

## Management & prevention of type 2 diabetes



### Treatment burden: An overlooked aspect of diabetes management

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Vijan et al have performed a fascinating study (summarised alongside) that estimated the effects of HbA<sub>1c</sub> reduction on diabetes outcomes and overall quality-adjusted life-years (QALYs) using a Markov simulation model. It is not an easy read, and its results rely on the quality of the model and the data inputs used in it. However, the authors seem to have used the best available evidence for the benefits of glucose control and accepted published data on glycaemic treatment disutility. Published studies demonstrate quite high levels of disutility for insulin therapy. Disutility from oral therapies comes from adverse effects such as weight gain and hypoglycaemia and, for metformin, its gastrointestinal side effects.

The results show that in a “best-case” scenario (in which improving HbA<sub>1c</sub> lowers coronary heart disease event risk and treatment has minimal patient burden and/or adverse effects), lowering HbA<sub>1c</sub> produces substantial benefits, particularly among younger individuals. As an example, in a 45-year-old, lifetime treatment to reduce HbA<sub>1c</sub> from 69.4 mmol/mol (8.5%) to 58.5 mmol/mol (7.5%) produces a gain of 0.906 QALYs. The benefit gets smaller with age. At 65 years, the benefit declines to 0.269 QALYs, and at 75 years it is only 0.104 QALYs.

However, a patient’s perception of the level of treatment burden has a profound impact on the net benefits of HbA<sub>1c</sub> reduction. In the above example of a 45-year-old, a high treatment burden of 0.05 (equivalent to 18.2 days of high-quality life lost per year – a level often reported by people who are prescribed insulin) outweighs all benefits of glycaemic control. In fact, the model predicts that patients will lose between 0.653 and 0.818 QALYs at this level of treatment disutility,

even when treatment improves HbA<sub>1c</sub> by 1%! The finding that older people experience smaller benefits from glycaemic control is becoming accepted wisdom, and this article quantifies that as a gain of 0.06 QALYs (22 days) for a 1% drop in HbA<sub>1c</sub> in a 75-year-old.

The authors conclude that their study challenges current practice. They say that instead of current recommendations and performance measures based on achievement of a specific HbA<sub>1c</sub> goal, the quality of diabetes care could be more accurately defined by assessing whether high-benefit treatment is provided and whether an informed decision-making process is used when potential benefits are more modest. High-quality decision making is best achieved by individualising treatment decisions by asking “what are the burdens and benefits of prescribing a new medication for this patient?”, not by just asking “what should this patient’s HbA<sub>1c</sub> target be?” The authors feel that currently we are failing our patients by not recognising that their preferences and views of treatment burden are the most important factor in helping them make glycaemic treatment decisions that are best for them.

Putting these ideas into practice in diabetes clinics is not going to be easy or straightforward. Many diabetes healthcare professionals now use a chronic disease management model in which they encourage patients to discuss their goals of therapy. If we implement the findings of this study, it will no longer just be a question of “what HbA<sub>1c</sub> goal do you wish to set for yourself in the next 6 months?”, but “which medication would be the best one (i.e. the one with the least disutility) to get you to that goal?” ■

### JAMA Intern Med

### The treatment burden of intensive glycaemic control

Readability ////

Applicability to practice ////

WOW! Factor ////

**1** The authors used a Markov model of diabetes outcomes to evaluate the benefits of glycaemic control in relation to treatment burden.

**2** Data from the UK Prospective Diabetes Study (UKPDS) were used to inform the risk of early and progressive microvascular and neuropathic outcomes, and the Framingham risk calculator was used to inform pretreatment risks of coronary heart disease (CHD) and stroke.

**3** Various analyses of glycaemic treatment disutilities were used to inform treatment burden and adverse effects. The model assumed quite optimistic benefits of HbA<sub>1c</sub> control (e.g. a reduction in CHD risk of 15%).

**4** Assuming a very low treatment burden, treatment that lowered HbA<sub>1c</sub> by 1% (from 69.4 mmol/mol [8.5%] to 58.5 mmol/mol [7.5%]) resulted in very little benefit in terms of quality-adjusted life-years [QALYs] in older people, and only modest benefit (0.906 QALYs) in those aged 45 years at diagnosis.

**5** However, a higher treatment burden, as is often reported in studies of insulin therapy, resulted in a net loss of QALYs in all age groups.

**6** The authors conclude that the net benefits of glycaemic treatments depend on a person’s age at diagnosis, pretreatment HbA<sub>1c</sub> level and, above all, the burden of the specific treatment. Using HbA<sub>1c</sub> targets alone to inform treatment decisions, therefore, is a flawed strategy. They also suggest that treatments should be evaluated using clinical outcomes rather than HbA<sub>1c</sub> as endpoints.

