

Adrenal tuberculosis causing Addison's disease - a case report

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Background/Introduction:

Primary insufficiency of the adrenal glands is mostly caused by autoimmune reactions in the Western world (i.e. Morbus Addison). But also other diseases may cause adrenal insufficiency (i.e. Addison's disease), and in developing countries tuberculous adrenalitis remains a dominant cause. We describe an otherwise healthy man who presented with typical signs of primary adrenal insufficiency which was caused by tuberculosis.

Methods:

Case report

Results:

A 49-year old man, originally from Sri Lanka (living in Switzerland for 31 years), presented to his general practitioner with nausea, fatigue, sleep disorders, and weight loss for one year. Clinical examination showed hyperpigmentation of the neck, palms, and oral mucosa. Blood sodium (135mmol/l) and basal cortisol levels (147nmol/l) were in the lower range of normal, the latter with an inadequate rise after stimulation with ACTH (147nmol/l, cutoff 500nmol/l). Renin (335.8mU/l, UNL: 46.1mU/l) and ACTH (1317ng/l, UNL: 48.8ng/l) were elevated. Autoimmune antibodies specific for M.Addison were negative. Abdominal CT showed bilateral nodular enlargement and calcifications of the adrenal glands, as well as non-specific mesenterial, mediastinal and axillary lymphadenopathy. CT-guided biopsy of an adrenal gland and fine needle aspirations of axillary lymph nodes showed necrotizing granulomatous inflammation but no pathogen, neither in pathogen-specific staining, nor in molecular-based diagnostics (PCR) and culture. The interferon-gamma release assay (IGRA), urinary histoplasma antigen and serologies for syphilis and HIV were negative. Only excision of an axillary lymph node led to the final diagnosis of adrenal tuberculosis with a positive PCR and culture for *Mycobacterium tuberculosis*.

Conclusion:

Bilateral adrenal tuberculosis is a rare cause of primary adrenal insufficiency. In patients originating from endemic areas for tuberculosis, having negative autoantibodies but typical radiological and histopathological findings for adrenal tuberculosis, identification and susceptibility testing of the causing pathogen are important, as resistant *M. tuberculosis* is increasing worldwide. A negative IGRA never excludes active tuberculosis, therefore tissue sampling is essential.

Microwave Ablation for the Treatment of Amiodarone Induced Thyrotoxicosis: Case Report

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Background/Introduction: Amiodarone-induced thyrotoxicosis (AIT) is a thyroid dysfunction induced by amiodarone, an antiarrhythmic drug. The incidence of AIT varies widely, ranging from 0.003% to 10%. Type 1 AIT is a form of hyperthyroidism that occurs in patients with a pre-existing thyroid disease (goiter or latent Graves' disease) due to excessive thyroid hormone production by autonomous thyroid tissue exposed to the iodine load. Type 2 AIT develops in an otherwise normal thyroid gland and is caused by a destructive, toxic effect of amiodarone on thyroid tissue. Type 1 AIT is usually treated with antithyroid drugs (ATD), whereas type 2 AIT is treated with high dose of corticosteroids. However, mixed or unclear forms are not uncommon, and they can be treated with a combination of ATD and glucocorticoids. Sometimes AIT may be refractory to medical treatment. Other possibilities for the definitive treatment include radioiodine treatment (for type I, but only after several months after amiodarone withdrawal) and thyroidectomy. As these patients are often at high anesthesiologic risk due to the cardiac comorbidities, alternative treatments have been studied, and a treatment by radiofrequency ablation was suggested by investigators at Mayo Clinic in 2018 ([Study Details | Radiofrequency Ablation for Amiodarone-induced Thyrotoxicosis | ClinicalTrials.gov](#)). This trial was terminated due to very low enrollment.

Case presentation: We describe the case of a 56-year-old woman with heart failure with reduced ejection fraction (HFrEF), secondary to valvular, arrhythmic, and ischemic etiologies, and a prior cardiac arrest requiring implantation of an implantable cardioverter-defibrillator (ICD). She presented with thyrotoxicosis developed while under amiodarone treatment. AIT type 2 was suspected but due to cardiac instability she was initially treated with prednisone and carbimazole. Given the cardiac comorbidities, prednisone worsened cardiac decompensation and every attempted dose lowering was followed by a worsening of thyrotoxicosis. Due to persistent and clinically significant thyrotoxicosis, and the high risk associated with general anesthesia and potential complications of thyroidectomy, we discussed a thermal ablation. Since the patient is carrying an ICD, microwave ablation was chosen over radiofrequency ablation, which could potentially interfere with the device. Thermal ablation was performed in two sessions, first on the left thyroid lobe, achieving approximately 70% of devascularization, and 3 weeks later a second one, resulting in an almost complete devascularization of the right thyroid lobe and the isthmus.

Results: At presentation, free T3 was 8.36 pmol/L and free T4 was 56 pmol/L. Clinically, the patient presented with symptomatic ventricular bigeminy and trigeminy, accompanied by a new episode of heart failure. Just prior to the first thermal ablation session, free T3 was 12.1 pmol/L and free T4 was 72 pmol/L. Twelve days after the second thermal ablation session, free T3 had normalized (6.8 pmol/L) and free T4 had decreased to 36 pmol/L. Microwave ablation of the thyroid tissue allowed a progressive reduction of pharmacological treatment. No recurrence of arrhythmia is noted, and the patient reports an improvement of her general condition following the second thermal ablation session.

Conclusion: Microwave ablation of thyroid tissue represents an alternative treatment option for AIT in patients with compromised cardiac function in whom high-dose prednisone is contraindicated or not tolerated.

Temozolomide as an Alternative Treatment for Aggressive Pituitary Tumors: A Case Series

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Background/Introduction:

Aggressive pituitary tumors (APTs) are rare but challenging entities due to their invasive behavior and resistance to conventional treatment. While most pituitary adenomas are effectively managed by surgery with or without medical therapy, APTs may require alternative strategies. Temozolomide (TMZ), an alkylating agent used in brain tumors, has emerged as a salvage treatment in APTs after failure of standard modalities. The aim is to evaluate the efficacy and safety of TMZ in patients with APTs treated in our institution.

Methods:

Seven patients with histologically confirmed APTs (Trouillas grades 1b, 2b, or 3) were treated with TMZ at a dose of 150–300 mg/m²/day for 5 days every 4 weeks. All tumors were invasive (Knosp grade 4 on at least one side) and classified radiologically as giant in six cases. Immunohistochemistry included Ki-67 and MGMT expression. Tumor response was assessed using RANO (Response Assessment in Neuro-Oncology) criteria.

Results:

The cohort included two females and five males (mean age: 46 years, range: 31–71). Tumor types were: 4 non-functioning adenomas, 2 prolactinomas, and 1 somatotropinoma. Trouillas grading showed five cases of grade 2b, one grade 1b, and one grade 3. Ki-67 index was >3% in six patients. TMZ was administered for 6 to 71 cycles (mean: 40). It was indicated after surgery and / or radiotherapy in all patients. The treatment was generally well tolerated. One case of transient thrombocytopenia and one case of myelodysplastic syndrome (MDS) after prolonged exposure (71 cycles) were recorded; the latter led to patient death. RANO evaluation showed stable disease in all patients over a mean follow-up of five years. Two additional deaths occurred: one from tumor progression and one from stroke.

Conclusion:

Temozolomide appears effective in stabilizing tumor progression in aggressive pituitary adenomas, including giant and invasive forms. However, long-term use may lead to serious adverse effects such as MDS. Careful patient monitoring, dose adjustment, and limiting cumulative exposure are essential to minimize toxicity while maintaining therapeutic benefit.

Mild Androgenic insensitivity syndrome - a case report

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Background/Introduction:

Androgen insensitivity syndrome is a common cause of sexual development disorders in individuals with a 46,XY karyotype. It is caused by mutations in the X-linked androgen receptor (AR) gene, resulting in variable resistance to androgens and a spectrum of phenotypes: complete (CAIS), partial (PAIS), and mild (MAIS) forms. Unlike complete or partial forms, MAIS is associated with minimal to no genital ambiguity and normal male secondary sexual characteristics, but with evidence of androgen receptor dysfunction. Due to the subtle clinical presentation, MAIS is often underdiagnosed or misinterpreted as idiopathic male infertility. Diagnosis is confirmed by genetic testing revealing pathogenic variants in the AR gene, often in combination with hormonal profiles indicative of androgen resistance. Early recognition is essential to guide appropriate management and genetic counseling.

Methods:

We describe the clinical presentation, laboratory and genetic findings of a patient with MAIS

Results:

We introduce a 54-year-old patient who presented for osteological evaluations after multiple vertebral body fractures following inappropriate traumas. Laboratory findings showed a total Testosterone of 37nmol/l, free Testosterone 116nmol/l, SHBG of 82.3nmol/l with normal FSH and slightly elevated FSH of 9.4U/l. Assay interference was ruled out by confirming the results in three different laboratories. History taking revealed normal pubertal development. In addition, clinically no signs of hypogonadism with preserved fertility (father of 2 children). The laboratory constellation led to suspicion of mild androgen insensitivity syndrome. The genetic clarification confirmed the detection of a probable pathogenic, hemizygous missense variant in the AR gene, c.2382G>C p.(Glu794Asp). The patient has a monozygotic twin brother with similar laboratory findings, but genetic testing was not performed in this case yet.

Conclusion:

This case demonstrates the subtle presentation of MAIS and highlights the diagnostic value of AR gene analysis. Mild androgen insensitivity syndrome should be part of the differential diagnosis in males with unexpectedly high testosterone levels and near-normal gonadotropins, in those with infertility or even in the absence of hypogonadal features. Early genetic diagnosis can guide appropriate management, avoid unnecessary investigations, and facilitate family counseling.

Observational Study for Digital Biomarker Development in Prediabetes Screening and Lifestyle Phenotyping: A Study Protocol of the GLOW UP Study

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Background:

The Glucose Observation and Wearable Use for Prevention (GLOW UP) study investigates the potential of wearable-derived lifestyle data, including physical activity, sleep, nutrition, and stress, for identifying individuals with prediabetes and understanding lifestyle phenotypes. The primary aim is to assess whether real-world data from commercially available wearables and smartphones can predict prediabetes, as defined by Fasting Plasma Glucose (FPG) and Hemoglobin A1c (HbA1c). By leveraging continuous lifestyle and glucose monitoring in free-living conditions, the study seeks to inform scalable, data-driven approaches to early detection and prevention of type 2 diabetes (T2D).

Methods:

This is a single-center, prospective, case-control study involving 200 adults aged ≥ 45 years with a BMI > 25 kg/m², recruited in Switzerland. Participants are classified as individuals with prediabetes or metabolically healthy controls based on baseline FPG and HbA1c levels. Over 4 weeks, participants undergo continuous lifestyle monitoring via a fitness tracker and image-based dietary logging through a smartphone app, in conjunction with blinded continuous glucose monitoring (CGM). Baseline and follow-up measures of FPG, HbA1c, BMI, and visceral fat are collected. Predictive modeling using machine learning techniques (e.g., logistic regression, random forests, gradient boosting methods) will assess the performance of wearable-based features in classifying individuals with prediabetes. Secondary analyses will explore within- and between-person relationships between lifestyle behaviors and CGM-based glucose dynamics.

Results:

The primary outcome is the predictive performance (AUC, sensitivity, specificity) of wearable- and smartphone-derived lifestyle metrics in predicting prediabetes (vs. controls). Secondary outcomes include the prediction of time-varying CGM metrics (e.g., postprandial glucose excursions) and the evaluation of lifestyle patterns across metabolic phenotypes (derived from FPG, HbA1c, BMI, and visceral fat). Findings will elucidate which lifestyle factors most influence glucose regulation and offer insights into metabolic variability at the individual level.

Conclusions:

GLOW UP is among the first studies in Switzerland to integrate consumer-grade wearables, image-based diet tracking, and CGM with clinical biomarkers in a real-world setting. It aims to advance the development of digital biomarkers for the early detection of metabolic risk. Insights from this study will inform personalized, low-burden, and scalable strategies for T2D prevention, contributing to digital health innovation and public health efforts in Switzerland and globally.

Novel deuterium metabolic imaging technique reveals distinct patterns of postprandial hepatic glucose homeostasis in patients with type 1 diabetes and healthy controls – a case control study.

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Background/Introduction:

Subcutaneous (SC) insulin delivery in insulin-deficient type 1 diabetes bypasses the portal circulation, disrupting the physiological porto-systemic insulin gradient, affecting postprandial hepatic glucose regulation. However, direct, non-invasive measurement of these liver-specific dynamics in type 1 diabetes and their deviation from normal physiology has been challenging. To address this, we integrated metabolic imaging coupled with whole-body tracer dilution to map postprandial glucose metabolism both in the liver and systemically in adults with type 1 diabetes and healthy controls.

Methods:

In this cross-sectional study, ten adults with type 1 diabetes and ten age-, BMI-, and sex-matched healthy controls were enrolled. After an overnight fast, participants ingested 60 g of [6,6'-²H₂]-glucose (D-Glc); insulin was administered subcutaneously in type 1 diabetes as needed. Interleaved Deuterium Metabolic Imaging (DMI) and ¹³C-Magnetic Resonance Spectroscopy (¹³C-MRS) at 7T were performed from pre-ingestion to 150 min post-ingestion to quantify hepatic D-Glc and glycogen. Blood samples were collected to measure plasma glucose, insulin, and glucagon. Endogenous and D-Glc fluxes were estimated using a single tracer model, and glucose-insulin dynamics were derived using an adapted Single Tracer Oral Minimal Model accounting for non-steady-state insulin exposure.

Results:

At baseline, type 1 diabetes patients had significantly higher plasma glucose concentrations (10.7 ± 2.3 vs. 5.2 ± 0.4 mmol/l, $p < 0.001$), while pre-prandial glycogen levels did not differ significantly. Following D-Glc administration, hepatic D-Glc increased more markedly in the type 1 diabetes vs. control group (peak value: 4.7 ± 2.0 vs. 3.0 ± 0.8 mmol/l, $p = 0.02$). In the postprandial period, glycogen levels did not significantly rise at 150 min in type 1 diabetes, whereas a clear increment was observed in controls (iAUC₀₋₁₈₀ = 2.4 mol/l*min). Despite similar systemic insulin exposure and no significant differences in postprandial glucagon concentrations between groups, type 1 diabetes subjects demonstrated significantly reduced suppression of endogenous glucose production (EGP, $p = 0.001$), but similar insulin-dependent glucose disposal. Hierarchical clustering identified two distinct type 1 diabetes subgroups: Subgroup 1 exhibited a steeper increase in both hepatic and systemic D-Glc profiles, while Subgroup 2 showed a divergent D-Glc trajectory and net glycogen depletion relative to accumulation in Subgroup 1 (iAUC₀₋₁₈₀ = -3.0 vs. 2.5 mol/l*min, $p = 0.04$), despite no overt clinical differences between subgroups.

Conclusion:

By integrating interleaved DMI/¹³C-MRS liver imaging with systemic stable isotope modelling, this comparative study demonstrates significantly altered hepatic glucose metabolism in well-controlled adults with type 1 diabetes versus matched controls, alongside substantial phenotypic heterogeneity within the type 1 diabetes cohort. These findings highlight the potential of non-invasive metabolic phenotyping to resolve metabolic alterations and inter-individual variation in type 1 diabetes, essenti

Finerenone Treatment in Patients with Type 2 diabetes and Chronic Kidney Disease in Tertiary Care in Switzerland

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Background/Introduction:

Finerenone is a relatively new treatment option for chronic kidney disease in type 2 diabetes with beneficial effects on kidney (FIDELIO-DKD trial) and cardiovascular (FIGARO-DKD trial) outcomes. Finerenone was approved in Switzerland in 2021 and listed on the Swiss specialties list in 2023, with reimbursement criteria based on the FIDELIO-DKD trial. Data regarding the use of finerenone in Switzerland are lacking. The aim of this study was to assess the eligibility for treatment with finerenone according to the Swiss specialties list, the FIDELIO-DKD, and the FIGARO-DKD trial criteria, as well as the current use of finerenone in Switzerland.

Methods:

This is a multicentre, retrospective, cross-sectional study assessing patients with type 2 diabetes from two cohorts: the SwissDiab registry and two outpatient clinics in Lausanne. Descriptive data include demographic, clinical, and laboratory parameters. The primary outcome is the number and characteristics of eligible patients. Secondary outcomes are number and characteristics that are not eligible, but were included in the FIDELIO-DKD and FIGARO-DKD trial, and number and characteristics of patients that are already treated with finerenone.

Results:

Preliminary results include data from the Lausanne cohort. Among 741 patients, 104 (14.0%), 79 (10.7%), 120 (16.2%) are eligible for treatment with finerenone according to the Swiss specialties list, the FIDELIO-DKD, and the FIGARO-DKD criteria, respectively. Mean age, sex, BMI, and blood pressure were similar across the different groups. Mean (\pm SD) HbA1c, eGFR, urinary albumin to creatinine ration, and maximum serum potassium were $7.2 \pm 1.5\%$, 45 ± 12 ml/min/1.73m², 78 ± 12.5 mg/g, and 4.5 ± 0.4 mmol/L (Swiss specialties list); $7.7 \pm 1.4\%$, 47 ± 11 ml/min/1.73m², 16 ± 13 mg/g, and 4.4 ± 0.3 mmol/L (FIDELIO-DKD); and $7.6 \pm 1.7\%$, 60 ± 18 ml/min/1.73m², 13 ± 11 mg/g, and 4.3 ± 0.4 mmol/L (FIGARO-DKD), respectively. Differences were seen in pretreatment with medications. Use of SGLT2 inhibitors was 26 (25%), 39 (49%), and 60 (50%), and use of renin-angiotensin system blockers was 80 (76.9%), 60 (76%), and 95 (79%) for the Swiss specialties list, FIDELIO-DKD, and FIGARO-DKD criteria. Of eligible patients, only 18 (17.3%, Swiss specialties list), 10 (13.0%, FIDELIO-DKD), and 14 (12.0%, FIGARO-DKD) patients are currently treated with finerenone.

Conclusion:

Number and characteristics of patients eligible for treatment with finerenone vary according to different criteria. Despite a significant proportion of patients with type 2 diabetes meeting eligibility criteria for finerenone treatment, actual numbers of patients remain low, suggesting a potential gap between clinical trial-based eligibility and real-world practices.

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Real-World Performance of the Omnipod® 5 Automated Insulin Delivery System in Children, Adolescents, and Adults with Type 1 Diabetes in Germany

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Background/Introduction:

The Omnipod® 5 Automated Insulin Delivery (AID) System, which allows for personalized therapy through customizable glucose targets from 6.1-8.3mmol/L in 0.55mmol/L increments, is CE marked for use in individuals ages two years and older with type 1 diabetes (T1D) and is commercially available in some European countries. This study aimed to evaluate the real-world performance of the system in children, adolescents, and adults in Germany.

Methods:

A retrospective analysis of continuous glucose monitoring (CGM) and insulin data from Omnipod 5 users with T1D aged ≥ 2 years in Germany who provided consent (guardian provided consent for those aged < 18 years) was conducted for those with sufficient CGM data (≥ 30 days of data with ≥ 1 reading and $\geq 75\%$ of days with ≥ 220 readings) between December 1, 2024 to May 20, 2025. Results are shown as median.

Results:

Data from 18,056 users (32% aged 2 to 17y; 68% aged ≥ 18 y) meeting the inclusion criteria were included in the analysis. Adult users ($n=12,234$) achieved a time in target range (TIR; 3.9-10.0 mmol/L) of 71%, 66%, and 57% with use of the 6.1 mmol/L, 6.7 mmol/L, and 7.2-8.3 mmol/L targets, respectively, with minimal time below range (TBR; < 3.9 mmol/L) (1.1%, 0.9%, and 0.6%, respectively). Across glucose targets, pediatric users ($n=5,822$) achieved a similar TIR and TBR, with a TIR of 66%, 66%, and 65% with use of the 6.1 mmol/L, 6.7 mmol/L, and 7.2-8.3 mmol/L targets, respectively, and a TBR of 1.6% with each glucose target. Use of the lowest target (used by 54% of the study sample) was associated with higher TIR with some age-related variability (2-5y: 68% [$n=105$]; 6-12y: 69% [$n=1,169$]; 13-17y: 64% [$n=1,540$]; 18-25y: 65% [$n=1,217$]; 26-49y: 71% [$n=3,690$]; 50-64y: 73% [$n=1,683$]; ≥ 65 y: 77% [$n=375$]). Across all age groups, use of the lowest target was also associated with higher time in tight range (3.8-7.8 mmol/L; 41-49%), low TBR (0.9-2.3%), and a high percentage of time spent in Automated Mode (94-97%).

Conclusion:

Collectively, these results in $> 18,000$ children, adolescents, and adults with T1D in Germany demonstrate that favorable glycemic outcomes are achievable with real-world Omnipod 5 use and support that users seeking to further improve TIR should consider decreasing their glucose target toward the lowest setting whenever possible.

Paraneoplastic Cushing syndrome in acinar cell carcinoma

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Background/Introduction:

Acinar cell carcinoma of the pancreas is a rare malignant tumor, accounting for about 0.2–4.3% of all pancreatic cancers. This tumor differs from the more common pancreatic ductal adenocarcinoma in terms of its epidemiology, molecular characteristics, and clinical behavior. A rare aspect of acinar cell carcinoma is its potential to exhibit endocrine differentiation and secrete ectopic adrenocorticotrophic hormone (ACTH). This ectopic ACTH production can lead to Cushing's syndrome, which is characterized by hypercortisolism, hypokalemia, and various metabolic disturbances. Such occurrences are extremely rare and are usually associated with a more aggressive clinical course and poor prognosis. Immunohistochemical analysis is necessary to confirm the production of ACTH by the tumor cells.

Methods:

Case report on a rare ACTH-producing acinar cell carcinoma

Results:

Emergency presentation of a 76-year-old patient with pancreatic acinar cell carcinoma (ED 04/2023) due to hypertensive crises and hypokalemia of 2.5 mmol/l.

Despite the establishment of 5x antihypertensive therapy inadequate blood pressure control was still found. Screening for secondary forms of hypertension detected Hypercortisolism (morning cortisol 1700 nmol/l, urine cortisol > 1180 ug, midnight salivary cortisol 607 nmol/l). ACTH was detectable at 25 ng/l. Primary aldosteronism and a pheochromocytoma could be ruled out. Clinical signs of cortisol excess developed rapidly (myopathia, edema, weight gain).

Treatment with osilodrostat was initiated up to 2x 5 mg/d. However no significant reduction of morning cortisol could be achieved.

A CT Scan showed extensive tumor progression with nodal, hepatic and peritoneal metastasis. A fine-needle biopsy of cervical lymph nodes finally revealed malignant cells with acinar and neuroendocrine expression with positivity for BCL-10 and synaptophysin.

Due to paraneoplastic ACTH-dependent hypercortisolism and tumorprogression a second-line chemotherapy with Gemcitabine was initiated. Treatment was discontinued after only one cycle because of the poor general condition and best supportive care was established.

Conclusion:

Acinar cell carcinoma of the pancreas are typically exocrine tumors but can show mixed or focal neuroendocrine features. Synaptophysin positivity in tumor cells supports the diagnosis of a neuroendocrine origin responsible for ectopic ACTH production leading to paraneoplastic Cushing syndrome.

Congenital adrenal hyperplasia, Addison's disease and OARTs: coincidence or consequence?

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Background/Introduction:

Congenital adrenal hyperplasia (CAH) is a genetic disorder caused by enzyme deficiencies in the adrenal glands, leading to impaired cortisol and overproduction of androgens. In Addison's disease, primary adrenal dysfunction results in deficiency of glucocorticoids and, sometimes, mineralocorticoids. Both cause similar hormonal deficiencies and treatment is glucocorticoid replacement, but their management differs, and co-occurrence is rarely reported. Ovarian adrenal rest tumors (OARTs) consist of ectopic adrenal tissue and are very rare in women in CAH, while their equivalent in CAH men, testicular adrenal rest tumors (TARTs), have a prevalence of around 40%. They are associated with poor CAH control and stimulation through high ACTH.

Methods:

Case study and literature review.

Diagnostics: In 2014, a 25-year-old patient was referred with unfulfilled desire to conceive, oligomenorrhoea, hirsutism and clitoromegaly. A transvaginal ultrasound revealed bilateral ovarian lesions (left 4 x 2 x 1.5 cm; right 2 x 2 cm), later confirmed through MRI, as well as enlarged adrenal glands. Diastolic blood pressure was elevated, laboratory testing showed normal electrolytes and low cortisol (82 nmol/l [80-638]), however the patient had no clinical signs of hypocortisolism. Further evaluation showed: testosterone 12.1 nmol/l [0.3-1.7], DHEA-sulfate 3.99 μ mol/l [1.7-9.7], androstendione^o >35.0 nmol/l [2.0-9.0], aldosterone 47 pmol/l [32-654], renin 0.6 ng/l [1.7-23.9], 17-OH-progesterone (stimulated) 19.4 nmol/l [<43], 11-desoxycortisol^o >180 nmol/l [<12], ACTH 2008.0 pg/ml [<46.0]. We diagnosed CAH with 11- β -hydroxylase deficiency and OARTs.

Results:

Glucocorticoids were initiated to control androgen excess. Subsequently she became pregnant spontaneously in 2017. After delivery, glucocorticoids were discontinued; nevertheless, she became pregnant again and now has two healthy sons.

In 2021, she presented with severe fatigue and low blood pressure of 92/61 mmHg (heart rate 69/min). Androgens were almost unmeasurable and cortisol very low. She was diagnosed with an Addisonian crisis and substitution with hydrocortisone was started. 21-hydroxylase antibodies were positive (1.2 U/ml [<0.4]), suggesting autoimmune origin. In 2022, aged 32 years, she presented with premature ovarian failure (cessation of menstruation, hot flashes, estradiol 26.5 pmol/l [114-1959], LH 48.1 IU/l [<95.6], FSH 21.8 IU/l [1.7-21.5]) and hormone replacement was started. Surprisingly, the OARTs regressed and had not been detectable in imaging since 2019. While glucocorticoid treatment is an established treatment for early TARTs in men, it is exceptional that it led to such pronounced radiological shrinkage of OARTs in our patient. Also, her ability to become pregnant twice spontaneously with large bilateral OARTs and CAH has rarely been reported.

Conclusion:

While the simultaneous presence of CAH, Addison's disease and premature ovarian failure could be purely coincidental, further investigation into their potential associations is warranted. Prospective evidence and established treatment protocols are lacking when it comes to CAH, OARTs and fertility.

