Type 2 Diabetes
Current Awareness Bulletin
November 2019

A number of other bulletins are also available – please contact the Academy Library for further details.

If you would like to receive these bulletins on a regular basis please contact the library.

If you would like any of the full references we will source them for you.

Contact us: Academy Library 824897/98
Email: ruh-tr.library@nhs.net

Citation: Diabetic Medicine; Nov 2019; vol. 36 (no. 11); p. 1510-1511
Author(s): McGough, B.; Murray, E.; Brownlee, L.; Barron, E.; Smith, J.; Valabhji, J.

Abstract: The article offers information on National Health Service (NHS) Diabetes Prevention Programme which aim to prevent or delay the onset of Type 2 diabetes in adults in England. Topics discussed include information on behavioural interventions that encourage weight loss for people who are overweight; assessment of clinical effectiveness compared with face-to-face interventions; and need to address inequalities of access according to age.

Title: Early Outcomes From the English National Health Service Diabetes Prevention Program.

Citation: Diabetes care; Nov 2019
Author(s): Valabhji, Jonathan; Barron, Emma; Bradley, Dominique; Bakhai, Chirag; Fagg, Jamie; O'Neill, Simon; Young, Bob; Wareham, Nick; Khunti, Kamlesh; Jebb, Susan; Smith, Jenifer

Objective: To assess weight and HbA1c changes in the Healthier You: National Health Service Diabetes Prevention Program (NHS DPP), the largest DPP globally to achieve universal population coverage.

Research Design and Methods: A service evaluation assessed intervention effectiveness for adults with nondiabetic hyperglycemia (HbA1c 42-47 mmol/mol [6.0-6.4%] or fasting plasma glucose 5.5-6.9 mmol/L) between program launch in June 2016 and December 2018, using prospectively collected, national service-level data in England.

Results: By December 2018, 324,699 people had been referred, 152,294 had attended the initial assessment, and 96,442 had attended at least 1 of 13 group-based intervention sessions. Allowing sufficient time to elapse, 53% attended an initial assessment, 36% attended at least one group-based session, and 19% completed the intervention (attended >60% of sessions). Of the 32,665 who attended at least one intervention session and had sufficient time to finish, 17,252 (53%) completed: Intention-to-treat analyses demonstrated a mean weight loss of 2.3 kg (95% CI 2.2, 2.3 kg) and an HbA1c reduction of 1.26 mmol/mol (1.20, 1.31 mmol/mol) (0.12% [0.11, 0.12%]); completer analysis demonstrated a mean weight loss of 3.3 kg (3.2, 3.4 kg) and an HbA1c reduction of 2.04 mmol/mol (1.96, 2.12 mmol/mol) (0.19% [0.18, 0.19%]). Younger age, female sex, Asian and black ethnicity, lower socioeconomic status, and normal baseline BMI were associated with less weight loss. Older age, female sex, black ethnicity, lower socioeconomic status, and baseline overweight and obesity were associated with a smaller HbA1c reduction.

Conclusions: Reductions in weight and HbA1c compare favorably with those reported in recent meta-analyses of pragmatic studies and suggest likely future reductions in participant type 2 diabetes incidence.

Title: Cost-effectiveness of the SLIMMER diabetes prevention intervention in Dutch primary health care: economic evaluation from a randomised controlled trial.

Citation: BMC health services research; Nov 2019; vol. 19 (no. 1); p. 824
Author(s): Duijzer, Geerke; Bukman, Andrea J; Meints-Groenveld, Aafke; Haveman-Nies, Annemien; Jansen, Sophia C; Heinrich, Judith; Hiddink, Gerrit J; Feskens, Edith J M; de Wit, G Ardine

Background: Although evidence is accumulating that lifestyle modification may be cost-effective in patients with prediabetes, information is limited on the cost-effectiveness of interventions implemented in public health and primary health care settings. Evidence from well-conducted pragmatic trials is needed to gain insight into the realistic cost-effectiveness of diabetes prevention
interventions in real-world settings. The aim of this study is to assess the cost-effectiveness of the SLIMMER lifestyle intervention targeted at patients at high risk of developing type 2 diabetes compared with usual health care in a primary care setting in the Netherlands.

**Methods:** Three hundred and sixteen high-risk subjects were randomly assigned to the SLIMMER lifestyle intervention or to usual health care. Costs and outcome assessments were performed at the end of the intervention (12 months) and six months thereafter (18 months). Costs were assessed from a societal perspective. Patients completed questionnaires to assess health care utilisation, participant out-of-pocket costs, and productivity losses. Quality Adjusted Life Years (QALY) were calculated based on the SF-36 questionnaire. Cost-effectiveness planes and acceptability curves were generated using bootstrap analyses.

**Results:** The cost-effectiveness analysis showed that the incremental costs of the SLIMMER lifestyle intervention were €547 and that the incremental effect was 0.02 QALY, resulting in an incremental cost-effectiveness ratio (ICER) of €28,094/QALY. When cost-effectiveness was calculated from a health care perspective, the ICER decreased to €13,605/QALY, with a moderate probability of being cost-effective (56% at a willingness to pay, WTP, of €20,000/QALY and 81% at a WTP of €80,000/QALY).

**Conclusions:** The SLIMMER lifestyle intervention to prevent type 2 diabetes had a low to moderate probability of being cost-effective, depending on the perspective taken.

**Trial Registration:** The SLIMMER study is retrospectively registered with ClinicalTrials.gov (Identifier NCT02094911) since March 19, 2014.

---

**Title:** Insulin degludec/liraglutide (IDegLira) maintains glycaemic control and improves clinical outcomes, regardless of pre-trial insulin dose, in people with type 2 diabetes that is uncontrolled on basal insulin.

**Citation:** Diabetic medicine : a journal of the British Diabetic Association; Nov 2019

**Author(s):** Meneghini, L; Doshi, A; Gouet, D; Vilsbøll, T; Begtrup, K; Örsy, P; Ranthe, M Flyvholm; Lingvay, I

**Aims:** To assess whether people with type 2 diabetes transferring from higher basal insulin doses (> 20 units) to a starting dose of 16 units of insulin degludec/liraglutide (IDegLira) benefit from IDegLira with/without transient loss of glycaemic control.

**Methods:** Post hoc analysis of DUAL V and VII assessed fasting self-measured blood glucose (SMBG) over weeks 1-8, changes in HbA1c, body weight and mean insulin dose over 26 weeks, and percentage of participants achieving HbA1c < 53 mmol/mol (7.0%) by end of trial in participants with Type 2 diabetes uncontrolled with basal insulin. IDegLira was compared with continued up-titration of insulin glargine (IGlar U100) in DUAL V, or switching to basal-bolus therapy in DUAL VII (IGlar U100 and insulin aspart), across pre-trial insulin dose groups (20-29, 30-39 and 40-50 units/day).

