Management & prevention of type 2 diabetes

Testing times for blood glucose testing?

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The important, high profile, well-conducted study summarised alongside suggests that routine blood glucose testing in type 2 diabetes may be more trouble than it's worth. Certainly, frequent blood glucose testing in the well-controlled individuals with type 2 diabetes participating in this trial did not deliver significant improvements in HbA_{1c} or reduce the rates of hypoglycaemia. The authors' conclusion is modest and can hardly be taken issue with: 'evidence is not convincing of an effect of self monitoring blood glucose, with or without instruction in incorporating findings into self-care, in improving glycaemic control on reasonably controlled non-insulin treated patients with type 2 diabetes'.

But care is required. The difficulty, as always, is interpreting the evidence carefully and not extrapolating inappropriately. Of the 8457 people with type 2 diabetes open to study, 1616 (19 %) were excluded owing to regular blood glucose meter use and 3855 (46 %) for other reasons. In other words, over half of the available population were ineligible for the study and, in the majority of cases (70 %), we are not told why. Additionally, those who were recruited had a short duration of diabetes (median 3 years) that was relatively well-controlled ($HbA_{1c} \leq 7.5$ %).

Participants were allocated to either standardised usual care without monitoring; less intensive self-monitoring of blood glucose (three tests daily twice a week and healthcare professional advice on interpretation and action); or more intensive self-monitoring (free-testing and self-training in interpretation and application). There was no difference in the primary end point of change in HbA_{1c}, but there were significant differences in the secondary end points of total cholesterol and hypoglycaemia rates: total cholesterol was lower and hypoglycaemia rates higher in the intensively monitoring group compared with control. This is intriguing and difficult to explain considering the failure to improve HbA_{1c}. However, it seems clear that even in individuals empowered with the ability to make changes to diet, lifestyle and medication, monitoring did not result in improved glycaemic control.

The authors quote existing systematic reviews as estimating a 0.4 % reduction in HbA_{1c} with self-monitoring and calculate the incremental cost of QALY gained of between £4500 and £15 515. If, as this study suggests, this is an overestimate of the reduction in HbA_{1c} achieved, then the cost of monitoring becomes much more significant. Perhaps when treatment choices are discussed with these individuals, relieving them of the burden of blood glucose monitoring could make way for more intensive lipid-lowering or blood pressure lowering, which arguably, would be more valuable.

DIABETES CARE

Initiating insulin in groups saves time

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

1 A randomised, multicentre, two-arm, parallel-design study compared insulin initiation in groups of 4–8 with individual initiation.

2 Using the same personnel and education programme, 121 people with non-insulin-treated type 2 diabetes and an HbA_{1c} of 7.0–12.0 % were randomised to bedtime insulin glargine.

3 Insulin doses were self-adjusted to achieve a fasting plasma glucose of 4.0–5.5 mmol/l.

4 The mean HbA_{1c} had decreased by a similar amount in each group at week 24 (8.7 ± 0.2 to 6.9 ± 0.1 % for individually treated people and 8.8 ± 0.2 to 6.8 ± 0.1 % for groups; P = ns).

5 Mean insulin doses were 62 ± 5IU and 56 ± 5IU, respectively (P = ns) and the frequency of hypoglycaemia was similar.

6 Total time spent initiating insulin in groups (2.2±0.1 hours) was 48 % less than for those seen individually (4.2±0.2 hours). Therefore, time could be saved by group initiation without affecting outcomes.

Yki-Järvinen H, Juurinen L, Alvarsson M et al (2007) Initiate Insulin by Aggressive Titration and Education (INITIATE): a randomized study to compare initiation of insulin combination therapy in type 2 diabetic patients individually and in groups. *Diabetes Care* **30**: 1364–9

BMJ

SMBG does not improve glycaemic control in non-insulin-treated people with type 2 diabetes

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

1 The effect of self-monitoring of blood glucose (SMBG) was investigated in 453 people with non-insulin-treated diabetes from 48 general practices in Oxfordshire and South Yorkshire.

2 Participants in this three-arm, open, parallel-group randomised trial had a mean age of 65.7 years and a median diabetes duration of 3 years. Mean HbA_{1c} was 7.5 %.

3 The control group consisted of 152 people with usual standardised care. SMBG was introduced to a further 150 individuals who were advised to contact their GP for interpretation of the results. In addition, 151 people used SMBG and were trained in interpreting and applying their own results to enhance motivation.

4 The main outcome measure was HbA_{1c}. At 12 months, the differences between the three groups (adjusted for baseline measures) were not statistically significant (P = 0.12).

5 The difference in HbA_{1c} between controls and those using SMBG was -0.14 % (95 % CI: -0.35–0.07 %). The difference between controls and those using more intensive self-monitoring was -0.17 (95 % CI: -0.37–0.03 %).