Long-term radiologic monitoring remains mandatory in patients with non-functioning PitNET even after gross total resection or stable residual tumor

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Background/Introduction:

The objective of the study was to investigate whether radiologic monitoring can be discontinued in non-functioning pituitary neuro-endocrine tumors (NF-PitNET) with satisfactory therapeutic response at 3 years (3Y) post transsphenoidal surgery (TSS) and to determine specific factors associated with early and late recurrences.

Methods:

This was a retrospective longitudinal unicentric study. A cross-sectional analysis was performed in patients who underwent TSS for NF-PitNET at Lausanne University Hospital between 2000-2022. Based on MRI at 3Y post-TSS, participants were classified as exhibiting gross-total resection (GTR), stable residual tumor (SRT) or progressive residual tumor (PRT). We then conducted a longitudinal analysis of patients with favorable outcome (GTR and SRT) to check for new-onset recurrence / regrowth at 5 years (5Y) post TSS and at the last available FU (LAFU, 7.7 ± 3.6 years).

Results:

Out of eighty-five eligible patients, forty-two had GTR, twenty presented with SRT and twenty-three with PRT status. Tumor size and extension to cavernous sinus (Knosp grade) at baseline were significantly more elevated in patients with PRT at 3Y post-TSS ($p=0.0007$ and $p=0.037$, respectively). Enrichment for proliferative tumors (and Ki-67 index $\geq 3\%$) showed a similar trend, although non-significant ($p=0.0560$). Late recurrence was observed in 19% (11/52) and 25% (14/51) of GTR+SRT group at 5Y and LAFU, respectively. The presence of residual tumor (SRT status vs GTR) at 3Y after TSS was significantly more frequent in progressive than in stable cases at LAFU ($p=0.0007$), regardless of residual tumor size ($p=0.68$).

Conclusion:

No single parameter could effectively predict the therapeutic outcome of NF-PitNET at 3Y post-TSS. Late tumor recurrence/regrowth beyond 3Y was not an infrequent finding and occurred more often in patients with residual tumor after surgery but was also observed in few cases with more favorable predictive markers (complete resection at 3Y, non-proliferative tumors). Our results stresses the need to maintain long-term MRI monitoring in cases with NF-PitNET even if early remission is achieved.

Adverse health outcomes of people with rare bone diseases across ages: a population-based cohort study

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Background/Introduction:

Rare bone diseases are a heterogeneous group of complex, disabling diseases with unique health patterns. Poor current understanding leads to unmet needs of people with rare bone diseases, their families, and care providers: diagnostic delays, limited access to expert care, and lack of specialized treatments. Few if any studies have investigated the major health outcomes of multiple rare bone diseases across age, including hospitalization rates, reasons for hospitalization, and in-hospital outcomes.

Methods:

This nationwide population-based cohort study uses an administrative claims database, comprising a near-complete sample of all hospitalizations in Switzerland between 01/2012 and 12/2021. Of the 11 million hospitalizations in the dataset, we included 2,876 hospitalizations of 1,996 individuals with a rare bone disease, as defined by ERN BOND and well classified in ICD-10:

X-linked hypophosphatemia (XLH), osteogenesis imperfecta (OI), fibrous dysplasia (FD), achondroplasia (ACH), pseudohypoparathyroidism (PHP), fibrodysplasia ossificans progressiva (FOP).

Results:

Compared to the general population, people with rare bone diseases had more frequent hospitalizations during childhood, and people with each rare bone disease showed very distinct major health outcomes. In XLH, 23% of hospitalized patients had malignancies and 13% had diabetes mellitus which has not been previously reported. Diabetes mellitus was also common in pseudohypoparathyroidism (15%). Fractures were the leading cause of hospitalization only in people with osteogenesis imperfecta (OI). Arthropathies and dorsopathies were frequent across all groups. In XLH, bacterial infections and digestive malignancies were the top causes. Achondroplasia showed high rates of hospitalizations due to episodic/paroxysmal disorders. Emergency admissions were common in early childhood in OI and in late adulthood in XLH. Planned admissions were frequent in late childhood/early adulthood in achondroplasia and fibrous dysplasia. XLH patients had higher diagnostic complexity. Across all rare bone diseases and compared to the general population, hospital stays were twice as long, ICU admission odds were 3.1 times higher, mortality odds 2.3 times higher, and readmission odds 1.3 times higher in rare bone diseases.

Conclusion:

Distinct hospitalization patterns and health outcomes of the individual rare bone diseases highlight the importance of disease- and age-specific diagnosis, treatment, and care strategies. The findings of this paper may help to shorten diagnostic delays and anticipate emergency hospitalizations across age groups and bone diseases.

The high malignancy rate of people with XLH warrants further investigation.

The implementation of guideline-directed therapies in diabetic kidney disease in a renal and diabetic outpatient clinic at the Lausanne University Hospital

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Background/Introduction:

The management of DKD requires a multidisciplinary approach and adherence to recent Swiss guidelines, including the use of renin-angiotensin system (RAS) blockers, sodium-glucose cotransporter 2 (SGLT2) inhibitors, non-steroidal mineralocorticoid inhibitors (finerenone), and GLP-1 receptor agonists (GLP1-RA), forming a four-pillar therapeutic approach. This study aimed to evaluate the therapeutic targets and the implementation of guidelines for the management of DKD in patients followed at the nephrology and diabetes outpatient clinics of the Centre Hospitalier Universitaire Vaudois (CHUV).

Methods:

Data from 1,101 patients followed in 2024 were collected. The inclusion criteria were an estimated glomerular filtration rate (eGFR) of less than 60 mL/min/1.73 m² and/or an albumin-to-creatinine ratio (ACR) of more than 30 mg/mmol at least once since 2014. Therapeutic targets (HbA1c, blood pressure, LDL cholesterol) were assessed as well as implementation of the four-pillar approach. Descriptive analyses and comparisons (Student's t-tests, chi-square tests) were performed, as well as exploratory logistic regression models.

Results:

The cohort consisted of 1,101 patients (64.1% men), with a mean age of 64.4 years and a mean BMI of 29.4 kg/m². A significant proportion (58%) of patients were classified as high or very high risk according to the KDIGO classification.

Achieved treatment goals were: 58.1% for HbA1c, 46.2% for blood pressure and only 32.5% for LDL cholesterol (<1.8 mmol/L). Patients off target were younger.

The prescription rates for eligible nephroprotective therapies were: RAS blockers (72.4%), GLP1-RA (59.7%), SGLT2i (37.1%), and finerenone (17%). Combination therapy with GLP-1 RA + SGLT2i was observed in 40% of eligible patients, and triple combination therapy (+RASb) in 36.6%, despite reimbursement difficulties in Switzerland. Prescription of RAS blockers and finerenone increased with KDIGO risk stage. The prescription rates were generally higher than other countries although comparison is limited due to differences in cohorts studied. A gradual improvement in target achievement was observed between 2016 and 2024.

Conclusion:

The study reveals improved but partial implementation of Swiss DKD recommendations at CHUV. Barriers to the implementation need to be further evaluated in order to improve the care of DKD patients.

The Use of Teprotumumab in Thyroid Eye Disease: A Case Series

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Introduction: Thyroid eye disease (TED) is a potentially severe, disfiguring and sight-threatening complication of autoimmune thyroid disorders, affecting up to 25% of patients with Graves' disease. Since May 2025, Teprotumumab (Tepezza®), an anti-IGF-1 receptor monoclonal antibody, has been approved by Swissmedic. Clinical trials and real-world data have demonstrated that Teprotumumab significantly reduces disease activity - as assessed by the Clinical Activity Score (CAS) - and leads to improvements in proptosis, diplopia and quality of life. Reported side effects include infusion reactions, hyperglycemia and inner ear dysfunction.

Methods: We describe three patients with TED successfully managed with Teprotumumab. Teprotumumab was used as part of a compassionate use program. All patients had audiometry before, after the 4th infusion and after termination of treatment.

Results: Patient 1 (57y, m) had active, longstanding thyroid eye disease (TED) since 2009 due to Graves' disease, with multiple relapses despite repeated high-dose glucocorticoid pulses (5 pulses between 2009–2023) and total thyroidectomy (2016). In August 2024, he presented with bilateral exophthalmos (32 mm), limited upgaze, diplopia in upgaze, and a Clinical Activity Score (CAS) of 4/10. Teprotumumab was initiated in January 2025. Following 4 infusions, exophthalmos decreased by 3 mm (right) and 2 mm (left), CAS improved to 1/10 and the patient reported better nocturnal eyelid closure. Audiometric monitoring after 4 and 8 infusions revealed no hearing changes. No adverse effects occurred.

Patient 2 (39y, f) presented in October 2024 with retrobulbar pain and newly diagnosed active TED, following a transition from hypothyroidism (under treatment with levothyroxine 75 µg daily) to TRAb-positive hyperthyroidism. Clinical findings included severe orbital inflammation (CAS 6–7/10), bilateral exophthalmos (22 mm), and upgaze as well as lateral gaze restriction. High-dose intravenous glucocorticoid therapy for 12 weeks resulted in only transient improvement (reduction of CAS to 3/10 no improvement of ocular motility). Three weeks post-therapy visual acuity declined and contrast sensitivity worsened - raising suspicion of early compressive optic neuropathy. After interdisciplinary review, Teprotumumab was initiated and urgent orbital decompression deferred. After just 2 infusions improvement in CAS (1/10) and exophthalmos occurred but also contrast sensitivity and visual acuity improved as surrogate for regression of optic neuropathy, thus orbital decompression could be avoided. Diabetes mellitus, which had developed during glucocorticoid therapy, required insulin therapy (basal-bolus regimen), but could be well controlled. No otologic symptoms or infusion reactions were observed.

Patient 3 (53y, m) presented himself in August 2024 with periorbital swelling, diplopia, and newly diagnosed Graves' disease. TED was confirmed with a CAS of 5/10 and disabling diplopia, resulting in working inability as a truck driver. Despite 12 weeks of high-dose intravenous glucocorticoids, TED progressed (CAS 6/10) with worsening extraocular motility. Teprotumumab was initiated after interdisciplinary discussion. Rapid symptomatic relief occurred within days. After 3 infusions, CAS improved to 0–1/10 and motility almost completely normalized, allowing return to work. No side effects including hyperglycemia, otologic symptoms or infusion reactions were observed.

Conclusion: Teprotumumab demonstrated rapid and clinically meaningful improvements in disease activity, proptosis, ocular motility and quality of life in patients with moderate-to-severe and glucocorticoid-refractory thyroid eye disease. All three cases underscore its efficacy even in chronic or vision-threatening presentations, with a favourable safety profile under regular monitoring. These real-world data support Teprotumumab as a valuable targeted treatment option in the evolving management of TED.

Advancing Primary Care for Type-2 Diabetes Management: Stakeholder Perspectives on Digital Quality Monitoring in Switzerland

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Background

Primary care physicians manage the majority of type 2 diabetes (T2D) patients worldwide, yet they face increasing workload pressures, fragmented care systems, and limited infrastructure. Quality monitoring tools, such as the SGED score developed by the Swiss Society of Endocrinology and Diabetology—offer promising solutions to managing T2D outcomes. However, such tools are often paper-based and administratively burdensome. This study examines key barriers and facilitating factors to implementing a digital T2D quality monitoring score in primary care, with Switzerland as a case study.

Methods

We conducted 38 semi-structured interviews following the COREQ guidelines with key stakeholders involved in T2D care in Switzerland: 12 healthcare providers, 12 patients, five health insurers, and nine healthcare application developers. Data were analyzed using thematic analysis.

Results

Participants highlighted general challenges in T2D management, including time pressure, fragmented care, and lack of personalized support. Barriers to adopting tools like the SGED score included poor integration with clinical systems, misaligned incentives, and limited relevance to complex real-world cases. To address these issues, stakeholders recommended embedding tools into existing workflows, enabling task-shifting, improving data sharing, and designing more patient-centered features.

Conclusion

Digital quality monitoring tools (e.g., SGED score) can improve diabetes care through features such as patient-entered data, automated alerts, and pharmacy-supported follow-ups. Their success depends on aligning with GP workflows, enabling task shifting, and ensuring system interoperability. Stakeholder involvement and incentive-aligned implementation are crucial for integrating T2D management into routine GP care.

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A case of familial hypobetalipoproteinemia

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Background/Introduction:

Hypocholesterolemia is a heterogeneous group of disorders, defined by LDL-cholesterol (LDL-C), apolipoprotein B (ApoB) and triglycerides levels below the 5th percentile for age. Etiologies include genetic causes (polygenic or monogenic), secondary causes (hyperthyroidism, liver failure, inflammation, inflammatory bowel disease, pancreatic insufficiency), and syndromic causes (Shwachman-Diamond syndrome, Smith-Lemli-Opitz syndrome).

Method/Case presentation:

A 33-years old female, known for thrombophilia (PAI-1 4G/5G mutation), was referred to the lipid clinic of CHUV for evaluation of hypocholesterolemia. The lipid profile showed undetectable ApoB (< 0.26 g/l) and LDL-C of 0.6 mmol/l. Family history revealed hypolipidemia in the sister, brother, father and paternal aunts, suggesting a genetic cause.

Results:

There was no secondary cause identified. Given the family history, genetic testing was performed and showed a heterozygous mutation on ApoB (NM_000384.3:c.3365del), compatible with familial hypobetalipoproteinemia (FHBL). Work-up identified hepatic steatosis, without fibrosis, with no other complications of the disease.

Discussion:

Over 120 mutations have been identified, most commonly resulting in premature truncation of ApoB, with the phenotype depending on the mutation's position relative to the ApoB protein. Homozygous or compound heterozygous mutations leads to a phenotype identical to abetalipoproteinemia (MTTP mutation) and is observed in fewer than fifty reported cases, while heterozygous mutations—found in 1 in 700 to 1 in 3000 individuals according to observational studies—result in a milder phenotype. ApoB is essential for the structural integrity of chylomicrons and VLDL, ApoB-48 is synthesized in enterocytes and ApoB-100 in hepatocytes; mutations in the ApoB gene—depending on the length of the truncated protein—can impair the secretion of both chylomicrons and VLDL if the protein is shorter than 48% of the normal length, while only VLDL secretion is affected if the length is between 48% and 100%. The mutation identified in our patient does only affect ApoB-100. Clinical manifestations of familial hypobetalipoproteinemia range from asymptomatic cases to fat malabsorption, steatorrhea, and growth retardation in severe forms, with possible complications including hepatic steatosis/cirrhosis, fat-soluble vitamin deficiencies, and neurological or ophthalmological symptoms.

Conclusion:

Familial hypocholesterolemia is a rare entity, often underdiagnosed. Correct identification of these patients is essential to prevent complications.

Biallelic CPOX mutations presenting as adrenal insufficiency, disorder of sexual development, optic neuropathy and unexplained anemia: expanding the phenotype

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Background

Coproporphyrinuria is a rare genetic disorder caused by a deficiency of the enzyme coproporphyrinogen oxidase (CPOX), which is involved in the biosynthesis of heme. Mono-allelic inactivation of *CPOX* causes hereditary coproporphyrinuria. Bi-allelic mutations of *CPOX* are very rare and lead to harderoporphyria, a condition with a distinct phenotype characterized mainly by hematologic manifestations. Primary adrenal insufficiency (PAI) was recently described as part of this clinical syndrome in two case series.

Methods

We report a 23-year-old male of Middle Eastern origin (Iraqi Kurdistan), diagnosed with PAI at age of 3 years. A classic form of congenital adrenal hyperplasia was presumed, because of high unstimulated 17OH-progesterone (> 30 nmol/L) and very high ACTH (> 500 ng/L). Despite therapy with glucocorticoids, he developed bilateral testicular lesions, considered as Testicular Adrenal Rest Tumors (TART). Physical examination was notable for microphallus and history of cryptorchidism treated by orchidopexy. He also presented with microcytic anemia of unknown origin since birth, transient neonatal jaundice, as well as a bilateral optic nerve atrophy. Family history was remarkable for consanguineous parents (first cousins). Moreover, his two younger sisters presented with similar phenotype of transient neonatal jaundice, unexplained anemia, optic atrophy and adrenal insufficiency.

Results

Sequencing of all major genes involved in adrenal steroidogenesis came back negative. Further genetic analysis revealed a homozygous p.(Ser28Ter) *CPOX* (NM_000097.7) mutation in the three affected subjects, establishing the diagnosis of harderoporphyria. The detected mutation is absent in control and is predicted as pathogenic according to the American College of Medical Genetics guidelines. Recently, the same mutation was found in two male siblings of similar ethnicity as our patient, who also presented with harderoporphyria and PAI. Impaired heme biosynthesis affecting steroidogenic enzyme activity, as well as progressive adrenal cortex damage due to mitochondrial dysfunction were suggested as the underlying mechanisms. Hormonal assessment in our index patient showed a compensated hypergonadotropic hypogonadism and oligozoospermia, suggesting an underlying gonadal dysgenesis. Conversely, the two affected sisters had history of precocious puberty. Notably, none of the affected siblings exhibited acute porphyria crisis.

Conclusion

This case further expands the phenotype of congenital coproporphyrinuria, demonstrating that biallelic *CPOX* mutations can cause multisystemic manifestations even in the absence of classic porphyria symptoms. Early recognition in atypical presentations, especially with a supportive family history, may avoid unnecessary investigations and allow for appropriate management and counseling.

Endocrine Conditions among Swiss Childhood Cancer Survivors and Their Association with Health-related Quality of Life

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Background: Endocrine conditions, including thyroid disorders, growth hormone deficiency (GHD), early and late puberty onset, and diabetes mellitus, are common among childhood cancer survivors (CCS). Limited evidence exists on how endocrine conditions in CCS affect their health-related quality of life (HRQOL). We determined the prevalence of endocrine conditions in CCS and investigated associations with HRQOL.

Methods: This study included CCS from the Swiss Childhood Cancer Survivor Study (SCCSS), who were registered in the Swiss Childhood Cancer Registry, had been diagnosed at age <21 years, were resident in Switzerland, alive and aged ≥16 years at time of study. Siblings of CCS served as comparison group. We assessed HRQOL (SF-36), endocrine conditions (thyroid disorders, GHD, medication for early/late puberty, diabetes mellitus) and sociodemographic characteristics using questionnaires. Cancer-related data originated from the Swiss Childhood Cancer Registry. We compared HRQOL between CCS with and without endocrine conditions using t-tests. To compare HRQOL between CCS and siblings, we used multivariable linear regression, adjusting for sociodemographic characteristics (age at study, sex, parental education, region) and presence of any endocrine condition. To investigate associations between endocrine conditions and HRQOL in CCS, we used multivariable linear regression, adjusting for clinical factors (age at cancer diagnosis, cancer type, chemotherapy, radiotherapy, surgery, haematopoietic stem cell transplantation) in addition to sociodemographic characteristics.

Results: With an overall response rate of 59%, we included 2422 CCS (48% women; median age 24 [IQR 20-31]) and 795 siblings (58% female; median age 27 [IQR 21-33]) with data on HRQOL and endocrine conditions. Twenty percent of CCS (506/2422) and three percent of siblings (25/795) reported at least one endocrine condition. For CCS, thyroid disorders were most common (15%, n=367), followed by GHD (8%, n=183), early/late onset puberty (4%, n=101), and diabetes mellitus (2%, n=43). CCS with endocrine conditions had reduced HRQOL in all SF-36 dimensions (difference in mean norm-based score for physical functioning -2.8; role physical -3.3; bodily pain -1.7; general health -4.4; vitality -3.3; role emotional -2.4; social functioning -3.0; mental health -1.6; all p<0.001). In multivariable linear regression analyses, physical HRQOL (coef. -0.2, 95%CI -0.9 to 0.4) and mental HRQOL (0.5, 95%CI -0.2 to 1.3) was similar between

CCS and siblings. Thyroid disorders (-1.5, 95%CI -2.5 to -0.50), GHD (-2.9, 95%CI -4.4 to -1.4) and diabetes mellitus (-3.7, 95%CI -6.2 to -1.1) were associated with reduced physical HRQOL, and thyroid disorders (-1.6, 95%CI -2.8 to -0.45) and diabetes mellitus (-3.3, 95%CI -6.2 to -0.4) with reduced mental HRQOL. Having received medication for early/late puberty onset was not associated with physical or mental HRQOL and GHD was not associated with mental HRQOL.

Conclusion: Endocrine conditions affect twenty percent of CCS and are associated with reduced physical and mental HRQOL. Survivors with thyroid disorders, GHD and diabetes mellitus are particularly vulnerable to low HRQOL. Adhering to survivorship guidelines enables early detection and may reduce this impact.

Follicular cell-derived thyroid cancer: impact of the changes of the recurrence risk level classifications on postoperative radioactive iodine administration

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Background/Introduction:

Postoperative management of follicular cell-derived thyroid cancer (TC) is based on the risk of recurrence. Compared with the 2006 ETA and the 2009 ATA classifications, there were more low-risk patients and fewer high-risk patients in the 2015 ATA classification, reducing the indications for postoperative radioactive iodine (RAI) administration.

Methods:

The aim was to evaluate the consequences of the changes in the risk level classification of the latest ATA classification on postoperative RAI indications. This is a single-center retrospective study, including 474 consecutive patients operated for follicular cell-derived TC between January 2016 and December 2022.

Results:

The patients (76% women, mean age: 51 years), had papillary TC in 87% of the cases. According to AJCC 8th edition, TC were pT1, pT2, pT3 and pT4 in 61%, 25%, 13% and 1%, respectively. Tumors were pN0/Nx in 73% of the cases and pN1 in 27%.

According to the 2006 ETA, 2009 and 2015 ATA classifications, patients were classified in the lowest-risk level in 22%, 37%, and 58% of the cases, as intermediate-risk level in 36%, 53%, and 31% of cases and as high risk in 42%, 10%, and 11% of cases, respectively. Based on each guideline, RAI was considered or indicated in 70%, 56% and 46% of the cohort, respectively.

Using the next ATA classification, 40% of the cases will be low risk, 24% low-intermediate risk 21% intermediate-high and 15% high risk. Compared to the 2015 classification, 25% of the patients will increase their risk level and 4% will decrease it. RAI will be considered or indicated in 60% of the patients, an increase of 30%.

Conclusion:

While the 2015 ATA guidelines led to a decrease in recurrence risk classification, the next ATA classification will have the opposite effect with a 30% increase in RAI indications.

Hospitalization trends and clinical outcomes in Congenital Adrenal Hyperplasia: A population-based cohort study in Switzerland

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Background/Introduction:

Congenital adrenal hyperplasia (CAH) comprises autosomal recessive disorders characterized by impaired cortisol and aldosterone synthesis and excess adrenal androgens due to enzyme deficiencies. CAH is associated with increased cardiovascular and metabolic morbidity and a lifelong risk of adrenal crises. We evaluated the comorbidity burden, hospitalization trends, and associated outcomes among individuals with CAH in Switzerland.

Methods:

This population-based, retrospective cohort study used national hospital data from Switzerland between 2011 and 2022. People with CAH were identified using the ICD-10-GM code E25 and compared to individuals hospitalized for any cause without CAH (referred to as the general population). We assessed incidence rates of hospitalizations, main reasons for admission, number of diagnoses per hospitalization across the lifespan, and hospital-associated outcomes, stratified by four age groups.

Results:

Out of 12,569,835 hospitalizations, 2,020 involved individuals with CAH. In the CAH population, hospitalization incidence rates were highest during the neonatal and early childhood periods, whereas in the general population most hospitalizations occurred later in life. Most important causes for admissions in CAH individuals were endocrine and metabolic disorders (neonates and infants: OR 66.5 [95% CI 8.88-498.07], young children: OR 21.42 [95% CI 4.67-98.20], children and adolescents: OR 53.32 [95% CI 7.08-401.72], adults: OR 2.61 [95% CI 1.53-4.46]). Across the lifespan, individuals with CAH exhibited a higher burden of comorbidities, averaging 5.5 diagnoses at birth, while individuals in the general population did not reach this average number of diagnoses until around 60 years of age. CAH patients were also more likely to experience serious in-hospital outcomes, such as intensive care unit admission (OR 1.55 [95% CI 1.2–2.01]), with the greatest differences observed among neonates and infants – indicating that this subgroup largely accounts for the increased risk in the overall CAH population.

Conclusion:

This analysis revealed unique hospitalization patterns in individuals with CAH, whose main reasons for admission differed from those in the general population. Individuals with CAH experienced more complex hospital stays and a greater risk for severe in-hospital outcomes, underscoring the importance for improved patient education, increased clinical awareness, and tailored management strategies – particularly for newborns and children, who are most vulnerable.

AGP Score: A Simple and Comprehensive Metric for Glycemic Control in Type 1 Diabetes

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Background/Introduction:

Hemoglobin A1c (HbA1c) remains a standard for assessing glycemic control in type 1 diabetes (DMT1), yet it fails to capture daily glucose fluctuations. Continuous glucose monitoring (CGM)-derived metrics such as time in range (TIR), time below range (TBR), and coefficient of variation (CV) offer complementary insights, prompting development of composite indices. However, existing scores are often complex, inconsistently weighted, or omit HbA1c.

Methods:

We developed and validated the Ambulatory Glucose Profile (AGP) Score, a transparent, ADA-guideline-aligned composite index integrating HbA1c, TIR, TBR, and CV into a 4–16-point scale. In a retrospective cohort of 247 DMT1 patients from University Hospital Zurich, AGP Scores were computed and compared across insulin delivery modalities (MDI, CSII, AID). Performance was benchmarked against four established composite scores (ADRR, PGS, COGI, GRI).

Results:

The AGP Score differentiated glycemic profiles across delivery methods, with AID users showing superior control. It demonstrated strong associations with CGM metrics, especially TBR ($\rho = -0.63$) and CV ($\rho = -0.64$), and correlated significantly with all comparator indices. Case analyses illustrated the score's superiority in capturing clinically relevant differences not reflected by HbA1c or TIR alone.

Conclusion:

The AGP Score offers a clinically meaningful, easy-to-interpret tool for comprehensive glycemic assessment in DMT1. By integrating both laboratory and CGM data, it overcomes limitations of existing metrics and may support individualized diabetes management and risk stratification.

The Influence of menstrual cycle on metabolic control and diet in patients with phenylketonuria

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Background/Introduction:

Based on experiences from everyday clinical practice and indications from the literature, the menstrual cycle might impact on metabolic stability in patients with urea cycle disorders and organic acidurias. However, this connection has not yet been systematically investigated. Phenylketonuria (PKU) as the most prevalent inborn error of metabolism with its easily determinable biomarker is a suitable model disease to shed light on this question.