Vijan S, Sussman JB, Yudkin JS, Hayward RA (2014) Effect of patients’ risks and preferences on health gains with plasma glucose level lowering in type 2 diabetes mellitus. *JAMA Intern Med* **174**: 1227–34

## Diabetes Care

### Patient preferences for non-insulin diabetes medications

Readability ✓✓✓  
 Applicability to practice ✓✓✓  
 WOW! Factor ✓✓✓

- The authors conducted a systematic review of preferences of people with T2D when choosing non-insulin medications.
- A total of 10 studies, with sample sizes of 129–1355, met the inclusion criteria and were analysed.
- Key patient concerns were glycaemic control, weight loss, treatment burden (e.g. route and frequency of administration and cost) and side effects (e.g. hypoglycaemia, weight gain and gastrointestinal [GI] effects).
- When preferences were compared, weight loss, glycaemic control and GI effects were particularly important. Weight loss became increasingly important in those with a BMI >30 kg/m<sup>2</sup>.
- Although preferences should always be assessed on an individual level, the consistency of these results should raise clinicians' awareness of their importance when initiating and evaluating therapies.

Purnell TS, Joy S, Little E et al (2014) Patient preferences for noninsulin diabetes medications: a systematic review. *Diabetes Care* **37**: 2055–62

## Curr Med Res Opin

### Genital mycotic infections with canagliflozin

Readability ✓✓  
 Applicability to practice ✓✓✓  
 WOW! Factor ✓✓

- The prevalence of genital mycotic infections in people receiving canagliflozin 100 mg or 300 mg was evaluated in two pooled populations from phase III studies of the agent.
- In the first cohort ( $n=2313$ ), over a mean exposure of around 24 weeks, infections were more common with the two doses of canagliflozin than with placebo (10.4–11.4% vs 3.2% in women; 3.7–4.2% vs 0.6% in men).
- In the second cohort ( $n=9439$ ), over a longer exposure of around 64 weeks, the incidences were similar to those in the first cohort (13.9–14.7% vs 3.1% in women; 7.3–9.3% vs 1.6% in men).
- The infections tended to occur within the first 4 months in women and the first year in men, and were typically mild to moderate in intensity, responding to standard treatments.

Nyirjesy P, Sobel JD, Fung A et al (2014) Genital mycotic infections with canagliflozin, a sodium glucose co-transporter 2 inhibitor, in patients with type 2 diabetes mellitus: a pooled analysis of clinical studies. *Curr Med Res Opin* **30**: 1109–19

## Diabetes Obes Metab

### All-cause mortality risks with metformin and sulphonylureas

Readability ✓✓  
 Applicability to practice ✓✓✓  
 WOW! Factor ✓✓

- In this retrospective analysis, the authors assessed all-cause mortality rates in people with T2D who were taking metformin or sulphonylureas (SUs) compared with people without T2D.
- In total, 78 241 people receiving metformin and 12 222 receiving SUs were matched with the same numbers of untreated controls without diabetes.
- Compared with the controls, the mortality rate was lower in the metformin group (14.4% vs 15.2%) but higher in the SU group (50.9% vs 28.7%).
- Compared with metformin recipients, adjusted median survival time was 15% lower in the general population and 38% lower in SU recipients. Those who initiated SU therapy at a younger age ( $\leq 53$  years) were at particular risk.
- The prospect that metformin may benefit people without diabetes warrants evaluation in controlled trials.

Bannister CA, Holden SE, Jenkins-Jones S et al (2014) Can people with type 2 diabetes live longer than those without? A comparison of mortality in people initiated with metformin or sulphonylurea monotherapy and matched, non-diabetic controls. *Diabetes Obes Metab* **16**: 1165–73

“The authors conclude that the net benefits of glycaemic treatments depend on a person's age at diagnosis, pretreatment HbA<sub>1c</sub> level and, above all, the burden of the specific treatment. Using HbA<sub>1c</sub> targets alone to inform treatment decisions, therefore, is a flawed strategy.”

## Diabetes Obes Metab

### Effectiveness of different treatments in preventing T2D

Readability ✓✓  
 Applicability to practice ✓✓✓  
 WOW! Factor ✓✓✓

- In this systematic review and meta-analysis of 71 studies and 490 813 people, the effectiveness of 15 different treatment strategies in the prevention of T2D was evaluated.

- Three treatment strategies – vitamins, beta-cell-stimulating drugs and estrogens – had no significant preventive effect.
- The other treatments, in descending order of effectiveness, were bariatric surgery (odds ratio [OR], 0.16), glitazones (OR, 0.37), diet plus physical activity (OR, 0.43), diet (OR, 0.44), physical activity or education (OR, 0.53), alpha-glucosidase inhibitors (OR, 0.54), metformin (OR, 0.65), lipid-lowering drugs (OR, 0.66), alcohol (OR, 0.65) and antihypertensive drugs (OR, 0.74–0.76).

- In most studies, the participants were overweight; however they were obese in the bariatric surgery studies, which makes comparison difficult. The authors conclude that bariatric surgery is the most effective strategy for obese people, while normal-weight and overweight people might benefit from the other treatments.
- Significant heterogeneity was found in the physical activity, glitazone and antihypertensive studies; therefore, those results may be less reliable.

Merlotti C, Morabito A, Pontiroli AE (2014) Prevention of type 2 diabetes: a systematic review and meta-analysis of different intervention strategies. *Diabetes Obes Metab* **16**: 719–27