Type 2 Diabetes
Current Awareness Bulletin
March 2018

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Prevention

Title: Case study of an adaptation and implementation of a Diabetes Prevention Program for individuals with serious mental illness.

Citation: Translational behavioral medicine; Mar 2018; vol. 8 (no. 2); p. 195-203

Author(s): Quiñones, Maria M; Lombard-Newell, Judy; Sharp, Daryl; Way, Valerie; Cross, Wendi

Abstract: The Diabetes Prevention Program (DPP) is an evidence-based lifestyle intervention developed to decrease the risk for type 2 diabetes and promote weight loss in individuals at risk for diabetes. Individuals with serious mental illness have a greater risk for developing diabetes compared with the general population. In this article, the authors provide a detailed description of the adaptation process of the DPP for individuals with serious mental illness (DPP-SMI). The adaptation process was based on a cultural adaptation framework for modifying evidence-based interventions. To assess the effectiveness of the DPP-SMI, 11 individuals from a community mental health residential agency completed a 22-session pilot study of the adapted program and provided physiological measures before and after the intervention. As primary outcomes, participants were expected to report decreased body weight and increased physical activity per week. Completers had an average weight loss of 19 lbs (8%) and their physical activity increased from 161 to 405 min per week. These preliminary results together with participants’ feedback informed further refinement of the DPP-SMI. This case study supports that individuals with serious mental illness can benefit from the DPP-SMI, which is tailored to meet the unique needs of this population group.

Title: Fibre supplementation for the prevention of type 2 diabetes and improvement of glucose metabolism: the randomised controlled Optimal Fibre Trial (OptiFiT).

Citation: Diabetologia; Feb 2018

Author(s): Honsek, Caroline; Kabisch, Stefan; Kemper, Margrit; Gerbracht, Christiana; Arafat, Ayman M; Birkenfeld, Andreas L; Dambeck, Ulrike; Osterhoff, Martin A; Weickert, Martin O; Pfeiffer, Andreas F H

Aims/Hypothesis: Insoluble cereal fibres have been shown in large prospective cohort studies to be highly effective in preventing type 2 diabetes, but there is a lack of interventional data. Our 2 year randomised double-blind prospective intervention study compared the effect of an insoluble oat fibre extract with that of placebo on glucose metabolism and incidence of diabetes.

Methods: A total of 180 participants with impaired glucose tolerance underwent a modified version of the 1 year lifestyle training programme PRevention of DIAbetes Self-management (PREDIAS) and were randomised to receive a fibre supplement (n = 89; 7.5 g of insoluble fibre per serving) or placebo (n = 91; 0.8 g of insoluble fibre per serving) twice daily for 2 years. Eligible participants were men and women, were at least 18 years old and did not report corticosteroid or other intensive anti-inflammatory treatment, fibre intolerance or any of the following disorders: overt diabetes, chronic or malignant disease, or severe cardiopulmonary, endocrine, psychiatric, gastrointestinal, autoimmune or eating disorder. Participants were recruited at two clinical wards in Berlin and Nuthetal. The allocation was blinded to participants and study caregivers (physicians, dietitians, study nurses). Randomisation was conducted by non-clinical staff, providing neutrally numbered supplement tins. Both supplements were similar in their visual, olfactory and gustatory appearance. Intention-to-treat analysis was applied to all individuals.

Results: After 1 year, 2 h OGTT levels decreased significantly in both groups but without a significant difference between the groups (fibre -0.78 ± 1.88 mmol/l [p ≤ 0.001] vs placebo -0.46 ± 1.80 mmol/l [p = 0.020]; total difference 0.32 ± 0.29 mmol/l; not significant). The 2 year incidence of diabetes was 9/89 (fibre group) compared with 16/91 (placebo group; difference not significant). As secondary outcomes, the change in HbA1c level was significantly different between the two groups (0.2 ± 4.6 mmol/mol [-0.0 ± 0.0%; not significant] vs +1.2 ± 5.2 mmol/mol [+0.1 ± 0.0%; not significant]; total difference 1.4 ± 0.7 mmol/mol [0.1 ± 0.0%]; p = 0.018); insulin sensitivity and hepatic insulin clearance increased in both groups. After 2 years, improved insulin sensitivity was still present in both
groups, although the effect size had diminished. Separate analysis of the sexes revealed a significantly greater reduction in 2 h glucose levels for women in the fibre group (-0.88 ± 1.59 mmol/l [p ≤ 0.001] vs -0.22 ± 1.52 mmol/l [p = 0.311]; total difference 0.67 ± 0.31 mmol/l; p = 0.015). Levels of fasting glucose, adipokines and inflammatory markers remained unchanged in the two groups. Significantly increased fibre intake was restricted to the fibre group, despite dietary counselling for both groups. No severe side effects occurred.

**Conclusions/Interpretation:** We cannot currently provide strong evidence for a beneficial effect of insoluble cereal fibre on glycaemic metabolism, although further studies may support minor effects of fibre supplementation in reducing glucose levels, insulin resistance and the incidence of type 2 diabetes.

**Trial Registration:** clinicaltrials.gov NCT01681173 Funding: German Diabetes Foundation (grant no. 232/11/08).

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**Title:** "I Want to Walk with My Moko." The Application of Social Cognitive Theory in the Creation of a Diabetes Prevention Documentary with New Zealand Māori.

**Citation:** Journal of health communication; Feb 2018; p. 1-7

**Author(s):** Farmer, Alison; Edgar, Timothy; Gage, Jeffrey; Kirk, Ray

**Abstract:** Type 2 diabetes is almost three times more prevalent in the indigenous people of New Zealand (Māori) than non-Māori. Despite the high rate of diabetes there is a low level of diabetes knowledge and awareness in the Māori community. Several studies of Māori health identify a need for new health communication approaches to diabetes prevention in order to reduce the gap between Māori and non-Māori disease rates. We applied a Community-Based Participatory Research (CBPR) framework and behavioral theory to create a culturally appropriate documentary for Māori at risk for type 2 diabetes. We discuss how we utilized Bandura’s social cognitive theory to provide a culturally sensitive theoretical basis for behavior change messaging. We outline why social cognitive theory was a culturally appropriate foundation and describe the role of the community in shaping the documentary messaging. A culture-centered approach utilizing participatory methodologies and culturally sensitive behavioral change theory might serve as a model for creating health communication resources in collaboration with other indigenous communities.

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**Title:** Effective translation of a type-2 diabetes primary prevention programme into routine primary care: The PreDE cluster randomised clinical trial.

**Citation:** Diabetes research and clinical practice; Feb 2018; vol. 139; p. 32-42

**Author(s):** Sanchez, Alvaro; Silvestre, Carmen; Campo, Natalia; Grandes, Gonzalo; PredDE Group

**Aims:** We assessed the effectiveness of a Type 2 diabetes mellitus (T2D) prevention programme in routine primary health care (PHC) in high-risk patients.

**Methods:** Phase IV cluster clinical trial involving 14 PHC centres in the Basque Health Service were randomised to the DE-PLAN educational healthy lifestyle promotion programme or standard care. All non-diabetic 45- to 70-year-old PHC attendees considered at high risk of T2D (FINDRISC ≥ 14 points) were eligible. The primary outcome was the 24-month cumulative incidence of T2D confirmed by oral glucose tolerance testing. Secondary outcomes were self-reported physical activity and dietary changes at 12 months in a subsample.

**Results:** Of the 4170 patients screened, 2128 (51%) were considered high risk, but 355 (33%) and 459 (43.6%) refused to participate in the control and intervention groups, respectively. Of all eligible non-diabetic patients, 634 and 454 were included in the control and intervention arms, 545 (85.9%) and 411 (90.5%) completed the follow-up. Intention-to-treat cumulative incidences of T2D were 12.1% (77/634) in the control group and 8.4% (38/454) in intervention group, with an absolute difference of 3.8% (95% CI: 0.18%-7.4%, p = 0.045) and a relative risk reduction of 32% (0.68; 95% CI: 0.47-0.99, p = 0.048) in favour of the intervention. Intervention patients were 1.83-fold more likely to meet recommended physical activity levels at 12 months (95% CI: 1.06-3.17, p = 0.03).
Conclusions: The DE-PLAN programme was effective in reducing T2D incidence in PHC high-risk patients. Research on implementation strategies to improve its feasible and sustainable adoption, reach and public health impact is warranted.

Title: NHS Diabetes Prevention Programme in England: formative evaluation of the programme in early phase implementation.

Citation: BMJ open; Feb 2018; vol. 8 (no. 2); p. e019467

Author(s): Penn, Linda; Rodrigues, Angela; Haste, Anna; Marques, Marta M; Budig, Kirsten; Sainsbury, Kirby; Bell, Ruth; Araújo-Soares, Vera; White, Martin; Summerbell, Carolyn; Goyder, Elizabeth; Brennan, Alan; Adamson, Ashley J; Sniehotta, Falko F

Objectives: Evaluation of the demonstrator phase and first wave roll-out of the National Health Service (NHS) Diabetes Prevention Programme (DPP) in England. To examine: (1) intervention design, provision and fidelity assessment procedures; (2) risk assessment and recruitment pathways and (3) data collection for monitoring and evaluation. To provide recommendations informing decision makers on programme quality, improvements and future evaluation.

Design: We reviewed programme documents, mapping against the NHS DPP specification and National Institute for Health and Care Excellence (NICE) public health guideline: Type 2 diabetes (T2D) prevention in people at high risk (PH38), conducted qualitative research using individual interviews and focus group discussions with stakeholders and examined recruitment, fidelity and data collection procedures.

Setting: Seven NHS DPP demonstrator sites and, subsequently, 27 first wave areas across England.

