Management of type 1 diabetes

Type 1 diabetes and life expectancy

Daniel Flanagan
Consultant Physician, Derriford Hospital, Plymouth

Studies of diabetes registers, although rather removed from clinical practice, can help answer some of the key questions asked in the diabetes clinic. A fundamental question is "How does having a diagnosis of diabetes alter life expectancy?" We could perhaps hope and expect that modern studies would show that life expectancy with diabetes, in the absence of significant kidney disease, might be approaching that of the population without the condition. Observational studies cannot answer the question of whether or not our interventions are influencing mortality, but they can at least tell us whether a low HbA_{1c} is associated with a lower risk of death. This is particularly important when considering the concern that severe hypoglycaemia is under-reported and might be an underestimated cause of death.

The study by Lind and colleagues (summarised alongside) gives us an up-to-date picture of the mortality risk in a population of people receiving state-of-the-art diabetes treatment in a Western health economy. This was a large study of 34 000 people with type 1 diabetes. The populations are well defined and well studied. The results, therefore, are reliable and believable. The participants were followed between 1998 and 2011, so the treatments and glycaemic targets used reflect modern practice.

The results are startling and perhaps disappointing. The headline result is that people with type 1 diabetes have a significantly reduced life expectancy compared with a matched population without the condition. Even the group with what would be regarded as optimal blood glucose control and modern lipid and blood pressure management had an all-cause mortality risk that was twice that of the controls. For those people with higher HbA_{1c} levels, the risk of death was significantly higher again: 8–10 times that of the general population. Although the risk was lower than in studies from 20–30 years ago, the authors were not able to show that it was continuing to improve over the time course of the study.

A linked analysis of the Scottish Diabetes Register shows a similar picture (Livingstone et al, 2015). These data would suggest that having a diagnosis of type 1 diabetes at age 20 years contributes to a loss of life expectancy of 11 years in men and 13 years in women. One might think, based on previous studies, that the excess risk was due to the development of kidney disease, but even the population with normal renal function showed a similar (if smaller) increased risk of death.

What these studies clearly show is that, although we have made giant strides in the management of type 1 diabetes, we still have a long way to go. ■

Livingstone SJ, Levin D, Looker HC et al (2015) Estimated life expectancy in a Scottish cohort with type 1 diabetes, 2008–2010. *JAMA* **313**: 37–44

N Engl J Med

Mortality risk and glycaemic control in T1D

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

1 In this observational study, Lind and colleagues sought to compare the risk of all-cause and cardiovascular (CV) mortality between people with T1D and varying levels of glycaemic control and the general population.

2 A total of 33 915 people with T1D from the Swedish National Diabetes Register were compared with 169 249 matched controls (5:1 ratio) for approximately 8 years.

3 Overall, 2701 participants with T1D (8.0%) and 4835 controls (2.9%; hazard ratio [HR], 3.52) died.

4 The majority of deaths in the T1D population were due to diabetes complications (33.8%) or CV causes (34.3%), and the rate of CV death was significantly higher in the T1D population than in controls (2.7% vs 0.9%; HR, 4.60).

5 Among the T1D population, mortality risk increased in line with glycaemic control, with the greatest risk occurring in those with an HbA_{1c} of ≥9.7% (83 mmol/mol; HR, 8.51 for all-cause death and 10.46 for CV death). However, even those who met the national HbA_{1c} target of <7.0% (53 mmol/mol) were at greater risk than the general population (HR, 2.36 for all-cause death and 2.92 for CV death).

6 The authors note that the history of HbA_{1c} levels was incomplete in many participants; therefore, they were unable to conclude whether those who achieved consistently good glycaemic control from the time of diagnosis were still at risk. Nonetheless, it appears that people with T1D remain at risk of death, particularly from CV causes, even if they achieve a low HbA_{1c}.

Lind M, Svensson AM, Kosiborod M et al (2014) Glycemic control and excess mortality in type 1 diabetes. *N Engl J Med* **371**: 1972–82

BMJ

Long-acting versus intermediate-acting insulin for T1D

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

1 The authors performed a systematic review and meta-analysis of 39 studies to compare the effectiveness, safety and cost-effectiveness of long-acting (glargine and detemir) and intermediate-acting (neutral protamine Hagedorn [NPH] and lente) insulins in adults with T1D.

