The medical records of patients treated by the GCT from February 2020 to September 2021 were retrospectively reviewed. Glycaemic control was assessed by percent patient days in target blood glucose range (4–10mmol/L). Glycaemic control before, after GCT intervention and between different subgroups were compared by Student's t tests. The association between glycaemic control and clinical outcomes were analysed with regression models.

Results: Percent patient days in range increased from 25.5% to 36.9% ($p<0.001$) and percent patient days in hyperglycaemia decreased from 70.6% to 59.9% ($p<0.001$) after GCT intervention. There was no significant change in time in hypoglycaemia. No strong correlation was found between percent days in range and hospital or ICU LOS. Lower percent days in range was associated with increased surgical site infection ($p=0.037$). Higher baseline HbA1c was associated with greater 28-day readmission ($p=0.003$). Patients with HbA1c ≥ 7.5% and those on insulin therapy had less time in target range but no significant differences in LOS, surgical site infection or 28-day readmission rate.

Conclusion: The GCT was effective in improving inpatient glycaemic control in surgical patients with diabetes without increasing hypoglycaemia. Patients with HbA1c ≥ 7.5% and on insulin therapy prior to admission have high risk of inpatient dysglycaemia and require more intensive management strategies.

The effectiveness of the Glucose Management Team in optimising Perioperative Blood Glucose levels in people with Diabetes undergoing Surgical procedures

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Background: Poorly managed diabetes in hospitalised individuals is associated with negative clinical outcomes. In 2020, Royal North Shore Hospital introduced the Glucose Management Team (GMT), whose primary purpose is to improve inpatient glycaemic management, alongside clinical outcomes, in people with diabetes undergoing surgery. The GMT proactively manages people with diabetes, circumventing the usual routes of referral.

Aim: This retrospective study assessed the effectiveness of the GMT in improving inpatient glycaemic levels in people with diabetes undergoing surgery and assessed the characteristics of individuals who developed perioperative dysglycaemia and adverse clinical outcomes.

Method: We reviewed the medical records of hospitalised individuals with diabetes managed by the GMT from February 2020 to September 2021, capturing baseline characteristics, including HbA1c. Glycaemic level was measured by time in range (TIR) defined as percent patient days in target blood glucose range (4.0-10mmol/L), hypoglycaemia and hyperglycaemia. Glycaemic measures were compared before and after GMT involvement. The association between TIR and clinical outcomes, including hospital length of stay (LOS), surgical site infection (SSI), and 28-day readmission rate, was analysed by logistic regression.

Results: Percent patient days in range increased from 25.5% to 36.9% ($p<0.001$) and percent patient days in hyperglycaemia decreased from 70.6% to 59.9% ($p<0.001$) after GMT intervention. There was no change in time in hypoglycaemia. No association was found between TIR and LOS. A shorter TIR was associated with increased SSI ($p<0.05$). Higher HbA1c was associated with a greater 28-day readmission rate ($p<0.005$). People with HbA1c ≥ 7.5% and those on insulin therapy had less TIR but no significant differences in LOS, SSI or 28-day readmission rate.

Conclusion: The GMT was effective in improving TIR in people with diabetes undergoing surgery without increasing hypoglycaemia. People with HbA1c ≥ 7.5% and on insulin therapy before admission have high risk of inpatient dysglycaemia and require intensive management.

The effects of the JAK1/JAK2 Inhibitor Baricitinib on proportions of Immune cells in the Peripheral Blood of patients with newly diagnosed Type 1 Diabetes

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Background: The BANDIT clinical trial showed that the JAK1/JAK2 inhibitor baricitinib slowed the progressive decline in C-peptide in participants newly diagnosed with type 1 diabetes. JAK inhibitors block signalling downstream of cytokines that regulate cells of the immune system, including interferons and cytokines that use the common gamma chain of the IL-2 receptor.

Aim: To determine whether treatment with baricitinib affected the proportions of immune cell populations in peripheral blood.

Method: Peripheral blood was collected from participants at baseline, week 24 (during treatment) and week 96 (one year after treatment). PBMC were analysed by flow cytometry to determine proportions of NK cells, CD4+ and CD8+ T cells, B cells and monocytes. The placebo and baricitinib treatment groups were compared at all three timepoints.

Results: Baricitinib treatment resulted in a significant decrease in the proportion of both CD56dim and CD56bright NK cells. Amongst T cells, there was a reduction in the proportion of CD4+ T follicular helper cells and effector memory CD4+ and CD8+ T cell subsets in the baricitinib group. Regulatory CD4+ T cells were not affected by baricitinib treatment. B cells were increased in proportion with baricitinib treatment. All cell subsets returned to the same as placebo treated individuals after 1 year of follow up. Over time, we observed an increase in the proportion of exhausted CD8+ T cells in both baricitinib and placebo groups, suggesting a disease, but not treatment, related effect on these cell types.

Conclusion: Reduced proportion of effector cell populations, including NK and T cells, are consistent with previous reports for JAK inhibitors in human studies and with our NOD mouse studies. In future work we will use 10x single cell RNA-seq to examine cell proportions and gene expression changes in cell populations in more detail.

The evidence behind the hype: a retrospective study of the efficacy of semaglutide 1mg for the treatment of obesity in adults with prediabetes or normoglycaemia

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Background: Semaglutide, a potent glucagon-like peptide 1 receptor agonist (GLP-1 RA), represents a significant advancement in diabetes pharmacotherapy. Although semaglutide 1mg is not indicated for obesity management, global prescribing patterns suggest its effectiveness for weight loss as 'off-label' therapy. However, current evidence for this practice in non-diabetic populations is limited.

Methods: We retrospectively analysed records from a large private multidisciplinary clinic in Western Sydney. Non-diabetic adults with obesity (BMI > 30 kg/m²) who started semaglutide therapy from July 2020 to December 2022 were included. Patients followed a very low/low energy diet (800-1200 Kcal/day), time-restricted eating, physical activity targets, and received lifestyle coaching. Outcomes included 12-month changes in weight, BMI, waist circumference (WC), blood pressure, liver function tests, and lipid profile.

Results: We identified 171 patients with the majority (n=113) receiving weekly semaglutide for 12 months, and 58 continuing for 3-6 months. At baseline, mean age was 44.8 ± 1.05 years, 78.9% female. Medical comorbidities included prediabetes (8.8%), hyperlipidaemia (32.2%), fatty liver disease (32.2%), hypertension (25.1%), GORD (24.6%), OSA (21.1%), PCOS (21.1%), osteoarthritis (17.5%), and cardiovascular disease (10.5%). Mean weight was 105.02 ± 2.25 kg, BMI 37.95 ± 0.61 kg/m^2, and WC 112.81 ± 1.37 cm. After 12 months, there was mean reductions in body weight of -13.28 kg (95% CI, 12.01 to 14.55, p<0.0001), BMI -4.77 kg/m2 (95% CI, 4.36 to 5.19, p<0.0001), and WC -13.97 cm (95% CI, 11.30 to 16.44, p<0.0001). Proportional weight loss of ≤ 5% loss was achieved by 10.5% of the cohort, 5.1-10% loss in 28.1%, 10.1-15% loss in 25.7%, and >15% in 35.7%. All secondary outcomes including BP, liver enzymes, and lipid profile saw global improvements.

Conclusion: Weekly semaglutide 1mg in non-diabetic patients with obesity was effective for significant weight loss when combined with a multidisciplinary approach. Further evaluation of long-term outcomes is warranted.

The FIND survey: Fiona Stanley Fremantle Hospital Group INpatient Diabetes Point Prevalence and Management Survey

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Background: Diabetes is common amongst hospital inpatients, and management can be complex. A previous survey at Fiona Stanley Fremantle Hospital Group (FSFHG) in 2016 identified an inpatient diabetes point prevalence of 20.1%.

Aims: To determine the contemporary inpatient diabetes prevalence at FSFHG and describe in-hospital diabetes management and complications.

Methods: A multidisciplinary working group designed and implemented a point prevalence survey of inpatients admitted at FSFHG with diabetes, conducted during a 4 hour period on 19th July 2023. Data was captured regarding biochemistry, blood glucose monitoring, hypoglycaemia, medication management and good diabetes days (defined as a day with appropriate blood glucose monitoring, no hypoglycaemia, and no more than one blood glucose level outside the range 5–10 mmol/L).

Results: There was a diabetes prevalence of 26.2% (n=208) across FSFHG, with individual site prevalence; Fiona Stanley Hospital 27.7% (n=152) and Fremantle Hospital 22.9% (n=56). The prevalence of diabetes at FSFHG in 2023 was higher than recorded at the previous FSFHG diabetes point prevalence survey in 2016 (26.2% vs 20.1%; p= 0.006). The mean age of included patients was 67.9 years, range 22 to 98 years old. 68.3% (142) patients were admitted for non-diabetes related medical conditions with 19.2% (40) admitted for non-medical indications, such as surgery. There were 16 episodes of hypoglycaemia identified, with 12 episodes occurring with blood glucose levels between 3 and 3.9 mmol/L and 4 episodes occurring with blood glucose levels less than 3 mmol/L.
Good diabetes days were documented for inpatients with diabetes at FSFHG on 53.2% days. Haemoglobin A1C levels were checked during admission in 36.5% (n=76) of patients.

Conclusions: The prevalence of diabetes amongst inpatients at FSFHG has increased. Episodes of hypoglycaemia are uncommon however serious episodes of less than 3 mmol/L are occurring, and this warrants further education and intervention.

The first thousand screens: outcomes of the Type1Screen national type 1 diabetes screening program since implementation of in-home testing in 2022.

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Background: Type1Screen provides islet autoantibody testing for Australians with a family history of type 1 diabetes with the dual aims of preventing ketoacidosis at diagnosis and providing access to immunotherapy to preserve beta cell function. We describe screening outcomes since July 2022, when we implemented online registration and consent, and offered in-home capillary blood spot sampling as an alternative to venesection at a community collection centre.

Method: Data from participants who registered to be screened between July 2022 and April 2024 were extracted. Key outcomes were the geographical distribution and clinical characteristics of participants, rates of antibody positivity and specificity of blood spot testing, determined by comparing blood spot results with those derived from a subsequent confirmatory venous sample.

Results: Of the 1218 participants, 946 (45% male) opted for in-home blood spot screening and the remaining 272 (43% male) for venesection. The median [Q1, Q3] age of blood spot registrants was lower (12 [7, 26] v 15 [9, 36]; p<0.001) and they were more likely to reside in regional communities. A total of 49 (4.0%) and 32 (2.6%) participants screened positive for single and multiple autoantibodies respectively, consistent with the expected 6% rate of positive screens. Of the 946 blood spot participants, 31 (3.5%) screened positive for a single antibody and 18 (2.0%) for multiple antibodies. So far, venous samples have been collected from 25 antibody-positive blood spot participants and all but one has been confirmed positive (specificity 96%).

Conclusions: Type1Screen has national reach. In-home blood spot screening is popular and highly feasible, particularly for younger participants living in the regions. We identified the expected number of positive screens with high specificity. The lower cost, increased convenience and greater reach of blood spot screening will help meet the global need to screen large populations for type 1 diabetes risk.

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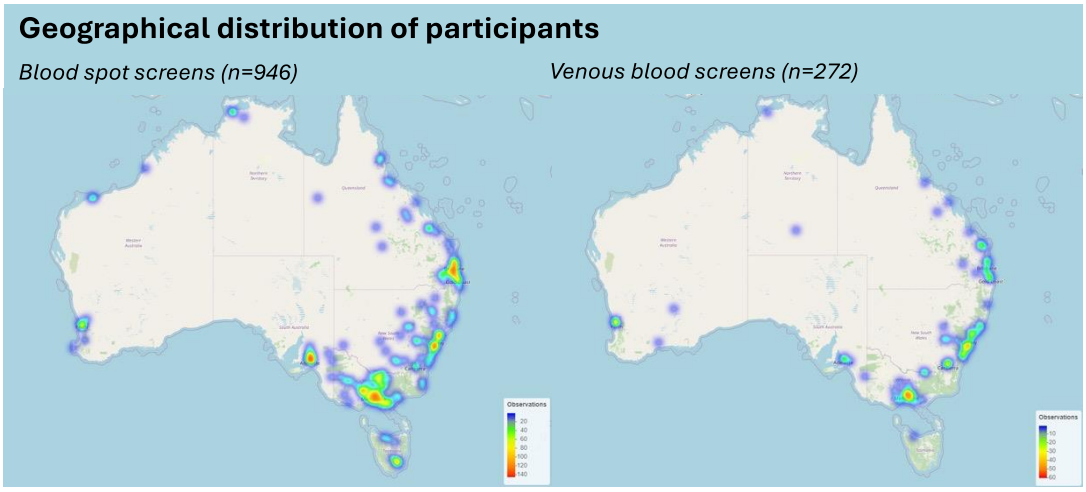

The Global Economic Burden of Type 1 Diabetes: Current estimates and projections to 2040

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[1]University of Southern California, [2]T.H. Chan School of Public Health, Harvard University, [3]College of the Holy Cross Economics and Accounting, [4]Monash University, [5]The global economic burden of type 1 diabetes: Current estimates and projections to 2040, [6]Macquarie University, [7]The University of Queensland, [8]The University of Adelaide

Introduction: The health burden of type 1 diabetes (T1D) has been rising globally over the past decades, especially in low- and middle-income countries. Yet, estimates of T1D's global economic burden and country-specific distribution is lacking.