Interventions: Intensive behavioural intervention with weight loss, diet and physical activity goals. The national programme specifies at least 13 sessions over 9 months, delivered face to face to groups of 15-20 adults with non-diabetic hyperglycaemia, mainly recruited from primary care and NHS Health Checks.

Participants: Participants for qualitative research were purposively sampled to provide a spread of stakeholder experience. Documents for review were provided via the NHS DPP Management Group.

Findings: The NHS DPP specification reflected current evidence with a clear framework for service provision. Providers, with national capacity to deliver, supplied intervention plans compliant with this framework. Stakeholders highlighted limitations in fidelity assessment and recruitment and retention challenges, especially in reach and equity, that could adversely impact on implementation. Risk assessment for first wave eligibility differed from NICE guidance.

Conclusions: The NHS DPP provides an evidence-based behavioural intervention for prevention of T2D in adults at high risk, with capacity to deliver nationally. Framework specification allows for balance between consistency and contextual variation in intervention delivery, with session details devolved to providers. Limitations in fidelity assurance, data collection procedures and recruitment issues could adversely impact on intervention effectiveness and restrict evaluation.

Title: Assessing the risk of type 2 diabetes mellitus among children and adolescents with psychiatric disorders treated with atypical antipsychotics: a population-based nested case-control study.

Citation: European child & adolescent psychiatry; Feb 2018

Author(s): Lee, Hankil; Song, Dong-Ho; Kwon, Jin-Won; Han, Euna; Chang, Min-Jung; Kang, Hye-Young

Abstract: To examine the associations between atypical antipsychotic (AAP) exposure and the development of type 2 diabetes mellitus (T2DM) in Korean pediatric patients with psychiatric disorders, we conducted a nested case-control study using the claims data of the National Health Insurance system of Korea between 2010 and 2014. A cohort of patients with psychiatric disorders was identified, and enrollment was taken as the date of the first psychiatric diagnosis. Cases involved patients with a diagnosis of T2DM or prescriptions for glucose lowering drugs after enrollment, and
the identification of T2DM was defined as the index date. We performed a conditional logistic regression analysis for matched case-control data to assess associations between AAP exposure and T2DM, and adjusted odds ratios (aORs) with 95% confidence intervals (CIs) are presented. From 1,092,019 patients aged 2-19 years, we identified 20,263 cases with T2DM and 80,043 controls, matched by sex, age, enrollment date, and primary psychiatric diagnosis. After adjusting for comorbidities, psychotropic medication history, and the healthcare institution characteristics, the aOR of having T2DM was significantly higher in multi-AAP users compared with non-users (aOR 1.89; 95% CI 1.63-2.20). Particularly high ORs for T2DM were observed in clozapine users compared with non-users (aOR 3.47; 95% CI 1.88-6.41). We observed a linear relationship between the increase in risperidone dose and the increase in the risk of developing T2DM. Our findings suggest a significantly increased risk of developing T2DM in child or adolescent patients with psychiatric disorders exposed to AAPs compared with those not exposed to AAPs.

Title: Diabetes UK evidence-based nutrition guidelines for the prevention and management of diabetes.

Citation: Diabetic medicine : a journal of the British Diabetic Association; Feb 2018
Author(s): Dyson, P A; Twenefour, D; Breen, C; Duncan, A; Elvin, E; Goff, L; Hill, A; Kalsi, P; Marsland, N; McCardle, P; Mellor, D; Oliver, L; Watson, K

Abstract: A summary of the latest evidence-based nutrition guidelines for the prevention and management of diabetes is presented. These guidelines are based on existing recommendations last published in 2011, and were formulated by an expert panel of specialist dietitians after a literature review of recent evidence. Recommendations have been made in terms of foods rather than nutrients wherever possible. Guidelines for education and care delivery, prevention of Type 2 diabetes, glycaemic control for Type 1 and Type 2 diabetes, cardiovascular disease risk management, management of diabetes-related complications, other considerations including comorbidities, nutrition support, pregnancy and lactation, eating disorders, micronutrients, food supplements, functional foods, commercial diabetic foods and nutritive and non-nutritive sweeteners are included. The sections on pregnancy and prevention of Type 2 diabetes have been enlarged and the weight management section modified to include considerations of remission of Type 2 diabetes. A section evaluating detailed considerations in ethnic minorities has been included as a new topic. The guidelines were graded using adapted ‘GRADE’ methodology and, where strong evidence was lacking, grading was not allocated. These 2018 guidelines emphasize a flexible, individualized approach to diabetes management and weight loss and highlight the emerging evidence for remission of Type 2 diabetes. The full guideline document is available at: This article is protected by copyright. All rights reserved.

Title: Risk of type 2 diabetes: health care provider perceptions of prevention adherence.

Citation: Applied Nursing Research; Nov 2016; vol. 32 ; p. 1-6
Author(s): Thomas, Jenifer J.; Moring, John C.; Harvey, Terra; Hobbs, Talisha; Lindt, Adara

Abstract: The aim of the current study was to describe health care providers' perceptions as to why individuals may or may not follow recommendations for reducing risk of developing type 2 diabetes. A grounded theory research design guided data collection and analysis. Data were collected from 16 health care providers through semi-structured interviews. Results demonstrated that health care providers perceived prevention adherence as related to individual characteristics of the patient and activities of the provider. Specifically, providers described assessment of patient-based characteristics associated with behavior, context, and traits. In addition, providers discussed giving attention to the patient-provider relationship and helping the patient incorporate small lifestyle changes. Providers might utilize social cognitive theory to understand personal and socio-structural aspects of adherence. In addition, providers should focus assessment and relationship building efforts on factors that support self-efficacy.
Title: Mental Models of Cause and Inheritance for Type 2 Diabetes Among Unaffected Individuals Who Have a Positive Family History.

Citation: Qualitative Health Research; Mar 2018; vol. 28 (no. 4); p. 534

Author(s): Daack-Hirsch, Sandra; Shah, Lisa L; Cady, Alyssa D

Abstract: Using the familial risk perception (FRP) model as a framework, we elicited causal and inheritance explanations for type 2 diabetes (T2D) from people who do not have T2D but have a family history for it. We identified four composite mental models for cause of T2D: (a) purely genetic; (b) purely behavioral/environmental; (c) direct multifactorial, in which risk factors interact and over time directly lead to T2D; and (d) indirect multifactorial, in which risk factors interact and over time cause a precursor health condition (such as obesity or metabolic syndrome) that leads to T2D. Interestingly, participants described specific risk factors such as genetics, food habits, lifestyle, weight, and culture as "running in the family." Our findings provide insight into lay beliefs about T2D that can be used by clinicians to anticipate or make sense of responses to questions they pose to patients about mental models for T2D.
**Control**

**Title:** Glycaemic control and treatment of type 2 diabetes in adults aged 75 years or older.

**Citation:** International journal of clinical practice; Mar 2018

**Author(s):** Rodriguez-Poncelas, Antonio; Barrot-de la Puente, Joan; Coll de Tuero, Gabriel; López-Arpí, Carles; Vlacho, Bogdan; Lopéz-Simarro, Flora; Munset Tudurí, Xavier; Franch-Nadal, Josep

**Aim:** The aim of this study was to assess glycaemic control and prescribing practices of antihyperglycaemic treatment in patients with diabetes mellitus type 2 aged 75 years or older.

**Methods:** We analysed data from health electronic records from 4,581 persons attended at primary healthcare centres of the Institut Català de la Salut (ICS), in the Girona Sud area of Catalonia, Spain, during 2013 and 2016. Variables such as age, gender, body mass index (BMI), diabetes duration, age at diabetes diagnosis, glycated haemoglobin (HbA1c), creatinine, glomerular filtrate rate and the albumin/creatinine ratio in urine were collected. A descriptive analysis of the study variables was done to determine the percentage of persons on antidiabetic treatment.

**Results:** We identified 4,421 persons aged 75 years or older who provided data on HbA1c and antidiabetic treatment. Mean age was 82.3 (5.1) years. In 58.1% of patients, the level of HbA1c was below 7.0%, while in 36.8% it was below 6.5%. Between patients with HbA1c below 7.0%, antidiabetic drugs were taken by 70.2%, where 15.2% were either on insulin, sulphonylureas or repaglinide therapy.

**Conclusion:** Intensive treatment among older adults with diabetes mellitus type 2 is common in primary care clinical practice in our area. Intensive glycaemic control confers an increased risk of hypoglycaemia and little benefit among older individuals with diabetes. Physicians should take care more not to harm those populations and treatment should be de-intensified to reduce the risk of hypoglycaemia.

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**Title:** Effects of Psychological Intervention in Glycemic Control of Patients with Type 2 Diabetes in Integrated Primary Care Setting.

**Citation:** Psychotherapy and psychosomatics; Mar 2018

**Author(s):** Brusadelli, Emanuela; Tomasich, Alessandra; Bruno, Samantha; Romanazzi, Alessia; Dagani, Regina; Porcelli, Piero

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**Title:** Is Cognitive Behavioural Therapy focusing on Depression and Anxiety Effective for People with Long-Term Physical Health Conditions? A Controlled Trial in the Context of Type 2 Diabetes Mellitus.

**Citation:** Behavioural and cognitive psychotherapy; Mar 2018; vol. 46 (no. 2); p. 129-147

**Author(s):** Wroe, Abigail L; Rennie, Edward W; Sollesse, S; Chapman, J; Hassy, A

**Background:** It is unclear as to the extent to which psychological interventions focusing specifically on depression and anxiety are helpful for people with physical health conditions, with respect to mood and condition management.

**Aims:** To evaluate the effectiveness of a modified evidence-based psychological intervention focusing on depression and anxiety for people with type 2 diabetes mellitus (T2DM), compared with a control intervention.