Methods:

In ten patients with classic PKU on a low protein diet and on an amino acid mixture, phenylalanine (Phe) was measured from dried blood spots twice a week for 6 months. During this time, the patients documented their menstrual cycle and filled in nutrition protocols since it is known that the menstrual cycle also influences nutritional behavior

Results:

Based on this cohort, we found a significant correlation between the phases of the menstrual cycle and Phe concentration, with the lowest concentrations in the early luteal phase and the highest in the early follicular phase, during menstrual bleeding. This effect did not appear to be due to a change in eating behavior, as both protein and calorie intake were not significantly different in relation to the menstrual cycle. Since the increase in Phe began before menstrual bleeding, it does also not appear to be a pure effect of catabolism due to bleeding.

Conclusion:

A significant effect of the menstrual cycle on Phe concentration could be demonstrated with the lowest Phe concentrations shortly after ovulation and highest concentrations in the late luteal phase. The etiology of this effect couldn't be completely clarified with this current study, possible explanations include catabolism due to blood loss, changes in nutritional habits depending on the cycle phase and a direct hormonal effect.

Assessing the proportion of patients with type 2 diabetes in tertiary care eligible for combination therapy with GLP-1 receptor agonist and SGLT2 inhibitor

Author/Address of institution:

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Background/Introduction:

Based on distinctive mechanisms of action, the combination therapy with GLP-1 receptor agonist (GLP-1 RA) and SGLT2 inhibitor (SGLT2i) is currently the recommended treatment for certain indications based on national and international guidelines. However, the current Swiss health care reimbursement standard do not generally reimburse this. The degree to which this is a concern for quality of care is partly dependent on the magnitude of patients affected. The aim of the current study was therefore to estimate the proportion of outpatients with type 2 diabetes in tertiary care that would be eligible for combination therapy with GLP-1 RA and SGLT2i.

Methods:

Patients enrolled in SwissDiab with a visit in 2021 or later were eligible for the study, the most recent visit was used for the analysis. For the results to better reflect the patient population at one tertiary care centre, the analysis was limited to the study centre at Kantonsspital St.Gallen. As a first step, patients with a BMI ≥ 28 kg/m² and thus eligible for GLP-1 RA were identified. This included patients who were currently prescribed GLP-1 RA and had a BMI ≥ 28 kg/m² at the time of treatment initiation. Of these, patients with heart failure, chronic kidney disease (persistent albuminuria and/or eGFR < 60 ml/min/1.73 m²) and/or insufficient glycaemic control (HbA1c $> 8\%$) were considered eligible for the addition of SGLT2i. For patients with BMI ≥ 28 kg/m² that were SGLT2i and GLP-1 RA naïve, insufficient glycaemic control was set to “no” regardless of HbA1c, assuming that treatment with either agent would lower HbA1c below 8%.

Results:

Out of 401 patients, 293 (73.1%) were eligible for GLP-1 RA based on a BMI ≥ 28 kg/m². Of these, 179 (61.1%) had heart failure, chronic kidney disease and/or insufficient glycaemic control, i.e. an indication warranting the addition of SGLT2i in accordance with current treatment recommendations. The prevalence of heart failure was 25.7%, chronic kidney disease 77.7%, and insufficient glycaemic control 37.4%. Overall, 44.6% (n=179) of the patients with type 2 diabetes in tertiary care would stand to benefit from a combination therapy with GLP-1 RA and SGLT2i. Of these, 27.9% were treated accordingly, 26.3% were prescribed GLP-1 RA, 31.3% SGLT2i, and 14.5% were not prescribed either GLP-1 RA or SGLT2i. Overall, almost 1 in 6 patients (16.0%; n=64) had insufficient glycaemic control (median [IQR] HbA1c 8.7, [8.3, 9.3]%) while currently prescribed either GLP-1 RA or SGLT2i. Of these, 35.9% were prescribed GLP-1 RA. Of the 64.1% prescribed SGLT2i, 63.4% had a BMI ≥ 28 kg/m² (33.9 [30.3, 36.7] kg/m²).

Conclusion:

Of the patients in tertiary diabetes care enrolled in SwissDiab at Kantonsspital St. Gallen, almost half were eligible for combination therapy with GLP-1 RA and SGLT2i. However, less than one in three patients were treated accordingly. The discrepancy between real-life and best clinical practice recommendations may partly be explained by the lack of reimbursement.

Performance of Large Language Model-based Nutrition Tracking Services: A Comparative Study of Claude, Gemini, GPT, and AI-Powered Mobile Apps

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Background: Accurate nutrition tracking plays a vital role in predicting and preventing type 2 diabetes (T2D). Although commercial image-based food tracking applications are widely used, they frequently exhibit limitations, including low food recognition accuracy, limited integration with wearable devices, and substantial subscription costs. Recent advancements in large language models (LLMs) present new opportunities to enhance digital nutrition tools by increasing both their accuracy and cost-effectiveness. This study evaluates the performance of state-of-the-art large language models (LLMs) for image-based nutrition tracking and compares their outputs with those of commercial mobile applications to assess their potential in supporting the development of digital technologies aimed at preventing T2D.

Methods: We evaluate the accuracy of three LLM-based (Claude-3.7, Gemini 2.0, and GPT-4o-mini) nutrition tracking services (NTS) in estimating caloric and carbohydrate content from food images. These models are compared against three commercially available mobile applications (Snaq, January.ai, and Cal.ai). We utilized the open-source Nutrition5k dataset, focusing specifically on estimating total caloric content (in kilocalories) and total carbohydrate content (in grams), two key nutritional components highly relevant to glycemic control. Mean absolute errors (MAE) in calorie and carbohydrate estimation were computed for each model and compared to those from the three mobile applications.

Results: The Claude-3.7-based NTS achieved the lowest mean absolute error (MAE) in calorie estimation at 92.2 kcal, followed by GPT-4o-mini (101.7 kcal), Gemini 2.0 (103.3 kcal), Cal.ai (110.5 kcal), January.ai (120.9 kcal), and Snaq (183.8 kcal). In carbohydrate estimation, the Claude-3.7-based NTS again outperformed other NTSs with an MAE of 9.9 g, followed by Gemini 2.0 (11.0 g), January.ai (11.0 g), Cal.ai (13.4 g), GPT-4o-mini (15.7 g), and Snaq (20.6 g). These results indicate that the Claude-3.7-based NTS consistently provided the most accurate nutritional estimates among all evaluated platforms. Nevertheless, it is important to acknowledge the absence of clinically validated thresholds for acceptable error margins in nutrition tracking, which represents a limitation for comparative interpretation in healthcare contexts.

Conclusion: LLM-based NTS, particularly those leveraging Claude-3.7 and Gemini 2.0, demonstrate improved accuracy compared to current commercial applications in estimating nutritional content from food images in a T2D nutrition context. These findings highlight the potential of LLM-based NTS in supporting the prevention and management of T2D through enhanced digital nutrition monitoring.

Future research should prioritize the development of consensus-driven evaluation frameworks and further refine model accuracy across diverse dietary contexts.

Swiss Precision Digital Therapeutics for the Prevention of Type-2 Diabetes

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Background: In Switzerland, type 2 diabetes (T2D) is among the most prevalent non-communicable diseases, contributing to significant health complications and imposing substantial costs on the healthcare system. Effective prevention of T2D holds the potential to alleviate both the medical and economic burdens on the Swiss population and its healthcare infrastructure. Our new Innosuisse Flagship project seeks to address three critical systemic challenges: (1) limited long-term engagement with lifestyle interventions, which diminishes the effectiveness of preventive care; (2) the absence of sustainable business models for T2D prevention among healthcare, health insurance and technology providers; and (3) insufficient utilization of individual's health and lifestyle data to enable AI-driven diabetes risk detection and personalized preventive interventions.

Method: To address these challenges and enable systemic change in the prevention of T2D, we have established a multidisciplinary consortium comprising partners with expertise in digital health interventions, wearable body monitoring, health insurance, food retail, and food processing. The consortium also includes hospitals, a Swiss Innovation Park, and a cantonal government. We will apply a mixed-methods approach, integrating design science research, focus group discussions, joint case studies, and simulation studies.

Results: First, we aim to develop scalable digital biomarkers for identifying individuals at risk of developing type 2 diabetes (T2D). This includes data-driven analytics derived from consumer behavior on online shopping platforms, as well as app-tracked eating and cooking habits. Second, we will deliver human-supported, AI-driven precision interventions for T2D prevention, with a specific focus on women, older adults, and individuals with lower socio-economic status. The interventions will focus on diet and nutrition, while also addressing other key lifestyle factors such as physical activity, stress management, and sleep. In parallel, we will develop sustainable business models to support the long-term implementation of preventive interventions.

Conclusion: Our project's health insurers and food retailers reach up to 60% of the Swiss population. Our integrated, digital T2D prevention service could significantly reduce the health and economic burden of T2D in Switzerland and help lower socioeconomic inequalities in health.

IGF-2-associated refractory hypoglycemia in a patient with a solitary fibrous tumor

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Background/Introduction:

Hypoglycemia in adult patients without diabetes can be a challenging condition for diagnostic workup. Non-islet cell tumor hypoglycemia is a rare cause of hypoglycemia. It mostly arises from paraneoplastic secretion of incompletely processed insulin-like growth factor 2 (pro-IGF-2) and is associated with tumors of mesenchymal origin, among others. IGF-2 stimulates insulin receptors and thus increases glucose utilization, mainly by skeletal muscle, and inhibits glucose release from the liver. Therapeutic measures in IGF-2-associated hypoglycemia include acute management of hypoglycemia, dietary modification, treatment of the underlying malignancy, and medical therapy, e.g. with glucocorticoids.

Methods:

We present the case of a 76-year-old male patient with a known solitary fibrous tumor (12 cm in diameter) in the gluteal region, who presented with new-onset hypoglycemia. We report the diagnostic workup for non-islet cell tumor hypoglycemia and discuss the challenges in managing hypoglycemia in this patient.

Results:

Eleven years after the initial tumor diagnosis, the patient presented to the emergency department with severe hypoglycemia (1.7 mmol/L) and neuroglycopenic symptoms; the Whipple triad was fulfilled. There were no signs of adrenal or hepatic insufficiency.

Further tests showed suppressed insulin (< 1 mU/L) and C-peptide (0.17 ng/mL), as well as suppressed ketogenesis (3 beta hydroxybutyrate < 20 μmol/L) at a glucose level of 3.1 mmol/L. IGF 1 was reduced (20.5 ng/mL; reference range 35.1–216 ng/mL) and IGF 2 elevated (1333 ng/mL; reference range 373–1000 ng/mL), consistent with paraneoplastic production of IGF 2 as the underlying mechanism of the hypoglycemia.

Despite dietary interventions with frequent meals every two hours and increasing prednisone doses up to 80 mg/day after initial stabilization, the patient again required continuous glucose infusion (8 g of glucose/h). As treatment or debulking of the underlying progressive tumor was not considered feasible, and due to significantly reduced quality of life from tumor progression, the patient decided to stop treatment. He died of hypoglycemia after discontinuing the glucose infusion.

Conclusion:

IGF 2-associated hypoglycemia should be considered as a cause of hypoglycemia, especially in patients with a known malignancy. Contrary to many cases described in the literature, where IGF 2-associated hypoglycemia often can be stabilized with glucocorticoids, this patient showed treatment refractory hypoglycemia. This highlights the need for further data regarding alternative treatment options in these rare cases.

Impact of assessing Lp(a) on cardiovascular risk management in tertiary type 2 diabetes care – a SwissDiab study

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Background/Introduction:

Lipoprotein(a) [Lp(a)] is a risk factor for atherosclerotic cardiovascular disease (ASCVD) that is independent of LDL-cholesterol (LDL-C). The level of Lp(a) is primarily genetically determined and guidelines recommend at least one measurement to better assess overall ASCVD risk. Conventional LDL-C assays measure cholesterol from both Lp(a) and LDL particles. Elevated Lp(a) levels might thus lead to an overestimation of LDL-C and associated ASCVD risk. The aim of the study was to assess the prevalence of elevated Lp(a) in patients with type 2 diabetes mellitus (T2DM) and evaluate how accounting for Lp(a)-cholesterol could affect clinical decision making with respect to cardiovascular risk assessment and lipid management.

Methods:

Patients enrolled in SwissDiab with a visit in 2021 or later were eligible for analysis. ASCVD risk and recommended lipid targets were defined according to the 2021 European Society of Cardiology guidelines on cardiovascular prevention. Lp(a) was measured with an immun-nephelometric assay. Lp(a)-attributable cardiovascular risk was determined as follows; <300 mg/L=rule-out risk, 300-500 mg/L=intermittent risk, >500 mg/L=rule-in risk. Lp(a)-corrected LDL-C (LDL-Ccorr) was estimated by subtracting the assumed cholesterol content in Lp(a) (estimated at 17-30% of particle mass) from the conventionally measured LDL-C level as follows; LDL-Ccorr (mmol/L) = LDL-C (mmol/L) – X*Lp(a) (mg/L)*0.002586 where X equals 0.17 or 0.30 assuming Lp(a)-cholesterol content of 17% and 30%, respectively and 0.002586 is the conversion factor for LDL-C from mg/L to mmol/L.

Results:

Of 454 eligible patients, 371 (81.7%) had data available for analysis. The median (IQR) age was 67.2 (59.5, 74.0) years, diabetes duration 15 (10, 23) years, 25.3% were females, and 44.5% were at high, and 55.5% at very high ASCVD risk. The median Lp(a) level was 97 (30, 269) mg/L, with the highest measurement observed 1720 mg/L. In total, 16% had elevated Lp(a) levels (>500 mg/L), of which 37.3% had high and 62.7% very high ASCVD risk. Adjusting LDL-C for the estimated cholesterol content in Lp(a), the biggest reduction in median LDL-C was observed among patients with Lp(a) >500 mg/L (from 2.1 to 1.7 mmol/L and 1.4 mmol/L, assuming 17% and 30% Lp(a)-cholesterol content, respectively), with more modest reductions among patients with Lp(a) levels <500 mg/L. Patients with elevated Lp(a) levels were prescribed more intensive lipid-lowering therapy without any differences observed in LDL-cholesterol levels or target attainment as compared to patients with low or intermediate levels of Lp(a). Overall, LDL-cholesterol target attainment was low, 13.5%. The proportion increased to 18% (p=0.11) and 22% (p=0.002) when correcting LDL-C levels, assuming 17% resp. 30% Lp(a)-cholesterol content. Improvement was primarily seen among patients with elevated Lp(a) at very high ASCVD risk.

Conclusion:

One in seven patients with T2DM had elevated Lp(a) levels (>500 mg/L). The results indicate that for these patients it would be clinically meaningful to correct LDL-C levels for Lp(a)-cholesterol content to ensure more accurate lipid and cardiovascular risk management and understanding of therapeutic responses, thereby underscoring the importance of measuring Lp(a) at least once.

Personalized Insulin Management with Reinforcement Learning: Feasibility Study of ABBA in MDI-Treated Diabetes

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Background/Introduction:

Multiple daily injections insulin (MDI) therapy remains challenging, highlighting the need for innovative solutions in diabetes care. The Adaptive Basal-Bolus Advisor (ABBA) is a reinforcement learning-based algorithm for personalized insulin management, designed for use with self-monitoring of blood glucose (SMBG) and MDI therapy, and integrated into a smartphone. The primary endpoint is to assess whether ABBA performs as effectively as standard care; adherence ($\pm 20\%$ of the recommended dose) is also monitored.

Methods:

The feasibility study, conducted at Geneva University Hospital, involves 15 insulin-treated participants with a basal/bolus regimen over the course of four weeks, divided into two phases with a crossover design. During Phase 1 (first 2 weeks), participants managed their insulin therapy conventionally while wearing continuous glucose monitoring (CGM) devices. The CGM and insulin data collected during this phase were used to initialize ABBA by tailoring it to each participant's individual characteristics.

In Phase 2 (following 2 weeks), participants received insulin dose recommendations from ABBA, which operated based on SMBG. As a minimum, participants measured their blood glucose before meals, in the morning, and before administering basal insulin. These values, along with estimated CHO content of meals, were entered into ABBA to enable ongoing adaptation and generation of personalized bolus insulin suggestions.

Results:

To date, 7 participants have completed the study; the rest will finish by the end of July. Among those with adherence $>50\%$ ($73.7 \pm 10.02\%$), time-in-target range improved by $5.7 \pm 4.2\%$, time in hyperglycemia decreased by $6.1 \pm 3.7\%$, and severe hyperglycemia decreased by $1.4 \pm 4.6\%$, with no significant change in severe hypoglycemia, compared to standard treatment. No adverse event were reported.

Conclusion:

Preliminary results indicate that ABBA improves glycemic control and supports daily diabetes care. These promising findings highlight its potential for safer, more personalized treatment in insulin-treated individuals living with diabetes.

Objective and subjective sleep from pregnancy to one year postpartum: associations with eating behavior and metabolic health in women with gestational diabetes

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Background/Introduction:

Gestational diabetes mellitus (GDM) increases the risk of adverse maternal and neonatal outcomes and long-term metabolic complications. Sleep, an often-underappreciated factor, plays a key role in eating behavior and metabolic health, yet little is known about its impact beyond pregnancy. This study aimed to describe subjective and objective sleep quality and duration during the third trimester of pregnancy and at one-year postpartum in women with GDM, compare these measurement approaches and examine their associations with intuitive eating and metabolic health both cross-sectionally and longitudinally.

Methods:

Data from 199 participants in the MySweetHeart Trial were analyzed. Subjective sleep was assessed using the Pittsburgh Sleep Quality Index (PSQI) during pregnancy while objective sleep was measured using wrist-worn GENEActiv accelerometers during pregnancy (24-32 weeks) and at one-year postpartum. Eating behavior was evaluated using the Intuitive Eating Scale-2. Metabolic health was assessed via BMI, fasting glucose, post oral glucose tolerance test glucose (OGTT), and glycated hemoglobin (HbA1c). Linear regressions were used to explore associations, adjusted for relevant confounders.

Results:

During pregnancy, mean objective sleep duration was 6.9 ± 1.5 hours, while subjective duration was 7.7 ± 1.7 hours ($p < 0.001$). Objective sleep efficiency was 74.9 ± 8.2 %, compared with 89.1 ± 16.1 % for subjective efficiency ($p < 0.001$). The mean PSQI score during pregnancy was 6.8, with 31.0% of women experiencing poor sleep quality (PSQI > 5). At one-year postpartum, objective sleep duration was 6.8 ± 1.1 hours and the objective sleep efficiency was 77.4 ± 6.7 %. Comparisons between pregnancy and postpartum showed no significant difference in sleep duration ($p = 0.69$), whereas sleep efficiency was significantly higher at one-year postpartum ($p = 0.002$). In adjusted analyses, subjective sleep duration in pregnancy was negatively associated with HbA1c levels ($\beta = -0.04$, $p = 0.03$). At one-year postpartum, objective sleep duration was significantly associated with lower 2-hour glucose levels during the OGTT ($\beta = -0.25$, $p = 0.03$), independently of confounders. No other significant associations were observed between sleep measures and eating behavior or metabolic outcomes, either cross-sectionally or longitudinally.

Conclusion:

Poor sleep was common in pregnant women with GDM, with subjective reports overestimating sleep quality and duration. Sleep showed only weak associations with glycemic control and no clear associations to eating behavior or metabolic health. These findings highlight the importance of using objective sleep measures and suggest that sleep issues are frequent in high-risk pregnancies but their impact may be masked by stronger metabolic factors.

The influence of sex and age on lipid management in type 1 diabetes mellitus - a SwissDiab Study

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Background/Introduction:

As a result of younger age of onset and a longer lifetime burden of disease, adult patients with type 1 diabetes mellitus (T1DM) have been shown to have similar, and in some cases higher, cardiovascular disease risk than age-matched patients with type 2 diabetes mellitus. This study aimed to assess the proportion of adult patients with T1DM in the Swiss Diabetes Registry (SwissDiab) that meet recommended lipid treatment targets and evaluate to what extent lipid management is dependent on sex and age.

Methods:

SwissDiab is a multicenter, longitudinal observational study of outpatients in tertiary diabetes care at Kantonsspital St.Gallen (coordinating center), and Basel, Bern, Geneva, and Zürich University Hospital. The analysis included patients with T1DM and a study visit in 2021 or later. The most recent visit was used unless missing data required the use of an earlier visit. Patients arrived fasted (>8 hours), and lipid parameters (low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], and apoB) were measured using routine methods at each hospital, and non-HDL-C was determined. Only patients with a complete lipid profile (LDL-C, non-HDL-C, and apoB) were included. Atherosclerotic cardiovascular disease (ASCVD) risk and recommended lipid targets were defined based to the 2021 European Society of Cardiology guidelines on cardiovascular prevention. Differences in proportions were determined with the Chi-Square test, or Fisher Exact test as appropriate.

Results:

Out of 322 eligible patients, 216 patients had data available for analysis. Median (IQR) age was 43.6 (31.9-58.2) years, diabetes duration 16 (10-25) years, 39.4% were females, 13.4% were at moderate, 75.0% at high, and 11.6% at very high ASCVD risk, and 33.6% were prescribed lipid-lowering therapy (LLT). Target attainment was low for LDL-C (7.9%), and significantly higher for non-HDL-C (30.6%, $p < 0.00001$) and apoB (59.7%, $p < 0.00001$), with no significant differences observed between males and females. LLT was associated with improved target attainment (all $p \leq 0.004$, except LDL-C, $p = 0.08$). Females were less likely than males to be prescribed LLT (21.2% vs 41.2%, $p = 0.002$), with similar trends observed accounting for ASCVD risk. Patients below median age was less likely to be prescribed LLT compared to patients above median age, specifically among patients at high (11.9% vs 47.4%, $p < 0.00001$) and very high (0% vs 95.2%, $p = 0.0004$) ASCVD risk.

Conclusion:

Currently recommended LDL-C targets were met by a small minority of the patients with T1DM enrolled in SwissDiab, whereas a substantially higher proportion reached non-HDL-C and apoB targets. LLT significantly improved target attainment, and the results highlight the need for improved awareness of the importance of lipid management, particularly among women and younger patients.

Body composition and energy expenditure in patients receiving thyroxin replacement for primary and secondary hypothyroidism.

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Background/Introduction:

Primary hypothyroidism (PH) is a frequent endocrine disorder, in which the thyroid gland does not produce enough thyroid hormones. The replacement therapy is guided by measurement of the pituitary gland hormone thyrotropin (TSH). Patients with central hypothyroidism in whom pituitary insufficiency leads to hypothyroidism, TSH cannot be used to guide therapy. So far there are no reliable methods for therapy control in patients with central hypothyroidism.

Resting energy expenditure (REE) and body composition are known to be influenced by thyroid hormone levels and may reflect metabolic activity more directly than serum markers.

We investigated whether REE and body composition can serve as potential markers to guide replacement therapy.

Methods:

The study was performed as a prospective observational study. A large cohort of healthy volunteers spanning all ages from 18 to 80 years and an equal proportion of males and females served as control population (n=141). Patients with primary (n=33) and secondary hypothyroidism (n=28) undergoing thyroxin replacement therapy were recruited from the outpatient clinic. On a single study visit we measured resting energy expenditure (REE) by indirect calorimetry and body composition by dual x-ray absorptiometry (DXA). We sampled plasma for the analysis of thyroid hormone levels and metabolites. To adjust REE to body composition we used a linear regression model based on the log-transformed fat-mass and muscle mass of the control population and fitted the values from the two patient groups to the model. Values are given as fraction of the expected REE (adjREE).

Statistical analysis was by ANOVA followed by Tukey's test for multiple comparisons. Values are given as mean±SD.

Results:

Levels of TSH were 2.1±1.1 µU/l in the control group, 1.6±1.4 µU/l in patients with treated PH, and 0.4±0.6 µU/l in patients with secondary hypothyroidism (sec.hypo.) undergoing T4 replacement (ANOVA p<0.0001). Levels of free T4 were 15.6±2.2 pM, 18.0 ±4.0 pM (p<0.0001), and 17.3±2.8 pM (p=0.0027), respectively (ANOVA p<0.0001).

The mean replacement dosage was 1.34±0.45 µg per kg body weight in patients with PH and 1.1 ±0.46 µg/kg body weight in SH

Percentage body fat was higher in patients with PH (32±9%, p=0.0006) than in controls (25±9%), but not different in SH (28±6%, p=0.44). Conversely, percentage muscle mass was lower in PH (63±8%, p=0.0013) than in controls (68±8%), but similar in SH (66±6%, p=0.29).

Patients with substituted secondary hypothyroidism had significantly lower adjREE (0.92±0.1, p=0.0005) than healthy controls (1.00±0.11), while adjREE was only slightly lower in substituted PH (0.96±0.13, p=0.12). The replacement dosage was not associated with adjREE in both primary and SH. While levels of free T4 and free T3 were weakly associated with adjREE in healthy controls, this was not the case in patients with primary or SH receiving T4 replacement.

Conclusion:

In patients with secondary hypothyroidism REE adjusted for body composition was lower than in healthy controls but was not affected by the replacement dose or levels of free T4 and free T3.

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“From skin to hormones”

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Background/Introduction:

Laugier-Hunziker syndrome is a rare acquired disorder characterized by diffuse macular hyperpigmentation of the oral mucosa and sometimes longitudinal melanonychia. It's considered a benign disease with no systemic involvement or malignant potential and remains a diagnosis of exclusion. The pathogenesis is unknown. Its differential diagnosis is broad and includes Peutz-Jegher syndrome (PJS), Bandler syndrome, Cronkhite-Canada syndrome, lichen planus, Addison disease, smoking, drugs, heavy metal exposure, acquired immune deficiency syndrome (AIDS), idiopathic melanoplakia and melanonychia.

Methods:

We describe the the case of a young woman who presented at the dermatology department and was initially suspected of having Laugier-Hunziker syndrome.

Results:

The 23-year-old woman presented to our dermatology colleague in 10/2024 for brown-spotted changes in the red of her lips since a vacation in Portugal in autumn 2023. In addition, there had been streaky pigmented nail changes on several fingernails for around 2 years and hyperpigmentation on the elbows and above the spine. For several weeks, she had been experiencing symptoms such as palpitations and increased sweatings, dizziness (during the summer) and salt cravings. Her past medical history was unremarkable.

Laboratory work-up revealed an unclear thyroid profile, prompting endocrine referral.