2 In the efficacy analysis, glargine once daily, detemir once daily and detemir twice daily resulted in a statistically significant reduction in HbA_{1c} compared with NPH once daily (mean difference, –0.39%, –0.26% and –0.36%, respectively); however, these differences were smaller than the 0.5% difference required to infer clinical relevance.

3 Regarding weight gain, the network meta-analysis showed that detemir once or twice daily was least likely to cause weight gain, followed by glargine once daily.

4 Detemir once or twice daily had a lower risk of severe hypoglycaemia compared with NPH once or twice daily (odds ratio, 0.62).

5 The cost-effectiveness analyses were inconsistent, but the majority of studies showed that detemir and glargine were more expensive but more effective than NPH. In the two studies comparing glargine with detemir, the former was not cost-effective.

6 The authors conclude that long-acting insulins are probably superior to intermediate-acting insulins, although the differences in terms of HbA_{1c} are not clinically significant. The choice of insulin can thus be made based on preference and cost.

Tricco AC, Ashoor HM, Antony J et al (2014) Safety, effectiveness, and cost effectiveness of long acting versus intermediate acting insulin for patients with type 1 diabetes: systematic review and network meta-analysis. *BMJ* **349**: g5459

Diabetes Obes Metab

Basal insulin degludec non-inferior to insulin detemir

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

1 In this 26-week, open-label, non-inferiority trial, basal insulin degludec was compared with insulin detemir, both in combination with mealtime bolus insulin aspart.

2 After 26 weeks, mean HbA_{1c} reduced by 8 mmol/mol (0.73%) in the degludec group (n=302) and by 7 mmol/mol (7.1%) in the detemir group (n=153). The estimated treatment difference was –0.09%, confirming the non-inferiority of degludec.

3 Mean fasting plasma glucose levels fell by 2.60 mmol/L with degludec and by 7.29 mmol/L with detemir (P<0.0001). However, the authors note that the difference did not translate into a difference in HbA_{1c}.

4 The rates of hypoglycaemia were similar in the two groups, at around 46 episodes per patient-year of exposure (PYE) in both arms; however, nocturnal hypoglycaemia was less common in the degludec group (4.14 vs 5.93 episodes per PYE).

Davies MJ, Gross JL, Ono Y et al (2014) Efficacy and safety of insulin degludec given as part of basal–bolus treatment with mealtime insulin aspart in type 1 diabetes: a 26-week randomized, open-label, treat-to-target non-inferiority trial. *Diabetes Obes Metab* **16**: 922–30

Diabetes Care

Mortality risk after cardiovascular events in T1D

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

1 The authors estimated mortality risk in 1839 people with T1D who had a cardiovascular (CV) event, comparing those with and without a prior episode of hypoglycaemia.

2 Prior hypoglycaemia was associated with an additional risk of death both in the first month after the CV event (hazard ratio [HR], 1.79) and after 1 month (HR, 1.25).

3 Compared with people with T1D and no history of hypoglycaemia, the estimated 5-year cumulative mortality risk at age 60 years increased by 12.3% (to 52.4%) for myocardial infarction and 9.4% (to 39.8%) for stroke in those with a prior hypoglycaemic event.

Lung TW, Petrie D, Herman WH et al (2014) Severe hypoglycemia and mortality after cardiovascular events for type 1 diabetic patients in Sweden. *Diabetes Care* **37**: 2974–81

Diabet Med

The relationships between T1D and OSA

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

1 These authors assessed the relationships between T1D, obstructive sleep apnoea (OSA) and the prevalence of microvascular and macrovascular complications in 67 consecutive people with T1D.

2 OSA was observed in 46% of the cohort and severe OSA in 19%.

3 OSA was associated with longer diabetes duration, diabetic retinopathy, neuropathy, cardiovascular disease and hypertension, but not with age, gender, BMI or HbA_{1c}. Obesity and excessive daytime sleepiness were uncommon in the cohort.

4 OSA may have different causes in T1D compared with T2D, as it was associated with neuropathy and diabetes duration, but not BMI as in people with T2D. The authors suggest that it may be a result of upper airway dilator muscle dysfunction in T1D.

Manin G, Pons A, Baltzinger P et al (2015) Obstructive sleep apnoea in people with type 1 diabetes: prevalence and association with micro- and macrovascular complications. *Diabet Med* **32**: 90–6

"People with T1D remain at risk of death, particularly from cardiovascular causes, even if they achieve a low HbA_{1c}."