Management & prevention of type 2 diabetes

Closing the gap: Growing evidence for earlier diabetes diagnosis in high-income countries

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Once upon a time it was thought that in many, diabetes was diagnosed several years after its true onset, so that years of untreated hyperglycaemia exposure had already caused considerable damage in some individuals. Indeed, at the point of diagnosis in the UKPDS study, one in five participants already had retinopathy, and rates of other complications were also high (UKPDS Research Group, 1990). Thankfully, in many high-income countries the gap between actual diabetes onset and clinical diagnosis appears to have decreased. In this regard, the paper by Thomsen et al (summarised alongside) takes us a little further by demonstrating that pre-drug treatment HbA_{1c} levels in people with incident type 2 diabetes have decreased substantially in Northern Denmark: from 74 mmol/mol (8.9%) in 2000–2003 to 53 mmol/mol (7.0%) in 2010–2012. Thomsen et al also demonstrated that more patients in 2010–2012 achieved good glycaemia levels (<6.5% [48 mmol/mol]) upon treatment within the first 3–6 months post diagnosis than in 2000–2003 (53% vs 37% respectively), and that this was due, in part, to many more receiving metformin in recent years (90% in 2011–2012 vs 32% in 2000–2003).

The results of this large population-based database fit with emerging data in other high-income countries (Hoerger et al, 2008). Collectively, such data concur with the more widespread glycaemia testing in recent years, something that the recent adoption of HbA_{1c} as a diagnostic tool may further aid, due to its ability to be measured anytime of the day. Further indirect but powerful evidence for contemporary earlier diagnosis comes from recent Scottish data demonstrating far lower rates of retinopathy in recent years (Looker et al, 2012). This is all good news since, as we all know, unchecked hyperglycaemia rapidly begets microvascular disease and has a "slower burn" effect on macrovascular risk.

Two other advantages of earlier diagnosis also merit discussion. The first is that patients may be somewhat more receptive ("plastic") to lifestyle changes or more responsive to treatments if the disease is picked up early and before much damage has accrued. Second, earlier diagnosis means earlier use of cardio-protective therapies, such as statins and anti-hypertensive medications, which lead to lower cardiovascular risks since, as discussed (Sattar, 2013), cholesterol and blood pressure reductions more rapidly lessen cardiovascular risk in diabetes than intensive glucose control. But the battle is not yet won, and there is much to do. Many patients, especially younger ones who tend to be more obese, have glucose levels that are difficult to control early on and much more work is needed in this rising population. We must also remember the challenges of early diabetes control and treatment that are particularly pertinent to many low- and middle-income countries where continuing westernisation is leading to explosions in diabetes rates, which is often diagnosed late in the disease progression. Solving these latter issues will not be easy, but they are of global importance and there is much work to be done. ■

Hoerger TJ, Segel JE, Gregg EW, Saaddine JB (2008) Is glycemic control improving in U.S. adults? *Diabetes Care* **31**: 81–6

Looker HC, Nyangoma SO, Cromie D et al (2012) Diabetic retinopathy at diagnosis of type 2 diabetes in Scotland. *Diabetologia* **55**: 2335–42

Sattar N (2013) Revisiting the links between glycaemia, diabetes and cardiovascular disease. *Diabetologia* **56**: 686–95

UKPDS Research Group (1990) UK Prospective Diabetes Study 6. Complications in newly diagnosed type 2 diabetic patients and their association with different clinical and biochemical risk factors. *Diabetes Res* **13**: 1–11

Diabetes Obes Metab

Trends in early glycaemic control and glucose-lowering treatment

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

1 The aim of this study was to examine real-life trends in early glycaemic control in people with T2D. In particular, it was examined whether there were any trends with the initiation of glucose-lowering drug therapy and subsequent HbA_{1c} control.

2 A large cohort of 38 418 people in Northern Denmark was identified and the observation period was from 2000–2012. In total, 91% of the group started on a monotherapy regimen of an oral glucose-lowering drug. The remainder of the cohort started on two or more therapies.

3 Baseline HbA_{1c} was taken as the most recent recording in the 12 months prior to the first medicines prescription, and HbA_{1c} was then measured again in the following 3–6 months.

4 One of the lead findings was the increase in the percentage of the cohort who were initiated with metformin over the observation period: from 32% in 2000–2003 to 90% in 2011–2012.

5 During the same time, the proportion of those initiated on sulphonylureas decreased 10-fold.

6 The authors also noted that the median pre-treatment HbA_{1c} decreased from 74 mmol/mol (8.9%) in 2000–2003 to 53 mmol/mol (7.0%) 2010–2012.

7 In more recent times, the percentage of those achieving an HbA_{1c} target of <53 mmol/mol (<7%) and <48 mmol/mol (<6.5%) have increased.