**Results:** In all subgroups, participants treated with IDegLira experienced significant improvements in HbA1c by end of trial, which were greater than with IGlar U100 up-titration (estimated treatment difference -5.86, -6.59 and -6.91 mmol/mol for pre-trial insulin doses of 20-29, 30-39 and 40-50 units/day, respectively) and similar to basal-bolus therapy (estimated treatment difference -0.16, -1.0 and -0.01 mmol/mol for pre-trial insulin doses of 20-29, 30-39 and 40-50 units/day, respectively). Compared with IGlar U100 and basal-bolus therapy, IDegLira participants experienced weight loss vs. weight gain, lower rates of hypoglycaemia and a lower mean end of trial daily insulin dose. In both trials, mean fasting SMBG decreased from weeks 1 to 8 across all subgroups, despite a temporary increase in mean fasting SMBG in the 40-50 units pre-trial insulin dose group during week 1 [mean increase (sd) +1.1 (2.0) mmol/l for DUAL V and +1.1 (2.1) mmol/l for DUAL VII], which reverted to baseline by week 4.

**Conclusions:** Regardless of pre-trial insulin dose, IDegLira resulted in improved clinical outcomes, even in participants transferring from 40-50 units of basal insulin, despite a transient (< 4 weeks), clinically non-relevant, elevation in pre-breakfast SMBG.
Title: Benefits and harms of intensive glycemic control in patients with type 2 diabetes.

Citation: BMJ (Clinical research ed.); Nov 2019; vol. 367 ; p. l5887

Author(s): Rodriguez-Gutierrez, René; Gonzalez-Gonzalez, José Gerardo; Zuñiga-Hernandez, Jorge A; McCoy, Rozalina G

Abstract: Diabetes is a major and costly health concern worldwide, with high morbidity, disability, mortality, and impaired quality of life. The vast majority of people living with diabetes have type 2 diabetes. Historically, the main strategy to reduce complications of type 2 diabetes has been intensive glycemic control. However, the body of evidence shows no meaningful benefit of intensive (compared with moderate) glycemic control for microvascular and macrovascular outcomes important to patients, with the exception of reduced rates of non-fatal myocardial infarction. Intensive glycemic control does, however, increase the risk of severe hypoglycemia and incurs additional burden by way of polypharmacy, side effects, and cost. Additionally, data from cardiovascular outcomes trials showed that cardiovascular, kidney, and mortality outcomes may be improved with use of specific classes of glucose lowering drugs largely independently of their glycemic effects. Therefore, delivering evidence based, patient centered care to people with type 2 diabetes requires a paradigm shift and departure from the predominantly glucocentric view of diabetes management. Instead of prioritizing intensive glycemic control, the focus needs to be on ensuring access to adequate diabetes care, aligning glycemic targets to patients’ goals and situations, minimizing short term and long term complications, reducing the burden of treatment, and improving quality of life.

Title: SGLT2 inhibitors for the prevention of kidney failure in patients with type 2 diabetes: a systematic review and meta-analysis.

Citation: The lancet. Diabetes & endocrinology; Nov 2019; vol. 7 (no. 11); p. 845-854

Author(s): Neuen, Brendon L; Young, Tamara; Heerspink, Hiddo J L; Neal, Bruce; Perkovic, Vlado; Billot, Laurent; Mahaffey, Kenneth W; Charytan, David M; Wheeler, David C; Arnott, Clare; Bompoint, Severine; Levin, Adeera; Jardine, Meg J

Background: The effects of sodium-glucose co-transporter-2 (SGLT2) inhibitors on kidney failure, particularly the need for dialysis or transplantation or death due to kidney disease, is uncertain. Additionally, previous studies have been underpowered to robustly assess heterogeneity of effects on kidney outcomes by different levels of estimated glomerular filtration rate (eGFR) and albuminuria. We aimed to do a systematic review and meta-analysis to assess the effects of SGLT2 inhibitors on major kidney outcomes in patients with type 2 diabetes and to determine the consistency of effect size across trials and different levels of eGFR and albuminuria.

Methods: We did a systematic review and meta-analysis of randomised, controlled, cardiovascular or kidney outcome trials of SGLT2 inhibitors that reported effects on major kidney outcomes in people with type 2 diabetes. We searched MEDLINE and Embase from database inception to June 14, 2019, to identify eligible trials. The primary outcome was a composite of dialysis, transplantation, or death due to kidney disease. We used random-effects models to obtain summary relative risks (RRs) with 95% CIs and random-effects meta-regression to explore effect modification by subgroups of baseline eGFR, albuminuria, and use of renin-angiotensin system (RAS) blockade. This review is registered with PROSPERO (CRD42019131774).

Findings: From 2085 records identified, four studies met our inclusion criteria, assessing three SGLT2 inhibitors: empagliflozin (EMPA-REG OUTCOME), canagliflozin (CANVAS Program and CREDENCE), and dapagliflozin (DECLARE-TIMI 58). From a total of 38 723 participants, 252 required dialysis or transplantation or died of kidney disease, 335 developed end-stage kidney disease, and 943 had acute kidney injury. SGLT2 inhibitors substantially reduced the risk of dialysis, transplantation, or death due to kidney disease (RR 0·67, 95% CI 0·52-0·86, p=0·0019), an effect consistent across studies (I²=0%, pheterogeneity=0·53). SGLT2 inhibitors also reduced end-stage kidney disease (0·65, 0·53-0·81, p=0·0001), and acute kidney injury (0·75, 0·66-0·85, p<0·0001), with consistent benefits across studies. Although we identified some evidence that the proportional effect of SGLT2 inhibitors might attenuate with declining kidney function (ptrend=0·073), there was clear,
separate evidence of benefit for all eGFR subgroups, including for participants with a baseline eGFR 30-45 mL/min per 1·73 m² (RR 0·70, 95% CI 0·54-0·91, p=0·0080). Renoprotection was also consistent across studies irrespective of baseline albuminuria (ptrend=0·66) and use of RAS blockade (pheterogeneity=0·31).

**Interpretation:** SGLT2 inhibitors reduced the risk of dialysis, transplantation, or death due to kidney disease in individuals with type 2 diabetes and provided protection against acute kidney injury. These data provide substantive evidence supporting the use of SGLT2 inhibitors to prevent major kidney outcomes in people with type 2 diabetes.

**Funding:** None.

---

**Title:** Prevention of Type 2 Diabetes by Lifestyle Changes: A Systematic Review and Meta-Analysis.

**Citation:** Nutrients; Nov 2019; vol. 11 (no. 11)

**Author(s):** Uusitupa, Matti; Khan, Tauseef A; Viguiliouk, Effie; Kahleova, Hana; Rivellese, Angela A; Hermansen, Kjeld; Pfeiffer, Andreas; Thanopoulou, Anastasia; Salas-Salvadó, Jordi; Schwab, Ursula; Sievenpiper, John L

**Abstract:** Prevention of type 2 diabetes (T2D) is a great challenge worldwide. The aim of this evidence synthesis was to summarize the available evidence in order to update the European Association for the Study of Diabetes (EASD) clinical practice guidelines for nutrition therapy. We conducted a systematic review and, where appropriate, meta-analyses of randomized controlled trials (RCTs) carried out in people with impaired glucose tolerance (IGT) (six studies) or dysmetabolism (one study) to answer the following questions: What is the evidence that T2D is preventable by lifestyle changes? What is the optimal diet (with a particular focus on diet quality) for prevention, and does the prevention of T2D result in a lower risk of late complications of T2D? The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was applied to assess the certainty of the trial evidence. Altogether seven RCTs (N = 4090) fulfilled the eligibility criteria and were included in the meta-analysis. The diagnosis of incident diabetes was based on an oral glucose tolerance test (OGTT). The overall risk reduction of T2D by the lifestyle interventions was 0.53 (95% CI 0.41; 0.67). Most of the trials aimed to reduce weight, increase physical activity, and apply a diet relatively low in saturated fat and high in fiber. The PREDIMED trial that did not meet eligibility criteria for inclusion in the meta-analysis was used in the final assessment of diet quality. We conclude that T2D is preventable by changing lifestyle and the risk reduction is sustained for many years after the active intervention (high certainty of evidence). Healthy dietary changes based on the current recommendations and the Mediterranean dietary pattern can be recommended for the long-term prevention of diabetes. There is limited or insufficient data to show that prevention of T2D by lifestyle changes results in a lower risk of cardiovascular and microvascular complications.