Aims: To estimate the global economic burden of T1D, its distribution across different country categories and geographies, and to project its future trends.

Methods: We determined the economic burden of T1D using two alternative methodologies: a cost-of-illness study (COI) and a value-per-statistical-life (VSL) approach. Data on T1D prevalence and mortality by country and broad age groups up to 2040 are derived from the T1D Index. For the COI study, we conducted a literature review to estimate the healthcare costs, the labour income losses, and the caregiver costs associated with T1D across different countries. For the VSL study, we estimated country-specific VSLs using standard methods from the literature.

Results: The current economic burden of T1D is substantial and ranges from $84.4 billion (COI approach) to $479 billion (VSL approach) globally, depending on the adopted economic evaluation method (Table 1). The largest burden is estimated in high-income countries. The economic burden of T1D is expected to more than double by 2040 at the global level. The largest percentage increases in economic burden over time are expected to occur in Africa and South Asia. The COI approach produces more conservative burden estimates since it neglects to account for the intrinsic value of health.

Conclusions: Regardless of the evaluation method used, the economic burden of T1D is high and expected to increase over time, thereby calling for more investment in prevention, early detection, and better treatments for T1D. Our findings can serve as a tool for advocacy, targeted funding choices, and as guidance in investment decisions.

The Impact of GLP-1 Receptor Agonist Shortages on Glycaemic Control: Findings from an Australian Specialist Diabetes Clinic

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Aim: To evaluate the real-world impact of the 2022-2023 glucagon-like peptide-1 receptor agonist (GLP-1 RA) medication shortage on glycaemia and cardiometabolic parameters in adults with type 2 diabetes (T2D) managed at an Australian specialist diabetes clinic.

Method: This retrospective audit analysed electronic medical records of 811 T2D adults attending the Baker Heart and Diabetes Institute, Melbourne, who received ≥2 prescriptions for GLP-1 RA before (01/2019 – 03/2022) and during (04/2022–10/2023) the nationwide GLP-1 RA shortage. Data on HbA1c, weight, lipids and medications were extracted. The "pre-shortage" period comprised Quarter (Q1) 2019 – Q1 2022, while "during shortage" was Q2 2022–Q2 2023. Non-parametric tests evaluated changes in glycaemia and weight.

Results: Significant increases in HbA1c were observed between Q3 2022-Q2 2023 (During shortage) vs. Q1 2022, the quarter immediately preceding the shortage. Median HbA1c peaked in Q1 2023 at 7.9% (***mmol/mol) and was higher (p<0.0001) than Q3 2019-Q1 2022. HbA1c levels increased by 0.3% (5.1 mmol/mol; p<0.0001) During-shortage (7.8%) compared with Pre-shortage (7.5%;) (figure 1). The percentage of patients with HbA1c≤7% was 28.6% pre-shortage vs. 23.6% during the shortage. Weight decreased by 1.6 kg during the shortage (n=701; p<0.0001). Total cholesterol (3.75 [3.2,4.3] vs. 3.7 [3.3,4.3]; p<0.05) marginally decreased, both HDL-C (1.12 [0.94,1.4] vs. 1.20 [1.0,1.4] mmol/l; p<0.0001) and LDL-C (1.5 [1.1,2.0] vs. 1.6 [1.2,2.1] mmol/l; p<0.01) increased Pre-shortage vs. During shortage.

Conclusion: Australia's recent GLP-1 RA shortage led to clinically meaningful deterioration in glycaemic control among adults with T2D established on GLP-1 RA therapy at a specialist diabetes centre. Thea small weight reduction during the shortage supports disparate effects of this drug class on short-term glycaemia and weight. Strategic measures are needed to prevent and mitigate the impacts of drug shortages on optimal diabetes care.

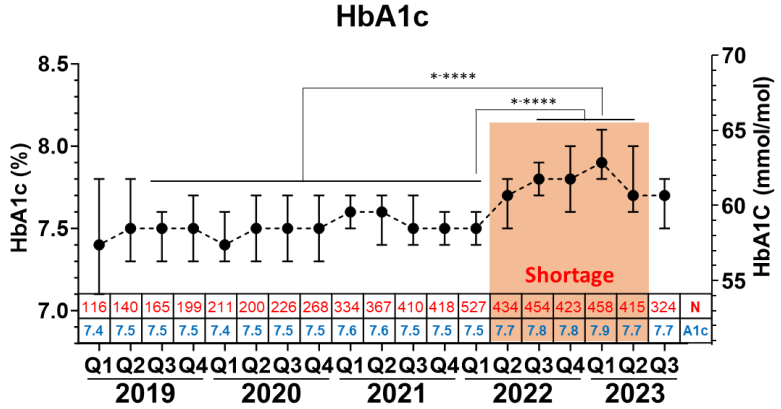

Figure 1. Effect of the GLP 1 shortage on median HbA1c levels (a) Shading indicates the time points affected by the shortage. Kruskal-Wallis test with Dunn's post-hoc test for multiple comparisons. * p<0.05; ** p<0.01; *** p<0.001; **** p<0.000

The Impact of Socioeconomic Disadvantage on Medication use in Australians with Type 1 Diabetes

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Aim: This study sought to explore trends in medication use among people with type 1 diabetes (T1D) in Australia, and disparities in medication use across socioeconomic status (SES).

Method: Australians with T1D, registered on the National Diabetes Services Scheme between 1/1/2013 and 31/12/2019 were linked to dispensed medications via the Australian pharmaceutical claims database. Commonly used medication classes among people with T1D across their life course were investigated (including glucose lowering, lipid modifying and anti-hypertensive therapies, proton pump inhibitors, anti-thrombotics as well as medications for asthma, auto-immune conditions and mental health). Trends in dispensing over time as well as variation in dispensing by SES were assessed. Medication use was calculated as the number of people dispensed ≥1 prescription for that year, divided by the number of people with T1D, among those who survived the full year.

Results: A total of 68,990 Australians with T1D were included. Medication use among people with T1D has remained relatively stable over the 5-year interval. Compared to people in the least disadvantaged areas, those in the most disadvantaged areas were more likely to receive adjuvant glucose lowering therapy (in addition to insulin) [with 2019 data showing rates of 21.5% in the most disadvantaged areas vs 11.6% in the least disadvantaged areas], lipid modifying [35.7% vs 29.7%] and anti-hypertensive therapy [36.1% vs 28.8%], as well as proton pump inhibitors [25.2% vs 17.1%] and anti-thrombotics [8.9% vs 5.6%]. Medication use was also higher among people in the most disadvantaged areas for asthma [13.2% vs 8.4%], autoimmune conditions [19.1% vs 17.0%] and mental health [27.5% vs 21.5%].

Conclusion: People with T1D diabetes in more disadvantaged areas are more likely to be prescribed a range of medications, which may reflect the worse health and health outcomes in these areas.

The Inpatient Diabetes and Advisory Teaching Service (IDAATS) Improves Confidence and Competence in the Inpatient Management of Diabetes among the Junior Meical Officers

Shi H[1,2], Yu C[1], Choy K[5,6,7], Touke R[1], Clifford L[1,2], Templer S[1], Chalak S[1], Alleyn R[2,3], Cohen-Hallaleh R[2,3], Abdo S[1,4], Collins S[2,3], O'Rourke F[3], Flack J[1,2,4], Wong T[1,2,4]
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Background: Although junior medical officers (JMOs) are frequently involved in treating patients with diabetes, a previous study undertaken at our facility demonstrated a lack of confidence and competence in providing inpatient diabetes related care.

Aim: To introduce and validate the effectiveness of the Inpatient Diabetes and Advisory Teaching Service (IDAATS) in improving JMOs' confidence and competence in managing inpatient diabetes.

Methods: IDAATS, led by an Endocrinology registrar/consultant, JMO-champion and diabetes educator is a novel program that involved four case-based weekly sessions teaching the theory of diabetes management alongside discussing contemporaneous inpatient consultations. Prior to IDAATS, an anonymised five-point Likert-scale questionnaire was administered to evaluate self-reported confidence levels in eight domains of diabetes management. An eight-item quiz corresponding to each of these domains was administered to assess competence. The identical questionnaire and another eight-question quiz of equivalent difficulty level were administered post-IDAATS.

Results: Among the 25 participating JMOs from Bankstown-Lidcombe Hospital, IDAATS increased average confidence levels across eight aspects from a mean of 2.4±0.4 (out-of-5) to 3.4±0.2, ($p<0.01$, paired t-test) with significant improvements observed in each domain. The most notable enhancement occurred in the domain "managing steroid-induced hyperglycaemia", with confidence levels rising from 1.7±0.6 to 3.3±0.5 ($P<0.0001$). Similarly, IDAATS enhanced JMO competence, with the total quiz score significantly increasing from 3.2±1.5 (out-of-8) to 6.2±1.2 ($p<0.05$; Figure 1). The most remarkable improvement was observed in "managing steroid-induced hyperglycaemia," with correct responses increasing from 28% pre-IDAATS to 92% post-IDAATS. While postgraduate Year2 JMOs (n=6, 24%) displayed increased confidence compared to Year 1 graduates/interns (n=19, 76%), there were no significant differences in competence. Hence clinical exposure alone did not necessarily translate to acquisition of adequate knowledge. This emphasises the need for authentic case-based teaching to consolidate didactic/conventional teaching methodologies.

Conclusion: IDAATS improves JMO confidence and competence, optimising diabetes care through experiential learning.

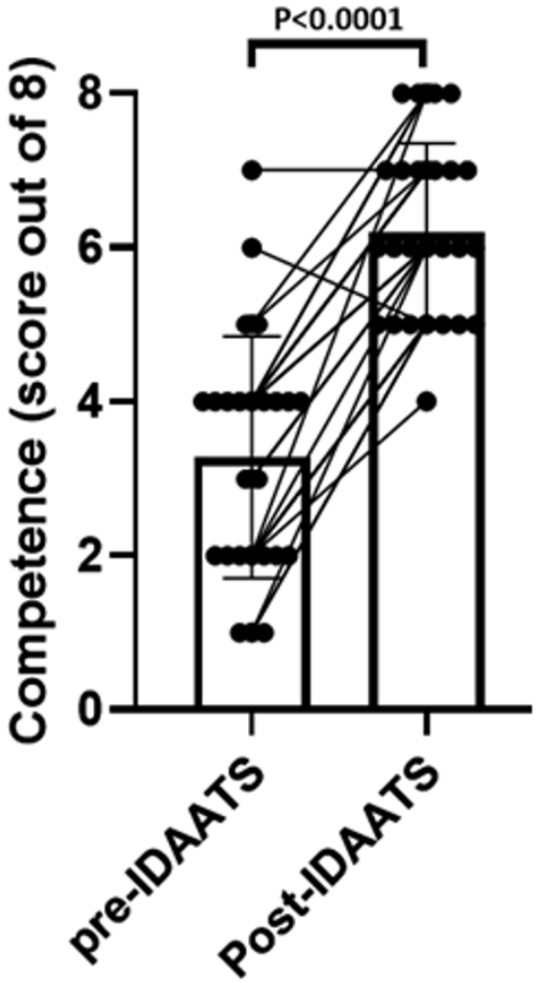

Figure 1. Pre- and post-IDAATS competence measured by a score out of 8. Paired T-test.

The Metabolic Syndrome and its Components as Risk Factors for Peripheral Sensory Neuropathy in Humans: A Systematic Review of the Published Literature

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Background: Recent research has demonstrated an epidemiological association between the metabolic syndrome and peripheral neuropathy in people with type 2 diabetes and in the general population. However, findings regarding the association of individual components of the metabolic syndrome with peripheral neuropathy have been mixed.

Aims: A systematic review of published literature was conducted to assess the relationship between the metabolic syndrome and peripheral neuropathy in observational studies, in order to synthesise the mixed existing evidence in the field.

Methods: Medline, Embase and CINAHL were searched and relevant articles were selected and assessed for risk of bias. Key study characteristics and results were tabulated, and a narrative synthesis of the findings was produced.

