Action to Control CardiOvascular Risk in Diabetes

Reference

The Action to Control Cardiovascular Risk in Diabetes Study Group (2008) Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med* **358**:2545–59.

Synopsis

Objective: To investigate the effects of intensive glycaemic control on CV events in people with type 2 diabetes at high risk.

Methods: ACCORD was a randomized, double-blind, multicentre trial in which 10,251 people with type 2 diabetes mellitus and additional CV risk factors were assigned to receive intensive therapy (target HbA_{1c}, <6.0%) or standard therapy (target HbA_{1c}, 7.0–7.9%) for a planned average follow-up time of 5.6 years.

The primary end point was the time to occurrence of one of a composite of non-fatal MI, non-fatal stroke or mortality from CV causes. Secondary end points included all-cause mortality and individual components of the primary end point.

Results: At 1 year, HbA_{1c} levels had stabilized in both treatment groups and were lower in the intensive therapy group (Figure 3.7).

Intensive therapy did not significantly reduce the incidence of CV events and was associated with an increase in all-cause mortality (Figure 3.8).

Critical appraisal

ACCORD, ADVANCE (p. 60) and VADT (p. 52) were set up to build on the success of UKPDS (p. 50), by choosing older high-risk individuals and driving HbA_{1c} down lower. ACCORD participants had an average age of >62 years, obesity and diabetes for 10 years; 35% had suffered a previous MI. Instead of reducing mortality, there was a relative increase of 22% in the intensive therapy group, causing this arm to be abandoned. Some blame the target HbA_{1c} being too low and combination of drugs, including high insulin usage; others blame rapid reduction of HbA_{1c} early in the trial. It is generally thought that hypoglycaemia – the incidence of which was significantly higher in the intensive treatment group – had a role, either directly or by increasing CV risk in the ensuing period. Almost 28% of those on the over-intensive regimen gained >10 kg. By contrast, after the intensive arm was abandoned but while recruits were still being monitored, a reduction in the primary end point was signalled, suggesting intensive treatment was initially harmful but lower HbA_{1c} might later confer benefit. So, aggressive treatment in high-risk patients late in the illness should be avoided. Sadly, it took 54 extra deaths to illustrate this.

ACCORD

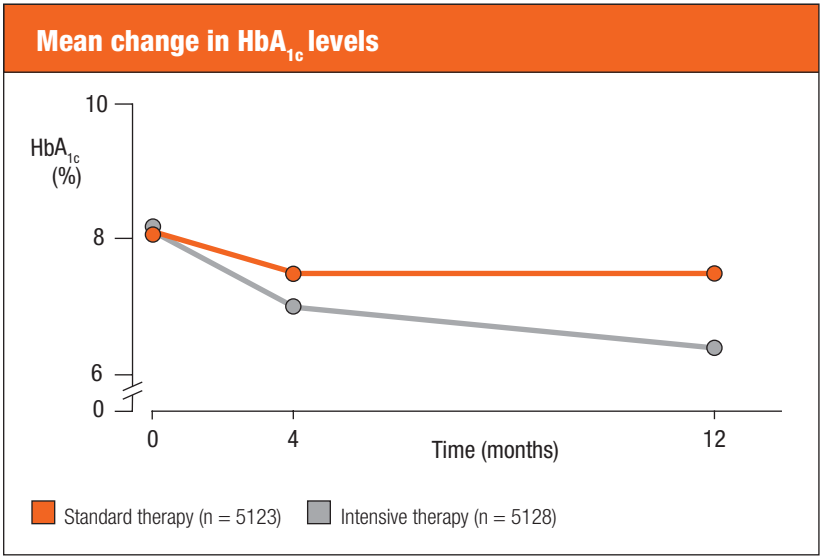

Figure 3.7

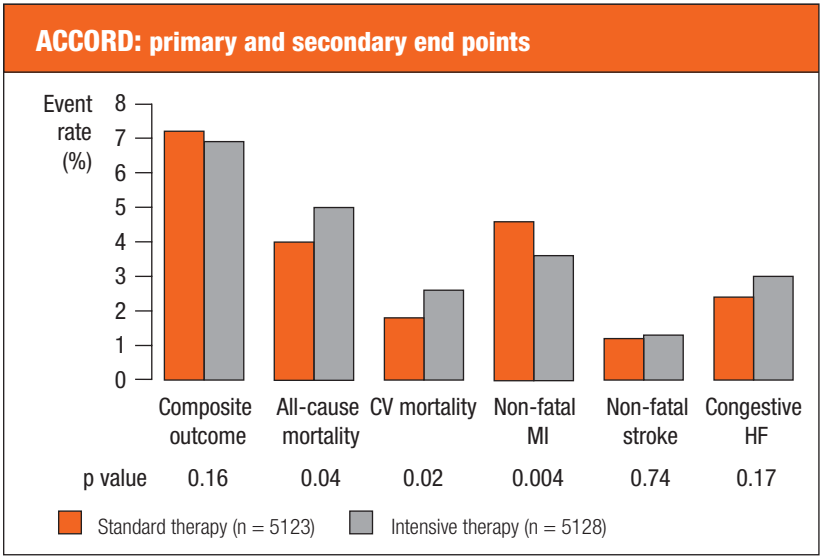

Figure 3.8