Management & prevention of type 2 diabetes

HbA_{1c} overtesting and overtreatment in the US: Might it also be happening in the UK?

Roger Gadsby
Honorary Associate Clinical Professor, Warwick Medical School, University of Warwick

The fascinating paper by McCoy et al (summarised alongside) sheds a lot of light on HbA_{1c} overtesting and overtreatment in the US. The study was a retrospective data analysis of 31 545 people with type 2 diabetes from a national administrative database. The participants were aged 18 years and over, had type 2 diabetes with stable glycaemic control (two consecutive HbA_{1c} measurements <53 mmol/mol [7.0%] within a 2-year period), did not use insulin, had no history of severe hypoglycaemia or hyperglycaemia and were not pregnant. HbA_{1c} test frequency was assessed within 24 months of the second index HbA_{1c} test. The frequency of HbA_{1c} testing was classified as recommended (once or twice per year), frequent (three or four times per year) or excessive (five or more times per year). Changes in treatment regimen were ascertained within 3 months of the index test.

The mean age of the cohort was 58 years and the mean index HbA_{1c} was 44 mmol/mol (6.2%). Testing frequency was defined as frequent in 55% of participants and excessive in 6%. Despite good glycaemic control at baseline, treatment was further intensified by addition of glucose-lowering agents or insulin in 7% of those tested as per guidelines, 9% of those tested frequently and 13% of those tested excessively.

The authors conclude that in this US cohort of adults with stable and well-controlled type 2 diabetes, 60% received too many HbA_{1c} tests, a practice associated with potential overtreatment with hypoglycaemic drugs. Excessive testing contributes to the growing problem of waste in healthcare and increased patient burden in diabetes management.

Could this overtesting and potential overtreatment be happening in England and Wales? The most recent National Diabetes Audit (NDA) report for England and Wales shows that, among the 8198 participating practices, 94.8% of people with a diagnosis of type 2 diabetes in their GP records had at least one HbA_{1c} measurement in the previous 12 months (Health and Social Care Information Centre, 2016). Such results are usually interpreted as "5.2% have not had an HbA_{1c} measurement. How scandalous." The idea that the 94.8% figure might include people who have had too many HbA_{1c} measurements has not, in my opinion, really been considered or measured.

The NDA report also shows that 66.1% of people with type 2 diabetes in the audit achieve an HbA_{1c} of ≤58 mmol/mol (7.5%). Again, this result is usually interpreted as "32.9% fail to achieve good control. How scandalous." However, we know that some older frail people with diabetes, especially nursing home residents, are being overtreated, putting them at increased risk of hypoglycaemia (Gadsby et al, 2012). In addition, might the NDA's 66.1% also include some people who are not old and frail, whose HbA_{1c} levels are inappropriately low and who might benefit from a reduction in their glucose-lowering medications? ■

Gadsby R, Galloway M, Barker P, Sinclair A (2012) Prescribed medicines for elderly frail people with diabetes resident in nursing homes – issues of polypharmacy and medication costs. *Diabet Med* **29**: 136–9

Health and Social Care Information Centre (2016) *National Diabetes Audit 2013–2014 and 2014–2015. Report 1: Care Processes and Treatment Targets*. HSCIC, Leeds. Available at: http://bit.ly/1UsDzOC (accessed 05.05.16)

BMJ

High rates of HbA_{1c} overtesting in people with stable T2D

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

1 In this retrospective analysis of a commercially insured population with T2D in the US, the authors assessed the rate of HbA_{1c} overtesting and potential overtreatment.

2 Participants were all adults with good, stable glycaemic control (two consecutive HbA_{1c} measurements of <53 mmol/mol (7.0%) within a 2-year period) without insulin therapy and with no history of severe hypo- or hyperglycaemia.

3 Testing frequency was assessed within 2 years of the second index HbA_{1c} test and was classified according to international guidelines as recommended (once or twice per year), frequent (three or four times per year or with tests taken 3–6 months apart) or excessive (five or more times per year or with tests taken <3 months apart).

4 Of 31 545 participants (mean age, 58 years; mean HbA_{1c}, 44 mmol/mol [6.2%]), 54.5% underwent frequent testing and 5.8% underwent excessive testing. Those who received too many tests were older, had more comorbidities, were receiving more antidiabetes drugs and had a higher index HbA_{1c}.

5 Treatment intensification occurred in 7% of those tested as per guidelines, 9% of those tested frequently and 13% of those tested excessively.

6 Compared with those who were tested at the recommended frequency, those tested excessively were more likely to receive treatment intensification (odds ratio, 1.35) despite no clinical indication to do so.

