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Type 2 Diabetes Current Awareness Bulletin

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Systematic Review / Meta-Analysis

Title: Association of Type 2 Diabetes With Cancer: A Meta-analysis With Bias Analysis for Unmeasured Confounding in 151 Cohorts Comprising 32 Million People.

Citation: Diabetes Care 2020;43(9):2313-2322.
Author(s): Ling S.

Abstract: [This analysis (151 cohorts; over 32 million people) found evidence for an association between type 2 diabetes and incidence of various types of cancer; bias analysis for unmeasured confounding suggested causal associations for liver, pancreatic and endometrial cancer.]
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Title: Lifestyle Changes Observed among Adults Participating in a Family- and Community-Based Intervention for Diabetes Prevention in Europe: The 1st Year Results of the Feel4Diabetes-Study.

Citation: Nutrients; Jul 2020; vol. 12 (no. 7); p. 1949-1949

Author(s): Manios ; Lambrinou, Christina-Paulina; Mavrogianni, Christina; Cardon, Greet; Lindström, Jaana; Iotova, Violeta; Tankova, Tsvetalina; Rurik, Imre; Van Stappen, Vicky; Kivelä, Jemina; Mateo-Gallego, Rocío; Moreno, Luis A.; Makrilakis, Konstantinos; Androutsos, Odysseas

Abstract: The Feel4Diabetes intervention was a school and community-based intervention aiming to promote healthy lifestyle and tackle obesity and obesity-related metabolic risk factors for the prevention of type 2 diabetes (T2D) among families at risk of developing this disease. The current study aims to present the results on lifestyle behaviors obtained from parents during the first year of the Feel4Diabetes intervention. This multicomponent intervention had a cluster randomized design and was implemented in Belgium, Bulgaria, Finland, Greece, Hungary and Spain over two years (2016–2018). Standardized protocols and procedures were used by the participating centers in all countries to collect data on parents' lifestyle behaviors (diet, physical activity, sedentary behavior). The Feel4Diabetes intervention was registered at clinicaltrials.gov (registration number: NCT02393872). In total, 2110 high-risk parents participated in the baseline and 12-month follow-up examination measurements. Participants allocated to the intervention group reduced their daily consumption of sugary drinks ($p = 0.037$) and sweets ($p = 0.031$) and their daily screen time ($p = 0.032$), compared with the control group. In addition, participants in the intervention group in Greece and Spain increased their consumption of breakfast ($p = 0.034$) and fruits ($p = 0.029$), while in Belgium and Finland they increased their water intake ($p = 0.024$). These findings indicate that the first year of the Feel4Diabetes intervention resulted in the improvement of certain lifestyle behaviors in parents from high-risk families.

Title: Knowledge and Perceptions towards Cardiovascular Disease Prevention among Patients with Type 2 Diabetes Mellitus: A Review of Current Assessments and Recommendations.

Citation: Current diabetes reviews; Sep 2020

Author(s): Elnaem, Mohamed Hassan; Elrggal, Mahmoud E; Syed, Nabeel; Naqvi, Atta Abbas; Hadi, Muhammad Abdul

Introduction: Patients with type 2 diabetes mellitus (T2DM) are at significantly higher risk of developing cardiovascular disease (CVD). There is scarcity of literature reviews that describes and summarises T2DM patients' knowledge and perception about CVD prevention.

Objectives: To describe and summarise the assessment of knowledge and perceptions about CVD risk and preventive approaches among patients with T2DM.

Methods: A scoping review methodology was adopted, and three scientific databases, Google Scholar, Science Direct and PubMed were searched using predefined search terms. A multistage

screening process that considered relevancy, publication year (2009-2019), English language, and article type (original research) was followed. We formulated research questions focused on the assessment of levels of knowledge and perceptions of the illness relevant to CVD prevention and the identification of associated patients' characteristics.

Results: A total of 16 studies were included. Patients were not confident to identify CVD risk and other clinical consequences that may occur in the prognostic pathway of T2DM. Furthermore, patients were less likely to identify all CV risk factors indicating a lack of understanding of the multi-factorial contribution of CVD risk. Patients' beliefs about medications were correlated with their level of adherence to medications for CVD prevention. Many knowledge gaps were identified, including the basic disease expectations at the time of diagnosis, identification of individuals' CVD risk factors and management aspects. Knowledge and perceptions were affected by patients' demographic characteristics, e.g., educational level, race, age, and area of residence.

Conclusion: There are knowledge gaps concerning the understanding of CVD risk among patients with T2DM. The findings necessitate educational initiatives to boost CVD prevention among patients with T2DM. Furthermore, these should be individualised based on patients' characteristics and knowledge gaps, disease duration and estimated CVD risk.

Title: The development and testing of a nurse-led smartphone-based self-management programme for diabetes patients with poor glycaemic control.

Citation: Journal of advanced nursing; Sep 2020

Author(s): Wang, Wenru; Cheng, Michelle Tze Min; Leong, Foon Leng; Goh, Antoinette Wei Ling; Lim, Suan Tee; Jiang, Ying

Aims: To describe a systematic process for the development of a nurse-led smartphone-based self-management programme for type 2 diabetes patients with poor glycaemic control in Singapore.