Clinical evaluation revealed low blood pressure, hyperpigmentation of the oral mucosa, palate, lips, hand lines and on the elbows. Addison's disease was suspected and confirmed by low cortisol levels, strongly elevated ACTH, hyponatremia and positive adrenal antibodies.

In addition we found subclinical hypothyroidism, positive TPO antibodies and sonographic findings consistent with Hashimoto's thyroiditis suggesting polyglandular autoimmune syndrome.

Conclusion:

This case illustrates how early cutaneous signs such as lip and nail hyperpigmentation may serve as key clinical clues to underlying endocrine disease.

In the presence of unexplained pigmentation, Addison's disease should be considered. Prompt testing of basal cortisol is essential to avoid delayed diagnosis and potential adrenal crisis.

Interim Results From the APHENITY Extension Study: Sepsiapterin Reduces Blood Phe With Improved Dietary Phe Tolerance in Participants With Phenylketonuria

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Background/Introduction:

Phenylketonuria (PKU) is an autosomal-recessive inborn error of metabolism caused by deficiency of the enzyme phenylalanine hydroxylase (PAH). This results in elevated phenylalanine (Phe) levels, associated with neurological, cognitive, psychiatric and behavioral impairments. The standard of care is a Phe-restricted diet. Sepsiapterin is an endogenous precursor of tetrahydrobiopterin (BH4), an essential cofactor for PAH; it increases intracellular BH4 bioavailability and acts as a pharmacologic chaperone, leading to increased PAH enzymatic activity in both BH4-responsive and non-responsive PAH variants. Sepsiapterin is being developed as a novel oral treatment for PKU. The Phase 3 APHENITY trial (NCT05099640) was a global, two-part study evaluating sepsiapterin in a broad PKU population. Upon completion, participants could enroll directly into the APHENITY open-label extension study (NCT05166161). Here, we describe updated results from the extension study (30.06.2024 data cut).

Methods:

The extension study includes both participants with PKU who have completed the APHENITY Phase 3 trial, and participants who have not been included before in a PTC-sponsored Phase 3 trial. All participants received oral sepsiapterin once daily for ≥ 12 months. At the Month 2 Day 1 visit, mean blood Phe from Month 1 was reviewed. Participants with mean blood Phe < 360 $\mu\text{mol/L}$ underwent a concurrent Dietary Phe Tolerance Assessment. For a 26-week period, mean blood Phe was assessed along with dietary Phe consumption from 3-day diet records every 2 weeks, with changes in prescribed Phe allowed. Those with mean blood Phe ≥ 360 $\mu\text{mol/L}$ continued receiving daily treatment but without active Phe Tolerance Assessment.

Results:

As of the June 30, 2024 data cut, 169 participants (median age, 14.0 years [min, max: 0.2, 55.0]) were treated with sepsiapterin. Dietary Phe Tolerance Assessments were performed in 100 participants. The median (min, max) treatment exposure was 465.0 (26, 868) days for the participants who undertook Dietary Phe Tolerance Assessments. For all participants undertaking the Dietary Phe Tolerance Assessment, the least-square mean change (95% confidence interval) for change in dietary Phe consumption from baseline to Week 26 was 38.0 mg/kg/day (32.1, 43.9) (protein: 0.76 g/kg/day [0.64, 0.88]). An approximately 2.3-fold increase from baseline (27.6 mg/kg/day [protein: 0.55 g/kg/day]) in mean daily Phe consumption was achieved at Week 26 (63.6 mg/kg/day [protein: 1.27 g/kg/day]) in the overall Dietary Phe Tolerance Assessments. Mean blood Phe remained within the recommended target of < 360 $\mu\text{mol/L}$ during the Dietary Phe Tolerance Assessment commensurate with increase in Phe consumption. Overall, sepsiapterin showed a favorable safety profile and was well tolerated in the study. In the overall group (n=169), treatment-related TEAEs reported in $\geq 2\%$ of participants were diarrhea, headache, discolored feces, vomiting, and fatigue. There were no treatment-related serious TEAEs during the study.

Diagnosing Vasopressin deficiency using Mannitol-stimulated Copeptin

Author/Address of institution:

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Background/Introduction:

The differential diagnosis between arginine vasopressin (AVP) deficiency (formerly known as central diabetes insipidus) and primary polydipsia remains challenging. To date, the method with the highest diagnostic accuracy is osmotically-stimulated copeptin – a surrogate marker of AVP – measured during hypertonic saline infusion. However, this method is often limited to experienced hospitals, requires close monitoring, and is contraindicated in some patients. An alternative simpler osmotic stimulation test would be highly desirable. Intravenous mannitol has been shown to increase plasma osmolality and stimulate AVP release. In this study, we investigated the effects of mannitol infusion on copeptin and its potential as a diagnostic tool in diagnosing AVP-deficiency.

Methods:

In part 1 we conducted a randomized double-blind placebo-controlled cross-over trial to investigate the effect of mannitol infusion on copeptin in 22 healthy adults. Participants presented for two visits, each receiving either mannitol infusion (1g/kg in 30 minutes, maximum 80g) or placebo (normal saline) in random order. Serum copeptin was measured at baseline and at 30, 45, 60, 90, and 150 minutes.

In part 2 we included 10 patients with AVP-deficiency and 10 patients with primary polydipsia. Participants presented for one visit, receiving open label mannitol infusion (1.5 g/kg in 30 minutes, maximum 120g), and blood samples were taken at baseline, 30 and 90 minutes. The primary endpoint was copeptin levels after infusion of mannitol versus placebo (part 1) and in patients with AVP-deficiency versus patients with primary polydipsia (part 2).

Results:

In healthy adults, median [IQR] baseline copeptin was 4.5 pmol/L [<2.7 , 7.0] before mannitol infusion and 4.4 pmol/L [3.1, 6.7] before placebo infusion. Mannitol infusion was associated with a significant treatment effect, increasing copeptin at 30 minutes by +9.3 pmol/L compared to placebo (95% CI: +7.8, +10.8; $p < 0.001$).

In patients, baseline copeptin was <2.7 pmol/L [<2.7 , <2.7] in primary polydipsia and <2.7 pmol/L [<2.7 , <2.7] in AVP deficiency. After 30 minutes, the treatment effect on copeptin was +9.0 pmol/L in primary polydipsia (95% CI: +5.6, +12.3; $p < 0.001$) compared to AVP-deficiency. The best cutoff for differentiating AVP-deficiency from primary polydipsia was at 5.5 pmol/L with 100% sensitivity and 100% specificity.

Conclusion:

Mannitol infusion represents a promising new approach for differentiating AVP deficiency from primary polydipsia. Its short test duration, straightforward dosing, minimal monitoring requirements and no relevant side effects make it accessible, cost-effective and safe, with the potential to become the new diagnostic standard of care.

Impact of Semaglutide on Kidney, Cardiovascular, and Mortality Outcomes by Baseline BMI and Weight Loss in People with T2D and CKD: Data from the FLOW Trial

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Background/Introduction:

In FLOW, semaglutide reduced the risk of kidney, cardiovascular (CV), and mortality outcomes in people with type 2 diabetes (T2D) and chronic kidney disease (CKD). We now test how the benefit of semaglutide relates to baseline BMI and change in body weight (BW).

Methods:

Participants were randomized to once-weekly subcutaneous semaglutide 1.0 mg or placebo (N= 3,533). The primary kidney outcome was a composite of kidney failure, sustained estimated glomerular filtration rate reduction of $\geq 50\%$, or kidney or CV death. Key secondary outcomes included major adverse CV events and all-cause death. Subgroup analyses by BMI used a Cox proportional hazards model; mediation analyses by change in BW used a repeated regression approach.

Results:

Mean baseline BMI and BW were 32.0 kg/m² and 89.6 kg, respectively. The effect of semaglutide on the primary kidney outcome, major adverse CV events, and all-cause death was consistent across baseline BMI categories (interaction p value range, 0.6217 to 0.9471). The estimated percentage mediation (95% CI) of BW loss was -0.5% ($-29.8, 37.8$) on the primary kidney outcome; -33.4% ($-273.1, 82.0$) for major adverse CV events; and -25.6% ($-150.5, 34.3$) for all-cause death.

Conclusion:

Semaglutide benefits on kidney, CV, and mortality outcomes were independent of baseline BMI, and did not seem to be explained by change in BW.

Unintended Pregnancy Following Possible Reversal of Hypogonadotropic Hypogonadism: A Case Report

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Background

Patients with congenital hypogonadotropic hypogonadism (CHH) represent a group of oligogenic disorders characterised by a wide range of phenotypic manifestations. Some individuals have a complete absence of pubertal development and infertility, while others have a partial gonadotropin deficiency with delayed sex development, and some may even have normal reproductive function. CHH is caused by an isolated defect in gonadotropin-releasing hormone (GnRH) secretion and action. More than 60 genes have been associated with CHH, which can be transmitted in an autosomal dominant, autosomal recessive, or X-linked recessive manner. The phenotypic variability observed within the same family reflects the oligogenic mode of inheritance and incomplete penetrance. Approximately 10 - 20% of men with CHH show reversibility after gonadotropin replacement therapy. However, reversal of CHH has been reported far less frequently in women. The genetic profile linked to reversal is poorly defined, although several patients with mutations in the FGFR1 gene have been identified.

Case Presentation

A 41-year-old male presented to his orthopaedist due to shoulder complaints. Because of generalised muscle weakness, laboratory testing was initiated, revealing undetectable testosterone levels. Further evaluation confirmed clinical and biochemical hypogonadotropic hypogonadism (HH) (see Table 1), and the patient was subsequently referred to our outpatient clinic. Despite classic clinical signs and lack of puberty (see Table 2), the patient had not undergone prior endocrine evaluation. MRI of the brain demonstrated hypoplasia of the olfactory bulb, and the patient reported anosmia since early childhood. Genetic testing revealed a mutation in the FGFR1 gene, consistent with an autosomal dominant inheritance pattern. Family history revealed that several relatives suffer from HH (see pedigree). Although details on the laboratory evaluation were not available and genetic testing was declined, the patient's mother is likely affected by the same genetic mutation. She reported lifelong oligo-/amenorrhoea and infertility due to HH. At the age of 31, she became pregnant following ovulation induction therapy. Approximately nine years later, she experienced an unexpected spontaneous pregnancy, seemingly "out of the blue". This clinical course suggests that she experienced a reversal of HH.

Conclusion

Reversal of CHH is an increasingly recognised phenomenon that challenges the traditional view of CHH as a lifelong condition. Careful long-term monitoring and re-evaluation of therapy are recommended, particularly in patients with fluctuating clinical symptoms or family history suggestive of reversible forms. Awareness of the potential reversibility is crucial, as patients may regain endogenous sex hormone production resulting in fertility. In such cases, it is essential to provide appropriate counselling regarding effective contraception to minimise the risk of unintended pregnancy. This case and his family history highlight the variable expressivity of the clinical features and underscore the importance of genetic evaluation in patients with HH.

Inconsistent Management of High Fracture Risk in CKD Patients: An International Survey

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Background/Introduction:

Optimisation of bone health in patients with severe chronic kidney disease (CKD G3b to G5) and high fracture risk lacks a robust evidence base. We explored current approaches among experts in metabolic bone health using virtual case studies.

Methods:

An online survey featuring 5 virtual cases was sent to clinical experts in metabolic bone health across various countries. The first case involved a 72-year-old woman with CKD G4 and high fracture risk, and low calcium intake (300 mg/day). She experienced 3 new vertebral fractures after a fall and had a history of a humerus fracture. DXA showed a T score of -3.6 SD at the femoral neck. Biochemical analysis showed stable CKD (eGFR 25 ml/min/1.73m²), normal adjusted serum calcium, elevated PTH (4x ULN), high fasting serum phosphate, normal ALP, and low 25-OH vitamin D (<20 nmol/L).

Results:

Sixty specialists (rheumatology (n=24), endocrinology (n=17), nephrology (n=15), and geriatric medicine (n=4)) from 14 countries responded to the survey. Among them, 87% were consultants and 75% managed specialist metabolic bone clinics. In general, one third of experts do not routinely test ionised calcium and 82% do not routinely use of bone biopsies. For the case, 49 specialists agreed to initiate calcium supplementation, 25 would start a maintenance dose vitamin D supplement while 22 aimed for a high-dose. Specific osteoporosis treatment was recommended by 55 experts, while 4 would offer calcium and vitamin D only. Antiresorptive treatment was suggested by 47 participants, with 40 recommending the standard dose, 28 opted for denosumab, 8 for oral bisphosphonates, and 4 for intravenous bisphosphonates. Seven suggested an antiresorptive treatment with a reduced dose. Additionally, 8 experts recommended anabolic treatment, 3 suggested teriparatide and 5 romosozumab, with variability within countries and between specialities. Biochemical follow-up after treatment initiation showed significant variability. Only 17/28 (61%) experts routinely check serum calcium levels within 14 days of standard dose denosumab, despite the risk of hypocalcaemia and regulator recommendations.

Conclusion:

The lack of standardised clinical practice for managing bone health in patients with severe CKD leads to some patients receiving no osteoporosis treatment or unlicensed doses of antiresorptive or anabolic treatments. These results highlight the consequences of the evidence gap in patients with CKD at high fracture risk.

Digital Diabetes Screening in Switzerland: A cost-effectiveness analysis

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Background: Early identification of individuals at risk for type 2 diabetes (T2D) is critical for timely lifestyle intervention and prevention. While digital health applications offer a scalable and accessible approach to risk screening, their value depends on achieving sufficient accuracy to justify widespread use. This study aims to assess the cost-effectiveness of digital diabetes screening in Switzerland.

Methods: A decision-analytic model was developed comprising a 1-year budget impact component and a 5-year cost-effectiveness analysis, consistent with established economic evaluation frameworks for diabetes screening. The target population consisted of 7 million Swiss adults aged 20 and above, with a 6% prevalence of T2D, of which 33% were assumed to be undiagnosed. The risk score was modeled as a two-step screening process, with assumed sensitivities ranging from 60% to 95% and specificities ranging from 90% to 99%, followed by confirmatory laboratory testing (e.g., HbA1c, FPG). Uptake scenarios ranged from 20% to 80%. Screening costs were considered based on available market prices, ranging from CHF 5 to CHF 120 per user, confirmatory testing at CHF 40, and initial treatment at CHF 200. Outcomes included new cases of T2D detected and quality-adjusted life years (QALYs) gained. Early detection was assumed to reduce the incidence of diabetes-related complications by 15% over 5 years. All parameters were sourced from published literature and Swiss public health data.

Results: In the base-case scenario (50% uptake, CHF 5 screening cost), the program identified 55,440 new T2D cases, with a 1-year net cost of CHF 38 million, equating to CHF 680 per case for statutory insurers (LaMal). Outpatient providers experienced a predominantly positive or neutral financial impact, benefiting from a larger diabetic population that allowed for earlier disease management. Over five years, the screening cost CHF 528.5 million and generated 528,917 QALYs, compared to CHF 657.2 million and 522,000 QALYs without screening. The incremental cost-effectiveness ratio (ICER) was –CHF 18,565 per QALY gained, indicating that the screening was dominant (lower cost, higher benefit). Sensitivity analysis showed cost-effectiveness was maintained when specificity exceeded 90% and uptake surpassed 30%. These thresholds mark critical conditions under which the screening remains economically viable.

Conclusion: Our analysis indicates that integrating digital diabetes screening into outpatient care in Switzerland is economically dominant under realistic assumptions. This approach offers substantial potential for cost-effective early detection and significant system-level savings, making it a valuable addition to national preventive health strategies.

Intravenous [Pyr1]apelin-13 increases Sodium Levels in Healthy Volunteers with Artificially-Induced SIAD - a randomized double-blind placebo-controlled cross-over study - the escAPe Study

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Background/Introduction:

Hyponatremia often results from inappropriate arginine vasopressin (AVP) activity, leading to free water retention. The hormone apelin, secreted by the posterior pituitary, antagonizes AVP in salt and water homeostasis. Observational data in hyponatremic patients have not only shown an elevation in copeptin, a surrogate marker for AVP, but also a relative apelin deficit. The subcutaneous administration of apelin analogs in hyponatremic rodent models led to an increase in urine output and sodium levels, but data in humans are lacking. We hypothesized that restoring a physiological AVP/apelin ratio by intravenously administering exogenous [Pyr1]apelin-13 would increase urinary excretion in healthy participants with artificially-induced syndrome of inappropriate antidiuresis (SIAD).

Methods:

This is a double-blind randomized placebo controlled cross-over study involving 15 healthy adults who presented for three visits. SIAD was induced with intravenous 4- μ g desmopressin, oral water intake of 30 ml/kg body weight and subsequent infusion of 300 ml hypotonic (0.45%) saline. Thereafter, the study infusion with [Pyr]apelin-13 in a concentration of 10 nmol/ml (high dose) or 1 nmol/ml (low dose) or placebo was administered during three hours. Blood samples were taken every 30 minutes during the study infusion and every 60 minutes thereafter. Urine output was assessed every 60 minutes. The primary endpoint was the total urinary volume excreted from the start to one hour after the end of infusion (4 hours in total). Secondary endpoints were changes in plasma sodium during the observation period of 9 hours.

Results:

Seven of 15 participants were female (47%). Median [IQR] age was 26 years [24, 29] and median [IQR] body mass index was 23.2 kg/m² [20.6, 27.5]. The primary analysis showed no difference in 4-hour urine output after infusion of either dose of apelin compared to placebo, i.e. mean 4-hour urine output was the highest during infusion of placebo with 173 ml (95% CI: 136 – 209) and 17 ml lower (95% CI: -52 – 19; p = 0.36) during low dose apelin and 15 ml lower (95% CI: -51 – 20; p = 0.40) during high dose apelin. In contrast, plasma sodium adjusted for sodium levels at the start of infusion slightly increased upon infusion of high dose apelin with +0.7 mmol/L (95% CI: 0.2 – 1.1) over 4 hours and +1 mmol/L (95% CI: 0.5 – 1.4) over the entire observation period. No differences in sodium were observed between placebo and low dose apelin.

Conclusion:

Intravenous apelin increases sodium levels in healthy volunteers with artificially induced SIAD, highlighting its potential as a novel therapeutic option for SIAD. However, because of its lack of effect on urine output, the underlying mechanism remains to be elucidated.

Clinical and radiological characteristics of secondary neoplasms to the thyroid gland

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Background/Introduction:

Metastases to the thyroid gland are rare, with a prevalence of 0.16–7.5% in fine-needle aspiration cytology (FNAC) series and 1.2–3% in thyroid surgeries for suspected malignancy, reaching up to 24% in autopsy series of patients dying from non-thyroid cancers. They most commonly originate from renal, lung, breast, and gastrointestinal primaries, and appear typically in the setting of widespread metastatic disease. They present mainly as palpable neck masses, while 15–25% are incidental findings on imaging. Data on ultrasound characteristics are incomplete, but ultrasound features often show solid, heterogeneous, hypoechoic nodules with irregular margins and no calcifications.

Methods:

This study involved a retrospective review of all thyroid FNAC performed at HUG between 2000 and 2024. We selected all cytologically or histologically proven diagnosis of thyroid metastases from extra-thyroid malignancy, and we retrospectively reviewed patients' files

Results:

Twenty-four patients (62.5% women) had thyroid involvement from extra-thyroidal malignancies. Median age at diagnosis was 64.5 years (range: 24-86). Primary tumors were lymphomas (25%), gastrointestinal tract cancers (25%), lung cancers (20.8%), head and neck cancers (8.3%), kidney cancers (4.1%) and breast cancers (4.1%). The mean interval between primary tumor diagnosis and thyroid metastasis was 18 months (SD: 33).

Detection occurred via routine follow-up imaging (75%), local symptoms (20%), or hypothyroidism evaluation. In two patients, no active extra-thyroid malignancy was present, so thyroid metastasis was not initially suspected at the time of FNAC.

Ultrasound data were available for 18 of the 24 patients (75%). Most nodules were EU-TIRADS 5, with an mean size of 35 mm (SD 17.9). Multiple nodules were present in 33% of patients. They were often markedly hypoechoic (68%) with heterogeneous echotexture (87%). Irregular margins and microcalcifications were observed in 12.5% and 5.5% of cases, respectively.

Only 6 patients underwent surgery and median survival after diagnosis of thyroid involvement was 8 months (range 1-27).

Conclusion:

Thyroid metastases are rare and often detected incidentally during cancer follow-up. They usually appear as EU-TIRADS 5 lesions, though typical malignant features may be lacking. Diagnosis often occurs in the setting of active disease, but may precede primary detection or signal relapse. Prognosis is poor, warranting an individualized, context-based approach.

Unrecognized Macro-TSH as Cause of Isolated TSH Elevation — A Case Report

Authors

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Background/Introduction

Thyrotropin (TSH) elevation with free thyroid hormones within the reference range is a common finding in clinical practice and is usually recognized as subclinical hypothyroidism. Depending on the clinical and laboratory course, there are several differential diagnoses to consider (table 1). Macro-TSH is usually formed by the binding of IgG immunoglobulins to TSH and has low or absent biological activity. Immunoassays detect both monomeric TSH and macro-TSH, so the result does not reflect only biologically active TSH (figure 1). The reported prevalence of macro-TSH is between 0.6 - 1.6 %. The gold standard for diagnosis is gel chromatography, but due to high costs and low availability, it is not suitable for routine use. An initial diagnostic step in suspected macro-TSH is polyethylene glycol (PEG) precipitation.

Case presentation

We present the case of a 40-year-old, normal-weight patient with TSH elevation (TSH 28 mU/l, n 0.27 – 4.2) and free thyroid hormones within the reference range (fT4 17.8 pmol/l, n 12.0 - 22.0 and fT3 5.08 pmol/l, n 3.1 – 6.8) detected in a routine check in the context of ischemic cardiomyopathy and ongoing amiodarone therapy. Clinically, the patient was euthyroid. An endocrinological workup was performed. Thyroid ultrasonography was unremarkable, and thyroid autoantibodies were negative. Given the unchanged laboratory constellation over several months, a non-thyroidal illness syndrome and an amiodarone-related effect were considered unlikely. A TSH-secreting adenoma was excluded based on normal pituitary imaging and normal alpha-subunit levels. In the absence of clinical symptoms and with free thyroid hormone levels within the reference range, a watchful waiting approach was adopted.

Subsequently, the patient was lost to endocrinological follow-up for an extended period. In the meantime, he underwent a heart transplant and, because of fatigue and persistently elevated TSH levels, the treating team initiated levothyroxine. The laboratory course under continuous dose adjustment of levothyroxine is summarized below (table 2). Due to persistent TSH elevation despite high-dose levothyroxine therapy, a repeat endocrinological evaluation was requested and further workup was performed. Interference due to heterophilic antibodies was excluded and the laboratory constellation was confirmed using different immunoassays and in repeated measurements. Following PEG precipitation, the measured TSH level was markedly lower, suggesting the presence of macro-TSH. Finally, size exclusion chromatography confirmed the presence of macro-TSH. Levothyroxine was discontinued, and the patient remained asymptomatic.

Conclusion

This case highlights the importance of considering macro-TSH as a potential cause of isolated TSH elevation with normal free thyroid hormones, particularly when the clinical presentation and laboratory findings are inconsistent. Failure to recognize macro-TSH led to extensive diagnostic procedures and unnecessary, prolonged levothyroxine treatment over several years. Early identification of macro-TSH can prevent misdiagnosis and avoid unwarranted therapy.

Response to Fluid Restriction in Patients with SIAD – A Validation Analysis

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Background

Fluid restriction is the current first-line therapy for hyponatremia due to the syndrome of inappropriate antidiuresis (SIAD), but up to 50% of patients do not achieve a sufficient increase in plasma sodium levels. European guidelines identify a urine osmolality >500 mOsm/kg as a predictor of non-response. As additional predictors, high urine sodium (>130 mmol/L) and serum urea (>5 mmol/L) have been proposed but have never been validated. This study aimed to validate these predictors and potentially identify new predictors.

Methods

This predefined secondary analysis was based on an international, prospective study that included patients with moderate to severe hyponatremia (serum sodium <130 mmol/L). Response to treatment with fluid restriction was defined as an increase in serum sodium of >3 mmol/L within the first 24 hours, while non-response was defined as an increase of ≤3 mmol/L. Baseline laboratory parameters—particularly urine sodium, urine osmolality, and serum urea—were analyzed using univariate logistic regression.

Results

Of 613 patients with SIAD who had not received fluid restriction prior to study enrollment, 163 were treated exclusively with fluid restriction within the first 24 hours. Among these, 59 patients (36%) were classified as responders, while 104 (64%) did not show a sufficient increase in serum sodium and were considered non-responders. Univariate logistic regression revealed no significant association between treatment non-response and urinary osmolality >500 mOsm/kg (OR 1.87, 95% CI 0.90–3.91, $p = 0.095$), urinary sodium levels >130 mmol/L (OR 3.39, 95% CI 0.95–12.18, $p = 0.061$), or serum urea >5 mmol/L (OR 1.01, 95% CI 0.52–2.00, $p = 0.967$). However, baseline plasma sodium >127 mmol/L, determined by ROC analysis, was statistically significantly associated with non-response to fluid restriction (OR 2.51, 95% CI 1.17–5.41, $p = 0.019$), suggesting that patients with higher initial sodium levels were less likely to benefit from this intervention.

Conclusion

In this cohort, the response rate to fluid restriction after 24 hours was low. The proposed cutoffs for urinary osmolality, urinary sodium, and serum urea did not significantly predict treatment non-response. In contrast, baseline plasma sodium >127 mmol/L was associated with a reduced likelihood of response, indicating that higher baseline plasma sodium may serve as a negative predictor in clinical decision-making.

A challenging a case of familial chylomicronemia syndrome with post-pancreatitis thrombocytopenia treated by Volanesorsen

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Background/Introduction:

Familial chylomicronemia syndrome (FCS) is a rare genetic disorder caused by biallelic mutations in the lipoprotein lipase (LPL) gene or related genes, resulting in severe hypertriglyceridemia and an increased risk of acute pancreatitis. Despite the use of conventional pharmacological interventions and strict dietary management, these approaches are often insufficient. Volanesorsen, an antisense oligonucleotide targeting APOC3 messenger RNA (mRNA), reduces apo-CIII levels thereby decreasing triglyceride (TG) level by relieving its inhibitory effect on LPL activity.

Method/Case presentation:

We describe a challenging case of the case of a 29-year-old patient with a homozygous LPL gene deletion, who suffered from multiple episodes of pancreatitis despite maximal medical therapy and lifestyle changes. The patient has a homozygous deletion which slices exons 9 and 10 of the LPL gene. Volanesorsen was initiated as last-line therapy despite the presence of moderate thrombocytopenia and treatment was closely monitored.

