Preventing type 2 diabetes: A role for pioglitazone?

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A number of studies have shown that the rate of conversion from impaired glucose tolerance (IGT) to T2D can be reduced with lifestyle modification, bariatric surgery, and acarbose, metformin and thiazolidinedione (TZD) medication (Alberti et al, 2007). In one study, the use of rosiglitazone decreased the risk of T2D in adults with IGT by 62% (DREAM [Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication] Trial Investigators et al, 2006). However, due to concerns about an increased risk of cardiovascular (CV) ischaemic events, the marketing authorisation for rosiglitazone was suspended in the EU in 2010. Pioglitazone is now the only TZD currently available in the EU. It has recently come off patent and the cost to the NHS is expected to drop as a result.

In the ACT NOW Study (DeFronzo et al, 2011; summarised alongside), 602 people aged ≥18 years in the USA with IGT were randomly allocated to receive pioglitazone or placebo. Both groups received 30 minutes of dietary instruction, which was reinforced at follow-up visits; median follow-up was 2.4 years. Fasting blood glucose levels were measured quarterly and oral glucose tolerance tests undertaken annually. Compared with placebo, pioglitazone treatment reduced the risk of conversion to T2D by 72%. Weight gain was 3.9 kg compared with 0.77 kg in the placebo group. Oedema occurred in 12.9% of people on pioglitazone compared with 6.4% on placebo. Withdrawal rates and baseline characteristics were similar in the two groups.

Pioglitazone treatment was associated with lower systolic blood pressure, higher levels of HDL-cholesterol, and reduced rates of carotid intima–media thickening compared with placebo. The authors suggest that pioglitazone may, therefore, provide some protection against the development of atherosclerotic CV disease.

Nine fractures occurred in the pioglitazone group compared with eight in the placebo group; all were associated with trauma. There was one case of congestive cardiac failure in each group. The number of participants that need to be treated for 1 year to prevent one case of T2D was 18.

This study shows that pioglitazone is the most effective therapy yet tested in preventing conversion to T2D in people with IGT. Lifestyle modification is likely to remain the cornerstone of T2D prevention, but when medication is needed, metformin and now pioglitazone have a good evidence base.

Alberti KG, Zimmet P, Shaw J (2007) International Diabetes Federation: a consensus on type 2 diabetes prevention. *Diabet Med* **24**: 451–63

DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators, Gerstein HC, Yusuf S et al (2006) Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. *Lancet* **368**: 1096–105

DIABETES CARE

Burden of diabetes in south Asian children and young people

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The authors explored the incidence of diabetes in all south Asian (SA) and non-SA children and young people aged 0–29 years in West Yorkshire.

2 Annual incidence per 100 000 and time trends were assessed in 2889 individuals diagnosed with diabetes between 1991 and 2006.

3 A total of 83% had T1D, 12% had T2D, 0.7% (n=19) had maturity-onset diabetes of the young, 0.1% (n=1 of each) had "J" type or other, and 4% uncertain/unclassified.

4 A lower incidence of T1D and a 3-fold excess of T2D was observed in SA compared with non-SA people. The incidence of T1D levelled out and T2D increased after the first SA person was diagnosed with T2D in 1999.

5 It was concluded that the burden of diabetes increased over time in both ethnic groups, with an excess of T2D in SA children and young people.

Harron KL, Feltbower RG, McKinney PA et al (2011) Rising rates of all types of diabetes in south Asian and non-south Asian children and young people aged 0-29 years in West Yorkshire, U.K., 1991-2006. *Diabetes Care* **34**: 652–4

NEW ENGLAND JOURNAL OF MEDICINE

Reduced progression from IGT to T2D with pioglitazone

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 This study was undertaken to examine whether the thiazolidinedione pioglitazone (Pio) can reduce the risk of T2D in adults with impaired glucose tolerance (IGT).

2 Participants (n=602) were randomised to receive Pio or placebo, and were followed-up for 2.4 years. Quarterly measurements for fasting blood glucose were taken, and oral glucose tolerance tests were undertaken annually.

3 Annual incidence rates for T2D were 2.1% and 7.6% in the Pio group and placebo group, respectively; hazard ratio for conversion to T2D in the Pio group was 0.28 (95% confidence interval [CI], 0.16–0.49; P<0.001).

4 Conversion to normal glucose tolerance was observed in 48% of the Pio group compared with 28% of the placebo group (P<0.001).

5 Compared with placebo, Pio treatment was associated with significantly reduced fasting blood glucose levels (P<0.001), 2-hour blood glucose levels (P<0.001) and HbA_{1c} levels (P<0.001).

6 Pio treatment was also associated with a decrease in diastolic blood pressure (P=0.03), a reduced rate of carotid intima–media thickening (P=0.047), and a greater increase in HDL-cholesterol (P=0.008).