---

**Title:** Effectiveness of Shared Decision-making for Diabetes Prevention: 12-Month Results from the Prediabetes Informed Decision and Education (PRIDE) Trial.

**Citation:** Journal of general internal medicine; Nov 2019; vol. 34 (no. 11); p. 2652-2659

**Author(s):** Moin, Tannaz; Duru, O Kenrik; Turk, Norman; Chon, Janet S; Frosch, Dominick L; Martin, Jacqueline M; Jeffers, Kia Skrine; Castellon-Lopez, Yelba; Tseng, Chi-Hong; Norris, Keith; Mangione, Carol M

**Importance:** Intensive lifestyle change (e.g., the Diabetes Prevention Program) and metformin reduce type 2 diabetes risk among patients with prediabetes. However, real-world uptake remains low. Shared decision-making (SDM) may increase awareness and help patients select and follow through with informed options for diabetes prevention that are aligned with their preferences.

**Objective:** To test the effectiveness of a prediabetes SDM intervention. DESIGN Cluster randomized controlled trial.
**Setting:** Twenty primary care clinics within a large regional health system.

**Participants:** Overweight/obese adults with prediabetes (BMI ≥ 24 kg/m² and HbA1c 5.7-6.4%) were enrolled from 10 SDM intervention clinics. Propensity score matching was used to identify control patients from 10 usual care clinics.

**Intervention:** Intervention clinic patients were invited to participate in a face-to-face SDM visit with a pharmacist who used a decision aid (DA) to describe prediabetes and four possible options for diabetes prevention: DPP, DPP ± metformin, metformin only, or usual care.

**Main Outcomes and Measures:** Primary endpoint was uptake of DPP (≥ 9 sessions), metformin, or both strategies at 4 months. Secondary endpoint was weight change (lbs.) at 12 months.

**Results:** Uptake of DPP and/or metformin was higher among SDM participants (n = 351) than controls receiving usual care (n = 1028; 38% vs. 2%, p < .001). At 12-month follow-up, adjusted weight loss (lbs.) was greater among SDM participants than controls (-5.3 vs. -0.2, p < .001).

**Limitations:** Absence of DPP supplier participation data for matched patients in usual care clinics.

**Conclusions And Relevance:** A prediabetes SDM intervention led by pharmacists increased patient engagement in evidence-based options for diabetes prevention and was associated with significantly greater uptake of DPP and/or metformin at 4 months and weight loss at 12 months. Prediabetes SDM may be a promising approach to enhance prevention efforts among patients at increased risk.

**Trial Registration:** This study was registered at clinicaltrials.gov (NCT02384109)).

---

**Title:** Glycemic Control and Insulin Treatment Alter Fracture Risk in Older Men With Type 2 Diabetes Mellitus.

**Citation:** Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research; Nov 2019; vol. 34 (no. 11); p. 2045-2051

**Author(s):** Lee, Richard H; Sloane, Richard; Pieper, Carl; Lyles, Kenneth W; Adler, Robert A; Van Houtven, Courtney; LaFleur, Joanne; Colón-Emeric, Cathleen

**Abstract:** Diabetes mellitus among older men has been associated with increased bone mineral density but paradoxically increased fracture risk. Given the interactions among medication treatment, glycemic control, and diabetes-associated comorbidities, the relative effects of each factor remains unclear. This retrospective study includes 652,901 male veterans aged ≥65 years with diabetes and baseline hemoglobin A1c (HbA1c) value. All subjects received primary care in the Veterans Health Administration (VHA) from 2000 to 2010. Administrative data included ICD9 diagnoses and pharmacy records and was linked to Medicare fee-for-service data. Hazard ratios (HR) for any clinical fracture and hip fracture were calculated using competing risk hazards models, adjusted for fracture risk factors including age, race/ethnicity, body mass index (BMI), alcohol and tobacco use, rheumatoid arthritis, corticosteroid use, as well as diabetes-related comorbidities including cardiovascular disease, chronic kidney disease, and peripheral neuropathy. HbA1c <6.5% was associated with a higher risk of any clinical fracture (HR = 1.08, 95% confidence interval [CI] 1.06-1.11) compared with the reference HbA1c of 7.5% to 8.5%. Fracture risk was not increased among those with A1c ≥8.5%, nor among those with A1c 6.5% to 7.5%. Use of insulin was independently associated with greater risk of fracture (HR = 1.10, 95% CI 1.07-1.12). There was a significant interaction between insulin use and HbA1c level, (p < 0.001), such that those using insulin with HbA1c <6.5% had HR = 1.23 and those with HbA1c 6.5% to 7.5% had HR = 1.15. Metformin use was associated with decreased fracture risk (HR = 0.88, 95% CI 0.87-0.90). We conclude that among older men with diabetes, those with HbA1c lower than 6.5% are at increased risk for any clinical and hip fracture. Insulin use is associated with higher fracture risk, especially among those with tight glycemic control. Our findings demonstrate the importance of the treatment regimen and avoiding hypoglycemia for fracture prevention in older men with diabetes. © 2019 American Society for Bone and Mineral Research.
Title: GLP-1 receptor agonists for prevention of cardiorenal outcomes in type 2 diabetes: An updated meta-analysis including the REWIND and PIONEER 6 trials.

Citation: Diabetes, obesity & metabolism; Nov 2019; vol. 21 (no. 11); p. 2576-2580
Author(s): Giugliano, Dario; Maiorino, Maria Ida; Bellastella, Giuseppe; Longo, Miriam; Chiodini, Paolo; Esposito, Katherine

Abstract: A meta-analysis of cardiovascular outcome trials (CVOTs) comparing glucagon-like peptide-1 receptor agonists (GLP-1RAs) and placebo concerning cardiorenal outcomes in patients with type 2 diabetes (T2D) is presented. An electronic search without language restrictions up to June 15, 2019 was conducted to determine eligible trials. A meta-analysis of available trial data was undertaken, using a random-effects model to calculate overall hazard ratios (HRs) and 95% confidence intervals (CIs). Data from seven CVOTs, comprising 56,004 patients (68.9% with established cardiovascular disease) were included. GLP-1RA reduced major cardiovascular events (MACE) by 13% (HR, 0.87; 95% CI, 0.80-0.96; P = 0.011) with a non-significant heterogeneity between subgroups of patients with and without cardiovascular disease (CVD) (P = 0.220). GLP-1RA also reduced the risk of cardiovascular death by 12%, of non-fatal stroke by 16%, of hospitalization for heart failure by 9%, of all-cause mortality by 11%, and the broad composite kidney outcome by 17%; the latter appeared to be driven only by a reduction in macroalbuminuria (HR, 0.76 [0.68-0.86]; P = 0.003). GLP-1RAs have moderate benefits concerning MACE, and also reduce hospitalization for heart failure and all-cause mortality; they also robustly reduce the incidence of macroalbuminuria, without affecting the progression of diabetic renal disease.