Results:

Over a two-month treatment period (from mid-October to early December 2024), serum TG were efficiently reduced to below 10 mmol/L. This reduction was sustained throughout the course of therapy, even after adjusting the injection intervals to biweekly due to decline in platelet count.

Discussion:

This case highlights the effectiveness of Volanesorsen in reducing TG even in patient with LPL gene deletion. These findings suggest that apo-CIII inhibition may exert its lipid lowering effect through LPL-independent mechanisms. This case also demonstrates that Volanesorsen can be safely initiated with close monitoring in patients with moderate thrombocytopenia.

Conclusion:

Volanesorsen represents a promising therapeutic option for patients with FCS including those with LPL mutation. Volanesorsen and eventually other apoCIII inhibitors such as Olezarsen may lower TG through alternative pathways beyond LPL-dependent mechanism.

Efficacy and Safety of Palopegteriparatide Treatment in Adults With Hypoparathyroidism: 3-Year Results From The Phase 3 PaTHway Trial

Author/Address of institution:

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Background/Introduction:

Hypoparathyroidism is an endocrine disease caused by insufficient levels of parathyroid hormone (PTH) and is associated with reduced quality of life and a high comorbidity burden. Conventional therapy for hypoparathyroidism (active vitamin D and elemental calcium) aims to alleviate hypocalcemia but does not address insufficient PTH and may increase the risk of renal complications. Palopegteriparatide is a prodrug of PTH(1-34), administered subcutaneously once daily, designed to provide active PTH within the physiological range for 24 hours/day. It is approved by the Food and Drug Administration, European Commission, and Medicines and Healthcare products Regulatory Agency. This analysis evaluated the long-term efficacy and safety of palopegteriparatide in adults with chronic hypoparathyroidism through week 156 of the PaTHway trial.

Methods:

PaTHway was a phase 3 trial with a 26-week randomized, double-blind, placebo-controlled period followed by an open-label extension period. Serum biochemistries were assessed at baseline and regular intervals. Renal function was assessed by estimated glomerular filtration rate (eGFR). Safety assessments included 24-hour urine calcium and treatment-emergent adverse events (TEAEs).

Results:

At week 156, 89% (73/82) of participants remained in the trial; of those, 96% were independent from conventional therapy (no active vitamin D and ≤ 600 mg/day elemental calcium) and 88% had normal albumin-adjusted serum calcium levels (8.3-10.6 mg/dL) with a mean (SD) of 8.9 (0.6) mg/dL. Mean (SD) serum phosphate (3.4 [0.6] mg/dL) and calcium x phosphate product (30.6 [5.4] mg²/dL²) levels remained within normal ranges through week 156. Mean (SD) eGFR at week 156 was 78.0 (14.5) mL/min/1.73 m², reflecting a mean (SD) increase of 8.8 (11.9) mL/min/1.73 m² from baseline ($P < 0.0001$); 59% and 43% of participants had an increase in eGFR of ≥ 5 mL/min/1.73 m² and ≥ 10 mL/min/1.73 m², respectively. Among participants with baseline eGFR < 60 mL/min/1.73 m² ($n = 23$), the mean (SD) increase in eGFR was 14.0 (8.9) mL/min/1.73 m² from baseline to week 156. Mean (SD) 24-hour urine calcium levels normalized with palopegteriparatide treatment, remaining below the upper limit of normal (≤ 250 mg/day) through week 156 (162.1 [117.8] mg/day). TEAEs were mostly grade 1 or 2, with no new safety signals identified.

Conclusion:

Through year 3 of the PaTHway trial, retention rate was high and palopegteriparatide demonstrated consistent longer-term safety and efficacy, which included the maintenance of serum and urine biochemistries within normal levels and sustained improvement in renal function.

Long-Term Efficacy and Safety of Palopegteriparatide Treatment in Adults With Chronic Hypoparathyroidism: 4-Year Results From the Phase 2 PaTH Forward Trial

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Background/Introduction:

Hypoparathyroidism is an endocrine disease caused by insufficient levels of parathyroid hormone (PTH). Conventional therapy for hypoparathyroidism (active vitamin D, elemental calcium) aims to alleviate hypocalcemia but does not address insufficient PTH. Palopegteriparatide is a prodrug of PTH (1-34), administered once daily, designed to provide active PTH within the physiological range for 24 hours/day in adults with chronic hypoparathyroidism. It is approved by the EC, MHRA, and FDA. This analysis investigated the long-term efficacy and safety of palopegteriparatide in adults with chronic hypoparathyroidism through week 214 of the PaTH Forward trial.

Methods:

PaTH Forward was a phase 2 trial with a 4-week randomized, double-blind, placebo-controlled period, followed by an open-label extension period. Renal function was assessed by estimated glomerular filtration rate (eGFR). Bone turnover markers C-terminal telopeptide of type 1 collagen (CTX) and procollagen type 1 N-terminal propeptide (P1NP), and bone mineral density (BMD) measured by DXA, were assessed at baseline and regular intervals through week 214. Safety assessments included 24-hour urine calcium and treatment-emergent adverse events (TEAEs).

Results:

At week 214, 95% (56/59) of participants remained in the trial; of those, 93% were independent from conventional therapy (no active vitamin D and ≤ 600 mg/day elemental calcium) and 98% had normal albumin-adjusted serum calcium levels (2.07-2.64 mmol/L) with a mean (SD) of 2.24 (0.10) mmol/L. Mean CTx and P1NP increased from the low end of normal at baseline, peaked by week 26, and declined thereafter and remained stable above baseline levels through week 214. The elevated baseline mean BMD Z-scores trended towards age- and sex-matched norms at the lumbar spine, femoral neck, and total hip and largely stabilized after 26 weeks of treatment, remaining above zero through week 214. Changes in Z-scores were larger in participants with longer duration of hypoparathyroidism but were similar across the population when considering sex and age/menopausal status. Mean (SD) eGFR at week 214 was 86.0 (21.7) mL/min/1.73 m², reflecting a mean (SD) increase of 7.6 (13.7) mL/min/1.73 m² from baseline. Mean (SD) 24-hour urine calcium levels normalized with palopegteriparatide treatment, remaining below the upper limit of normal (≤ 6.2 mmol/day) through week 214 (4.4 [2.1] mmol/day). TEAEs were mostly mild or moderate; no new safety signals were identified.

Conclusion:

These results demonstrate sustained efficacy and safety of palopegteriparatide in adults with chronic hypoparathyroidism through week 214 of the PaTH Forward trial, highlighting continued benefits in skeletal dynamics and renal function.

Smartphone-Based Automated Meal Analysis for Type 1 Diabetes: User Engagement, Usability Perceptions, and Impact on Glycaemic Control in AID Users

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Background/Introduction:

Precise meal carbohydrate estimation persists as a critical challenge in type 1 diabetes management. Image-based food recognition technologies represent emerging solutions for optimizing prandial decision support. In this real-world study, we quantified engagement metrics, usability perceptions of SNAQ - a smartphone application deploying artificial intelligence and computer vision for automated meal macronutrient analysis – in adult AID user with type 1 diabetes. We further related pre/post usage changes in glucose control with subjective experiences.

Methods:

Forty-one adults with type 1 diabetes using variable AID systems received complimentary SNAQ access and were instructed to consistently utilize the application for meal management during a 3-week observation period, with optional use thereafter. Participants completed a user experience questionnaire post-intervention. Change in Time in Range (TIR; sensor glucose 3.9-10.0mmol/L) was assessed by comparing sensor glucose concentrations during the 3-week intervention period versus a 2-3 week pre-intervention baseline under usual care. Using ordinal logistic regression adjusted for age and sex, we examine associations between changes in TIR and user-reported experience measures.

Results:

Mean baseline TIR was $73.7 \pm 13.6\%$. Following SNAQ implementation, the cohort demonstrated a mean change in TIR of $+3.5 \pm 6.9\%$. Application engagement averaged 1.6 ± 1.0 daily uses during the 3-week intervention but exhibited declining utilization over time, and was negligible during the follow-up period with optional SNAQ use. Participants rated SNAQ highly for usability: 80.5% endorsed its simple design and 87.8% reported ease of use. Greater TIR improvements correlated positively with perceived benefits in dietary choices ($p = 0.026$), nutrition literacy ($p < 0.001$), and glucose control perception ($p < 0.001$). Conversely, larger TIR gains predicted lower satisfaction with the application's estimation performances ($p < 0.001$). Reported carbohydrate estimation burden during SNAQ use remained unchanged from baseline.

Conclusion:

Participants with greater TIR improvements credited meal management benefits to enhanced food awareness and nutrition literacy rather than automated carbohydrate estimation. Despite positive usability ratings, sustained interest in the application was lacking across the entire cohort. These findings suggest that effective nutritional support in type 1 diabetes requires approaches beyond carbohydrate quantification, warranting further research in this field.

A case of severe Myxedema Coma and Literature Review.

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Background/Introduction:

Myxedema coma is a nowadays rare but still life-threatening medical emergency caused by severe and prolonged hypothyroidism and associated with multi-organ dysfunction. We present a case of myxedema coma from our hospital, complicated by cardiorespiratory failure and requiring intensive care unit admission.

Methods:

A 72-year-old woman presented in a somnolent state with anasarca, hemodynamic instability, and profound hypoventilation (arterial pCO₂ 12.4kPa). Her medical history included depression and psoriasis. In the days prior to the admission, the patient complained about persistent fatigue, dry cough, and cold intolerance. Imaging showed bilateral pleural effusions, significant pericardial effusion, and ascites. Her respiratory failure was initially managed with non-invasive ventilation, followed by intubation and transfer to the intensive care unit. The pericardial effusion was drained urgently because of hemodynamic instability, characterized by hypotension, pulsus paradoxus, and corresponding findings on transthoracic echocardiography (TTE). Drainage led to immediate hemodynamic improvement. The right-sided pleural effusion was subsequently drained to relieve respiratory compromise in addition to diuretic therapy. Cytology of the effusions was negative for malignancy.

Given the high clinical suspicion for overt hypothyroidism based on her symptoms, laboratory tests were performed, which revealed markedly elevated TSH (47.800 µE/ml, normal range: 0.27 - 4.20 µE/ml), unmeasurably low fT3 (< 0.6 pmol/l, normal range: 3.1 - 6.8 pmol/l) and fT4 levels (< 0.5 pmol/l, normal range: 12 - 22 pmol/l). Thyroid Peroxidase (TPO) antibodies were markedly elevated (3112 kIU/L, normal range: < 60 kIU/L), consistent with Hashimoto's thyroiditis.

Intravenous levothyroxine was initiated for severe hypothyroidism. A random cortisol level was within the normal range, but not relatively elevated under stress (276 nmol/L, normal range: 145 – 619 nmol/L). Relevant hypocortisolism was excluded by an ACTH-stimulation test (Cortisol 60' after ACTH: 808 nmol/L, normal: > 500 nmol/L), so there was no need for corticosteroid substitution.

Results:

The patient regained consciousness rapidly after initiation of levothyroxine therapy and demonstrated hemodynamic stability as well as an overall improvement in clinical condition. After an 11-day hospitalisation, the patient was discharged from the hospital in improved condition. Right before hospital discharge, the TSH was only reduced to 39 µE/ml, as expected due to delayed pituitary-thyroid axis feedback. However, the peripheral values were significantly improved (fT3 2.27 pmol/l, fT4 levels 8.67 pmol/l).

Conclusion:

Myxedema is a rare but life-threatening manifestation of severe hypothyroidism that requires prompt recognition and aggressive therapy. Despite advancements in intensive care and hormone replacement, mortality remains high—especially in older patients with delayed diagnosis. A high index of suspicion is essential in patients presenting with altered mental status, hypothermia, and bradycardia in the setting of known or suspected hypothyroidism. Early intravenous levothyroxine, supportive care, and stress-dose glucocorticoids, when indicated, remain the cornerstone of management.

Normalization of mild to moderate hyponatremia in hospitalized patients decreases osteoclast activation

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Background/Introduction:

Hyponatremia is the most common electrolyte disorder in hospitalized patients. Over the past decades, studies have shown an association between hyponatremia and increased risk of bone fragility and fractures. While preclinical studies suggest that hyponatremia stimulates osteoclast activation, secondary analyses in patients with syndrome of inappropriate antidiuresis showed an improvement in osteoblast function after correction of hyponatremia. This study aimed to evaluate whether the normalization of hyponatremia of any origin in hospitalized patients with mild to moderate hyponatremia impacts bone metabolism.

Methods:

In this prospective, observational study we included patients with serum sodium levels <135 mmol/l hospitalized at the University Hospital of Basel, Switzerland, between March 2020 and February 2025. Premenopausal women, patients receiving steroid therapy, patients with hypogonadism, fractures, hyperparathyroidism or undergoing specific osteoporotic treatment were excluded. Serum sodium levels and biochemical markers of bone resorption (CTX) and bone formation (P1NP) were measured at baseline and after 10(\pm 3) days. Descriptive analyses were applied to compare patients who achieved normonatremia versus those who remained hyponatremic at day 10. A multivariable model was implemented to adjust for baseline characteristics and comorbidities

Results:

Forty-one patients, 66% male, with mean age of 68.6 years and median(IQR) body mass index (BMI) of 23.2 (21.7-26.4) kg/m² completed the study. Median (IQR) sodium at baseline was 130 (127-132 mmol/l), with 60% of the patients showing mild hyponatremia (sodium 130-134 mmol/l). Serum-CTX levels at baseline between patients with persistent hyponatremia (n=19, 46.3%) and patients reaching normonatremia at day 10 were similar: median (IQR) 0.41 (0.29-0.53) ng/ml vs 0.41 (0.37-0.66) ng/ml, p=0.35. In contrast, significantly higher CTX levels at day 10 were observed for patients with persistent hyponatremia: median (IQR) 0.54 (0.37-0.58) ng/ml vs 0.35 (0.26-0.45) ng/ml, p=0.02. P1NP levels showed no differences between the groups at both baseline and day 10 (p>0.05). Length of hospitalization was similar in the two groups (11(6.5-28) days in the normonatremia vs 11(6.5-15) days in persistent hyponatremia, p=0.30). The multivariable linear model adjusted per age, sex, BMI, comorbidities, smoking habits, 25OH vitamin D levels and volume status confirmed an independent association between normonatremia at day 10 and a decrease in CTX (estimate β coefficient -0.18, 95%CI -0.29 to -0.08, p=0.002).

Conclusion:

In hospitalized patients with mild to moderate hyponatremia, normalization of sodium levels is associated with a decrease of CTX levels, suggesting an attenuation of osteoclast activity. Hyponatremia correction could thus be beneficial for bone health.

Associations between cardiorespiratory fitness and muscle strength with metabolic health outcomes and inflammatory parameters at 1-year postpartum in women after gestational diabetes

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Background/Introduction:

Women with gestational diabetes mellitus (GDM) have increased risk of insulin resistance, glucose intolerance, and low-grade systemic inflammation in the postpartum. Higher cardiorespiratory fitness (CRF) and muscular strength (MS) are associated with improved metabolic outcomes in the general population, but data in women with GDM are lacking. We investigated the longitudinal associations between CRF and MS during pregnancy with glucose intolerance, insulin resistance and inflammation parameters at 1-year postpartum in women with GDM.

Methods:

This is a secondary analysis of the MySweetHeart trial, which included 179 women with GDM. During pregnancy, CRF was assessed using the Chester Step test, and MS was measured via handgrip strength and adjusted for body mass index (BMI) during pregnancy. At one-year postpartum, participants underwent a 75g oral glucose tolerance test, and we calculated HOMA-IR and MATSUDA index. We calculated glucose intolerance and assessed metabolic syndrome (MetS) and c-reactive protein (CRP) at 1-year postpartum.

Results:

Higher CRF during pregnancy was associated with lower risk of glucose intolerance, MetS, and insulin resistance at one-year postpartum (all $p \leq 0.047$). These associations were attenuated after adjusting for classical diabetes risk factors including family history of diabetes, age, ethnicity, and pre-pregnancy BMI. Higher MS during pregnancy was associated with lower CRP, HOMA-IR, higher MATSUDA index, and reduced MetS (BMI-based) at one-year postpartum, the latter three even independent of classical diabetes risk factors (all $p \leq 0.043$).

Conclusion:

In this longitudinal cohort of women with GDM, higher CRF and MS during pregnancy were protective of adverse metabolic health outcomes at 1-year postpartum. The relationship between MS and metabolic health was independent of classical diabetes risk factors.

Long-term evolution of cardiovascular complications and risk factor control in type 1 diabetes mellitus – a SwissDiab Study

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Background/Introduction:

Cardiovascular disease remains the leading cause of morbidity and mortality in individuals with type 1 diabetes mellitus (T1DM). End of the 2010s, the importance of cardiovascular risk management in T1DM gradually gained more focus in national and international treatment guidelines. The current status of cardiovascular risk management, and to what extent it has developed over time is unclear. The aim of the current study was to assess the prevalence and prior development of cardiovascular risk factors and complications in adults with T1DM in tertiary diabetes care in Switzerland.

Methods:

A retrospective analysis based on data from the Swiss Diabetes Registry (SwissDiab), a multicentre longitudinal observation study of patients in tertiary diabetes care. Patients with T1DM and a study visit in 2022/23 were included. Cardiovascular risk and risk factor control was mainly defined according to the 2021 European Society of Cardiology (ESC) guideline. Control of the following six cardiovascular risk factors was determined; low-density lipoprotein cholesterol (LDL-C, based on cardiovascular risk according to the 2021 ESC guideline), blood pressure (<130/80 mmHg if ≤65 years; <140/80 mmHg if >65 years), glycaemic control (HbA1c <7%), weight (BMI <25 kg/m²), smoking, and albuminuria (ACR ≤3 mg/mmol), as well as the prevalence of cardiovascular complications. To assess prior development, the analysis was repeated among the sub-group of patients with data from a SwissDiab visit back in 2015/16, applying the same treatment targets for cardiovascular risk factor control.

Results:

Of 285 patients with a visit in 2022/23, 280 had data available for analysis. Median (IQR) age was 44.7 (32.5, 59.2) years, diabetes duration 18 (11, 27) years, HbA1c 7.3 (6.8, 8.0)%, BMI 24.9 (22.6, 27.6) kg/m², 20.9% were active smokers, 71.2% had hypertension, and 2.4% were at moderate, 76.1% at high, and 21.5% at very high cardiovascular risk. A prior history of myocardial infarction, coronary heart disease and stroke was present in 2.5, 5.0 and 0.7%. Of the 125 patients with data available back in 2015/16 (follow-up time 7.5 [7.0, 8.1] years), the number with controlled LDL-C and HbA1c had increased in 2022/23, and less were active smokers. However, the only significant changes were impaired weight control (50.0% vs 60.5%) and an increased prevalence of albuminuria (89.2% vs 82.0%). Although the majority of patients had 3 or less risk factors under control in both 2015/16 and 2022/23 (74.3 vs 69.5%), more patients had only 2 risk factors controlled in 2022/23 (37.1 vs 23.8%, p=0.016). The prevalence of coronary heart disease (12.8 vs 3.2%, p=0.03) and of patients with at least one cardiovascular event (13.6% vs 8.8%, p=0.03) increased significantly between 2015/16 and 2022/23, reflecting a slowly increasing burden of cardiovascular complications.

Conclusion:

Overall, cardiovascular risk management in T1DM was suboptimal and resulted in an increasing prevalence of ASCVD. The results illustrate the need for a more aggressive management in daily clinical practice in patients with T1DM.

Diagnostic Performance of Urine Sodium to Assess Volume Status in hyponatremic patients: Data from a Prospective Study

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Background/Introduction:

Hyponatremia (serum sodium < 135 mmol/l) is common in hospitalized patients. Accurate assessment of extracellular fluid volume state (ECFV) is key to appropriate treatment, but remains challenging. Current European guidelines suggest urine sodium ≥ 30 mmol/l indicates euvolemia. However, this is based on scarce evidence and may be unreliable in case of diuretic therapy. This analysis aimed to determine the optimal urine sodium threshold for predicting ECFV in a large hyponatremic cohort.

Methods:

This preplanned secondary analysis used data from an international, randomized-controlled trial (2018-2024) of hospitalized adults with hypotonic hyponatremia (serum sodium < 130 mmol/l), randomized to either targeted plasma sodium correction or standard care. Urine sodium was measured at baseline. Treatment response (≥ 2 mmol/l plasma sodium increase on day 1 following treatment based on initial clinical evaluation) served as the reference standard. ROC analysis was performed to detect the optimal urine sodium threshold.

Results:

Treatment response on day 1 was documented in 684 patients with available urine sodium values. The standard threshold of 30 mmol/L provided a high sensitivity of 85% and a specificity of 39% for identifying euvolemia. Raising the threshold to 40 mmol/l showed slightly lower sensitivity 75% but enhanced specificity to 54%. A higher cutoff of 50 mmol/L further decreased sensitivity (64%) with a modest gain in specificity (66%).

For identifying hypovolemia, the standard threshold of 30 mmol/l showed a sensitivity of 43% and specificity of 80%. Increasing the threshold to 40 mmol/l improved sensitivity to 58% but reduced specificity (69%).

Conclusion:

The standard threshold of 30 mmol/l for detecting euvolemia showed higher sensitivity at the cost of lower specificity. A higher threshold of 40 mmol/l offered a better compromise between sensitivity and specificity in this analysis.

Associations of eating and sleep patterns with daily values of overnight glucose measures using ecological momentary assessments in women with GDM

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Background/Introduction:

The influence of diet and sleep on daily glucose control in women with gestational diabetes (GDM) remains unclear. We used ecological momentary assessment (EMA) to assess real-time associations between time, eating and sleep patterns with overnight and morning glucose measures.

Methods:

We included 34 untreated women with GDM (28 ± 2 weeks of gestational age) followed at the Lausanne University Hospital. We assessed the relationship of evening eating and sleep patterns with glucose measures using EMA. Predictors included the effect of time, daily food diaries and sleep questionnaire (Spiegel sleep questionnaire). Outcomes were derived from continuous glucose monitoring (CGM) over 5 days, after removal of day 1, assessing 5-day averaged and daily values of overnight mean glucose, variability (SD), total glycemic exposure during the night measured as the mean overnight glucose area under the curve (AUC), and glucose levels upon waking. We performed multivariate stepwise regressions to identify the most relevant predictors and ANOVAs to investigate the effect of time on glucose measures.

Results:

Higher day-to-day variability in number of snacks was associated with increased 5-day average values of overnight mean glucose levels and AUC (all, $p \leq 0.03$). Later dinner was associated with both greater 5-day average levels of overnight glucose variability and daily values of overnight glucose variability (SD) (both $p \leq 0.01$). Overnight mean glucose levels, AUC, and glucose levels upon waking showed significant differences across days (all $p \leq 0.03$).

Conclusion:

Reinforcing regular dinner time and reducing variability in eating habits may represent a strategy to help optimize overnight glycemic values in women with GDM. A still unexplained daily variation in overnight and waking glucose CGM should be also considered.

The impact of arginine vasopressin deficiency on bone turnover markers: a comparative analysis with primary polydipsia and healthy controls

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Background/Introduction:

Arginine vasopressin (AVP) and oxytocin (OXT) are neurohypophyseal hormones known to exert opposing effects on bone metabolism. Based on animal models, AVP has been shown to reduce bone formation and promote resorption via AVP V1a receptor signaling, whereas OXT promotes osteoblast differentiation and activity. Despite the well-established cellular actions of these hormones on osteoblasts and osteoclasts in preclinical studies, data from human studies are lacking, particularly regarding bone metabolism in populations with a deficiency of AVP and possibly OXT, such as individuals with AVP deficiency (AVP-D, previously referred to as central diabetes insipidus). This study aimed to evaluate bone turnover markers in patients with AVP-D compared to individuals with primary polydipsia (PP) and healthy controls (HC).

Methods:

This was a secondary analysis of a prospective trial including adult HC and patients with PP and AVP-D undergoing a novel copeptin stimulation test with urea. Laboratory assessments were performed at baseline and included markers for bone resorption (C-terminal telopeptide of type I collagen, CTX) and bone formation (N-terminal propeptide of type I procollagen, P1NP), as well as 25OH vitamin D, serum calcium, and phosphate. The bone formation index (defined as P1NP/CTX ratio) was calculated. Patients on chronic steroid therapy (except budesonide and corticosteroid replacement therapy), prior osteoporotic fractures, or long-term antiresorptive treatment were excluded from the analysis.

Results:

Forty-seven subjects were included (HC=22, AVP-D=12, PP=13). Serum calcium, phosphate, 25OH vitamin D and P1NP levels were comparable across all groups. Median (IQR) CTX levels were significantly lower in AVP-D patients (0.376 [0.295-0.580] ng/ml) compared to HC (0.592 [0.427-0.729] ng/ml, $p=0.036$), with no difference between PP (0.514 [0.411-0.618] ng/ml) and the other two groups ($p>0.05$). In the multivariable linear regression model, the P1NP/CTX ratio adjusted for confounders was significantly higher in AVP-D compared to HC ($\beta = 38.3$, $p=0.041$) while no difference was observed compared to PP.

Conclusion:

Patients with AVP-D exhibited an increased P1NP/CTX ratio compared to HC, whereas the ratio in patients with PP was similar to both groups. Overall, our findings do not clearly indicate altered bone metabolism in AVP-D; if present, it is unlikely to be harmful.

Refractory Cough Revealing an Ectopic Parathyroid Adenoma: A Case Report

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Background/Introduction:

Primary hyperparathyroidism (PHPT) is an endocrine disorder characterized by hypercalcemia due to excessive parathyroid hormone (PTH) secretion. It affects approximately 1% of the population and is most often caused by a single parathyroid adenoma. Less commonly, it results from multiglandular disease (multiple adenomas or hyperplasia) or, rarely, parathyroid carcinoma. While parathyroid glands are usually located near the thyroid, ectopic locations occur in 10–22% of cases due to abnormal embryologic migration. The superior parathyroid glands originate from the fourth pharyngeal pouch and typically migrate to the posterior thyroid, with the retroesophageal space being the most common ectopic site (2–58%). Inferior parathyroids arise from the third pharyngeal pouch, along with the thymus, and can be located anywhere from the mandible to the pericardium. Due to their variable and often atypical locations, ectopic adenomas are often difficult to localize preoperatively and challenging in the initial surgical management.

Methods:

We hereby describe the clinical presentation, imaging, laboratory findings and short-term follow-up of a patient with ectopic primary hyperparathyroidism.

