Diabetes journals

Multiple risk factor intervention: Is it effective early in the course of diabetes?

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Type 2 diabetes is associated with significantly elevated all-cause and cardiovascular disease (CVD)-related mortality, as well as a higher incidence of microvascular and macrovascular disease. These risks can be reduced by multiple risk factor intervention, particularly in people who are at higher baseline risk, with a longer diabetes duration (Gaede et al, 1999). Less is known, however, about the potential utility of intensive multiple risk factor intervention earlier in the course of type 2 diabetes. Such a question is becoming increasingly pertinent in the context of a greater focus on opportunistic screening for diabetes in at-risk individuals, ultimately leading to a larger number of people being diagnosed at an earlier point within the natural history of the condition.

The study by Black et al (summarised alongside) was a pragmatic, cluster-randomised, parallel-group trial conducted in Denmark, the Netherlands and the UK. A total of 3057 people with screen-detected type 2 diabetes were grouped by general practice and randomised to receive routine diabetes care according to national guidelines (*n*=1379) or intensive, multifactorial, target-driven management (*n*=1678). In the intensively managed group, treatment targets included an HbA_{1c} of <53.0 mmol/mol (7.0%) if HbA_{1c} was higher than 47.5 mmol/mol (6.5%); a blood pressure of ≤135/85 mmHg if higher than 120/80 mmHg; a cholesterol level of <5.0 mmol/L in people without ischaemic heart disease and <4.5 mmol/L in those with ischaemic heart disease; and a prescription of aspirin in those being treated with antihypertensive medication. Statins were recommended to all individuals with a cholesterol level ≥3.5 mmol/L.

The participants were followed for a mean of 5.7 years. The primary endpoint was 10-year CVD risk, estimated using the UK Prospective Diabetes Study (UKPDS) model at 5 years post-diagnosis. The UKPDS model is a diabetes-specific risk assessment tool that estimates the absolute risk of fatal or non-fatal CVD within a defined time frame up to 20 years (Coleman et al, 2012).

In all three participating countries, 10-year CVD risk was significantly lower in the intensive treatment group compared with the routine care group at 5 years, although both groups demonstrated a reduction in long-term CVD risk. As with all evaluations using modelled outcomes, there are some limitations that need to be considered, primarily the degree of uncertainty arising from modelled outcomes and how these may differ from true clinical outcomes. However, the model used in this study is both disease-specific and well validated. Another issue is that the participants were predominantly of white ethnic origin (93%), which may limit the extrapolation of these findings to more ethnically diverse populations.

The results of this study, in essence, support the potential long-term outcome benefit associated with intensive multiple risk factor intervention in newly diagnosed people with type 2 diabetes, whilst illustrating that even if such an approach is not adopted, current guideline-based treatment also delivers a reduction in long-term risk. The study, therefore, provides further rationale to support the implementation of widespread screening to facilitate earlier diagnosis of type 2 diabetes. ■

Coleman R, Stevens R, Holman R (2012) Updated UKPDS risk engine that estimates primary and secondary cardiovascular disease risk in people with recently-diagnosed or established type 2 diabetes. *Diabetes* **61** (Suppl 1): A103 (poster 395-P)

Gaede P, Vedel P, Parving HH, Pedersen O (1999) Intensified multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: the Steno type 2 randomised study. *Lancet* **353**: 617–22

Diabet Med

Early multifactorial therapy reduces cardiovascular risk in T2D

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

1 This was a parallel-group, randomised controlled trial conducted in three countries to evaluate the effects of an intensive, multifactorial treatment on cardiovascular (CV) risk in people with screen-detected T2D.

2 Five-year results showed a statistically insignificant 17% reduction in CV events. In the absence of longer-term data to evaluate the effects of this treatment, the authors modelled the 10-year CV risk in this cohort.

3 A total of 3057 participants from 343 general practices across Denmark, the Netherlands and the UK were evaluated and were randomised to either routine care or intensive therapy.

4 The intensive therapy included tight control of HbA_{1c}, blood pressure and cholesterol levels, as well as statin and aspirin use if required.

5 After a mean follow-up of 5.7 years, 196 people had died (24% owing to CV causes) and were excluded, and 760 were excluded owing to lack of complete data, leaving 2101 participants for analysis.

6 In the total cohort, 10-year modelled CV risk decreased from 27.3% at baseline to 21.3% at 5 years. Across the three countries combined, after adjustment for baseline risk and clustering, the risk was 2.0% lower (95% confidence interval, –3.1 to –0.9%) in the intensive treatment group.

7 The authors, therefore, recommend that clinicians intensively treat multiple CV risk factors as early as possible in the course of T2D.