7 The Pio group experienced greater weight gain (P<0.001) and more frequent oedema (P=0.007) than the placebo group.

8 The authors concluded that Pio reduced the risk of conversion from IGT to T2D, but was associated with weight gain and oedema.

DeFronzo RA, Tripathy D, Schwenke DC et al (2011) Pioglitazone for diabetes prevention in impaired glucose tolerance. *N Engl J Med* **364**: 1104–15

"Electronic feedback to GPs on the quality of T2D care provision resulted in significantly improved quality of care."

DIABETIC MEDICINE

Improved T2D care following electronic feedback to GPs

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 To evaluate the effect of an electronic feedback system to GPs on the quality of T2D care, the authors undertook a 15-month cluster randomised controlled trial.

2 Eighty-six general practices (totalling 158 GPs) with 2458 people with T2D (aged 40–70 years) were randomised to receive electronic feedback on the quality of care, or to receive no feedback.

3 Primary endpoints were processes of care according to guidelines on prescriptions for T2D treatments, measurement of HbA_{1c} and cholesterol levels, and ophthalmology visits.

4 Secondary endpoints were changes in HbA_{1c} level and serum cholesterol.

5 During follow-up, people with T2D in the intervention group redeemed recommended prescriptions significantly more often than those in the control group, respectively, for oral antidiabetes drugs (32.8 vs 12.0%; $P=0.002$), insulin therapy (33.8 vs 12.4%; $P<0.001$), lipid-lowering drugs (38.3 vs 18.6%; $P=0.004$) and blood pressure treatment (27.6 vs 16.3%; $P=0.026$).

6 No differences were observed between the two groups regarding mean HbA_{1c} level or serum cholesterol.

7 The authors concluded that electronic feedback to GPs on the quality of T2D care provision resulted in significantly improved quality of care regarding processes according to the Danish evidence-based diabetes guidelines for general practitioners.

Guldberg TL, Vedsted P, Kristensen JK, Lauritzen T (2011) Improved quality of type 2 diabetes care following electronic feedback of treatment status to general practitioners: a cluster randomized controlled trial. *Diabet Med* **28**: 325–32

DIABETIC MEDICINE

Liraglutide versus sitagliptin: Treatment satisfaction in T2D

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 This patient-reported outcomes evaluation – which was a substudy of a 26-week trial comparing the glucagon-like peptide-1 (GLP-1) receptor agonist liraglutide (Lira) and dipeptidyl peptidase-4 (DPP-4) inhibitor sitagliptin (Sita) – aimed to assess treatment satisfaction at baseline and 26 weeks.

2 In the main 26-week study, participants ($n=658$) were randomised to treatment with Lira 1.2 mg, 1.8 mg or Sita 100 mg once-daily, as an add-on to metformin monotherapy. Lira was associated with greater HbA_{1c} reduction ($P<0.0001$ for both Lira doses) and weight loss ($P<0.0001$) than Sita.

3 Treatment satisfaction in participants in this patient-reported outcomes substudy study (Lira 1.8 mg, $n=171$; 1.2 mg, $n=164$; Sita, $n=170$) was assessed using the Diabetes Treatment Satisfaction Questionnaire.

4 An overall increase in treatment satisfaction was observed in all groups at 26 weeks, with greater improvement with Lira (4.35 and 3.51 vs 2.96 for Lira 1.8 mg and 1.2 mg vs Sita; $P=0.03$).

5 Participants perceived themselves to be hyperglycaemic significantly less frequently with Lira 1.8 mg (difference, –0.88; $P<0.0001$) and 1.2 mg (difference, –0.49; $P=0.01$) compared with Sita. The perceived hypoglycaemia frequency was similar in all groups.

6 The authors concluded that treatment satisfaction in people on Lira therapy may be greater than in those on Sita therapy.

Davies M, Pratley R, Hammer M et al (2011) Liraglutide improves treatment satisfaction in people with type 2 diabetes compared with sitagliptin, each as an add on to metformin. *Diabet Med* **28**: 333–7

DIABETES CARE

Ultra-long-acting basal insulin with a bolus boost

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓✓

1 Insulin degludec (IDeg 70%), when combined with insulin aspart (IAsp 30%), produces a soluble coformulation – IDegAsp1.

2 In this 16-week, randomised controlled trial the authors compared the safety and efficacy of IDegAsp1, IDegAsp2 (IDeg 55% and IAsp 45%) and insulin glargine (IGlar) in insulin-naïve people with T2D with suboptimal glycaemic control on oral medication.

3 Participants (mean age, 59.1 years; HbA_{1c} level, 8.5% [69 mmol/mol]; BMI, 30.3 kg/m^2) were randomised to receive once-daily IDegAsp1 ($n=59$), IDegAsp2 ($n=59$) or IGlar ($n=60$); all in combination with metformin.

