Major journals

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

Pioglitazone slows CIMT progression

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

1 Increased carotid intima-media thickness (CIMT) is associated with an increased CV risk and is used as a surrogate marker for CVD risk.

2 In a long-term, randomised, comparator-controlled trial in the US the progression of CIMT was measured in 462 people with type 2 diabetes administered pioglitazone (15–45 mg/d) or glimepiride (1–4 mg/d).

3 The pioglitazone group CIMT measurements at final visit from baseline were 0.013 mm thinner than those of the glimepiride group ($P=0.02$).

4 A significant difference in HbA_{1c} levels emerged at 48 weeks and when the study concluded at 72 weeks the difference was 0.32 % ($P=0.002$).

5 Those participants prescribed pioglitazones showed significant improvements in levels of triglycerides and HDL-c at final visit compared to those on glimepiride, however there were no significant differences between the groups in LDL-c levels and blood pressure, and weight gain was significantly greater in the pioglitazone group ($P<0.001$).

6 The authors infer that over 18 months pioglitazone slowed CIMT progression and therefore incurred a CV benefit. They hypothesise that this is due to modification of non-traditional markers such as circulating inflammatory and coagulation markers and improvement in endothelial cell functioning.

Mazzone T, Meyer PM, Feinstein SB et al (2006) Effect of pioglitazone compared with glimepiride on carotid intima-media thickness in type 2 diabetes: a randomized trial. *Journal of the American Medical Association* **296**: 2572–81

Using carotid artery intimal thickness to investigate the cardiovascular risk of pioglitazone versus glimepiride

Jiten Vora, Consultant Physician, Royal Liverpool University Hospital

Carotid artery intimal thickness (CIMT) has been demonstrated to be a marker of coronary atherosclerosis and independently predict cardiovascular events.

Previous short-term studies have suggested that thiazolidinediones such as pioglitazone may reduce the progression of CIMT in persons with type 2 diabetes. This randomised double-blind comparator controlled multicentred trial in people with type 2 diabetes evaluated the effect of pioglitazone versus glimepiride on changes in CIMT of the common carotid artery over a period of 72 weeks (Mazzone et al, 2006; summarised on left). CIMT images were obtained by a single ultrasonographer and read by a single treatment-blinded reader using automated edge-detection technology. Participating were 462 patients with type 2 diabetes who were either newly diagnosed or currently treated with lifestyle changes, metformin, insulin or a combination of these. They were then randomised to receive additional therapy with either pioglitazone, the study drug, or glimepiride, the active comparator. Absolute changes in CIMT were evaluated from first to final visit.

The changes in CIMT were less with pioglitazone versus glimepiride throughout the study period of 72 weeks. At 72 weeks the primary end point of progression of CIMT was less with pioglitazone than glimepiride, suggesting a slowing of progression of maximum CIMT. The beneficial effect of pioglitazone on reduced rate of progression of CIMT was independent of age, sex, systolic blood pressure, duration of diabetes, BMI, HbA_{1c} and statin usage. Consequently, over an 18-month period those treated with pioglitazone demonstrated reduced progression of CIMT compared with glimepiride.

ARCHIVES OF INTERNAL MEDICINE

Cardiovascular disease burden elevated with chronic kidney disease

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

1 Diabetes is reported to occur in up to 40 % of people with chronic kidney disease (CKD). Both conditions increase risk of CVD. This paper reports the outcomes of a study into CVD risk factors in 3258 people with CKD.

2 Participants with CKD were found to have significantly higher rates of CVD, coronary heart disease, MI and congestive heart failure ($P<0.001$).

3 Diabetes was found in nearly twice as many participants with CKD than those without (23.5 % versus 11.9 %, $P=0.02$). Where diabetes was treated, CKD participants were still more likely to miss a target HbA_{1c} level of 7 %.

4 The study provided evidence that a significant burden of CVD risk factors are linked to CKD.

5 The authors admit limitations in the diversity of the participants, who were geographically clustered and predominantly Caucasian.