**Method:** Clients (n = 140) who experienced mild to moderate depression and/or anxiety and had a diagnosis of T2DM were allocated to either diabetes specific treatment condition (n = 52) or standard intervention (control condition, n = 63), which were run in parallel. Each condition received a group intervention offering evidence-based psychological interventions for people with depression and anxiety. Those running the diabetes specific treatment group received additional training and
supervision on working with people with T2DM from a clinical health psychologist and a general practitioner. The diabetes specific treatment intervention helped patients to link mood with management of T2DM.

**Results:** Both conditions demonstrated improvements in primary outcomes of mood and secondary outcome of adjustment [95% confidence interval (CI) between 0.25 and 5.06; p < 0.05 in all cases]. The diabetes specific treatment condition also demonstrated improvements in secondary outcomes of self-report management of T2DM for diet, checking blood and checking feet, compared with the control condition (95% CIs between 0.04 and 2.05; p < 0.05 in all cases) and in glycaemic control (95% CI: 0.67 to 8.22). The findings also suggested a non-significant reduction in NHS resources in the diabetes specific treatment condition. These changes appeared to be maintained in the diabetes specific treatment condition.

**Conclusions:** It is concluded that a modified intervention, with input from specialist services, may offer additional benefits in terms of improved diabetic self-management and tighter glycaemic control.

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**Title:** Improved glycemic control with once-weekly dulaglutide in addition to insulin therapy in type 2 diabetes mellitus patients on hemodialysis evaluated by continuous glucose monitoring.

**Citation:** Journal of diabetes and its complications; Mar 2018; vol. 32 (no. 3); p. 310-315

**Author(s):** Yajima, Takahiro; Yajima, Kumiko; Hayashi, Makoto; Takahashi, Hiroshi; Yasuda, Keigo

**Aims:** To evaluate the efficacy and safety of adding once-weekly dulaglutide to insulin therapy in type 2 diabetes mellitus (T2DM) patients on hemodialysis.

**Methods:** Fifteen insulin-treated T2DM patients on hemodialysis were enrolled. Continuous glucose monitoring was performed before (1st hospitalization) and after the fifth dulaglutide administration (2nd hospitalization). The insulin dose was reduced after the first administration of dulaglutide (1st hospitalization day 6). Parameters of glycemic control were compared on 1st hospitalization days 4-5, 2nd hospitalization days 3-4, and days 6-7.

**Results:** The median total daily insulin dose was reduced significantly from 12 (12-25) to 0 (0-12) U (p < 0.0001) after treatment with dulaglutide. Mean glucose level on 2nd hospitalization days 3-4 significantly decreased and that on days 6-7 tended to decrease compared with that on 1st hospitalization days 4-5 (median, 8.2 to 6.7 mmol/L, P = 0.006 and 8.2 to 6.9 mmol/L, P = 0.053, respectively). %CV of glucose levels decreased significantly after dulaglutide administration (28.1 to 19.8, P = 0.003 and 28.1 to 21.0, P = 0.019). However, the incidence of hypoglycemia remained unchanged.

**Conclusions:** Dulaglutide may improve glycemic control and excursion and allow total daily insulin to be reduced without increasing the risk of hypoglycemia in T2DM patients on hemodialysis.

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**Title:** Better glycaemic control and less hypoglycaemia with insulin glargine 300 U/mL vs glargine 100 U/mL: 1-year patient-level meta-analysis of the EDITION clinical studies in people with type 2 diabetes.

**Citation:** Diabetes, obesity & metabolism; Mar 2018; vol. 20 (no. 3); p. 541-548

**Author(s):** Ritzel, Robert; Roussel, Ronan; Giaccari, Andrea; Vora, Jiten; Brulle-Wohlhueter, Claire; Yki-Järvinen, Hannele

**Aims:** To investigate the efficacy and safety of insulin glargine 300 U/mL (Gla-300) vs insulin glargine 100 U/mL (Gla-100) over 12 months in a patient-level meta-analysis, using data from the EDITION studies in people with type 2 diabetes (T2DM).

**Methods:** EDITION 1, 2 and 3 were multicentre, randomized, open-label, 2-arm, parallel-group, treat-to-target phase IIIa studies. Similar study designs and endpoints enabled a meta-analysis to be conducted. RESULTS Reductions in glycated haemoglobin (HbA1c) were better sustained over 12 months with Gla-300 than with Gla-100 (least squares [LS] mean difference in change from baseline: -0.10 % [95% confidence interval (CI) -0.18 to -0.02] or -1.09 mmol/mol [95% CI -2.01 to -
Risk of confirmed (≤3.9 mmol/L) or severe hypoglycaemia was 15% lower with Gla-300 vs Gla-100 at night (relative risk 0.85 [95% CI 0.77-0.92]) and 6% lower at any time of day (relative risk 0.94 [95% CI 0.90-0.98]). Rates of hypoglycaemia were 18% lower with Gla-300 vs Gla-100 at night (rate ratio 0.82 [95% CI 0.67-0.99]), but comparable at any time of day. HbA1c <7.0% without nocturnal hypoglycaemia was achieved by 24% more participants with Gla-300 than with Gla-100 (relative risk 1.24 [95% CI 1.03-1.50]). Severe hypoglycaemia was rare; in both treatment groups the incidence of events at any time of day was ≤3.6%, while rates were ≤0.08 events per participant-year.

Conclusions: In a broad population of people with T2DM over 12 months, use of Gla-300 provided more sustained glycaemic control and significantly lower hypoglycaemia risk at night and at any time of day compared with Gla-100.
Treatment

Title: Relationship and variation of diabetes related symptoms, sleep disturbance and sleep-related impairment in adults with type 2 diabetes.

Citation: Journal of Advanced Nursing; Mar 2018; vol. 74 (no. 3); p. 689
Author(s): Zhu, Bingqian; Quinn, Laurie; Fritschi, Cynthia

Aim: The objective of this study was to examine whether diabetes-related symptoms (e.g. fatigue, neuropathic pain, diabetes distress and depressive symptoms) were related to sleep disturbance and sleep-related impairment in adults with type 2 diabetes while controlling for potential covariates.

Background: In people with type 2 diabetes, sleep disturbance and sleep-related impairment are common and likely associated with diabetes-related symptoms. However, limited research has investigated the predictive ability of diabetes-related symptoms on sleep.

Design: A correlational, cross-sectional design was used.

Methods: Data were collected at a large university in the Midwestern United States from September 2013-March 2014. Multiple linear regression analyses were used to examine the relationship of diabetes-related symptoms (fatigue, neuropathic pain, distress and depressive symptoms) to sleep disturbance and sleep-related impairment. The instruments included Patient-Reported Outcomes Measurement Information System instruments, Diabetes Symptom Checklist and Diabetes Distress Scale.

Findings: In this study of adults with type 2 diabetes (N = 90; 52.2% female, mean age 57.4 years), gender, A1C, neuropathic pain and fatigue were significantly related to sleep disturbance when age, diabetes duration, depressive symptoms and distress were controlled. Those variables collectively explained 52% of the variation in sleep disturbance. Fatigue was significantly associated with sleep-related impairment when the same covariates were controlled.

Conclusion: Findings suggested that diabetes-related symptoms, including neuropathic pain and fatigue, are strongly related to sleep disturbance and sleep-related impairment in adults with type 2 diabetes, underscoring the need to include detailed assessments of neuropathic pain and fatigue when evaluating sleep.

Title: Fixed-ratio combination therapy for type 2 diabetes: the top ten things you should know about insulin and glucagon-like peptide-1 receptor agonist combinations.

Citation: Postgraduate medicine; Mar 2018
Author(s): Blumer, Ian; Pettus, Jeremy H; Santos Cavaiola, Tricia

Abstract: Many individuals with type 2 diabetes (T2D) will eventually require insulin therapy to help achieve and maintain adequate glycemic control. However, the use of insulin can be associated with adverse effects such as hypoglycemia and weight gain, and in some patients the addition of insulin to treatment regimens is often still insufficient to achieve target glycemic control. Combining basal insulin with a glucagon-like peptide-1 receptor agonist (GLP-1 RA) for the treatment of patients with T2D has been demonstrated to be effective and well tolerated, while mitigating many of the adverse events associated with giving either of these drug classes alone. Two titratable, fixed-ratio combination therapies, iGlarLixi and IDegLira, that combine basal insulin and a GLP-1 RA in a once-daily subcutaneous injection are currently approved by the US Food and Drug Administration (FDA) for the treatment of patients with T2D. The fixed-ratio combination iGlarLixi combines insulin glargine 100 Units/mL with lixisenatide, while IDegLira combines insulin degludec 100 Units/mL with liraglutide. While these new fixed-ratio combinations contain antihyperglycemic medications that are familiar to most health care providers, there are many questions relating to their use when formulated as a fixed-ratio combination therapy. This article discusses the ‘top 10’ considerations that health care providers should know about these novel combination therapies as these agents begin to gain an increasing presence in clinical practice.
Title: Pharmacological management of diabetes in severe mental illness: a comprehensive clinical review of efficacy, safety and tolerability.

Citation: Expert review of clinical pharmacology; Mar 2018 ; p. 1-14

Author(s): Lally, John; O’Loughlin, Aonghus; Stubbs, Brendon; Guerandel, Allys; O'Shea, Donal; Gaughran, Fiona

Introduction: The increased prevalence of Type 2 diabetes mellitus (T2DM) in severe mental illness (SMI) contributes to increased cardiovascular morbidity and reduced life expectancy for people with SMI.

Areas covered: In the present clinical review, we summarize the efficacy, safety and tolerability of selected diabetic pharmacotherapy options in SMI and discuss the quality and strength of evidence.