Methods: A three-step process involving the application of a theoretical framework, evidence from literature, content validity, and pilot tests were conducted for the content and technical development of the programme. Content experts and lay patients evaluated the appropriateness, relevance, and comprehensibility of the newly developed Care4Diabetes application. A pilot randomized controlled trial was conducted with 40 patients recruited in Singapore. Twenty patients each were randomly allocated to the control and intervention groups. The study outcomes were collected at baseline and at 3 months thereafter.

Results: The nurse-led smartphone-based self-management programme was developed with integration of the Care4Diabetes application and the web-portal system. The pilot results indicated that the effects of this smartphone-based programme on patient's health-related outcomes were comparable with those of the currently available nurse-led diabetes service.

Conclusion: The smartphone-based self-management intervention was deemed effective, yet full-scale randomized controlled trials are still ongoing and the results of these may provide strong evidence of the effectiveness of such an approach in improving patient care.IMPACTThe uniqueness of this study lies in the integrated system used, which offers a clinical platform for diabetes nurses to provide personalized coaching and care to patients remotely, while monitoring patients' progress closely. By adopting such an approach, it would free up more time for nurses to cater to patients who are more critically in need of their direct attention.

Title: Effect of nutrition on postprandial glucose control in hospitalized patients with type 2 diabetes receiving fully automated closed-loop insulin therapy.

Citation: Diabetes, obesity & metabolism; Sep 2020

Author(s): Banholzer, Nicolas; Herzig, David; Piazza, Camillo; Alvarez Martinez, Mario; Nakas, Christos T; Kosinski, Christophe; Feuerriegel, Stefan; Hovorka, Roman; Bally, Lia

Abstract: Fully automated closed-loop insulin delivery may offer a novel way to manage diabetes in hospital. However, postprandial glycaemic control remains challenging. We aimed to assess the effect of nutritional intake on postprandial glucose control in hospitalized patients with type 2 diabetes receiving fully closed-loop insulin therapy. The effects of different meal types and macronutrient composition on sensor glucose time in target (TIT, 3.9-10.0 mmol/L) and mean sensor glucose (MGL) were assessed with hierarchical linear models using a Bayesian estimation approach. TIT was lower, and MGL slightly higher, after breakfast compared to lunch and dinner whilst insulin dose was higher. Across meals, when carbohydrates were replaced by fat, or to a lesser extent by protein, postprandial glucose control improved. For breakfast, a 3.9% improvement in TIT was observed when 10% of the energy from carbohydrates was replaced by fat. Improvements were slightly lower during lunch and dinner (3.2 and 3.4%) or when carbohydrates were replaced by protein (2.2-2.7%). We suggest that reducing carbohydrate at the expense of fat or protein, could further improve glucose control during fully closed-loop insulin therapy in hospital.

Title: Patients With Type 2 Diabetes Have an Increased Demand for Pacemaker Treatment: A Comparison With Age- and Sex-Matched Control Subjects From the General Population.

Citation: Diabetes care; Sep 2020

Author(s): Rautio, Elina; Gadler, Fredrik; Gudbjörnsdottir, Soffia; Franzén, Stefan; Rydén, Lars; Svensson, Ann-Marie; Mellbin, Linda G

Objective: Patients with type 2 diabetes have an increased risk for cardiovascular disease, including arrhythmias. The prevalence of bradyarrhythmia and the subsequent need for treatment with pacemakers (PMs) is less well explored in a contemporary patient population. The current study explores 1) whether patients with type 2 diabetes have an increased demand for PM implantation compared with an age- and sex-matched control population without diabetes and 2) patient characteristics associated with an increased demand for receiving a PM.RESEARCH DESIGN AND

Methods: In this population-matched registry study, a total of 416,247 patients with type 2 diabetes from the Swedish National Diabetes Registry and 2,081,235 age- and sex-matched control subjects selected from the general population were included between 1 January 1998 and 31 December 2012 and followed until 31 December 2013. Mean follow-up time was 7 years. Cox proportional hazard regression analyses were performed to estimate the demand of PM treatment and the factors identifying patients with such demand.

Results: Type 2 diabetes was associated with an increased need of PM treatment (hazard ratio 1.65 [95% CI 1.60-1.69]; P < 0.0001), which remained (1.56 [1.51-1.60]; P < 0.0001) after adjustments for age, sex, educational level, marital status, country of birth, and coronary heart disease. Risk factors for receiving a PM included increasing age, HbA1c, BMI, diabetes duration, and lipid- and blood pressure-lowering medication.

Conclusions: The need for PM treatment is higher in patients with type 2 diabetes than in matched population-based control subjects. Age, diabetes duration, and HbA1c seem to be risk factors for PM treatment.

Title: Flash Glucose Monitoring Improves Glucose Control in People with Type 2 Diabetes Mellitus Receiving Anti-diabetic Drug Medication.

Citation: Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association; Aug 2020

Author(s): Chen, Maoyuan; Li, Huiqin; Shen, Yun; Liu, Bingli; Yan, Renna; Sun, Xiaojuan; Ye, Lei; Lee, Kok-Onn; Ma, Jianhua; Su, Xiaofei

Objective: To investigate the effects of Flash Glucose Monitoring (FGM) on glucose profile in people with Type 2 Diabetes Mellitus (T2DM) receiving anti-diabetic drug medication.