Results:

In a 75-year-old female patient, a thoracic CT scan was performed by her general practitioner due to therapy-resistant cough and fatigue. The imaging revealed an unclear retroesophageal mass in the upper mediastinum measuring 2.2 × 1.6 × 5.3 cm. Laboratory tests showed pronounced albumin-corrected hypercalcemia (up to 3.1 mmol/L) and significantly elevated PTH levels (up to 606 ng/L), with normal vitamin D levels. Due to the severity of hypercalcemia, the patient was admitted to inpatient care and referred for endocrine evaluation. The patient denied classic symptoms of hyperparathyroidism such as bone pain, pathological fractures, proximal muscle weakness, cramps, loss of appetite, constipation, polyuria, or polydipsia. However, she reported a history of bilateral nephrolithiasis (2015) and a chronic kidney disease (KDIGO G4). Previous calcium levels were not available. Based on the biochemical findings, an oligosymptomatic primary hyperparathyroidism was suspected. Neck ultrasound did not reveal any enlarged parathyroid gland in typical locations. However, a choline PET-CT scan demonstrated an ectopic parathyroid adenoma with increased choline uptake, correlating with the known retroesophageal lesion in the upper mediastinum. Given the biochemical abnormalities and clinical history, a focused minimally-invasive trans-thoracic parathyroidectomy from the right side was performed using the Da Vinci Xi robotic system. A 2.5 × 2.0 × 6.0 cm hypercellular adenoma was removed without histological signs of malignancy. Intraoperatively, PTH dropped from 339 ng/L to 36 ng/L, and calcium levels normalized postoperatively (2.5 mmol/L). Notably, the previously persistent cough – the leading symptom of this rare ectopic primary hyperparathyroidism – resolved completely after surgery.

Conclusion:

This case report aims to raise the awareness of an atypical presentation of ectopic primary hyperparathyroidism, the relative rarity of ectopic parathyroid adenomas, and the associated diagnostic and therapeutic challenges.

Sustained Glycemic Improvements with Extended Use of the Omnipod® 5 Automated Insulin Delivery (AID) System: Results of the RADIANT 13-week Extension Study

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Background/Introduction:

The efficacy and safety of the Omnipod® 5 AID System compared with multiple daily injections (MDI) and continuous glucose monitor (CGM) therapy in adults and children with type 1 diabetes (T1D) and suboptimal glycemia was recently demonstrated in the RADIANT study, a multinational randomized controlled trial (RCT). This analysis evaluated glycemic outcomes during the extension phase of the RADIANT study.

Methods:

In the 13-week RCT, adults and children aged 4-70y with T1D and screening HbA1c 58-97 mmol/mol currently using MDI with a FreeStyle Libre 2 CGM for ≥ 3 months were enrolled across 19 institutions in France, the United Kingdom, and Belgium. Participants completed 14 days of baseline data collection with MDI+CGM, then were randomly assigned 2:1 to AID (intervention) or to continue with MDI+CGM (control). During the extension phase (weeks 14-26), participants in the control group initiated AID (MDI-AID group) and participants in the intervention group continued to use the AID system (AID-AID group).

Results:

A total of 187 participants (MDI-AID: n=63, AID-AID: n=124) continued into the extension phase, of which 96% (180/187) completed it. Improvements in HbA1c were observed at 26 weeks in the MDI-AID group (week 13 vs 26: 64 vs 56 mmol/mol, $p < 0.0001$), while the initial improvements from baseline were maintained in the AID-AID group (baseline vs week 26: 65 vs 55 mmol/mol, $p < 0.0001$). Similarly, time in range (3.9-10.0 mmol/L) during the extension phase increased in the MDI-AID group (week 13 vs 26: 43% vs 65%, $p < 0.0001$) and was maintained in the AID-AID group (baseline vs week 26: 39% vs 66%, $p < 0.0001$). In both groups, time < 3.9 mmol/L remained low at 26 weeks: median 2.3% vs 2.2% at week 13 in the MDI-AID group and 2.5% vs 2.2% at baseline in the AID-AID group (both $p > 0.05$).

Conclusion:

These extension phase results demonstrated significant improvements in glycemic outcomes with AID, providing further evidence of sustained benefit of Omnipod 5 use following direct transition from MDI in adults and children with T1D not meeting glycemic targets.

Brain Age in Adult Patients with Early-Treated Phenylketonuria

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Background/Introduction:

Structural brain alterations have been observed in individuals with phenylketonuria (PKU), however the potential impact of PKU on brain aging remains unexplored. This study investigated brain age in adults with early-treated classical PKU compared to healthy controls.

Methods:

Thirty early-treated adults with classical PKU (age 19–48 years) and 59 age-, sex-, and education-comparable healthy controls underwent structural magnetic resonance imaging (MRI), cognitive and mood assessment, and blood sampling for phenylalanine (Phe) levels. Brain age was estimated using machine learning models trained to predict brain age from MRI-derived features across various brain regions. The brain age gap (BAG), defined as the difference between brain age and chronological age, was calculated. In addition, white matter lesion load was quantified for each patient.

Results:

Patients with PKU showed a higher BAG than healthy controls in four out of eight brain regions; however, after false discovery rate (FDR) correction, only the difference in the insula remained statistically significant ($p = 0.006$, $\eta^2 = 0.07$). In patients, cingulate BAG was positively correlated with both concurrent and historical Phe levels ($r_s = 0.41$ – 0.69 , $p < 0.05$), as well as with white matter lesion load ($r_s = 0.40$, $p = 0.034$). Moreover, subcortical and cingulate BAG were associated with cognitive performance ($r_s = -0.41$ – 0.38 , $p < 0.05$), though none of the correlations above survived FDR correction.

Conclusion:

In conclusion, the elevated insular BAG observed in adults with early-treated PKU may reflect the cumulative effects of early-life or lifelong metabolic disturbances. Longitudinal studies are warranted to further elucidate brain aging trajectories and their cognitive implications in PKU.

Sleep duration but not sleep variability is associated with markers of glucose metabolism. Multiple cross-sectional studies.

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Background

Sleep duration has been suggested to be associated with insulin resistance or high glucose levels. However, sleep is characterized by its duration and variability, and few studies have explored the relationship between sleep variability and markers of glucose metabolism.

Objective

Assess the associations between sleep duration and variability and glucose metabolism in a Swiss population-based sample.

Methods

Cross-sectional analyses from survey periods 2014-2017 (second follow-up, N=2310, 64.1±10.9 years, 43.0% female) and 2018-2021 (third follow-up, N=1843, 65.5±10.2 years, 42.6% female) of the CoLaus|PsyCoLaus study. Sleep metrics were assessed using accelerometers (processed via two MACRO, and GGIR algorithms) and ecological momentary assessment (EMA) for one week. Variability was determined by standard deviations (SD), coefficient of variation (CV), and range.

Results

In the second follow-up, after multivariable adjustment, for the MACRO algorithm, sleep duration was negatively associated with glucose (standardized beta: -0.055, p=0.016), insulin (beta=-0.070, p<0.001) and HOMA (beta=-0.077, p<0.001), while no association was found with sleep variability. Similar findings were obtained for sleep duration as assessed by EMA, but not for the GGIR algorithm. In the third follow-up, similar findings were obtained for MACRO, while sleep duration as assessed by GGIR was also negatively associated with all glucose markers: betas -0.087, -0.067 and -0.078 for glucose, insulin and HOMA, respectively, all p<0.05, while no association was found for sleep as assessed by EMA. No U-shaped association was found.

Conclusion

Sleep duration but not sleep variability are associated with glucose, insulin, HOMA, but the results differ according to the sleep assessment method.

Little or no association between sleep duration or variability and diabetes. Cross-sectional and prospective studies.

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Background:

Sleep duration has been suggested to be associated with diabetes. However, few large-scale longitudinal studies have comprehensively explored the relationship between sleep variability and Type-2 diabetes mellitus (T2DM).

Objective:

Assess the associations between sleep variability with T2DM prevalence and incidence in a Swiss population-based sample.

Methods:

Cross-sectional and longitudinal analyses from survey periods 2014-2017 (second follow-up, N=2571, 61.9±9.9 years, 53.4% female) and 2018-2021 (third follow-up, N=1908, 65.1±9.5 years, 53.8% female) of the CoLaus|PsyCoLaus study. Diabetes was assessed by fasting plasma glucose ≥ 7.0 mmol/L. Sleep metrics were assessed using accelerometers (processed via two MACRO, and GGIR algorithms) and ecological momentary assessment (EMA) for one week. Variability was determined by standard deviations (SD), coefficient of variation (CV), and range.

Results:

In cross-sectional analysis, after multivariable adjustment, sleep variability as assessed by EMA were higher among participants with diabetes than in participants without, average±standard error 61±5 vs 51±1 minutes for SD and 161±11 vs. 128±4 minutes for range, respectively. Bedtime range as assessed by GGIR was shorter among participants with diabetes than in participants without, 90±4 vs. 100±1 minutes. No other differences were found. In the prospective study, on bivariate analysis, participants who developed T2DM had a shorter sleep duration at baseline than participants who remained free of the disease: 353±63 vs. 402±63, but no differences were found after multivariable adjustment.

Conclusion:

Sleep variability appears to be associated with diabetes, but results depend on the sleep assessment method. We found no association between sleep duration or variability and incident T2DM.

Towards Scalable Digital Studies in Type 2 Diabetes: An Infrastructure for Sensor Integration, Diet Logging, and Customizable Messaging

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Background: Observational and intervention studies in type 2 diabetes (T2D) increasingly utilize digital tools, such as smartphone applications and smartwatches, to collect lifestyle data (e.g., physical activity, sleep, stress, and nutrition). While existing research platforms ensure regulatory compliance, they typically offer limited support for detailed food logging (e.g., meal photos) and lack flexible customization and control over in-app messaging. This limitation constrains researchers' ability to deliver behavioral prompts and support participant adherence throughout the study. As a result, many research teams develop custom data collection applications, which can be twice as costly as out-of-the-box solutions, harder to replicate, and make it difficult to pass regulatory requirements, posing barriers to scalability and reproducibility in metabolic health research.

Methods: We developed and evaluated a modular, low-cost infrastructure to support digital metabolic health studies. The system leverages a pre-existing clinical data collection platform (MyDataHelps) to handle core functionalities such as survey administration, wearable data integration, and daily food logging, thereby minimizing development burden. A lightweight, open-source software component was developed to connect this platform to custom logic (i.e., configurable by the research team) for message timing and content, supporting rule-based and randomized message delivery based on near real-time participant data.

Results: The infrastructure was deployed in a 30-day feasibility study with five participants. The system delivered over 1,500 smartphone-based reminders to support participants' adherence to a food logging protocol. Message timing was randomized within participant-defined time windows, and message contents were adapted to each participant's prior logging behavior. Participants received up to four prompts per day. The infrastructure operated at a minimal cost (~0.03 CHF per participant per month). All code developed for the infrastructure was made openly available on GitHub and designed for reuse in future digital metabolic health studies.

Conclusions: This work presents a practical, low-cost blueprint for conducting digital studies in T2D and other metabolic health studies that integrate wearable monitoring, nutrition logging, and participant messaging. By extending existing platforms through a modular open-source component, we demonstrate that reliable digital data collection and customizable messaging can be implemented without custom app development. This approach reduces cost and technical burden while enabling scalability and reproducibility in clinical research.

Incidence and hospital outcomes of acute adrenal crisis amongst different etiologies and age groups: a population-based study

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Background/Introduction:

Adrenal crises (AC) are potentially life-threatening emergencies, yet epidemiology is underreported, particularly in older adults. The objective of this study is to assess the incidence, clinical outcomes and predictors of outcomes of AC-related hospitalizations focusing on age- and etiology-specific differences in Switzerland from 2012- 2022.

Methods:

Nationwide retrospective cohort study analyzing Swiss hospital discharge data linked to the national death registry. Hospitalizations with AC were identified and stratified by age group and AI etiology - primary (PAI), central (CAI) and unspecified (UN). Incidence rates were calculated per 100,000 person years. The primary outcome was AC hospitalization incidence; main secondary outcome was a composite endpoint of in-hospital mortality, ICU admission and 30-day rehospitalization. Additional outcomes were length of stay, length of ICU-stay and 1-year all-cause mortality. To reduce allocation bias, 3:1 propensity score matching was performed. Predictors of adverse outcomes were analyzed using multivariate logistic regression.

Results:

2,302 AC hospitalizations were identified. AC hospitalization incidence increased over the study period with the highest overall incidence in patients >80 with the steepest rise in cases with CAI. Compared to matched controls, AC was associated with a higher risk of the secondary composite outcome (OR 1.33; 95% CI 1.23-1.43) driven primarily by ICU admissions (OR 1.72; 95% CI 1.55-1.90). The UN group showed the highest in-hospital mortality (OR 1.66; 95% CI 1.35-2.02) and 1-year all-cause mortality (OR 1.20; 95% CI 1.04-1.39). Key predictors of adverse outcomes included UN etiology, advanced age, male sex, diabetes insipidus, sepsis and cancer.

Conclusion:

The incidence of AC-related hospitalizations has increased in Switzerland, especially among the elderly, who are particularly vulnerable to adverse outcomes. Steepest rise in hospitalizations occurred in CAI, possibly linked to increased use of glucocorticoids and immune checkpoint inhibitors. Patients in the UN group experienced the poorest outcomes but reasons remain elusive. These findings underscore the need to improve identification and management of AI - especially in older populations.

Associations between conscientiousness personality trait, self-efficacy, and health literacy with mental and metabolic health in women with Gestational Diabetes Mellitus in the perinatal period.

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Background/Introduction:

Gestational Diabetes Mellitus (GDM) is associated with increased long-term maternal metabolic and mental health risks. An effective management of GDM requires sustained changes in diet, eating behavior and perinatal weight control. Psychosocial factors, such as self-efficacy, conscientiousness personality trait, and health literacy may be protective factors for metabolic and mental health including both depression and eating behavior. We investigated the associations between these psychosocial factors with metabolic and mental health outcomes in the perinatal period in women with GDM.

Methods:

This is a secondary analysis of the MySweetheart treatment trial, which included 211 women with GDM. Predictors included dietary (diet) self-efficacy, physical activity (PA) self-efficacy, and social support (soc) self-efficacy, conscientiousness (Big5C), and health literacy (HL), all assessed using validated self-report questionnaires. Outcomes included weight, BMI, Reliance on Hunger and Satiety Cues (RHSC) and Eating for Physical rather than emotional Reasons (EPR) subscales of the Intuitive Eating Scale-2. Depressive symptoms were measured with the Edinburgh Postnatal Depression Scale (EPDS). Outcomes were measured during pregnancy (24-32 weeks of gestational age), 6-8 weeks and at 1-year postpartum (pp). Regression models were adjusted for group allocation as well as for socio-demographic, behavioral, anthropometric, and psychological covariates if they were significantly related to the respective outcome measure.

Results:

During pregnancy and at 1-year pp, diet self-efficacy and Big5C were associated with higher scores of both EPR and RHSC, with soc self-efficacy only associated with higher EPR (all $p \leq 0.040$). Only diet self-efficacy was associated with lower pp BMI ($p = 0.003$). Soc self-efficacy, Big5C, and HL were associated with lower EPDS during pregnancy, whereas all psychosocial factors were related to lower EPDS at 1-year pp (all $p \leq 0.030$). In longitudinal analyses, soc self-efficacy and Big5C during pregnancy predicted higher scores of EPR at 6-8 weeks and 1-year pp, whereas all predictors except soc self-efficacy were associated with higher RHSC at 1-year pp (all $p \leq 0.035$). In a multiple linear regression model including all significant psychosocial predictors, diet self-efficacy was the only predictor associated with higher RHSC at 1-year pp ($p = 0.031$). Both soc self-efficacy and Big5C during pregnancy were associated with lower EPDS at 6-8 weeks pp (both $p \leq 0.017$), whereas at 1-year pp, only Big5C remained associated ($p = 0.001$). Only diet self-efficacy during pregnancy predicted higher RHSC at 1-year pp in the model ($p < 0.001$).

Conclusion:

In women with GDM, conscientiousness personality trait and dietary self-efficacy were consistently associated with healthier eating behavior during the perinatal period. All psychosocial predictors by themselves were associated with lower EPDS scores.

Thyroidectomy for drug refractory amiodarone-induced thyrotoxicosis – A retrospective, single-centre analysis

Author/Institution

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Background

Amiodarone-induced thyrotoxicosis (AIT) is a difficult to treat and therefore challenging complication. Uncontrolled thyrotoxicosis may lead to progressive cardiac deterioration and adverse outcomes. Whether urgent thyroidectomy in patients refractory to drug therapy is advisable has been a matter of debate since some previous retrospective studies documented a significant increase in perioperative complications and mortality while other series reported favourable outcomes and even improved cardiac function.

Methods

Retrospective, single centre analysis of all patients with AIT who required urgent total thyroidectomy at our tertiary hospital between 2011 and 2024, focussed on perioperative complications and changes in left ventricular ejection fraction (LVEF). Data are presented as median [IQR]. Wilcoxon signed rank tests were used to compare LVEF before and after thyroidectomy.

Results

In total, 34 patients (79.4% male) with a median age of 63.5 [58.2-67.3] years were identified, all of which presented with overt thyrotoxicosis at diagnosis. AIT was preoperatively classified as type 1 in 7 (20.6%), type 2 in 21 (61.8%) and mixed or unclear type in 6 (17.6%) patients. 26 received treatment with antithyroid drugs and 31 with glucocorticoids (missing data in 1 case). Sodium perchlorate was added in 6 patients and iopanoic acid in 1. All thyroidectomies were performed by two high-volume endocrine surgeons 68 [42.5-95.8] days after AIT diagnosis. At the time of surgery, 28 had persistent overt thyrotoxicosis (fT4 49.1 [32.7-67.7] pmol/l), 5 had subclinical thyrotoxicosis (fT4 12.4 [11.1-13.2] pmol/l) and euthyroidism had been restored in 1 (fT4 15.2pmol/l). One unplanned ICU admission became necessary due to postoperative delirium. Median time to hospital discharge was 3 days. No perioperative deaths occurred within 30 days and 33 patients (97.1%) were alive 1 year postoperatively. At postoperative laryngoscopy, no case of laryngeal nerve injury was observed. Transient hypoparathyroidism occurred in 4 cases but no bleeding or wound infection.

Median LVEF at baseline (13 [8-27] months before AIT diagnosis) was 50% [35-56.25] and remained stable at postoperative follow-up (48.5% [34.8-55.8]; median 9 months postoperatively [4-13.5], n=30, p=0.21). In patients with baseline LVEF ≥50%, a significant decline (48% [38-57] vs 56% [52-59], n=12, p=0.03) was observed preoperatively, which had fully recovered at postoperative follow-up (55% [51-59], p=0.41).

Conclusion

Urgent thyroidectomy for AIT was not associated with increased perioperative morbidity or mortality and can be safely recommended in drug refractory cases. Normal LVEF was rapidly restored in patients with a preoperative decline associated with AIT.

Acknowledgement

Parts of the data were drawn from the EUROCRINE registry (eurocrine.eu).

Thyroid tuberculosis: a case report on echographic evolution under antituberculous drugs

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Background / Introduction :

Thyroid tuberculosis is a rare disease due to the organ's natural resistance to mycobacterial infection. Clinical presentation ranges from asymptomatic swelling to compressive mass or acute abscess and is most often localized to the thyroid gland with a minority of cases associated with pulmonary tuberculosis. Ultrasound typically shows a heterogeneous, hypoechoic, poorly defined lesion which may mimic thyroid neoplasia. In other cases, imaging shows cystic lesions, multiple nodules or diffuse goiter. Thyroid hormone levels are usually normal but hyperthyroidism, due to parenchymal destruction, or hypothyroidism, in advanced disease, are possible. Diagnosis is based on positive Ziehl Neelsen stain, culture or PCR on thyroid tissue through fine-needle aspiration (FNA) or biopsy, or occasionally after surgery when FNA is inconclusive. Anti-tuberculous drugs are first-line treatment and prognosis is generally good.

Methods

A 22-year-old Somali male patient presented to the emergency department with progressive swelling of the left neck, mild dysphagia, a 10 Kg weight loss and occasional cough. Clinical examination revealed a firm, painless left thyroid enlargement. He was subfebrile with otherwise normal vital signs. Workup showed elevated CRP (110 mgr/l), normal leukocyte count, slightly elevated free T4 (22.3 pmol/l) and normal TSH.

Results

Neck ultrasound revealed a diffusely enlarged, heterogeneous, left thyroid lobe (36 ml) with a honeycomb pattern and normal vascularity, as well as reactive-appearing cervical lymph nodes. Contrast-enhanced computed tomography showed a cavitory mass in the left lung, and signs of necrosis on the left thyroid lobe. FNA cytology showed inflammation, necrosis, epithelioid and multinucleated giant cell granulomas. Ziehl Neelsen stain and PCR for mycobacteria were negative. Eventually, culture of the FNA aspirated fluid revealed *Mycobacterium africanum*, also detected by PCR in sputum sampled. The patient was started on rifampicin, isoniazid, pyrazinamid, myambutol. One month later, ultrasound revealed a paradoxical increase in left thyroid lobe volume (45 ml) prompting biopsy which excluded malignancy and showed persistent granulomatous inflammation without acid-fast bacilli. Three-month after treatment, the left thyroid lobe had significantly decreased in size (7.1 ml) and thyroid function was normal. At 6 months, shortly after completing anti-tuberculous therapy, the left lobe measured 2.15 ml and remained hypoechoic and heterogeneous.

Conclusion

Thyroid tuberculosis is difficult to diagnose, with variable clinical features that may mimic other thyroid disease. Pulmonary manifestations and granulomas on FNA cytology, as in our case, may help to establish diagnosis, but are not always present. This case demonstrates a paradoxical increase in thyroid lesion size after one month of well-conducted therapy, a phenomenon well described in pulmonary lesions, followed by regression of the thyroid lesion 3-6 months later.

Social determinants of health and disparities in pregnancies affected by gestational diabetes mellitus in Switzerland – a population-based cohort study

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Background/Introduction:

Lifestyle and pharmacological interventions can prevent adverse outcomes in women with gestational diabetes (GDM) and their offspring. However, social determinants of health (SDOH) - including ethnicity, socioeconomic status, and area of residence - may influence GDM management and contribute to disparities in prevalence and outcomes. Despite rising GDM rates and growing social inequities, these factors remain underexplored in high-income settings. Therefore, our aim was to assess whether citizenship, insurance class, or regional area, proxies for key SDOH, modify GDM prevalence and the burden of GDM-related maternal and neonatal adverse outcomes in Switzerland.

Methods:

We conducted a population-based retrospective cohort study using Swiss claims data from the Federal Statistical Office (January 2012 to December 2023), including all singleton childbirth hospitalizations. Trends in GDM prevalence and its association with adverse outcomes were analysed, stratified by SDOH variables. The primary composite endpoints comprised maternal complications during pregnancy (1), childbirth (2), and the postpartum period (3), as well as neonatal adverse outcomes (4).

Results:

Among 963,302 birth hospitalizations, 7.7% were affected by GDM. Between 2012 and 2023, GDM prevalence increased from 4.9% to 9.5%, with greater absolute annual increases among women without Swiss citizenship, with basic insurances, and from urban areas. Overall, GDM was associated with a higher risk of obstetric complications (OR 2.11 [95% CI 2.06-2.15]), with stronger association in women with basic versus supplementary insurance (OR 2.16 [2.11-2.21] vs 1.75 [1.64-1.87]; p for interaction <0.001). The GDM-associated risk of postpartum complications was more pronounced in non-Swiss women (OR 1.31 [1.24-1.39] vs 1.2 [1.13-1.27] ; p for interaction 0.022). Neonates of mothers with GDM had a higher risk of adverse outcomes (OR 1.35, 95% CI 1.33-1.38), with stronger associations among those with basic insurance (OR 1.36 [1.33-1.38] vs 1.29 [1.23-1.36]); p for interaction 0.009).

Conclusion:

We found evidence of a widening gap in GDM prevalence, with clear disparities in GDM-associated adverse outcomes for both women and neonates. Basic insurance status and non-Swiss nationality emerged as negative modifiers. These findings merit further investigation into causal factors and the development of strategies to improve health equity in women and neonates affected by GDM.

Protein-Induced Thermogenesis Depends on the Absolute Amount of Ingested Protein rather than on Bodyweight

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Background/Introduction:

Diet-induced thermogenesis (DIT) represents the increase in energy expenditure following food intake. Previous studies using mixed-meal tests have shown that both energy content and protein proportion are key determinants of diet-induced thermogenesis (DIT). This study is the first to investigate the temporal profile of DIT after consumption of nearly isolated protein (88% of energy from protein) and to assess whether its magnitude depends on protein quantity or individual characteristics such as bodyweight.

Methods:

A total of 12 healthy adults (6 women, 6 men; age 18–40 years; BMI 18.5–28 kg/m²) participated in a randomized, controlled crossover study. Following ≥8 hours of fasting, resting energy expenditure (REE) was measured using indirect calorimetry. Participants then received, in randomized order across three visits, one of three nutritional challenges: 400 mL water (control), proteins in grams equal to bodyweight, or a fixed dose of 93g of protein. Postprandial energy expenditure was assessed hourly for seven hours.

Results:

During the visit when only water was consumed, REE remained relatively stable. Using fasting EE as baseline, EE increased by 25% following the fixed dose protein, peaking 4 hours postprandially (mean AUC 8.20). Protein-induced thermogenesis was significantly affected by the protein dose with minimal influence of participants' bodyweight. When protein intake was adjusted relative to bodyweight, EE peaked 3 hours after the meal with a maximum increase of 23% (AUC 7.92). Again, thermogenesis was influenced by the protein dose rather than by bodyweight. Direct comparison of the two treatments using a mixed-effects model confirmed that the increment in EE was more dependent on the absolute protein amount ingested than on the participants' bodyweight ($p= 0.025$).

Conclusion:

These findings highlight the substantial impact of protein on diet-induced thermogenesis, with protein dose identified as its key determinant, irrespective of the size of the study subjects. They may help nutritionists in planning nutritional strategies to target energy balance and weight management.

