EASD 2024 Abstract Highlights

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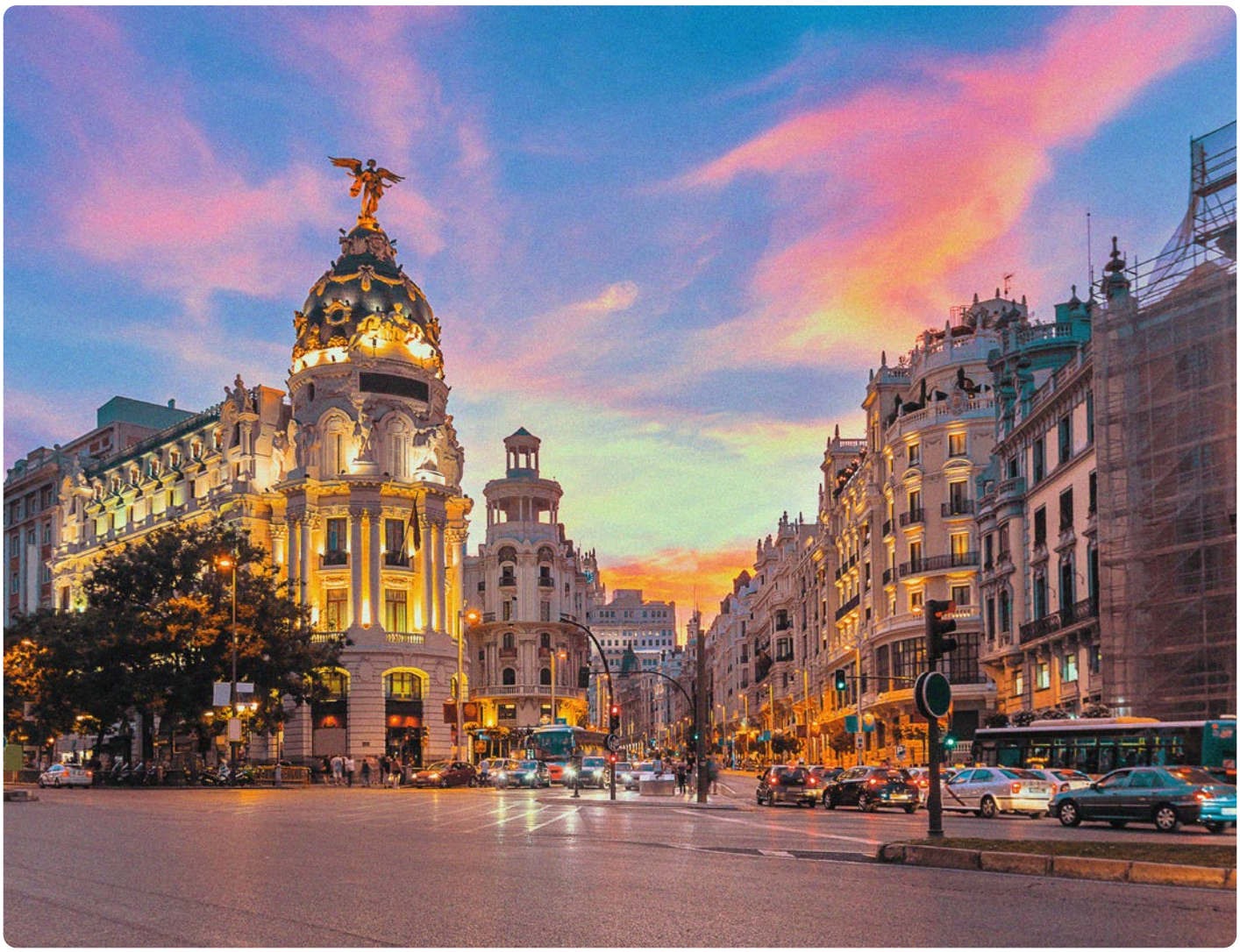
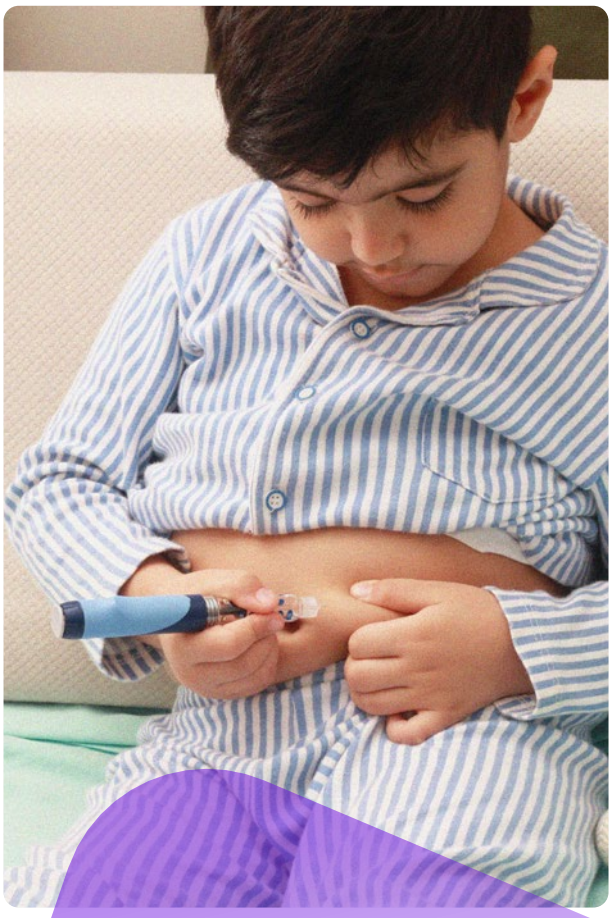
The following highlights showcase late-breaking research presented at the European Association for the Study of Diabetes (EASD) Annual Meeting 2024. Topics covered ranged from maternal effects on Type 1 diabetes development to the impact of diabetic peripheral neuropathy on patient mental health. Additionally, a common theme was the connection between Type 1 diabetes and other autoimmune diseases, such as coeliac disease and Graves' disease.