Methods: This is a prospective non-randomized uncontrolled study. 111 people with T2DM were enrolled and received FGM for 14 days. There was no change of anti-diabetic medication during the

14 days. The plasma glucose concentration on day 2 was used as baseline and the day 13 was considered as study end point. The parameters to compare were mean plasma glucose (MPG), glucose variations, and incidence of hypoglycemia during the FGM period. The multivariate linear stepwise regression analysis was applied to determine the independent factors that affect MPG difference.

Results: This study analyzed the data of a total of 111 people with T2DM (male 60 and female 51). The general clinical data of these patients were as follows: age: 65.0±6.7 years old; duration of diabetes: 11.6±6.8 years; HbA1c: 61.2±13.3 mmol/mol; body mass index (BMI): 25.2±3.2 kg/m². Using FGM, people with T2DM were able to change daily diet and exercise through which significant reductions in MPG on days 12 or 13 were achieved as compared with that of day 2 (P=0.04 or P=0.003, respectively). The glucose variations, such as standard deviation (SD) of plasma glucose, coefficient of variation (CV), and mean amplitude of glycemic excursion (MAGE), progressively declined starting from day 6 as compared with baseline (P=0.016, P=0.003, or P=0.012, respectively). The incremental area over the curve (AOC) of the hypoglycemia (66.1 mmol/mol).

Title: Association and relative importance of multiple risk factor control on cardiovascular disease, end-stage renal disease and mortality in people with type 2 diabetes: A population-based retrospective cohort study.

Citation: Primary care diabetes; Aug 2020

Author(s): Usman, Muhammad; Khunti, Kamlesh; Davies, Melanie J; Gillies, Clare L

Aims: To evaluate the risk of cardiovascular disease (CVD), end-stage renal disease (ESRD), and mortality, when implementing a multifactorial optimal control approach in primary care in the United Kingdom (UK), in individuals with newly diagnosed type 2 diabetes.

Materials and Methods: A retrospective cohort of 53 942 patients were stratified into 1 of the 8 groups according to whether glycated haemoglobin (HbA1c), blood pressure (BP) and total cholesterol (TC) target values were achieved or not from baseline to the date of last follow-up. Those with single or combinations of risk factor control targets achieved, were compared to those who achieved no targets in any of the risk factor. Hazard ratios from the Cox proportional hazards models were estimated against patients who achieved no targets.

Results: Of 53 942 patients with newly diagnosed type 2 diabetes, 28%, 55%, and 68% were at target levels for HbA1c <48mmol/mol (<6.5%), BP<140/85mm Hg, and TC<5mmol/L respectively, 36%, 40%, and 12% were at target levels for any one, two, or all three risk factors respectively. Being at HbA1c, BP, and TC targets was associated with an overall 47%, 25%, 42%, 55% and 42% reduction in the risk of ischemic heart disease, cerebrovascular disease, ESRD, cardiovascular-mortality, and all-cause-mortality respectively. Among all subgroups, the risk reduction of study outcome events was greater in the subgroups of patients with microalbuminuria, males, smokers, and patients with BMI≥30kg/m2.

Conclusions: Optimal levels of HbA1c, BP, and TC occurring together in patients with newly diagnosed type 2 diabetes are uncommon. Achieving multiple risk factor control targets could substantially reduce the risk of CVD, ESRD and mortality.

Title: Vitamin D supplementation for prevention of type 2 diabetes mellitus. To D or not to D?

Citation: The Journal of clinical endocrinology and metabolism; Aug 2020

Author(s): Pittas, Anastassios G; Jorde, Rolf; Kawahara, Tetsuya; Dawson-Hughes, Bess

Context: Over the last decade, vitamin D has emerged as a risk determinant for type 2 diabetes and vitamin D supplementation has been hypothesized as a potential intervention to lower diabetes risk. Recently, several trials have reported on the effect of vitamin D supplementation on diabetes prevention in people with prediabetes.

Evidence Acquisition: A comprehensive literature review was performed using PubMed, Embase, and ClinicalTrials.gov to identify: 1) recent meta-analyses of longitudinal observational studies that report on the association between blood 25(OH)D level and incident diabetes and 2) clinical trials of adults with prediabetes that have reported on the effect of vitamin D supplementation on incident diabetes.

Evidence Synthesis: Longitudinal observational studies report highly consistent associations between higher blood 25(OH)D levels and lower risk of incident diabetes in diverse populations, including populations with prediabetes. Trials in persons with prediabetes show risk reduction in new-onset diabetes with vitamin D supplementation. In the three large trials that were specifically designed and conducted for prevention of diabetes, vitamin D supplementation when compared with placebo, reduced risk of diabetes by 10 to 13% in persons with prediabetes not selected for vitamin D deficiency.

Conclusions: Results from recent trials are congruent with a large body of evidence from observational studies indicating that vitamin D has a role in modulating diabetes risk. Participant-level meta-analysis of the three largest trials should provide a more refined estimate of risk reduction and identify patient populations likely to benefit the most.