Parikh NI, Hwang SJ, Larson MG et al (2006) Cardiovascular disease risk factors in chronic kidney disease: overall burden and rates of treatment and control. *Archives of Internal Medicine* **166**: 1884–91

'...simvastatin is potentially cost-effective across age ranges in people who have a 5% 5-year risk of a major CV event'

BMJ

Simvastatin cost-effective as a lifetime treatment

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

1 It is currently recommended that statins are given to all people who are at risk of major CV events to lower LDL-c and help prevent such CV events.

2 This study involved 32 536 people aged 40–80 years with a cholesterol level >3.5 mmol/l who were allocated either placebo or simvastatin 40 mg daily and monitored for on average 5 years for CV events warranting hospital admission.

3 Relative risk reduction was 25% for CVD in the simvastatin group compared to the placebo group. Estimated life years gained were 0.64 in participants aged over 70 years who initially had a 12% 5-year risk of a major CV event, and 2.49 years in participants aged 40–49 years who had a 42% 5-year risk.

4 Only in people over 70 years of age who had a 12% 5-year risk of a major CV event was simvastatin not cost-effective in terms of cost per life year gained.

5 These data can be extrapolated to show that simvastatin is potentially cost-effective across age ranges in people who have a 5% 5-year risk of a major CV event.

6 The authors suggest that this data should be used as evidence to initiate statin therapy across a wider age range of people and in those at lower risk than is currently the trend in the UK.

Heart Protection Study Collaborative (2006) Lifetime cost effectiveness of simvastatin in a range of risk groups and age groups derived from a randomised trial of 20,536 people. *BMJ* **333**: 1145

'... for every 25% increase in adherence to oral hypoglycaemics and statins, HbA_{1c} decreased by 0.05%...'

ARCHIVES OF INTERNAL MEDICINE

Chlorthalidone raises fasting blood glucose

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

1 Analysing ad hoc data from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) the differences between fasting glucose levels, incidence of type 2 diabetes and risk of CVD and renal disease were assessed in 18 411 participants without diabetes at baseline who were allocated chlorthalidone, amlodipine or lisinopril.

2 Those taking chlorthalidone were significantly more likely to have a fasting blood glucose level above 125 mg/dl than those taking amlodipine and lisinopril ($P<0.001$ in both comparisons).

3 After 2 years the probability of developing type 2 diabetes was significantly higher in the chlorthalidone group versus either of the two comparators. By 4 years this difference was no longer significant.

4 Elevated fasting blood glucose levels in patients receiving lisinopril and incident diabetes were significantly associated with an increased risk of CHD.

5 No incident associated with diabetes was recorded in any significantly greater numbers in the chlorthalidone group than the other two treatment arms. The amlodopine group were found to be at increased risk of CHD and heart failure.

6 Independent of treatment, fasting blood glucose levels were shown to increase in participants with hypertension.

Barzilay JI, Davis BR, Cutler JA et al (2006) Fasting glucose levels and incident diabetes mellitus in older nondiabetic adults randomized to receive 3 different classes of antihypertensive treatment: a report from the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *Archives of Internal Medicine* **166**: 2191–201

ARCHIVES OF INTERNAL MEDICINE

Nonadherence linked to poor outcomes

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

1 The authors set out to investigate whether the fact that only 43% of people with diabetes achieve treatment targets may be due to a lack of adherence to treatment regimens.

2 Analysis of a retrospective cohort of 11 532 patients with types 1 and 2 diabetes revealed that 2456 (21.3%) were nonadherent (where 'nonadherent' was defined as <80% of 240–365 days covered by medication).

3 Poor adherence to treatment regimens was associated with an increased risk of hospitalisation ($P<0.001$) and all-cause mortality ($P<0.001$).

4 It was found that for every 25% increase in adherence to oral hypoglycaemics and statins, HbA_{1c} decreased by 0.05%, and that similar adherence increases to antihypertensives reduced systolic BP by 1.0 mmHg and diastolic BP by 1.2 mmHg.

5 While the correlation between negative outcomes and medication nonadherence was evident, the results may also be due to improved overall self-care behaviour, such as following healthy-living guidance.

6 This study highlights the danger that practitioners may attribute no improvement in glycaemic control with inadequate doses. Thus, subsequent dose increases may put the individual with diabetes at risk of hypoglycaemia and other adverse consequences.

Ho PM, Rumsfeld JS, Masoudi FA et al (2006) Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. *Archives of Internal Medicine* **166:** 1836–41