McCoy RG, Van Houten HK, Ross JS et al (2015) HbA_{1c} overtesting and overtreatment among US adults with controlled type 2 diabetes, 2001–13: observational population based study. *BMJ* **351**: h6138

BMJ

DPP-4 inhibitors and SUs: The risk of hypoglycaemia

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

1 The authors of this systematic review and meta-analysis set out to quantify the risk of hypoglycaemia associated with the concomitant use of dipeptidyl peptidase-4 (DPP-4) inhibitors and sulfonylureas (SUs) compared with placebo and SUs.

2 After screening, 10 placebo-controlled randomised trials of at least 50 participants with T2D were identified for inclusion. These comprised a total of 6456 participants, 4020 of whom received DPP-4 inhibitors plus SUs and 2526 placebo plus SUs.

3 The risk ratio of hypoglycaemia associated with the addition of DPP-4 inhibitors to SUs in people with T2D was calculated to be 1.52 (95% confidence interval [CI], 1.29–1.80).

4 The number needed to harm was 17 (95% CI, 11–30) for a treatment duration of 6 months or less, 15 (95% CI, 9–26) for 6.1–12 months, and 8 (95% CI, 5–15) for >12 months. A subgroup analysis found no difference between full and low doses of DPP-4 inhibitors for risk of hypoglycaemia.

5 The authors conclude that the 50% increase in risk of hypoglycaemia (leading to one excess case for every 17 patients in the first 6 months) highlights the need to respect existing recommendations for dose reductions of SUs when treatment with DPP-4 inhibitors is initiated.

6 They further recommend that the efficacy of this risk minimisation strategy is assessed urgently.

Salvo F, Moore N, Arnaud M et al (2016) Addition of dipeptidyl peptidase-4 inhibitors to sulphonylureas and risk of hypoglycaemia: systematic review and meta-analysis. *BMJ* **353**: i2231

BMJ

DPP-4 inhibitors: Possible risk of HF

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

1 This meta-analysis of 43 randomised controlled trials (n=68 775) and 12 observational studies (n=1 777 358) compared dipeptidyl peptidase-4 (DPP-4) inhibitors against placebo, lifestyle modification or other antidiabetes drugs in terms of heart failure (HF) risk.

2 Moderate-quality evidence from five randomised controlled trials showed that, compared with controls, DPP-4 inhibitors increased the risk of hospital admission for HF among people with known cardiovascular disease (odds ratio [OR], 1.13).

3 Low-quality evidence from the 38 randomised controlled trials evaluating risk of HF not limited to hospital admissions demonstrated no significant risk (OR, 0.97). Evidence from observational studies was of very low quality.

Li L, Li S, Deng K et al (2016) Dipeptidyl peptidase-4 inhibitors and risk of heart failure in type 2 diabetes: systematic review and meta-analysis of randomised and observational studies. *BMJ* **352**: i610

Ann Intern Med

Behavioural interventions for T2D: What works?

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

1 In this systematic review and meta-analysis, the authors sought to identify factors that affect the effectiveness of behavioural programmes to improve T2D outcomes.

2 Bayesian network meta-analysis showed that most lifestyle and diabetes self-management education and support programmes led to clinically significant improvements in glycaemic control, while education programmes without added support provided little benefit.

3 More effective programmes had ≥10 contact hours and were delivered in person rather than over technology.

4 Reductions in HbA_{1c} were generally greater in people with a baseline HbA_{1c} of ≥53 mmol/mol (7.0%), adults younger than 65 years, and ethnic minorities.

Pillay J, Armstrong MJ, Butalia S et al (2015) Behavioral programs for type 2 diabetes mellitus: a systematic review and network meta-analysis. *Ann Intern Med* **163**: 848–60

ADA 2016

Efficacy and safety: the LixiLan-L trial

1 In this open-label trial, the efficacy and safety of LixiLan (a fixed-ratio combination of insulin glargine and lixisenatide) was compared with glargine alone in individuals with T2D.

2 Individuals with inadequate glycaemic control were included if their HbA_{1c} remained >53 mmol/mol (7.0%) following a 6-week run-in phase during which insulin glargine was introduced or optimised.

3 Participants (n=736) were randomised to a LixiLan or insulin glargine treatment arm.

4 After 30 weeks, the LixiLan group showed a superior reduction from baseline HbA_{1c} compared with insulin glargine (–12 mmol/mol vs –7 mmol/mol [–1.1% vs –0.6%]; P<0.0001).

5 Furthermore, body weight decreased by 0.7 kg in the LixiLan group and increased by 0.7 kg in the insulin glargine group (difference 1.4 kg; P<0.0001). The rate of symptomatic hypoglycaemia was comparable between groups.

Aroda V et al (2016) Efficacy and safety of the insulin glargine/lixisenatide fixed-ratio combination vs. insulin glargine in patients with T2DM: the LixiLan-L trial. *ADA 76th Scientific Sessions*: abstract 238-OR

> *"Moderate-quality evidence from five randomised controlled trials showed that, compared with controls, dipeptidyl peptidase-4 inhibitors increased the risk of hospital admission for heart failure among people with known cardiovascular disease."*