Black JA, Sharp SJ, Wareham NJ et al (2014) Does early intensive multifactorial therapy reduce modelled cardiovascular risk in individuals with screen-detected diabetes? Results from the ADDITION-Europe cluster randomized trial. *Diabet Med* **31**: 647–56

Diabetes Care

Sulphonylurea use associated with CVD in women with T2D

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

1 In this study, the authors prospectively evaluated the association of long-term sulphonylurea use with incident cardiovascular disease (CVD) in a cohort of diabetes nurses with T2D but no CVD at baseline.

2 A total of 4902 participants were followed up for 5–10 years. In this time, 2435 received sulphonylureas and 2467 did not. There were 339 incidences of CVD, including 191 cases of coronary heart disease (CHD) and 148 cases of stroke.

3 Compared with non-users, participants who took sulphonylureas for 1–5, 6–10 and >10 years had a relative risk of CVD of 1.20, 1.40 and 1.65, respectively. When CHD and stroke were analysed separately, only CHD was significantly associated with sulphonylurea use.

4 Combination therapy with metformin and a sulphonylurea resulted in a three-times greater risk of CHD compared with metformin alone.

5 This study population comprised older women with long-standing T2D, so further studies to assess this risk in other populations are warranted.

Li Y, Hu Y, Ley SH et al (2014) Sulfonylurea use and incident cardiovascular disease among patients with type 2 diabetes: prospective cohort study among women. *Diabetes Care* **37**: 3106–13

Diabetes Care

Effects of overweight in youth on CIMT and T2D in adulthood

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

1 The authors assessed the 21-year progression of carotid intima–media thickness (CIMT) and risk of T2D and metabolic syndrome in youths according to BMI and metabolic status.

2 In 1986, a total of 1617 youths (age 9–24 years) were categorised as normal-weight, metabolically healthy (group 1); normal-weight, metabolically abnormal (group 2); overweight, metabolically healthy (group 3) or overweight, metabolically abnormal (group 4).

3 In 2007, CIMT progressively increased from group 1 through to group 4. CIMT was also significantly higher in group 4 than in group 2.

4 After adjustment for baseline metabolic parameters, CIMT in group 2 was not significantly different from that in group 1.

5 Groups 3 and 4 had a significantly higher risk of developing metabolic syndrome or T2D compared with group 1.

6 Youth overweight, therefore, appears to be independently associated with later cardiovascular and metabolic risk.

Koskinen J, Magnussen CG, Sabin MA et al (2014) Youth overweight and metabolic disturbances in predicting carotid intima–media thickness, type 2 diabetes, and metabolic syndrome in adulthood: the Cardiovascular Risk in Young Finns study. *Diabetes Care* **37**: 1870–7

Diabetes

Association between hyperglycaemia, infarct size, area at risk and myocardial salvage in STEMI

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

1 Hyperglycaemia occurs in up to half of hospital admissions for ST-elevation myocardial infarction (STEMI) and has been linked to worse prognosis; however, the causal direction of this relationship is unknown.

2 The authors sought to determine the associations between hyperglycemia and infarct size, myocardial salvage, and area at risk in 210 patients with STEMI.

3 Hyperglycaemia was associated with increased area at risk and infarct size; however, after adjustment for area at risk, infarct size and salvage index did not differ between the two groups.

4 Thus, hyperglycaemia is an indicator of area at risk and infarct size, but does not appear to affect myocardial salvage or the risk of reperfusion injury.

5 Exenatide treatment resulted in increased salvage index both in hyper- and normoglycaemic patients; therefore, its cardioprotective effects seem to be independent of glucose levels.

Lønborg J, Vejlstrup N, Kelbæk H et al (2014) Impact of acute hyperglycemia on myocardial infarct size, area at risk, and salvage in patients with STEMI and the association with exenatide treatment: results from a randomized study. *Diabetes* **63**: 2474–85

Diabetes Care

No effect of vitamin D supplementation in prediabetes

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

1 In addition to its effects on skeletal health, a low vitamin D concentration is associated with increased insulin resistance and is a predictor of future T2D and cardiovascular disease.

2 Therefore, the authors evaluated the effect of vitamin D supplementation on glycaemic parameters in a cohort of people with prediabetes (impaired fasting glucose and/or impaired glucose tolerance). They present the 1-year results of this 5-year trial.

3 Participants (n=511) were randomised 1:1 to receive weekly vitamin D supplementation or placebo.

4 At 1 year, after adjustment for baseline levels, vitamin D supplementation had no significant effect compared with placebo on glycaemic indices, lipid profiles, blood pressure or C-reactive protein levels.

Sollid ST, Hutchinson MY, Fuskevåg OM et al (2014) No effect of high-dose vitamin D supplementation on glycemic status or cardiovascular risk factors in subjects with prediabetes. *Diabetes Care* **37**: 2123–31

> *"At 1 year, after adjustment for baseline levels, vitamin D supplementation had no significant effect compared with placebo on glycaemic indices, lipid profiles, blood pressure or C-reactive protein levels."*