Type 2 Diabetes
Current Awareness Bulletin
June 2020

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Title: Effects of high-protein diet on glycemic control, insulin resistance and blood pressure in type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials.

Citation: Clinical Nutrition; Jun 2020; vol. 39 (no. 6); p. 1724-1734

Author(s): Yu ; Nan, Fengwei; Wang, Leslie Yingzhijie; Jiang, Hua; Chen, Wei; Jiang, Yu

Abstract: Obesity is a well-known risk factor of type 2 diabetes mellitus (T2DM), and it is commonly accompanied by T2DM. It is estimated that almost two thirds of the population with T2DM is also affected by hypertension. Elevated arterial blood pressure would increase the risk for diabetes development. Recently some studies indicated that a high-protein diet was effective for weight loss, and therefore we hypothesized that a high-protein diet could help control blood glucose, mitigate insulin resistance (IR) and improve blood pressure by weight management in T2DM patients. The study aimed to systematically review the effects of a high-protein diet on glycemic control, IR and blood pressure in T2DM patients. We searched four electronic databases until May 1st 2018 and included all randomized clinical trials comparing a high-protein diet with other diets. Two reviewers independently identified the trials for inclusion and independently extracted data. Either a fixed- or a random-effects model was used to combine the changes in each outcome from baseline to the end of the intervention. The meta-analysis was performed with RevMan 5.3 software. Twelve articles (thirteen studies) including 1138 T2DM patients met our inclusion criteria. Glycemic control was not significantly different between the high-protein diet and control group, with the changes in fasting plasma glucose (FPG) (−0.13 (95% CI (−0.46, 0.19), p = 0.43) mmol/L) and HbA1c% (−0.05 (95% CI (−0.18, 0.08), p = 0.92))) from baseline to the end of intervention. However, the difference in IR between the two groups was statistically significant. Most changes in lipids profiles were favorable. The changes in HDL, LDL, TC, and TG were +0.03 (95% CI (−0.04,0.11), p = 0.35) mmol/L, −0.10 (95% CI (−0.18,−0.02), p = 0.02) mmol/L, −0.21 (95% CI (−0.31,−0.12), p < 0.01) mmol/L and −0.19 (95% CI (−0.33,−0.05), p < 0.01) mmol/L, respectively. The result of HOMA-IR was −0.27 (95% CI (−0.47,−0.06), p < 0.01). Additionally, the difference in blood pressure in terms of systolic blood pressure (−0.57 (95% CI (−2.45, 1.32), p = 0.55)) and diastolic blood pressure (−0.73 (95% CI (−2.48, 1.02), p = 0.41)) was not significant. This review showed that a high-protein diet does not significantly improve glycemic control and blood pressure, but can lower LDL, TC, TG and HOMA-IR levels in T2DM patients. Further studies are needed to clarify the effects of a high-protein diet on glycemic control, IR and blood pressure control in T2DM patients.

Title: Improving type 2 diabetes mellitus glycaemic control through lifestyle modification implementing diet intervention: a systematic review and meta-analysis.

Citation: European Journal of Nutrition; Jun 2020; vol. 59 (no. 4); p. 1313-1328

Author(s): García-Molina ; Lewis-Mikhael, Anne-Mary; Riquelme-Gallego, Blanca; Cano-Ibáñez, Naomi; Oliveras-López, Maria-Jesús; Bueno-Cavanillas, Aurora

Purpose: Type 2 diabetes mellitus represents a significant health problem. Many studies have reported that intensive nutritional intervention by itself or in addition to medications is the best method to improve glycaemic control in type 2 diabetes mellitus. However, in clinical practice, dietary education is not implemented as an integral part in the management of type 2 diabetes mellitus. The purpose of this systematic review and meta-analysis is to analyse the scientific evidence concerning the role of nutritional intervention in the glycaemic control of type 2 diabetes mellitus.

Methods: We searched Pubmed, Scopus, Cochrane Library and Web of Science databases from inception till May 2019 for randomised controlled trials (RCTs) that include dietary interventions in the management of patients with type 2 diabetes mellitus.

Results: A total of 28 studies were included. Our results demonstrated that lifestyle interventions significantly lowered glycosylated haemoglobin (HbA1c) levels compared to the usual care for patients with type 2 diabetes mellitus, overall weighted mean difference, WMD = − 0.51 (− 0.67, −0.35). Strategies combining individualized and group-based activities were the most effective, WMD = − 0.95 (− 1.24, − 0.66). Most of stratified analyses did not totally resolve heterogeneity, but improvement in HbA1c levels has been consistently observed.
Conclusions: The available evidence from RCTs shows that lifestyle intervention is more effective than the standard care regarding the glycaemic control of type 2 diabetic patients, particularly when there is a weight loss. It is time to translate this evidence to the primary health care practice. The protocol of the present systematic review was registered in PROSPERO, registration number CRD42018090469.

Title: Gestational diabetes and progression to type two diabetes mellitus: missed opportunities of follow up and prevention?