Title: Durability of glycaemic control with dapagliflozin, an SGLT2 inhibitor, compared with saxagliptin, a DPP4 inhibitor, in patients with inadequately controlled type 2 diabetes.

Citation: Diabetes, obesity & metabolism; Nov 2019; vol. 21 (no. 11); p. 2564-2569
Author(s): Bailey, Clifford J; Del Prato, Stefano; Wei, Cheryl; Reyner, Daniel; Saraiva, Gabriela

Abstract: Dapagliflozin is associated with greater reductions in HbA1c and weight than saxagliptin in management of type 2 diabetes mellitus (T2DM). The present post hoc analyses compared the durability of these effects over short- and long-term follow-up in patients with T2DM who were inadequately controlled with metformin (≥1500 mg/day) and who were receiving either dapagliflozin (10 mg/day) or saxagliptin (5 mg/day). Failure of glycaemic control was assessed using the slope of the change in HbA1c from baseline-over-time regression line (coefficient of failure [CoF]). CoF was compared directly (dapagliflozin vs saxagliptin) over the short term (NCT01606007, 24 weeks) and indirectly (placebo-adjusted) over the long term (NCT00528879 and NCT00121667, 102 weeks). A low CoF value indicated greater durability. CoF was lower for dapagliflozin versus saxagliptin over 18-24 weeks (-1.38%/year; 95% CI, -2.41 to -0.35; P = .009) and 20-102 weeks (-0.37%/year; 95% CI, -0.73 to -0.02; P = .04). Fewer dapagliflozin-treated patients versus saxagliptin-treated patients required rescue medication or discontinued the study because of failure to achieve glycaemic control at 24 weeks (3.4% vs 9.4%; P = .0191). In patients with T2DM who were inadequately controlled with metformin, dapagliflozin was associated with greater durability of glycaemic control than saxagliptin over 18-24 and 20-102 weeks.

Title: Efficacy and safety of linagliptin to improve glucose control in older people with type 2 diabetes on stable insulin therapy: A randomized trial.

Citation: Diabetes, obesity & metabolism; Nov 2019; vol. 21 (no. 11); p. 2465-2473
Author(s): Ledesma, Gilbert; Umpierrez, Guillermo E; Morley, John E; Lewis-D’Agostino, Diane; Keller, Annett; Meinicke, Thomas; van der Walt, Sandra; von Eynatten, Maximilian
**Aim:** To assess the addition of linagliptin as an alternative to insulin uptitration in older people with type 2 diabetes on stable insulin therapy.

**Materials And Methods:** This phase 4, randomized, multicentre, double-blinded, placebo-controlled, 24-week study recruited individuals on stable insulin, with baseline HbA1c 7.0%-10.0%, aged ≥60 years and body mass index ≤45 kg/m². HbA1c and fasting plasma glucose were measured at study visits, and participants assessed glycaemic control with a self-monitoring blood glucose device. Adverse events (AEs) were reported during the study.

**Results:** Three hundred and two participants were randomized 1:1 to linagliptin 5 mg qd and placebo, with one third of patients from Japan. Study population age and HbA1c (baseline mean ± SD) were 72.4 ± 5.4 years and 8.2 ± 0.8%, respectively; ~80% of participants were aged ≥70 years; 80% had macrovascular complications, one third had a baseline estimated glomerular filtration rate 15 years. Linagliptin significantly improved glucose control at 24 weeks (HbA1c-adjusted mean change vs. placebo: -0.63%; P <0.0001) and the probability of achieving predefined HbA1c targets without hypoglycaemia (HbA1c <8.0%; OR 2.02; P <0.05 and HbA1c <7.0%; OR 2.44; P <0.01). Linagliptin versus placebo was well tolerated, with similar incidences of AEs, including clinically important hypoglycaemia (blood glucose <54 mg/dL) or severe hypoglycaemia.

**Conclusions:** Addition of linagliptin improves glucose control without an excess of hypoglycaemia in older patients with type 2 diabetes on stable insulin therapy.

---

**Title:** Effectiveness of short message service intervention to improve glycated hemoglobin control and medication adherence in type-2 diabetes: A meta-analysis of prospective studies.

**Citation:** Primary care diabetes; Oct 2019

**Author(s):** Zhuang, Qianling; Chen, Fengmei; Wang, Ting

**Background:** Distance education or reminder by texting short message may improve HbA1c level and medication adherence to type-2 diabetes.

**Methods:** Electronic databases (PubMed, EBSCO, Elsevier, Springer, Wiley, and Cochrane) were searched systematically for published studies up to Mar 2019. SMD and 95% confidence interval (CI) were used to evaluate the intervention effect on HbA1c level and medication adherence. The heterogeneity of the study was estimated with the I2 statistic. The publication bias was described by Beggs’ test, Egger’s test and plot.

**Results:** Ten studies with 380 interventions and 275 controls were included in this meta-analysis. The Hba1c overall SMD was -0.49%, 95% CI -0.75 to 0.22%, and the overall SMD was 0.96%, 95% CI 0.45-1.47 for medication adherence. The I2 and P were 64.90%, 0.002 and 56.40%, 0.10 respectively for Hba1c level and medication adherence.

**Conclusion:** SMS intervention was effective for HbA1c level and medication adherence according to this study for T2DM over first 6 months.

---

**Title:** The Role of Diet in the Prevention of Diabetes among Women with Prior Gestational Diabetes: A Systematic Review of Intervention and Observational Studies.

**Citation:** Journal of the Academy of Nutrition and Dietetics; Oct 2019

**Author(s):** D'Arcy, Ellie; Rayner, Jessica; Hodge, Allison; Ross, Lynda J; Schoenaker, Danielle A J M

**Background:** Women with prior gestational diabetes (GDM) have an increased lifetime risk of developing type 2 diabetes mellitus (T2DM). There are no up-to-date systematic reviews analyzing the relationship of diet with risk of developing T2DM following GDM.

**Objective:** To systematically review the evidence from intervention and observational studies on effects of dietary interventions and associations of dietary intake with T2DM outcomes in women with a GDM history.
Methods: Six electronic databases were searched (Cumulative Index to Nursing and Allied Health Literature, Embase, Medline, Cochrane Central, Proquest, and Scopus) for articles published until May 2019. This review includes intervention and observational studies among women of any age with a history of GDM that reported on the effects of dietary interventions or association of dietary intake (energy, nutrients, foods, dietary patterns) with T2DM, impaired glucose tolerance, impaired fasting glucose, or prediabetes.

Results: The systematic review identified five articles reporting results from four intervention studies, and seven articles reporting results from four observational studies. Findings from intervention studies indicated trends toward beneficial effects of a low-glycemic index diet, a low-carbohydrate diet, and a diet in line with general population dietary guidelines, but studies had unclear or high risk of bias. Findings from two cross-sectional and one prospective study indicated poorer diabetes outcomes for women with higher intakes of branched-chain amino acids, total and heme iron, and a diet relatively low in carbohydrates and high in animal fat and protein, and better outcomes among those consuming diets rich in fruit, vegetables, nuts, fish, and legumes, and low in red and processed meats and sugar-sweetened beverages, after adjustment for confounders, including body mass index.

