

All-cause mortality in type 1 diabetes

In this section, a panel of multidisciplinary team members give their opinions on a recently published diabetes paper. In this issue, the focus is on the publication of up-to-date all-cause mortality rates in people with type 1 diabetes versus those without diabetes.



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This study's findings have verified the results of an earlier UK-based study that investigated risk for all-cause mortality associated with insulin-treated diabetes, published in 1999 (Laing et al, 1999).

In a subsequent publication from the same group (Laing et al, 2003) a cohort of 23751 patients

with insulin-treated diabetes, diagnosed under the age of 30 years and from throughout the UK, were identified during the period 1972 to 1993 and followed for mortality until December 2000. Age- and sex-specific heart disease mortality rates and standardised mortality ratios were calculated and the results show that at all ages the ischaemic heart disease mortality rates in the cohort were higher than in the general population. The authors stated in conclusion that their observations emphasised the need to identify and treat coronary risk factors in these young patients.

Unfortunately, in the most recent publication using the General Practice Research Database (summarised right), risk factor identification is also not available. Although current approaches to cardiovascular risk calculation are the same for both type 1 and type 2 diabetes, this strategy assumes a similar influence of risk factors in both diseases. It is plausible that the relative influence(s) of certain risk factors could be very different in type 1 compared to type 2 diabetes and the effect of different risk factors and their interaction with age needs to be determined. It will be interesting to repeat this analysis in subsequent years to investigate whether the diabetes National Service Framework and the new General Medical Services contract have had an effect in reducing excess mortality among people with type 1 diabetes.

Laing SP, Swerdlow AJ, Slater SD et al (1999) The British Diabetic Association Cohort Study. I: all-cause mortality in patients with insulin-treated diabetes mellitus. *Diabetic Medicine* **16**: 459–65

Laing SP, Swerdlow AJ, Slater SD et al (2003) Mortality from heart disease in a cohort of 23,000 patients with insulin-treated diabetes. *Diabetologia* **46**: 760–5

'It is plausible that the relative influence(s) of certain risk factors could be very different in type 1 compared to type 2 diabetes and the effect of different risk factors and their interaction with age needs to be determined.'



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The findings of this study come as no surprise to those who have worked with people with type 1 diabetes for a number of years and have to come to terms with the early death of some of their patients, yet this has never been quantified in a UK study such as this before. We now have conclusive evidence that people with type 1 diabetes have a high mortality rate due to cardiovascular disease (CVD).

What can we do about reducing this risk? The recent publication of the results of the follow-up of patients in the Diabetes Control and Complications Trial (DCCT; Nathan et al, 2005) may provide some guidance. The change in HbA_{1c} during 6.5 years of treatment in the DCCT was significantly associated with most of the positive effects of intensive treatment on CVD. The authors concluded that intensive glycaemic therapy

reduces the risk of CVD in patients with type 1 diabetes.

The success of the DCCT was not just about the use of continuous subcutaneous insulin infusion (CSII)/multiple injection regimens but also the intensive education and ongoing support provided to this group of patients over a period of time. Within the UK, many centres are providing intensive insulin self-management courses (e.g. DAFNE, BERTIE) to help people with type 1 diabetes, but perhaps a one-off programme within a person's life is not enough – and we need to seriously consider the care pathway for people with type 1 diabetes, from the diagnosis onwards.

In my view, the current 'surveillance' model of care needs to be scrapped and replaced with an educational model of care that seeks to support all people with type 1 diabetes to effectively intensify their insulin regimens (using injections, pumps or inhalers – whatever works best for the individual) to offset the risks to their long-term health.

Nathan DM, Cleary PA, Backlund JY et al; The DCCT/EDIC Study Research Group (2005) Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *New England Journal of Medicine* **353**: 2643–53

All-cause mortality rates in patients with type 1 diabetes mellitus compared with a non-diabetic population from the UK general practice research database, 1992–1999

Soedamah-Muthu SS, Fuller JH, Mulnier HE et al (2006) *Diabetologia* **49**(4): 660–6

DIABETOLOGIA

Mortality in those with type 1 diabetes in the UK continues to be much greater than in those without diabetes

1 While it is well accepted that type 1 diabetes is associated with greater all-cause mortality compared to the general population, the extent of this risk has not been very precisely estimated. Reasons for this include small sample sizes and comparisons being made with general population groups (containing those with diabetes) in previous studies.

2 As it is not clear to what extent recent developments in diabetes care have improved the magnitude of excess mortality associated with type 1 diabetes, the authors of this study used data from the General Practice Research Database (GPRD) to generate up-to-date estimates of relative and absolute mortality rates.

3 The GPRD is a comprehensive source of primary care data, containing over 35 million patient-years of →

→ information, and was set up in 1987.

