Diabetes journals

Mortality trends: Improved rates for coronary heart disease without diabetes, but why not with diabetes?

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It is well recognised that mortality rates for coronary heart disease (CHD) and other circulatory diseases (such as stroke and peripheral arterial disease) have declined in developed countries, which has been attributed to factors, including a reduction in the prevalence of cardiovascular risk factors in the population and improvements in pharmacological and surgical interventions for cardiovascular conditions. Despite such considerations, cardiovascular disease remains a leading cause of morbidity and mortality representing a significant clinical and economic burden to healthcare systems. This is particularly pertinent for people with diabetes, for whom cardiovascular disease represents the most common and costly complication of the condition (Hex et al, 2012).

With these issues in mind, the study by Ecclestone et al (summarised alongside) aimed to compare trends in population-based mortality for CHD without diabetes on the death certificate with trends for CHD with diabetes mentioned on the same certificate. The authors analysed an all-England dataset with multiple-cause coded mortality records from 1995 to 2010. A dataset from Oxford was also analysed due to it being the longest run, starting from 1979, of multiple-cause coded mortality in England. Age-specific and age-standardised mortality rates were calculated. In the all-England dataset, there were nearly 2 million deaths with CHD and no mention of diabetes; and over 170 000 deaths with CHD and diabetes mentioned on the same death certificate.

Of deaths with CHD without a mention of diabetes, the rates per million approximately halved from 1995 to 2010 for men and women. Of deaths with CHD where diabetes was mentioned, the rates per million increased for men and fell slightly for women. The dataset from Oxford showed that mortality rates with CHD in men and women without diabetes had fallen by two-thirds; but that rates for CHD with diabetes had not fallen. These data illustrate a spectacular reduction in CHD mortality; however, there is no such fall in people with diabetes.

The reasons behind such an observation remain unclear. Medical interventions may have less effect in people with diabetes than those without; for example, recent trials of the use of fibrates to lower cholesterol have found these medications to be less effective in people with diabetes (Keech et al, 2005). Similarly, the efficacy of surgical interventions for CHD in people with type 2 diabetes may differ; for example, unlike in people without diabetes, coronary artery bypass grafting was superior to percutaneous coronary intervention in terms of reducing cardiovascular mortality and rate of myocardial infarction in those with multi-vessel CHD (Farkouh et al, 2012). Penetration of cardiovascular-modifying medication may be a factor; however, recent data illustrate that people with diabetes were found to have higher rates of risk-factor monitoring and medication than people without diabetes (Taylor et al, 2013).

The authors conclude there are some important limitations to this analysis; firstly, the trends in CHD mortality rates with and without diabetes described in the article are based on death certification data and their accuracy is, therefore, reliant on recording practices by certifying doctors. Secondly, this study did not distinguish between type 1 and type 2 diabetes because certification of type was inconsistent and type was often not available on death certificates. However, given that both types confer increased risk of CHD and that type 2 is by far the commoner form, the authors suggest that it is unlikely that the inclusion of both would have altered the general trends found.

Further studies should include analysis of trends in stroke and cancer in people with and without diabetes, while additional studies are warranted to investigate whether the data seen in this study reflects an increase in diabetes (and therefore in people at risk of CHD); whether people with diabetes are refractory to changes in other risk factors for CHD that have benefited people without diabetes; whether people with diabetes do not benefit as much as others from treatments for CHD; or whether the findings result from a combination of these. ■

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Diabet Med

Trends in mortality from CHD with and without diabetes

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

1 The authors investigated the trends in population-based mortality for coronary heart disease (CHD) with and without a mention of diabetes on the death certificate.

2 Using the all-England dataset, which has multiple-cause coded mortality records from 1995 to 2010, and the Oxford dataset, which began in 1979, the authors calculated age-specific and age-standardised mortality rates.

3 In the all-England dataset from 1995 to 2010, there were 1 772 760 deaths with CHD and no mention of diabetes and 173 184 deaths where both CHD and diabetes were mentioned on the same death certificate.

4 Of deaths with no mention of diabetes, deaths per million for women fell by half and deaths per million for men more than halved between 1995 and 2010. Of deaths that mentioned CHD and diabetes, there was an increase in rates per million for men and there was a slight decrease for women.

5 From the Oxford dataset, the data showed that mortality rates in men and women without diabetes had dropped by two-thirds, but that rates for CHD with diabetes on the same death certificate had not fallen.

6 The fall in mortality referring to CHD without diabetes may be attributed to improvements in risk factors for CHD and improvements in survival from CHD.

7 This study highlights that diabetes is associated with CHD and mortality, and asks why mortality rates have not declined for those with diabetes and CHD.

Ecclestone TC, Yeates DG, Goldacre MJ (2015) Fall in population-based mortality from coronary heart disease negated in people with diabetes mellitus: data from England. *Diabet Med* 28 Mar [Epub ahead of print]

Diabetologia

Blood pressure, cardiovascular events and renal impairment

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

1 In this study, the relationship between blood pressure (BP) and risk of cardiovascular events (CVEs) and all-cause mortality in people with T2D and renal impairment was investigated.

