

Sizeable declines in cardiovascular mortality in T2D: Causes and consequences



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Whilst some recent reports suggest diabetes care is not all it should be, cardiovascular risks have substantially reduced over the past decades and mortality rates have likewise declined. A very nice illustration of this comes from the analyses of the Icelandic population-

based Reykjavik and AGES-Reykjavik cohort studies (paper summarised alongside). The authors show that whilst mortality rates had declined in people with and without diabetes, the declines were greater in those with diabetes, so that adjusted hazard ratio of cardiovascular mortality in individuals with diabetes compared to those without diabetes fell from 1.88 in 1993 to 1.46 in 2004. In absolute risk terms, the adjusted cardiovascular disease mortality (CVD) mortality rates for diabetes patients were 18.9 per 1000 person-years in 1993 but only 10.2 per 1000 person in the 2004 (AGES-Reykjavik) diabetes cohort, with the latter rate notably similar to the non-diabetes rates from 1993.

The findings almost perfectly mirror recent meta-analysis data from the Emerging Risk Factor Collaboration (ERFC) of a halving in mortality from 1970s to 2000s (Seshasai et al, 2011), and together with other data from the US (Gregg et al, 2012), confirm a steep decline in CVD mortality in diabetes patients in westernised countries. Why have CVD mortality rates come down so much in people with diabetes? The major reason for recent gains appears to be better management of CVD

risk factors, in particular cholesterol and blood pressure levels, as recently documented (Ford et al, 2011). Of course, whilst this is good news, for newer agents to prove CVD risk reduction in diabetes now necessitates trials of ever increasing size, or better identification of very high-risk subgroups (Preiss et al, 2011).

Furthermore, and as recently reviewed (Sattar, 2013), as CVD death rates continue to decline and more people with T2D live longer, this may present newer problems, including rising levels of cognitive decline or, potentially, greater heart failure and cancer rates. Additionally, at the same time, there is an increasing population of younger, more obese patients with T2D, a group likely to have more rapid glycaemia progression, as well as a general rise in T2D rates worldwide. Consequently, diabetes will increasingly account for a higher percentage of the total CVD burden in society. These shifting patterns of disease will present unique problems in the future and mandate even greater efforts at slowing or reversing the diabetes epidemic. For the time being, however, good blood pressure and lipid control must remain cornerstones of CVD prevention in people with diabetes.

Ford ES (2011) Trends in the risk for coronary heart disease among adults with diagnosed diabetes in the U.S. *Diabetes Care* **34**: 1337–43

Gregg EW, Cheng YJ, Saydah S et al (2012) Trends in death rates among U.S. adults with and without diabetes between 1997 and 2006. *Diabetes Care* **35**: 1252–57

Preiss D, Sattar N, McMurray JJ (2011) A systematic review of event rates in clinical trials in diabetes mellitus. *Am Heart J* **161**: 210–9

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

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

DIABETES OBES METAB

BP lowering efficacy of GLP-1 RAs

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

1 The authors conducted a meta-analysis to evaluate the blood pressure-lowering activity of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) exenatide and liraglutide in people with T2D. An electronic database search identified 16 randomised controlled trials consisting of 3443 participants and 2417 controls for inclusion.

2 Exenatide was effective in reducing systolic blood pressure (SBP) compared to insulin glargine ($P < 0.00001$; $P < 0.00001$) and decreasing diastolic blood pressure (DBP; $P < 0.00001$) compared to sitagliptin. Liraglutide efficiently (1.2 mg) reduced SBP compared with placebo and glimepiride ($P < 0.00001$ and $P = 0.05$).

3 The authors concluded that exenatide and liraglutide decreased SBP and DBP by 1 to 5 mmHg compared to other common drugs, and may offer an effective treatment for people with T2D.

Wang B, Zhong J, Lin H et al (2013) Blood pressure-lowering effects of GLP-1 receptor agonists exenatide and liraglutide. *Diabetes Obes Metab* 22 Feb [Epub ahead of print]

BMC PUBLIC HEALTH

CV mortality continues to decline in diabetes

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

1 Decreased cardiovascular disease and all-cause mortality rates have lengthened life expectancy in the Western world. However, the incidence of T2D has increased, which is independently associated with elevated cardiovascular disease and mortality risk.