Maternal Type 1 Diabetes Protects Offspring From the Disease

NEW RESEARCH presented at EASD 2024 revealed that maternal Type 1 diabetes (T1D) provides long-term relative protection against the development of the disease in offspring, compared to paternal T1D.

> **The findings suggest that *in utero* exposure to maternal T1D plays a role in reducing the offspring's risk of developing the disease**



The study analysed data from over 11,000 individuals diagnosed with T1D and found that children of fathers with T1D are nearly twice as likely to develop the disease compared to children of mothers with T1D.

The study analysed data from five major studies, including BOX, Better Diabetes Diagnosis, TrialNet Pathway to Prevention, Type 1 Diabetes Genetic Consortium, and StartRight. The results showed that participants were significantly more likely to have an affected father than an affected mother. This pattern held true for both individuals diagnosed with T1D before and after the age of 18 years.

However, the protective effect of maternal T1D was only observed when the mother was diagnosed before the child's birth. If the mother was diagnosed after the birth, there was no significant difference in T1D risk compared to children of affected fathers. The T1D genetic risk score did not differ between individuals with mothers or fathers with T1D, indicating that the protection is not related to genetic factors.

The findings suggest that *in utero* exposure to maternal T1D plays a role in reducing the offspring's risk of developing the disease, offering new insights into the mechanisms underlying maternal protection. The researchers emphasised that this is the largest study to date that explores this phenomenon and provides further evidence for understanding familial transmission of T1D.

Early Screening Reduces Risk of Type 1 Diabetes and Coeliac Disease

A 7-YEAR population-based screening study conducted from 2017–2023 has demonstrated the effectiveness of early detection for Type 1 diabetes (T1D) and coeliac disease (CD) in children aged 1–17 years old. The study, presented at EASD 2024, has shown that screening for autoantibodies offers a way to prevent significant morbidity from delayed diagnoses, enabling early intervention.

