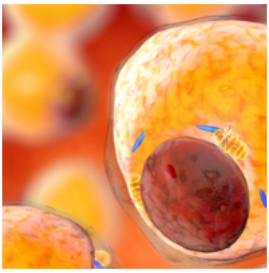
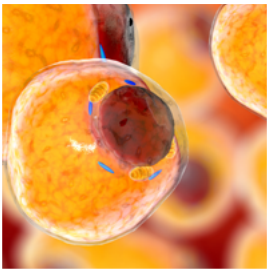
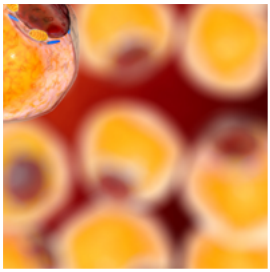
CONGRESS REPORT

The 56th Annual Meeting of the European Association for the Study of Diabetes







EASD 2021

28 September - 1 October 2021

SCIENTIFIC SEMINARS
INTERNATIONAL FOUNDATION

BIOGRAPHY

Raffaella Buzzetti

Raffaella Buzzetti is full Professor of Endocrinology at the Department of Experimental Medicine, Sapienza University, Rome, Italy. She is a member of the certifying committee of the specialty of endocrinology and serves on the doctorate teaching committee for molecular medicine, working on internationalizing the project. Professor Buzzetti has led the Diabetes Unit at Policlinico Umberto I Hospital in Rome since 2017, where she provides constant and integrated care for patients with diabetes and metabolic diseases. Professor Buzzetti balances her clinical activity with lecturing and training medical students.

Professor Buzzetti's major clinical and research interests are in the genetic susceptibility to polygenic diseases (such as type 1 diabetes), the pathogenesis and clinical features of type 1 diabetes and adult-onset autoimmune diabetes, and phase II and III clinical trial studies. During her career she has been an active principal investigator for national and international research projects on diabetes and metabolic diseases, including the NIRAD project, which clarified the pathogenetic and clinical characteristics of adult-onset autoimmune diabetes. Professor Buzzetti has been an active member of the Italian Society of Diabetology (SID), President of SID Lazio region and a member of the Scientific Committee of the Italian Society of Endocrinology, where she acted as coordinator of the teaching committee.

Professor Buzzetti has authored or co-authored more than 250 articles, 40 of these in the last 3 years, which have been published in peer-reviewed journals (H. Index Scopus: 45). She serves on the editorial board of Diabetes Metabolism Research and Reviews and PLOS ONE, and is a reviewer of numerous scientific journals including, Diabetes, Diabetes Care and Nature Endocrinology. She was a reviewer for the Horizon 20/20 Program, and worked on IMI2 EU as an expert for the 10th call for proposals (Brussels). In addition, Professor Buzzetti has been the recipient of several competitive national and international grants, serves as a board member of the ethical committee at Policlinico Umberto I and St Andrea Hospital in Rome, was vice-president of the National Committee of Research Guarantors and is now a board member of the National Committee of Research Evaluators at the Italian Ministry of University and Research.

CONGRESS REPORT

The European Association for the Study of Diabetes (EASD) 57th annual meeting was once again transformed into a virtual meeting due to the COVID-19 pandemic. However, the fact that it was virtual, did not prevent it from being an extraordinary congress, full of stimulating ideas across the 45 symposia, 9 prize lectures, 2 debates, 47 oral and 65 short oral presentations. Professor Stefano Del Prato (EASD President) opened the virtual meeting with the presidential address. Using a scenic, virtual background, he precisely detailed the structure of the congress, and then recognised the scientific commission for their excellent work and thanked all those who have given their time and expertise to organize the congress and to support the work of the EASD in the last year.

Professor Del Prato introduced the lecture winners for 2021: the 53rd Claude Bernard lecture was awarded to Dr Juleen Zierath (Sweden), who presented **How exercise keeps the rhythm in metabolism**. The 36th Camillo Golgi lecture was won by Dr Hiddo Lampres Heerspinks (The Netherlands) with his presentation, **Personalizing treatment for patients with type 2 diabetes: the mean is meaningless**. Dr Pedro Herrera (Switzerland) was the winner of the Albert Renold lecture for **Diabetes remission through insulin secretion by islet non-β cells**. The 56th Minkowsky lecture was presented by Professor Amelie Bonnefond (France), **Hunt for rare genetic variants of pretty little things in the genetics of diabetes** and the 7th Diabetes Prize for Excellence was awarded to Professor John Todd (UK), a very well-known researcher in genetic susceptibility to metabolic diseases and, in particular, to type 1 diabetes, who presented a very interesting lecture **From HLA-DQ position 57 and back again**. Professor Del Prato completed his presentation by defining EASD as not just an association, as much as a galaxy: continually expanding through the rejuvenating annual congress, the high standard of the Diabetologia journal and the many, many initiatives by EASD for people affected by diabetes mellitus.