Title: SGLT2 inhibitors for prevention of cardiorenal events in people with type 2 diabetes without cardiorenal disease: A meta-analysis of large randomized trials and cohort studies.

Citation: Pharmacological research; Aug 2020; vol. 161 ; p. 105175

Author(s): Qiu, Mei; Ding, Liang-Liang; Zhang, Miao; Lin, Jin-Hao; Gu, Jin-Song; Zhou, Xian; Tang, Ying-Xi; Wei, Xu-Bin; Liu, Shu-Yan

Abstract: To investigate whether sodium glucose cotransporter 2 inhibitors (SGLT2is) can reduce important cardiorenal endpoints in type 2 diabetic adults without established cardiovascular disease (ECD), in those without heart failure (HF), and in those without chronic kidney disease (CKD). We searched PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL) and clinicaltrials.gov. Event-driven randomized controlled trials (RCTs) and cohort studies were included. We conducted random-effects meta-analysis, respectively based on RCTs and cohort studies, on eight cardiorenal endpoints in three type 2 diabetic subgroups. Thirteen large studies were included. Meta-analysis of RCTs showed the high quality evidences: compared with placebo, SGLT2is significantly reduced the risk of major adverse cardiovascular events, cardiovascular death or hospitalization for HF, and progression of CKD in type 2 diabetic adults without ECD [HRs (95 % CIs): 0.88 (0.82, 0.94), 0.76 (0.70, 0.82), and 0.59 (0.52, 0.66), respectively; risk differences (95 % CIs): -1.6 (-2.4, -0.8), -2.6 (-3.3, -2.0), and -2.4 (-2.8, -2.0) per 1000 patient-years, respectively], in those without HF [HRs (95 % CIs): 0.89 (0.82, 0.95), 0.74 (0.67, 0.81), and 0.61 (0.55, 0.67), respectively; risk differences (95 % CIs): -1.7 (-2.9, -0.8), -5.8 (-7.3, -4.2), and -2.3 (-2.6, -1.9) per 1000 patient-years, respectively], and in those without CKD [HRs (95 % CIs): 0.88 (0.82, 0.94), 0.77 (0.71, 0.83), and 0.63 (0.57, 0.70), respectively; risk differences (95 % CIs): -2.4 (-3.6, -1.2), -6.1 (-7.6, -4.5), and -2.2 (-2.6, -1.8) per 1000 patient-years, respectively]. Meta-analysis of cohort studies also showed the benefits of SGLT2is on the three composite outcomes in the three diabetic subgroups. SGLT2is also significantly reduced some other cardiorenal endpoints in these diabetic subgroups. SGLT2is can significantly reduce important cardiorenal events in type 2 diabetic adults without ECD, in those without HF, and in those without CKD; which supports SGLT2is used in these diabetic subpopulations to prevent cardiorenal events.

Title: Global Patterns of Comprehensive Cardiovascular Risk Factor Control in Patients with Type 2 Diabetes Mellitus: Insights from the DISCOVER Study.

Citation: Diabetes, obesity & metabolism; Aug 2020

Author(s): Patel, Krishna K; Gomes, Marilia B; Charbonnel, Bernard; Chen, Hungta; Cid-Ruzafa, Javier; Fenici, Peter; Hammar, Niklas; Ji, Linong; Kennedy, Kevin F; Khunti, Kamlesh; Kosiborod, Mikhail; Pocock, Stuart; Shestakova, Marina; Shimomura, Iichiro; Surmont, Filip; Watada, Hirotaka; Arnold, Suzanne V

Aims: Optimal control of cardiovascular risk factors reduces the risk of micro- and macrovascular complications in patients with type 2 diabetes mellitus (T2D). Our aim was to investigate global patterns of cardiovascular risk factor control in patients with T2D.

Methods: DISCOVER is an international, observational cohort study of patients with T2D beginning second-line glucose-lowering therapy. Risk factor management was examined among eligible patients (i.e those with the risk factor) at study baseline. Inter-country variability was estimated using median odds ratios (MOR).

Results: Among 14,343 patients with T2D from 34 countries, the mean age was 57.4±12.0 years and the median duration of T2D was 4.2 (interquartile range 2.0-8.0) years; 11.8% had documented atherosclerotic cardiovascular disease (ASCVD). Among eligible patients, blood pressure was controlled in 67.5% (9284/13,756); statins were prescribed in 43.7% (5775/13,208); angiotensin-converting enzyme inhibitor/angiotensin II receptor blockers were prescribed in 55.6% (5292/9512); aspirin was prescribed in 53.3% of those with established ASCVD (876/1645); and 84.4% (12,102/14,343) were nonsmoking. Only 21.5% (3088/14,343) of patients had optimal risk factor management (defined as control of all eligible measures), with wide intercountry variability (10-44%), even after adjusting for patient and site differences (median odds ratio 1.47; 95% confidence interval: 1.24-1.66).

Conclusion: Globally, comprehensive control of ASCVD risk factors is not being achieved in most patients, with wide variability among countries unaccounted for by patient and site differences. Better country specific strategies are needed to implement comprehensive cardiovascular risk factor control consistently in patients with T2D to improve long-term outcomes.

Title: PERsistent Sitagliptin treatment & Outcomes (PERS&O 2.0) study, long-term results: a real-world observation on DPP4-inhibitor effectiveness.