Over this period, 34,110 children were screened for islet autoantibodies associated with T1D and transglutaminase autoantibodies linked to CD. The majority of these children (94%) did not have a first-degree relative with T1D, underscoring the importance of screening beyond family history. Most screenings were conducted in paediatric care clinics and outpatient labs.

The programme employed both radio-binding assays and the more specific electrochemiluminescence to measure islet and transglutaminase autoantibodies. The electrochemiluminescence method was especially valuable for distinguishing predictive, high-affinity autoantibodies from non-predictive ones. Children with positive results underwent further testing, which included assessments of autoantibodies by both methods, haemoglobin A1c, random blood glucose levels, and a thorough review of symptoms. Follow-up care was provided to those with confirmed multiple autoantibodies or high-affinity single autoantibodies, offering education to prevent diabetic ketoacidosis and referrals to clinical services or prevention trials.

Results showed that 0.54% of the children had multiple islet autoantibodies, predicting a 70% chance of developing T1D within 10 years, and 0.42% had a single high-affinity ab with a 30% risk. Notably, 90% of these high-risk children lacked a family history of T1D. Over a 3-year follow-up period, 77 children were diagnosed with clinical diabetes, and an additional 105 were identified at Stage 2 T1D. The screening also detected CD in 2.3% of participants, with 93% of those testing positive for transglutaminase autoantibodies receiving a confirmed diagnosis of CD.

The programme highlights the utility of widespread screening for early diagnosis of T1D and CD, significantly reducing diabetic ketoacidosis rates and enabling proactive disease management.

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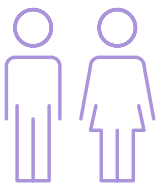
2.3% of participants were detected to have CD in the screening

> The researchers emphasised the potential of voice-based screening as a cost-effective and widely accessible tool for early T2D detection

Voice Analysis Shows Potential for Detecting Type 2 Diabetes

A NEW study presented at EASD 2024 found that voice analysis could be a non-invasive, scalable method for detecting Type 2 diabetes (T2D).

Researchers found that the voice-based algorithm accurately predicted T2D in 71% of male participants and 66% of females.



The study involved 607 participants from the USA and aimed to assess how well AI could differentiate between individuals with and without T2D based solely on their voices. Researchers found that the voice-based algorithm accurately predicted T2D in 71% of male participants and 66% of females. The predictive accuracy improved in specific groups, such as females over 60 years (74% accuracy) and participants with hypertension (75% accuracy in both genders).

The AI model was trained using voice recordings of participants reading text and cross-validated to ensure robustness. The study compared the AI's performance to the American Diabetes Association (ADA) risk score for T2D and found over 93% agreement between the two methods, demonstrating that voice analysis can be as effective as traditional risk assessment tools.

The researchers emphasised the potential of voice-based screening as a cost-effective and widely accessible tool for early T2D detection, particularly in at-risk populations. The researchers also noted that their findings are a promising first step toward using voice analysis as a first-line screening strategy for T2D. However, they emphasised the need for further research and validation, especially targeting early-stage cases of the disease.

This new approach could revolutionise diabetes screening by providing a simple, non-invasive method that can be easily deployed through digital platforms, potentially helping to reduce the global burden of undiagnosed T2D.

Diabetic Peripheral Neuropathy, Neuropathic Pain, and Mental Health

A RECENT study presented at EASD 2024 by researchers at Aalborg University Hospital and Steno Diabetes Center North Denmark sheds light on the significant impact of diabetic peripheral neuropathy (DPN) and neuropathic pain on the quality of life (QoL) and mental health of people with diabetes.

The observational, cross-sectional study included 7,743 participants, excluding 781 due to incomplete socioeconomic and mental health data. The remaining participants were divided into those with DPN (n=1,601) and those without (n=5,361). Of those with DPN, 1,085 also suffered from neuropathic pain, while 516 had painless DPN. Researchers utilised the Short Form Health Survey (SF36) and the Hospital Anxiety and Depression Scale (HADS) to assess QoL, depression, and anxiety levels.

