

# Congress Review

## Review of the European Association for the Study of Diabetes (EASD) Virtual Meeting 2020

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VIENNA, Austria's cultural, economic, and political centre is rich in architectural ensembles, including Baroque palaces and gardens, casting a spell on all its visitors with its majestic charm. More famous composers have lived here than in any other city in the world, including the likes of Wolfgang Amadeus Mozart, Ludwig van Beethoven, Joseph Haydn, Franz Schubert, and Johann Straus, earning the city the prestigious title of the 'World's Capital of Music'. Vienna is also known as the 'City of Dreams', serving as the home to the world's first psychoanalyst, Sigmund Freud. Accommodating over 1,000 research facilities and 35% of Austria's research and development expenses, the city is a major hotpot for science and research. Annually, over 2,000 large-scale meetings and events are hosted here, and between 2005 and 2013 Vienna was the world's primary destination for international congresses and conventions. It should come as no surprise that the European Association for the Study of Diabetes

(EASD) chose Vienna as the host city for their 56<sup>th</sup> annual meeting.

Like many recent congresses, the physical meeting was cancelled and replaced virtually as a result of the coronavirus disease (COVID-19) pandemic. The EASD Virtual Meeting 2020 prevailed over other congresses by providing a truly three-dimensional virtual reality experience, demonstrated by Prof Stefano Del Prato, EASD President, in the Opening Ceremony. The platform provided each attendee with an avatar, capable of moving throughout the entire venue to chat, exchange information, and attend sessions and incorporated 35 symposia, 264 oral presentations, 712 poster sessions, 114 invited speakers, and 190 chairs. "It is really a new opportunity. I understand it is not like meeting people in person, but we did as much as possible to encourage you to have a real meeting," Prof Del Prato conveyed.

After the initial COVID-19 outbreak, the disease spread throughout the globe,

undermining the health of millions of people, including patients with chronic conditions such as diabetes; it is estimated that 10% of the patients with COVID-19 have diabetes. Prof Del Prato exclaimed: “It has been a tough and terrible fight, one requiring long hours, days, and weeks of generous dedication until exhaustion, but a fight that has allowed us to reduce and limit the number of our losses. To all of you, to all who have been assisting the patients with or without diabetes at the time of COVID-19, we would like to say a big thank you.” The ceremony continued with a special 1 minute of silence to commemorate the victims of the COVID-19 pandemic and individuals of the EASD community, including Profs John Fuller, Angelo Gnudi, Arnold Gries, Robert Henry, Lelio Orci, and Roger Unger.

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“Knowledge is key. The scientific method is the tool and generating and fostering research in science in diabetes is at the core of EASD,” Prof Del Prato noted while explaining the aims of the EASD and presenting the award winners of this year. The scientific content presented at the EASD Virtual Meeting 2020 was tremendous,

and so were the awards bestowed to recognise excellence in research and science in the field of diabetes and related disorders. Awards were presented to the winners of the 55<sup>th</sup> Minkowski Lecture, 52<sup>nd</sup> Claude Bernard Lecture, 35<sup>th</sup> Camillo Golgi Lecture, and the 14<sup>th</sup> Albert Renold Lecture, to Prof Gian Paolo Fadini, Prof Takashi Kadowaki, Prof Naveed Scattar, and Prof Guy A. Rutter, respectively. The winner of the 6<sup>th</sup> EASD/Novo Nordisk Foundation Diabetes Prize for Excellence Lecture was Prof Jens C. Brüning and the winners of the EFSD/Novo Nordisk Rising Star Fellowship programme and Symposium were Ms Beatriz Merino Antolín, Dr Pierre Larraufie, Dr Lucille Dollet, and Dr Alexandra Smink. Lastly, for the first time presented at EASD, the Morgagni Prize was bestowed to Drs Olga Ramich and Giuseppe Daniele.

Concluding the opening ceremony, Prof Del Prato stated: “This is a virtual meeting, but a meeting to be remembered in the years to come because together we want EASD to continue representing **Excellence** in science, to provide an **Advanced** virtual experience, to be **Superior** to any other virtual meeting, and remain **Dedicated** to reach a worldwide audience.” Next year, EASD will celebrate the 100-year anniversary of the discovery of insulin, a landmark achievement for humankind and the beginning of modern diabetology, which brought hope to many patients with diabetes. As the EASD looks forward to welcoming you to next year’s congress in Stockholm, Sweden, Prof Del Prato proudly concluded: “EASD will continue working to provide hope and to provide solutions.”



