

## Management & prevention of type 2 diabetes

### More evidence for the use of HbA<sub>1c</sub> as the tool for diabetes screening



Roger Gadsby, GP and Senior Lecturer, Centre for Primary Healthcare Studies, Warwick University, Warwick

The article by Zang et al (2010; summarised alongside) presents a high-quality systematic review, using Cochrane Collaboration methods, that investigated the relationship between HbA<sub>1c</sub> level and type 2 diabetes (T2D) incidence.

HbA<sub>1c</sub> was modeled as a function of annualised T2D incidence using aggregate study-level data, with incidence ranging from 0.1% at an HbA<sub>1c</sub> level >5.0% (>31 mmol/mol) to 54% at an HbA<sub>1c</sub> level ≥6.1% (≥43 mmol/mol). Examination of the studies revealed three important

pieces of information. First, the risk of incident T2D increased steeply in the HbA<sub>1c</sub> range 5.0–6.5% (31–48 mmol/mol). Second, the HbA<sub>1c</sub> range 6.0–6.5% (42–48 mmol/mol) was associated with an increased risk of T2D (25–50% incidence over 5 years). Finally, the HbA<sub>1c</sub> range 5.5–6.0% (37–42 mmol/mol) was associated with a moderate increase in T2D

risk (9–25%) and an HbA<sub>1c</sub> level of 5.0–5.5% (31–37 mmol/mol) was associated with an increased incidence relative to HbA<sub>1c</sub> levels <5.0% (<31 mmol/mol), although the absolute incidence of T2D was low (<9% over 5 years).

The authors suggest that the progression of risk of T2D with HbA<sub>1c</sub> level is similar in magnitude and shape to that previously described for fasting plasma glucose and 2-hour oral glucose tolerance tests. Thus, HbA<sub>1c</sub> may have a similar application as an indicator of future risk, with an HbA<sub>1c</sub> range of 5.5–6.5% (37–48 mmol/mol) capturing a large proportion of people at high risk.

Zhang et al (2010) conclude that, given the cost-effectiveness of intensive interventions in clinical trials, the use of

an HbA<sub>1c</sub> threshold somewhere between 5.5% (37 mmol/mol) and 6.0% (42 mmol/mol) is likely to ensure that people who will benefit from preventive measures are efficiently identified.

This is an important study of great relevance to screening for T2D as HbA<sub>1c</sub> becomes the preferred measurement.

**“This is an important study of great relevance to screening for diabetes as HbA<sub>1c</sub> becomes the preferred measurement.”**

### DIABETES CARE

### HbA<sub>1c</sub> range can identify people at risk of diabetes

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

**1** HbA<sub>1c</sub> is considered by some to be a reliable test to identify people with undiagnosed T2D or to determine those at high risk of developing T2D.

**2** The American Diabetes Association has recommended that an HbA<sub>1c</sub> level of ≥6.5% (≥48 mmol/mol) be used as the cut-off point for the diagnosis of diabetes; however, no trials have determined HbA<sub>1c</sub> ranges that predict the risk of developing T2D.

**3** A systematic literature search identified 16 studies that examined the relationship between HbA<sub>1c</sub> and future diabetes incidence; the studies comprised 44 203 participants with a mean follow-up of 5.6 years.

**4** Study data were used to determine HbA<sub>1c</sub> as a function of annualised diabetes incidence, which ranged from 0.1% at HbA<sub>1c</sub> <5.0% (<31 mmol/mol) to 54.1% at HbA<sub>1c</sub> ≥6.1% (≥43 mmol/mol).

**5** Findings from studies that examined incident diabetes across a range of HbA<sub>1c</sub> values showed the risk of incident diabetes increased steeply with HbA<sub>1c</sub> 5.0–6.5% (31–48 mmol/mol).

**6** Additionally, a highly increased risk of incident diabetes (25–50% incidence over 5 years) was associated with an HbA<sub>1c</sub> between 6.0% and 6.5% (42 and 48 mmol/mol), and a moderately increased relative risk (9–25% incidence over 5 years) was associated with an HbA<sub>1c</sub> level 5.5–6.0% (37–42 mmol/mol).

**7** The results suggest that the HbA<sub>1c</sub> range 5.5–6.5% (37–48 mmol/mol) identifies a large proportion of people at high risk of developing diabetes, enabling referral to appropriate preventive interventions.

Zhang X, Gregg EW, Williamson DF et al (2010) A<sub>1c</sub> level and future risk of diabetes: a systematic review. *Diabetes Care* **33**: 1665–73

### DIABETIC MEDICINE

### Increasing costs of glucose-lowering therapies in the UK

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

**1** This study aimed to determine dispensing patterns and financial costs of glucose-lowering therapies in the UK from 2000–2008.