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

Author(s): Bossi, Antonio Carlo; De Mori, Valentina; Galeone, Carlotta; Bertola, Davide Pietro; Gaiti, Margherita; Balini, Annalisa; Berzi, Denise; Forloni, Franco; Meregalli, Giancarla; Turati, Federica

Introduction: Sitagliptin is a dipeptidyl peptidase 4 inhibitor for the treatment of type 2 diabetes (T2D). Limited real-world data on its effectiveness and safety are available from an Italian population.

Research Design And Methods: We evaluated long-term clinical data from the single-arm PERsistent Sitagliptin Treatment & Outcomes (PERS&O) study, which collected information on 440 patients with TD2 (275 men, 165 women; mean age 64.1 years; disease median duration: 12 years) treated with sitagliptin 'add-on'. For each patient, we estimated the 10-year cardiovascular (CV) risk using the UK Prospective Diabetes Study (UKPDS) Risk Engine (RE). Drug survival was evaluated using Kaplan-Meier survival curves; repeated measures mixed effects models were used to evaluate the evolution of glycated hemoglobin (HbA1c) and CV risk during sitagliptin treatment.

Results: At baseline, most patients were overweight or obese (median body mass index (BMI) (kg/m2) 30.2); median HbA1c was 8.4%; median fasting plasma glucose: 172 mg/dL; median UKPDS RE score: 24.8%, being higher in men (median 30.2%) than in women (median 17.0%) as expected. Median follow-up from starting sitagliptin treatment was 5.6 years. From Kaplan-Meier curves, the estimated median drug survival was 32.8 months when considering discontinuation for any cause and 58.4 months when considering discontinuation for loss of efficacy. A significant improvement in HbA1c was evident during treatment with sitagliptin ($p<0.01$): the reduction was rapid (median HbA1c after 4-6 months: 7.5%) and continued at longer follow-up. When comparing patients treated with sitagliptin versus those stopping sitagliptin and switching to another antihyperglycemic drug, we detected a significant difference in the evolution of HbA1c in favor of patients who continued sitagliptin treatment. The UKPDS RE score at 10 years and the BMI significantly improved during treatment with sitagliptin ($p<0.001$). Adverse events were relatively uncommon.

Conclusion: Patients with T2D treated with sitagliptin achieved an improvement in metabolic control and a reduction in CV risk and did not experience relevant adverse events.

Title: Circulating adhesion molecules and associations with HbA1c, hypertension, nephropathy, and retinopathy in the Treatment Options for type 2 Diabetes in Adolescent and Youth study.

Citation: Pediatric Diabetes; Sep 2020; vol. 21 (no. 6); p. 923-931

Author(s): Tryggestad ; Shah, Rachana D.; Braffett, Barbara H.; Bacha, Fida; Gidding, Samuel S.; Gubitosi-Klug, Rose A.; Shah, Amy S.; Urbina, Elaine M.; Levitt Katz, Lorraine E.

Background: The Treatment Options for type 2 Diabetes in Adolescent and Youth study, a randomized clinical trial of three treatments for type 2 diabetes (T2DM) in youth, demonstrated treatment failure (defined as sustained HbA1c ≥8%, or inability to wean insulin after 3 months after acute metabolic decomposition) in over half of the participants. Given that binding of mononuclear cells to vascular endothelium, initiated by cellular adhesion molecules and chemokines, is an early step in vascular injury, we sought to evaluate (a) changes in cellular adhesion molecule levels during the trial; (b) effect of diabetes treatment; and (c) association of markers with HbA1c, hypertension, hypercholesterolemia, nephropathy, and retinopathy.

Methods: Participants (n = 515 of 699) that had baseline assessment of adhesion molecules (monocyte chemoattractant protein-1 [MCP-1], vascular cell adhesion marker [VCAM], intercellular adhesion marker [ICAM], and E-Selectin) and at least one other assessment, measured at month 12, 24, or 36, were included.

Results: Over 1 to 3 years, significant increases in MCP-1 and decreases in VCAM (both P <.0001) concentrations were found; however, no significant interactions were identified with treatment group for any molecule. For every 1% increase in HbA1c, ICAM increased by 1.8%, VCAM by 1.5%, and E-selectin by 6.8% (all P <.0001). E-selectin increased by 3.7% and 4.2% for every 10 mm Hg increase in systolic and diastolic blood pressure, respectively (both P <.0001). ICAM was 10.2% higher and E-selectin was 15.5% higher in participants with microalbuminuria (both P <.01). There was no significant association of adhesion molecule levels with retinopathy.

Conclusion: Concentrations of cellular adhesion molecules rise with increasing HbA1c in youth with T2DM, and are associated with blood pressure and microalbuminuria, markers of vascular injury.

Title: Challenges and Strategies for Diabetes Management in Community-Living Older Adults.

Citation: Diabetes Spectrum; Aug 2020; vol. 33 (no. 3); p. 217-227

Author(s): Sinclair ; Abdelhafiz, Ahmed H.