Results: The metabolic syndrome was found to be a risk factor for clinical signs and symptoms of peripheral neuropathy in longitudinal and cross-sectional analyses, and predict poorer outcomes of structural and electrophysiological investigations. Obesity, lower high density lipoprotein cholesterol (HDL-C), and inflammation appeared to predict future clinical signs and symptoms of peripheral neuropathy. In cross-sectional analyses, obesity and hypertriglyceridemia were consistently found to be risk factors for poor structural investigation results. Obesity, across populations, and hypertension, in the general population, were predictors of poorer findings in electrophysiological investigations. Clinical signs and symptoms of neuropathy were not consistently related to any metabolic syndrome components in cross-sectional analyses.

Conclusions: These findings helped to clarify the relationship between the metabolic syndrome and peripheral neuropathy and can inform appropriate clinical screening. This review was limited by the heterogeneity in the literature and the restriction of included articles to published literature. However, it demonstrated that further research regarding the longitudinal association between the metabolic syndrome and peripheral neuropathy, the role of inflammation, and the potential of antihypertensive and lipid lowering medications as preventative interventions is warranted.

The New Zealand PREDICT-1 Cardiovascular Risk Equation and Cardiovascular Mortality in an Australian Diabetes Cohort

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Background – Cardiovascular disease (CVD) is the leading cause of death, accounting for 25% of all deaths in Australia in 2021. Management of CVD risk using validated risk equations is central to primary CVD prevention. The New Zealand-based PREDICT-1 equation (1) is predicated on data from contemporary diabetes populations, utilising multiple diabetes-related predictors, and has greater discrimination in diabetes populations than older risk equations. The PREDICT-1 equation forms the basis for the new AusCVDRisk calculator, applicable to type 2 diabetes. It is notable that the performance of the PREDICT-1 equation has not been examined in a relevant Australian population.

Aim – To assess the correlation between five-year CVD risk-scores using the PREDICT-1 equation and observed CVD mortality rates, in a large diabetes cohort.

Methods – The RPAH Diabetes Centre Database holds systematically collected clinical data from over 20,000 people with diabetes, collected from 1986 to 2010. Via linkage with the National Death Index, mortality outcomes censored in 2011 have been ascertained for this dataset. For those without pre-existing CVD, who had their index visit to the RPA Diabetes Centre from 1986-2006 and for whom baseline data are available, five-year risk scores are generated using the New Zealand based PREDICT-1 algorithm. The observed 5-year event rate is plotted against the mean sex-specific predicted event rate within deciles of predicted 5-year risk. Separate plots are generated for men, women, diabetes sub-type, year of diagnosis and by 15-year age bands. Additionally, the prevalence of lipid- lowering and antihypertensive use is examined for each quintile of predicted risk.

Conclusion/Significance – These data provide real-world insight into the utility of the PREDICT-1 algorithm in forecasting 5-year fatal CVD events in an Australian cohort. Additionally, we report on the performance of the PREDICT-1 algorithm in T1DM and the prevalence of real-world treatment gaps for CVD risk.

1. Pylypchuk R, Wells S, Kerr A, Poppe K, Harwood M, Mehta S, et al. Cardiovascular risk prediction in type 2 diabetes before and after widespread screening: a derivation and validation study. The Lancet. 2021 Jun 12;397(10291):2264–74.

The Promoting Resilience in Stress Management for Parents (PRISM-P) intervention: A pilot randomised controlled trial in parents of young children with Type 1 Diabetes

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Aim: Parents of children with type 1 diabetes (T1D) are vulnerable to experiencing elevated stress due to their responsibilities as caregivers. These stressors are particularly relevant to parents of young children who require significant adult supervision to manage their condition. Despite this, there are limited interventions designed to enhance resilience in this population of parents. This pilot randomised controlled trial aimed to examine the acceptability, appropriateness, and feasibility of the Promoting Resilience in Stress Management for Parents (PRISM-P) intervention in parents of young children with T1D.

Method: Parents of children (aged 11 years and younger) with T1D participated in this study (*N* = 30). Participants were randomly assigned (1:1) to a waitlist control or intervention group, with the intervention group participating in three one-on-one sessions via telemedicine with a trained coach. Intervention acceptability and appropriateness were assessed through a survey and semi-structured interview. Feasibility was defined by a minimum study enrolment rate of 50% and a minimum retention rate of 70%. Validated instruments to assess psychosocial wellbeing were completed at baseline, 6 weeks post-baseline, and 12 weeks post-baseline as secondary outcomes.

Results: The enrolment rate for the study was 27% and the retention rate was 87%. Mixed methods findings provided support for the acceptability and appropriateness of PRISM-P, and there were improvements in psychosocial outcomes across timepoints.

Conclusion: PRISM-P was deemed an acceptable and appropriate intervention. Despite initially modest enrolment rates, participant completion and intervention satisfaction were high. Further, changes in psychosocial outcomes provided preliminary support for the efficacy of PRISM-P. To improve enrolment rates, future large-scale trials should employ additional recruitment strategies.

The Relationship between Health literacy, Well-being and General health in Type 2 diabetes, considering Cultural and Linguistic diversity - the Diabetes MILES-Australia Study

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Aim: Low health literacy is associated with poorer health and well-being, yet little is known about these associations among people with type 2 diabetes mellitus (T2DM), particularly those from culturally and linguistically diverse (CALD) backgrounds. This study examined the relationships between health literacy, well-being and general health status among adults with T2DM, considering CALD backgrounds.

Method: Data from the first cross-sectional Diabetes MILES-Australia study were analysed, including adults with T2DM who completed validated measures of health literacy (seven scales of the Health Literacy Management Scale; HeLMS); subjective wellbeing (Personal Well-being Index; PWI), and general health status (EuroQOL Group Visual Analogue Scale; EQ-VAS). Participants from 'CALD' backgrounds (overseas born in a primarily non-English speaking country; primary non-English language) were identified. Multiple linear regression examined associations between HeLMS Domains and outcomes (PWI; EQ-VAS) overall, CALD and Non-CALD.

Results: Data from n=1962 participants (aged 59±9 years; 51% men; 15% CALD) were analysed. There are ≤30% of participants reported low health literacy (across HeLMS Domains). Greater health literacy was associated with greater well-being and health status. Specifically, 'attitudes toward health' (Domain 1; PWI: β=5.7, 95% CI (3.2-8.3); EQ-VAS: β=8.4, (5.9-10.9) and 'socioeconomic considerations' (Domain 4; β=8.2, 95% CI (5.8 – 10.6); β=6.2, 95% CI (3.8-8.5) were associated with both well-being and health status. 'Social support (Domain 3; β=4.9 95% CI [2.3-7.5) and 'being proactive' (Domain 7; β=5.2 95% CI (2.6 – 7.7) were associated with well-being only. Among participants from CALD backgrounds; Domain 1 was predictive of well-being; while Domains 1, 3 and 4 were predictive of health status.

Conclusion: The findings suggest the importance of health literacy in protecting well-being and general health among adults with T2DM, including those from CALD backgrounds. Longitudinal studies are needed to understand these inter-relationships more and to inform the development of appropriate interventions.

The role of Continuous Glucose Monitoring in Hospitalised Patients with Insulin- requiring Type 2 Diabetes having an Operation: Operation Glucose Protocol

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Improving perioperative glucose monitoring and diabetic management is crucial in optimising the clinical outcomes of patients with diabetes undergoing surgery. Continuous glucose monitoring (CGM) is an effective means of monitoring glucose levels in people with diabetes. There is evidence to support the use of CGM to improve glycaemic control, reduce glucose fluctuations or glycaemic variability and to improve quality of life in community dwelling individuals with diabetes [5]. The utility of CGM in perioperative diabetes management is not yet elucidated. The following protocol has been developed to address this question.

Aim: To determine if real-time continuous glucose monitoring (CGM) facilitates improves glycaemic control, as defined by percent time in target range 4.0-10.0 mmol/L, in patients admitted to hospital for surgical procedures with insulin-requiring type 2 diabetes (T2D).
Method: Participants will be recruited from pre-operative admission clinics and randomised into 2 groups: (1) CGM group – real-time CGM with standard point of care (POC) testing versus (2) control group: blinded CGM with standard POC testing. The blinded CGM consists of a blinded Libre ProIQ, in which neither the patient nor the clinical/research staff will be able to view the data until the end of the 14-day wear. The CGM group will have visible CGM data which can be used clinically, in addition to POC testing, with a low alert set at 4.5mmol/L.

The study endpoints include 1)POC-derived metrics (hypoglycaemic and hyperglycaemic episodes), 2) Standardised CGM-derived metrics (Time in range, Time below range, Time above range, Glucose variability. 3) Discordance between POC and CGM in clinical decision making and 4) Hospitalisation-related endpoints (length of stay, readmission rates).

Results: This study is underway. We hypothesize that our study design, with randomisation to real-time versus blinded CGM, will provide much needed evidence about the benefits of CGM in perioperative patients with insulin requiring T2D.

The Type 1 Diabetes National Screening Pilot: Monitoring Program – A protocol for evaluating the feasibility and acceptability of early stage T1D monitoring.

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Aim: Monitoring and education for children with early-stage, presymptomatic type 1 diabetes (T1D) is imperative to detect progression, allow timely commencement of insulin therapy and prevent diabetic ketoacidosis (DKA) at symptom-onset. New ADS-endorsed International guidance recommends regular metabolic monitoring, however the feasibility and acceptability to Australian general population families is unknown. We hypothesise that ongoing clinical monitoring for T1D is feasible and acceptable without causing excessive anxiety.

Methods: Up to 30 children identified with a single or multiple islet autoantibodies in the Type 1 Diabetes National Screening Pilot (T1D NSP) from six sites across Australia, will be offered monitoring based on their antibody status and age, in concordance with the JDRF *Consensus guidance for monitoring persons with islet autoantibody-positive pre-Stage 3 type 1 diabetes.* Single antibody children will be offered antibody testing, HbA1c and glucose levels 6-12 monthly for 3 years. Multiple antibody positive children will be offered HbA1c and glucose levels as well as continuous glucose monitoring (CGM) at 3-6 monthly for 3 years. Surveys will be completed prior to and after each monitoring visit to assess feasibility, satisfaction, beliefs and attitudes towards monitoring as well as parental anxiety (State Anxiety Inventory) and decision regret. Differences in study outcomes will be assessed using multiple comparison tests and logistic or multinomial regression analysis for dichotomous or multiple outcome categories, respectively.

Conclusion: This is the first national study monitoring children with early stage T1D identified from general population screening. Evaluation of acceptability and feasibility of monitoring will underpin the integration of these strategies into widespread clinical practice.

Tirzepatide for the Treatment of Concurrent Type 1 Diabetes and Overweight or Obesity: A Randomised Controlled Trial

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The increasing prevalence of overweight/obesity among individuals with type 1 diabetes (T1D) complicates glycaemic control and escalates insulin resistance, necessitating innovative therapeutic strategies. Tirzepatide, a dual agonist for glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) receptors, shows promise in managing weight and glycaemic control in type 2 diabetes but is unexplored in the context of T1D.

Aim: This double-blinded, placebo-controlled randomised trial evaluates the efficacy of tirzepatide in adults with T1D and overweight/obesity over 32 weeks.

Methods: 40 participants (age 18-70 years) with a body mass index ≥ 27 kg/m^2 and HbA1c ≤ 10% will be randomised 1:1 to receive either tirzepatide or a placebo, alongside standard insulin therapy. Primary outcomes include reduction in body weight (%) and HbA1c levels. Secondary measures involve changes in insulin dosage, time in range by continuous glucose monitoring (CGM) criteria, and severity of comorbidities. Compliance, adverse events, and medication interactions will be closely monitored, with adjustments made for tolerability. Patient reported outcomes and experiences will be measured to capture the benefits on glycaemic management, weight management, and quality of life.

Expected results and conclusion: This study addresses an urgent need for effective weight management interventions in T1D patients, potentially reducing long-term diabetic complications. Outcomes will clarify tirzepatide's role in T1D treatment paradigms, offering new insights into dual incretin receptor agonism as a therapeutic strategy for individuals with T1D. Findings from this study could redefine standard care practices for a growing demographic of patients with T1D and obesity, enhancing quality of life and reducing healthcare burdens associated with diabetes management.

Tirzepatide for the Treatment of Metabolic Dysfunction-associated Steatohepatitis with Liver Fibrosis: results of the SYNERGY-NASH phase 2 trial

Loomba R[1], Hartman M[2], Lawitz E[3], Vuppalanchi R[4], Boursier J[5], Bugianesi E[6], Yoneda M[7], Behling C[8], Cummings O[4], Tang Y[2], Brouwers B[2], Robins D[2], Nikooie A[2], Bunck M[2], Haupt A[2], Sanyal A[9], Obaid M[10], Piya M

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Aim: This study evaluated efficacy and safety of tirzepatide (TZP), a GIP/GLP-1 agonist, in treatment of non-cirrhotic metabolic dysfunction-associated steatohepatitis (MASH) with significant liver fibrosis.