Citation: Primary care diabetes; Jun 2020
Author(s): Walker, Emma; Flannery, Orla; Mackillop, Lucy

Background: The incidence of type 2 diabetes (T2DM) is increasing. Having a pregnancy complicated by gestational diabetes mellitus (GDM) is a potent risk factor for the later development of T2DM. AIMSTo explore the characteristics of women diagnosed with GDM in a single centre and their follow up for progression to T2DM.

Methods: A retrospective cohort study using anonymised data of one hundred and fifty four (154) women with GDM receiving maternity care at the Oxford University Hospitals NHS Foundation Trust (OUHFT) in 2010 and their follow up until 2018.

Results: The prevalence of GDM in women delivering in Oxfordshire in 2010 was 3.4%. 70% of pregnant women were overweight or obese (with 51% being obese) at booking. Gestational weight gain (GWG) was excessive in 29% of women, when compared to Institute of Medicine (IOM) guidelines. Almost a quarter of women (23.4%) had no follow up after delivery. Over a median follow up of 3.5 years (range 0-8 years) nearly one in six (16.9%) of the total cohort (22% of those tested) went on to develop T2DM. 74% of women with GDM were multiparous, and 65% of nulliparous women were tested compared to 81% of multiparous women. There was a significant difference between multiparous women (53.8%) compared to nulliparous women (46.2%) developing T2DM (p=0.01). There was no significant difference in BMI (p=0.866) or GWG (p=0.83) in women who progressed to T2DM versus those who did not.

Conclusion: The risk of T2DM after GDM is substantial however, follow up rates of this population is poor. Subsequent screening of women with GDM and their management crosses secondary and primary care with scope for improvement in counselling of women of the importance of annual reviews, in data collection and follow up in both obstetrics and general practice. The implementation of a recall system, an education programme for general practitioners and/or a registry of women diagnosed with GDM could be useful to identify those at high risk of developing T2DM as well as providing a platform for the potential development of interventions to prevent progression to T2DM after GDM.

Title: Diabetic Kidney Disease in Older People with Type 2 Diabetes Mellitus: Improving Prevention and Treatment Options.

Citation: Drugs & aging; Jun 2020
Author(s): Abdelhafiz, Ahmed H

Abstract: Age-related metabolic and renal changes predispose older people to an increased risk of diabetes mellitus and diabetic kidney disease, respectively. As the prevalence of the ageing population is increasing, because of increased life expectancy, the prevalence of older people with diabetic kidney disease is likely to increase. Diabetic kidney disease is associated with an increased risk of adverse outcomes and increased costs to healthcare systems. The management includes promotion of a healthy lifestyle and control of cardiovascular risk factors such as hyperglycaemia, hypertension and dyslipidaemia. Older people are a heterogeneous group of people from a community-living fit and independent person to a fully dependent individual residing in a care home. Therefore, management in this age group should be based on a patient's functional level adopting tight metabolic control in the fit individual and relaxed targets in the frail person. However, despite the
maximum available therapy, a significant number of patients with diabetic kidney disease still progress to renal failure and experience adverse cardiac outcomes. Therefore, future research is required to explore methods of early detection of diabetic kidney disease and to investigate novel therapeutic interventions to further improve the outcomes.

Title: Flash glucose monitoring helps achieve better glycemic control than conventional self-monitoring of blood glucose in non-insulin-treated type 2 diabetes: a randomized controlled trial.

Citation: BMJ open diabetes research & care; Jun 2020; vol. 8 (no. 1)

Author(s): Wada, Eri; Onoue, Takeshi; Kobayashi, Tomoko; Handa, Tomoko; Hayase, Ayaka; Ito, Masaaki; Furukawa, Mariko; Okui, Takayuki; Okada, Norio; Iwama, Shintaro; Sugiyama, Mariko; Tsunekawa, Taku; Takagi, Hiroshi; Hagiwara, Daisuke; Ito, Yoshihiro; Suga, Hidetaka; Banno, Ryoichi; Kuwatsuka, Yachiyo; Ando, Masahiko; Goto, Motomitsu; Arima, Hiroshi

Introduction: The present study aimed to evaluate the effects of flash glucose monitoring (FGM) and conventional self-monitoring of blood glucose (SMBG) on glycemic control in patients with non-insulin-treated type 2 diabetes.

Research Design and Methods: In this 24-week, multicenter, open-label, randomized (1:1), parallel-group study, patients with non-insulin-treated type 2 diabetes at five hospitals in Japan were randomly assigned to the FGM (n=49) or SMBG (n=51) groups and were provided each device for 12 weeks. The primary outcome was change in glycated hemoglobin (HbA1c) level, and was compared using analysis of covariance model that included baseline values and group as covariates.

