Major journals

ARCHIVES OF INTERNAL MEDICINE

Intensive glycaemic control does not reduce risk of CV or all-cause mortality

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The authors undertook a systematic review to synthesise the benefits and harms of intensive versus conventional blood glucose control among people with T2D.

2 A systematic search of MEDLINE was undertaken for randomised trials (published between January 1950 and April 2009) that reported outcomes in people with T2D receiving intensive and conventional glucose control.

3 Five trials (cumulative participants n=27 802) met the criteria for inclusion and study variable and outcomes (severe hypoglycaemia, cardiovascular disease, and all-cause mortality) were analysed.

4 Intensive blood-glucose control reduced the risk of cardiovascular disease (relative risk [RR], 0.90; 95% confidence interval [CI], 0.83–0.98) but not cardiovascular death (RR, 0.97; 95% CI, 0.76–1.24) or all-cause mortality (RR, 0.98; 95% CI, 0.84–1.15] compared with conventional blood glucose control.

5 Intensive blood glucose control increased the risk of severe hypoglycemia (RR, 2.03; 95% CI, 1.46–2.81).

6 It was concluded that intensive blood glucose control increased the risk of severe hypoglycaemia and reduced the risk of some cardiovascular disease outcomes, but not cardiovascular death or all-cause mortality.

Kelly TN, Bazzano LA, Fonseca VA et al (2009) Systematic review: glucose control and cardiovascular disease in type 2 diabetes. *Ann Intern Med* **151**: 394–403

Adding up the evidence: Intensive glycaemic control and cardiovascular risk

Jiten Vora, Consultant Physician, Royal Liverpool University Hospital

The clinician has been confronted with a variety of trials examining the effect of glycaemic control on macrovascular disease. The results have been conflicting, on the grounds of differing and heterogeneous study populations. Kelly et al (2009; summarised alongside) present a meta-analysis that summarises clinical benefits and harms of intensive verses conventional glycaemic control in adults with type 2 diabetes.

The studies evaluated by Kelly et al (2009) included ACCORD (Action to Control Cardiovascular Risk in Diabetes; ACCORD Study Group et al, 2008), ADVANCE (Action in Diabetes and Vascular Disease; ADVANCE Collaborative Group et al, 2008), UKPDS (UK Prospective Diabetes Study; UKPDS Group, 1998), and VADT (Veterans Affairs Diabetes Trial; Duckworth et al, 2009). These trials involved a cumulative total of 27 802 people.

Kelly et al (2009) found that intensive glycaemic control reduced the risk of cardiovascular disease (relative risk, 0.9), but did not reduce the risk of cardiovascular death or all-cause mortality. Not surprisingly, intensive glucose control was found to increase the risk of severe hypoglycaemia (relative risk, 2.0).

Thus, the view that intensive glycaemic control reduces non-fatal myocardial infarction – especially in younger people without established cardiovascular disease – at the risk of increasing severe hypoglycaemia is becoming widely held. This position may be supported by recent data that suggests mortality among people with type 2 diabetes is reduced most when HbA_{1c} levels are between 7.0% (53 mmol/mol) and 7.5% (58 mmol/mol; Currie et al, 2010).

> ***"The view that intensive glycaemic control reduces non-fatal myocardial infarction at the risk of increasing severe hypoglycaemia is becoming widely held among clinicians."***

ACCORD Study Group et al (2008) Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med* **358**: 2545–59

ADVANCE Collaborative Group et al (2008) Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med* **358**: 2560–72

Currie CJ, Peters JR, Tynan A et al (2010) Survival as a function of HbA_{1c} in people with type 2 diabetes: a retrospective cohort study. *Lancet* **375**: 481–89

Duckworth W, Abraira C, Moritz T et al (2009) Glucose control and vascular complications in veterans with type 2 diabetes. *N Engl J Med* **360**: 129–39

UK Prospective Diabetes Study Group (1998) Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ* **317**: 703–13

ARCHIVES OF INTERNAL MEDICINE

T2D incidence linked to health resources

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The authors hypothesised that the availability of neighbourhood resources supporting physical activity and healthy diet would be associated with lower incidence of T2D.

2 Data were drawn from the US-based prospective Multi-Ethnic Study of Atherosclerosis.

3 Participants (n=2285) were aged 45–84 years at baseline. At 5-year follow-up, 233 new cases of T2D were diagnosed in the study population.

4 Better neighbourhood resources were associated with a 38% lower incidence of T2D (hazard ratio, 0.62; 95% confidence interval 0.43–0.88).

5 The lower T2D incidence in well-resourced neighbourhoods remained significant after adjustment for age, sex, family history of T2D, race/ethnicity, income, education level, alcohol use and smoking status.

Auchincloss AH, Diez Roux AV, Mujahid MS et al (2009) Neighborhood resources for physical activity and healthy foods and incidence of type 2 diabetes mellitus: the Multi-Ethnic study of Atherosclerosis. *Arch Intern Med* **169**: 1698–704

"Despite improving glycaemic control, neither insulin nor metformin significantly reduced inflammatory biomarkers over 14 weeks."