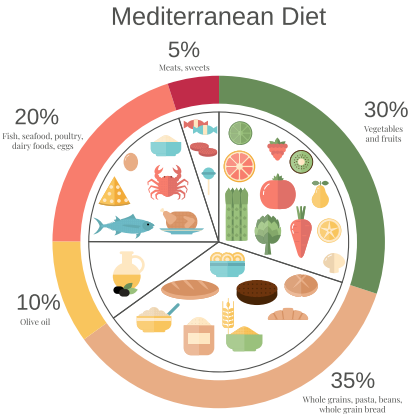
The annual meeting itself encompassed many interesting posters and oral presentations, among them, a short talk by J Strelitz (UK), **Association between weight change and incidence of cardiovascular disease events and mortality among adults with type 2 diabetes: a systematic review and meta-analysis**. The topic of body weight changes and incidence of cardiovascular disease (CVD) events and mortality in adults with type 2 diabetes

(T2D) has stimulated thousands of studies in recent years. In the study by Strelitz, et al, observational studies of weight changes and CVD events in adults with T2D and trials of behavioural interventions targeting weight loss were identified through searches of MEDLINE, EMBASE, Web of Science, CINAHL and The Cochrane Library (CENTRAL). Only studies reporting a measurement of change in weight and CVD and/or mortality outcomes among adults with T2D, or alternatively, reported the effect of a behavioural intervention on CVD events and/or mortality among adults with T2D were sought. Risk of bias was assessed using modified ROBINS-I and RoB2 tools. Out of an impressive number of 13,227 identified articles, 17 (14 observational studies, three trials) met the inclusion criteria. Weight gain after diabetes diagnosis (vs. no weight change) was associated with higher risks of CVD events [HRs (95% CI) ranged from 1.13 (1.00, 1.28) to 1.63 (1.11, 2.39)] and all-cause mortality [HRs (95% CI) ranged from 1.26 (1.12, 1.42) to 1.57 (1.33, 1.85)]. On the other hand, evidence of the effect of weight loss on CVD events was conflicting. Unintentional weight loss was associated with increased all-cause mortality, but associations with intentional weight loss were unclear. Trials of behavioural interventions targeting weight loss showed no effect on CVD events [pooled hazard ratio: 0.95 (95% CI: 0.72, 1.24)] over a range of 5–10 years. Risk of bias was low to moderate in 14 studies but high in 3 studies, due to potential uncontrolled confounding factors and the method of weight assessment. The presenter concluded that there was a small amount of evidence supporting weight loss for CVD prevention. Furthermore, long-term follow-up of behavioral intervention trials is needed to understand the effects on CVD and mortality and to inform policy regarding weight management support for patients with T2D.

Most significant studies in the literature, such as the Look AHEAD trial published in the New England Journal of Medicine, 20131[1] clearly showed that weight loss (at least the amount achieved in the trial), does not reduce CVD in patients with diabetes. A sub-analysis of this trial[2] suggests that those who lost >10% of their body weight during the first year did experience a reduction in CVD. However, as this result was from a post-hoc analysis there is less basis on which to make recommendations.

In contrast, the PREDIMED study (with all the limitations of this study) showed that a diet supplemented with healthy unsaturated fat-rich foods, like olive oil and

mixed tree nuts, without calorific restriction and weight loss, was associated with a ~30% relative risk reduction for the composite outcome of CVD.[3] Supplementary analyses of the PREDIMED study showed no heterogeneity based on diabetes status, suggesting that the benefits were similar in those with and without diabetes.



Moreover, PREDIMED showed a marked reduction in both the incidence of diabetes and the joint outcome of incidence of diabetes and mortality, again, without calorific restriction. To date, despite some limitations, this is the strongest evidence suggesting that we can reduce CV risk with diet. It should be acknowledged that PREDIMED-Plus is currently ongoing, comparing the original PREDIMED diet with some calorific restriction to find out whether this might confer added benefits on CVD risk. Based on all of the above, improving dietary quality becomes of paramount importance for patients at risk from CVD. For instance, we should encourage an increase in the consumption of healthy fats, and, if that is achieved, we should aim at encouraging patients to lose weight to improve the quality of their life, although, not necessarily for a CV benefit. Weight loss improves quality of life across a spectrum of diseases, including diabetes.