2 The total cohort were followed until 2011 or death and comprised 33 346 adults with diabetes and a mean age of 75±9 years.

3 Time-dependent Cox models were implemented to estimate hazard ratios, adjusting for cardiovascular risk factors and ongoing medications.

4 Over the follow-up period, 11 317 CVEs and 10 738 deaths occurred. Those who had a systolic BP of 135–139 mmHg and a diastolic BP of 72–74 mmHg had the lowest risk of CVEs and all-cause mortality.

5 A low pulse pressure was associated with a high risk of death, while a high pulse pressure was associated with an increased risk of a CVE.

6 Most participants were normoalbuminic which suggests that renal impairment is an independent risk factor for CVEs and all-cause mortality. Of interest, the author noticed that those that were normoalbumunic had a slightly higher mortality rate than those with albuminuria at the lowest BP range.

7 The risk of CVEs and all-cause mortality were increased for both high and low systolic and diastolic BPs, presenting a U-shaped relationship.

Afghahi H, Svensson MK, Pirouzifard M et al (2015) Blood pressure level and risk of major cardiovascular events and all-cause of mortality in patients with type 2 diabetes and renal impairment: an observational study from the Swedish National Diabetes Register. *Diabetologia* **58**: 1203–11

Diabetes Care

Empagliflozin and blood pressure

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

1 As part of the EMPA-REG blood pressure (BP) investigation, the aim of this analysis was to study the efficacy, safety and tolerability of empagliflozin (a sodium–glucose co-transporter 2 inhibitor) in people with T2D and hypertension.

2 A total of 825 people with T2D and hypertension were randomised to 10 and 25 mg empagliflozin or placebo once daily for 12 weeks.

3 At 12 weeks, 10 mg and 25 mg empagliflozin both significantly reduced BP from baseline compared to placebo.

4 A similar number of adverse events were reported in each of the three test groups. Serious adverse events were reported in a higher proportion of individuals receiving placebo than empagliflozin.

5 Empagliflozin was well tolerated by users and resulted in reductions in systolic and diastolic BP and HbA_{1c} versus placebo.

Tikkanen I, Narko K, Zeller C et al (2015) Empagliflozin reduces blood pressure in patients with type 2 diabetes and hypertension. *Diabetes Care* **38**: 420–8

Diabetologia

HbA_{1c} and blood pressure change with canagliflozin

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

1 Canagliflozin, a sodium–glucose co-transporter 2 inhibitor, is known to reduce HbA_{1c}, body weight and systolic blood pressure (SBP) in people with T2D. The authors planned to investigate the contribution of weight loss to reductions in HbA_{1c} and SBP as a result of canagliflozin treatment.

2 Pooled data from four placebo-controlled Phase III studies with 2250 people were analysed. Participants were either treated with canagliflozin 100 mg, 300 mg or placebo once daily for 26 weeks.

3 Canagliflozin 100 mg and 300 mg lowered body weight, HbA_{1c} and SBP significantly more than placebo.

4 The authors calculated that ~85% of HbA_{1c} lowering and ~60% of SBP lowering was independent of weight loss. The mechanism of weight-loss-independent BP reduction may be due to mild osmotic diuresis or alterations in sodium reabsorption as a result of canagliflozin treatment.

Cefalu WT, Stenlöf K, Leiter LA et al (2015) Effects of canagliflozin on body weight and relationship to HbA_{1c} and blood pressure changes in patients with type 2 diabetes. *Diabetologia* **58**: 1183–7

Diabetes Care

Physical activity

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

1 The authors investigated the contribution of leisure-time physical activity (LTPA) and an exercise training intervention to cardiovascular (CV) risk in people with coronary artery disease (CAD) and T2D. LTPA was measured by the frequency of physical activity periods lasting over 30 minutes.

2 During 2 years of follow up, people with no or low levels of LTPA at baseline compared to high levels of LTPA had an increased risk of CV events.

3 Alongside, among those who completed the 2-year exercise intervention, there were significant improvements in exercise capacity both in people who had CAD with T2D and without T2D compared with the control group.

Karjalainen JJ, Kiviniemi AM, Hautala AJ et al (2015) Effects of physical activity and exercise training on cardiovascular risk in coronary artery disease patients with and without type 2 diabetes. *Diabetes Care* **38**: 706–15

"This study highlights that diabetes is associated with coronary heart disease (CHD) and mortality, and asks why mortality rates have not declined for those with diabetes and CHD."

References for commentary

Farkouh ME, Domanski M, Sleeper LA et al (2012) Strategies for multivessel revascularization in patients with diabetes. *N Engl J Med* **367**: 2375–84

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Keech A, Simes RJ, Barter P et al (2005) Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial. *Lancet* **366**: 1849–61

Taylor KS, Heneghan CJ, Farmer AJ et al (2013) All-cause and cardiovascular mortality in middle-aged people with type 2 diabetes compared with people without diabetes in a large U.K. primary care database. *Diabetes Care* **36**: 2366–71