Clinical reviews

Our panel of GPs review recent research papers in their specialist areas that may influence the way you practise

Reviewers

Addiction
Dr Jez Thompson
MB ChB MSc MRCGP
GPwSI substance misuse, Leeds

Cardiovascular disease
Dr Peter Savill
BSc (Hons) MBBS PGDipCard
Former GP, Community Cardiology Specialist, Southampton and Mid Hampshire

Diabetes
Dr Matthew Lockyer
MB BS DCH DRCOG DFFP MRCGP
GP with an interest in diabetes, Suffolk

Mental health
Dr Phillip Bland
BA BM BCh MRCGP DRCOG
Former GP with an interest in mental health, Dalton-in-Furness

Obstetrics and gynaecology
Dr Chris Barclay
MB ChB FRCOG
GP with an interest in O&G, Suffolk

Paediatrics
Dr Chris Barclay
MB ChB FRCOG
GP with an interest in paediatrics, Suffolk

Respiratory disease
Dr Peter Saul
MB ChB DCH DRCOG FRCGP
GP with an interest in respiratory disease, Wrexham and Associate GP Dean for North Wales

Sexual health
Dr Richard Ma
MRCGP DFSRH DCH DRCOG DipGUM DrPH
GP with an interest in sexual health and NIHR Research Fellow, Imperial College, London

Smoking cessation
Dr Jez Thompson
MB ChB MSc MRCGP
GPwSI substance misuse, Leeds

Diabetes

Lack of legacy effect from tight glycaemic control in type 2 diabetes

Adults with type 2 diabetes who had received intensive glucose lowering therapy for nearly six years had a lower risk of cardiovascular events than those who received standard therapy only during the prolonged period in which the HbA_{1C} curves were separated, a study from the US has found. There was no evidence of a legacy effect or a mortality benefit with intensive glucose control 15 years after commencement of the study.

The study, published with an accompanying editorial in *The New England Journal of Medicine*, reports on a follow-up to the Veterans Affairs Diabetes Trial (VADT), a prospective study of the benefits of tight control of glycaemic levels.

The VADT originally enrolled 1,791 US military veterans with type 2 diabetes, mean age 61 years, who were randomised to two study arms, standard therapy (n = 899) or intensive glucose lowering therapy (n = 892). The majority of the participants were men, they were mostly overweight or obese, with a mean duration of diabetes of 11.5 years.

Intensive glucose-lowering therapy was given for a median of 5.6 years. A between-group difference of 1.5 percentage points in the median HbA_{1C} was achieved (6.9% in the intensive therapy group vs 8.4% in the standard therapy group).

The difference in HbA_{1C} between the intensive and routine care groups narrowed to 0.2-0.3% within three years of study completion.

An interim analysis ten years after commencement of the trial (active treatment period plus post-trial follow-up) showed that the intensive therapy group had a significant 17% lower incidence of cardiovascular events than the standard therapy group, hazard ratio (HR) 0.83 (95% CI: 0.70-0.99).

At 15 years (active treatment period plus post-trial follow-up) there was no significant difference in the risk of major cardiovascular events and death between the groups: HR 0.91 (95% CI: 0.78-1.06), and HR 1.02 (95% CI: 0.88-1.18) respectively.

The risk of major cardiovascular disease outcomes was only reduced during an extended interval of separation of the HbA_{1C} curves, but this benefit did not continue after equalisation of the HbA_{1C} levels.

The suggestion that intensive control of glucose in the early years had a long-term benefit in reducing cardiovascular risk, referred to as the legacy effect, derived from the UKPDS study (new onset type 2 diabetes) and the DCCT trial (type 1 diabetes), both seminal trials from the 1980s and 90s. Later trials of tight glycaemic control, the ACCORD and ADVANCE trials, did not replicate this finding.

The accompanying editorial[1] discusses the possible reasons for the observation of a legacy effect in the UKPDS and DCCT trials that was not replicated in more modern studies.

The authors note that older patients with longer duration of diabetes in the VADT might have already passed the point where intensive therapy might exert its benefit. Second, the early trials were done before widespread use of cardioprotective strategies including antiplatelet agents, ACE inhibitors and statins.

The authors of the editorial conclude: 'A major implication of the VADT follow-up study is that older patients with advanced diabetes should not expect long-term cardiovascular benefits from intensive glycaemic control. Instead, interventions that clearly reduce cardiovascular risk - such as smoking cessation, blood pressure control, statin therapy, use of antiplatelet agents, and the use of glucose-lowering agents with proven cardiovascular benefits in patients with established cardiovascular disease - should be prioritized.'

DR MATTHEW LOCKYER

Reaven PD, Emanuele NV, Wiitala WL et al for the VADT investigators. Intensive glucose control in patients with type 2 diabetes – 15-year follow-up. *N Engl J Med* 2019:380;2215-24

REFERENCE

1 Lipska KJ, Laiteerapong N. Lack of glycaemic legacy effects in the Veterans Affairs Diabetes Trial. *N Engl J Med* 2019:380;2266-67