4 HbA_{1c} decreased to comparable levels in all groups by study end (IDegAsp1, 7.0% [53 mmol/mol]; IDegAsp2, 7.2% [55 mmol/mol]; IGlar, 7.1% [54 mmol/mol]).

5 A comparable proportion of participants achieved an HbA_{1c} level of <7.0% (<53 mmol/mol) without confirmed hypoglycaemia in the last 4 weeks of the trial (IDegAsp1, 51%; IDegAsp2, 47%; IGlar, 50%).

6 A lower mean 2-hour post-dinner plasma glucose increase was observed in the IDegAsp1 and IDegAsp2 groups compared with IGlar; mean fasting plasma glucose was similar across the groups.

7 Rates of hypoglycaemia were lower for IDegAsp1 and IGlar than IDegAsp2, as were the rates of nocturnal hypoglycaemic events.

8 The authors concluded that IDegAsp1 was well tolerated and provided comparable glycaemic control to IGlar with similar low rates of hypoglycaemia.

Heise T, Tack CJ, Cuddihy R et al (2011) A new-generation ultra-long-acting basal insulin with a bolus boost compared with insulin glargine in insulin-naive people with type 2 diabetes: a randomized, controlled trial. *Diabetes Care* **34**: 669–74

DIABETIC MEDICINE

Exclusion from QOF may worsen health disparities

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 The authors undertook a serial cross-sectional study of exception reporting from the first 3 years of the Quality and Outcomes Framework (QOF).

2 Three analyses were undertaken using data from the electronic medical records of people with diabetes from 23 general practices in a deprived, ethnically diverse area of North West London between 2004/5 and 2006/7.

3 Individuals excluded from QOF were found to be less likely to achieve the treatment indicators for HbA_{1c} (2004/5 and 2006/7) blood pressure (2005/6 and 2006/7) and cholesterol (2005/6). Black and south Asian people were more likely to be excluded from the HbA_{1c} indicator than white people (adjusted odds ratio [OR], 1.64 [1.17–2.29] in 2005/6).

4 People with a diagnosed diabetes duration >10 years (adjusted OR, 2.01 [1.65–2.45] for HbA_{1c} in 2006/7) and comorbidities (adjusted OR, ≥three comorbidities compared with no comorbidity for HbA_{1c} adjusted OR, 1.90 [1.24–2.90] in 2004/5) were more likely to be excluded.

5 More people were excluded from the HbA_{1c} indicator in larger practices (adjusted OR, practice size ≥7000 compared with <3000, 3.52 [2.35–5.27] in 2005/6.

6 Practices in the more deprived areas consistently excluded more people from all indicators.

7 It was concluded that people excluded from QOF may have a reduced likelihood of achieving diabetes treatment goals, and that these individuals disproportionately come from disadvantaged areas.

Dalton AR, Alshamsan R, Majeed A, Millett C (2011) Exclusion of patients from quality measurement of diabetes care in the UK pay-for-performance programme. *Diabet Med* **28**: 525–31

LANCET

Glycaemic control with insulin degludec comparable to that with insulin glargine

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓✓

1 This 16-week, randomised, open-label, parallel-group phase II trial aimed to assess the efficacy and safety of insulin degludec (IDec) taken once-daily (OD) or three times a week (TTW) compared with OD insulin glargine (IGlar) in insulin-naïve people with T2D and suboptimal glycaemic control on oral antidiabetes drugs.

2 Participants (n=245; aged 18–75 years) with T2D were randomised in a 1:1:1:1 ratio to receive IDec OD or TTW, or IGlar OD; all in combination with metformin. The primary outcome was HbA_{1c} level after 16 weeks.

3 Sixty-two participants were randomised to IDec TTW (starting dose, 20 U [1 U=9 nmol]), 60 to IDec OD (starting dose, 10 U [1 U=6 nmol]; Group A), 61 to IDec OD (starting dose 10 U [1 U=9 nmol]; Group B) and 62 to IGlar (starting dose, 10 U [1 U=6 nmol]).

4 Mean HbA_{1c} levels were similar across all groups by study end: IDec TTW, 7.3% (56 mmol/mol); Group A, 7.4% (57 mmol/mol); Group B, 7.5% (58 mmol/mol); IGlar, 7.2% (55 mmol/mol).

5 Estimated mean HbA_{1c} treatment differences from IDec compared with IGlar were: 0.08% (95% confidence interval [CI], –0.23 to 0.40) for IDec TTW, 0.17% (–0.15 to 0.48) for Group A, and 0.28% (–0.04 to 0.59) for Group B.

6 The authors concluded that, in this cohort of people with T2D, IDec provided comparable glycaemic control to IGlar without additional adverse events.

Zinman B, Fulcher G, Rao PV et al (2011) Insulin degludec, an ultra-long-acting basal insulin, once a day or three times a week versus insulin glargine once a day in patients with type 2 diabetes: a 16-week, randomised, open-label, phase 2 trial. *Lancet* **377**: 924-31