Expert commentary: General principles for treating T2DM in SMI involve identifying treatments which promote weight loss and which have low or no risk of hypoglycemia. Patient engagement in decision making about treatment choices is an important factor to ensure adherence and successful use of the chosen therapy. The first line therapeutic option for T2DM in SMI for which there is most evidence is metformin. Based on general population data, second line treatment options in combination with metformin to achieve glycated haemoglobin treatment goals include GLP-1R agonists, DPP-4 inhibitors, sulphonylureas, SGLT2 inhibitors, pioglitazone and insulin, with most evidence for the use of GLP-1R agonists in SMI. Alongside efficacy and tolerability, treatment for T2DM in SMI should be considered on a patient-tailored basis.

Title: Changes in metformin use and other antihyperglycemic therapies after insulin initiation in patients with type 2 diabetes.

Citation: Diabetes research and clinical practice; Mar 2018

Author(s): Pilla, Scott J; Dotimas, James R; Maruthur, Nisa M; Clark, Jeanne M; Yeh, Hsin-Chieh

Aims: When patients with type 2 diabetes initiate insulin, metformin should be continued while continuation of other antihyperglycemics has unclear benefit. We aimed to identify practice patterns in antihyperglycemic therapy during the insulin transition, and determine factors associated with metformin continuation.

Methods: We performed a retrospective analysis of the Look AHEAD (Action for Health in Diabetes) trial which randomized overweight/obese adults under ambulatory care for type 2 diabetes to an intensive lifestyle intervention or diabetes support and education. Among the 931 participants who initiated insulin over ten years, we described longitudinal changes in antihyperglycemic medications during the insulin transition, and performed multivariable logistic regression to estimate the association between patient characteristics and metformin continuation.

Results: Before insulin initiation, 81.0% of patients used multiple antihyperglycemics, the most common being metformin, sulfonylureas, and thiazolidinediones. After insulin initiation, metformin was continued in 80.3% of patients; other antihyperglycemics were continued less often, yet 58.0% of patients were treated with multiple non-insulin antihyperglycemics. Metformin continuation was inversely associated with age (fully adjusted (a) OR 0.60 per 10 years [0.42-0.86]), serum creatinine above safety thresholds (aOR 0.09 [0.02-0.36]), lower income (P=0.025 for trend), taking more medications (aOR 0.92 per medication [0.86-0.98]), and initiating rapid, short, or premixed insulin (aOR 0.59 [0.39-0.89]).

Conclusions: The vast majority of patients with type 2 diabetes continue metformin after insulin initiation, consistent with guidelines. Other antihyperglycemics are frequently continued along with insulin, and further research is needed to determine which, if any, patients may benefit from this.
Title: Effects of testosterone supplement treatment in hypogonadal adult males with T2DM: a meta-analysis and systematic review.

Citation: World journal of urology; Mar 2018

Author(s): Zhang, Jianzhong; Yang, Bin; Xiao, Wenhui; Li, Xiao; Li, Hongjun

Purpose: Testosterone supplement treatment (TST) is a classic therapy for hypogonadal men with type 2 diabetes mellitus (T2DM), but the effects of TST in different studies are inconsistent. We conducted this meta-analysis to evaluate the precise role of TST in hypogonadal men with T2DM.

Methods: PubMed, Embase, Cochrane Library and Web of Science were searched to identify qualified randomized controlled trials (RCTs). Pooled mean differences (MDs) with 95% confidence intervals (CIs) were calculated to measure the specific effects of TST. Trial sequential analysis was performed to verify the pooled results.

Results: A total of eight RCTs were enrolled in our meta-analysis, including 596 hypogonadal participants with T2DM. Compared with comparators, TST can significantly improve glycemic control by reducing homeostatic model assessment of insulin resistance (MD -0.79, 95% CI -1.23 to -0.34), fasting glucose (MD -0.98, 95% CI -1.13 to -0.54), fasting insulin (MD -2.47, 95% CI -3.99 to -0.95) and HbA1c% (MD -0.45, 95% CI -0.73 to -0.16). In addition, TST can result in a decline in cholesterol (MD -0.29, 95% CI -0.38 to -0.19) and triglyceride (MD -0.37, 95% CI -0.59 to -0.15).

Conclusion: Our results indicated that TST can improve glycemic control and decrease TC and TG in hypogonadal patients with T2DM. We recommend TST during the anti-diabetic therapy in these patients.

Title: Glucose-Lowering Therapies and Heart Failure in Type 2 Diabetes Mellitus: Mechanistic Links, Clinical Data, and Future Directions.

Citation: Circulation; Mar 2018; vol. 137 (no. 10); p. 1060-1073

Author(s): Vijayakumar, Shilpa; Vaduganathan, Muthiah; Butler, Javed

Abstract: Diabetes mellitus independently increases the risk of and mortality from heart failure in a manner that is well established but inadequately understood. Glycemic optimization does not eliminate this risk, and measures of glycemic control are insufficient markers of cardiovascular risk. In response to a regulatory guidance from the US Food and Drug Administration, glucose-lowering agents are now routinely evaluated in large cardiovascular outcome trials. These recent trial experiences of novel and established glucose-lowering therapies have shown variable risks and benefits with respect to heart failure. Cardiovascular outcome trials have increasingly included heart failure events as either a component of the primary end point or a secondary adjudicated end point. We comprehensively review each established and novel currently marketed glucose-lowering therapy, their biological targets, mechanisms of action, and relationships with heart failure. We then highlight gaps in available evidence and directions for future research regarding the ascertainment of heart failure-related data in the evaluation of emerging glucose-lowering therapies.

Title: Adherence to a lifestyle program for youth with type 2 diabetes and its association with treatment outcome in the TODAY clinical trial.

Citation: Pediatric diabetes; Mar 2018; vol. 19 (no. 2); p. 191-198

Author(s): Berkowitz, Robert I; Marcus, Marsha D; Anderson, Barbara J; Delahanty, Linda; Grover, Nisha; Kriska, Andrea; Laffel, Lori; Syme, Amy; Venditti, Elizabeth; Van Buren, Dorothy J; Wilfley, Denise E; Yasuda, Patrice; Hirst, Kathryn; TODAY Study Group

Objective: To assess the association of proxies of behavioral adherence to the Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) lifestyle program with changes in glycemic control and obesity in a multi-ethnic sample of youth with type 2 diabetes.
**Methods:** The TODAY clinical trial included an intensive lifestyle intervention to promote weight reduction. Adherence was assessed with measures of attendance at intervention sessions and rates of self-monitoring of diet and physical activity by participants and their caregivers. The relation between participant characteristics and consistency of proxies of adherence were examined across 3 phases of intervention.

**Results:** A total of 234 TODAY youth were randomized to the lifestyle program. Overall rate of session attendance was approximately 60% of planned sessions. Participants with an adequate dose of session attendance (≥75% attended) did not differ from those who attended <75% of sessions in glycemic control, but did have significantly greater reductions in percent overweight compared with those who attended fewer than 75% of sessions. Rates of self-monitoring were low and additional analysis was not possible.

**Conclusions:** Rates of session attendance were moderate in a lifestyle program for youth with type 2 diabetes, but levels of self-monitoring, considered a key lifestyle change behavior, were low. Glycemic control was not significantly associated with session attendance but reductions in percent overweight were. Given the salience of program attendance and self-monitoring to lifestyle weight management established in other populations, future research is needed to understand, develop, and promote strategies and interventions targeting weight loss to achieve improved glycemic control in youth diagnosed with type 2 diabetes.
pharmacokinetics, and safety profiles of FFAR1 agonists, with a brief introduction to the biology and pharmacology of related targets.

**Title:** A comparative safety review between GLP-1 receptor agonists and SGLT2 inhibitors for diabetes treatment.

**Citation:** Expert opinion on drug safety; Mar 2018; vol. 17 (no. 3); p. 293-302

**Author(s):** Consoli, Agostino; Formoso, Gloria; Baldassarre, Maria Pompea Antonia; Febo, Fabrizio

**Abstract:** Glucagon-like peptide-1 receptor agonists (GLP-1RA) and sodium glucose cotransporter 2 inhibitors (SGLT2i) are of particular interest in type 2 diabetes treatment strategies, due to their efficacy in reducing HbA1c with a low risk of hypoglycaemia, to their positive effects on body weight and blood pressure and in light of their effects on cardiovascular risk and on nephroprotection emerged from the most recent cardiovascular outcome trials. Since it is therefore very likely that GLP-1RA and SGLT2i use will become more and more common, it is more and more important to gather and discuss information about their safety profile. Area Covered: adverse events and the safety concerns most often emerged in trials with GLP-1RA namely, exenatide long acting release (LAR), dulaglutide, liraglutide, semaglutide, lixisenatide or SGLT2i, namely empagliflozin, dapagliflozin, canagliflozin and SGLT2i with an attempt at comparing the safety profiles of molecules of these two classes. Expert opinion: GLP-1RA and SGLT2i, although each associated with different specific side effects, share a 'similar' safety profile and are both drugs relatively easy to handle. The potentially complementary mechanisms of action, the cardio and nephroprotective effects demonstrated by molecules of both classes, make these drugs potentially useful even in add on to each other.

**Title:** The cardiovascular effect of incretin-based therapies among type 2 diabetes: a systematic review and network meta-analysis.

**Citation:** Expert opinion on drug safety; Mar 2018; vol. 17 (no. 3); p. 243-249

**Author(s):** Wu, Shanshan; Cipriani, Andrea; Yang, Zhirong; Yang, Jun; Cai, Ting; Xu, Yang; Quan, Xiaochi; Zhang, Yuan; Chai, Sanbao; Sun, Feng; Zhan, Siyan

**Objective:** To evaluate the comparative cardiovascular safety of incretin-based therapies in patients with type 2 diabetes mellitus (T2DM).

