Management & prevention of type 2 diabetes

DIABETIC MEDICINE

Weight loss is linked to T2D reversal

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

1 The use of very low energy diets for T2D reversal has generated great public interest. Following this, the authors created a website containing general information about diabetes reversal for people with T2D and healthcare professionals.

2 In this study, feedback of personal experiences using energy restriction for T2D reversal including emails, letters and telephone communications were analysed from 66 men and 11 women.

3 Participants reported significant weight loss, decreasing from 96.7±17.5 kg at baseline to 81.9±14.8 kg (P<0.001) after the intervention period. Fasting blood glucose levels also decreased from 8.3 mmol/L (5.9–33.0) to 5.5 mmol/L (4.0–10.0; P<0.001).

4 Diabetes reversal occurred in 61% of participants. Reversal was reported in 80% of participants who lost more than 20 kg, 63% in those with a weight loss between 10 and 20 kg, and 53% who lost less than 10 kg.

5 The extent of weight loss significantly correlated to reported fasting glucose levels (Spearman rank-order coefficient [Rs]= -0.38; P=0.006). Reversal rates varied with diabetes duration, with shorter durations (<4 years) displaying a higher percentage of reversal compared to longer durations (>8 years; 73% versus 43%).

6 The authors concluded that intentional weight loss can lead to the reversal of T2D, and should be incorporated as a goal in diabetes management.

Steven S, Lim EL, Taylor R (2013) Population response to information on reversibility of Type 2 diabetes. *Diabet Med* **4**: e135–8

Stay motivated: Energy restriction may reverse T2D

Roger Gadsby, GP and Associate Clinical Professor, Warwick Medical School, University of Warwick, Coventry

Do you believe that long-duration T2D results in an inevitable and irreversible decline in insulin secretion, with the inevitable need for insulin after an average of around 10 years?

Data to suggest that this may not always be the case come from observations in people with diabetes who have had bariatric surgery (Hall et al, 2010), and from the effects of maintaining a very low calorie diet for 3 months (Lim et al, 2011). The extent of public interest following the publication of this latter study (Lim et al, 2011) prompted the authors to make available on a website, general information about reversing T2D (Taylor, 2011). In this, it is explained that a very low calorie diet was chosen in the study to mimic the effects of gastric bypass surgery. However, steady but substantial weight loss achieved by reducing portion size was recommended as the preferred method. All individuals were advised to discuss their plan for energy restriction with their own doctors, particularly with a view to adjusting glucose lowering medications. No alterations to habitual physical activity levels were advised.

Within a few months of the website going live, individuals began to feed back their experiences of attempting to reverse their diabetes, via email, letters and telephone communications. Steven et al (summarised alongside) collate responses from between July 2011 and September 2012. There were 66 men and 11 women, 56.4 years of age ± 9.7 years, with median diabetes duration of 5.5 years. Liquid meal replacements were used by 38 individuals and energy intake was restricted without the use of special products in 34 individuals. Self-reported weight fell from 96.7 kg (±17.5) to 81.9 kg (±14.8). Diabetes reversal was considered to have happened in 61% of the population, and occurred in 80% of those with a weight loss of over 20 kg.

The authors conclude that very significant improvements in glycaemic control can be made by energy restriction undertaken by motivated individuals in their usual environment. The responses clearly show that this minority of health-motivated people strongly resent being told that there is nothing that can be done to escape from T2D, and that they must take medication.

The overwhelming impression gained by doctors from their routine practice is that people with T2D rarely succeed in losing weight. The important conclusion from this study is that there is a subgroup of people with T2D who are strongly motivated by a desire to regain health. One individual contrasted the battle to "beat" a life threatening disease such as cancer with the learned helplessness induced by advice that T2D was inevitably progressive. Perhaps if we gave the information to all our newly diagnosed overweight patients with T2D that diabetes reversal is possible if very significant weight loss occurs more people might rise to the challenge and become free of the condition.

Hall TC et al (2010) Preoperative factors predicting remission of type 2 diabetes after Roux-on-Y gastric bypass surgery for obesity. *Obes Surg* **20**: 1245–50

Lim EL et al (2011) Reversal of type 2 diabetes. *Diabetologia* **54**: 2506–14

Taylor R (2011) *Reversing type 2 diabetes*. Newcastle University, Newcastle upon Tyne. Available at: http://bit.ly/oswAxG (accessed 10.05.13)

DIABETOLOGIA

DDP-4 inhibitors are more effective in Asian people

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

1 Research suggests that the pathophysiology of T2D varies with ethnicity. The authors investigated the glucose-lowering activity of dipeptidyl peptidase-4 (DPP-4) inhibitors in Asian and non-Asian people with T2D.

2 A systematic review and meta-analysis of 55 trials identified from online databases and conference proceedings was conducted.

3 DPP-4 inhibitors were found to lower HbA_{1c} more effectively in trials with ≥50% Asian participants (weighted mean difference [WMD] -0.92%; 95% CI, -1.03 to -0.82) compared to <50% Asian participants (WMD -0.65%; 95% CI, -0.69 to -0.60).

4 The risk ratio of lowering HbA_{1c} to <7.0% (53.0 mmol/mol) was higher in trials with ≥50% Asian participants (3.4 [95% CI, 2.6–4.7] versus 1.9 [95% CI, 1.8–2.0]).

5 The authors concluded that DDP-4 inhibitors are more effective at lowering HbA_{1c} in people of an Asian origin, suggesting that ethnic-specific guidelines may be useful in treatment.

Kim YG, Hahn S, Oh TJ et al (2013) Differences in the glucose-lowering efficacy of DDP-4 inhibitors between Asians and non-Asians. *Diabetologia* **56**: 696–708

DIABETIC MEDICINE

Non-adherence and insulin therapy

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

1 Failure to adhere to insulin therapy can result in poor glycaemic control and the development of long-term, diabetes-related complications.