Anxiety levels were highest in the painful DPN group, with a median score of 6.0 compared to 4.0

Results showed a significant difference in QoL between participants with and without DPN. The median SF36 score for those with DPN was 55.1 (interquartile range [IQR]: 36.7–73.6) compared to 82.2 (IQR: 63.6–90.9) for those without DPN (P<0.001). Mental health was similarly affected, with HADS depression scores of 4.0 (IQR: 1–8) for those with DPN, versus 1.0 (IQR: 0–3) for those without (P<0.001). Anxiety scores followed a similar trend, with median HADS anxiety scores of 5.0 (IQR: 2–9) for those with DPN and 2.0 (IQR: 1–5) for those without (P<0.001).

The impact was even more severe for participants with both DPN and neuropathic pain. Their median SF36 score dropped to 50.7 (IQR: 34.8–69.8), compared to 61.2 (IQR: 45.2–79.0) for those with painless DPN (P<0.001). Depression and anxiety scores also worsened, with HADS depression scores of 4.0 (IQR: 1–8) for those with painful DPN and 1.0 (IQR: 0–3) for those without pain. Anxiety levels were highest in the painful DPN group, with a median score of 6.0 (IQR: 3–10), compared to 4.0 (IQR: 1–8) for those without pain (P<0.001).

This study highlights the need for comprehensive care that addresses both physical symptoms and mental health in people with diabetes, especially those with DPN and neuropathic pain.

Imaging Biomarkers Reveals Pancreatic Changes in Type 1 Diabetes

OVER TIME, the chronic inflammation of the pancreatic islets, which leads to the destruction of insulin-producing beta cells in patients with Type 1 diabetes (T1D), spreads to the surrounding exocrine pancreas, causing increased immune cell infiltration and pancreatic atrophy.

In some cases, the development of parenchymal fibrosis may also occur, further complicating the disease. Due to the pancreas's location and sensitivity, tissue biopsies are risky. This makes non-invasive imaging techniques like multi-parametric magnetic resonance imaging (mpMRI) valuable for studying pancreatic changes in people with T1D. A UK Biobank study, presented at EASD 2024, aimed to characterise the pancreas in T1D using mpMRI markers to assess fibro-inflammation, fat content, and pancreatic volume, comparing these parameters with individuals who have Type 2 diabetes (T2D) and healthy controls.

The study analysed data from the UK Biobank using mpMRI to extract three key metrics: fibro-inflammation (srT1), fat content (proton density fat fraction, PDFF), and pancreatic volume. These were compared across individuals with T1D (n=106), T2D (n=1,190), and healthy controls (n=17,433).

Several key findings emerged, the first of which was that individuals with T1D showed significantly higher pancreatic fibro-inflammation, indicated by elevated srT1 values, compared to the other groups. Patients with T1D averaged 813 ms, compared to 763 ms in patients with T2D and 759 ms in healthy controls. This heightened inflammation in T1D reflects the autoimmune processes in the disease.

Pancreatic volume was also smaller in patients with T1D, averaging 59 mL compared to 68 mL in patients with T2D and 66 mL in healthy individuals. The smaller size is likely due to beta-cell loss and long-term inflammation. Additionally, patients with T1D had significantly lower pancreatic fat content (2.99%) compared to T2D (4.75%) and healthy controls (3.65%), suggesting a distinct metabolic profile in T1D.

The study found a negative correlation between fibro-inflammation and pancreatic volume, indicating that as inflammation increased, pancreatic size decreased. The use of mpMRI revealed that individuals with T1D have increased fibro-inflammation, smaller pancreatic size, and lower fat content. The results suggest that non-invasive imaging could become a key tool for monitoring T1D progression and treatment effects, offering a safer alternative to biopsies.