BMJ

Asprin use unproven in prevention of major CV events

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 By meta-analysis of randomised controlled trials (RCTs) the authors sought to evaluate the benefits and harms of low-dose aspirin among people with diabetes and no cardiovascular (CV) disease.

2 A search of MEDLINE, the Cochrane Library and the reference lists of retrieved articles was undertaken. RCTs included were those published between 1966 and November 2008 in which aspirin was compared with placebo or no aspirin in people with diabetes without existing CV disease.

3 Six articles were eligible for inclusion (cumulative participants n=10 117). Data on major CV events and all-cause mortality were extracted, pooled and analysed using a random effect model.

4 No significant risk reduction was seen for major CV event (relative risk [RR], 0.90; 95% confidence interval [CI], 0.81–1.00), CV mortality (RR, 0.94; 95% CI, 0.72–1.23) or all-cause mortality (RR, 0.93; 95% CI, 0.82–1.05) when aspirin was compared with placebo.

5 Asprin significantly reduced the risk of myocardial infarction in men (RR 0.57; 95% CI 0.34–0.94) but not women (RR 1.08; 95% CI 0.71–1.65; interaction P=0.056), suggesting that sex is an important effect modifier.

6 The authors concluded that no clear benefit of low-dose aspirin in the primary prevention of major CV events in people with DM could be proven.

De Berardis G, Sacco M, Strippoli GF et al (2009) Aspirin for primary prevention of cardiovascular events in people with diabetes: meta-analysis of randomised controlled trials. *BMJ* **339**: b453

AMERICAN JOURNAL OF MEDICINE

CHD and hypertension highest population risks for heart failure

Readability	✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 The relative contribution, change over time, and difference by sex of risk factors for heart failure (HF) remain controversial. The authors sought to establish the population attributable risk (PAR) associated with the key risk factors.

2 Using data from the US-based Rochester Epidemiology Project, 962 cases of HF occurring between 1979 and 2002 were age- and sex-matched to population-based controls.

3 Risk factors for HF (coronary heart disease [CHD], hypertension, diabetes, obesity, smoking) were investigated for frequency, odds ratios (ORs) and PAR of each individual factor.

4 Mean number of risk factors for HF were 1.9±1.1/case and the number of risk factors per case increased significantly over time (P<0.001).

5 The most common risk factors were hypertension (66%) and smoking (51%). Along with obesity, these risk factors increased over time.

6 The ORs for HF were highest for the risk factors CHD (OR, 3.05; 95% confidence interval [CI], 2.36–3.95) and diabetes (OR, 2.65; 95% CI, 1.98–3.54). However, PAR was highest for CHD and hypertension, which each accounted for 20% of HFs in the population.

7 CHD (PAR 23%) and hypertension (PAR 28%) accounted for the largest proportion of HFs in men and women, respectively.

8 At the population level, the largest impact on preventing HF will be the prevention of CHD and hypertension, but risk relationships vary over time and between the sexes.

Dunlay SM, Weston SA, Jacobsen SJ, Roger VL (2009) Risk factors for heart failure: a population-based case-control study. *Am J Med* **122**: 1023–8

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

Insulin and metformin fail to reduce inflammatory biomarkers

Readability	✓✓✓
Applicability to practice	✓✓
WOW! factor	✓✓✓

1 Given that diabetes is, in part, an inflammatory condition, the authors investigated whether insulin alone, or in combination with metformin, lowered inflammatory biomarker levels in people with recent-onset type 2 diabetes.

2 Participants (n=500; median time from diagnosis, 2 years) were randomised in a 2×2 factorial trial to receive: (i) placebo metformin; (ii) placebo metformin and insulin glargine; (iii) active metformin; or (iv) active metformin and insulin glargine (dose titration targeting fasting blood glucose <110 mg/dL [<6.1 mmol/L]).

3 The primary outcome was change in high-sensitivity C-reactive protein (hsCRP) levels from baseline to week 14.

4 hsCRP levels dropped by study end in all four treatment groups, but no significant difference in hsCRP reduction was seen between those randomised to receive insulin or no insulin (–11.8% and –17.5%, respectively; P=0.25), or between those receiving active or placebo metformin (–18.1% and –11.2%, respectively; P=0.17)

5 hsCRP was not reduced significantly more in either of the active treatment groups (i.e. metformin; metformin plus insulin glargine) compared with placebo alone (P=0.67 and P=0.87, respectively).

6 Despite improving glycaemic control (both active treatment groups, P<0.001), neither insulin nor metformin significantly reduced inflammatory biomarkers over 14 weeks.

Pradhan AD, Everett BM, Cook NR et al (2009) Effects of initiating insulin and metformin on glycemic control and inflammatory biomarkers among patients with type 2 diabetes: the LANCET randomized trial. *JAMA* **302**: 1186–94