Abstract: The prevalence of diabetes is increasing, especially in older people, mainly because of an increase in life expectancy. The number of comorbidities also increases with increasing age, leading to a unique diabetes phenotype in old age that includes vascular disease, physical and neuropathic complications, and mental dysfunction. These three categories of complications appear to have a synergistic effect that can lead to a vicious cycle of deterioration into disability. Early assessment and appropriate, timely interventions may delay adverse outcomes. However, this complex phenotype constitutes a great challenge for health care professionals. This article reviews the complex diabetes phenotype in old age and explores management strategies that are predominantly based on the overall functional status of patients within this heterogeneous age-group.

Title: Dipeptidyl peptidase 4 inhibitors in the treatment of type 2 diabetes mellitus.

Citation: Nature reviews. Endocrinology; Sep 2020

Author(s): Deacon, Carolyn F

Abstract: Dipeptidyl peptidase 4 inhibitors (DPP4i) have been available for treating type 2 diabetes mellitus since 2006. Although they are a diverse group, DPP4i are all small, orally available molecules

that interact with the catalytic site of DPP4 without disturbing any of its other known functions, including its effects on the immune system. DPP4i have no intrinsic glucose-lowering activity, so their efficacy as anti-diabetic agents is related directly to their ability to inhibit DPP4 activity and is mediated through the effects of the substrates they protect. Of these, the incretin hormone, glucagon-like peptide 1, is probably the most important. As the effects of glucagon-like peptide 1 are glucose-dependent, the risk of hypoglycaemia with DPP4i is low. Class effects, which are directly related to the mechanism of action, are common to all DPP4i; these include their overall good safety profile and tolerability, as well as their efficacy in improving glycaemic control, but also, potentially, a small increased risk of acute pancreatitis. Compound-specific effects are those related to their differing chemistries and/or pharmacokinetic profiles. These compound-specific effects could affect the way in which individual DPP4i are used therapeutically and potentially explain off-target adverse effects, such as hospitalization for heart failure, which is seen only with one DPP4i. Overall, DPP4i have a favourable therapeutic profile and are safe and effective in the majority of patients with type 2 diabetes mellitus.

Title: Efficacy of mesenchymal stem cells therapy on glucose levels in type 2 diabetes mellitus: A systematic review and meta-Analysis.

Citation: Journal of diabetes investigation; Sep 2020

Author(s): Ranjbaran, Hossein; Mohammadi-Joubani, Bahareh; Amirfakhrian, Elham; Alizadeh-Navaei, Reza

Aims/Introduction: In recent years, mesenchymal cellular therapies have received much attention in treatment of diabetes. In this meta-analysis we aimed to evaluate the efficacy of mesenchymal stem cell therapy in type 2 diabetes mellitus.

Materials and Methods: A comprehensive literature search was performed using PubMed, Scopus, Web of Science, and Central databases. A total of 1721 articles were identified from which nine full-text clinical trials were qualified to enter the current meta-analysis. The assessment groups included patients with type 2 diabetes, and levels of C-peptide, HbA1c, and insulin dose were analyzed before and after mesenchymal stem cell infusion. Data analysis was done in STATA V11. and the Jaded Score Scale was applied for quality assessment.RESULTSChanges on levels of C-peptide after mesenchymal stem cell therapy were: SMD=0.20, 95% CI= -0.61 to 1.00, on HbA1c levels: SMD= -1.45, 95%CI= -2.10 to -0.79, and on insulin dose were: SMD= -1.40, 95% CI= -2.88 to 0.09.

Conclusions: This meta-analysis of prospective studies showed associations between mesenchymal stem cell therapy and control of glucose level in patients with type 2 diabetes.

Title: Current Concepts in the Management of Diabetic Polyneuropathy.

Citation: Journal of diabetes investigation; Sep 2020

Author(s): Ziegler, Dan; Papanas, Nikolaos; Schnell, Oliver; Bich, Dao Thi Nguyen; Nguyen, Khue Thy; Kulkantrakorn, Kongkiat; Deerochanawong, Chaicharn

Abstract: Diabetic sensorimotor polyneuropathy (DSPN) is encountered in around one third of people with diabetes. This, in turn, may markedly impoverish their quality of life, mainly owing to neuropathic pain and foot ulcerations. Painful DSPN may be as frequent as 25% in diabetes. Symptoms due to DSPN typically comprise pain, paresthesias, and numbness in the distal lower limbs. Asymptomatic DSPN may reach 50% among subjects with this condition. Unfortunately, DSPN is still not adequately diagnosed and treated. Its management has three priorities: 1) lifestyle improvement, near-normoglycemia and multifactorial cardiovascular risk intervention, 2) pathogenesis-oriented pharmacotherapy, and 3) symptomatic alleviation of pain. Intensive diabetes therapy showed evidence for favorable effects on the incidence and deterioration of DSPN in type 1 but not type 2 diabetes. Among pathogenesis-oriented treatments, α-lipoic acid, actovegin, benfotiamine, and epalrestat are currently authorized to treat DSPN in several countries. Symptomatic therapy uses analgesics, notably antidepressants, opioids, and anticonvulsants, reducing pain by ≥50% in

approximately 50% of subjects, but may be limited particularly by CNS related adverse events. Local treatment with the capsaicin 8% patch may offer an alternative. In addition to pain relief, therapy should improve sleep, mobility, as well as quality of life. In conclusion, multimodal treatment of DSPN should consider the individual risk profile, pathogenetic treatment, and pain management using pharmacotherapy (combinations, if needed) as well as non-pharmacological options.