Results: Forty-eight participants in the FGM group and 45 in the SMBG group completed the study. The mean HbA1c levels were 7.83% (62.1 mmol/mol) in the FGM group and 7.84% (62.2 mmol/mol) in the SMBG group at baseline, and the values were reduced in both FGM (-0.43% (-4.7 mmol/mol), p=0.001) and SMBG groups (-0.30% (-3.3 mmol/mol), p=0.001) at 12 weeks. On the other hand, HbA1c was significantly decreased from baseline values in the FGM group, but not in the SMBG group at 24 weeks (FGM: -0.46% (-5.0 mmol/mol), p<0.001; SMBG: -0.17% (-1.8 mmol/mol), p=0.124); a significant between-group difference was also observed (difference -0.29% (-3.2 mmol/mol), p=0.022). Diabetes Treatment Satisfaction Questionnaire score was significantly improved, and the mean glucose levels, SD of glucose, mean amplitude of glycemic excursions and time in hyperglycemia were significantly decreased in the FGM group compared with the SMBG group.

Conclusions: Glycemic control was better with FGM than with SMBG after cessation of glucose monitoring in patients with non-insulin-treated type 2 diabetes.

Trial Registration Number: UMIN000026452, jRCTs041180082.

Title: The experience of type 2 diabetes self-management in adults with intellectual disabilities and their caregivers: A review of the literature using meta-aggregative synthesis and an appraisal of rigor

Citation: Journal of Intellectual Disabilities; Jun 2020; vol. 24 (no. 2); p. 253

Author(s): Maine, Andrew; Brown, Michael; Dickson, Adele; Truesdale, Maria

Abstract: People with intellectual disabilities (ID) experience significant barriers to diabetes self-management (DSM), yet there remains a paucity of research within this population. An overview of the literature on people with ID and their caregivers’ experiences of living with and self-managing type 2 diabetes is provided. Meta-aggregative methods were adopted to synthesize results, and an appraisal was reported of rigor. A total of eight studies met the inclusion criteria and four themes were extracted: (i) "Frustration over lifestyle adjustments," (ii) "Limited understanding and inadequate educational resources," (iii) "Limited training and knowledge in staff," and (iv) "Potential for effective DSM with appropriate support." Current support is inadequate to meet the needs of people with ID
and their caregivers self-managing diabetes. Structured education to improve health literacy and diabetes knowledge in people with ID is required, together with training for caregivers which leads to a culture of nurturing autonomy.

Title: Eating well, living well and weight management: A co-produced semi-qualitative study of barriers and facilitators experienced by adults with intellectual disabilities

Citation: Journal of Intellectual Disabilities; Jun 2020; vol. 24 (no. 2); p. 158
Author(s): Doherty, A J; Jones, S P; Chauhan, U; Gibson JME

Abstract: Adults with intellectual disabilities in England experience health inequalities. They are more likely than their non-disabled peers to be obese and at risk of serious medical conditions such as heart disease, stroke and type 2 diabetes. This semi-qualitative study engaged adults with intellectual disabilities in a co-production process to explore their perceived barriers and facilitators to eating well, living well and weight management. Nineteen participants with intellectual disabilities took part in four focus groups and one wider group discussion. They were supported by eight of their carers or support workers. Several barriers were identified including personal income restrictions, carers' and support workers' unmet training needs, a lack of accessible information, inaccessible services and societal barriers such as the widespread advertising of less healthy foodstuffs. A key theme of frustration with barriers emerged from analysis of participants' responses. Practical solutions suggested by participants included provision of clear and accessible healthy lifestyle information, reasonable adjustments to services, training, ‘buddying’ support systems or schemes and collaborative working to improve policy and practice.

Title: Understanding Reasons for Treatment Discontinuation, Attitudes and Education Needs Among People Who Discontinue Type 2 Diabetes Treatment: Results from an Online Patient Survey in the USA and UK.

Citation: Diabetes therapy : research, treatment and education of diabetes and related disorders; Jun 2020
Author(s): de Climens, Aude Roborel; Pain, Emilie; Boss, Anders; Shaunik, Alka

Introduction: Type 2 diabetes mellitus (T2DM) requires long-term treatment to achieve and maintain glycaemic control; however, up to 50% of people with T2DM discontinue treatment by 1 year. It is therefore important to understand the patient perspective of therapeutic adherence and persistence.

Methods: An online questionnaire was presented to people with T2DM in the USA and UK on PatientLive®, a platform of Carenity, an online patient community. Those who discontinued at least one T2DM treatment within the last 6 months answered open-ended questions aimed to assess the reasons for discontinuation, how discontinuation could have been prevented, and what would have improved the experience with the discontinued treatment. Thematic qualitative analysis was performed on respondents' answers to these questions.

Results: Oral antidiabetics were the most commonly discontinued treatments (93/161), followed by insulin (40/161) and glucagon-like peptide 1 receptor agonists (13/161). Main reasons for treatment discontinuation overall were side effects (57/161), mostly gastrointestinal side effects and weight gain. The second most reported reason was drug efficacy issues (42/161). Key factors stated to prevent discontinuation were an improved care pathway (45/161) and more efficacious treatments with fewer side effects (41/161). In the USA, treatment cost played an important role in discontinuation (14/161) and discontinuation prevention (12/161). More information about T2DM and associated treatments (56/161), help with T2DM management (24/161), and increased and informative patient-physician interaction (12/161) would have been helpful for many respondents in both countries, while some patients noted that no additional information would have been useful to improve their understanding and experience with their T2DM treatment (64/161).