EASD 2020 REVIEWED →



## What is the Difference in Life Expectancy with Diabetes?

IMPACT on lifespan of Type 1 and Type 2 diabetes mellitus (T1DM, T2DM) has been assessed in large-scale modelling studies. The shortened life expectancy in both groups was revealed in a study presented at the EASD Virtual Meeting 2020 and in a press release dated 21<sup>st</sup> September 2020.

The study utilised data from the UK National Diabetes Audit (NDA) and the Office for National Statistics (ONS) to calculate future life expectancy for T1DM, T2DM, and nondiabetic populations, for subgroups of age and sex. 'Lost life years' (LLY) were calculated as the difference between total life expectancy with and without diabetes. Data from 41.3 million individuals (217,000 with T1DM, 2.5 million with T2DM) from 6,165 general practices were used in the modelling analysis.

Analysis compared an 'average' person with T1DM (age 42.8 years) to an equivalent without T1DM; the person with T1DM had a life expectancy of 32.6 years (living to 75.4 years), compared with a life expectancy of 40.2 years (living to 83 years) without T1DM. The mean LLY with T1DM were 7.6

years. In a similar comparison, the average person with T2DM (age 65.4 years) life expectancy (18.6 years; living to 84.0 years) was also less than those without T2DM (life expectancy: 20.3 years, living to 85.7 years), a mean LLY of 1.7 years.

LLY were 21% greater for females with T1DM and 45% greater for females with T2DM, compared with males in each group. For both T1DM and T2DM, life expectancy may be shortened by 100 days for each year that an individual spends with their HbA1c >58 mmol/mol. The authors of the study highlighted: "Knowledge of this may act as an incentive for clinicians to ensure that all people are on the best therapy to keep their blood sugar in the target range, and for those people to engage more strongly with their therapy and lifestyle recommendations."

Other factors likely contribute to the difference in life expectancy, including smoking, physical activity, weight, hypertension, and use of statin therapy. However, the authors believe that HbA1c will remain a strong independent determinant of mortality in their planned follow-up study using general practice-level data.

*"Knowledge of this may act as an incentive for clinicians to ensure that all people are on the best therapy to keep their blood sugar in the target range..."*





## Type 2 Diabetes Mellitus Linked to Vascular Dementia, But Not Alzheimer's Disease

OVER 37,000 adults with Type 2 diabetes mellitus (T2DM) have been involved in an observational study that compared their risk of various dementia types with that of nearly 2 million matched controls. The results of this study were presented at the EASD Virtual Meeting 2020 and reported in a press release dated 21<sup>st</sup> September 2020.

Dementia has long been linked to poor blood sugar control, but results of the observational study, led by researchers from the University of Glasgow, Glasgow, UK, and the University of Gothenburg, Gothenburg, Sweden, have conveyed that individuals with T2DM were 36% more likely to develop vascular dementia and 9% more likely to develop nonvascular dementia, though no more likely to develop Alzheimer's disease, than their matched counterparts.

Prof Naveed Sattar, coleader of the study and from the University of Glasgow, commented on the findings: "A 36% higher risk is in itself an argument for preventive measures such as healthier lifestyle. The importance of prevention is underscored by the fact that, for the majority of dementia diseases, there is no good treatment."

Though the findings do not suggest that most patients with T2DM will go onto develop vascular dementia, they do suggest that a healthy lifestyle, absent of obesity, smoking, and lack of physical activity, can reduce the risk of developing vascular or nonvascular dementia.

Coauthor Dr Carlos Celis, University of Glasgow, summarised the importance of the results: "With the number of people with T2DM doubling over the past 30 years, the importance of a healthy lifestyle is clearer than ever."

The authors did point out that although their study was large, it was observational, and therefore no conclusions can be drawn about direct cause and effect.

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## Residual Nonfunctioning $\beta$ Cells in Patients with Longstanding Type 1 Diabetes Mellitus

RESTORING insulin-producing cells that are lost in Type 1 diabetes mellitus (T1DM) is now one step closer, as researchers have developed a noninvasive imaging technique to detect residual, nonfunctioning  $\beta$  cells in patients with longstanding T1DM. This breakthrough in  $\beta$ -cell regeneration research was presented at the EASD Virtual Meeting 2020 and reported in a press release dated 21<sup>st</sup> September 2020.

Scientists have struggled up until now to provide evidence for the existence of small numbers of nonfunctioning residual  $\beta$  cells, as it was widely believed that within years after T1DM diagnosis a complete destruction of the insulin-producing cells would occur. Now, single photon emission CT (SPECT) medical imaging, which has been used on a cohort of 10 adults aged 21–54 years with T1DM, has been able to confirm that most individuals with T1DM maintain a low level of residual  $\beta$  cells for years after diagnosis.

