Major journals

Emerging Risk Factors Collaboration study: Diabetes is associated with substantial premature death

Jiten Vora, Professor of Diabetes, Royal Liverpool University Hospital, Liverpool

The presence of diabetes doubles the risk of death from vascular causes. Furthermore, relationships between diabetes and certain cancers have been identified. However, the precise nature of these relationships with glycaemia has not been evaluated, nor indeed the contributions of other associated risk factors which may produce general ill-health in individuals with diabetes. Additionally, previous studies have only included relatively small numbers of participants.

> ***"This study confirms the views of clinicians that after adjustment of age, sex, smoking status and BMI there is nearly a two-fold increase in risk of death from any cause."***

The study summarised alongside is yet another excellent analysis from the Emerging Risk Factors Collaboration, of individual participant data on 123 205 deaths among 820 900 people in 97 prospective studies. What the results provide is confirmation of the views of clinicians that after adjustment of age, sex, smoking status and BMI there is nearly a two-fold increase in risk of death from any cause, death from cancer, death from vascular causes and death from other causes. The authors of the study also identify the cancers that particularly affect people with diabetes as those of the liver, pancreas, ovary, colorectum, lung, bladder and breast. The risk of death from varying causes is reduced when corrected for ambient glucose levels but not for corrections for systolic blood pressure, lipid levels, or renal function. Indeed fasting glucose values above 5.6 mmol/L (but not below) were associated with increased risk. This confirms the presence of substantial premature death in diabetes particularly from several cancers, infectious diseases and some external causes. Practically, this translates to a life-expectancy reduction of 6 years for a 50-year-old, of which 40% is due to non-vascular causes.

There will, no doubt, be further discussion regarding not only the contribution of diabetes to an increased rate of death and cancer, but also the effect of diabetes therapies on this increased risk.

ANNALS OF INTERNAL MEDICINE

Comparative review of drugs for T2D

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

1 The authors of this review set out to summarise the benefits and harms of antidiabetes drugs for type 2 diabetes (not including insulin).

2 Studies were identified by searching online databases, such as MEDLINE, and 140 trials and 26 observational studies of head-to-head comparisons of monotherapy or combination therapy that reported intermediate or long-term clinical outcomes or harms were analysed.

3 It was found that most medications decreased HbA_{1c} level by about 1 percentage point, with similar reductions for most dual-therapy combinations.

4 Compared with sulphonylureas, thiazolidinediones increased the risk of congestive heart failure and increased the risk of bone fracture compared with metformin.

5 The evidence reviewed supports use of metformin first-line.

Bennett WL, Maruthur NM, Singh S et al (2011) Comparative effectiveness and safety of medications for type 2 diabetes: an update including new drugs and 2-drug combinations. *Ann Intern Med* **154**: 602–13

NEJM

Diabetes associated with death from non-vascular causes

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

1 The relationship between diabetes or hyperglycaemia and death from cancer or other non-vascular causes was analysed in this study. The authors aimed to estimate the effect of diabetes on life-expectancy.

2 Hazard ratios were calculated for cause-specific death, according to baseline diabetes status or fasting glucose level. Data were from 97 prospective studies involving 820 900 people and 123 205 deaths.

3 Hazard ratios in people with diabetes compared with people without diabetes (after adjustment for age, sex, smoking status and BMI) were: 1.80 (95% confidence interval [CI], 1.17–1.90) for death from any cause; 1.25 (95% CI, 2.11–2.56) for death from cancer; 2.32 (95% CI, 2.11–2.56) for death from vascular causes; and 1.73 (95% CI, 1.62–1.85) for death from other causes.

4 Compared with people without diabetes, those with diabetes were at moderately higher risk of death from cancers of the liver, pancreas, ovary, colorectum, lung, bladder and breast.

5 Diabetes was also associated with death from renal disease, liver disease, pneumonia and mental disorders among others.

6 On average, a 50-year-old individual died 6 years earlier than someone without diabetes with 40% of the difference in survival attributable to excess non-vascular deaths.

7 It was concluded that, independent of other major risk factors, diabetes was associated with substantial premature death.

Emerging Risk Factors Collaboration, Seshasai SR, Kaptoge S et al (2011) Diabetes mellitus, fasting glucose, and risk of cause-specific death. *N Engl J Med* **364**: 829–41

AMERICAN JOURNAL OF MEDICINE

Impact of hypertension and diabetes on coronary intervention outcome

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

1 The outcome of people undergoing percutaneous coronary intervention was compared in people with diabetes or hypertension.