Conclusions: These results emphasise the need for focused medical education and improved communication to enhance patient experience and prevent treatment discontinuation. Understanding
of attributes preferred by people with T2DM can help improve therapeutic adherence and outcomes with current medications, and guide development of future therapies.

Title: Type 2 diabetes in older people: pathophysiology, identification and management.

Citation: Nursing older people; Jun 2020
Author(s): Mayo, Paula

Abstract: The general population is now living longer, with increasing numbers of older people living with more than one long-term condition. The number of older people diagnosed with type 2 diabetes is also rising because of the changes resulting from the ageing process and the significant increase in obesity levels, which are affecting the provision of healthcare and individuals' quality of life. This article explores the implications of increased longevity and how this is linked to the development of type 2 diabetes. It explains how the presentation of type 2 diabetes differs in older people compared with younger people, making initial diagnosis increasingly challenging. Frailty and anti-diabetes medicines can affect quality of life and an older person's risk of falls; therefore, linked to these, the article details the effects of declining functional ability and increasing cognitive impairment, and emphasises the need for regular medication reviews. The article also provides an analysis of the care required for older people with type 2 diabetes living in care homes, including the need for flexibility in treatment targets.

Title: A disease state approach to the pharmacological management of Type 2 diabetes in primary care: A position statement by Primary Care Diabetes Europe.

Citation: Primary care diabetes; Jun 2020
Author(s): Seidu, S; Cos, X; Brunton, S; Harris, S B; Jansson, S P O; Mata-Cases, M; Neijens, A M J; Topsever, P; Khunti, K

Abstract: Type 2 diabetes and its associated comorbidities are growing more prevalent, and the complexity of optimising glycaemic control is increasing, especially on the frontlines of patient care. In many countries, most patients with type 2 diabetes are managed in a primary care setting. However, primary healthcare professionals face the challenge of the growing plethora of available treatment options for managing hyperglycaemia, leading to difficulty in making treatment decisions and contributing to therapeutic inertia. This position statement offers a simple and patient-centred clinical decision-making model with practical treatment recommendations that can be widely implemented by primary care clinicians worldwide through shared-decision conversations with their patients. It highlights the importance of managing cardiovascular disease and elevated cardiovascular risk in people with type 2 diabetes and aims to provide innovative risk stratification and treatment strategies that connect patients with the most effective care.

Title: Incretin mimetics and sodium-glucose co-transporter 2 inhibitors as monotherapy or add-on to metformin for treatment of type 2 diabetes: a systematic review and network meta-analysis.

Citation: Acta diabetologica; Jun 2020
Author(s): Jia, Shubing; Wang, Zhiying; Han, Ruobing; Zhang, Zinv; Li, Yuping; Qin, Xiaotong; Zhao, Mingyi; Xiang, Rongwu; Yang, Jingyu

Purpose: Although there are many different methods of treating type 2 diabetes (T2D), it is still difficult to draw coincident conclusions concerning the efficacy and safety of different classes of new drugs, and the recommendation level of them has still kept uncertain as second anti-diabetic agents.
Therefore, the aim of this study was to summarize evidence on the efficacy and safety of DPP-4is, GLP-1RAs and SGLT-2is as monotherapy or add-on to metformin (Met) for treatment of T2D.

Materials and Methods: We searched PubMed, Embase, Cochrane library and ClinicalTrials.gov for relevant articles in keeping with established methods using terms associated with anti-diabetic agents up to February, 2020, with no start date restriction. Weighted mean difference and risk ratios with 95% confidence intervals were calculated within traditional and network meta-analysis. Primary outcomes were the mean change in hemoglobin A1c (HbA1c), fasting plasma glucose (FPG) change and the frequency of hypoglycemic events from baseline after 12 weeks of treatment.

Results: In total, 64 eligible studies comprising 37,780 patients and 7 treatment strategies were included. The results of primary outcomes showed that GLP-1RAs were significantly more effective than DPP-4is or SGLT-2is in reducing HbA1c when add-on to Met. For FPG, both GLP-1RAs and SGLT-2is significantly reduced FPG compared with DPP-4is whether add-on to Met or not. For hypoglycemia, monotherapy has a lower risk than combination therapy except for SGLT-2is. Ranking probability analysis indicated that GLP-1RAs and SGLT-2is, respectively, reduced HbA1c and FPG most when add-on to Met. Meanwhile, GLP-1RAs took the lowest risk to induce the hypoglycemia, whereas GLP-1RAs plus Met the highest.

Conclusions: Both GLP-1RAs and SGLT-2is have their own advantages in efficacy and safety. Monotherapy is beneficial for reducing the risk of hypoglycemia. The recommendation should be a patient-centered approach when selecting treatment choices.