Conclusions: Findings from observational studies support current dietary guidelines for the prevention of T2DM. Further dietary intervention studies are needed to confirm whether or not dietary modification following a GDM pregnancy reduces women's risk of developing T2DM.

Title: Effectiveness of a Social Media–Based, Health Literacy–Sensitive Diabetes Self-Management Intervention: A Randomized Controlled Trial

Citation: Journal of Nursing Scholarship; Nov 2019; vol. 51 (no. 6); p. 661

Author(s): Kim, Su Hyun, PhD, RN; Utz, Sonja, PhD

Aims: The purpose of the study was to evaluate the effects of a social media-based, health literacy-sensitive diabetes management intervention on patient activation, self-care behaviors, and glucose control compared to telephone-based, health literacy-sensitive diabetes management intervention and usual care. Additionally, this study aimed to identify how patient health literacy influenced the effectiveness of health literacy-sensitive diabetes management interventions.

Design: 3 (treatment condition) x 2 (health literacy level) randomized factorial trial.

Methods: In total, 151 patients diagnosed with type 2 diabetes were randomly assigned to the social media-based or telephone-based, health literacy-sensitive diabetes management interventions or the usual care control. The health literacy-sensitive diabetes management intervention consisted of an initial face-to-face diabetes nurse education using easy-to-read educational materials, the teach-back method, and eight weekly action-planning sessions guided with the use of social media or phone calls for each group.

Findings: Patients with high health literacy at the 9-week follow-up showed higher levels of patient activation than those with low health literacy in the control group, but the effect of health literacy was no longer significant when patients were provided with social media-based or telephone-based interventions. Patients who received the telephone-based, health literacy-sensitive diabetes management intervention had a significantly higher score for self-care behaviors than the usual care control group at 9 weeks’ followup. No other effects for self-care behaviors or glycated hemoglobin were significant at follow-up.

Conclusions: The social media-based, health literacy-sensitive diabetes management intervention was effective at mitigating the disadvantages faced by people with low health literacy when attempting to improve self-care activation. Clinical Relevance: Social media-based self-management interventions accommodating low health literacy have the potential to help people overcome their disadvantages associated with low health literacy.

Title: Cost-effectiveness analysis of empagliflozin treatment in people with Type 2 diabetes and established cardiovascular disease in the EMPA-REG OUTCOME trial.

Citation: Diabetic Medicine; Nov 2019; vol. 36 (no. 11); p. 1494-1502
**Author(s):** Kansal, A.; Reifsnider, O. S.; Proskorovsky, I.; Zheng, Y.; Pfarr, E.; George, J. T.; Kandaswamy, P.; Ruffolo, A.

**Aim:** In the EMPA-REG OUTCOME trial, empagliflozin therapy reduced cardiovascular death by 38% compared with placebo when added to standard of care. Using the trial results, we created a discrete-event simulation model to assess lifetime health economic outcomes in people with Type 2 diabetes and established cardiovascular disease.

**Methods:** Time-dependent survival regression analysis was performed on data from EMPA-REG OUTCOME for 10 cardiovascular and renal events (e.g. stroke, heart failure hospitalization, macroalbuminuria, cardiovascular mortality) to capture event rates over time, and interaction between events. Model performance was assessed by comparing predicted and observed outcomes at 3 years. Costs in the United Kingdom (UK) and health utilities were obtained from published literature. Outcomes included cumulative event rates, life-years, costs and quality-adjusted life-years (QALYs).

**Results:** The model predicted an 18% relative increase (by 2.1 life-years) in survival for empagliflozin (14.0 life-years) vs. standard of care (11.9 life-years), attributable to direct treatment effect on cardiovascular mortality, and to indirect effect via reductions in other events. Participants treated with empagliflozin may experience improved quality of life (1.0 QALY) and higher costs (£3737/participant), yielding an incremental cost-effectiveness ratio (ICER) of £4083/QALY. Sensitivity analyses confirmed the robustness of these results to changes in input parameters.

**Conclusions:** Based on extrapolation of EMPA-REG OUTCOME trial data using a participant-level simulation model, empagliflozin in addition to standard of care is projected to be highly cost-effective using UK healthcare costs. The impact in other countries will vary due to differences in drug pricing and accrual of other costs. (Clinical Trial Registry No: NCT01131676) What's new?: The sodium–glucose co-transporter 2 inhibitor empagliflozin has been shown to mitigate cardiovascular risk and cardiovascular death in people with Type 2 diabetes with established cardiovascular disease. An economic model was developed to extrapolate the outcomes of empagliflozin plus standard of care compared with standard of care alone over peoples' remaining lifetime in the United Kingdom. Patient-level data from EMPA-REG OUTCOME were analysed to generate time-to-event distributions for 10 cardiovascular and renal outcomes, including myocardial infarction, stroke, heart failure hospitalization, development of chronic kidney disease and cardiovascular mortality. Empagliflozin may have a positive benefit for people at costs acceptable to payers.

**Title:** Glycaemic, weight, and blood pressure changes associated with early versus later treatment intensification with dapagliflozin in United Kingdom primary care patients with type 2 diabetes mellitus.

**Citation:** Diabetes Research & Clinical Practice; Sep 2019; vol. 155

**Author(s):** Wilding, John P.H.; Rigney, Una; Blak, Betina T.; Nolan, Stephen T.; Fenici, Peter; Medina, Jesús

**Aims:** Early treatment intensification for type 2 diabetes mellitus (T2DM) is often required to achieve glycaemic control and avoid longer-term complications. We assessed associations between early versus later dapagliflozin initiation with changes in glucose control, weight, and blood pressure using UK Clinical Practice Research Datalink (CPRD) data.

**Methods:** People with T2DM aged ≥18 years, initiating dapagliflozin between November 2012 and August 2016 and with prior oral T2DM therapy (N = 3774), were included. The relationship between early (first intensification after metformin or sulfonylurea monotherapy) and later (second or higher-order intensification) dapagliflozin use and baseline changes in glycated haemoglobin A1c (HbA1c; ≥1.0% absolute reduction), weight (≥5.0% relative loss), and systolic blood pressure (SBP; ≥2 mmHg absolute reduction) after 6-12 months were assessed.

**Results:** Overall, 25% of patients (951 of 3774) were early users and 75% (2823 of 3774) were later users. Later users were older, more likely to be men, and had longer disease duration. Early and later users had similar baseline mean HbA1c levels. For early versus later users, respectively, baseline-adjusted mean (95% confidence interval [CI]) reductions were 1.54% (-1.65, -1.44) versus 1.02% (-1.03, -1.01).
1.08, -0.97) in HbA1c, 3.31% (-4.37, -2.25) versus 4.06% (-5.05, -3.07) in weight, and 2.50 mm Hg (-3.89, -1.11) versus 2.84 mm Hg (-3.67, -2.01) in SBP. Early versus later use was associated with a greater likelihood of adjusted HbA1c reduction of ≥1% (odds ratio: 1.68, 95% CI: 1.15-2.45).

**Conclusions:** Glycaemic benefits were greater with early versus later dapagliflozin intensification. These results support broader and earlier dapagliflozin use.