2 Data on 44268 people who had undergone their first percutaneous coronary intervention between 1 January 2006 and 31 December 2008 were extracted from five Swedish national registers.

3 Mortality was 6.4% and was highest in people with diabetes and hypertension. Hypertension did not increase mortality but did increase the risk for subsequent myocardial infarction by 10%. This increased to a 4-fold risk if the person had diabetes.

4 It was concluded that diabetes had a negative effect on the outcome of percutaneous coronary intervention, especially if the individual also has hypertension.

Lingman M, Albertsson P, Herlitz J et al (2011) The impact of hypertension and diabetes on outcome in patients undergoing percutaneous coronary intervention. *Am J Med* **124**: 265–75

ARCHIVES OF INTERNAL MEDICINE

Only early-onset diabetes is a CHD risk equivalent

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

1 The influence of age at onset and duration of diabetes on cardiovascular disease risk and all-cause mortality was assessed in 4045 men aged 60–79 years.

2 During the 9 years of follow-up, there were 372 major coronary heart disease (CHD) events, 455 deaths from cardiovascular disease (CVD) and 1112 deaths from all causes.

3 A significantly increased risk of major CHD events was associated with both early and late onset of diabetes compared with men who had no CHD.

4 Only men with early-onset diabetes had a CHD risk similar to those with a previous myocardial infarction.

5 The authors concluded that early onset of diabetes (duration >10 years) has the equivalent CHD risk of a previous MI.

Wannamethee SG, Shaper AG, Whincup PH et al (2011) Impact of diabetes on cardiovascular disease risk and all-cause mortality in older men: influence of age at onset, diabetes duration, and established and novel risk factors. *Arch Intern Med* **171**: 404–10

LANCET

The place of blood glucose lowering

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

1 The authors of this editorial begin by questioning whether the cardiovascular benefit of intensive blood glucose lowering justifies population screening for diabetes.

2 The American Diabetes Association concluded that regular screening (every 3–5 years) of people aged 30–45 years is cost-effective, however they point out that the analysis does not take into account the effect of intensive blood glucose lowering on quality of life.

3 The authors argue that the pharmaceutical industry has a part to play in the recommendation that blood glucose levels (rather than lipids or blood pressure) should be controlled for cardiovascular prevention despite this not being appropriate in certain patient groups.

4 The authors concluded that good blood glucose control has benefits when appropriately applied but not if it distracts from other treatment priorities.

Yudkin JS, Richter B, Gale EA (2011) Intensified glucose control in type 2 diabetes – whose agenda? *Lancet* **377**: 1220–2

LANCET

Cardiovascular safety and drug development

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

1 The authors of this editorial looked at the means of assessing cardiovascular risk of new medications. Concern about the long-term cardiovascular safety of diabetes drugs has led to the US Food and Drug Administration issuing new guidance on the subject.

2 The most recently approved drug classes (glucagon-like peptide-1 [GLP-1] receptor agonists and dipeptidyl peptidase-4 [DPP-4] inhibitors) seem to fulfil two of the main criteria for new diabetes drugs – they have advantages over previous drugs and have neutral or beneficial effects on cardiovascular health.

3 The GLP-1 receptor is expressed on cardiomyocytes as well as other cells and therefore produces direct and indirect actions on blood vessels and the heart in people with diabetes that are thought to be cardioprotective.

4 DPP-4 inhibition may also be cardioprotective as this review cites one study of saxagliptin where cardiovascular events did not increase in participants. However, the authors recommend healthy scepticism and remind readers that rosiglitazone initially showed protective and anti-inflammatory actions in pre-clinical studies.

6 The authors concluded that withdrawal of rosglitazone from the market due to cardiovascular concerns has led to earlier initiation of cardiovascular outcome studies for diabetes drugs such as sitagliptin, saxagliptin, liraglutide and exenatide once-weekly.

Bansal S, Wackers FJ, Inzucchi SE et al (2011) Drucker DJ, Goldfine AB (2011) Cardiovascular safety and diabetes drug development. *Lancet* **377**: 977–9

"Diabetes had a negative effect on the outcome of percutaneous coronary intervention, especially if the individual also has hypertension."