2 The authors of this study aimed to measure incidence of cardiovascular and all-cause mortality in two cohorts of older people with and without T2D.

3 A total of 1506 participants from the Reykjavik Study (1993) were compared to 4514 individuals taking part in the AGES-Reykjavik Study (2004) over two consecutive follow-up periods of 5.7 and 5.3 years.

4 The prevalence of diabetes was similar between the groups between 1993 and 2004 (men: 16.7% versus 16% and women: 9% versus 10%, respectively). A decrease in cardiovascular mortality rate (-32%) and all-cause mortality rate (-19%) was observed from 1993 and 2004.

5 This decrease was greatest in participants with T2D (hazard ratio, 1.88; 95% CI, 1.24–2.85 in 1993; and 1.46; 95% CI, 1.11–1.91 in 2004). The number of people with T2D receiving glucose-lowering, hypertensive and lipid-lowering medication was larger in 2004.

6 The authors concluded that cardiovascular and all-cause mortality rates declined in older people with and without T2D between 1993–2004.

Olafsdottir E, Aspelund T, Sigurdsson G et al (2013) Similar decline in mortality rate of older persons with and without type 2 diabetes between 1993 and 2004 the Icelandic population-based Reykjavik and AGES-Reykjavik cohort studies. *BMC Public Health* 15 Jan

Type 2 diabetes

DIABETES CARE

Menopause timing associated with T2D risk

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

1 Although the relationship between age at menopause and cardiovascular disease has been well established, the association between menopause timing and T2D is unknown.

2 The authors prospectively determined the relationship between menopausal age, reproductive life span and T2D risk in a cohort of postmenopausal women ($n=8099$).

3 After a median follow-up of 10.7 years (interquartile range 6.6–12.6), T2D had developed in a total of 3691 women. Menopause occurring at a younger age was significantly associated with an increased risk of T2D.

4 Hazard ratios (HRs) for T2D were 1.32 (95% CI, 1.04–1.69), 1.09 (0.90–1.31), 0.97 (0.86–1.10) and 0.85 (0.70–1.03) for menopause occurring at 40, 40–44, 45–49 and 55 years or over, compared with menopause at 50–54 years of age. Women experiencing menopause before 40 were 32% more likely to develop T2D compared to those with menopause at 50–54 years.

5 Higher T2D risk was also associated with shorter reproductive life span (HR per standard deviation [SD] 1.06 [1.01–1.12]). BMI, waist circumference and smoking did not display an effect modification ($P>0.05$).

6 The authors concluded that a younger age at menopause and a shorter reproductive life span are associated with an increased risk of T2D.

Brand JS, van der Schouw YT, Onland-Moret NS (2012) Age at menopause, reproductive life span, and type 2 diabetes risk. *Diabetes Care* **4**: 1012–9

DIABETES CARE

Factors linked to severe hypoglycaemia

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

1 The authors aimed to investigate the factors associated with severe hypoglycaemia (SH) in people with T2D.

2 Participants aged 25–75 years without renal disease ($n=1217$) were followed up for a median of 10.4 years. SH was associated with longer diabetes duration and macroalbuminuria (hazard ratio, 2.52; 95% CI, 1.31–4.84; $P=0.006$). SH incidence increased with older age ($P<0.001$), insulin ($P<0.001$) and sulphonylurea ($P=0.003$) use.

3 The authors concluded that SH was associated with T2D duration and macroalbuminuria.

Yun JS, Ko SH, Ko SH et al (2012) Presence of macroalbuminuria predicts severe hypoglycemia in patients with type 2 diabetes mellitus. *Diabetes Care* **17** Dec [Epub ahead of print]

DIABETOLOGIA

Low BR predicts amputation risk

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

1 The authors investigated the incidence of amputation in 9795 participants with T2D.

2 Plasma bilirubin (BR) was inversely correlated to lower-limb amputation (HR 1.38 per 5 $\mu\text{mol/L}$ decrease in BR, 95% CI, 1.07–1.79, $P=0.013$), with lower levels associated with increased risk.

3 The authors concluded that low BR is associated with an increased risk of lower-limb amputation in people with T2D.

Chan KH, O'Connell RL, Sullivan DR et al (2013) Plasma total bilirubin levels predict amputation events in type 2 diabetes mellitus. *Diabetologia* **56**: 724–36