6 The authors conclude that in people with non-insulin-treated type 2 diabetes, there is no convincing evidence from this data that SMBG improves glycaemic control compared with regular care, even when instruction on interpreting the results is provided.

Farmer A, Wade A, Goyder E et al (2007) Impact of self monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group randomised trial. *BMJ* **335**: 132

DIABETES

Carvedilol improves endothelial function more than metoprolol

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

1 In this small study, individuals who had previously been diagnosed with type 2 diabetes and hypertension were randomised to receive either carvedilol (n = 16) or metoprolol (n = 18) in addition to their current antihypertension medications.

2 At baseline, the mean age of both groups was around 61 years, BMI was approximately 34 kg/m^2 and 75 % were taking an ACE inhibitor and/or an ARB.

3 Target blood pressures for the trial were <135 mmHg (systolic) and <85 mmHg (diastolic). In the carvedilol group 8 % required the addition of a calcium channel blocker, 17 % required an additional diuretic and none required an alpha-blocker. For the metoprolol group these figures were 17 %, 0% and 8%, respectively.

4 From baseline to 5 months follow up, both treatments significantly reduced systolic ($P < 0.05$) and diastolic ($P < 0.0001$) blood pressure. The difference between treatments was not significant

5 Carvedilol significantly improved brachial–artery flow-mediated dilation compared with metoprolol ($P < 0.001$).

6 HDL-c decreased significantly with metoprolol ($P < 0.05$) but not carvedilol; however, there were no other glycaemic or lipid-variable differences between treatments.

7 Changes in oxidative stress, as measured by 8-isoprostane, asymmetric dimethylarginine and oxidised LDL-c, were not observed in the duration of this study.

8 Endothelial function is therefore significantly improved with carvedilol compared with metoprolol in people with type 2 diabetes and this difference is not explained by changes in glycaemic control and oxidative stress.

Bank AJ, Kelly AS, Thelen AM et al (2007) Effects of carvedilol versus metoprolol on endothelial function and oxidative stress in patients with type 2 diabetes mellitus. *Diabetes* **20**: 777–83

DIABETES CARE

Glycaemic control and weight reduction achieved with long-acting release exenatide

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

1 This phase 2 placebo-controlled study set out to ascertain the effects of long-acting release (LAR) exenatide on HbA_{1c}, postprandial glucose levels, fasting glucose levels and weight.

2 Forty-five individuals with type 2 diabetes poorly controlled by metformin and/or lifestyle alterations (HbA_{1c} 7.1–11.0 %) were randomly assigned to received either 0.8 mg LAR exenatide (n=16), 2.0 mg LAR exenatide (n=15) or placebo (n=14) once weekly for 15 weeks.

3 At baseline, average HbA_{1c} was 8.5 ± 1.2 % and mean diabetes duration was 5 ± 4 years.

4 LAR exenatide significantly reduced HbA_{1c} by 1.4 % in the 0.8 mg group and 1.7 % in the 2.0 mg group compared with those taking placebo (+0.4 %; $P < 0.0001$ for both comparisons).

5 An HbA_{1c} of ≤7 % was achieved by 4 people (36%) receiving 0.8mg LAR exenatide and 13 people (86 %) receiving 2.0 mg LAR exenatide, compared with no participants in the placebo group.

6 A significant level of weight reduction was observed in the 2.0 mg LAR exenatide group versus placebo: 3.8 ± 1.4 kg versus 0.03 ± 0.7 kg ($P<0.05$). Significant weight change was not observed in the placebo or 0.8 mg LAR exenatide groups.

7 Both exenatide doses also reduced fasting plasma glucose and self-monitored postprandial hyperglycaemia, and body weight was reduced with the 2.0 mg dose.

8 The authors suggest that a once-weekly formulation of exenatide could provide a novel method of delivering multiple positive metabolic effects in type 2 diabetes.

Kim D, MacConell L, Zhuang D et al (2007) Effects of once-weekly dosing of a long-acting release formulation of exenatide on glucose control and body weight in subjects with type 2 diabetes. *Diabetes Care* **30**: 1487–93

"Type 2 diabetes has a negative effect on the outcome of TB treatment. In light of this, screening for diabetes, and subsequent glycaemic control is recommended in people with TB."

ARCHIVES OF INTERNAL MEDICINE

Adding rosiglitazone to insulin therapy improves HbA_{1c}

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

1 The aim of this study was to examine the efficacy and safety of adding low-dose rosiglitazone to insulin therapy in comparison to continuing insulin alone in people with poorly controlled type 2 diabetes.