**Methods:** Medline, Embase, the Cochrane Library and www.clinicaltrials.gov were searched for randomized controlled trials (RCTs) with duration≥12 weeks. Network meta-analysis was performed, followed by subgroup analysis and meta-regression. The Grading of Recommendations Assessment, Development and Evaluation system was used to assess the quality of evidence. The outcome of interest was a composite of cardiovascular death, myocardial infarction, stroke and heart failure. Odds ratio (OR) with 95% confidence interval (CI) was calculated as the measure of effect size.

**Results:** 281 RCTs (76.9% double-blinded) with 180,000 patients were included, comparing incretin-based therapies with other six classes of anti-diabetic drugs or placebo. A statistically significant reduction in the risk of cardiovascular events was found in favour of GLP-1RAs when compared with placebo (OR 0.89, 95%CI: 0.80-0.99) and sulfonylurea (OR 0.76, 95%CI: 0.59-0.99), whereas DPP-4 inhibitors showed a neutral effect compared with placebo (OR 0.92, 95%CI: 0.83-1.01).

**Conclusions:** Incretin-based therapies show similar cardiovascular risk in comparison with metformin, insulin, thiazolidinediones, alpha-glucosidase inhibitor and sodium-glucose co-transporter 2. GLP-1RA could decrease the risk compared with sulfonylurea or placebo, while DPP-4I appears to have neutral effect on cardiovascular risk.

**Title:** Subcutaneous semaglutide (NN9535) for the treatment of type 2 diabetes.

**Citation:** Expert opinion on biological therapy; Mar 2018; vol. 18 (no. 3); p. 343-351

**Author(s):** Hedrington, Maka S; Tsiskarishvili, Ana; Davis, Stephen N
Abstract: It is critical for individuals with type 2 diabetes mellitus (T2DM) to maintain optimal glycemia while avoiding hypoglycemia, control body weight, and reduce cardiovascular risk. The GLP-1 receptor agonists stimulate glucose-dependent insulin release (low risk of hypoglycemia), inhibit glucagon secretion, slow gastric emptying and suppress appetite (weight loss). The new members of the class are available as once daily or weekly injections. Additionally, some members of the class have demonstrated reduced cardiovascular risk. Areas covered: This manuscript describes semaglutide - a new investigational long acting GLP-1 receptor agonist. The key trials from the clinical development process are reviewed and important end-points highlighted. Expert opinion: Once-weekly semaglutide has shown superiority in reducing glycosylated hemoglobin and body weight in comparison with placebo and active comparators when used as monotherapy or in combination treatment. In addition, semaglutide improved markers of β-cell function and have shown cardiovascular risk reduction similar to once daily liraglutide. Although, overall semaglutide safety was comparable to other GLP-1 receptor agonists (low risk of hypoglycemia and high frequency of gastrointestinal side effects), increase in retinopathy complications requires further investigation.

Title: The interpretation and effect of a low-carbohydrate diet in the management of type 2 diabetes: a systematic review and meta-analysis of randomised controlled trials.

Citation: European journal of clinical nutrition; Mar 2018; vol. 72 (no. 3); p. 311-325

Author(s): Huntriss, Rosemary; Campbell, Malcolm; Bedwell, Carol

Background/Objectives: Recently, the role of a low-carbohydrate diet in diabetes management has generated interest with claims being made regarding its superiority over the traditional high-carbohydrate, low-fat dietary approach. This systematic review and meta-analysis evaluated the interpretation and effect of a low-carbohydrate diet in the management of type 2 diabetes.

Subjects/Methods: Randomised controlled trials were searched for which included adults with type 2 diabetes aged 18 years or more. The intervention was a low-carbohydrate diet as defined by the author compared to a control group of usual care. MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials, ISRCTN, ProQuest and opengrey.eu were searched. Independent experts were contacted and reference lists of selected papers were checked. Results were analysed descriptively and meta-analyses were completed to include trials that presented data at 1 year.

Results: Eighteen studies (n = 2204) were eligible for inclusion within the systematic review. The definition of a low-carbohydrate diet varied. At trial end, the descriptive analysis suggested that the low-carbohydrate intervention arm (LCIA) may promote favourable outcomes in terms of HbA1c, triglycerides and HDL cholesterol. The LCIA demonstrated reduced requirements for diabetes medication, which may have reduced the observed benefit of dietary carbohydrate restriction on HbA1c. Seven studies provided data to be included in the meta-analyses at 1 year. The meta-analyses showed statistical significance in favour of the LCIA for HbA1c (estimated effect = -0.28%, 95% CI -0.53 to -0.02, p = 0.03; $\chi^2 = 13.15$, df = 6, p = 0.03; I² = 54%), HDL cholesterol (estimated effect = 0.06 mmol/L, 95% CI 0.04-0.09, p < 0.00001; $\chi^2 = 6.05$, df = 6, p = 0.42; I² = 1%), triglycerides (estimated effect = -0.24 mmol/L, 95% CI -0.35 to -0.13, p < 0.0001; $\chi^2 = 1.88$, df = 6, p = 0.93; I² = 0%) and systolic blood pressure (estimated effect = -2.74 mmHg, 95% CI -5.27 to -0.20, p = 0.03; $\chi^2 = 10.54$, df = 6, p = 0.10; I² = 43%). Meta-analyses for weight, total cholesterol, LDL cholesterol and diastolic blood pressure did not demonstrate a statistically significant difference between interventions. Dietary adherence was an issue in most studies. A very low-carbohydrate diet (<50 g/day) seems unrealistic in this population, however, a low-carbohydrate diet (<130 g/day) appears to be achievable. Improved clinical outcomes were observed in some studies as a result of achieving a low- or moderate-carbohydrate diet. Fifteen out of 18 studies were considered high risk of bias, with performance bias being a common issue.

Conclusions: Reducing dietary carbohydrate may produce clinical improvements in the management of type 2 diabetes. Further research is needed to understand the true effect of dietary carbohydrate restriction on HbA1c independent of medication reduction and to address known issues with adherence to this dietary intervention. Clarity is needed regarding appropriate classification of a low-carbohydrate diet.
Title: Heart Failure: Epidemiology, Pathophysiology, and Management of Heart Failure in Diabetes Mellitus.

Citation: Endocrinology and metabolism clinics of North America; Mar 2018; vol. 47 (no. 1); p. 117-135
Author(s): Jorsal, Anders; Wiggers, Henrik; McMurray, John J V

Abstract: This article briefly discusses the epidemiology of heart failure and diabetes and summarizes the key findings from the recent cardiovascular outcome trials in patients with type 2 diabetes, with a focus on heart failure as an endpoint.

Title: Initiating therapy in patients newly diagnosed with type 2 diabetes: Combination therapy vs a stepwise approach.

Citation: Diabetes, obesity & metabolism; Mar 2018; vol. 20 (no. 3); p. 497-507
Author(s): Cersosimo, Eugenio; Johnson, Eric L; Chovanes, Christina; Skolnik, Neil

Abstract: There is clear evidence that achieving glycaemic targets reduces the risk of developing complications as a result of type 2 diabetes (T2D). Many patients, however, continue to have suboptimal glycaemic control because of issues that include unclear advice on how to achieve these targets as well as clinical inertia. The two management approaches recommended for patients newly diagnosed with T2D are stepwise and combination therapy, each of which has advantages and disadvantages. Stepwise therapy may result in good patient adherence and allow greater individualization of therapy, and minimization of side effects and cost, and so may be appropriate for patients who are closer to goal. Stepwise therapy, however, may also lead to frequent delays in achieving glycaemic goals and longer exposure to hyperglycaemia. Combination therapy, which is now emerging as an important therapy option, has a number of potential advantages over stepwise therapy, including reduction in clinical inertia and earlier and more frequent achievement of glycated haemoglobin goals by targeting multiple pathogenic mechanisms simultaneously, which may more effectively delay disease progression. Compared with stepwise therapy, the disadvantages of combination therapy include reduced patient adherence resulting from complex, multi-drug regimens, difficulty determining the cause of poor efficacy and/or side effects, patient refusal to accept disease, and higher cost. Fixed-dose and fixed-ratio combinations are novel therapeutic approaches which may help address several issues of treatment complexity and patient burden associated with combination therapy comprising individual drugs. The choice of which drugs to administer and the decision to use stepwise vs combination therapy, however, should always be made on an individualized basis.

Title: Identification of barriers to insulin therapy and approaches to overcoming them.

Citation: Diabetes, obesity & metabolism; Mar 2018; vol. 20 (no. 3); p. 488-496
Author(s): Russell-Jones, David; Pouwer, Frans; Khunti, Kamlesh

Abstract: Poor glycaemic control in type 2 diabetes (T2D) is a global problem despite the availability of numerous glucose-lowering therapies and clear guidelines for T2D management. Tackling clinical or therapeutic inertia, where the person with diabetes and/or their healthcare providers do not intensify treatment regimens despite this being appropriate, is key to improving patients’ long-term outcomes. This gap between best practice and current level of care is most pronounced when considering insulin regimens, with studies showing that insulin initiation/intensification is frequently and inappropriately delayed for several years. Patient- and physician-related factors both contribute to this resistance at the stages of insulin initiation, titration and intensification, impeding achievement of optimal glycaemic control. The present review evaluates the evidence and reasons for this delay, together with available methods for facilitation of insulin initiation or intensification.
Title: Characteristics Associated With Decreased or Increased Mortality Risk From Glycemic Therapy Among Patients With Type 2 Diabetes and High Cardiovascular Risk: Machine Learning Analysis of the ACCORD Trial.

Citation: Diabetes care; Mar 2018; vol. 41 (no. 3); p. 604-612

Author(s): Basu, Sanjay; Raghavan, Sridharan; Wexler, Deborah J; Berkowitz, Seth A

Objective: Identifying patients who may experience decreased or increased mortality risk from intensive glycemic therapy for type 2 diabetes remains an important clinical challenge. We sought to identify characteristics of patients at high cardiovascular risk with decreased or increased mortality risk from glycemic therapy for type 2 diabetes using new methods to identify complex combinations of treatment effect modifiers.