2 The authors conducted a systemic literature review to investigate the factors influencing insulin adherence in adults with either T1D or T2D.

3 A search of PubMed and EMBASE identified 17 studies for inclusion. Of these, six studies used self-reported measures of insulin adherence and 11 used calculated measures. The majority of studies (13/17) were completed in the US.

4 The analysis revealed that factors associated with non-adherence could be clustered into four groups, including predictive factors for non-adherence, patient perceived barriers, medication cost and delivery device.

5 In the predictive factors and patient perceived barriers groups, female sex, age, travelling, fear of injection and embarrassment of public injections were all associated with non-adherence.

6 Adherence was generally low, but was improved when patients switched to a pen device or arranged insurance to lower the financial burden of pharmacological therapies.

7 The authors concluded that a more flexible insulin regimen could improve adherence. Future studies are warranted to aid the development of improved treatment strategies.

Davies MJ, Gagliardino JJ, Gray LJ at al (2013) Real-world factors affecting adherence to insulin therapy in patients with Type 1 or Type 2 diabetes mellitus: a systematic review. *Diabet Med* 16 Jan [Epub ahead of print]

J CLIN ENDOCRINOL METAB

Clinical outcomes in sulphonylurea monotherapy

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

1 If metformin monotherapy does not achieve adequate glycaemic control in patients with T2D, numerous second-line, glucose-lowering agents can be introduced into the individual's treatment regimen.

2 The authors set out to compare clinical outcomes associated with second-line glucose-lowering therapies in a cohort of 27 457 people with T2D. Individuals using alternative regimens were retrospectively identified after the initial failure of metformin monotherapy.

3 Data was obtained from the UK-based General Practice Research Database. Sulphonylurea (SU) monotherapy was associated with significantly increased hazard ratios (HRs) for all-cause mortality (HR 1.459, 95% CI, 1.207–1.763), major adverse cardiovascular events (MACE, HR 1.578, 1.187–2.099), stroke (HR 1.444, 1.050–1.987) and a combined end point (HR 1.381, 1.194–1.597). Metformin used with pioglitazone had lower HRs for all-cause mortality (HR 0.707, 0.515–0.970) and a combined end point (HR 0.747, 0.612–0.911). Mean HbA_{1c} improved in all regimens besides SU monotherapy.

4 The authors concluded that metformin combined with pioglitazone resulted in improved clinical outcomes compared metformin and sulfonylurea.

Morgan CL, Poole CD, Evans M et al (2012) What next after metformin? A retrospective evaluation of the outcome of second-line, glucose-lowering therapies in people with type 2 diabetes. *J Clin Endocrinol Metab* **97**: 4605–12

DIABETES CARE

IDeg injection time can be varied

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

1 The issue of injecting basal insulin analogues at a fixed time each day could negatively impact on adherence and thus impede glycaemic control in people with diabetes.

2 The authors conducted a randomised controlled trial to investigate the effects of changing the daily injection time of an ultra-long-acting basal insulin named insulin degludec (IDeg) on glycaemic control.

3 Participants with T2D were randomised to receive once-daily (OD) IDeg with 8–40 hour intervals (IDeg OD Flex; *n*=229), OD IDeg with an evening meal (IDegOD; *n*=228), or OD insulin glargine at the same time daily (*n*=230) for 26 weeks.

4 After 26 weeks, all regimens were found to be associated with an improved HbA_{1c}. HbA_{1c} was improved by 1.28% points (13.98 mmol/mol) with IDeg OD Flex, 1.07% points (11.69 mmol/mol) with IDeg OD, and 1.26% points (13.77 mmol/mol) with IGlar OD.

5 Overall, hypoglycemic episodes did not differ between the groups and the rates of adverse events were comparable. Glycaemic control was similar between IDeg OD Flex and IDeg OD.

6 The authors concluded that glycaemic control is not compromised by varying the injection time of OD IDeg by 8–40 hours.

Meneghini L, Atkin SL, Gough SC et al (2013) The efficacy and safety of insulin degludec given in variable once-daily dosing intervals compared with insulin glargine and insulin degludec osed at the same time daily: A 26-week, randomized, open-label, parallel-group, treat-to-target trial in individuals with type 2 diabetes. *Diabetes Care* **36**: 858–64

DIABETIC MEDICINE

Pioglitazone use increases risk of bladder cancer

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

1 Pioglitazone is a hypoglycaemic agent that is approved for use in people with T2D. However, great controversy surrounds the potential link between pioglitazone and bladder cancer.

2 The authors conducted a systematic review and meta-analysis. Electronic database searches of MEDLINE, EMBASE and the Cochrane Central Register of Controlled Trials (CENTRAL) identified six controlled studies which had longitudinally analysed the effects of pioglitazone in 215 142 individuals. Participants were follow-up for a median time of 44 months.

3 The risk of developing bladder cancer was significantly higher in people treated with pioglitazone compared to people who were not exposed to pioglitazone. Hazard of bladder cancer increased by 23% (95% CI, 9–39%) in people that were receiving pioglitazone at the end of the follow-up period. This increased hazard was consistently observed across all six studies ($I^2 = 0\%$).

4 The authors concluded that people treated with pioglitazone have an increased risk of bladder cancer. This hazard must be taken into consideration by prescribing physicians, particularly when treating patients with pre-disposing risk factors such as smoking or previous family history.

Ferwana M, Firwana B, Hasan R et al (2013) Pioglitazone and risk of bladder cancer: a meta-analysis of controlled studies. *Diabet Med* 28 Jan [Epub ahead of print]