---

**Title:** Tolerability and acceptability of real-time continuous glucose monitoring and its impact on diabetes management behaviours in individuals with Type 2 Diabetes - A pilot study.

**Citation:** Diabetes Research & Clinical Practice; Sep 2019; vol. 155

**Author(s):** Taylor, P.J.; Thompson, C.H.; Luscombe-Marsh, N.D.; Wycherley, T.P.; Wittert, G.; Brinkworth, G.D.; Zajac, I.

**Introduction:** Emerging evidence suggests use of real-time continuous glucose monitoring systems (RT-CGM), can assist to improve glucose control in Type 2 Diabetes (T2D) treatment, however the impact of these devices on patients’ stress levels and behaviour is poorly understood. This study aimed to examine the effects of RT-CGM on tolerance and acceptability of device wear, stress and diabetes management and motivation to change.

**Methods:** Twenty adults (10 men, 10 women) with T2D (aged 60.6 ± 8.4 years, BMI 34.2 ± 4.7 kg/m2), were randomised to a low-carbohydrate lifestyle plan whilst wearing a RT-CGM or an 'offline-blinded' (Blinded-CGM) monitoring system continuously for 12 weeks. Outcomes were glycaemic control (HbA1c), weight (kg) perceived stress scale (PSS), CGM device intolerance, acceptability, motivation to change and diabetes management behaviour questionnaires.

**Results:** Both groups experienced significant reductions in body weight (RT-CGM -7.4 ± 4.5 kg vs. Blinded-CGM -5.5 ± 4.0 kg) and HbA1c (-0.67 ± 0.82% vs. -0.68 ± 0.74%). There were no differences between groups for perceived stress (P = 0.47) or device intolerance at week 6 or 12 (both P > 0.30). However, there was evidence of greater acceptance of CGM in the RT-CGM group at week 12 (P = 0.03), improved blood glucose monitoring behaviour in the RT-CGM group at week 6 and week 12 (P ≤ 0.01), and a significant time x group interaction (P = 0.03) demonstrating improved diabetes self-management behaviours in RT-CGM.

**Conclusion:** This study provides preliminary evidence of improved behaviours that accompany RT-CGM in the context of diabetes management and glucose self-monitoring. RT-CGM may provide an alternative approach to glucose management in individuals with T2D without resulting in increased disease distress.

---

**Title:** Occurrence of First and Recurrent Major Adverse Cardiovascular Events With Liraglutide Treatment Among Patients With Type 2 Diabetes and High Risk of Cardiovascular Events: A Post Hoc Analysis of a Randomized Clinical Trial.

**Citation:** JAMA cardiology; Nov 2019

**Author(s):** Verma, Subodh; Bain, Stephen C; Buse, John B; Idorn, Thomas; Rasmussen, Søren; Ørsted, David D; Nauck, Michael A

**Importance:** After the occurrence of nonfatal cardiovascular events, recurrent events are highly likely. Most cardiovascular outcomes trials analyze first events only; extending analyses to first and recurrent (total) events can provide clinically meaningful information.

**Objective:** To investigate whether liraglutide is associated with reduced first and recurrent total major adverse cardiovascular events (MACE) compared with placebo among patients with type 2 diabetes and high risk of cardiovascular events.

**Design, Setting, and Participants:** This post hoc analysis of the Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER) randomized, double-blind, clinical trial included data from patients with type 2 diabetes who had established or were at high risk for cardiovascular disease at 410 sites in 32 countries from August 2010, to December 2015. Data
Analysis was performed from August 15, 2016, to July 5, 2019. Interventions Patients were randomized 1:1 to receive liraglutide (up to 1.8 mg per day) or placebo, both with standard care, for 3.5 to 5.0 years.

**Main Outcomes and Measures:** Assessed outcomes were MACE (cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke), expanded MACE (primary MACE plus coronary revascularization and hospitalization for heart failure or unstable angina pectoris), and the individual end points.

**Results:** The 9340 LEADER trial participants (6003 [64.3%] male; mean [SD] age, 64.3 [7.2] years) experienced 1605 total MACE (1302 first and 303 recurrent events; median follow-up, 3.8 years [range, 0-5.2 years]). Patients who experienced any MACE were older (1 MACE: mean [SD] age, 65.6 [8.0] years; >1 MACE: 65.7 [7.9] years) and had diabetes for longer duration (1 MACE: mean [SD] duration, 13.4 [8.3] years; >1 MACE: 14.4 [8.7] years) compared with patients without MACE (mean [SD] age, 64.1 [7.1] years; mean [SD] duration, 12.7 [7.9] years). Fewer first and recurrent MACE occurred in the liraglutide group (n = 4668; 608 first and 127 recurrent events) than in the placebo group (n = 4672; 694 first and 176 recurrent events). Liraglutide was associated with a 15.7% relative risk reduction in total MACE (hazard ratio [HR], 0.84; 95% CI, 0.76-0.93) and a 13.4% reduction in the total expanded MACE (HR, 0.87; 95% CI, 0.81-0.93) compared with placebo. For most individual cardiovascular end points, liraglutide was associated with lower risk vs placebo.

**Conclusions and Relevance:** These results suggest that liraglutide treatment is associated with reduced total MACE compared with placebo among patients with type 2 diabetes and high risk of cardiovascular events. This analysis supports the findings of an absolute benefit of liraglutide treatment with respect to the overall burden of cardiovascular events in this high-risk patient population.

**Trial Registration:** ClinicalTrials.gov identifier: NCT01179048.

---

**Title:** Alirocumab therapy in individuals with type 2 diabetes mellitus and atherosclerotic cardiovascular disease: analysis of the ODYSSEY DM-DYSLIPIDEMIA and DM-INSULIN studies.

**Citation:** Cardiovascular diabetology; Nov 2019; vol. 18 (no. 1); p. 149

**Author(s):** Ray, Kausik K; Del Prato, Stefano; Müller-Wieland, Dirk; Cariou, Bertrand; Colhoun, Helen M; Tinahones, Francisco J; Domenger, Catherine; Letierce, Alexia; Mandel, Jonas; Samuel, Rita; Bujas-Bobanovic, Maja; Leiter, Lawrence A

**Background:** Individuals with diabetes often have high levels of atherogenic lipoproteins and cholesterol reflected by elevated low-density lipoprotein cholesterol (LDL-C), non-high-density lipoprotein cholesterol (non-HDL-C), apolipoprotein B (ApoB), and LDL particle number (LDL-PN). The presence of atherosclerotic cardiovascular disease (ASCVD) increases the risk of future cardiovascular events. We evaluated the efficacy and safety of the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor, alirocumab, among individuals with type 2 diabetes (T2DM), high LDL-C or non-HDL-C, and established ASCVD receiving maximally tolerated statin in ODYSSEY DM-DYSLIPIDEMIA (NCT02642159) and DM-INSULIN (NCT02585778).