Method: This multicenter, double-blind, placebo (PBO)-controlled Phase 2 dose-finding trial in patients with biopsy-confirmed MASH, stage 2 or 3 fibrosis and a nonalcoholic fatty liver disease activity score (NAS) ≥ 4, randomized (1:1:1:1) participants (n=190) to once-weekly s.c. TZP (5, 10 or 15 mg) or PBO for 52-weeks. The primary endpoint was MASH resolution without worsening of fibrosis at 52-weeks.

Results: 157 participants had evaluable end-of-treatment liver biopsies, with missing values imputed assuming they follow a pattern in placebo arm. The proportion of participants who achieved primary endpoint was 9.8% for PBO and for TZP 5,10,15 mg was 43.6%, 55.5% and 62.4% ($p<0.001$). Among 155 participants who completed the study on treatment, the primary endpoint was achieved by 51.8%, 62.8%, and 73.3% for TZP 5, 10 and 15 mg, respectively vs. 13.2% for PBO ($p<0.001$). The proportion who achieved ≥ 1-stage fibrosis improvement without worsening of MASH was 29.7% for PBO and for TZP 5, 10, 15 mg was 54.9%, 51.3% and 51.0% ($p<0.05$). A reduction in NAS by ≥ 2 points was achieved by 71.7% to 78.3% across the three TZP groups vs. 36.7% with PBO ($p<0.001$ for all doses). Body weight was reduced by up to 17.3% with TZP. Liver enzymes, liver fat, and serum/imaging biomarkers of liver inflammation and fibrosis significantly ($p<0.01$) improved in the TZP groups vs. PBO. Adverse events with TZP were mostly gastrointestinal, and mild to moderate in severity.

Conclusion: In this study of patients with MASH and significant fibrosis, TZP treatment for 52-weeks was more effective than placebo in achieving the primary endpoint. Fibrosis also improved with TZP treatment but without an apparent dose-response effect.

Tirzepatide for Weight and Glycaemic management in a Preclinical model of concurrent Type 1 Diabetes and Obesity

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The rising prevalence of obesity in individuals with type 1 diabetes (T1D) threatens optimal glycaemic control and increases insulin resistance, highlighting the need for innovative therapeutic strategies. Tirzepatide (TZP) is a synthetic peptide that agonises both glucagon-like peptide -1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) receptors, resulting in weight loss and improved insulin sensitivity. TZP is yet to be explored in the context of T1D and obesity.

Aim: This study evaluates the efficacy of TZP to improve body weight and metabolic outcomes in a preclinical model of T1D and obesity.

Methods: 8-week-old male C57BL/6 mice were separated into control (CON) and diabetic (DM) groups, with diabetes induced by streptozotocin (STZ; 55 mg/kg/day for 5 days). Confirmed diabetic mice (blood glucose > 15 mmol/L) were assigned to treatments for 24 weeks: DM (standard chow, saline injections), DMO (high-fat diet, saline injections), and DMO-TZP (HFD, TZP injections every third day, dose incremented to 1.5mg/kg).

Results: 2 weeks post STZ injections, DM mice exhibited significant glucose intolerance; an oral glucose tolerance test revealed a significantly higher mean $AUC_{glucose}$ in the DM mice compared to the CON mice (2913 mmol/L/min vs 1562 mmol/L/min, $p<0.0001$). 6 weeks after treatment initiation, fasting blood glucose in the DM mice (21.4 mmol/L) and the DMO mice (28.4mmol/L) were significantly higher than the CON mice (10.3mmol/L, $p<0.0001$). Remarkably, after just 1 week of TZP treatment, DMO-TZP mice exhibited normoglycaemia comparable with CON mice (7.9 mmol/L vs 9.6 mmol/L). TZP also induced significant weight loss in the DMO-TZP mice, with an 8% reduction in mean body weight from week 0 to 4.

Conclusions: The results from this study show that TZP treatment improves glycaemic control and induces significant weight loss. These findings support the potential of TZP as an effective therapeutic option for improving metabolic outcomes and managing obesity in T1D.

TIRzepatide in Type 1 Diabetes: CardiometaboLic effects (the TIRTLE study). Study protocol of a double-blinded randomized placebo-controlled trial

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Background: Cardiovascular disease and its risk factors are prominent issues in type 1 diabetes (T1D). There is a need to identify therapies that can address weight, glycaemia and other cardiometabolic indices in T1D. Whether tirzepatide, a dual gastric inhibitory polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist, improves weight, glycaemia and cardiometabolic health in T1D has not been studied.

Methods: We will recruit 24 adults aged 18-60 years with T1D (diabetes duration > 2 years and body mass index ≥ 30 kg/m^2. Subjects will be randomized to treatment with tirzepatide, titrated to 5.0 mg weekly, or placebo, for 12 weeks. The primary endpoint is change in weight over 12 weeks. Secondary metabolic indices are arterial stiffness (augmentation index), serum inflammatory markers, body composition (Bodpod; using air-displacement plethysmography), energy expenditure (calorimetry), fasting free fatty acids, fasting glucagon and incretin hormone profile, lipid profile, anthropometry, HbA1c, continuous glucose monitoring metrics and total daily insulin dose. We will also assess gastrointestinal symptoms, eating behaviour, and physical activity levels by questionnaires (PAGISYM, TFEQ-r18, IPAQ), and diet patterns (collected via Easy Diet Diary^{TM}) at baseline and at 12 weeks. The trial is registered (Australian New Zealand Clinical Trial Registry ACTRN12624000111572) and will be conducted at the Garvan Institute of Medical Research, Sydney, Australia (HREC approval 2023-ETH02366).

Conclusion: The role of adjunctive therapies in the management of T1D requires further assessment. The TIRTLE study is the first placebo-controlled study to assess the effect of tirzepatide on cardiometabolic health, in adults with T1D. The study will use detailed physiological measures to explore predictors and mechanisms for metabolic improvements.

Tirzepatide reduced Sleep Apnea severity in Adults with Obstructive Sleep Apnea and Obesity: Results from the SURMOUNT-OSA trial.

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Aim: To investigate efficacy and safety of tirzepatide in treating moderate-to-severe obstructive sleep apnea (OSA) in adults with obesity.

Method: SURMOUNT-OSA (NCT05412004) was a randomized, placebo-controlled, 52-week phase 3 trial comparing the efficacy and safety of tirzepatide to placebo in adults living with moderate-to-severe OSA and obesity. Under a master protocol, the trial was composed of Study 1, which included participants who were unable or unwilling to use positive airway pressure (PAP) therapy, and Study 2, which included participants who were and planned to stay on PAP therapy during the duration of the trial.

Overall, the trials randomized 469 participants in a 1:1 ratio to receive tirzepatide maximum tolerated dose (MTD) 10 or 15 mg once weekly, or placebo.
Participants who tolerated 15 mg continued on 15 mg as their MTD. Participants who tolerated 10 mg but did not tolerate 15 mg continued on 10 mg as their MTD.

Results: At baseline, mean body mass index was 38.8 kg/m^2 and mean apnea-hypopnea index (AHI) was 50.1 events/hour. At 52 weeks, tirzepatide led to a mean AHI reduction from baseline of 27.4 (55.0%) and 30.4 (62.8%) events per hour compared to 4.8 (5.0%) and 6.0 (6.4%) events per hour for placebo in Study 1 and Study 2, respectively.
Moreover, tirzepatide led to a mean body weight reduction from baseline of 18.1% and 20.1%, compared to 1.3% and 2.3% for placebo, in Study 1 and Study 2, respectively.
The overall safety profile of tirzepatide in SURMOUNT-OSA studies was similar to previously reported SURMOUNT and SURPASS trials. The most commonly reported adverse events in SURMOUNT-OSA studies were gastrointestinal-related and generally mild to moderate in severity.

Conclusion: Tirzepatide 10 mg or 15 mg significantly reduced the AHI compared to placebo in adults with moderate-to-severe OSA and obesity, with and without PAP therapy.

Topical mirabegron's potential in diabetic foot ulcers. Using DESI-MSI and LC-MS/MS to confirm its transdermal delivery with novel gel.

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Intro: Mirabegron is a beta-3 adrenoreceptor (β3AR) agonist, approved by the TGA for use in overactive bladder syndrome, causing smooth muscle dilation. Stimulating the β3AR reduces oxidative stress and improves blood supply by increasing nitric oxide production and causing arterial smooth muscle dilation. These mechanisms enhance wound healing in diabetic tissue, from improved function of ischaemic tissue and immune cell infiltration.

Aim: We aimed to detect the ability of mirabegron in our novel gel to permeate the skin and be delivered to the dermis where it can affect the microvasculature and ischaemic tissue.

Methods: Desorption electrospray ionisation mass spectrometry imaging (DESI-MSI) connected to a SynaptG2 TOF mass spectrometer was used to spatially determine the location of mirabegron in ex vivo cultured human skin. Skin was cultured with drug applied to the epidermis for 18 hours. After incubation, it was frozen for later analysis. LC-MS/MS on a Sciex 7500 triple-quad was used to determine the presence of mirabegron in mouse plasma treated topically. Supported liquid extraction was used.

Results: Mirabegron in gel can permeate the stratum corneum and enter the dermis with our novel topical gel formulation, where it can then be absorbed and functionally affect microvasculature. This is shown by both DESI-MSI and LC-MS/MS using an *m/z* of 397.2 and is contrasted against negative controls of methanol in plasma and vehicle gel application on cultured skin and systemic administration positive controls.

Conclusion: We used DESI-MSI to show the successful topical delivery of small-molecule drugs in the dermis of human skin and LC-MS/MS to confirm this in plasma. Using mirabegron in a topical form may improve wound healing via improved redox conditions and blood supply in diabetic foot ulcers.

Total and excess type 1 and type 2 Diabetes related Bed days in Australia.

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Aim: The study was conducted to describe the bed days rate and excess bed days rate related to diabetes and to investigate contributors for the excess bed days.

Methods: We collected hospital admission data on the population with diabetes and on the general population. For the diabetes population, data were obtained from the Australian National Diabetes Services scheme, National Morbidity Inpatient Register, and National Death Index databases from 2014 to 2017. General population data were sourced from the National Morbidity Inpatient register. We modelled Poisson regression to estimate total and excess bed days using disease-specific bed days as the numerator and population size as the denominator. Age, sex, and fiscal year-adjusted rates were reported per 100,000 corresponding population.

Results: In the diabetes cohort, 6,298,792 total bed days were recorded over the follow up period, with cardiovascular disease (CVD) being the largest contributor of bed days. Total bed days for the general population were 115,306,000 days, with mental health diseases being the largest contributor. The annual all-cause bed days rate per 100,000 people was 241,375 (95% CI: 240,879, 241,872) and 119,804 (119,782, 119,826) for the diabetes and general population cohort, respectively, leading to an annual all-cause excess bed days rate of 121,571 (121,097, 122,046) being associated with diabetes. The higher excess admissions and moderately longer stays in endocrine disorders, total infections, CVD, genitourinary, digestive, and skin diseases contributed to most excess bed days. The cancer bed days rate was lower in people with diabetes compared to the general population. Compared to men with diabetes, the excess bed days rate was higher among women with diabetes.

Conclusion: People with diabetes had higher bed days rate compared to the general population. Excess bed days related to diabetes were primarily attributed to higher excess admissions and longer lengths of stay.

Transition from Insulin Degludec-insulin aspart to Glargine-based Basal-bolus Insulin in Hospitalised patients: An audit of current practice and outcomes

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Background: Insulin degludec-insulin aspart (IDegAsp70/30) has glucose-lowering effects persisting longer than that of insulin glargine. Basal-bolus insulin remains the recommended standard of inpatient management. There is no literature guiding transition from IDegAsp to glargine-based BBI regimens (GBBI).

Aim: To evaluate current practice and outcomes in transitioning from IDegAsp to GBBI.

Method: Single-centre, retrospective review of all inpatients prescribed IDegAsp and transitioned to GBBI at a tertiary center (June 2022–June 2023). Baseline characteristics, diabetes management, glucometric data and outcomes were evaluated. The proportion of patients experiencing ≥1 hypoglycaemic event (<4mmol/L) within 72-hours of IDegAsp cessation and glargine commencement, and proportion experiencing hyperglycaemia (>10mmol/L), were compared between patients initiated on glargine doses <70% vs ≥70% of their last IDegAsp.