Title: Type 2 diabetes and cognitive dysfunction-towards effective management of both comorbidities.

Citation: The lancet. Diabetes & endocrinology; Jun 2020; vol. 8 (no. 6); p. 535-545
Author(s): Srikanth, Velandai; Sinclair, Alan J; Hill-Briggs, Felicia; Moran, Chris; Biessels, Geert Jan

Abstract: Type 2 diabetes and cognitive dysfunction are highly prevalent disorders worldwide. Although type 2 diabetes is associated with an increased risk of dementia, awareness of the link between the two conditions is poor, and few recommendations are available to guide clinicians about how to approach cognitive dysfunction in people with diabetes. Clinical guidelines in diabetes have only recently begun to emphasise the importance of cognitive impairment in diabetes and its management. This Series paper aims to synthesise knowledge about the link between diabetes and cognitive dysfunction, issues pertaining to screening and diagnosis of cognitive impairment and dementia in those with type 2 diabetes, management of diabetes in people with cognitive dysfunction (accounting for age and frailty), and emerging therapies for prevention. A conceptual framework for approaching screening and diagnosis is included, and future research directions to guide the field forward are suggested.

Title: Beyond general resistance training. Hypertrophy versus muscular endurance training as therapeutic interventions in adults with type 2 diabetes mellitus: A systematic review and meta-analysis.

Citation: Obesity reviews : an official journal of the International Association for the Study of Obesity; Jun 2020; vol. 21 (no. 6); p. e13007
Author(s): Acosta-Manzano, Pedro; Rodriguez-Ayllon, Maria; Acosta, Francisco M; Niederseer, David; Niebauer, Josef

Abstract: Resistance training (RT) is a powerful first-line intervention for the management of type 2 diabetes mellitus (T2DM). Nonetheless, the effects of the most frequent RT (hypertrophy training [HT] and muscular endurance training [MERT]) employed for the management of T2DM, and which type of RT might exert superior effects, remain elusive. Thus, this review aims to assess the effects of HT and MERT on glycaemic control, physical fitness, body composition, lipid profile, blood pressure, C-reactive protein, and quality of life in patients with T2DM; to analyse which particular RT is more effective; to assess the effects of general RT; and to identify RT components, characteristics of
patients, and medications that could mediate the effects of RT. Randomized controlled trials (RCT) and non-RCT (RT≥ 4 weeks) in adults with T2DM were selected. Both HT and MERT improved HbA1c, insulin levels and sensitivity, muscle strength, body mass index, waist circumference, and fat mass. Additionally, HT improved glucose, cardiorespiratory fitness, fat percentage, lean body mass, lipid profile, systolic blood pressure, and C-reactive protein, and MERT improved weight. Overall, HT and MERT exert beneficial effects well comparable with aerobic training. Both types of RT can be used as potent therapeutic interventions for the management of T2DM depending on patients' limitations/preferences.

Title: Semaglutide injection for the treatment of adults with type 2 diabetes.

Citation: Expert review of clinical pharmacology; Jun 2020
Author(s): Chudleigh, Richard A; Bain, Stephen C

Introduction: Current estimates suggest that approximately 10% of the global adult population have type 2 diabetes. In recent years there has been a significant increase in the therapeutic options available for its treatment. This article examines the use of injectable semaglutide in the treatment of type 2 diabetes.

Areas Covered: We will describe the global problem posed by type 2 diabetes followed by consideration of the glucagon-like peptide 1 receptor agonist class of glucose lowering therapies. The focus is then shifted to semaglutide and a description of the large phase 3 pre-approval trial programme known as SUSTAIN. There is consideration of glucose control, the primary end-point of the phase 3 programme, as well as secondary end-points such as weight and blood pressure. There follows a précis of the cardiovascular outcomes trial for subcutaneous semaglutide (SUSTAIN 6) and the post-approval publications. As well as the SUSTAIN trial programme we used PubMed to identify relevant publications.

Expert Opinion: This section discusses the position of semaglutide and the risks and benefits versus other once weekly GLP-1RAs and finally the development of an oral version of semaglutide, which has recently been approved in the United States.

Title: Combined effect of interventions with pure or enriched mixtures of (poly)phenols and anti-diabetic medication in type 2 diabetes management: a meta-analysis of randomized controlled human trials.

Citation: European journal of nutrition; Jun 2020; vol. 59 (no. 4); p. 1329-1343
Author(s): Raimundo, Ana F; Félix, Filipa; Andrade, Rita; García-Conesa, María-Teresa; González-Sarrias, Antonio; Gilso-Lopes, João; do Ó, Dulce; Raimundo, Ana; Ribeiro, Rogério; Rodriguez-Mateos, Ana; Santos, Cláudia N; Schär, Manuel; Silva, Ana; Cruz, Inês; Wang, Brian; Pinto, Paula; Menezes, Regina

Purpose: (Poly)phenols have been reported to confer protective effects against type 2 diabetes but the precise association remains elusive. This meta-analysis aimed to assess the effects of (poly)phenol intake on well-established biomarkers in people with type 2 diabetes or at risk of developing diabetes.