Androgen Production in Adrenocortical H295R Cells Is Regulated by Thyroid Hormone T3 Without Reciprocal Thyroid Axis Modulation in Pediatric CAH

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Background: Thyroid hormones (THs) are critical regulators of development, differentiation, and metabolism. While their systemic effects are well established, their role in adrenal androgen production remains poorly defined. Moreover, potential feedback regulation of the hypothalamic–pituitary–thyroid (HPT) axis by adrenal androgens has not been thoroughly investigated. Therefore, we explored the regulatory effects of THs on adrenal androgen synthesis in human adrenocortical H295R cells and assessed the interrelationship between THs and adrenal androgens in patients with congenital adrenal hyperplasia (CAH).

Methods: H295R cells were incubated with triiodothyronine (T3) [10^{-9} M] in serum-free media for either 48 h or 72 h. Gene expression was assessed by mRNA-sequencing, and steroid profiling of cell supernatants was examined via liquid chromatography-mass spectrometry (LC-MS). In addition, serum samples of pediatric CAH patients with 21-hydroxylase deficiency were analyzed, obtained from a prospective, observational multi-center cohort study. At 1 or 2 consecutive visits, a targeted and untargeted panel of conventional adrenal and additional peripheral steroids were measured by LC-MS. Data of 83 visits from 70 children (39 boys, 31 girls; 33 prepubertal, 37 postpubertal) were available. Mean age was 11.0 [1.2; 18.9] years and BMI z-score was 0.51 [-1.84; 2.91]. Free thyroxine (fT4) was measured via chemiluminescence immunoassays. Regression analyses were adjusted for age, sex, BMI-z score, pubertal status (pre- and postpubertal), CAH subtype (salt-wasting, simple-virilizing, late-onset) and treatment quality (under-, over- and well-treated).

Results: T3 downregulated dehydroepiandrosterone (DHEA) and DHEA-sulfate production in H295R cells by 29 % and 37 % respectively ($p < 0.01$), while slightly increasing T and 11OHA4 synthesis. This shift in the androgen profile is reflected by upregulated HSD3B2 ($\log_2FC = 1.24$) and AKR1C3 ($\log_2FC = 0.64$) gene expression, along with reduced CYP17A1 ($\log_2FC = -0.42$) transcripts. Likewise, in our CAH patients, we found a weak negative correlation for fT4 and serum DHEA ($R^2 = 0.251$; $p = 0.014$), androstenedione ($R^2 = 0.368$; $p = 0.018$) and androsterone ($R^2 = 0.323$; $p = 0.036$), as well as for TSH and serum DHEA ($R^2 = 0.247$; $p = 0.018$), androsterone ($R^2 = 0.338$; $p = 0.013$) and 5 α -DHT ($R^2 = 0.432$; $p = 0.023$). However, no differences in fT4 or TSH were observed between well-controlled and hyperandrogenic patients, suggesting a lack of feedback regulation by adrenal androgens on the HPT axis.

Conclusion: Our findings demonstrate that THs modulate adrenal androgen production via transcriptional regulation of key steroidogenic enzymes. This regulatory role is supported by hormone correlations in CAH patients. Conversely, adrenal androgens do not appear to influence TH levels, indicating unidirectional regulation from the HPT to the adrenal axis.

Disrupted α -cell function in human and murine islets devoid of other endocrine cells

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Background/Introduction:

Pancreatic α -cells release glucagon to counteract hypoglycemia and suppress its secretion during hyperglycemia. This regulation is influenced by glucose levels and paracrine signals from islet cells. In diabetes, glucagon secretion is dysregulated, with elevated plasma glucagon during hyperglycemia and blunted α -cell responses to hypoglycemia. While multiple diabetes-related factors have been linked to α -cell dysfunction, the exact mechanisms remain unclear. Here we investigate whether dysrupted intra-islet communication drives glucagon dysregulation.

Methods:

Monotypic pseudoislets were generated by sorting and re-aggregating purified human α - and β -cells. Glucagon and insulin secretion were measured at physiological glucose levels from basal (5.6 mM) to either 8.6 mM (postprandial glucose levels) or 3 mM (hypoglycemic levels) and compared with pseudoislets containing all cell types.

Plasmatic glucagon was assessed in α -only mice (Rip-DTR, Sst-DTR and Ppy-DTR transgenes) following diphtheria toxin (DT)-induced ablation of β -, δ - and γ -cells ("non- α -cells"). After islet remodeling, glucagon was measured during hypo and hyperglycemia and compared with control mice.

Results:

Human β -cells maintain proper secretory function without α -, δ - and γ -cells, whereas α -cells require paracrine regulation. In absence of non- α -cells, α -cells exhibit an inverted secretory pattern with increased glucagon release at 8.6 mM and reduced secretion at 3 mM. Similarly, α -only mice show impaired glucagon suppression during hyperglycemia and decreased secretion in hypoglycemia.

Conclusion:

Human and murine α -cells rely on intra-islet communication for proper function. Without non- α -cells, α -cells display a dysregulated secretory pattern, mirroring postprandial hyperglucagonemia and impaired α -cell hypoglycemic responses in diabetes. This suggest that glucagon dysregulation in diabetes stems from inadequate α -cell interactions within the islet.

Distinct response of human plasma lipidome to cold and fenoterol

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Background/Introduction:

Brown adipose tissue (BAT) plays a crucial role in thermoregulation. Upon cold exposure, the sympathetic nervous system releases norepinephrine, which activates β -adrenergic receptors (β -AR) on brown adipocytes. This activation stimulates lipolysis, leading to the release of free fatty acids that serve both as activators of uncoupling protein 1 (UCP1) and as substrates for mitochondrial oxidation, thereby generating heat. Recent research has indicated that the β 2-AR stimulation could activate human BAT. Here, we analysed the changes in lipidome in response to cold-exposure and β 2-AR stimulation with the selective agonist fenoterol.

Methods:

We performed a cross-over, randomized trial in twelve healthy volunteers (seven men and five women). We determined resting energy expenditure (REE) using indirect calorimetry during cold exposure or during continuous fenoterol infusion (145 μ g). Both interventions were performed over 2 hours. We sampled blood for metabolome analysis by gas chromatography-mass spectrometry (GC-MS) at every visit.

We compared the data to metabolomics data from another trial with cold exposure.

Results:

Both fenoterol and mild cold exposure increased REE in humans: before fenoterol 1502 \pm 281 kcal/24h, after fenoterol 1860 \pm 305 kcal/24h ($p < 0.0001$); before cold 1516 \pm 347 kcal/24h, after cold 1712 \pm 270 kcal/24h ($p = 0.02$).

Both interventions affected plasma lipid levels. Specifically, fenoterol increased levels of free fatty acid (FA); with FA18:3 ($\log_2FC = 1.21$, $p = 4 \times 10^{-8}$), FA20:3 ($\log_2FC = 0.76$, $p = 1.2 \times 10^{-7}$), FA14:0 ($\log_2FC = 0.82$, $p = 5.6 \times 10^{-7}$), FA20:2 ($\log_2FC = 0.73$, $p = 7.3 \times 10^{-7}$) and FA12:0 ($\log_2FC = 0.78$, $p = 8 \times 10^{-7}$).

In contrast to fenoterol, cold exposure increased FA levels only moderately, but increased triglycerides. TG 56:8-FA16:1 ($\log_2FC = 0.30$, $p = 0.00176$), TG 56:9-FA22:6 ($\log_2FC = 0.29$, $p = 0.028$), TG 56:7-FA22:6 ($\log_2FC = 0.25$, $p = 0.021$).

However, the levels of fatty acids FA18:1, FA 22:2, FA16:1 and FA20:1 were all related to cold-induced thermogenesis ($R^2 > 0.5$ and $p < 0.05$). The poly-unsaturated fatty acids FA22:2, FA20:3 and FA22:4 were correlated to BAT activity as determined by FDG-PET/CT ($R^2 > 0.7$, $p < 0.01$).

We replicated the analysis regarding changes in the lipid profile after cold exposure in a second cohort of healthy volunteers. Of note the polyunsaturated fatty acids C22:6 (docosahexaenoic acid, DHA; $\log_2FC = 0.68$, $p = 0.0036$) and C22:5 (docosapentaenoic

Conclusion:

Both cold exposure and stimulation of the β 2-AR increase lipolysis and REE in humans. Our findings indicate that enhanced lipolysis is a key mechanism driving β 2-AR-stimulated thermogenesis. However, the distinct lipidomic profile points towards different molecular mechanisms in response to cold. Polyunsaturated fatty acids seem to be especially important for BAT activation. Further investigation is required to distinguish BAT-dependent from BAT-independent pathways contributing to cold-induced.

Gut microbial signatures correlate with inflammation and glycemic impairment in HFD-fed mice

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Background/Introduction:

Elevated circulating lipopolysaccharide (LPS) observed in obesity and type 2 diabetes indicates not only increased intestinal permeability, but also a potential shift in gut microbial composition, specifically an enrichment of Gram- bacteria, the source of LPS. To better understand which microbial populations contribute to intestinal inflammation and glycemic dysregulation in obesity, we targeted either Gram+ or Gram- bacteria using distinct antibiotic regimens.

Methods:

Male mice aged 5-7 weeks were fed a high-fat diet (HFD) for one week and simultaneously treated with either vancomycin (vanco, targeting mostly Gram+ bacteria), neomycin (neo, targeting mostly Gram-), or water (control) via oral administration. Metabolic status was assessed by *in vivo* glucose tolerance tests. Intestinal inflammation was evaluated by quantitative qPCR and flow cytometric profiling of gut immune cell populations. Caecal samples were subjected to 16S rRNA gene sequencing, and microbial composition was analyzed using the Phyloseq package.

Results:

One week of treatment with either vanco or neo significantly improved glucose tolerance and reduced insulin secretion in HFD-fed mice, despite unchanged or even increased body weight. qPCR analysis of whole colon tissue revealed upregulation of inflammatory gene expression in the neo-treated group. This local inflammatory response was also reflected systemically, as indicated by elevated plasma TNF levels compared to vanco-treated mice. Furthermore, neo treatment was associated with increased frequencies of Foxp3⁺ regulatory T cells, pro-inflammatory macrophages (P2), and resident macrophage subsets (P4 and P5), along with elevated Th2 and Th17 cell frequencies. Both antibiotics induced a marked reduction in alpha diversity and caused substantial shifts in microbial composition. At the class level, these changes were characterized by a depletion of Clostridia, Bacteroidota, and Vampirivibrionia, and expansion of Campylobacteria (particularly in the vanco group) and Verrucomicrobia (particularly in the neo group). Notably, the relative abundance of Bacteroidaceae (family level) and Bacteroides (genus level) positively correlated with both the frequency of pro-inflammatory macrophages and impaired glucose tolerance across all three groups (vanco, neo, control).

Conclusion:

Using distinct antibiotic interventions, we identified Bacteroidaceae (family level) and Bacteroides (genus level) as positively correlating with both intestinal inflammation and glucose intolerance in HFD-fed mice. These findings point to a potential link between specific microbial taxa, gut immune activation, and metabolic dysfunction, highlighting the gut microbiota-immune axis as a modifiable regulator of metabolic health.

Brown Adipose Tissue as Nutrient Buffer through Diet-Induced Thermogenesis: The BANDIT-Study

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Background/Introduction:

Brown adipose tissue (BAT) dissipates energy into heat when activated, classically after cold exposure. While there is clear evidence for the correlation between the presence of active BAT and a lean phenotype as well as lower prevalence of cardiometabolic diseases, the exact mechanisms of these beneficial effects remain unclear, especially since BAT's contribution to the total energy expenditure is small.

In this study we tested the hypothesis that BAT operates as a nutrient buffer and prevents unfavourable postprandial peaks of glucose, free fatty acids, or branched-chain amino acids. The primary objective was to compare postprandial increases of metabolites in subjects with functional BAT to those without. Moreover, we assessed how the beforementioned macronutrients and BAT-activity contribute to diet-induced thermogenesis (DIT).

Methods:

This single center prospective observational study involved 30 healthy, normal weight volunteers. Participants were screened for presence or absence of cold induced BAT activity using a mild cold stimulus over two hours, followed by an ¹⁸F-FDG-PET/CT. BAT metabolic volume (BMV=SUV_{mean} x BAT volume)>200mL was chosen as cut-off value to discriminate between BAT-positive and BAT-negative subjects. At each of the following study visits, the participants consumed an iso-caloric test meal containing exclusively either carbohydrate, protein, or fat. We performed indirect calorimetry hourly and blood samples half-hourly before and during five hours following the test meal.

Results:

Overall, the data of 15 BAT-positive (BMV=639.05.±367.54) and 15 BAT-negative (BMV=75.83±63.55) subjects show no DIT after intake of fat. A 15-35% increase in energy expenditure was observed persistently for at least 5 hours after intake of protein and for 1 hour after glucose. No difference was seen between BAT-positive and BAT-negative subjects in this respect. The average fasting blood glucose level of all study visits was 4.80±0.38mmol/L with no difference between the groups. While all had similar glucose curves after the 100g OGTT, we detected consistently lower blood glucose values in BAT-positive subjects following the challenge with fat and protein.

Conclusion:

Our data show the impact of different macronutrients on DIT and contradict the notion that BAT status has an impact on DIT. Interestingly blood glucose seemed to be lower in BAT-positive subjects after intake of protein and fat while glucose tolerance in our healthy subjects did not correlate to BAT status.

Effect of Glyceroltrinitrate on human energy expenditure and brown adipose tissue thermogenesis

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Background/Introduction:

Weight loss regimens reduce resting energy expenditure (REE), which counteracts further weight loss and promotes weight regain. Brown adipose tissue (BAT) contributes to energy expenditure by generating heat and is associated with lower body weight. BAT activity can be stimulated by repeated cold exposure, via the sympathetic nervous system or pharmacologically, though traditional activation via norepinephrine is limited due to cardiovascular side effects. An alternative involves nitric oxide–induced cGMP signaling. The use of glycerol trinitrate, which releases nitric oxide, is proposed to enhance BAT activity and support weight reduction. In this study, the effect of short-term therapy with glycerol trinitrate (Nitroderm® TTS) on BAT activity was investigated.

Methods:

The primary analysis was conducted in 25 healthy volunteers (18-40 years). All participants received transdermal Nitroderm® TTS over a period of 15 days (5 mg/24 h for 5 days, followed by 10 mg/24 h for 10 days). REE was assessed via indirect calorimetry both before and after standardized cold exposure, and cold-induced thermogenesis (CIT) was calculated as the difference between these two measurements. In addition, supraclavicular BAT volume and activity were quantified using ¹⁸F-FDG-PET/CT, after cold exposure. Following a 2-week washout, measurements were repeated without treatment as a control in this randomized, open-label crossover trial.

Results:

Baseline REE before cold exposure did not significantly differ between treatment and control phase (1434±295 kcal/24h and 1400±287 kcal/24h respectively, p=0.26). Similarly, no significant difference in CIT was observed between the treatment and control phases (218±297 kcal/24h and 185±224 kcal/24h, p=0.43). However, cold exposure significantly increased energy expenditure during both the treatment and control phases (p=0.0019 and p=0.0003).

The mean standardized uptake value (SUV_{mean}) of supraclavicular BAT was 3.2±1.4 g/ml after 15 days of treatment with Nitroderm® TTS, and 3.3±1.5g/ml after the control phase (p=0.81).

Accordingly, the active BAT volume was 92±68 ml vs. 90±59 ml, (p=0.57). Moreover, no difference in total glycolytic volume (= metabolically active volume) was observed between the two study phases (1499±1782g vs. 1499±1771g, p=0.71).

Conclusion:

Glycerol trinitrate (Nitroderm TTS) was not associated with any significant alteration in energy expenditure at rest and after cold exposure. This finding is consistent with the PET/CT analysis results, which showed no difference in brown adipose tissue activity.

Mapping the metabolism of adrenal 11-oxy androgens in human primary hepatocytes

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Background/Introduction:

Adrenal steroid hormones and their metabolism play a vital role in human endocrinology. Their downstream metabolism mainly occurs in the liver, with steroidogenic enzymes catalysing their biosynthesis and metabolism. In adrenal androgen excess disorders, specifically 21-hydroxylase deficiency (21OHD), precursor adrenal hormones accumulate and are converted to androgens. More precisely, adrenal 11-oxy androgens (11OxyAs) are excessively produced, leading to the production of 11-ketotestosterone (11KT), which can bind and activate the androgen receptor equipotently to the classical androgen, testosterone (T). Despite the known biochemical route for classical androgen liver metabolism, it remains unclear how 11OxyAs are metabolised in the liver, which this study aimed to investigate in adult human primary hepatocytes.

Methods:

Normal hepatocytes (n=3 donors, 2 female, taken from the periphery of liver specimens from patients undergoing surgical resection for metastases) were incubated with steroid substrates (1 μ M) for 24 hours or a 1-8-hour time course assay. Steroid profiles were analysed in cell supernatants, with and without deconjugation, using liquid chromatography-mass spectrometry to quantify precursor and downstream steroid metabolites.

Results:

After 24 hours, all classical androgens and 11OxyAs were completely metabolised downstream and conjugated. Total steroid levels show that the classical androgens, T and androstenedione, were mainly 5 α / β - and 3 α -reduced, forming etiocholanolone: androsterone (1.8:1). The 11OxyAs favoured 5 α -reduction followed by 3 α -reduction forming the downstream products 11 β -hydroxyandrosterone (11OHAST) > 11-ketoandrosterone. Free steroid levels were only quantified for 11 β -hydroxyandrostenedione (11OHA4) and 11 β -hydroxytestosterone (11OHT). During the time course assay, T was more efficiently converted compared to 11KT, partly attributed to the more efficient conjugation of T (~4-fold). Over time, 11KT was first converted to 11-ketoandrostenedione, then to 11OHA4 after which 11OHAST was produced which indicates hepatic 11 β -hydroxysteroid dehydrogenase type 1 (HSD11B1) activity.

Conclusion:

In summary, our results show that the hepatic metabolism of the 11OxyAs is different compared to classical androgens, favouring 5 α - and 3 α -reduction, with marked hepatic HSD11B1 activity. Moreover, the 11-oxy testosterones are not as efficiently metabolised and conjugated compared to T in the liver, marking that the 11OxyAs are less efficiently inactivated. Ultimately, these data underscore the role of the 11OxyAs in 21OHD, distinguished by their unique hepatic metabolism.

Analysis of functionally uncharacterized variants of the GH1 gene from patients with Isolated Growth Hormone Deficiency (IGHD)

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Background/Introduction:

Human growth hormone (hGH), or somatotropin, a 217-amino acid glycoprotein produced by the somatotrophic cells in the anterior pituitary, is encoded by the GH1 gene, located on chromosome 17 (17q22-24). Mutations in GH1 are associated with Isolated Growth Hormone Deficiency (IGHD), characterized by a spectrum of pituitary hormone deficiencies and growth failure in children, and it can result from mutations in GH1 or related genes. IGHD is classified into four types based on inheritance patterns: Type IA and IB (autosomal recessive) Type II (Autosomal dominant), and Type III (X-linked), all of which result in short stature.

Methods:

We have investigated five functionally uncharacterized but clinically reported GH1 missense variants (A39T, R42L, C79G, Q110E, and R160W), identified in patients with IGHD of various types and genetic backgrounds. Pathogenicity analysis tools such as PANTHER, PhD-SNP, SIFT, Meta-SNP, and E-SNPs & GO were utilized to assess the pathogenicity scores for each mutation. To complement computational insights, the variants were introduced into the wild type GH1 gene via site-directed mutagenesis and expressed in *E. coli*. Recombinant proteins were purified using immobilized metal affinity chromatography (IMAC), yielding high-quality preparations suitable for downstream functional studies.

Results:

C79G and R42L were predicted to be the most deleterious mutations. Among the mutations, Q110E is predicted to have the most significant stabilizing effect. Protein free energy $\Delta\Delta G$ calculations (1.882 kcal/mol) suggested that it enhances protein stability, reducing the likelihood of denaturation or unfolding. Conversely, A39T appears to significantly decrease protein flexibility compared to the other five mutations, as indicated by $\Delta\Delta S_{Vib}$ (-4.925 kcal/mol*K) predictions, which suggests that A39T induces a more rigid and ordered protein structure. Additionally, multiple sequence alignment and phylogenetic analysis with Clustal Omega, phylogenetic analysis with MEGA, domain prediction with SMART, 3D structures modeling, and motif analysis with MEME, confirmed high conservation these residues among primates, underscoring their importance.

Conclusion:

These findings provide a detailed computational and experimental framework for understanding GH1 variant effects, offering a foundation for future in vitro studies aimed at advancing personalized approaches to IGHD diagnosis and treatment.

Tirzepatide vs semaglutide for the management of obesity and overweight: a subgroup indirect treatment comparison of body composition outcomes from SURMOUNT-1 and STEP 1

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Background/Introduction:

Changes in body composition (BC) are of key importance in the context of obesity management, with the distribution of fat and lean body mass linked to mortality risks, cardiometabolic complications and the challenge of weight regain. However, there is no published comparison of BC outcomes between the obesity management medications tirzepatide (TZP), a glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 (GLP-1) receptor agonist (RA) and semaglutide (SEMA), a GLP-1 RA. Here, BC outcomes were compared for TZP and SEMA in an indirect treatment comparison (ITC).

Methods:

A Bucher ITC was conducted on SURMOUNT-1 (SMT-1) and STEP-1 trial subgroups that underwent dual-energy X-ray absorptiometry: adults without type 2 diabetes and with obesity (BMI ≥ 30 kg/m²), or overweight (BMI ≥ 27 kg/m²) with ≥ 1 obesity-related complication, with BMI ≤ 40 kg/m² for STEP-1 and no upper BMI limit for SMT-1. Both populations were suitably similar for inclusion in an ITC. Each TZP dose (SMT-1: 5mg [n=38], 10mg [n=39], 15mg [n=43], all once weekly [QW]) was compared with SEMA 2.4mg QW (STEP-1: n=95) via placebo (SMT-1: n=36, STEP 1: n=45), all adjunct to reduced-calorie diet and increased physical activity. Efficacy estimand data (patients remaining on treatment with no rescue medication) were used at the primary timepoint (SMT-1: Week 72; STEP-1: Week 68) to investigate changes in absolute (kg) and relative (proportion of total BM, %) fat and lean mass (FM) (LM).

Results:

TZP 15mg had a statistically significant greater reduction in absolute and relative FM (mean difference [95% CI]: -4.87 kg [-9.64, -0.10], -3.50 %pt. [-6.66, -0.34], resp.) vs SEMA 2.4mg, while TZP 5 and 10mg had non-significant trends of greater or similar reductions in absolute (-0.57 kg [-5.41, 4.27], -4.17 kg [-8.94, 0.60], resp.) and relative FM (-0.80 %pt. [-4.03, 2.43], -2.40 %pt. [-5.60, 0.80], resp.) vs SEMA 2.4mg, TZP 5, 10 and 15mg had comparable reductions in absolute regional visceral FM (0.05 kg [-0.19, 0.29], -0.05 kg [-0.28, 0.18], -0.12 kg [-0.35, 0.11], resp.) as well as non-significant trends of smaller or similar reductions in absolute LM (2.14 kg [-0.01, 4.29], 0.04 kg [-2.11, 2.19], 0.84 kg [-1.28, 2.96], resp.) and greater increases in relative LM (0.90 %pt. [-2.14, 3.94], 2.30 %pt. [-0.74, 5.34], 3.40 %pt. [0.40, 6.40], resp.) with TZP 15mg reaching statistical significance for the latter.

Conclusion:

This ITC found, TZP 15mg led to statistically significant greater reductions in absolute and relative FM vs SEMA 2.4mg, indicating more favourable BC changes. Although all TZP doses and SEMA 2.4mg reduced absolute LM, TZP 15mg showed a statistically significant greater increase in relative LM (i.e., a smaller relative decrease in LM vs total BM) compared to SEMA 2.4mg. Small subgroups and supplementary nature of these outcomes in both trials limit the ITC's conclusions.

Characteristics of participants who regained weight after withdrawal of tirzepatide: A post hoc analysis of SURMOUNT-4

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Background/Introduction:

In the SURMOUNT-4 (SM) clinical trial, withdrawing tirzepatide maximally tolerated dose (MTD) after a 36-week open-label lead-in treatment period resulted in substantial regain of lost weight, whereas continued treatment maintained and augmented initial weight reduction. In this post hoc analysis, we investigated the baseline characteristics (week 0) and change in weight and waist circumference at the end of the open-label lead-in period (week 36) associated with varying degrees of weight regain after tirzepatide withdrawal.

Methods:

SM-4 participants who achieved $\geq 10\%$ weight reduction with 36 weeks of tirzepatide treatment (MTD of 10 or 15 mg) and randomized to placebo (N=308) were included in this post hoc analysis. Participants' baseline characteristics, and change in weight and waist circumference were calculated descriptively by the degree of weight regain, from Week 36 to 88, as a percentage of weight reduction, from Week 0 to 36; $<25\%$ (n=54, least weight regain), ≥ 25 to $<50\%$ (n=77), ≥ 50 to $<75\%$ (n=103), and $\geq 75\%$ (n=74, most weight regain).

Results:

Participants in the lower weight regain groups exhibited significantly greater mean reductions in weight (%) from the start of the lead-in period to randomization; -23.6% in the $<25\%$ group, -23.4% in the ≥ 25 to $<50\%$ group, -22.6% in the ≥ 50 to $<75\%$ group, and -18.3% in the $\geq 75\%$ group ($p < .001$). Similarly, greater reduction in mean waist circumference (cm) from the start of the lead-in period to randomization was also observed in participants with lower weight regain; -19.6 cm in the $<25\%$ group, -20.0 cm in the ≥ 25 to $<50\%$ group, -17.9 cm in the ≥ 50 to $<75\%$ group, and -16.2 cm in the $\geq 75\%$ group ($p = .022$).

Amongst participants in SM-4 who had treatment with tirzepatide withdrawn, there were no significant differences in the demographic characteristics at baseline (Week 0) across the weight regain groups including sex, age, years of education and duration of obesity. Similarly, no differences in baseline clinical characteristics were noted including weight, waist circumference, blood pressure, lipids, glycemic control, insulin, renal function and obesity-related complications.

Conclusion:

In this post-hoc analysis of participants who were withdrawn from tirzepatide-treatment in the SURMOUNT-4 clinical trial, participants with less body weight (BW) regain demonstrated greater reductions in BW and waist circumference during initial open-label lead-in period. There were no significant differences in baseline demographic or clinical characteristics across groups with different degrees of weight regain. These findings are consistent with multifactorial and complex nature of obesity.

Tirzepatide treatment and achieving weight reduction >5%, SBP reduction >5 mmHg and non-HDL cholesterol reduction >10%: A post hoc analysis from the SURMOUNT-1 3-year trial

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Background/Introduction:

This post-hoc analysis evaluated the proportion of participants who met the combined goal of weight reduction >5%, systolic blood pressure (SBP) reduction >5 mmHg and non-HDL cholesterol reduction >10% from baseline to Week-176 in SURMOUNT-1 3-year trial.