Research Design and Methods: The machine learning method of gradient forest analysis was applied to understand the variation in all-cause mortality within the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial (N = 10,251), whose participants were 40-79 years old with type 2 diabetes, hemoglobin A1c (HbA1c) ≥7.5% (58 mmol/mol), cardiovascular disease (CVD) or multiple CVD risk factors, and randomized to target HbA1c <6.0% (42 mmol/mol; intensive) or 7.0-7.9% (53-63 mmol/mol; standard). Covariates included demographics, BMI, hemoglobin glycosylation index (HGI; observed minus expected HbA1c derived from prerandomization fasting plasma glucose), other biomarkers, history, and medications.

Results: The analysis identified four groups defined by age, BMI, and HGI with varied risk for mortality under intensive glycemic therapy. The lowest risk group (HGI <0.44, BMI <30 kg/m2, age <61 years) had an absolute mortality risk decrease of 2.3% attributable to intensive therapy (95% CI 0.2 to 4.5, P = 0.038; number needed to treat: 43), whereas the highest risk group (HGI ≥0.44) had an absolute mortality risk increase of 3.7% attributable to intensive therapy (95% CI 1.5 to 6.0; P < 0.001; number needed to harm: 27).

Conclusions: Age, BMI, and HGI may help individualize prediction of the benefit and harm from intensive glycemic therapy.

Title: New treatment options for lipid-lowering therapy in subjects with type 2 diabetes.

Citation: Acta diabetologica; Mar 2018; vol. 55 (no. 3); p. 209-218

Author(s): Scicali, Roberto; Di Pino, Antonino; Ferrara, Viviana; Urbano, Francesca; Piro, Salvatore; Rabuazzo, Agata Maria; Purrello, Francesco

Abstract: Dyslipidemias represent a variety of quantitative and/or qualitative lipoprotein abnormalities. According to etiology, we distinguish primary dyslipidemias with strictly genetic background and secondary ones with their origin in other disease or pathological states. Diabetic dyslipidemia is a type of secondary dyslipidemia and plays an important role in determining the cardiovascular risk of subjects with type 2 diabetes. In these patients, insulin resistance is responsible for overproduction and secretion of atherogenic very low density lipoprotein. In addition, insulin resistance promotes the production of small dense low-density lipoprotein (LDL) and reduces high-density lipoprotein (HDL) production. Cardiovascular disease remains a leading cause of morbidity and mortality in diabetic patients. Previous results support the role for small, dense LDL particles in the etiology of atherosclerosis and their association with coronary artery disease. Moreover, lowering LDL cholesterol reduces the risk of cardiovascular death. Therefore, the European guidelines for the management of dyslipidemias recommend an LDL cholesterol goal 400 mg/dL, they recommend a non-HDL cholesterol goal < 130 mg/dL in diabetic individuals without cardiovascular events. Statins are the first line of LDL-lowering therapy in diabetic patients and combined therapy with ezetimibe and statins could be useful in very high cardiovascular risk diabetic subjects. Furthermore, the effect of a fibrate as an add-on treatment to a statin could improve the lipid profile in diabetic individuals with high TG and low HDL cholesterol. Regarding new therapies, recent data from phase III trials show that proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors considerably decrease LDL cholesterol. Thus, they may be useful in diabetic patients with concomitant diseases such as familial
dyslipidemia, recurrent cardiovascular events, and elevated LDL cholesterol after second drug administration in addition to maximal statin dose or statin intolerance.

Title: Treatment with insulin is associated with worse outcome in patients with chronic heart failure and diabetes.

Citation: European journal of heart failure; Feb 2018

Author(s): Cosmi, Franco; Shen, Li; Magnoli, Michela; Abraham, William T; Anand, Inder S; Cleland, John G; Cohn, Jay N; Cosmi, Deborah; De Berardis, Giorgia; Dickstein, Kenneth; Franzosi, Maria Grazia; Gullestad, Lars; Jhund, Pardeep S; Kjekshus, John; Køber, Lars; Lepore, Vito; Lucisano, Giuseppe; Maggioni, Aldo P; Masson, Serge; McMurray, John J V; Nicolucci, Antonio; Petrarolo, Vito; Robusto, Fabio; Staszewsky, Lidia; Tavazzi, Luigi; Teli, Roberto; Tognoni, Gianni; Wikstrand, John; Latini, Roberto

Aims: Up to one-third of patients with diabetes mellitus and heart failure (HF) are treated with insulin. As insulin causes sodium retention and hypoglycaemia, its use might be associated with worse outcomes.

Methods and Results: We examined two datasets: 24 012 patients with HF from four large randomized trials and an administrative database of 4 million individuals, 103 857 of whom with HF. In the former, survival was examined using Cox proportional hazards models adjusted for baseline variables and separately for propensity scores. Fine-Gray competing risk regression models were used to assess the risk of hospitalization for HF. For the latter, a case-control nested within a population-based cohort study was conducted with propensity score. Prevalence of diabetes mellitus at study entry ranged from 25.5% to 29.5% across trials. Insulin alone or in combination with oral hypoglycaemic drugs was prescribed at randomization to 24.4% to 34.5% of the patients with diabetes. The rates of death from any cause and hospitalization for HF were higher in patients with vs. without diabetes, and highest of all in patients prescribed insulin [propensity score pooled hazard ratio for all-cause mortality 1.27 (1.16-1.38), for HF hospitalization 1.23 (1.13-1.33)]. In the administrative registry, insulin prescription was associated with a higher risk of all-cause death [odds ratio (OR) 2.02, 95% confidence interval (CI) 1.87-2.19] and rehospitalization for HF (OR 1.42, 95% CI 1.32-1.53).

Conclusions: Whether insulin use is associated with poor outcomes in HF should be investigated further with controlled trials, as should the possibility that there may be safer alternative glucose-lowering treatments for patients with HF and type 2 diabetes mellitus.

Title: Why prescribe exercise as therapy in type 2 diabetes? We have a pill for that!

Citation: Diabetes/metabolism research and reviews; Feb 2018

Author(s): Ried-Larsen, Mathias; MacDonald, Christopher S; Johansen, Mette Y; Hansen, Katrine B; Christensen, Robin; Almdal, Thomas P; Pedersen, Bente K; Karstoft, Kristian

Abstract: The majority of T2D cases are preventable through a healthy lifestyle, leaving little room for questions that lifestyle should be the first line of defense in the fight against the development of T2D. However, when it comes to the clinical care of T2D, the potential efficacy of lifestyle is much less clear-cut, both in terms of impacting the pathological metabolic biomarkers of the disease, and long-term complications. A healthy diet, high leisure-time physical activity and exercise are considered to be cornerstones albeit adjunct to drug therapy in the management of T2D. The prescription and effective implementation of structured exercise and other lifestyle interventions in the treatment of T2D has not been routinely used. In this article, we critically appraise and debate our reflections as to why exercise and physical activity are not used to a satisfactory degree is multifaceted and primarily relates to a ‘vicious cycle’ with lack of proven efficacy on T2D complications and a lack of proven effectiveness on risk factors in the primary care of T2D. Furthermore, there is a lack of experimental research establishing the optimal dose of exercise. This precludes widespread and sustained implementation of physical activity and exercise in the clinical treatment of T2D will not succeed.
Title: Use of glucagon-like peptide-1 receptor agonists among individuals on basal insulin requiring treatment intensification.

Citation: Diabetic medicine : a journal of the British Diabetic Association; Feb 2018
Author(s): Trautmann, M E; Vora, J

Abstract: As Type 2 diabetes progresses, treatment is intensified with additional therapies in an effort to manage hyperglycaemia effectively and therefore avoid complications. When greater efficacy is required, options for injectable treatments include glucagon-like peptide-1 receptor agonists and insulin, which may be added on to oral glucose-lowering treatments. Among individuals receiving long-acting basal insulin as their first injectable treatment, ~40-60% are unable to achieve or maintain their target HbA1c goals. For these people, treatment intensification options are relatively limited and include the addition of short-acting prandial insulin or a glucagon-like peptide-1 receptor agonist. Glucagon-like peptide-1 receptor agonists vary in their effects, with short- and long-acting agents having a greater impact on postprandial and fasting hyperglycaemia, respectively. Studies comparing treatment intensification options have found both glucagon-like peptide-1 receptor agonists and prandial insulin to be effective in reducing HbA1c concentrations; however, recipients of glucagon-like peptide-1 receptor agonists lost weight and had a greater frequency of gastrointestinal adverse events, whereas those receiving prandial insulin gained weight and had a greater incidence of hypoglycaemia. In addition to the separate administration of a glucagon-like peptide-1 receptor agonist and basal insulin, fixed-ratio combinations of a glucagon-like peptide-1 receptor agonist and basal insulin offer a single administration for both treatments but have less flexibility in dose titration than treatment with their individual components. For individuals who require treatment intensification beyond basal insulin, use of these various options allows physicians to target the individual needs of their patients for the achievement of optimal long-term glycaemic control. This article is protected by copyright. All rights reserved.

Title: Educational and Psychological Aspects Prevalence and correlates of depressive disorders in people with Type 2 diabetes: results from the International Prevalence and Treatment of Diabetes and Depression (INTERPRET-DD) study, a collaborative study carried out in 14 countries.