2 This 24-week double-blind study randomised 630 individuals with type 2 diabetes who were poorly controlled on insulin therapy alone (HbA_{1c} >7.5 %) to receive either rosiglitazone (2 or 4 mg/day) or placebo in addition to their usual insulin regimen.

3 At 24 weeks, mean HbA_{1c} was significantly decreased in the rosiglitazone group versus placebo (-0.3 %; $P=0.02$ for 2 mg and -0.4%; $P<0.001$ for 4 mg) and versus baseline (-0.6 % for 2 mg and -0.8 % for 4 mg; both $P<0.001$).

4 Addition of rosiglitazone 2 or 4 mg/day reduced C-reactive protein by 22.0 % and 34.2 %, respectively, versus baseline ($P<0.001$, for both) and by 22.2 % ($P=0.003$) and 32.0 % ($P<0.001$) versus placebo.

5 Fibrinogen was reduced by 10.5 % versus baseline with rosiglitazone 2 mg and by 12.0 % with 4 mg (both $P<0.001$). The difference was also significant versus placebo for 2 mg (-7.9 %; $P=0.002$) and 4 mg (-7.6 %; $P=0.004$).

6 Rosiglitazone 4 mg/day reduced matrix metalloproteinase 9 levels versus baseline (-17.1 %; $P=0.007$) and vs placebo (-23.3; $P<0.001$).

7 Adverse events were similar between treatment groups.

Hollander P, Yu D, Chou HS (2007) Low-dose rosiglitazone in patients with insulin-requiring type 2 diabetes. *Archives of Internal Medicine* **167**: 1284–90

QJM

Poor adherence to insulin impacts on long-term metabolic control

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

1 This observational, records-based study investigated the associations between adherence to an insulin regimen and HbA_{1c} in people with type 2 diabetes.

2 The data were collected from residents in Tayside, Scotland, between 1995 and 2001.

3 Of the 1099 people studied, 574 (52 %) were male; the mean age of participants at baseline was 62 ± 12 years and the average diabetes duration was 10 ± 7 years.

4 Median time for which insulin was dispensed was 1107 days (range: 366–2446).

5 The amount of insulin prescribed was 58.0 ± 33.3 IU/day while 53.6 ± 27.1 IU/day of insulin were collected from pharmacies. These figures in addition to the annual number of days of insulin coverage on the recommended dose were calculated to measure adherence to insulin. The outcome was 70.6 ± 17.7 %.

6 Individuals who had an insulin regimen adherence rate ≥80 % were significantly more likely than those with lesser rates of adherence to have a greater age at baseline ($P=0.0004$), a lower BMI ($P=0.0188$), lower HbA_{1c} ($P<0.0001$), greater age at diagnosis of diabetes ($P=0.001$) and lower daily insulin doses ($P<0.0001$).

7 Significant predictors of HbA_{1c} were adherence to insulin ($P=0.0021$), BMI ($P=0.0001$) and diabetes duration ($P=0.0314$).

Donnelly LA, Morris AD, Evans JM et al (2007) Adherence to insulin and its association with glycaemic control in patients with type 2 diabetes. *QJM* **100**: 345–50

CLINICAL INFECTIOUS DISEASES

Type 2 diabetes negatively impacts on treatment of TB

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

1 Type 2 diabetes is a known risk factor for tuberculosis (TB) This study set out to assess the effect of diabetes on the clinical presentation and treatment outcome of TB.

2 In Indonesia, 737 people with pulmonary TB were screened for type 2 diabetes.

3 People with diabetes comprised 14.8 % of people with TB and the presence of diabetes was associated with older age and greater body weight.

4 More TB symptoms were present in those who also had diabetes, although there was no evidence that symptoms were more severe.

5 Sputum microscopic examination was used to measure specimens for *Mycobacterium tuberculosis* at 2 and 6 months.

6 At 2 months, more cultured sputum specimens tested positive for the bacteria in the people with diabetes (18.1 %) than those without (10 %).

7 At 6 months, positive results were 22.2% and 6.9%, respectively.

8 Diabetes is therefore significantly associated with positive sputum culture results after 6 months of TB treatment. This association remained when BMI, age, sex, chest radiograph abnormalities, sputum mycobacterium load after 2 months, noncompliance and drug resistance were controlled for (odds ratio: 7.65; $P=0.004$).

9 Type 2 diabetes therefore has a negative effect on the outcome of TB treatment. In light of this, screening for diabetes, and subsequent glycaemic control is recommended in people with TB. The authors suggest research into the underlying mechanisms of this association.

Alisjahbana B, Sahiratmadja E, Nelwan EJ (2007) The effect of type 2 diabetes mellitus on the presentation and treatment response of pulmonary tuberculosis. *Clinical Infectious Diseases* **45**: 428–35