Thomsen RW, Baggesen LM, Svensson E et al (2015) Early glycaemic control among patients with type 2 diabetes and initial glucose-lowering treatment. *Diabetes Obes Metab* **17**: 771–80

Diabetes Obes Metab

Fixed combination of insulin degludec and liraglutide: 52-week data

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

1 The efficacy and safety of a fixed combination of insulin degludec (100 U/mL) and liraglutide (3.6 mg/mL [IDegLira]) was compared to insulin degludec or liraglutide alone among people with T2D. Over 1300 people from the original 26-week DUAL I trial continued to participate for an additional 26 weeks.

2 After 52 weeks, HbA_{1c} was reduced from baseline by 20.2 mmol/mol (1.84%) in the IDegLira group, 15.3 mmol/mol (1.40%) for the insulin degludec group and 13.2 mmol/mol (1.21%) for the liraglutide group.

3 The IDegLira group had the highest proportion of individuals who achieved an HbA_{1c} of 53 mmol/mol (<7%) compared to the other treatment groups. At 52 weeks, the body weight change had remained stable for the IDegLira group and rates of hypoglycaemia were significantly lower that the insulin degludec group, but significantly higher than the liraglutide group.

4 The majority of adverse events were mild and did not appear to the trial investigators to be related to the trial products. It was concluded that the treatments were well tolerated, with no significant adverse events or safety issues.

5 The extended data of the DUAL I trial confirm that the positive results from the initial 26-week results can be sustained.

Gough SC, Bode BW, Woo VC et al (2015) One-year efficacy and safety of a fixed combination of insulin degludec and liraglutide in patients with type 2 diabetes: results of a 26-week extension to a 26-week main trial. *Diabetes Obes Metab* 15 May [Epub ahead of print]

Diabetes Res Clin Pract

Heart failure prediction in T2D

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

1 The study's aim was to improve the assessment of heart failure (HF) risk in people with T2D. To do this a systematic review and meta-analysis were carried out, which included articles published from 1946 to 2014.

2 Twenty-one studies comprising 1 111 569 people in total were included, 507 637 of whom had T2D. The studies' follow-up period ranged from 1 to 12 years.

3 Five factors were found to be associated with increased risk of HF among people with T2D: insulin use (hazard ratio [HR], 2.48), HbA_{1c} 7.0–8.0% (HR 2.41), 5 years increase in age (HR, 1.47), fasting glucose (HR, 1.28) and HbA_{1c} (HR 1.18 for each 1% increase).

Wang Y, Negishi T, Negishi K, Marwick TH (2015) Prediction of heart failure in patients with type 2 diabetes mellitus – a systematic review and meta-analysis. *Diabetes Res Clin Pract* **108**: 55–66

Diabet Med

T2D incidence in ethnic youth groups

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

1 The authors sought to determine the incidence of diabetes (T2D and diabetes using insulin only) among young South Asians, Chinese and White people (5–29 years) in a population-based study in British Columbia, Canada.

2 In 1997–2006, 712 South Asians, 498 Chinese and 6176 White young people were diagnosed with diabetes. Most youth with diabetes were diagnosed with T2D (South Asian 86.4%, Chinese 87.1% and White 61.8%)

3 Age-standardised average incidence of T2D for South Asians was more than double compared with the White population and three times higher compared with the Chinese population in those aged 20–29 years.

4 Rates of T2D were higher in the older group (20–29 years) than the younger group (5–19 years), and this was a trend seen across all ethnic groups.

Ke C, Sohal P, Qian H, Quan H (2015) Diabetes in the young: a population-based study of South Asian, Chinese and White people. *Diabet Med* **32**: 487–96

Diabetes Metab

Metformin in African Americans at high diabetes risk

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

1 The use of metformin for people with pre-diabetes is becoming more widespread, but it is unknown if there are any differences in glycaemic response among different racial groups.

2 The authors completed a secondary analysis of data from the randomised, multi-centre, Diabetes Prevention Program among people with pre-diabetes – 582 Whites and 210 African Americans received 850 mg of metformin twice daily and were followed for 3 years.

3 After 6 months on metformin, African Americans had a larger drop in fasting plasma glucose than Whites (0.3 vs 0.2 mmol/L; P=0.006), and this difference remained statistically significant at year 1 and 2.

Zhang C, Zhang R (2015) More effective glycaemic control by metformin in African Americans than in Whites in the prediabetic population. *Diabetes Metab* **41**: 173–5

> *"Five factors were found to be associated with increased risk of heart failure among people with type 2 diabetes: insulin use, HbA_{1c} 7.0–8.0%, 5 years increase in age, fasting glucose and increasing HbA_{1c}."*