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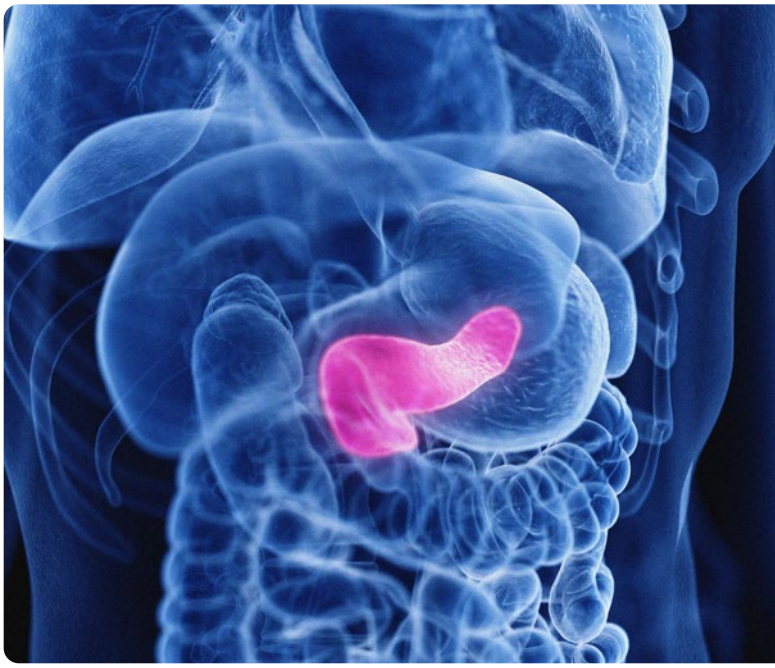


Genetic Risk Score Influences Response to Type 1 Diabetes Immunotherapies

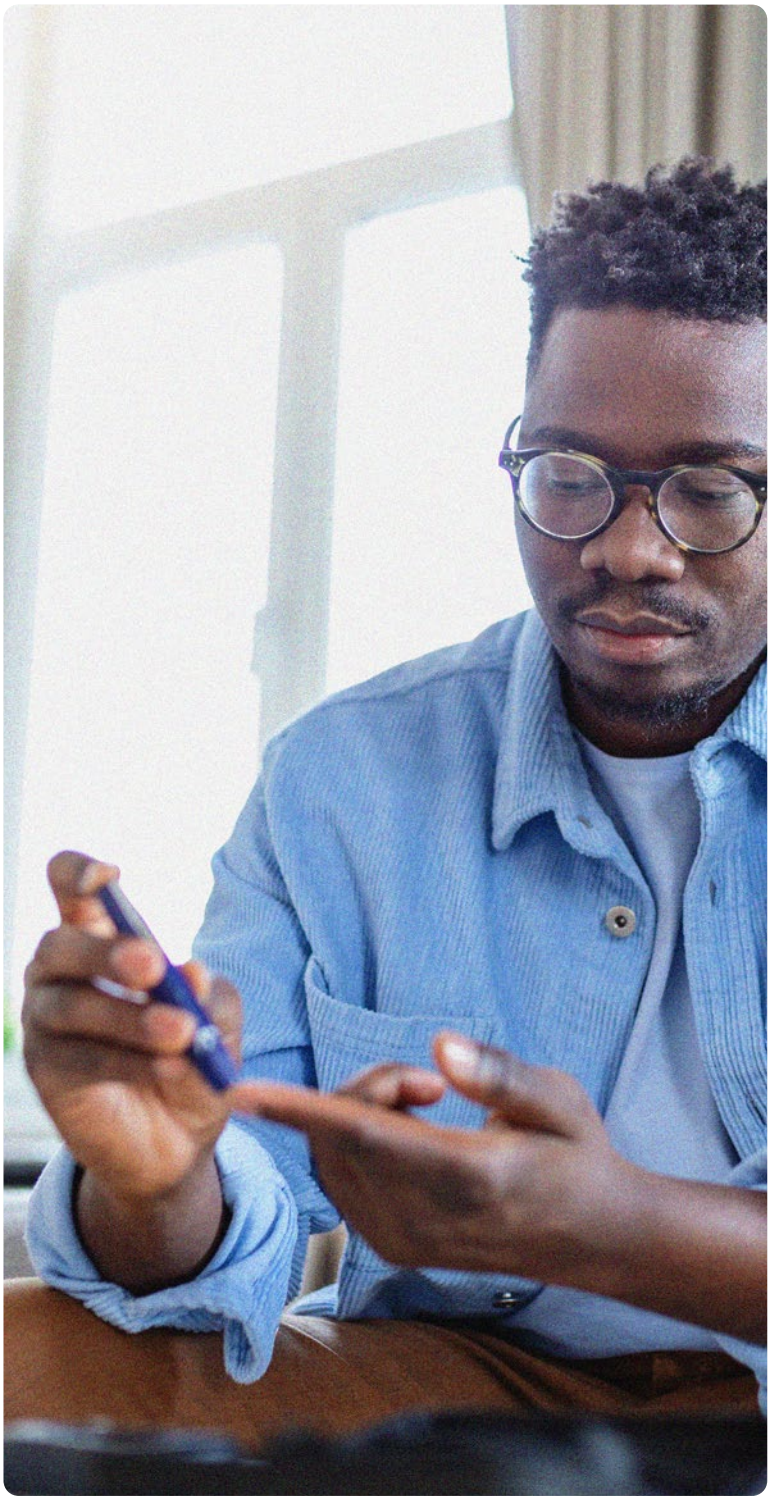
A NEW study presented at EASD 2024 demonstrated that the genetic risk score for Type 1 diabetes (T1D) may predict how well individuals respond to immunotherapies aimed at preventing the disease.