Results: Of 92 patients, 39 (42.4%) were commenced on glargine doses ≥70% of their last IDegAsp. Median glargine doses were 57.1% (<70% group) and 82.4% (≥70% group) of IDegAsp. There were no differences in age, sex, BMI and HbA1c between the groups. Hypoglycaemia occurred in 14/92 (15.2%) with no difference between the groups. Although age, HbA1c, total daily insulin pre-transition, eGFR, sulfonylurea use and timing of glargine after IDegAsp were not associated with hypoglycaemia incidence, in 12/14 (85.7%) contributing factor(s) such as fasting, acute kidney injury, glucocorticoid weaning and sulfonylurea recommencement were identified. 75/81 (92.6%) experienced hyperglycaemia pre-transition and 89/92 (96.7%) post-transition. Proportion of glucose 4-10mmol/L was greater with GBBI compared to pre-transition, and in the <70% group vs ≥70% within (p=0.01) and after 24 hours of transition (p=0.047).

Conclusion: Patients have high glycaemic lability during transition from IDegAsp to GBBI. Improved glycaemic control occurred following transition to GBBI. There was no correlation between incidence of hypoglycaemia and starting glargine dose in relation to pre-transition IDegAsp dose, but there were identifiable factors contributing to most cases of hypoglycaemia.

Transition from Paediatric to Adult Healthcare services for Emerging Adults and their Caregivers living in Western Australia: A qualitative study.

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Aim: The period known as 'emerging adulthood' is particularly challenging for young people living with Type 1 Diabetes (T1D): they must learn to manage their condition independently alongside milestones such as starting university or joining the workforce, moving out of the family home and assuming greater financial responsibility. Concurrently, emerging adults with T1D are transferred from paediatric to adult healthcare services. These significant stressors can complicate diabetes management. Under the current model, interruption of care is common, and these lapses are associated with worsening glycaemic control, increasing the risk of poor short and long-term physical and psychological outcomes. This qualitative study explored the experience of transition to adult services for emerging adults living with T1D in Western Australia and their caregivers.

Methods: We conducted focus groups and interviews with emerging adults with T1D (n=10) who transitioned to adult services in WA in the last 5 years; and their caregivers (n=9), to better understand (i) how the transition from paediatric to adult healthcare services is experienced; (ii) current shortfalls in care provision; and (iii) their needs to promote successful transition.

Results: Emerging adults with T1D and caregivers identified that transition from paediatric to adult services is currently experienced as a sudden and dramatic shift in support with a lack of clear information provided about clinical care pathways. Families also experienced transition as a loss of aspects of person-centred, wholistic care that was provided with paediatric services.

Conclusion: The findings of this study highlight that current support for transition from paediatric to adult services in WA falls short of guidelines which emphasise a guided, gradual and purposeful process. From here, we will work with multiple stakeholders, including emerging adults with T1D, caregivers and healthcare providers to co-design a new model of care that meets the needs of emerging adults living with T1D.

Travel Insulin Variations in Environmental Temperatures (TRIVET) study: An assessment of checked luggage

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Background/aim: Many insulin-treated people travel by aeroplanes. Current advice is to avoid transporting insulin in checked luggage due to risk of exposure to extreme temperatures. In-use insulin storage recommendations are 2-25 or 30 degrees C for up to 4-weeks.

We aimed to measure temperatures in checked luggage in domestic and international flights.

Methods: A temperature logger (Govee H5074, IL, US) approved for in-luggage air-travel, recording temperature every minute, was placed inside checked luggage without additional insulation, by travellers. Travellers provided their luggage check-in and pickup times and flight details. Data were downloaded from loggers on their return. Publicly available data re flight times, aircraft type and ambient (ground) temperatures were related to temperature recordings. Some flights had ≥1 traveller. Descriptive statistics were applied with significance taken at $p<0.05$.

Results: During Jun 2023 – May 2024 17 travellers took 105 (34 domestic, 71 international) flights, including 68 >2-hours and 35 >8-hours duration; range 0.5-17.3 hours. Ambient ground temperatures in airport regions ranged between 3-42 °C.
In-flight mean (SD) temperatures were 19.2 (3.6) °C, range 4.5-27.5 °C, with n=8 >25 °C and none >30°C. Including both pre- and post-flight baggage handling, mean (SD) temperature was 20.4 (3.3) °C, with n=12 >25°C and one >30°C. Those with in-flight temperatures >25°C reached this temperature pre-check-in.

Conclusions: Observed luggage temperatures pre-, during, and post-air flight were not outside the range of 2-30°C. When luggage temperatures were >25°C this temperature was reached 'on the ground' pre-flight. Results support checked luggage can be a reliable mode for insulin transport (temperature-wise). Further studies are merited and review of advice re insulin care on flights may be considered.

Treatment-induced Neuropathy of Diabetes: A nerve-racking diagnosis

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Introduction: Treatment-induced neuropathy of diabetes (TIND) is an under-recognised iatrogenic neuropathy associated with a rapid improvement in glycaemic control.

Case: A 45-year-old man with type 2 diabetes mellitus and obesity presented with a 4-week history of worsening bilateral neuropathic lower calf and foot pain associated with paraesthesia. Diabetes was diagnosed 5 years prior when he presented with polyuria and polydipsia. HbA1c was 10.8% at the time of diagnosis. He was initially commenced on metformin and twice-daily pre-mixed insulin but was non-adherent to treatment and follow-up care. HbA1c over the subsequent years ranged from 8% to 11%. Prior to the onset of calf and foot pain, improved treatment adherence and significant lifestyle modifications resulted in weight loss of 12 kg and rapid improvement in glycaemic control, evidenced by a reduction in HbA1c from 10.3% to 6.5% over 3 months. Physical examination was consistent with a lower limb sensory neuropathy with reduced sensation to monofilament testing up to the ankles bilaterally with normal power and tone. A nerve conduction study demonstrated moderate sensorimotor axonal polyneuropathy in the lower limbs with no evidence of demyelinating process. Investigations for autoimmune, endocrine and nutritional causes of neuropathy were normal. The acute onset of lower limb neuropathy following rapid glycaemic change was strongly suggestive of TIND. Furthermore, an ophthalmic examination demonstrated new-onset mild non-proliferative diabetic retinopathy. There were no symptoms of autonomic dysfunction. He was started on duloxetine, and pregabalin was subsequently commenced as an add-on therapy. He experienced symptomatic improvement following 6 months of treatment.

Conclusion: This case report highlights the clinical features of TIND to raise awareness of this entity. The current literature, albeit limited, demonstrates a clear relationship between a rapid rate of glycaemic improvement and the development of TIND. Prospective studies are essential to guide disease prevention and treatment recommendations.

Trends in Cause-specific Mortality in people with and without Diabetes: A multi-national population-based study

Magliano D[1,2], Morton J[1,3], Chen L[1], Sacre J[1], Carstensen B[4], Gregg E[5], Pavkov M[6], Arffman M[7], Braake J[8], Chu L[9,10], Fleetwood K[11], Fosse-Edorh S[12], Garbuviene M[13], Guion M[12], Ha K[14], Kaul P[15,16,17], Keskimäki I[7], Kim D[14], Laurberg T[18,19], Støvring H[18,20], Vos R[8], Wild S[11], Shaw J[1,2,21]
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Aim: Population-level trends in cause-specific mortality among people with diabetes are inadequately described. We aimed to examine trends in cause-specific mortality in people with and without diabetes across nine high-income jurisdictions.

Methods: We assembled aggregated mortality data from registries, national health insurance schemes, or other administrative sources in nine high-income jurisdictions from people with and without diabetes between 2000 and 2021. We estimated cause-specific mortality rates and mortality rate ratios (MRRs; for people with vs. without diabetes) for eleven causes of death defined via the underlying cause of death using Poisson models adjusted for age and sex.

Results: There were 2.2 million deaths over 66 million person-years of follow-up and 9.1 million deaths over 1.3 billion person-years of follow-up among people with and without diabetes, respectively. Mortality from Alzheimer's disease increased in people with and without diabetes in 7/9 jurisdictions (Australia, Canada, Denmark, Finland, Lithuania, Netherlands and Scotland) (Figure). MRRs for Alzheimer's disease increased in Australia, Denmark, Netherlands and Scotland, while there was no significant change in the MRR for other jurisdictions. Conversely, cardiovascular disease mortality decreased in all jurisdictions in both people with and without diabetes, with greater declines in people with diabetes than those without diabetes in Australia, Canada, Denmark, Finland and Lithuania. Cancer mortality declined in most jurisdictions in both people with and without diabetes, except stable in those with diabetes from Lithuania and Netherlands. MRRs for cancer were stable in Australia, Finland, Lithuania, Scotland and South Korea; increased in Denmark, France and Netherlands; and decreased in Canada. Trends in other causes of death varied across jurisdictions.

Conclusion: Mortality and excess mortality from cardiovascular disease has consistently declined among people with diabetes, while mortality from Alzheimer's disease has increased markedly independently of age.

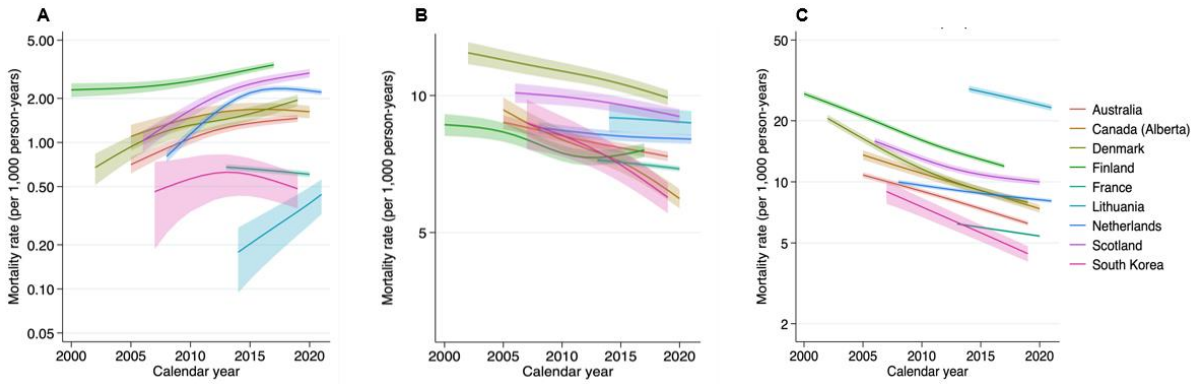

Figure. Age- and sex-standardised mortality rates for Alzheimer's disease (A), cancer (B) and cardiovascular disease (C) in people with diabetes

Trends in incidence of Young-onset Diabetes by Diabetes Type: A multi-national population-based study

Magliano D[1,2], Chen L[1], Morton J[1,3], Salim A[1,4,5], Carstensen B[6], Gregg E[7], Pavkov M[8], Arffman M[9], Colhoun H[10], Ha K[11], Imamura T[12], Jermendy G[13], Kim D[11], Kiss Z[14], Mauricio D[15,16,17], McGurnaghan S[10], Nishioka Y[12], Wild S[10], Winell K[9,18], Shaw J[1,2,19]

[1]Baker Heart And Diabetes Institute, [2]School of Public Health and Preventive Medicine, Monash University, [3]Centre for Medicine Use and Safety, Monash University, [4]Melbourne School of Population and Global Health, The University of Melbourne, [5]School of Mathematics and Statistics, The University of Melbourne, [6]Clinical Epidemiology, Steno Diabetes Centre Copenhagen, [7]Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, [8]Division of Diabetes Translation, Centers for Diseases Control and Prevention, [9]Department of Public Health and Welfare, Finnish Institute for Health and Welfare, [10]Usher Institute, University of Edinburgh, [11]Department of Endocrinology and Metabolism, Ajou University School of Medicine, [12]Department of Public Health, Health Management and Policy, Nara Medical University, [13]3rd Medical Department, Bajcsy-Zsilinszky Hospital, [14]2nd Department of Medicine and Nephrological Center, Medical Faculty, University of Pécs, [15]CIBER of Diabetes and Associated Metabolic Diseases, Instituto de Salud Carlos III (ISCIII), [16]Institut Català de la Salut, Unitat de Suport a la Recerca Barcelona Ciutat, Institut Universitari d'Investigació en Atenció Primària Jordi Gol (IDIAP Jordi Gol), [17]Department of Endocrinology, Hospital de la Santa Creu i Sant Pau, Autonomous University of Barcelona, [18]Unit of Public Health, University of Turku, [19]School of Life Sciences, La Trobe University

Aim: To examine secular trends in the incidence of diagnosed type 1 diabetes (T1DM) and type 2 diabetes (T2DM) with an age of onset between 15 and 39 years from 2000 to 2020 (or a subset thereof).

Methods: We used aggregated data from registries, national health insurance schemes, or other administrative sources in eight high-income countries or jurisdictions. Diabetes type was classified based on standard clinical criteria: time from diagnosis to initiation of insulin therapy, persistence of insulin use, and age at diagnosis of diabetes. We modelled T1DM and T2DM incidence rates using Poisson regression including age and calendar time (2000–2020) by sex.

