Management & prevention of type 2 diabetes

More evidence for the use of HbA_{1c} as the tool for diabetes screening

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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_{1c} level and type 2 diabetes (T2D) incidence.

HbA_{1c} was modeled as a function of annualised T2D incidence using aggregate study-level data, with incidence ranging from 0.1% at an HbA_{1c} level >5.0% (>31 mmol/mol) to 54% at an HbA_{1c} 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_{1c} range 5.0–6.5% (31–48 mmol/mol). Second, the HbA_{1c} 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_{1c} range 5.5–6.0% (37–42 mmol/mol) was associated with a moderate increase in T2D risk (9–25%) and an HbA_{1c} level of 5.0–5.5% (31–37 mmol/mol) was associated with an increased incidence relative to HbA_{1c} 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_{1c} level is similar in magnitude and shape to that previously described for fasting plasma glucose and 2-hour oral glucose tolerance tests. Thus, HbA_{1c} may have a similar application as an indicator of future risk, with an HbA_{1c} range of 5.5–6.5% (37–48 mmol/mol) capturing a large proportion of people at high risk.

> *"This is an important study of great relevance to screening for diabetes as HbA_{1c} becomes the preferred measurement."*

Zhang et al (2010) conclude that, given the cost-effectiveness of intensive interventions in clinical trials, the use of an HbA_{1c} 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_{1c} becomes the preferred measurement.

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-glucoside 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

HbA_{1c} range can identify people at risk of diabetes

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

1 HbA_{1c} 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_{1c} 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_{1c} ranges that predict the risk of developing T2D.

3 A systematic literature search identified 16 studies that examined the relationship between HbA_{1c} 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_{1c} as a function of annualised diabetes incidence, which ranged from 0.1% at HbA_{1c} <5.0% (<31 mmol/mol) to 54.1% at HbA_{1c} ≥6.1% (≥43 mmol/mol).

5 Findings from studies that examined incident diabetes across a range of HbA_{1c} values showed the risk of incident diabetes increased steeply with HbA_{1c} 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_{1c} 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_{1c} level 5.5–6.0% (37–42 mmol/mol).

7 The results suggest that the HbA_{1c} 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_{1c} level and future risk of diabetes: a systematic review. *Diabetes Care* **33**: 1665–73

DIABETES CARE

Exenatide QW further improves HbA_{1c}

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

1 In the first part of the DURATION-1 (Diabetes Therapy Utilisation: Tesearching Changes in HbA_{1c}, 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_{1c} 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_{1c} –0.32%) with minimal hypoglycaemia (1.30 episodes/patient-year).

4 Those who remained on liraglutide (*n*=199) maintained a mean HbA_{1c} 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 (≥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_{1c} reduction of –0.30%, whereas the dapagliflozin groups had a mean HbA_{1c} 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