Researchers analysed data from autoantibody-positive participants from three prevention trials, TrialNet Anti-CD3 (teplzumab), TrialNet Abatacept, and TrialNet Oral Insulin. The study found that individuals with a higher GRS2, an indicator of higher risk for T1D, were more likely to progress to the clinical stage of T1D when treated with abatacept or oral insulin. However, participants treated with teplizumab showed a different pattern. The participants with a GRS2 score of 13 or higher had a significantly reduced risk of developing T1D compared to those in the placebo group, suggesting that teplizumab is more effective in individuals with a higher genetic burden.

> **The participants with a GRS2 score of 13 or higher had a significantly reduced risk of developing T1D**

Additionally, the study found that individuals with a lower GRS2 score did not experience the same protective effect from teplizumab, indicating a decreased response to the therapy. These findings suggest that the genetic risk score could be used as a tool for identifying patients who are more likely to benefit from certain immunotherapies, particularly teplizumab, in preventing the onset of T1D.

The findings of the study indicate the potential for using genetic information to tailor treatments and improve outcomes for individuals at risk of developing T1D.



Maternal Stress Shown Not to Affect Childhood Diabetes Risk

A RECENT study conducted in Norway, involving the largest cohort to date, explored the potential link between maternal psychological stress and the onset of Type 1 diabetes (T1D) in children. Previous studies have suggested that psychological stress may influence the immune system, potentially playing a role in the development of T1D, but results have been inconclusive. This study, presented at EASD 2024, aimed to determine whether maternal stress during pregnancy or the child's early years increases the risk of T1D.

The study analysed data from

91,000

mother-child pairs born between 2000–2009 and were followed until 2021

The study analysed data from the Norwegian Mother, Father, and Child Cohort (MoBa) study, which included up to 91,000 mother–child pairs. These children were born between 2000–2009 and were followed until 2021. Information on maternal anxiety, depression, and negative life events was collected through repeated validated questionnaires. The study tracked whether the children developed T1D before age 18 years using the Norwegian Childhood Diabetes Registry, where 551 children were diagnosed.

The researchers used binary log-linear regression to estimate relative risks (aRR) of developing T1D, adjusting for several factors including maternal T1D, age, parity, education, smoking, and pre-pregnancy BMI. Maternal symptoms of anxiety or depression during pregnancy were not associated with an increased risk of T1D in children (aRR: 0.91; 95% CI: 0.71–1.17). Similarly, negative life events reported during pregnancy (aRR: 1.04; 95% CI: 0.96–1.12) showed no significant correlation with the onset of T1D. The results were consistent when examining maternal stress at 6, 18, and 36 months after childbirth.

Other aspects of stress, such as job-related stress, social support, self-esteem, and overall life satisfaction, were also not found to be significant contributors to T1D risk. The study found no evidence to support a link between maternal psychological stress and the development of T1D in children, and therefore, these findings suggest that other factors, beyond maternal stress, are more likely to influence the onset of T1D.