Results: There were 349591 incident diabetes cases from 346 million person-years of follow-up among people aged 15–39 years. Over time, the incidence of T1DM was stable in Hungary and Japan, and increased in Australia, Denmark, Finland, Scotland, South Korea, and Spain with annual changes ranging from 0.5% to 6.0%. Incidence of T2DM increased in 4 out of 8 jurisdictions (Denmark, Finland, Japan, and South Korea), with annual increases from 2.0% to 8.5%. The magnitude of increase in incidence of T2DM was greater in Asian (4.8% in South Korea and 8.5% in Japan) than non-Asian jurisdictions (2.0% in Denmark and 3.4% in Finland). T2DM incidence was stable in Australia and Hungary, and decreased in Scotland and in Spain, with annual changes of -0.7% and -1.5%, respectively (Figure).

Conclusion: T2DM incidence increased in half of the jurisdictions, but increases were markedly greater in Asian than non-Asian jurisdictions. T1DM increased modestly across most jurisdictions. Changing patterns of incidence of T1DM and T2DM in young adults may call for greater research focus on young people with diabetes.

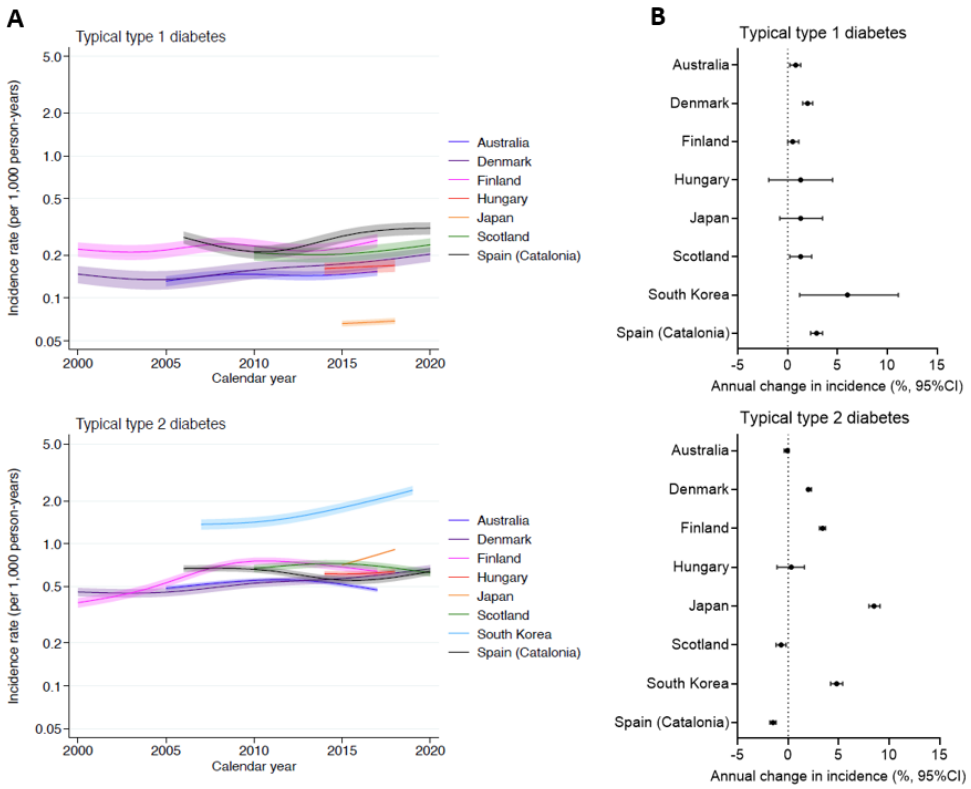

Figure: Age-standardised incidence of diabetes for people aged 15–39 years (A) and estimated annual changes in incidence of diabetes (B), by country and diabetes type

Trends in Liver Disease Mortality in People with and without Diabetes: A multi-national population-based study

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Aim: Although there is growing awareness of an association between diabetes and liver disease, population-level data on liver disease in people with diabetes are limited. This multi-country study examined trends in liver disease mortality in people with and without diabetes.

Methods: We assembled aggregated mortality data from registries, national health insurance schemes, or other administrative sources in nine high-income jurisdictions from people with and without diabetes between 2000 and 2021. Liver disease deaths were defined by the underlying cause-of-death recorded as K70-K76 using the International Classification of Disease, Tenth Revision codes. We modelled liver disease mortality rates and mortality rate ratios (MRRs) for liver disease in people with diabetes compared to those without diabetes using Poisson regression, adjusted for age and sex. An MRR above 1 indicates higher mortality risk to the age- and sex-matched population without diabetes.

Results: During 66 million and 1.3 billion person-years of follow-up, there were 2.2 million and 9.1 million deaths among people with and without diabetes, respectively. Among 9 jurisdictions, the proportions of deaths from liver disease of all deaths varied from 1.0% to 2.8% and from 0.6% to 2.3% in people with and without diabetes, respectively. Over time, liver disease mortality in people with diabetes increased in Finland and Netherlands, was stable in Australia, Canada, France, Lithuania and Scotland, and decreased in Denmark and South Korea (Figure). MRRs for liver disease remained stable or increased in 7/9 jurisdictions over time. People with diabetes had over double the risk of dying of liver disease compared to those without diabetes in 8/9 jurisdictions.

Conclusion: People with diabetes had more than double the risk of dying of liver disease than did those without diabetes in most high-income jurisdictions we assessed. Better screening methods for liver disease in people with diabetes should be considered.

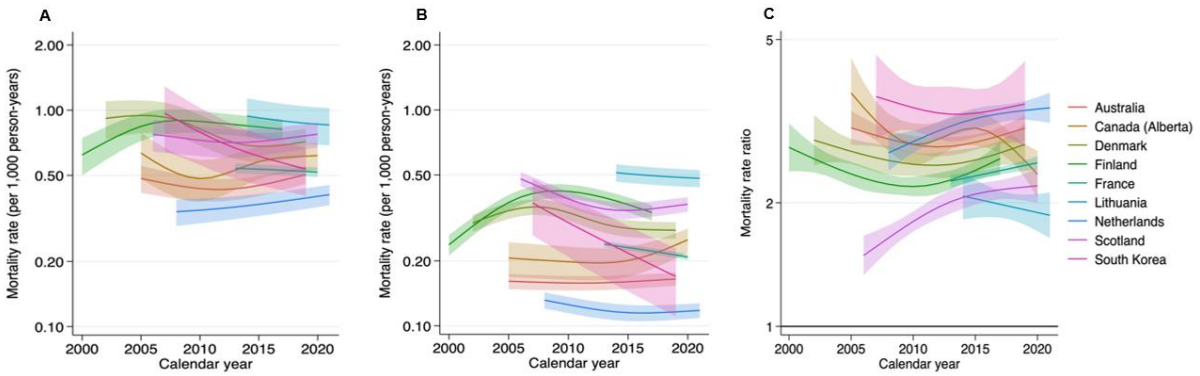

Figure. Age- and sex-standardised liver disease mortality rates in people with (A) and without (B) diabetes, and mortality rate ratios (C) for liver disease

Type 1 Diabetes Patient Treatment Journey – A Longitudinal Oservational study of a Young Adult Clinic (YAC)

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Background: The YAC is a multidisciplinary service that has expanded significantly over the last 10 years. In the last 5 years, access to advanced technologies (continuous glucose monitoring(CGM) and hybrid closed loop insulin pumps) for Type 1 diabetes(T1DM) management has increased.

Aim: To assess uptake of diabetes technologies, associated glycaemic control, and weight changes over time in our cohort.

Methods: A longitudinal observational study of T1DM patients in the YAC at Bankstown-Lidcombe Diabetes Centre who attended for minimum 2-5 years. Treatment type (MDI ± flexible dosing, CGM, Insulin pump), BMI, HbA1c and weight change were assessed at baseline and two subsequent timepoints. Exclusions: patients with incomplete data, >30 years at the end of the study period, and patients managed for less than 2 years. Paired T-tests and McNemar's tests were undertaken for repeated measure observations for continuous and categorical data, respectively. Student t-tests for unpaired continuous data. Statistical significance was defined as $p<0.05$. All time points in this study were within the date range: 14/04/2018 to 01/05/2024.

Results: A total of 38 patients met inclusion criteria, 22 female (58%) and 16 male (42%). The baseline and endpoint ages (mean+SD) were 20±3.0, and 24±3.4 years respectively. Patients were followed up for a mean 4.0 ± 3.4 years. The table demonstrates the treatment type, including uptake of advanced technology, BMI, weight change and HbA1c at each timepoint. There were no statistical differences in HbA1c or BMI according to flexible dosing, CGM, Pump versus MDI users or pump type at any timepoint, (interpretation limited by small sample sizes in subgroups)

Conclusions: In this cohort, there were significant increases in flexible dosing, CGM and hybrid closed loop pumps over the study period. Insulin pump uptake did not increase overall. HbA1c improved from baseline to midpoint but plateaued thereafter. There were significant increases in weight over time.

Table: Treatment type, weight and HbA1c at each time point:

N/A = Not applicable (unable to undertake McNemar's testing as 0 cases at baseline)

Treatment type	Baseline (B)	Midpoint (M)	Endpoint (E)	B vs M	M vs E	B vs E
MDI N (%)	24/38 (63)	26/38 (68)	24/38 (63)	NS	NS	NS
MDI +flexible dosing N (%)	9/24 (38)	16/26 (76)	20/24 (83)	NS	NS	<0.05
CGM N (%)	4/38 (11)	19/38 (50)	26/38 (68)	<0.0001	NS	<0.0001
Insulin Pump N (%) Medtronic AMSL Omnipod	14/38 (37) 12/14 (86) 2/14 (14) 0	12/38 (32) 10/12 (71) 2/12 (14) 0	14/38 (37) 10/14 (71) 3/14 (21) 1/14 (71)	NS	NS	NS
Hybrid closed loop system N (%)	0	1/12 (8)	10/14 (71)	N/A	<0.05	N/A
Senor augmented pump (SAP) N(%)	0	6/12 (50)	1/14 (7)	N/A	NS	N/A
Outcomes						
HbA1c (mean±SD)	9.1±2.2	8.3±1.5	8.4±1.5	<0.05	NS	NS
Weight (kg)	73.8±18.0	90.6±36.2	83.2±25.3	<0.01	NS	<0.001
BMI (mean±SD)	25.1±5.2	26.±4.5	28.6±7.0	<0.05	<0.001	<0.0001
Weight change (kgs), (mean±SD)	ref	+3.8 ± 9.0	+5.6 ± 9.7	<0.05	<0.01	<0.0001

NS = Not significant

Understanding Attitudes about Basal Insulin: Insights from a Global Survey of People with Type 2 Diabetes

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Aim: We aimed to understand the experiences of people with T2D treated with basal insulin, barriers to basal insulin therapy use among those who are insulin naïve, and perceptions of once-weekly insulin.

Methods: A cross-sectional, online survey was conducted from March-April 2023 among adults with T2D in Australia, France, India, Mexico, Saudi Arabia, South Korea, and United Kingdom. Descriptive statistical analyses were performed.

Results: A total of 700 people self-reporting a T2D diagnosis completed the survey (347 basal insulin treated/353 insulin naïve). The burden of managing T2D was higher among insulin treated who were more likely than insulin naïve people with T2D to strongly agree that they were tired of worrying about their T2D (47% vs 34%), worry about having a severe low glucose event (39% vs 27%) and were overwhelmed by both their T2D (36% vs 26%) and the number of all medicines they need to take (41% vs 29%). Only 52% of all people with T2D were satisfied with their current T2D medication; 58% of insulin treated were satisfied with their basal insulin. Although 86% of all people with T2D felt it was important for their T2D to be controlled, only 52% thought it was currently in control. Some people with T2D (31%) forgot to take their basal insulin/T2D medication at least sometimes. When shown a profile of a once-weekly basal insulin, 86% and 65% of insulin treated and insulin naïve people with T2D, respectively, reported being highly likely to use it if recommended by their healthcare provider. People with T2D agreed a once-weekly basal insulin would be convenient to take (73% insulin treated vs 56% insulin naïve) and easy to administer (71% vs 45%).

Conclusion: This survey identified challenges in T2D management and insulin use, some of which may be addressed by once-weekly basal insulin.

Understanding Diabetic Kidney Disease, COVID-19 infection, and Mitochondrial Dysfunction

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During previous years of the global pandemic, the presence of the comorbidities of diabetes and COVID-19 were strongly associated with increased morbidity and mortality. Previous studies have linked both diseases independently with kidney damage and mitochondrial dysfunction. Considering the importance of mitochondrial dysfunction in both diabetes and COVID-19, we hypothesized that improving mitochondrial function would be an effective strategy for preventing kidney damage when these diseases are concomitant.