Methods: A systematic search was conducted using the following selection criteria: (1) human randomized controlled trials involving individuals with prediabetes and type 2 diabetes; (2) one or more of the following biomarkers: glucose, glycated haemoglobin (HbA1c), insulin, pro-insulin, homeostatic model assessment of insulin resistance (HOMA-IR), islet amyloid polypeptide (IAPP)/amylin, pro-IAPP/pro-amylin, glucagon, C-peptide; (3) chronic intervention with pure or enriched mixtures of (poly)phenols. From 488 references, 88 were assessed for eligibility; data were extracted from 27 studies and 20 were used for meta-analysis. The groups included in the meta-analysis were: (poly)phenol mixtures, isoflavones, flavanols, anthocyanins and resveratrol.
Results: Estimated intervention/control mean differences evidenced that, overall, the consumption of (poly)phenols contributed to reduced fasting glucose levels (-3.32 mg/dL; 95% CI -5.86, -0.77; P = 0.011). Hb1Ac was only slightly reduced (-0.24%; 95% CI -0.43, -0.044; P = 0.016) whereas the levels of insulin and HOMA-IR were not altered. Subgroup comparative analyses indicated a stronger effect on blood glucose in individuals with diabetes (-5.86 mg/dL, 95% CI -11.34, -0.39; P = 0.036) and this effect was even stronger in individuals taking anti-diabetic medication (-10.17 mg/dL, 95% CI -16.59, -3.75; P = 0.002).

Conclusions: Our results support that the consumption of (poly)phenols may contribute to lower glucose levels in individuals with type 2 diabetes or at risk of diabetes and that these compounds may also act in combination with anti-diabetic drugs.

Title: Coronavirus Infections and Type 2 Diabetes-Shared Pathways with Therapeutic Implications.

Citation: Endocrine reviews; Jun 2020; vol. 41 (no. 3)

Author(s): Drucker, Daniel J

Abstract: Individuals with diabetes are at increased risk for bacterial, mycotic, parasitic, and viral infections. The severe acute respiratory syndrome (SARS)-CoV-2 (also referred to as COVID-19) coronavirus pandemic highlights the importance of understanding shared disease pathophysiology potentially informing therapeutic choices in individuals with type 2 diabetes (T2D). Two coronavirus receptor proteins, angiotensin-converting enzyme 2 (ACE2) and dipeptidyl peptidase-4 (DPP4) are also established transducers of metabolic signals and pathways regulating inflammation, renal and cardiovascular physiology, and glucose homeostasis. Moreover, glucose-lowering agents such as the DPP4 inhibitors, widely used in subjects with T2D, are known to modify the biological activities of multiple immunomodulatory substrates. Here, we review the basic and clinical science spanning the intersections of diabetes, coronavirus infections, ACE2, and DPP4 biology, highlighting clinical relevance and evolving areas of uncertainty underlying the pathophysiology and treatment of T2D in the context of coronavirus infection.

Title: Effects of ertugliflozin on renal function over 104 weeks of treatment: a post hoc analysis of two randomised controlled trials.

Citation: Diabetesologia; Jun 2020; vol. 63 (no. 6); p. 1128-1140

Author(s): Cherney, David Z I; Heerspink, Hiddo J L; Frederich, Robert; Maldonado, Mario; Liu, Jie; Pong, Annpay; Xu, Zhi J; Patel, Shrida; Hickman, Anne; Mancuso, James P; Gantz, Ira; Terra, Steven G

Aims/Hypothesis: This study aimed to evaluate the effect of ertugliflozin, a sodium-glucose cotransporter 2 (SGLT2) inhibitor, on eGFR and albuminuria (urine albumin/creatinine ratio [UACR]) vs glimepiride or placebo/glimepiride (non-ertugliflozin) over 104 weeks of treatment in participants with type 2 diabetes mellitus, using pooled data from two randomised controlled, active comparator studies from the eValuation of ERTugliflozin efficacY and Safety (VERTIS) programme (Clinicaltrials.gov NCT01999218 [VERTIS SU] and NCT02033889 [VERTIS MET]). In the VERTIS SU study, ertugliflozin was evaluated vs glimepiride over 104 weeks. In the VERTIS MET study, ertugliflozin was evaluated vs placebo over 26 weeks; eligible participants were switched from placebo to blinded glimepiride from week 26 to week 104. The glycaemic efficacy of ertugliflozin vs non-ertugliflozin was also assessed in the pooled population.METHODSPost hoc, exploratory analysis was used to investigate mean changes from baseline in eGFR and UACR over 104 weeks.