SGLT2 Inhibitor Reduces Risk of Neurodegenerative Diseases in Type 2 Diabetes

RESEARCH presented at EASD 2024 has revealed that sodium-glucose cotransporter 2 inhibitor (SGLT2i) use reduces the risk of Alzheimer's disease (AD), vascular dementia, and Parkinson's disease in patients with Type 2 diabetes.

The study included 1,348,362 participants aged 40 years and above with Type 2 diabetes who initiated antidiabetic therapy between 2014–2019. After matching participants based on propensity scores, 358,862 individuals were included in the final analysis (mean age: 57.8 years; 57.9% male). Over the follow-up period, 6,837 incidents of dementia or Parkinson's disease were recorded.

The results revealed that SGLT2i use was associated with a 19% reduction in Alzheimer's risk (adjusted hazard ratio[aHR]: 0.81; 95% CI: 0.76–0.87), a 31% reduction in vascular dementia risk (aHR: 0.69; 95% CI: 0.60–0.78), and a 20% reduction in Parkinson's disease risk (aHR: 0.80; 95% CI: 0.69–0.91). Furthermore, the use of SGLT2i lowered the risk of all-cause dementia by 21% (aHR: 0.79; 95% CI: 0.69–0.90) and the combined outcome of dementia and Parkinson's disease by 22% (aHR: 0.78; 95% CI: 0.73–0.83).

These effects were consistent across various subgroups, regardless of age, sex, BMI, blood pressure, glucose, lipid profiles, kidney function, health behaviours, Charlson comorbidity index, diabetic complications, comorbidities, and medications.

The study suggests that SGLT2i may play a protective role against neurodegenerative disorders in patients with Type 2 diabetes. Further research should explore the underlying mechanisms and long-term outcomes to confirm these benefits.

> **SGLT2i may play a protective role against neurodegenerative disorders in patients with Type 2 diabetes**

Autoimmune Conditions Linked to Higher Type 1 Diabetes Risk

TYPE 1 diabetes (T1D) often coexists with other autoimmune conditions, such as thyroid diseases and coeliac diseases. While the prevalence of these conditions in patients with T1D is well known, fewer studies have investigated the risk of developing T1D in individuals who already have other autoimmune conditions.

This study, presented at EASD 2024, aimed to assess whether individuals with specific autoimmune diseases, like coeliac disease, hyperthyroidism, and hypothyroidism, have a higher risk of developing T1D compared to those without any autoimmune conditions.

This retrospective, observational matched-cohort study utilised real-world data from the Optum Clinformatics claims database, including individuals with autoimmune conditions including coeliac disease, hyperthyroidism (such as Graves' disease), or hypothyroidism (like Hashimoto's thyroiditis). They had to have at least one diagnosis of the autoimmune condition during the identification period (between 1 January 2017–30 September 2023) and no prior diagnosis of T1D or Type 2 diabetes. These participants were followed for at least 1 month after diagnosis. The control group consisted of individuals without any autoimmune conditions, matched 1:1 on demographics and clinical characteristics. A Cox proportional hazards model was used to compare the risk of developing T1D between the cohorts.

The results showed that individuals with autoimmune conditions had a significantly higher risk of developing T1D. Specifically, T1D developed in 0.14% of those with coeliac disease, 0.17% with hyperthyroidism, and 0.16% with hypothyroidism, compared to 0.06%, 0.06%, and 0.05% of controls, respectively. The time to T1D onset was shorter in the autoimmune cohorts than in the controls. The hazard ratios were 2.54 for coeliac disease, 2.98 for hyperthyroidism, and 3.19 for hypothyroidism, indicating a 2.5- to 3-fold increased risk of developing T1D compared to individuals without autoimmune diseases.

In conclusion, this study found that individuals with coeliac disease and thyroid autoimmunity have a significantly higher risk of developing T1D. These findings suggest that screening individuals with autoimmune conditions for early signs of T1D could be beneficial for early diagnosis and intervention.

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