Another very interesting presentation at EASD 2021 was the short oral presentation by AT Andreeva (Russian Federation): Cholecalciferol therapy effect on glucose metabolism in patients with prediabetes. In this study, 65 patients with pre-diabetes but without diseases affecting their metabolism who were not taking vitamin D were randomized into two treatment groups: cholecalciferol 500 IU (group A) and cholecalciferol 4000 IU (group B) for 3 months. Anthropometric data, comorbidities and concomitant medications were assessed. In addition, before and after the 3 months of cholecalciferol therapy, all patients underwent an oral glucose tolerance test. Plasma glucose and GLP-1 were evaluated, as well as indices of insulin resistance with insulin and glucagon-like peptide (HOMA-IR), insulin sensitivity and functional β-cell activity (HOMA-B). Also measured were 25-hydroxycalciferol and parathyroid hormone (PTH) levels. Results showed that after 3 months of therapy, an increase in vitamin D and a decrease in PTH concentrations were found in both groups, but normal values of vitamin D were reached in only 10.7% of patients from group A compared with 73.3% of patients from group B. Reduction in HbA1c ($p<0.001$) and plasma glucose at 1 and 2 hours ($p<0.04$), increase in insulin levels at 2 hours ($p=0.03$) and gain in HOMA-B index (25.3%) at the end of the study were observed only in group B patients (those taking the higher dose of vitamin D, 4000 IU daily). After 3 months of therapy, normal glucose and HbA1c levels were observed in 63.3% of patients

from group B compared with 7% of patients from group A. The authors concluded that treatment with 4000 IU of vitamin D3 per day for 3 months is associated with a significant increase in vitamin D levels leading to an improvement of parameters of glucose metabolism in subjects with pre-diabetes. Although there are limitations to this study (i.e. the small sample size and the short period of observation), nevertheless, it is of interest that treatment with cholecalciferol over a relatively short time period (3 months) is effective in modifying glucose tolerance in subjects with pre-diabetes. These results prompted the authors to implement a large trial with long-term follow-up to find out whether treatment with high dose cholecalciferol is effective in preventing the development of T2D in subjects with pre-diabetes.

In the last few years, cholecalciferol (vitamin D3) has emerged as a potential risk modifier for diabetes, and the possibility of T2D prevention with vitamin D3 has been investigated.[4,5] However, the optimum dose of vitamin D3 has not yet been determined and further background information on the role of vitamin D3 in diabetes is required to highlight current issues and unmet needs.

In subjects with T2D, dysfunctional islet β-cells are due to decreased β-cell mass, and possibly also due to both abnormal ATP/Ca^{2+} signaling and free cholesterol levels. There is evidence that vitamin D may have an important role beyond the musculo-skeletal system, and, indeed, may modify the risk of developing T2D. Vitamin D has both direct and indirect effects, the latter via regulation of calcium effects on various mechanisms related to T2D, including pancreatic β-cell dysfunction, impaired insulin action and systemic inflammation. Vitamin D supplementation with calcium may be beneficial in controlling glucose levels since these nutrients act together on insulin secretion and sensitization. The potentially significant extra-skeletal role of vitamin D is highlighted in several recently published studies including the demonstration of expression of the vitamin D receptor in a large number of non-skeletal cells, including pancreatic β-cells. Evidence of the effect of vitamin D supplementation in T2D comes primarily from many cross-sectional and prospective observational studies, most of which showed an inverse association between vitamin D status and prevalence or incidence of T2D. All these observations have prompted investigators to study the effect of vitamin D3 supplementation in patients with pre-diabetes.

REFERENCES

1. Look AHEAD Research Group, Wing RR, et al. N Engl J Med. 2013 Jul 11;369(2):145-54. doi: 10.1056/NEJMoa1212914. Epub 2013 Jun 24. PMID: 23796131
2. Estruch R, et al, PREDIMED Study Investigators. N Engl J Med. 2018 Jun 21;378(25):e34.
3. Ros E. Endocrinol Diabetes Nutr. 2017 Feb;64(2):63-66. doi: 10.1016/j.endinu.2016.11.003. Epub 2017 Feb 1. PMID: 28440779
4. Mitri J, Pittas AG. Endocrinol Metab Clin North Am. 2014 Mar;43(1):205-32. doi: 10.1016/j.ecl.2013.09.010. Epub 2013 Dec 12. PMID: 24582099; PMCID: PMC3942667.
5. Santos RKF, et al. Diabetes Metab Res Rev. 2018 Mar;34(3). doi: 10.1002/dmrr.2969. Epub 2017 Dec 21.

This independent educational activity is made possible thanks to an educational grant received from Merck Healthcare KGaA, Darmstadt, Germany.

Scientific Seminars International Foundation
Via di Porta Pinciana, 6 - 00187 Roma
www.scientificseminars.com