Using  $^{111}\text{In}$ -exendin to measure pancreatic tracer uptake, six out of 10 patients were shown to have measurable pancreatic uptake after an average of 11 years post-T1DM diagnosis. Additionally, five out of the 10 displayed uptake similar to the lower levels observed in healthy controls; the indication is therefore that, despite years of T1DM, these  $\beta$  cells could have their function restored, if the right treatments become available.

*“The presence of a residual pool of dysfunctional  $\beta$  cells has important implications for treatment of Type 1 diabetes mellitus, since these cells could help people maintain some ability to make their own insulin.”*

Prof Martin Gotthardt, Radboud University Medical Center, Nijmegen, the Netherlands, who co-led the study, concluded the findings: “The presence of a residual pool of dysfunctional  $\beta$  cells has important implications for treatment of Type 1 diabetes mellitus, since these cells could help people maintain some ability to make their own insulin.” He did, however, issue some caution: “These results are hugely encouraging, but we need to do more studies.”



# Hot Baths as A Therapeutic Tool for Type 2 Diabetes Mellitus

HOT baths have been associated with beneficial effects on Type 2 diabetes mellitus (T2DM) on account of regular heat exposure. This new research was presented at the EASD Virtual Meeting 2020 on 21<sup>st</sup> September.

Heat therapy, in the form of saunas and hot-tub bathing, has been proven to positively impact glycaemic control and body fat percentage. There are, however, no large studies that have examined this form of heat therapy and the effects on metabolic parameters of patients with T2DM in a real-world setting to date.

*“Our results indicate that daily heat exposure through hot-tub bathing has beneficial influences on cardiovascular risk factors in patients with T2DM.”*

In this study led by Dr Hisayuki Katsuyama, Kohnodai Hospital, Ichikawa, Chiba, Japan, researchers investigated the effect of bathing in Japanese patients with T2DM, since bathing in a bath or hot tub is common practice in Japanese households. Dr Katsuyama and colleagues executed a questionnaire with 1,297 patients with T2DM between October 2018 and March 2019 and investigated the frequency of bathing with anthropometric measurements and blood test results.

The results from the study showed that increased bathing frequency was associated with decreased body weight, BMI, waist circumference, diastolic blood pressure, and HbA1c. After adjusting for age, sex, BMI, and drug therapy, analysis also showed that the patients who had the highest frequency of bathing had reduced HbA1c and diastolic blood pressure.

The authors commented on the positive results of their study: “Our results indicate that daily heat exposure through hot-tub bathing has beneficial influences on cardiovascular risk factors in patients with T2DM.”





## Restoration of Pancreas Size in Landmark Diabetes Remission Clinical Trial (DiRECT)

SHRUNKEN and small pancreas could result from Type 2 diabetes mellitus (T2DM), rather than lead to it, and reversal of T2DM can restore the pancreas to a normal size and shape. Smaller sized and abnormally shaped pancreases in people with T2DM have been evidenced but whether they are a consequence or cause of the metabolic disease was unknown until now. New research in this field from a team at Newcastle University, Newcastle, UK, was presented at the EASD Virtual Meeting 2020 on 21<sup>st</sup> September.

Increased postprandial insulin levels cause tissues to grow or at least maintain size. Imaging studies and past research have shown that achieving remission of T2DM through intensive weight loss regimes can restore the insulin-producing capacity of the pancreas to levels similar to those in people who have never been diagnosed with the disease. “This new study suggests that achieving remission of T2DM restores this healthy, direct effect of insulin on the pancreas,” commented Prof Roy Taylor, lead researcher.

Over the course of 2 years, 64 participants from the landmark Diabetes Remission Clinical Trial (DiRECT), and 64 age-, sex-, and weight-matched controls without T2DM, were measured for  $\beta$  cell function, pancreas volume and fat levels, and irregularity of pancreas borders using MRI. Individuals in remission, or responders, were those classified as achieving an HbA1c level

<6.5%, fasting blood glucose <7.0 mmol/L, and taking no medications.

At the beginning of the investigation, average pancreas volume was smaller, and the pancreas borders were more irregular in individuals with diabetes compared to the matched control group. Over a period of 5 months of weight loss, pancreas volume was unchanged in both groups. After 2 years, the pancreas had grown on average by one-fifth in size in responders compared with one-twelfth increase in size in those who were not in remission. Responders lost a significant amount of fat from their pancreas compared with nonresponders over the 2 years and achieved normal pancreas borders. They alone also showed early and sustained improvement in  $\beta$  cell function. After 5 months of weight loss, the amount of insulin being made by responders increased and was maintained at 2 years, but there was no change in nonresponders. Limitations of the study included the short follow-up time of 2 years and retrospective observations.