Citation: Diabetic medicine : a journal of the British Diabetic Association; Feb 2018
Author(s): Lloyd, C E; Nouwen, A; Sartorius, N; Ahmed, H U; Alvarez, A; Bahendeka, S; Basangwa, D; Bobrov, A E; Boden, S; Bulgari, V; Burti, L; Chaturvedi, S K; Cimino, L C; Gaebel, W; de Girolamo, G; Gondek, T M; de Braude, M Guinzbourg; Guntupalli, A; Heinze, M G; Ji, L; Hong, X; Khan, A; Kiejna, A; Kokoszka, A; Kamala, T; Lalic, N M; Lecic Tosevski, D; Mankovsky, B; Li, M; Musau, A; Müssig, K; Ndeitei, D; Rabbani, G; Srikanta, S S; Starostina, E G; Shevchuk, M; Taj, R; Vukovic, O; Wölwer, W; Xin, Y

Aims: To assess the prevalence and management of depressive disorders in people with Type 2 diabetes in different countries.

Methods: People with diabetes aged 18-65 years and treated in outpatient settings were recruited in 14 countries and underwent a psychiatric interview. Participants completed the Patient Health Questionnaire and the Problem Areas in Diabetes scale. Demographic and medical record data were collected.

Results: A total of 2783 people with Type 2 diabetes (45.3% men, mean duration of diabetes 8.8 years) participated. Overall, 10.6% were diagnosed with current major depressive disorder and 17.0% reported moderate to severe levels of depressive symptomatology (Patient Health Questionnaire scores >9). Multivariable analyses showed that, after controlling for country, current major depressive disorder was significantly associated with gender (women) (P<0.0001), a lower level of education (P<0.05), doing less exercise (P<0.01), higher levels of diabetes distress (P<0.0001) and a previous diagnosis of major depressive disorder (P<0.0001). The proportion of those with either current major...
depressive disorder or moderate to severe levels of depressive symptomatology who had a diagnosis or any treatment for their depression recorded in their medical records was extremely low and non-existent in many countries (0-29.6%).

**Conclusions:** Our international study, the largest of this type ever undertaken, shows that people with diabetes frequently have depressive disorders and also significant levels of depressive symptoms. Our findings indicate that the identification and appropriate care for psychological and psychiatric problems is not the norm and suggest a lack of the comprehensive approach to diabetes management that is needed to improve clinical outcomes. This article is protected by copyright. All rights reserved.

**Title:** Insulin Matters: A Practical Approach to Basal Insulin Management in Type 2 Diabetes.

**Citation:** Diabetes therapy : research, treatment and education of diabetes and related disorders; Feb 2018

**Author(s):** Berard, Lori; Antonishyn, Noreen; Arcudi, Kathryn; Blunden, Sarah; Cheng, Alice; Goldenberg, Ronald; Harris, Stewart; Jones, Shelley; Mehan, Upender; Morrell, James; Roscoe, Robert; Siemens, Rick; Vallis, Michael; Yale, Jean-François

**Abstract:** It is currently estimated that 11 million Canadians are living with diabetes or prediabetes. Although hyperglycemia is associated with serious complications, it is well established that improved glycemic control reduces the risk of microvascular complications and can also reduce cardiovascular (CV) complications over the long term. The UKPDS and ADVANCE landmark trials have resulted in diabetes guidelines recommending an A1C target of ≤7.0% for most patients or a target of ≤6.5% to further reduce the risk of nephropathy and retinopathy in those with type 2 diabetes (T2D), if it can be achieved safely. However, half of the people with T2D in Canada are not achieving these glycemic targets, despite advances in diabetes pharmacological management. There are many contributing factors to account for this poor outcome; however, one of the major factors is the delay in treatment advancement, particularly a resistance to insulin initiation and intensification. To simplify the process of initiating and titrating insulin in T2D patients, a group of Canadian experts reviewed the evidence and best clinical practices with the goal of providing guidance and practical recommendations to the diabetes healthcare community at large. This expert panel included general practitioners (GPs), nurses, nurse practitioners, endocrinologists, dieticians, pharmacists, and a psychologist. This article summarizes the panel recommendations.

**Title:** Pharmacogenetics of Glucagon-like Peptide-1 agonists for the treatment of Type 2 Diabetes Mellitus.

**Citation:** Current clinical pharmacology; Feb 2018

**Author(s):** Karras, Spyridon; Rapti, Eleni; Koufakis, Theocharis; Kyriazou, Angeliki; Goulis, Dimitrios; Kotsa, Kalliopi

**Background:** Pharmacogenetics is a promising area of medical research, providing methods to identify the appropriate pharmaceutical agent and dosing for each unique patient. Glucagon-like peptide-1 (GLP-1) agonists are a novel therapeutic choice used in the treatment of type 2 diabetes mellitus (T2DM), demonstrating efficacy regarding glycemic control and weight loss. Therapeutic response to GLP-1 agonist treatment is a complex biophenomenon, dependent on a plethora of modifiable (diet, exercise, adherence) and non-modifiable (genetic individual variants, ethnic characteristics) parameters. At this context, it has been hypothesized that genetic polymorphisms of GLP-1 related genes may be associated with the therapeutic response to GLP-1 agonist treatment. This review focuses on the most important polymorphisms of the GLP-1 biological network that could affect clinical response to GLP-1 agonist treatment.

**Methods:** Biomedical databases were searched to identify key articles in the field and their results are critically presented in this review.

**Results:** Recent pharmacological and clinical studies demonstrated a significant variation in GLP-1 agonist treatment, in cohorts with homogeneous adherence to diet, exercise and antidiabetic
treatment. These studies identified several cases of non-responders to GLP-1 agonist therapy, in association with specific allelic patterns of GLP-1 receptor or other biomolecules implicated in glucose homeostasis.

**Conclusion:** Although the exact DNA sequences that cause the molecular changes leading to a variable response to GLP-1 agonists have not been yet fully identified, these findings underline the importance of an individualized approach in anti-diabetic treatment.

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**Title:** Clinical Benefit of Basal Insulin Analogue Treatment in Persons with Type 2 Diabetes Inadequately Controlled on Prior Insulin Therapy: A Prospective, Noninterventional, Multicenter Study.

**Citation:** Diabetes therapy : research, treatment and education of diabetes and related disorders; Feb 2018

**Author(s):** Bjekić-Macut, Jelica; Živković, Teodora Beljić; Kocić, Radivoj

**Introduction:** Basal insulin analogues offer persons with type 2 diabetes mellitus (T2DM) adequate glycemic control combined with a favorable safety profile. BASAL-BALI-a prospective, noninterventional, multicenter disease registry-assessed the effectiveness and safety of basal insulin analogues in adult Serbians with T2DM previously inadequately controlled on other insulin types.

**Methods:** The primary objective was to assess the reduction in glycated hemoglobin (HbA1c) from basal insulin analogue initiation to the end of a 6-month observation period. Data collection was performed at three study visits: baseline, 3 months, and 6 months. All treatments and procedures were performed at the physicians’ discretion.

**Results:** In total, 460 subjects were included. Mean diabetes duration was 11.6 ± 6.6 years. Late complications of diabetes were present in 67% of subjects and comorbidities in 85%. After 6 months, the mean reduction in HbA1c was 1.8% (p < 0.01 vs. baseline); body weight (mean reduction of 0.9 kg, p < 0.01), waist circumference (1.5 cm, p < 0.01), and BMI (0.2 kg/m², p < 0.01) were also reduced. A total of 49.1% of subjects reached their individualized HbA1c treatment target, and 42.0% met the composite HbA1c and fasting plasma glucose (FPG) target. The incidence of symptomatic hypoglycemia was reduced from 96.3% in the 6 months prior to initiating basal insulin analogues to 15.4% over the 6-month treatment period.

**Conclusion:** Introducing basal insulin analogues in persons with T2DM previously inadequately controlled on other insulin types can significantly improve glycemic control and reduce the risk of hypoglycemia, without adversely affecting body weight.

**Funding:** Sanofi, Serbia

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**Title:** Safety and tolerability of dapagliflozin, saxagliptin and metformin in combination: post hoc analysis of concomitant add-on versus sequential add-on to metformin and of triple versus dual therapy with metformin.

**Citation:** Diabetes, obesity & metabolism; Feb 2018

**Author(s):** Del Prato, Stefano; Rosenstock, Julio; Garcia-Sanchez, Ricardo; Iqbal, Nayyar; Hansen, Lars; Johnsson, Eva; Chen, Hungta; Mathieu, Chantal

**Abstract:** The safety of triple oral therapy with dapagliflozin plus saxagliptin plus metformin, versus dual therapy with dapagliflozin or saxagliptin plus metformin, was compared in a post hoc analysis of three randomized trials of sequential or concomitant add-on of dapagliflozin and saxagliptin to metformin. In the concomitant add-on trial, patients with type 2 diabetes on stable metformin received dapagliflozin 10 mg/day plus saxagliptin 5 mg/day. In sequential add-on trials, patients on metformin plus either saxagliptin 5 mg/day or dapagliflozin 10 mg/day received add-on dapagliflozin 10 mg/day or saxagliptin 5 mg/day, respectively. After 24 weeks, incidences of adverse events and serious adverse events were similar between triple and dual therapy and between concomitant and sequential add-on regimens. Urinary tract infections were more common with sequential than with concomitant add-on therapy; genital infections were reported only with sequential add-on of dapagliflozin to
saxagliptin plus metformin. Hypoglycaemia incidence was <2.0% across all analysis groups. In conclusion, safety and tolerability of triple therapy with dapagliflozin, saxagliptin and metformin, as either concomitant or sequential add-on, were similar to dual therapy with either agent added to metformin.

Title: Weekly Versus Daily Dipeptidyl Peptidase 4 Inhibitor Therapy for Type 2 Diabetes: Systematic Review and Meta-analysis.