To investigate this, male C57Bl6/J mice (n=12-16/group) were assigned to 5 groups: 1) no-diabetes, placebo and non-infected; 2) non-diabetic, non-treated, and infected; 3) non-diabetic, treated, and infected; 4) diabetic, non-treated, and infected; and 5) diabetic, treated, and infected. MitoA is an antioxidant compound that has demonstrated potency and efficacy in ameliorating mitochondrial dysfunction in other mitochondrial diseases. Type 1 diabetes was induced by 5 daily x i.p. injections of low-dose streptozotocin (STZ, 55 mg/kg/day) at 5 weeks of age. Groups that received MitoA treatment were given a daily dose via oral gavage, with control groups receiving saline. At 18 weeks of age, the COVID-19 disease groups were infected with amouse-adapted strain of the SARS-CoV-2 virus via respiratory innoculation and monitored daily. When the average body weight of one group decreased by over 20% of the pre-infection body weight, mice from all groups were euthanased.
COVID-19 infection significantly decreased body weight, which was most significant in those with diabetes given placebo. The body weight decrease was significantly alleviated in groups receiving MitoA treatment, with or without diabetes.

Interestingly, the infected diabetic group that received daily MitoA treatment showed qualitatively less kidney damage (shown by less collagen staining in kidney tissue) when compared to the untreated group. MitoA treatment had no noticeable effect on blood glucose control. These results suggest that MitoA may ameliorate some of the effects of diabetes and COVID-19 co-infection on kidney health.

Understanding the Experiences and Unmet needs of Chinese Women in Australia at High Risk of Gestational Diabetes: a Photovoice Study

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Context and aim: Chinese people comprise the second largest group of permanent migrants in Australia. Chinese women born in China are 3.94 times as likely to develop Gestational Diabetes (GDM) than Australia-born White women. Women from culturally and linguistically diverse (CALD) backgrounds experience additional barriers when engaging in lifestyle modifications for GDM prevention. There are limited studies investigating Chinese women's experiences on GDM prevention. This study aims to explore the experiences and unmet needs of Chinese women when engaging with GDM related preventative care, to inform culturally appropriate preventive care.

Methods and analysis/research findings: Semi-structured interviews and photovoice were conducted with 12 women recruited through public advertising and purposive sampling across Chinese social media sites in Australia (July 2023-December 2023). All women identified as being of Chinese ethnicity and are immigrants. Photos, captions and interview transcripts (units of analysis) were inductively coded and grouped into sub-categories and themes of experiences or unmet needs. Experiences included positive and negative events that may have influenced GDM prevention engagement. Unmet needs were perceived barriers to engaging with GDM prevention. People (28.7%) and food (18.5%) are the two largest sub-categories of units of analysis for experience. Australian Healthcare System (30.3%) and cost (26.5%) are the two largest sub-categories for unmet needs.

Conclusion/future action: For Chinese immigrant women, the most prominent types of experiences influencing GDM prevention were related to people and food. The most prominent types of unmet needs relate to the Australian Health Care System and cost. When compared to the literature of other CALD groups, Chinese immigrants in Australia have experiences and unmet needs that are in-keeping with and novel to the literature. Co-design workshops based on the results of this study are currently underway between health professionals and women, which aim to discuss and suggest solutions collaboratively.

Understanding the Impact of Parental Anxiety in the context of caring for a Young child with Type 1 Diabetes: A qualitative study

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Aim: Children with type 1 diabetes (T1D) and their parents face unique challenges and are at a greater risk of developing anxiety disorders than the general population. Anxiety in children with T1D and their parents has been associated with poorer diabetes outcomes. This qualitative study aimed to understand parents' experiences of anxiety while raising a child with T1D, specifically focusing on the perceived impact of anxiety, and identifying potential modifiable parenting processes that may contribute to the development of anxiety in their children.

Methods: Participants (N=26) were parents of children aged 10 years and younger with T1D in Western Australia. Parents participated in one-to-one semi structured interviews via video conferencing with a trained researcher. Data was analysed inductively using reflexive thematic analysis. The analysis centred on lived experiences with anxiety while caring for a child with T1D and emphasised the meaning ascribed to these experiences by parents.

Results: Preliminary findings suggest that parents experience pervasive anxiety and use strategies such as constant monitoring for signs of ill health, avoidance of cognitions related to T1D and control of diet and activities to manage anxiety. Parents felt that anxiety impacted their parenting choices and relationship with their child. Parents reported that the uncertainty of T1D caused significant anxiety and that they worried about the impact of their anxiety on their children.

Conclusions: Understanding parents' experiences of anxiety may inform the development of a preventative anxiety intervention that targets parenting processes in order to reduce rates of anxiety in children with T1D. Addressing parental anxiety in this population has the potential to improve long-term health outcomes for children with T1D and their families.

Understanding the Molecular basis and Associated Genetic variants in Patients with a Hypoplastic Pancreas and Diabetes Mellitus

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Aim: To evaluate the aetiology of Diabetes Mellitus (DM) in young adults in Indians those presented with clinical and radiological feature of pancreatic diabetes.

Method: Eighty- One patients with young onset Diabetes mellitus who were negative for GAD-65 and IA2 Autoantibodies with imaging features of pancreatic structural abnormalities were included. They were divided into 4 groups based on the imaging features of pancreas into group with Classical Fibrocalcific pancreatic diabetes (FCPD), group with Atrophic pancreas, group with Dorsal agenesis and group with Lipomatosis. The genetic analysis was done using Inhouse Next generation sequencing technique (NGS) which included a 10 gene panel- peptide levels, the degree of malabsorption, pancreatic thickness and the other clinical features were also assessed.

Results: The genetic variants observed in the FCPD group were SPINK1 (commonest), CTRC, PRSS1, CaSR. Genetic variants such as PDX and RFX6 were positive in a few patients among the group with FCPD group.

In the group with the atrophic pancreas, none of them had a SPINK1 variant. However, PDX1 variants were most common variant, followed by the CTRC variants. CEL and HNF1B variants were the other genetic variants seen in the group with the atrophic pancreas.

Genetic profile of Dorsal agenesis of the pancreas differed from other groups with genetic variants positive for the genes involved in the development of the pancreas.

Clinical features, response to OADs, degree of exocrine insufficiency, associated systemic features are different in each of these forms of pancreatic DM.

Conclusion: Cross sectional imaging helps in evaluating the aetiology of DM in the young, who have negative GAD/IA2 and do not have features of Type 2 DM. Cross sectional Imaging along with genetic analysis helps us to differentiate between chronic pancreatitis, Dorsal agenesis, Pancreatic Lipomatosis, and the atrophic pancreas. Accurate diagnosis and differentiating between these entities have clinical, therapeutic, prognostic implications.

Understanding the Type 1 Diabetes models of care for Children and Young Adults in Australia: A mixed methods study of providers' perspectives.

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Abstract: The Juvenile Diabetes Research Foundation Global Centre of Excellence was established to study, develop and implement into practice optimal models of T1D care. This requires understanding what specific components of available models of care are currently being offered.

Aims: To identify currently offered models of care and model components offered to children and young adults living with T1D in Australia. To understand which components are functioning as intended and to identify opportunities for improvement from the perspective of service providers.

Methods: Providers from all major Australian T1D services were invited to complete a survey which was co-designed with T1D service providers and refined by a working group. Survey results were analysed in SPSS using descriptive statistics. Providers were also invited through the survey to participate in semi-structured interviews. Interview transcripts were deductively thematically analysed, and the main themes were synthesised by two analysts.

Results: Thirty-two T1D service clinicians (16 metropolitan; 16 from regional/rural areas) from all Australian states and territories completed the survey, and seven participated in an interview. In their interdisciplinary teams, the clinicians provided services included dieticians (94%), clinical nurse specialists (71%), general paediatricians (68%), and paediatric endocrinologists (61%). Eight clinics (29%) reported having a dedicated psychologist. Five (16%) services had links with their local primary health network (PHN). Themes emerging from the qualitative interview data suggest that providers felt they had skilled, cohesive teams that provide consistent care. However, concerns were expressed regarding staff shortages and limited access to psychologists.

Conclusion: The results reveal a clear gap in the current models of care components. Current T1D guidelines recommend that diabetes specific, psychological services be integrated into patient care and that services be linked to their primary health care network. Leveraging telehealth and strengthening linkages to psychological and wellbeing support services may address this gap.

Unmet Needs and Solutions for effective Type 2 Diabetes management reported by People with Lived experience: Results from a qualitative study.

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Aim: To identify the unmet needs of people with T2D and engage them in the co-design of effective self-management interventions. The prevalence of type 2 diabetes (T2D) is increasing worldwide and in Australia. Despite the efforts in healthcare and public health policy to tackle T2D, initiatives to support improved self-management have been unsuccessful, partly due to insufficient engagement of people with lived experience of T2D in developing and tailoring interventions to meet their needs.

Methods: Adults with T2D participated in two focus groups, and transcripts were coded in NVIVO14 (QSR International). Inductive thematic analysis was used to extract themes related to participants' unmet needs and proposed solutions for effectively self-managing their condition.

Results: Ten adults (3 females, 7 males; 58-78 years old) with T2D participated in two focus groups. Four main themes and 15 sub-themes were identified. Main themes were: (1) Misinformation; (2) Limited guidance; (3) Self-management; and (4) Prevention and Screening. Participants reported multiple unmet needs related to self-management, including maintaining motivation, managing T2D alongside other commitments, and mental health issues. They also reported feeling misinformed about self-management and noted a lack of guidance to address this misinformation from healthcare professionals and government organisations. Frequently participants resorted to using online or other information that was conflicting and untrustworthy. Those from culturally and linguistically diverse (CALD) backgrounds noted very limited information about diet that was relevant to their needs. Participants suggested multiple strategies for policymakers to address these unmet needs including training of primary care providers, boosting the role of diabetes nurse specialists, providing targeted mental health support, and working closely with CALD communities for culturally appropriate dietary information.

Conclusions: These findings are important, since they set the basis for consumer-driven intervention programs for the management of T2D, developed by people with T2D for people with T2D.

Unravelling the role of Renal Glycogen in Diabetic Kidney Disease

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Diabetes significantly alters tissue storage of glucose, as glycogen, including increased deposition in kidneys. Considering the contribution of kidneys to glucose homeostasis highlighted by the beneficial effects of SGLT2i, the role, distribution, and significance of kidney glycogen in diabetes and its impact on the development of kidney disease (DKD) warrants further investigation.

To investigate this, male kidney epithelial cell (Cadherin-16) -specific Gys1 homozygous knockout mice (n=3-8/group), were used for this study, with the wildtype variants as controls. Type 1 diabetes was induced via 5 x daily i.p. injections of low dose streptozotocin (STZ, 55 mg/kg/day). Mice were given standard chow and water ad libitum for 22 weeks before euthanasia.

WT diabetic mice had significantly lower body weight, worse blood glucose control (short-term, and long-term, with higher glycated hemoglobin levels and dysglycaemia during oral glucose tolerance tests and renal hyperfiltration assessed via measured Glomerular Filtration Rate (GFR, using FITC-sinistrin decay) as compared to WT non-diabetic group.

There were no significant differences between KO and WT diabetic groups in body weight, blood glucose control, or GFR. This may indicate that excess glycogen storage seen in the diabetic kidney does not directly impact blood glucose control and glomerular filtration rate in this model. Further studies of kidney structure and function are required to better elucidate the role of kidney glycogen in diabetes, whether it is beneficial, pathogenic, or inconsequential (as an indicator).

Unveiling the Digital Divide, Tech-driven improvements in Adolescent T1D Glycemic control but Rural patients lagging behind

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Introduction: Adolescents in Western Australia (WA) with T1D receive care through the Perth Children's Hospital (PCH) service; metropolitan patients within a dedicated adolescent clinic at PCH while those in regional/rural areas are managed within general (non-adolescent dedicated) outreach clinics. Technological advances have recently been introduced and become standard of care; wider access to continuous glucose monitoring (CGM) devices with national subsidy in 2017, and automated hybrid closed loop (aHCL) insulin pumps after this. Their use and impact on our adolescent cohort's glycaemic control is not clear.

Aim: To review glycaemic control of adolescents with T1D in WA, metropolitan and regional/rural, and the impact of each technological advance (CGM, aHCL).

Methods: Glycaemic data, HbA1c and CGM metrics, and utilisation of technology (CGM and aHCL insulin pump) of patients in regional/rural and metropolitan clinics across WA will be retrieved via the WA Children's Diabetes Database, for the years 2016, 2019 and 2023 (1st January to 31st December). These years are best able to review care prior to (2016) and after (2019) the widespread use of CGM, and combination with aHCL (2023).

Results: Significant improvement in HbA1c (mean ± SD, proportion <7%) between 2016 (8.7 ± 1.7, 10.7%) and 2023 (8.1 ± 1.8, 30.2%), $p < 0.001$. A gradient improvement with each advancement in technology, with the greatest improvement due to aHCL introduction, +13% target Hba1c (2019 to 2023).