**2** Open-source data from the four prescription pricing agencies in the UK were analysed to ascertain the volume of prescriptions dispensed between 2000 and 2008, and their cost.

**3** The total cost of glucose-lowering therapies in the UK in 2008 was £702 239 000; in England, dispensing costs increased from £290 million in 2000 to £591 million in 2008.

**4** Insulin costs increased from £128 million in 2000 to £286 million in 2008.

**5** The dispensing volume of glucose-lowering drugs increased over this time period, except for alpha-glucosidase inhibitors and prandial glucose regulators.

**6** Costs increased at a higher rate than volume, and changes in prescribing seemed to be more affected by commercial factors than by clinical evidence.

Currie CJ, Peters JR, Evans M (2010) Dispensing patterns and financial costs of glucose-lowering therapies in the UK from 2000–2008. *Diabet Med* **27**: 744–52

## DIABETES CARE

### Exenatide QW further improves HbA<sub>1c</sub>

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

**1** In the first part of the DURATION-1 (Diabetes Therapy Utilisation: Tesearching Changes in HbA<sub>1c</sub>, Weight and Other Factors Through Intervention with Exenatide Once-Weekly) trial, exenatide once-weekly (QW) significantly improved glycaemic control compared with exenatide twice-daily over 30 weeks in 295 people with T2D.

**2** This study is the second part of the DURATION-1 trial, where participants ( $n=258$ ) in the first part were randomised to continued exenatide QW 2 mg ( $n=128$ ) or switching from exenatide twice-daily to exenatide QW ( $n=130$ ) for an additional 22 weeks.

**3** Participants on exenatide QW treatment for a total of 52 weeks achieved a mean HbA<sub>1c</sub> level of 6.6% (49 mmol/mol) and reduced body weight; those who switched to exenatide QW in this study achieved further improvement in glycaemic control and sustained weight loss.

Buse JB, Drucker DJ, Taylor KL et al (2010) DURATION-1: exenatide once-weekly produces sustained glycaemic control and weight loss over 52 weeks. *Diabetes Care* **33**: 1255–61

## DIABETES CARE

### Liraglutide improves glycaemic control

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

**1** A previous 26-week study found that once-daily liraglutide (1.8 mg) resulted in better glycaemic control with fewer hypoglycaemic episodes than twice-daily exenatide (10 µg).

**2** This study was a 14-week extension to determine the safety and efficacy of either switching from twice-daily exenatide to once-daily

liraglutide or continuing once-daily liraglutide (for a total of 40 weeks).

**3** Participants who switched from exenatide to liraglutide ( $n=177$ ) improved their glycaemia (HbA<sub>1c</sub> -0.32%) with minimal hypoglycaemia (1.30 episodes/patient-year).

**4** Those who remained on liraglutide ( $n=199$ ) maintained a mean HbA<sub>1c</sub> level of 6.9% (52 mmol/mol) and experienced 0.74 minor hypoglycaemic episodes per patient-year.

**5** Switching from exenatide to liraglutide was found to be well tolerated and provided good glycaemic control.

Buse JB, Sesti G, Schmidt WE et al (2010) Switching to once-daily liraglutide from twice-daily exenatide further improves glycaemic control in patients with type 2 diabetes using oral agents. *Diabetes Care* **33**: 1300–3

## LANCET

### Dapagliflozin plus metformin improves glycaemic control

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

**1** The authors investigated whether the addition of dapagliflozin, a selective sodium–glucose cotransporter-2 inhibitor that reduces renal glucose reabsorption, to metformin would improve glycaemic control in people with T2D.

**2** The study comprised 546 adults with T2D inadequately controlled on metformin ( $\geq 1500$  mg/day), who were randomised to receive additional dapagliflozin 2.5 mg ( $n=137$ ), 5 mg ( $n=137$ ), 10 mg ( $n=135$ ) or placebo ( $n=137$ ) once daily for 24 weeks.

**3** At study end, the placebo group had a mean HbA<sub>1c</sub> reduction of -0.30%, whereas the dapagliflozin groups had a mean HbA<sub>1c</sub> reduction of -0.67% (2.5 mg group), -0.70% (5.0 mg group) and -0.84% (10 mg group).

Bailey CJ, Gross JL, Pieters A et al (2010) Effect of dapagliflozin in patients with T2D who have inadequate glycaemic control with metformin. *Lancet* **375**: 2223–33