Citation: Diabetes care; Feb 2018
Author(s): Yamada, Tomohide; Shojima, Nobuhiro; Noma, Hisashi; Yamauchi, Toshimasa; Kadowaki, Takashi

Title: Management of type 2 diabetes mellitus in people with severe mental illness: an online cross-sectional survey of healthcare professionals.

Citation: BMJ open; Feb 2018; vol. 8 (no. 2); p. e019400
Author(s): McBain, Hayley; Lamontagne-Godwin, Frederique; Haddad, Mark; Simpson, Alan; Chapman, Jacqui; Jones, Julia; Flood, Chris; Mulligan, Kathleen

Objectives: To establish healthcare professionals' (HCPs) views about clinical roles, and the barriers and enablers to delivery of diabetes care for people with severe mental illness (SMI).

Design: Cross-sectional, postal and online survey.

Setting: Trusts within the National Health Service, mental health and diabetes charities, and professional bodies.

Participants: HCPs who care for people with type 2 diabetes mellitus (T2DM) and/or SMI in the UK.

Primary And Secondary Outcome Measures: The barriers, enablers and experiences of delivering T2DM care for people with SMI, informed by the Theoretical Domains Framework.

Results: Respondents were 273 HCPs, primarily mental health nurses (33.7%) and psychiatrists (32.2%). Only 25% of respondents had received training in managing T2DM in people with SMI. Univariate analysis found that mental health professionals felt responsible for significantly fewer recommended diabetes care standards than physical health professionals (P<0.001). For those seeing diabetes care as part of their role, the significant barriers to its delivery in the multiple regression analyses were a lack of knowledge (P=0.003); a need for training in communication and negotiation skills (P=0.04); a lack of optimism about the health of their clients (P=0.04) and their ability to manage T2DM in people with SMI (P=0.003); the threat of being disciplined (P=0.02); fear of working with people with a mental health condition (P=0.01); a lack of service user engagement (P=0.006); and a need for incentives (P=0.04). The significant enablers were an understanding of the need to tailor treatments (P=0.04) and goals (P=0.02) for people with SMI.

Conclusions: This survey indicates that despite current guidelines, diabetes care in mental health settings remains peripheral. Even when diabetes care is perceived as part of an HCP's role, various individual and organisational barriers to delivering recommended T2DM care standards to people with SMI are experienced.

Title: Effectiveness of motivational interviewing for improving physical activity self-management for adults with type 2 diabetes: A review.

Citation: Chronic Illness; Mar 2018; vol. 14 (no. 1); p. 54-68
Author(s): Soderlund, Patricia Davern

Objectives: This review examines the effectiveness of motivational interviewing for physical activity self-management for adults diagnosed with diabetes mellitus type 2. Motivational interviewing is a
patient centered individually tailored counseling intervention that aims to elicit a patient's own motivation for health behavior change. Review questions include (a) How have motivational interviewing methods been applied to physical activity interventions for adults with diabetes mellitus type 2? (b) What motivational interviewing approaches are associated with successful physical activity outcomes with diabetes mellitus 2?

**Methods:** Database searches used PubMed, CINAHL, and PsycINFO for the years 2000 to 2016. Criteria for inclusion was motivational interviewing used as the principal intervention in the tradition of Miller and Rollnick, measurement of physical activity, statistical significance reported for physical activity outcomes, quantitative research, and articles written in English.

**Results:** A total of nine studies met review criteria and four included motivational interviewing interventions associated with significant physical activity outcomes.

**Discussion:** Findings suggest motivational interviewing sessions should target a minimal number of self-management behaviors, be delivered by counselors proficient in motivational interviewing, and use motivational interviewing protocols with an emphasis placed either on duration or frequency of sessions.

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**Title:** Optimising insulin therapy to individual need.

**Citation:** Practice Nursing; Feb 2018; vol. 29

**Author(s):** Hamson, Kim

**Abstract:** The author explains why optimisation of insulin therapy for patients with type 2 diabetes is needed and mentions related topics such as United Kingdom Prospective Diabetes Study, the National Institute for Health and Care Excellence, and neutral protamine Hagedorn insulin.

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**Title:** Real-world evaluation of the DESMOND type 2 diabetes education and self-management programme.

**Citation:** Practical Diabetes; Jan 2018; vol. 35 (no. 1); p. 19-23

**Author(s):** Chatterjee, Sudesna; Davies, Melanie J.; Stribling, Bernie; Farooqi, Azhar; Khunti, Kamlesh

**Abstract:** Diabetes education and self-management programmes are associated with improved biomedical, psychosocial and behavioural outcomes according to a number of randomised controlled trials (RCT) and systematic reviews. Observational studies are necessary to determine whether delivery of this education translates to improved outcomes in the real world. In 2008, the results of an RCT evaluating Diabetes Education and Self-Management for Ongoing and Newly Diagnosed (DESMOND) in a multi-ethnic population were published confirming the benefits of participating in this programme with sustained improvements at three years along with confirmed cost-effectiveness. DESMOND has therefore been recommended by NICE as a robust and validated national diabetes structured education programme. DESMOND courses have been offered by the Leicester City, Leicestershire and Rutland (LLR) clinical commissioning groups for people newly diagnosed or with pre-existing type 2 diabetes since 2008, and we reviewed the outcomes of participants who attended a course between January 2014 and March 2015. During this period, 1678 (53%) participants attended one of 244 courses in LLR compared with 5.3% attending any validated structured education programme nationally. Notably, there was a statistically significant reduction in HbA1c of 0.96% at six months and 0.70% at 12 months (both p < 0.005). Qualitative evaluation from surveys completed by 302/1678 (18%) respondents immediately after attending DESMOND found that the programme was well received by participants who noted improvements in their ability to self-manage diabetes. This 15-month evaluation of DESMOND confirms the benefits of attending the programme in the real world. Copyright © 2018 John Wiley & Sons.
Outcomes

Title: Risk of infection in type 1 and type 2 diabetes compared with the general population: A matched cohort study.

Citation: Diabetes Care; Mar 2018; vol. 41 (no. 3); p. 513-521
Author(s): Carey I.M.; Critchley J.A.; Dewilde S.; Harris T.; Hosking F.J.; Cook D.G.

Objective: We describe in detail the burden of infections in adults with diabetes within a large national population cohort. We also compare infection rates between patients with type 1 and type 2 diabetes mellitus (T1DM and T2DM). RESEARCH Design and Methods: A retrospective cohort study compared 102,493 English primary care patients aged 40-89 years with a diabetes diagnosis by 2008 (n = 5,863 T1DM and n = 96,630 T2DM) with 203,518 age-sex-practice-matched control subjects without diabetes. Infection rates during 2008-2015, compiled from primary care and linked hospital and mortality records, were compared across 19 individual infection categories. These were further summarized as any requiring a prescription or hospitalization or as cause of death. Poisson regression was used to estimate incidence rate ratios (IRRs) between 1) people with diabetes and control subjects and 2) T1DM and T2DM adjusted for age, sex, smoking, BMI, and deprivation. RESULTS: Compared with control subjects without diabetes, patients with diabetes had higher rates for all infections, with the highest IRRs seen for bone and joint infections, sepsis, and cellulitis. IRRs for infection-related hospitalizations were 3.71 (95% CI 3.27-4.21) for T1DM and 1.88 (95% CI 1.83-1.92) for T2DM. A direct comparison of types confirmed higher adjusted risks for T1DM versus T2DM (death from infection IRR 2.19 [95% CI 1.75-2.74]). We estimate that 6% of infection-related hospitalizations and 12% of infection-related deaths were attributable to diabetes.

Conclusions: People with diabetes, particularly T1DM, are at increased risk of serious infections, representing an important population burden. Strategies that reduce the risk of developing severe infections and poor treatment outcomes are under-researched and should be explored. Copyright © 2017 by The American Diabetes Association.

Title: BMI and Mortality in Patients With New-Onset Type 2 Diabetes: A Comparison With Age- and Sex-Matched Control Subjects From the General Population.

Citation: Diabetes care; Mar 2018; vol. 41 (no. 3); p. 485-493
Author(s): Edqvist, Jon; Rawshani, Araz; Adiels, Martin; Björck, Lena; Lind, Marcus; Svensson, Ann-Marie; Gudbjörnsdotir, Sofia; Sattar, Naveed; Rosengren, Annika

Objective: Type 2 diabetes is strongly associated with obesity, but the mortality risk related to elevated body weight in people with type 2 diabetes compared with people without diabetes has not been established.

Research Design and Methods: We prospectively assessed short- and long-term mortality in people with type 2 diabetes with a recorded diabetes duration ≤5 years identified from the Swedish National Diabetes Register (NDR) between 1998 and 2012 and five age- and sex-matched control subjects per study participant from the general population.

Results: Over a median follow-up of 5.5 years, there were 17,546 deaths among 149,345 patients with type 2 diabetes (mean age 59.6 years [40% women]) and 68,429 deaths among 743,907 matched control subjects. Short-term all-cause mortality risk (≤5 years) displayed a U-shaped relationship with BMI, with hazard ratios (HRs) ranging from 0.81 (95% CI 0.75-0.88) among patients with diabetes and BMI 30 to <35 kg/m2 to 1.37 (95% CI 1.11-1.71) with BMI ≥40 kg/m2 compared with control subjects after multiple adjustments. Long-term, all weight categories showed increased mortality, with a nadir at BMI 25 to <30 kg/m2 and a stepwise increase up to HR 2.00 (95% CI 1.58-2.54) among patients with BMI ≥40 kg/m2, that was more pronounced in patients <65 years old.

Conclusions: Our findings suggest that the apparent paradoxical findings in other studies in this area may have been affected by reverse causality. Long-term, overweight (BMI 25 to <30 kg/m2) patients
with type 2 diabetes had low excess mortality risk compared with control subjects, whereas risk in those with BMI ≥40 kg/m² was substantially increased.

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

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