Results: Overall, mean (SD) baseline eGFR was 88.2 (18.8) ml min^-1 (1.73 m^-2) and geometric mean (95% CI) of baseline UACR was 1.31 mg/mmol (1.23, 1.38). At week 6, the changes in eGFR from baseline were -2.3, -2.7 and -0.7 ml min^-1 (1.73 m^-2) for the ertugliflozin 5 mg, ertugliflozin 15 mg and non-ertugliflozin groups, respectively. Mean eGFR in the ertugliflozin groups increased over time thereafter, while it decreased in the non-ertugliflozin group. Week 104 changes in eGFR
from baseline were -0.2, 0.1 and -2.0 ml min-1 (1.73 m) for the ertugliflozin 5 mg, ertugliflozin 15 mg and non-ertugliflozin groups, respectively. Among 415 patients (21.4% of the cohort) with albuminuria at baseline, the ertugliflozin groups had greater reductions in UACR at all measured time points up to week 104. At week 104, the non-ertugliflozin-corrected difference in UACR (95% CI) was -29.5% (-44.8, -9.8; p < 0.01) for ertugliflozin 5 mg and -37.6% (-51.8, -19.2; p < 0.001) for ertugliflozin 15 mg. Least squares mean changes from baseline in HbA1c (mmol/mol [95% CI]) at week 104 were similar between treatment groups: -6.84 (-7.64, -6.03), -7.74 (-8.54, -6.94) and -6.84 (-7.65, -6.03) in the ertugliflozin 5 mg, ertugliflozin 15 mg and non-ertugliflozin groups, respectively. Least squares mean changes from baseline in HbA1c (% [95% CI]) at week 104 were: -0.63 (-0.70, -0.55), -0.71 (-0.78, -0.64) and -0.63 (-0.70, -0.55) in the ertugliflozin 5 mg, ertugliflozin 15 mg and non-ertugliflozin groups, respectively.

Conclusions/Interpretation: Ertugliflozin reduced eGFR at week 6, consistent with the known pharmacodynamic effects of SGLT2 inhibitors on renal function. Over 104 weeks, eGFR values returned to baseline and were higher with ertugliflozin compared with non-ertugliflozin treatment, even though changes in HbA1c did not differ between the groups. Ertugliflozin reduced UACR in patients with baseline albuminuria.

Trial Registration: clinicaltrials.gov NCT01999218 and NCT02033889.


Citation: Diabetic medicine : a journal of the British Diabetic Association; Jun 2020; vol. 37 (no. 6); p. 909-923

Author(s): Olesen, K; Folmann Hempler, N; Drejer, S; Valeur Baumgarten, S; Stenov, V

Aims: To synthesize primary research into the impact of person-centred diabetes self-management education, and support that targets people with type 2 diabetes, on behavioural, psychosocial and cardiometabolic outcomes and to identify effective mechanisms underlying positive outcomes of person-centred diabetes self-management education and support.

Methods: Using Whittemore and Knafl’s integrative review method, we conducted a systematic search of peer-reviewed literature published between January 2008 and June 2019 using PubMed, Scopus and CINAHL. After article selection according to established criteria, study quality was assessed using Critical Appraisal Skills Programme checklists for cohort studies, randomized controlled trials and qualitative research.

Results: From 1901 identified records, 22 (19 quantitative, two qualitative, and one mixed methods) were considered eligible for inclusion. Interventions were categorized by content, medium of delivery, and outcomes. Qualitative studies, quantitative cohort studies and randomized controlled trials demonstrated positive outcomes, with no differences in success rates across study design. Interventions were largely successful in improving HbA1c and patient-reported outcomes such as quality of life but had limited success in lowering cholesterol and weight, or initiating long-term improvements in lifestyle behaviours. Primary objectives were achieved more often than secondary objectives, and studies with fewer outcomes appeared more successful in achieving specific outcomes.

Conclusions: Person-centred diabetes self-management education and support has demonstrated a considerable impact on desired diabetes-related outcomes in people with type 2 diabetes. To advance the field further, new studies should take advantage of systematic and transparent approaches to person-centred diabetes self-management education.

Title: Fixed-dose combination of empagliflozin and linagliptin for the treatment of patients with type 2 diabetes mellitus: A systematic review and meta-analysis.

Citation: Diabetes, obesity & metabolism; Jun 2020; vol. 22 (no. 6); p. 1001-1005

Author(s): Katsiki, Niki; Ofori-Asenso, Richard; Ferrannini, Ele; Mazidi, Mohsen
Abstract: The present meta-analysis evaluated the efficacy and safety of empagliflozin + linagliptin combination compared with either monotherapy [n=6 randomized controlled trials; 2857 adults with type 2 diabetes (T2DM) on diet + exercise ± metformin; 39.7% women; mean age: 54.6-59.9 years]. The combination of empagliflozin 10 mg + linagliptin 5 mg led to significantly greater reductions in glycated haemoglobin (HbA1c) compared with either drug alone over 24 weeks: weighted mean difference [WMD; -0.72%, 95% confidence interval (CI): -1.04, -0.40], and fasting plasma glucose (-1.60 mmol/L 95% CI: -2.21, -1.00). Similar results were observed when empagliflozin 25 mg + linagliptin 5 mg was compared with linagliptin 5 mg monotherapy or with empagliflozin 10 or 25 mg monotherapy. Patients with T2DM treated with the drug combination had more than three times higher likelihood of achieving HbA1c <7% than those on either monotherapy. Weight reduction was significantly greater in the combination group only when compared with linagliptin monotherapy. Safety profile was similar between combination treatment and monotherapies. Overall, the empagliflozin + linagliptin combination had superior efficacy and similar safety in achieving euglycaemia compared with either monotherapy. This combination, administered once daily, has the potential to reduce regimen complexity, enhance adherence and improve outcomes in clinical practice.