Regional/rural clinics continually have a lower proportion target glycaemia, with this gap widening with each technological advancement, greatest in 2023, 7.9 ± 1.7, 35.5% and 8.2 ± 1.9, 27.8% (metropolitan and regional/rural respectively). The utilisation of CGM is comparable, however use of insulin pump and aHCL therapy is lower in regional/rural clinics.

Conclusion: Implementation of technology, particularly aHCL has seen significant improvement in glycaemic control for adolescents with T1D. Review of the non-adolescent dedicated regional/rural clinics is required, to determine ways to improve aHCL use and bridge the gap in glycaemic control with metropolitan services.

Use of Continuous Glucose monitoring in Young adults with Cystic Fibrosis-related Diabetes Mellitus - a pilot study

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Aims: Cystic fibrosis-related diabetes (CFRD) occurs in 20-30% of young people with cystic fibrosis (CF). Regular monitoring and early optimisation of glycaemic control is important to reduce associated morbidity and mortality. This is a pilot study to determine uptake, tolerability and utility of continuous glucose monitoring (CGM) in young adults with CFRD.

Methods: In a dedicated CF Endocrine Clinic, people under 21 years of age with insulin-requiring CFRD were offered CGM in addition to standard care, with comparison made to standard care alone. Outcomes were HbA1c and diabetes distress measured by the Problem Areas in Diabetes (PAID) scale over 3 months.

Results: Ten of 14 potential participants consented to study enrolment (median age 20 years, eight male, median diabetes duration seven years). Three participants commenced CGM. Amongst all participants, baseline median HbA1c was 5.9% (IQR 5.7-6.9) and median PAID score was 2.5 (IQR 0.3-8.8), consistent with minimal diabetes distress. At three months, median HbA1c was 6.4% (range 6.1-8%) in CGM users (n=3) and 6.0% (range 5.6-7.5%) in the standard care group (n=5). PAID score improved in 2 of 3 CGM users and 1 of 3 standard care recipients. Barriers to CGM use included pre-existing satisfactory glycaemia, desire to avoid further medical devices and future cost concerns.

Conclusions: Young people with insulin-requiring CFRD were reluctant to trial CGM and reported multiple barriers to engagement with diabetes technology.

Use of, time to, and type of first add-on Anti-hyperglycaemic Therapy to Metformin in Australian Clinical practice, 2018-2022

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Abstract title (max. 25 words):

Aim: To examine contemporary trends in the use of, time to and type of first add-on anti-hyperglycaemic therapy to metformin in Australia.

Method: We used the dispensing records of a 10% random sample of Pharmaceutical Benefits Scheme eligible people. We included people aged 40 years and older initiating metformin from 01/01/2018 to 31/12/2020. Our primary outcome was first add-on anti-hyperglycaemic medicine within two years of metformin initiation. We analysed time to dispensing of first add-on therapy. All analyses were stratified by year of metformin initiation.

Results: Overall, 38,747 people aged 40 years and older initiated metformin between 2018 and 2020. Approximately one-third (N=12,946) people received add-on therapy with the proportion increasing slightly by year of metformin initiation (32.3% in 2018 to 34.8% in 2020). Amongst people with add-on therapy, sodium-glucose cotransporter 2 inhibitors (SGLT2i) use increased from 28.8% in 2018 to 35.0% in 2020, and glucagon-like peptide-1 receptor agonists (GLP-1 RA) increased from 3.0% to 9.6%, respectively. Dipeptidyl peptidase-4 inhibitors and sulfonylureas as first-add on therapy decreased and insulin remained stable. The median time to add-on therapy was approximately two months with one-third of people with add-on therapy, initiating the therapy on the same day metformin was initiated.

Conclusion: Amongst people initiating metformin from 2018 to 2020, there was an increasing proportion of SGLT2i and GLP-1 RA being used as first add-on therapy. However, given the overall low prevalence of add-on therapy, increasing the proportion of people with add-on therapy specifically with medicines with cardiorenal benefits is critical. Given the popularity of initial combination therapy with metformin in our study, this approach should undergo review by the government to determine whether removing the need for failure on metformin or a sulfonylurea to enable subsidisation for an SGLT2i or GLP-1 RA is cost-effective.

Utilising CSII Hybrid closed-loop system to improve Glycaemic control in a complex patient with MODY 5 Diabetes, Eating disorder and Percutaneous Endoscopic Jejunostomy (PEJ) feeding.

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MODY is a monogenic non-autoimmune form of diabetes typically presenting in non-obese young adults, of age <25 years. MODY-5 is caused by an autosomal dominant mutation in the HNF 1b gene. Commonly this results in renal cysts and diabetes syndrome.

We report the case of a 41-year-old Caucasian lady with MODY-5 diabetes, who was diagnosed in her mid-20s. Recurrent DKAs (Diabetic ketoacidosis) and prolonged hospital admission with eating disorder, electrolyte imbalances and urinary tract infections were key issues. Her diabetes is further complicated by the sequence of diabetic Tripathy. She also has complex psychosocial issues with recent long-term overseas stay in a country with suboptimal health care facilities, domestic violence, depression and most recently PTSD with carer burnout.

Following a 3-month admission due to carer fatigue, deteriorating mental health, negligible oral intake in the context of eating disorder with further weight loss and dangerously low BMI (13Kgm^2) the management of her weight and general well-being became critical. PEJ feeding began under a guardianship order. Following PEJ feeding the management of her diabetes became significantly challenging. LIBRE 2 Continuous Glucose Monitoring (CGM) revealed significant glycaemic variability.

An Endocrine Nurse Practitioner proposed using CSII system with augmented basal (Medtronic 780-G CGM Smart-Guard) with predictive control, then this was commenced in domiciliary setting. A dearth of literature around prescription of algorithms suitable for this CSII start was a limitation.

Initially, the technology was met with extreme patient resistance, now the patient is mostly self-managing the system and averaging over 60 % Time in Range without hypoglycaemia and carer fatigue has been significantly reduced.

We report a complex case of MODY 5 diabetes with multiple complications, including psychosocial issues and eating disorder. According to literature, this is first case to support the use of this CSII system in such patients.

Vitamin C, vitamin D and zinc Deficiencies in Patients with Active Foot Wounds

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Diabetes-related foot ulceration (DFU) are a common complication of diabetes, peripheral neuropathy, and ischemia. Vitamin C, vitamin D and zinc are essential micronutrients that support immune function and play a critical role in tissue repair. However, the impact of these nutrients on healing of foot ulcers is unclear. This study aimed to determine the relationship between serum vitamin C, vitamin D and zinc on DFU healing in adults and compare time to healing in individuals who are deficient in these micronutrients to those who have adequate levels.
One hundred adults with active foot wounds were recruited from Blacktown high risk foot service. Serum vitamin C, D and zinc as well as routine baseline blood testing was undertaken. Wounds were measured using a three-dimensional wound camera and classified using the WIfI system. People were followed for 12 months or complete ulcer healing, whichever occurred sooner.
Vitamin C deficiency (<40µmol/L) was present in 75% of participants, 50% had vitamin D deficiency (<50nmol/L) and 38% had zinc deficiency (<10.7µmol/L). Wound chronicity and toe blood pressures were predictive of wound healing at 6 and 12 months. Vitamin C, vitamin D and zinc were not associated with differences in wound healing, or time to healing. There was a relationship between both vitamin C deficiency and zinc deficiency and history of a previous amputation. Increased severity of WIfI scoring was significantly correlated with a zinc deficiency. Deficiency in serum zinc was significantly correlated with increased C-Related Protein (CRP) levels.
This cohort had very high deficiency rates of vitamin C, D and zinc, however we did not identify any relationship between these deficiencies and wound healing. However, only 13 people had normal results for all nutrients, making that analysis underpowered. Randomised controlled trials of supplementation may determine if adequate levels of these nutrients improve wound healing outcomes.

VPS41 controls insulin content in pancreatic beta-cells

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Background: Vacuolar Protein Sorting Protein 41 (VPS41) was originally identified in secretory neuroendocrine cells as a genetic contributor to neurological defects associated with impaired lysosomal function. In pancreatic beta-cells, our lab has found that specific deletion of VPS41 in beta-cells of mice results in reductions in insulin secretion and insulin content.

Aim: Investigate how loss of VPS41 in beta-cells results in impaired insulin secretory function.

Methods: Proteomics of VPS41KO and VPS41KD INS1 cells, and islets from beta-cell specific VPS41KO mice were performed to uncover cellular pathways contributing to defects in the insulin secretory pathway.

Results: *In vivo,* loss of VPS41 in beta-cells is associated with dysregulated autophagy pathways, resulting in increased ER stress specifically in male mice. Chronic deletion of VPS41 in VPS41KO INS1 cells drives dedifferentiation of beta-cells and downregulation of insulin synthesis. Acute deletion of VPS41 in VPS41KD INS1 cells results in increased lysosomal degradation of mature insulin.

Conclusions: VPS41 is a regulator of the insulin secretory pathway, and a necessity for the maintenance of insulin content in beta-cells.

Which Type 1 Diabetes (T1D) guidelines, technologies and insulin regimens are used to manage T1D in Australian children? A survey of clinicians

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In addition to type 1 diabetes (T1D) guidelines released by the International Society for Pediatric and Adolescent Diabetes (ISPAD) and the New Zealand Society for Paediatric Endocrinology and Diabetes (ANZSPED), state-based and local hospital-based guidelines may also be used in practice. Furthermore, it is unclear to what extent shared care and sick-day plans, and T1D technologies are routinely used to manage T1D in children.

Aims: To describe the guidelines applied in clinical practice, use of T1D technologies and insulin regimens used in Australia.

Methods: Providers from T1D services completed an on-line survey which was co-designed with an interdisciplinary working group. Questions included guideline usage, developing shared care and sick day plans, use of continuous glucose monitors (CGM) and insulin pumps. Results were analysed in SPSS.

Results: Thirty-two T1D clinicians (16 metropolitan; 16 regional/rural) from all Australian states and territories completed the survey. A combination of local and state-based guidelines were used. Less than half (20-47%) indicated that their guidelines aligned with the ANZSPED guidelines. Twenty-one services (65%) developed shared-care plans, with access given to the patient/family (53%), general practitioners (47%), or with referral to other health providers (34%). Only 44% provided their patients with sick-day plans. The majority (78%) offered CGM within one month of diagnosis and most (78%) used hybrid closed loop pump systems; 34% routinely used insulin injection regimens. Providers from rural regions reported significantly lower proportions of patients in range > 70% of the time ($P<0.05$).

Conclusions: There is variation in the use of guidelines, shared care and sick day plans. CGM and hybrid closed loop pump systems are offered routinely by the majority of services. A more nuanced analysis of these results is progressing to identify contextual factors associated with variation in practice.

Younger-onset Type 2 Diabetes: UK Prospective Diabetes Trial (UKPDS) 30-Year Follow-Up

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Background: Younger-onset type 2 diabetes (T2D) is associated with accelerated complications. We assessed whether complications and mortality rates differed for younger compared with older age at diagnosis over 30-years of follow-up in the UKPDS.
Methods: Using 1977-2007 data from UKPDS participants aged 25–65 years with newly-diagnosed T2D with younger- (<40 years) or later-onset (≥40 years), and without diabetes autoantibodies, we analysed standardised mortality ratios (SMR) using UK general population data, and incidence rates of pre-specified outcomes by 10-year age intervals at diagnosis.
Results: Of 4550 participants (59% male, mean HbA_{1c} 9.1%) testing negative to all measured autoantibodies, 429 (9·4%) had younger-onset T2D. Their SMR was higher (3·72, 95% CI 2·98-4·64; median follow-up: 18·0 years) compared with later-onset T2D (1·54, 1·47-1·61; median follow-up: 17·4 years). When stratified by 10-year cohorts of age at diagnosis, the SMR was highest at 3·85 (2·62-5·66) in the youngest group diagnosed with T2D between 24-35 years of age and attenuated with increasing age at diagnosis. The absolute incidence rate was higher for all outcomes in later-onset T2D, except for microvascular disease [14·5 (younger-onset) vs 12·1 (later-onset) per 1000-person years]. However, at any given age, the 5-year incidence of any diabetes-related endpoint, all-cause mortality, microvascular disease, and myocardial infarction was higher with younger age at diagnosis. Annual mean HbA_{1c} was higher in the first 20 years in younger-onset compared with later-onset T2D. Among participants randomised to intensive vs. conventional glycaemic control, we observed no interactions by subgroup of younger- vs. later-onset T2D for any outcome.
Conclusion: The risk of dying relative to the general population is even greater for people diagnosed with T2D at younger ages. The increased risk of complications and poorer glycaemic control in younger-onset T2D supports developing services to identify and manage these individuals over their lifetimes.