Prof Taylor commented on possibilities created with this new discovery: “Our findings provide proof of the link between the main tissue of the pancreas which makes digestive juices and the much smaller tissue which makes insulin, and open up possibilities of being able to predict future onset of T2DM by scanning the pancreas.”



# Exercise Capacity and All-Cause Mortality Risk in People with Diabetes

EXERCISE capacity may be positively correlated with a decreased all-cause mortality risk, according to results from a study presented at the EASD 2020 Virtual Meeting on 21<sup>st</sup> September.

Physical activity has been shown to inhibit inflammatory cytokines, increased chronic production of which can largely contribute to inflammatory diseases such as diabetes. Thus far, investigations into the effect of exercise on all-cause mortality in people with Type 2 diabetes mellitus had not been fully explored. The new study by Dr Yun-Ju Lai and colleagues, at Puli Branch, Taichung Veterans General Hospital, Nantou, Taiwan, used data from the National Health Interview Survey (NHIS) and the National Health Insurance Research Database (NHIRD) in Taiwan to explore the link between higher levels of exercise and all-cause mortality risk.

Surveys performed between 2001 and 2013 used information about the characteristics of each participant, including their socioeconomic status, health behaviours, and exercise habits, and health status was followed-up until 31<sup>st</sup> December 2016.

A statistical analysis to evaluate the relationship between exercise capacity and all-cause mortality was also carried out.

The study enrolled, and obtained survey results for, 4,859 adult patients with Type 2 diabetes mellitus and a mean age of 59.5 years. Those with a higher exercise capacity were found to have a significantly lower risk of all-cause mortality compared with those who reported no physical activity or exercise. Participants who performed a moderate amount of exercise had a 25% lower all-cause mortality rate and individuals who were classed as having a high exercise level had a 32% lower all-cause mortality risk.

The team of researchers concluded: “Among people with Type 2 diabetes [mellitus], those with increased exercise capacity had a significantly decreased risk of all-cause mortality. Further studies should investigate the type and dose of exercise that is most helpful to promote health and prolong life expectancy.”



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# Should Individuals with Rheumatoid Arthritis Be Screened for Diabetes Risk Factors?

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RESEARCH from a new study presented at the EASD Virtual Meeting 2020 on Monday 21<sup>st</sup> September revealed that rheumatoid arthritis is linked with a 23% increased risk of Type 2 diabetes mellitus (T2DM), and may indicate that both conditions are associated with the body’s inflammatory response. Inflammation is considered a key factor in disease progression of T2DM and it has been established that rheumatoid arthritis is an autoimmune and inflammatory disease.

A team of researchers, led by Drs Zixing Tian and Adrian Heald from University of Manchester, Manchester, UK, suggested that the systemic inflammation associated with rheumatoid arthritis may increase the risk of an individual developing diabetes.



*“Agents that reduce systemic inflammatory marker levels may have a role in preventing T2DM. This may involve focussing on more than one pathway at a time.”*

A comprehensive search of a range of medical and scientific databases, and statistical analyses for relative risk and publication bias, were carried out, comparing the incidence of T2DM among people with rheumatoid arthritis to the diabetes risk within the general population. After identifying the eligible studies, which comprised 1,629,854 participants, the authors found that patients with rheumatoid arthritis had a 23% higher chance of developing T2DM compared to the risk of being diagnosed with T2DM within the general population. The findings support the hypothesis of the team that inflammatory pathways are indicated in the pathogenesis of diabetes.

The researchers shared their ideas for future research and management: “We suggest that more intensive screening and management of diabetes risk factors should be considered in



## Undiagnosed Diabetes Could be Identified Earlier Through Population Screening

*“Our study shows that population-level screening could identify cases of T2DM far earlier and potentially reduce complications.”*

SCREENING for Type 2 diabetes mellitus (T2DM) through population databases, such as the UK Biobank, using HbA1c levels could identify those with undiagnosed T2DM, according to a study presented at EASD Virtual Meeting 2020 and in a press release dated 21<sup>st</sup> September.

In the UK, diagnosis of T2DM is commonly established through HbA1c testing at a general practitioner practice when a patient is symptomatic. To reduce this potential delay in diabetes onset and initiation of treatment, researchers from the UK used the UK Biobank to test if population screening using the HbA1c levels measured at recruitment could identify those with undiagnosed T2DM.