Methods:

There were 568 participants with obesity and prediabetes who completed treatment with tirzepatide (n=454) or placebo (n=114) at Week-176 and had measures for all three outcomes (weight, blood pressure and lipids) or had any of the three measurements not meeting the threshold. Baseline characteristics were compared using ANOVA model for continuous data and Chi-square test for categorical data.

Results:

Total 145 (25.5%) participants met the combined goal at Week-176. Participants meeting vs. not meeting the combined goal had higher mean SBP (130.0 vs. 124.4 mmHg), total cholesterol (203.6 vs. 186.1 mg/dL), non-HDL cholesterol (155.4 vs. 138.2 mg/dL), LDL cholesterol (123.0 vs. 108.7 mg/dL), and triglycerides (175.2 vs. 148.8 mg/dL) at baseline. Significantly more tirzepatide-treated participants (n=139, 30.6%) met the combined goal vs. placebo (n=6, 5.3%), p<0.0001. Moreover, 94.2% (n=131) TZP participants who met the combined goal also had an HbA1c <5.7%, 41.0% (n=57) had a BMI ≤27 kg/m² and 28.8% (n=40) had a WHtR <0.53 (Figure 1, 2). Of the six placebo participants who met the combined goal, all had HbA1c < 5.7%, 1 had a BMI ≤27 kg/m² and 1 had a WHtR of <0.53.

Conclusion:

Treatment with tirzepatide led to significantly more participants achieving a combined clinical goal of weight reduction >5%, SBP reduction >5 mmHg and non-HDL cholesterol reduction >10% vs. placebo. Most of the tirzepatide participants meeting the combined goal also achieved normoglycemia, over 1 in 3 participants met the BMI goal, and 1 in 4 met the WHtR goal, suggesting central adiposity reduction. Outcomes trials are ongoing to further evaluate the cardiometabolic impact of tirzepatide.

Unbalanced IL-18 signaling alters anti-microbial peptides production and microbiota equilibrium in the gut aggravating diet-induced steatohepatitis in mice

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Background:

Metabolic Dysfunction-Associated Steatohepatitis (MASH) is an inflammatory complication of metabolic liver steatosis. If uncontrolled, MASH can evolve in fibrosis, cirrhosis and eventually in hepatocellular carcinoma (HCC). IL-18 binding protein (IL-18BP) is a secreted protein that binds to interleukin-18 (IL-18) to prevent its signaling, thus considered as an endogenous inhibitor. In the present study, we aim to delineate the implication of the IL-18/IL-18BP couple in gut-liver axis function and liver integrity during nutritional stress.

Methods:

Wild-type (WT) or *Il18bp*^{-/-} mice aged 2 months were fed 1) chow; 2) High Fat diet (HFD) for 10 weeks (60 kcal% from fat); or 3) Methionine- and Choline-Deficient (MCD) diet for 7 weeks. Gene expression was assessed by real-time quantitative PCR using a LightCycler Detection System (Roche Diagnostics). Gut microbiota composition was determined using an Illumina MiSeq instrument. Histochemistry was performed using PAS/ Lendrum phloxine-tartrazine protocols. In vivo modification of gut microbiota was performed using phages treatment and co-housing experiments.

Results:

Gut *Il18bp* and anti-microbial peptides (AMPs) expression were decreased in wild-type mice fed a high-fat or a MCD-diet. In contrast, *Il18/Il18bp* expression ratio was increased in the gut of wild-type mice on HFD and MCD diet, correlating to the proportion of different classes of proteobacteria. *Il18bp*^{-/-} mice exhibited a decrease in anti-microbial peptides (AMPs) production in the ileum and an enrichment in proteobacteria in their gut microbiota both on HFD and on MCD diet. *Il18bp*^{-/-} mice exhibited increased hepatic damage, inflammation, and fibrosis (independently of steatosis) compared to WT mice. Phages and co-housing experiments revealed that exacerbated liver inflammation and fibrosis in *Il18bp*^{-/-} mice are linked to their specific gut microbiota.

Conclusions:

IL-18BP appears as a gatekeeper of the gut-liver axis, tightly regulating AMPs production and gut microbiota balance. Unbalanced IL-18/IL-18BP signaling in the gut leads to dysbiosis and aggravates diet-induced steatohepatitis in mice.

Impact and implications:

IL-18BP presents a therapeutic interest to maintain a healthy gut/liver axis.

Baseline characteristics of participants who achieved normal BMI: post hoc analysis of SURMOUNT-1 3-year Study

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Background/Introduction:

While highly effective obesity medications have been shown to lead to substantial weight reduction, few data exist on achieving normal BMI. SURMOUNT (SM)-1 3-year study is a phase 3 trial of the dual GIP/GLP-1 receptor agonist tirzepatide (TZP). This study aimed to assess baseline characteristics of participants on TZP with prediabetes who reached normal BMI (< 25 kg/m²).

Methods:

SM-1 participants with obesity and prediabetes were randomized to TZP (5, 10 or 15mg) or placebo. Participants who received at least 75% of doses were included and baseline characteristics compared between those who reached normal BMI vs not.

Results:

Out of 714 TZP-treated participants, 17.6% (N=128) reached normal BMI by the end of the study. Compared to those who did not reach normal BMI, these participants were: more likely to be female (79.37% vs 60.54%), slightly older (mean age 50.33 vs 47.82), on higher doses of TZP (10 or 15mg), with lower baseline weight (mean 89.38 vs 111.49 kg), waist circumference (mean 104.77 vs 119.01 cm), BMI (mean 33.10 vs 39.95), HbA1c (5.67% vs 5.78%), insulin (11.31 vs 17.32), systolic blood pressure (123.38 vs 126.62 mmHg), eGFR (92.29 vs 95.69) and ALT (23.42 vs 29.80). Sensitivity analysis (normal BMI cutoff for Asian < 23) is consistent with main results.

Conclusion:

In this post-hoc analysis, nearly one in five reached normal BMI by the end of 176 weeks TZP treatment. Compared to participants who did not reach normal BMI, those who reached normal BMI had higher proportion of females, older age, on higher TZP doses, and lower baseline BMI. These findings may help tailor obesity treatment to individual health goals.

Mechanisms of Fasting Induced Reduction in Energy Expenditure – FIRE Trial

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Background/Introduction:

Therapeutic strategies for obesity involving surgical and medical interventions are limited in their efficacy with a fast weight loss during the first few months of therapy which then plateaus. In response to the limitation of energy intake mediated by these therapies, total energy expenditure (TEE) is reduced in part by adaptation of resting EE (REE). These adaptations are not uniform but differ substantially between individuals. Research has demonstrated that the fasting-induced reduction in EE (FIRE) correlates inversely with weight gain. The goal of this interventional trial is to elucidate endocrine regulation that contribute to FIRE and to assess the effect of fasting on diet-induced thermogenesis (DIT), i.e. the change in EE in response to a meal.

Methods:

The study was performed as a randomized open label cross-over, monocentric trial in healthy volunteers with a BMI 18-27 kg/m². After two screening visits with 12- and 24-hour fasting, the change in resting energy expenditure (REE) was calculated. Participants in the highest and lowest FIRE quartiles were selected for the main study. Primary endpoint was diet-induced thermogenesis (DIT), defined as increase in EE above baseline in response to a liquid mixed meal test with defined composition of macronutrients (450 kcal). This endpoint was measured after a 12 h- and 24 h- fast. REE was measured by indirect calorimetry. Blood samples were collected at baseline and at various time points during the main study visits.

Results:

We report the results of the first 20 participants who successfully completed the trial. Resting energy expenditure decreased in 8 participants after 24 h of fasting and increased or remained stable in 12 participants.

Levels of free triiodothyronine (fT3) decreased significantly after 24 h of fasting as compared to 12 hours of fasting (4.5 pM vs. 4.8 pM, $p=0.0025$). Conversely, free thyroxine levels increased from 15.5 pM to 16.6 pM ($p=0.0014$). Levels of fT3 but not fT4 correlated significantly with REE after an 12 h fast (fT3: $R^2=0.34$, $p=0.0059$, fT4: $R^2=0.01$, $p=0.73$).

DIT was significantly higher after an 12h fast as compared to the 24 h fast, 262 ± 88 kcal/24 h vs. 200 ± 74 kcal/24, $p=0.0087$. The change in DIT was not related to the change in thyroid hormone levels. After 24h of fasting pulse rate was lower than after 12 h, 65.9 ± 11.5 bpm vs. 70.8 ± 11.2 bpm, $p=0.011$. Tympanic temperature was not significantly affected, 36.5°C vs 36.6°C , $p=0.25$.

Conclusion:

Fasting for more than 24 hours leads to a significant reduction DIT. Thyroid function does not appear to contribute to this change. However, the autonomic nervous system may play a role in regulating DIT in the fasting state.

Sleep variability is associated with overweight and obesity levels, and with weight gain, cross-sectional and prospective studies.

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Background

Sleep variability has been suggested to be associated with diabetes by increasing BMI levels. However, few large-scale longitudinal studies have comprehensively explored the relationship between sleep variability and BMI levels.

Objective

Assess the associations between sleep variability and BMI or waist in a Swiss population-based sample.

Methods

Cross-sectional and longitudinal analyses from survey periods 2014-2017 (second follow-up, N=2530, 62.3±9.9 years, 53.5% female) and 2018-2021 (third follow-up, N=1917, 65.5±9.4 years, 53.8% female) of the CoLaus|PsyCoLaus study. Sleep duration was assessed using accelerometers (MACRO, and GGIR) or by ecological momentary assessment (EMA) for one week. Variability was determined by standard deviations (SD), coefficient of variation (CV), and range.

Results

On cross-sectional analysis, after multivariable adjustment, sleep duration average was lower and sleep variability was higher in participants with obesity relative to those with normal weight, but this association differed depending on the assessment method (MACRO, GGIR, EMA). Multivariable linear regression showed average sleep to be negatively associated, while sleep variability was positively associated with BMI and waist. Sleep duration variability remained positively associated with BMI and waist after adjusting for average sleep. On prospective analysis, participants who lost or gained 5+kg had higher baseline sleep variability than those who had <5 kg weight change, but this association was only observed with the MACRO method.

Conclusion

Sleep variability was associated with BMI, waist and weight change, but the results varied depending on the assessment method. Adequate identification and standardisation of sleep assessment methods is important for the related research.

Short-term erythritol and xylitol intake does not impact markers of platelet, endothelial, and coagulation activation

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Background/Introduction:

Metabolomic profiling trials have shown increased endogenous production of erythritol and xylitol in individuals with various clinical conditions, including cardiovascular disease. However, the underlying cause of this increase is unknown. Both substances are also widely consumed as alternative sweeteners. A recently published pilot trial suggested that acute intake of these sweeteners may enhance platelet activation, with increased aggregation observed 30 minutes after intake. However, it is important to note that platelet activation naturally fluctuates and can be modulated by external factors such as physical activity and diet. In a randomized, double-blind, placebo-controlled crossover design, we investigated the acute impact of orally administered erythritol, xylitol, and water on platelet, endothelial, and coagulation activation, as well as circulating concentrations of erythritol and xylitol.

Methods:

A total of 11 healthy, lean participants (mean \pm SD; age: 26.4 ± 5.7 years, BMI: 21.5 ± 1.9 kg/m²) were enrolled in the study. Each participant underwent three separate test sessions. During each session, they consumed one of the following test solutions: 50 g erythritol dissolved in 300 mL water, 33.5 g xylitol dissolved in 300 mL water, or 300 mL pure water as a control. Blood samples were obtained to measure (i) ex vivo maximum platelet aggregation in response to TRAP6 (10 μ M) pre- and 60 minutes post-administration, (ii) in vivo activation markers - including platelet activation (P-selectin), endothelial activation (sVCAM-1), and coagulation activation (D-dimers) - up to 180 minutes post-administration, and (iii) plasma erythritol and xylitol concentrations up to 48 hours post-administration.

Results:

Maximum adjusted platelet aggregation did not differ significantly pre- versus post- administration or between different treatment conditions. In addition, P-selectin, sVCAM-1, and D-dimers concentrations did not differ significantly between treatment conditions and showed no correlation with changes in platelet aggregation. Post-administration, plasma erythritol concentrations reached their maximum at 60 min and stayed mildly elevated for up to 48 hours. Contrarily, plasma xylitol concentrations reached their maximum at 30 min post-administration and decreased back to baseline within 24 hours.

Conclusion:

These findings indicate that acute administration of erythritol or xylitol does not exert a direct impact on platelet, endothelial, or coagulation activation markers.

Roux-en-Y gastric bypass partially resolves obesity-induced alterations in gut immunity

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Background/Introduction:

Obesity and obesity related co-morbidities are rising worldwide. The most effective treatment for morbid obesity and its long-term complications are bariatric surgeries. Obesity leads to systemic low-grade chronic inflammation and to changes in the immune cell composition in various tissues. The aim of this project was to assess the immunological changes in blood and colon immune cells upon obesity and whether these changes resolve after bariatric surgery, in comparison to a healthy control group.

Methods:

Peripheral blood mononuclear cells (PBMC) and immune cells from colon transversum were isolated from obese subjects before and 6-8 months after bariatric surgery. In addition, a healthy control group was assessed. Different immune cells were characterized by flow cytometry.

Results:

Obesity was associated with an expansion of colonic inflammatory macrophage subpopulation P2, naïve and IgA expressing B cells as well as Th22, Th17 and Th9 T cell subsets, while other T cells such as Th1 and regulatory T cells were reduced. Following bariatric surgery, regulatory T cells recovered and the anti-inflammatory macrophage subpopulation P5 increased, while the inflammatory P2 subpopulation as well as Th17 and Th9 cells declined. In addition, both the total macrophage population and the frequency of naïve B cells were reduced post-surgery. In peripheral blood, obesity was marked by elevated levels of classical monocytes and T cells, in particular CD4 and Th17 cells, whereas regulatory T cells and NK T cells were reduced. After bariatric surgery, monocytes, in particular classical monocytes, and naïve B cells decreased, while Th9 cells showed a relative increase.

Conclusion:

Obesity triggers inflammation in the colon and blood, as evidenced by increased inflammatory immune cells. This inflammation, however, is in part resolved by bariatric surgery as indicated by decreased inflammatory and increased anti-inflammatory macrophages and further changes in adaptive immunity. Bariatric surgery does not only drive weight loss, but also resolves tissue inflammation. However, further studies have to show whether this is related to the surgery or to weight loss in general.

No AgRP, No Sugar: Hypothalamic Disruption of Glucose Stability Under Starvation

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Background/Introduction:

Agouti-related peptide (AgRP) neurons in the hypothalamus are critical regulators of energy balance and feeding behavior. While their role in promoting food intake is well established, their contribution to glucose homeostasis, particularly during prolonged fasting, remains less understood. This study investigates the role of AgRP in maintaining blood glucose levels under extended fasting conditions using a genetic knockout mouse model.

Methods:

We used AgRP-Cre;DTA mice, in which AgRP-expressing neurons are selectively ablated during development, and compared them to wild-type littermates. Both groups were subjected to 48-72 hours of fasting. Blood glucose and plasma insulin levels were measured at multiple time points. Additionally, hepatic gluconeogenic gene expression (Pck1, G6pc) and liver glycogen content were assessed via RT-qPCR and biochemical assays, respectively. To evaluate the integrity of counter-regulatory mechanisms, plasma corticosterone and glucagon levels were also measured.

Results:

Under ad libitum feeding conditions, AgRP-KO mice maintained normal glucose levels compared to controls. However, during prolonged fasting, AgRP-KO mice exhibited significantly lower blood glucose levels starting at 18 hours and continuing through 72 hours ($p < 0.01$). Hypoglycemia in KO mice was accompanied by attenuated hepatic expression of Pck1 and G6pc ($p < 0.05$), reduced liver glycogen stores, and blunted glucagon and corticosterone responses. Despite similar body weights and fat mass, AgRP-KO mice displayed increased torpor-like behavior during fasting.

Conclusion:

These findings indicate that AgRP neurons are essential for maintaining glucose homeostasis during prolonged fasting. Their absence impairs counter-regulatory hormonal responses and hepatic gluconeogenesis, leading to fasting-induced hypoglycemia. This highlights a previously underappreciated role of hypothalamic circuits in systemic glucose regulation and could inform therapeutic strategies targeting central glucose-sensing pathways.

Real-World Experience of GLP 1 Receptor Agonist Liraglutide in Adolescents With Obesity: A First Cross-Sectional Single-Center Analysis From Switzerland

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Background/Introduction:

Adolescent obesity remains a major challenge with limited sustainable treatment options. GLP 1 receptor agonists such as liraglutide (Saxenda®) have shown efficacy in trials, but real-world data in youth are limited.

Methods:

This retrospective, cross-sectional, non-interventional study evaluated 20 adolescents treated with liraglutide at a Swiss pediatric endocrinology center. All participants received nutritional counseling and lifestyle guidance with three-monthly follow-up. BMI standard deviation scores (BMI SDS) and adverse effects were documented.

Results:

The mean age at treatment initiation was 14.9 years (range 12.5–17.5); 15 patients (75%) had Southern European immigrant background. Average treatment duration was 7.8 months (range 1–18). BMI SDS decreased significantly from $+2.6 \pm 0.28$ to $+2.4 \pm 0.32$ (mean intra-individual change -0.25 ± 0.18 SDS; p

Conclusion:

Liraglutide led to a modest yet significant BMI SDS reduction comparable to pivotal trials, with a favorable safety profile. However, the high discontinuation rate underscores the need for thorough pre-treatment counseling and proactive management of side effects. Prospective studies are needed to assess long term outcomes and the potential for broader use of GLP 1 receptor agonists in adolescent .

Treatment response to incretin mimetics in non-diabetic obese patients with and without insulin resistance (TRIM-IR)

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Background/Introduction:

Incretin mimetics such as semaglutide are effective and safe treatments for obesity, yet weight loss responses exhibit substantial variability. Non-diabetic individuals generally experience greater reductions than those with diabetes, yet up to 10% show little or no response. Most pronounced weight loss effects are seen in premenopausal women without diabetes. The underlying factors driving this heterogeneity remain poorly understood. Insulin resistance (IR), a central feature of adipose tissue dysfunction and impaired metabolic health, is a plausible determinant of differential responses to incretin mimetics as weight loss intervention. IR is associated with diminished metabolic flexibility, reduced muscle quantity and quality and a pro-inflammatory adipocyte profile - mechanisms that may blunt semaglutide's efficacy. Investigating the impact of insulin resistant states on weight loss interventions offers a mechanistic framework to explain observed variations in treatment outcomes.

Methods:

40 non-diabetic obese participants (gender-balanced) will be enrolled. IR will be assessed via hyperinsulinemic euglycemic clamp test. Fat and lean mass distribution will be measured with DEXA; adipose tissue function will be assessed via biopsies and scRNA sequencing. Additional tissue quality metrics include adipokine profiling and metabolomics. We hypothesize that GIR (glucose infusion rate) is inversely correlated with weight loss and explains $\geq 20\%$ of the outcome variability. Participants will be stratified by IR levels. Secondary endpoints include changes in fat/lean mass, visceral fat reduction, and adipose tissue quality over 16 weeks. Exploratory analysis will examine adipocyte subpopulations in relation to insulin sensitivity.

Results:

Baseline characteristics are reported for the initial 33 participants enrolled, since recruitment began in March of this year. The cohort includes 21 females and 12 males, with an average age of 41.2 years (SD 10.1) and a mean BMI of 35.3 kg/m² (SD 2.6). Mean HbA1c was 5.3% (SD 0.3) and fasting glucose 5.3 mmol/L (SD 0.4). Mean CRP was 4.5 mg/L (SD 3.5), and the glucose infusion rate (GIR) averaged 5.0 mg/kg/min (SD 3.2). Insulin resistance is typically defined by GIR below approximately 6.0 mg/kg/min. Based on this cut off, 6 female participants were insulin sensitive, while all men were insulin resistant. The study is ongoing, with over 65% of participants expected to complete data collection by November 2025, allowing for the presentation of preliminary findings.

Conclusion:

This single-center prospective cohort study explores how insulin resistance relates to weight loss, changes in body composition, and adipose tissue function in non-diabetic obese individuals treated with semaglutide. The study aims to improve personalized treatment strategies and enhance our understanding of adipose tissue plasticity.

Early time-restricted eating, but not a late eating window, improves body fat mass in adults with overweight/obesity and a morning chronotype – A randomized, open-label, multi-arm controlled trial

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Background/Introduction:

Time-restricted eating (TRE) is emerging as a promising alternative for weight loss and improving metabolic health. This chrononutrition approach may be more beneficial when mealtimes are personalized and aligned with the individual chronotype. We aimed to evaluate the changes in body composition following early TRE (e-TRE) vs. late TRE (l-TRE) vs. active control for 12 weeks among individuals with overweight/obesity.

Methods:

This three-arm parallel-group randomized controlled trial recruited adults aged 25-50 years with body mass index 25-34 kg/m², an eating window \geq 12 hours and a morning chronotype, as evaluated by the Horne-Ostberg Morningness-Eveningness Questionnaire. Eligible participants were randomized to e-TRE (eating from 8am to 2pm, n=19) vs. l-TRE (eating from noon to 8pm, n=17) vs. active control (three meals a day, n=18) for 12 weeks. At baseline and at the end of the study, body composition was measured by dual-energy X-ray absorptiometry, and meal timing and nutritional intake with the smartphone app MyFoodRepo. The primary outcome was the change in body fat mass after 12 weeks, which was analyzed using paired statistical tests to compare changes within each group and Analysis of Covariance (ANCOVA) between groups.

Results:

Overall, 54 participants (87% women, mean age $39.6 \pm$ SD 6.7 years, and body mass index $29.4 \pm$ 2.4 kg/m²) completed the intervention. e-TRE led to a significant weight loss ($-4.51 \pm$ 3.54 kg, $p < 0.001$), but not l-TRE ($-1.22 \pm$ 2.33 kg, $p = 0.052$) and active control ($-0.53 \pm$ 1.67 kg, $p = 0.21$). Body fat mass was significantly decreased in e-TRE (median -2.90 kg, IQR -3.61 to -1.74 , $p < 0.001$), but not in l-TRE (-1.37 kg, -2.16 to $+0.24$, $p = 0.05$) and active control ($+0.02$ kg, -1.63 to $+1.21$, $p = 0.93$). In group comparisons, this loss of body fat mass in e-TRE was greater compared to l-TRE ($p = 0.035$) and active control ($p = 0.001$), with no significant difference between l-TRE and active control. Of each intervention, only e-TRE significantly reduced visceral fat mass (median -48 g, IQR -107 to -21 , $p < 0.001$), but we found no between-group differences. Only e-TRE led to a significant loss of lean mass (median -1.82 kg, IQR -3.15 to -0.19 , $p = 0.002$), which was greater than in either l-TRE ($p = 0.017$) or active control ($p = 0.007$). In all interventions, no changes were observed in bone mass.

Conclusion:

Among adults with overweight/obesity and a morning chronotype, e-TRE is more effective in reducing body fat mass and visceral fat mass than l-TRE or active control, but is accompanied by a greater loss of lean mass. Future analyses will explore the mechanisms underlying the beneficial and adverse outcomes of TRE implementations tailored to morning chronotype.

Sex Differences Among Adults Seeking GLP-1 Pharmacotherapy for Weight Loss

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Background/Introduction:

Sex disparities in people seeking GLP-1 receptor agonist (GLP-1RA) pharmacotherapy remain insufficiently characterised. Understanding these differences is essential to optimize GLP-1RA therapy and deliver personalised weight management.

Methods:

In this cohort of 913 adults seeking GLP-1RA therapy (semaglutide/Wegovy®) for weight loss through Inselspital Bern's Metabolic Medicine Service (37% male [n=336], 63% female [n=577], of whom 39% [n=227] postmenopausal), we assessed sex differences in patient characteristics using both clinical and validated patient-reported baseline metrics. In a subgroup of 302 individuals, we further examined sex differences in initial 4 months treatment weight loss response. Sex/gender discordance was reported in 0.8% of participants (n=7) and was not considered in comparative analyses. Comparisons were conducted using t-tests or Mann-Whitney tests for continuous variables and chi-squared tests for categorical variables. Multivariable linear and logistic regression models were used to adjust for age and BMI. Values are reported as mean \pm SD or %.

Results:

Age was similar (47.1 \pm 11.8 vs 47.0 \pm 13.7yrs) but BMI was slightly lower in women vs men (37.2 \pm 5.3 vs 38.1 \pm 5.9kg/m², p<0.05). Women more often had children (75.1 vs 65.2%, p<0.01), were single parents (10.4 vs 4.2%, p<0.01), reported greater body dissatisfaction (60.9 vs 47.1%, p<0.01), poorer wellbeing, higher anxiety/depression (51.6 vs 34.8%, p<0.01), and more pain (59.6 vs 45.3%, p<0.01), especially postmenopause. Men more often lived alone (22.9 vs 12.1%, p<0.01) and had higher rates of hypertension (54.8 vs 42.4%, p<0.05), dyslipidemia (46.7 vs 32.1%, p<0.01), (pre)diabetes (27.5 vs 18.7%, p<0.05) and other comorbidities (sleep apnea, MASLD), and related medication. Metabolic burden was higher post- vs premenopausal (63.3 vs 48.2%, p<0.05). Physical activity was similar, but macronutrient shares differed. Men had lower fat mass (34.1 vs 43.8%, p<0.001), but more adverse cardiometabolic profiles (triglycerides, liver fat/stiffness, hsCRP, BP; lower insulin sensitivity and HDL-C, all p<0.05). Differences persisted after BMI/age adjustment. Postmenopausal status (age/BMI-adj.) related to higher HbA1c (5.9 \pm 0.8 vs 5.6 \pm 0.7%, p<0.05). Women set more ambitious target weights (-27% vs -25%, p<0.001) and achieved greater early weight loss at 4 months (-10.0 \pm 10.2 vs -8.8 \pm 3.8%, p<0.05).

Conclusion:

Significant sex differences exist among adults seeking GLP-1RA weight management, with menopausal status emerging as a pivotal additional factor. Men exhibit poorer cardiometabolic health, whereas women report greater psychological burden and achieve greater weight loss during treatment. Integrating sex-specific factors – including menopausal status – is fundamental to addressing obesity heterogeneity and advancing inclusive and personalised metabolic care.