Title: Glucagon-like peptide 1 receptor agonists and sodium glucose co-transporter 2 inhibitors as combination therapy for type 2 diabetes. A systematic review and meta-analysis.

Citation: Diabetes, obesity & metabolism; Jun 2020

Author(s): Mantsiou, Chrysanthi; Karagiannis, Thomas; Kakotrichi, Panagiota; Malandris, Konstantinos; Avgirinos, Ioannis; Liakos, Aris; Tsapas, Apostolos; Bekiari, Eleni

Aim: To assess the efficacy and safety of combination therapy with a glucagon-like peptide 1 receptor agonist (GLP-1 RA) and a sodium glucose co-transporter 2 inhibitor (SGLT2i) in patients with type 2 diabetes.

Methods: We searched Medline, Embase, the Cochrane Library, and grey literature sources until December 2, 2019 for randomized controlled trials in adults with type 2 diabetes assessing the combination of GLP-1 RA and SGLT2i, either as co-initiation therapy or as add-on to each other, against placebo or an active comparator. The primary outcome was change in HbA1c. Secondary outcomes included change in body weight, blood pressure, and eGFR, and incidence of severe hypoglycemia, all-cause mortality, cardiovascular mortality, myocardial infarction, stroke and hospitalization for heart failure. We pooled data using random effects meta-analyses.

Results: Seven trials (1913 patients) were eligible. Compared to GLP-1 RA, GLP-1 RA/SGLT2i combination therapy was associated with greater reduction in HbA1c (weighted mean difference -0.61%, 95% CI -1.09 to -0.14%, four studies), body weight (-2.59 kg, -3.68 to -1.51 kg, three studies), and systolic blood pressure (-4.13 mmHg, -7.28 to -0.99 mmHg, four studies). Compared to SGLT2i, GLP-1 RA/SGLT2i combination therapy reduced HbA1c (-0.85%, -1.19 to -0.52%, six studies) and systolic blood pressure (-2.66 mmHg, -5.26 to -0.06 mmHg, six studies), but not body weight (-1.46 kg, -2.94 to 0.03 kg, five studies). After excluding data for one trial that had a considerably longer duration than the remaining studies, body weight was also reduced versus SGLT2i (-1.79 kg, -2.99 to -0.59 kg, five studies). Combination therapy did not increase the incidence of severe hypoglycemia. Data for mortality and cardiovascular outcomes were scarce.

Conclusions: GLP-1 RA/SGLT2i combination therapy seems to reduce HbA1c, body weight and systolic blood pressure without increasing the risk for severe hypoglycemia compared to either GLP-1 RA or SGLT2i. No robust conclusions can be made regarding long-term effectiveness or effect on cardiovascular outcomes. This article is protected by copyright. All rights reserved.

Title: Positioning sulfonylureas in a modern treatment algorithm for patients with type 2 diabetes: expert opinion from a European Consensus Panel.

Citation: Diabetes, obesity & metabolism; Jun 2020

Author(s): Consoli, Agostino; Czupryniak, Leszek; Duarte, Rui; Jermendy, György; Kautzky-Willer, Alexandra; Mathieu, Chantal; Melo, Miguel; Mosenzon, Ofr; Nobels, Frank; Papanas, Nikolaos;
Abstract: The large number of pharmacological agents available to treat type 2 diabetes (T2D) makes choosing the optimal drug for any given patient a complex task. Since newer agents offer several advantages, whether and when sulfonylureas (SUs) should still be used to treat T2D is controversial. Published treatment guidelines and recommendations should govern the general approach to diabetes management. However, expert opinions can aid in better understanding local practices and in formulating individual choices. The present consensus paper aims to provide additional guidance on the use of sulfonylureas in T2D. We summarize current local treatment guidelines in European countries, showing that SUs are still widely proposed as second line treatment after metformin and often ranked at the same level as newer glucose-lowering medications. Strong evidence now shows that SGLT2-i and GLP-1RAs are associated with low hypoglycemia risk, promote weight loss, and exert a positive impact on vascular, cardiac, and renal endpoints. Thus, using SUs in place of SGLT2-i and GLP-1RAs may deprive patients of key advantages and potentially important cardiorenal benefits. In subjects with ascertained cardiovascular disease or at very high cardiovascular risk, SGLT2-i and/or GLP-1RAs should be used as part of diabetes management, in the absence of contraindications. Routine utilization of SUs as second line agents continues to be acceptable in resource-constrained settings. This article is protected by copyright. All rights reserved.

Sources Used:

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