Title: Ketogenic diets as treatment of obesity and type 2 diabetes mellitus.

Citation: Reviews in endocrine & metabolic disorders; Sep 2020; vol. 21 (no. 3); p. 381-397

Author(s): Casanueva, Felipe F; Castellana, Marco; Bellido, Diego; Trimboli, Pierpaolo; Castro, Ana I; Sajoux, Ignacio; Rodriguez-Carnero, Gemma; Gomez-Arbelaez, Diego; Crujeiras, Ana B; Martinez-Olmos, Miguel A

Abstract: During the last decades, several interventions for the management of overweight and obesity have been proposed. Among diets, the first studies focused on the effect of water only and total fasting diets with or without proteins. Unfortunately, they were found to be associated with adverse events which lead to the abandon of these strategies. Interestingly, despite the radical approach, total fasting was effective and generally well tolerated. A strict connection between protein-calorie malnutrition and increased in morbidity and mortality in hospitalized patients was found at that time. Then, the seminal works of Blackburn and his collaborators lead to the introduction of the protein-sparing modified fast. Encouraged by the early results using this intervention, diets evolved to the current very-low-calorie ketogenic diets (VLCKD). In the present review, results of studies on the VLCKDs are presented and discussed, with a particular reference to the protocolled VLCKD. Also, a recent proposal on the nomenclature on the ketogenic diets is reported. Available evidence suggests VLCKDs to be effective in achieving a rapid and significant weight loss by means of an easily reversible intervention which could be repeated, if needed. Muscle mass and strength are preserved, resting metabolic rate is not impaired, hunger, appetite and mood are not worsened. Symptoms and abnormal laboratory findings can be there, but they have generally been reported as of mild intensity and transient. Preliminary studies suggest VLCKDs to be a potential game-changer in the management of type 2 diabetes too. Therefore, VLCKDs should be considered as an excellent initial step in properly selected and motivated patients with obesity or type 2 diabetes, to be delivered as a part of a multicomponent strategy and under strict medical supervision.

Title: Oral antidiabetes agents for the management of inpatient hyperglycaemia: so far, yet so close.

Citation: Diabetic medicine : a journal of the British Diabetic Association; Sep 2020; vol. 37 (no. 9); p. 1418-1426

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Background: Hyperglycaemia is an ongoing challenge in hospital settings and is associated with poor outcomes. Current recommendations for the management of inpatient hyperglycaemia suggest insulin as the main glucose-lowering treatment choice and limit the administration of oral antidiabetes agents to a small proportion of cases because of safety concerns.

Aim: To present and critically appraise the available evidence on the use of oral antidiabetes agents in the hospital setting and the risk-benefit balance of such an approach in the era of cardiovascular outcomes trials.

Methods: PubMed, Embase and Google Scholar databases were searched to identify relevant published work. Available evidence on the efficacy and the safety profile of oral agents in the context of their use in hospitalized individuals are summarized and discussed in this narrative review.

Results: There is no robust evidence to suggest the use of metformin, thiazolidinediones, sulfonylureas and sodium-glucose co-transporter-2 inhibitors in the hospital setting, although some of their effects on acute outcomes deserve further evaluation in future studies. However, the use of dipeptidyl peptidase-4 inhibitors in inpatients with type 2 diabetes is supported by a few, well-

designed, randomized controlled trials. These trials have demonstrated good safety and tolerability profiles, comparable to insulin glucose-lowering efficacy, and a reduction in insulin dose when dipeptidyl peptidase-4 inhibitors are co-administered with insulin, in individuals with mild to moderate hyperglycaemia and a stable clinical condition.

Conclusion: The administration of dipeptidyl peptidase-4 inhibitors to specific groups of inpatients might be a safe and effective alternative to insulin.

Title: Long-Term Cost-Effectiveness Analyses of Empagliflozin Versus Oral Semaglutide, in Addition to Metformin, for the Treatment of Type 2 Diabetes in the UK.

Citation: Diabetes therapy : research, treatment and education of diabetes and related disorders; Sep 2020; vol. 11 (no. 9); p. 2041-2055

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Introduction: International guidelines recommend treatment with a sodium-glucose cotransporter-2 (SGLT-2) inhibitor or glucagon-like peptide-1 (GLP-1) receptor agonist for treatment intensification in type 2 diabetes mellitus (T2DM) patients with progression on metformin. In the randomised, controlled, Peptide Innovation for Early Diabetes Treatment (PIONEER) 2 trial, the SGLT-2 inhibitor empagliflozin was compared with the GLP-1 receptor agonist oral semaglutide, in addition to metformin. The aim of the current study was to assess the long-term cost-effectiveness of empagliflozin 25 mg versus oral semaglutide 14 mg, in addition to metformin, for T2DM patients in the UK.