4 Baseline in this study was 1 January 1992. Patients with type 1 diabetes (n=7713) were selected from the GPRD using an algorithm, and the validity of the selection process was verified by manual checking of a random sample of patients.

5 Five age- and sex-matched individuals without any record of diabetes were selected as comparison subjects for each person with diabetes (n=38518 in total).

6 Selected participants were followed until 1999. Deaths occurring during the follow-up period were recorded and cause of death was classified.

7 All-cause mortality rates were higher in the type 1 diabetes group compared to the group without diabetes (8.0 deaths per 1000 patient-years [95% confidence interval (CI) 7.2–8.9] versus 2.4 deaths per 1000 patient-years [95% CI 2.2–2.6]), corresponding to a hazard ratio (HR) of 3.7 (95% CI 3.2–4.3).

8 Participants were stratified according to age; increased mortality in those with type 1 diabetes compared to those without diabetes was observed across all age bands.

9 Sex-specific HRs were as follows: 4.5 (95% CI 3.5–5.6) for women with diabetes compared to women without diabetes; 3.3 (95% CI 2.7–4.0) for men with diabetes compared to men without diabetes. The mortality risk in men without diabetes was higher than in women without diabetes (HR=1.5; 95% CI 1.3–1.9; $P<0.0001$). However, there was no statistically significant difference in mortality rate between men and women with type 1 diabetes (HR=1.1; 95% CI 0.9–1.4; $P=0.3$).

10 HRs were also calculated for specific causes of death. While there was no statistically significant difference between the groups in cancer-related mortality risk, the HR for fatal cardiovascular disease (CVD) was significantly raised in people with type 1 diabetes versus those without diabetes.

11 The investigators concluded that, despite continuing improvements in diabetes care, type 1 diabetes is associated with greatly increased mortality rates, with CVD being the major cause of death.



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This important study confirms excess cardiovascular mortality in patients with type 1 diabetes matched to a cohort of patients in primary care without diabetes. Excess mortality was noted across all ages and was

most dramatic after the age of 40 years. Women with type 1 diabetes had a more striking excess mortality compared with their female peers without diabetes.

This study, conducted in the community, presents a considerable challenge to those working in primary care as it underlines the need to improve cardiovascular risk. The

'This study presents a considerable challenge to those working in primary care as it underlines the need to improve cardiovascular risk in diabetes'

principal framework available to primary care teams to address this excess cardiovascular risk in people with diabetes is the new General Medical Services (nGMS) contract. The recent modification of the contract asked for stratification of people with diabetes into type 1 and type 2 categories. Addressing cardiovascular risk in diabetes accounts for

approximately 40% of the diabetes points in the nGMS contract and includes rewarding practices for addressing hypertension, hyperlipidaemia, and smoking risks.

We know that long-term reduction of HbA_{1c} in people with type 1 diabetes can prevent excess mortality and there is also a framework for addressing this in the nGMS contract.

'Despite advances in health care, the "harvest of sorrow" goes on, and there is an urgent need to improve the way we look after our patients with type 1 diabetes.'



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Soedamah-Muthu et al use a large UK primary care database to estimate mortality rates for people with type 1 diabetes.

They provide important data that broadly agree with those of the Diabetes UK survey (Laing et al, 1999), reporting that the standardised mortality ratio for people with type 1 diabetes is 3–4 times higher than for those without, and that women are affected more than men. So, despite advances in health care, the 'harvest of sorrow' (Gale, 2005) goes on, and there is an urgent need to improve the way we look after our patients with type 1 diabetes.

Direction is provided by the cause-specific mortality data. Soedamah-Muthu et al show that the predominant cause of death in patients with type 1 diabetes is now cardiovascular disease

– and this supports previous publications (e.g. Laing et al, 1999; Skriverhaug et al, 2006). The study therefore reminds us to tackle risk factors that we have usually only addressed in our type 2 diabetes patients.

All people with type 1 diabetes over the age of 40 years should be considered for lipid-lowering therapy regardless of baseline cholesterol, aspirin should be recommended for those with features associated with the metabolic syndrome, we should be aiming for a target blood pressure of 130/80 mmHg (125/75 mmHg with proteinuria) and smoking should be discouraged. I would suggest this is the overall message of this article.

Gale EA (2005) Type 1 diabetes in the young: the harvest of sorrow goes on. *Diabetologia* **48**: 1435–8

Laing SP, Swerdlow AJ, Slater SD et al (1999) The British Diabetic Association Cohort Study. I: all-cause mortality in patients with insulin-treated diabetes mellitus. *Diabetic Medicine* **16**: 459–65

Skriverhaug T, Bangstad HJ, Stene LC et al (2006) Long-term mortality in a nationwide cohort of childhood-onset type 1 diabetic patients in Norway. *Diabetologia* **49**: 298–305