**Method:** Sln DM-DYSLIPIDEMIA, individuals with T2DM and mixed dyslipidemia (non-HDL-C ≥ 100 mg/dL; n = 413) were randomized to open-label alirocumab 75 mg every 2 weeks (Q2W) or usual care (UC) for 24 weeks, with UC options selected before stratified randomization. In DM-INSULIN, insulin-treated individuals with T2DM (LDL-C ≥ 70 mg/dL; n = 441) were randomized in a double-blind fashion to alirocumab 75 mg Q2W or placebo for 24 weeks. Study participants also had a glycated hemoglobin < 9% (DM-DYSLIPIDEMIA) or < 10% (DM-INSULIN). Alirocumab dose was increased to 150 mg Q2W at week 12 if week 8 LDL-C was ≥ 70 mg/dL (DM-INSULIN) or non-HDL-C was ≥ 100 mg/dL (DM-DYSLIPIDEMIA). Lipid reductions and safety were assessed in patients with ASCVD from these studies.

**Results:** This analysis included 142 DM-DYSLIPIDEMIA and 177 DM-INSULIN participants with ASCVD, including 95.1% and 86.4% with coronary heart disease, and 32.4% and 49.7% with microvascular diabetes complications, respectively. At week 24, alirocumab significantly reduced LDL-C, non-HDL-C, ApoB, and LDL-PN from baseline versus control. This translated into a greater proportion of individuals achieving non-HDL-C < 100 mg/dL (64.6% alirocumab/23.8% UC [DM-DYSLIPIDEMIA]; 65.4% alirocumab/14.9% placebo [DM-INSULIN]) and ApoB < 80 mg/dL (75.1%...
Alirocumab/35.4% UC and 76.8% alirocumab/24.8% placebo, respectively versus control at week 24 (all P < 0.0001). In pooling these studies, 66.4% (alirocumab) and 67.0% (control) of individuals reported treatment-emergent adverse events. The adverse event pattern was similar with alirocumab versus controls.

Conclusions: Among individuals with T2DM and ASCVD who had high non-HDL-C/LDL-C levels despite maximally tolerated statin, alirocumab significantly reduced atherogenic cholesterol and LDL-PN versus control. Alirocumab was generally well tolerated. Trial registration Clinicaltrials.gov. NCT02642159. Registered 30 December 2015 and Clinicaltrials.gov. NCT02585778. Registered 23 October 2015.

Title: Pan-European Economic Analysis to Identify Cost Savings for the Health Care Systems as a Result of Integrating Glucose Monitoring Based Telemedical Approaches Into Diabetes Management.

Citation: Journal of diabetes science and technology; Nov 2019; vol. 13 (no. 6); p. 1112-1122

Author(s): Fritzen, Katharina; Basinska, Kornelia; Rubio-Almanza, Matilde; Nicolucci, Antonio; Kennon, Brian; Vergès, Bruno; Zakrzewska, Katerina; Schnell, Oliver

Background: Self-monitoring of blood glucose supported by the diabetes-app OneTouch Reveal® has demonstrated to improve HbA1c. We aimed at analyzing costs savings related the integration of telemedical features into diabetes management.

Methods: Data from a randomized controlled trial were used to assess the 10-year risk of patients for fatal myocardial infarction (MI). On the basis of this risk assessments-also related to a 5% or 10% reduction of hypoglycemic episodes-cost savings for the health care systems of five European countries-France, Germany, Italy, Spain, and the United Kingdom-were modeled.

Results: HbA1c reduction of 0.92% in insulin-treated type 2 diabetes patients (T2DM) was associated with a 2.3% decreased 10-year risk for fatal MI. In combination with a 10% reduction of hypoglycemic events this risk reduction led to cost savings of €16.1 million (France), €57.8 million (Germany), €30.9 million (Italy), €23.8 million (Spain), and €5.8 million (UK), considering all insulin-treated T2DM patients in the respective countries.

Conclusion: Improving metabolic control and thus risk for comorbidities like MI by combining the glucose meter with CRI with telemedical features has the potential to reduce costs for European health care systems.

Title: The effects of popular diets on type 2 diabetes management.

Citation: Diabetes/metabolism research and reviews; Nov 2019; vol. 35 (no. 8); p. e3188

Author(s): Chester, Brittannie; Babu, Jeganathan Ramesh; Greene, Michael W; Geetha, Thangiah

Abstract: Type 2 diabetes can be managed with the use of diabetes self-management skills. Diet and exercise are essential segments of the lifestyle changes necessary for diabetes management. However, diet recommendations can be complicated in a world full of different diets. This review aims to evaluate the evidence on the effects of three popular diets geared towards diabetes management: low-carbohydrate and ketogenic diet, vegan diet, and the Mediterranean diet. While all three diets have been shown to assist in improving glycaemic control and weight loss, patient adherence, acceptability, and long-term manageability play essential roles in the efficacy of each diet.

Title: An evidence-based approach to developing low-carbohydrate diets for type 2 diabetes management: A systematic review of interventions and methods.

Citation: Diabetes, obesity & metabolism; Nov 2019; vol. 21 (no. 11); p. 2513-2525

Author(s): Turton, Jessica; Brinkworth, Grant D; Field, Rowena; Parker, Helen; Rooney, Kieron
Aim: To identify core diet and delivery components of low-carbohydrate (CHO) diets that have demonstrated efficacy for type 2 diabetes (T2D) management.

Materials and Methods: MEDLINE, Pre-MEDLINE, EMBASE, CINAHL and the Cochrane Library of Controlled Trials databases were systematically searched from inception until August 18, 2018. Primary intervention studies of low-CHO diets (≤130 g/d or 26% total energy intake [TEI]) were included. Content analysis was performed on the low-CHO diet protocols classified as safe and effective for T2D management.

Results: A total of 41 studies published between 1963 and 2018 were included, of which 40 were classified as safe and effective for inclusion in the primary analysis. Thirteen studies (13/40) were on very-low-CHO diets (35% TEI). Twenty-six studies reported a prescribed dietary protein amount, of which 22 were unrestricted or were high-protein (>25% TEI). The types of dietary CHO, fat and protein recommended were predominantly whole foods. Common delivery methods reported were dietician and/or physician involvement, moderate to high frequency of contact (≥1 session/month) and use of participant self-monitoring.

Conclusions: Multiple approaches for developing and delivering a low-CHO diet intervention for T2D management are safe and effective. A comprehensive set of core dietary components to consider in the formulation of low-CHO diet protocols were identified for use in clinical practice and to inform evidence-based guidelines for T2D management.

Title: Treatment patterns and associated factors in 14 668 people with type 2 diabetes initiating a second-line therapy: Results from the global DISCOVER study programme.

Citation: Diabetes, obesity & metabolism; Nov 2019; vol. 21 (no. 11); p. 2474-2485

Author(s): Nicolucci, Antonio; Charbonnel, Bernard; Gomes, Marília B; Khunti, Kamlesh; Kosiborod, Mikhail; Shestakova, Marina V; Shimomura, Ichiro; Watada, Hirotaka; Chen, Hungta; Cid-Ruzafa, Javier; Fenici, Peter; Hammar, Niklas; Surmont, Filip; Tang, Fengming; Pocock, Stuart

Aim: To evaluate treatment data from DISCOVER (NCT02322762 and NCT02226822), a global, prospective, observational study programme of patients with type 2 diabetes initiating a second-line glucose-lowering therapy.

Materials and Methods: Data were collected using a standardized case report form. First- and second-line treatments were assessed in 14 668 patients from 37 countries across six regions. Among patients prescribed first-line metformin monotherapy, Firth logistic regression models were used to assess factors associated with second-line treatment choices.