Methods: Analyses were conducted from the UK healthcare payer perspective, using the IQVIA Core Diabetes model, with a time horizon of 50 years. Patients received either empagliflozin or oral semaglutide, in addition to metformin, until Hba1c threshold of 7.5% (58 mmol/mol) was exceeded, following which treatment intensification with insulin glargine in addition to empagliflozin or oral semaglutide plus metformin was assumed. Baseline cohort characteristics and 52-week treatment effects were derived from the PIONEER 2 trial. Treatment effects of empagliflozin and GLP-1 receptor agonists on hospitalisation for heart failure (hHF) were based on the Empagliflozin Comparative Effectiveness and Safety (EMPRISE) real-world study. Utilities, treatment costs and costs of diabetes-related complications were obtained from published sources.

Results: Direct costs for empagliflozin plus metformin were considerably lower than those for oral semaglutide plus metformin (by more than GBP 6000). Compared with oral semaglutide plus metformin, empagliflozin plus metformin was a cost-effective treatment for T2DM patients in all scenarios tested. Probabilistic sensitivity analysis showed cost-effectiveness in > 95% of the iterations using a threshold of 20,000 GBP/QALY.

Conclusion: Empagliflozin 25 mg is a cost-effective treatment option versus oral semaglutide 14 mg, when used in addition to metformin, for the treatment of T2DM patients in the UK.

Title: Glucagon-like peptide-1 receptor agonists or sodium-glucose cotransporter-2 inhibitors as add-on therapy for patients with type 2 diabetes? A systematic review and meta-analysis of surrogate metabolic endpoints.

Citation: Diabetes & metabolism; Sep 2020; vol. 46 (no. 4); p. 272-279

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OBJECTIVE As sodium-glucose cotransporter-2 inhibitors (SGLT-2is) and glucagon-like peptide-1 receptor agonists (GLP-1RAs) are second-line treatment options in type 2 diabetes mellitus (T2DM), our study sought to provide precise effect estimates regarding the role of GLP-1RAs vs SGLT-2is as add-on treatments in patients uncontrolled by metformin monotherapy.

RESEARCH DESIGN AND METHODS: PubMed, the Cochrane Central Register of Controlled Trials (CENTRAL) and 'grey literature' were searched from their inception up to December 2019 for randomized controlled trials (RCTs) with durations≥12weeks to evaluate the safety and efficacy of adding a GLP-1RA vs an SGLT-2i in patients with T2DM.

Results: Three eligible RCTs were identified. Administration of GLP-1RAs vs SGLT-2is resulted in significant decreases in HbA1c with no significant impact on either body weight or fasting plasma glucose. GLP-1RA treatment led to a significant increase in odds for achieving an HbA1c5%. Significantly greater risk for any hypoglycaemia, nausea and diarrhoea, and lower risk for genital infections, was also observed with GLP-1RAs, while no differences regarding severe hypoglycaemia, treatment discontinuation and impact on blood pressure levels were identified. No other major safety issues arose.

Conclusion: Our meta-analysis suggests that GLP-1RAs provide better glycaemic effects than SGLT-2is in patients with T2DM uncontrolled by metformin, albeit while increasing risk for hypoglycaemia and gastrointestinal adverse events.

Title: DPP4 Inhibitors in the Management of Hospitalized Patients With Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomized Clinical Trials.

Citation: Advances in therapy; Sep 2020; vol. 37 (no. 9); p. 3660-3675

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Introduction: We studied the effects of dipeptidyl peptidase 4 (DPP4) inhibitors on glycemic control in non-critically ill patients admitted to hospital.

Methods: We searched MEDLINE and EMBASE for published studies in English up to July 2019. We included randomized clinical trials (RCTs) that compared DPP4 inhibitors plus insulin supplementation versus basal-bolus insulin regimen in the management of hyperglycemia non-critically ill patients with type 2 diabetes admitted to hospital. Mean difference (MD), relative risk (RR), and 95% confidence intervals (CI) were generated to interpret the data.

Results: Of 401 papers, four RCTs including 648 participants met inclusion criteria. There was no significant difference in mean daily blood glucose level between the two groups (MD 4.63; 95% CI = - 1.57, 10.83; p = 0.14) (I2 = 14%, p = 0.32). Total insulin dose per day was lower in patients receiving DPP4 inhibitors (MD - 14.27; CI = - 22.47, - 6.07; p = 0.001) (I2 = 92%, p = 0.001). Also, the number of insulin injection was significantly lower in patients receiving DPP4 inhibitors (MD - 0.79; CI = - 1.01, - 0.57; p = 0.001) (I2 = 0%, p = 0.68). The rate of hypoglycemia was not significantly different between the two groups (RR 0.60, CI = 0.34, 1.074; p = 0.08) (I2 = 37.3%, p = 0.18). Treatment failure was not significantly different between the two groups (RR 0.87, CI = 0.64, 4.8; p = 0.38) (I2 = 49%, p = 0.11).

Conclusion: The results indicate that using DPP4 inhibitors plus basal or supplemental insulin in hospitalized patients is non-inferior to a standard basal-bolus insulin regimen and leads to a lower amount of insulin use and a lower rate of insulin injection. Limitations of this study were heterogeneity of baseline characteristics of included patients, small sample size, short duration, and non-uniformly defined outcome assessment parameters in the included studies.

Sources Used:
The following databases are used in the creation of this bulletin: BNI, CINAHL, EMBASE, Medline, and KnowledgeShare