The UK Biobank comprises approximately 500,000 participants between the ages 40 and 70 years (at time of recruitment), for whom primary care records are available for around one-half. Patients without diabetes (n=201,465) were defined as those who did not self-report diabetes and had no evidence in their primary care records of diabetes prior to recruitment. The authors retrieved data on the time it took for participants who had undiagnosed diabetes at recruitment (Hb1Ac of  $\geq 48$  mmol/mol) to be clinically diagnosed, finding that the median time

was 2.3 years, with 23% having not received a diagnosis at the 5 years follow-up.

Using the UK Biobank, the authors found that 1.0% (n=2,022) of participants had an HbA1c measurement of  $\geq 48$  mmol/mol and therefore had undiagnosed diabetes. Resultant diagnosis of diabetes from this screening was predicted to be approximately 2 years earlier than a clinical diagnosis, potentially shortening the time to receiving treatment. Compared to those with an HbA1c of  $< 48$  mmol/mol at screening, these participants were older (median age: 61 years), had a higher BMI (median: 31), and were more likely to be male (60%).

Dr Katherine Young, University of Exeter, Exeter, UK, concluded: “Our study shows that population-level screening could identify cases of T2DM far earlier and potentially reduce complications.” She acknowledged that the implications of the delays in diabetes diagnosis seen here are unclear but advocated for further research to illuminate this and the potential of screening for diabetes.



# Increased Risk of Falls Seen in People with Diabetes

FALLS can occur for a multitude of reasons and potentially lead to fall-related injuries. The results from a study presented at EASD Virtual Meeting 2020 and in a press release dated 21<sup>st</sup> September showed that those with Type 1 diabetes mellitus (T1DM) were at a 33% increased risk of having a fall, and those with Type 2 diabetes mellitus (T2DM) were at a 19% increased risk, compared to the general population.

The study investigated the risk factors associated with increased falls in both those with diabetes and the general population using data from the Danish National Patient Register. Patients with T1DM (n=12,975) or T2DM (n=407,099) were matched for sex and age (1:1) with those from the general population, which formed the control group. Computer modelling was used to analyse the fall-related hospitalisations from 1996 to 2017.

The results for the adjusted analyses, which included risk factors such as age, sex, diabetic complications, history of alcohol abuse, and medication history, showed that there was a 33% increased risk of having a fall in those with T1DM, and a 19% increased risk in those with T2DM. Other risk factors that had a profound impact

on the risk of fall in T1DM and T2DM were female sex, age (>65 years), selective serotonin receptor inhibitor use, opioid use, and history of alcohol abuse.

When analysing the differences in risk of bone fracture compared to the general population, those with T2DM were at increased risk of fractures to the hip and femur, humerus, radius, and skull or face; those with T1DM were at an increased risk of fractures of the hip or femur. “Gaining further information on risk factors for falls could guide the management of diabetes treatment such as the choice of medication, which enables us to improve treatment, particularly in people with a high risk of falls and fractures associated with high mortality,” the authors concluded.

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## Spousal Concordance Can Influence Type 2 Diabetes Mellitus Risk Factors



BEHAVIOURS, such as those relating to diet and exercise, can reduce the likelihood of developing Type 2 diabetes mellitus (T2DM). According to a study presented at EASD Virtual Meeting 2020 and summarised in a press release dated 21<sup>st</sup> September, if one partner in a relationship displays high levels of behaviours that positively influence the risk of T2DM, then the other partner is also likely to do so.

In this cross-sectional study, the similarity in the pathophysiology mechanisms, including  $\beta$  cell function and insulin sensitivity, of T2DM and risk factors, such as BMI, percentage body fat, physical activity levels, and diet indicators, were analysed in 172 couples using data from the Maastricht Study. Glucose metabolism status was also assessed through fasting and 2-hour plasma glucose testing and HbA1c.

The Dutch Healthy Diet Index (DHDI) showed the strongest spousal concordance, with a 1-unit increase in the female partner's DHDI

correlated with a 0.53-unit increase in the male's DHDI. A similar association was seen with time spent in high intensity physical activity (HPA), for which a 1-unit increase in the male's time spent in HPA corresponded with a 0.36-unit increase in the female partner's time spent in HPA. The strong spousal concordances seen in the behavioural risk factors were not observed in the pathophysiological factors, with the weakest spousal concordance observed in  $\beta$  cell function measurements.

The authors concluded: "From a practical point of view, public health prevention strategies to mitigate diabetes risk may benefit from spousal similarities in health-related behaviours and diabetes risk factors to design innovative and potentially more effective couple-based interventions."