Results: The most common first-line therapies were metformin monotherapy (57.9%) and combinations of metformin with a sulphonylurea (14.6%). The most common second-line therapies were combinations of metformin with other agents (72.2%), including dipeptidyl peptidase-4 (DPP-4) inhibitors (25.1%) or sulphonylureas (21.3%). Among patients prescribed first-line metformin monotherapy, the most common second-line therapies were combinations of metformin with a DPP-4 inhibitor [32.8%; across-region range (ARR): 2.4%-51.3%] or a sulphonylurea (30.0%; ARR: 18.3%-63.6%); only a few patients received combinations of metformin with sodium-glucose co-transporter-2 inhibitors (6.7%; ARR: 0.0%-10.8%) or glucagon-like peptide-1 receptor agonists (1.9%; ARR: 0.1%-4.5%). Both clinical and non-medical factors were associated with choice of second-line therapy after metformin monotherapy.

Conclusions: Fewer patients than expected received metformin monotherapy at first line, and the use of newer therapies at second line was uncommon in some regions of the world. Patients’ socioeconomic status was associated with treatment patterns, suggesting that therapy choices are influenced by cost and access.

Title: Long-term efficacy and safety of combined insulin and glucagon-like peptide-1 therapy: Evidence from the LEADER trial.

Citation: Diabetes, obesity & metabolism; Nov 2019; vol. 21 (no. 11); p. 2450-2458
**Author(s):** Tack, Cees J; Jacob, Stephan; Desouza, Cyrus; Bain, Stephen C; Buse, John B; Nauck, Michael A; Petrie, John R; Poulter, Neil R; Pratley, Richard E; Stegmann, Helen Vanya B K; Bosch-Traberg, Heidrun; Startseva, Elena; Zinman, Bernard; LEADER Publication Committee on behalf of the LEADER Trial Investigators

**Aim:** Glucagon-like peptide-1 receptor agonist (GLP-1RA) and insulin combination therapy is an effective treatment option for type 2 diabetes, but long-term data are lacking. The aim was to assess the long-term efficacy of the GLP-1RA liraglutide in subgroups by insulin use in the LEADER trial.

**Materials and Methods:** LEADER assessed cardiovascular (CV) safety and efficacy of liraglutide (1.8 mg) versus placebo (plus standard of care therapy) in 9340 patients with type 2 diabetes and high risk of CV disease, for up to 5 years. We analyzed CV events, metabolic parameters and hypoglycaemia post hoc in three subgroups by baseline insulin use (basal-only insulin, other insulin or no insulin). Insulin was a non-random treatment allocation as part of standard of care therapy.

**Results:** At baseline, 5171 (55%) patients were not receiving insulin, 3159 (34%) were receiving basal-only insulin and 1010 (11%) other insulins. Insulin users had a longer diabetes duration and slightly worse glycaemic control (HbA1c) than the no-insulin subgroup. Liraglutide reduced HbA1c and weight versus placebo in all three subgroups (P < .001), and severe hypoglycaemia rate in the basal-only insulin subgroup. The need for insulin was less with liraglutide. CV risk reduction with liraglutide was similar to the main trial results in the basal-only and no-insulin subgroups.

**Conclusions:** In patients on insulin, liraglutide improved glycaemic control, weight and need for insulin versus placebo, for at least 36 months with no increased risk of severe hypoglycaemia, while maintaining CV safety/efficacy, supporting the combination of liraglutide and insulin for management of type 2 diabetes.

---

**Title:** The beneficial actions of SGLT-2 inhibitors beyond management of hyperglycemia.

**Citation:** Current medicinal chemistry; Oct 2019

**Author(s):** Loutradis, Charalampos; Papadopoulou, Eirini; Angeloudi, Elena; Karagiannis, Asterios; Sarafidis, Pantelis

**Abstract:** Type 2 diabetes mellitus (DM) is a public health burden and its co-existence with hypertension is long established in the context of the metabolic syndrome. Both DM and hypertension are major risk factors, for end-stage renal disease, cardiovascular events and mortality. Strict blood pressure (BP) control in diabetics has been associated with a cardiovascular and renal risk decrease. Inhibitors of the sodium-glucose co-transporter 2 (SGLT-2) in the proximal tubule is a relatively novel class of agents for treatment of type 2 DM. Inhibition of SGLT-2 co-transporter combines proximal tubule diuretic and osmotic diuretic action leading to glucose reabsorption reduction and mild natriuretic and diuretic effects. On this basis, several studies showed that treatment with SGLT-2 inhibitors can effectively decrease hyperglycemia but also increase BP control and reduce renal outcomes and cardiovascular mortality. Based on such evidence, the recent guidelines for the management of type 2 diabetes now suggest that SGLT-2 inhibitors should be preferred among oral agents in combination with metformin, in patients at increased cardiovascular risk, chronic kidney disease or heart failure. This review summarizes the existing data from studies evaluating the effect of SGLT-2 inhibitors on BP, and its potential value for cardio and nephroprotection.

---

**Title:** Benefit-Risk Assessment of Alogliptin for the Treatment of Type 2 Diabetes Mellitus.

**Citation:** Drug safety; Oct 2019

**Author(s):** Kaku, Kohei; Kisanuki, Koichi; Shibata, Mari; Oohira, Takashi

**Abstract:** The dipeptidyl peptidase-4 inhibitor (DPP-4i) alogliptin is an oral, antidiabetic treatment that is approved in many countries to treat patients with type 2 diabetes mellitus (T2DM), including the USA, Europe, and Japan. Alogliptin is efficacious both as monotherapy and as add-on/combination
therapy with other commonly prescribed T2DM treatments, such as metformin and pioglitazone. Overall, alogliptin is well-tolerated in patients with T2DM, including older patients, those with renal and/or hepatic impairment, and those at high risk of cardiovascular events. There is a low risk of hypoglycemia, weight gain, acute pancreatitis, and gastrointestinal adverse events with alogliptin treatment, as demonstrated in long-term trials (lasting up to 4.5 years) and in a real-world setting. Additionally, alogliptin has a generally favorable or similar safety profile in comparison to other antidiabetic agents (metformin, thiazolidinediones, sulfonylureas, glucagon-like peptide-1 receptor agonists, sodium-glucose cotransporter 2 inhibitors, α-glucosidase inhibitors, and insulin). However, further evaluation would be required to determine the mechanism and effect of alogliptin on heart failure, bullous pemphigoid, and inflammatory bowel disease. Of note, due to the ethnic diversity in the epidemiology of T2DM, alogliptin has been shown to be more efficacious in Asian patients than in non-Asian patients with T2DM, but with a similar tolerability profile. These data indicate that DPP-4is, including alogliptin, are important treatment options, especially for Asian patients with T2DM, for whom they have potential as a first-line therapy. This benefit-risk assessment aims to place alogliptin within the current armamentarium of T2DM and aid physicians when choosing optimal diabetes treatment for their patients.

**Sources Used:**

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

**Disclaimer:**

The results of your literature search are based on the request that you made, and consist of a list of references, some with abstracts. Royal United Hospital Bath Healthcare Library will endeavour to use the best, most appropriate and most recent sources available to it, but accepts no liability for the information retrieved, which is subject to the content and accuracy of databases, and the limitations of the search process. The library assumes no liability for the interpretation or application of these results, which are not intended to provide advice or recommendations on patient care.