## Clinical DIGEST 1

## **Major journals**

## LANCET

## Most MIs caused by potentially modifiable risk factors

Readability / / / / /
Applicability to practice / / / /
WOW! factor / / / /

Over 80 % of the worldwide burden of cardiovascular disease (CVD) occurs in low- and middle-income countries. Most studies, however, have been carried out in developed countries so the importance of CVD risk factors in populations from low- and middle-income countries is unknown.

The INTERHEART study was a standardised, case-control study aimed at determining the importance of modifiable risk factors in people from 52 countries worldwide (15 152 people with CVD and 14 820 people without).

Smoking, hypertension or diabetes, diet, physical activity, waist/ hip ratio, alcohol consumption, blood apolipoproteins (Apo) and psychosocial factors were analysed to determine their relation to myocardial infarction using odds ratios, 99 % confidence intervals and population attributable risks.

Smoking, history of hypertension, diabetes, ApoB/ApoA1 ratio, daily consumption of fruit and vegetables, abdominal obesity, psychosocial factors, regular alcohol consumption and regular physical activity were all significantly related to acute myocardial infarction (p<0.0001; except alcohol consumption p=0.03).

These results were the same regardless of age, gender or region of world and accounted for 94 % of population attributable risks in women and 90 % in men.

Prevention approaches worldwide can be based on the same principles and can potentially prevent most premature cases of myocardial infarction.

Yusuf S, Hawken S, Ôunpuu S et al (2004) Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study: case-control study). *Lancet* **364**: 937–52

#### Majority of MI cases preventable by risk factor modification



Marc Evans, Consultant Physician, Llandough Hospital, Cardiff ardiovascular disease (CVD) remains a leading cause of global mortality. Although there has been a reduction in cardiovascular death rates in recent years in developed countries, in poorer countries rates of CVD have continued to increase. Current knowledge about

CVD prevention is mainly derived from studies done in European populations. There is debate as to the extent to which these findings may apply worldwide, with data suggesting that the effect of individual risk factors may vary between populations and that the prevalence of any risk factor might also demonstrate ethnic variations resulting in differing populationattributable risks. To clarify whether the effects of risk factors vary in different populations, the INTERHEART Study was conducted – representing an international standardised case control study of 15152 cases versus 14822 controls in 52 countries. The objectives were to determine the association between nine easily measured risk factors; namely smoking, dyslipidaemia, hypertension, diabetes, obesity, diet, physical activity, alcohol consumption and psychosocial factors with

risk of myocardial infarction.

This study demonstrated that these potentially modifiable risk factors accounted for over 90 % of the proportion of risk for an initial myocardial infarction; this being consistent in men and women, across different geographic regions and by ethnic groups. The effect of risk factors appeared particularly striking in young men and women, while worldwide the two most important risk factors were smoking and abnormal lipids as defined by the apolipoprotein (Apo)B/Apo A1 ratio together accounting for nearly two-thirds of the population attributable risk.

The lipid observations further support the notion that measurement of total or LDL-cholesterol alone is insufficient to provide optimum assessment of the impact of dyslipidaemia on cardiovascular risk, since an ApoB/ApoA1 ratio provides true reflection of the atherogenic lipoprotein burden. The results of this study appear consistent across all ethnic groups, in men and women, young and old, and thus the prevention of CVD can be based on similar principles on a global basis. In essence, modification of currently known risk factors has the potential to prevent the majority of cases of myocardial infarction worldwide.

### ARCHIVES OF INTERNAL MEDICINE

# CV complications linked with post-prandial glucose

Readability / / / / /
Applicability to practice / / / /
WOW! factor / / /

There is increasing evidence that postprandial hyperglycaemia is linked to CVD development through its harmful effects on vasculature and contribution to HbA<sub>1c</sub> level.

This paper examines the hypothesis that controlling postprandial glucose level may be important in preventing diabetes complications.

The relationship between postprandial hyperglycaemia and

post-challenge hyperglycaemia is poorly understood but they are thought to be closely related.

The harmful effects of postprandial hyperglycaemia make controlling hyperglycaemia an essential part of good practice. Recent suggestions are that this, even with improved HbA<sub>1c</sub> levels, cannot be a strategy for controlling diabetes due to potential risks, especially that of hypoglycaemia.

In the authors' opinion, achieving control of near-normal blood glucose levels is important.

The authors suggest controlling postprandial glucose levels may be particularly important in preventing vascular complications in people with diabetes.

Ceriello A, Hanefeld M, Leiter L et al (2004) Postprandial glucose regulation and diabetic complications. *Archives of Internal Medicine* **164** 2090–95

## Cardiovascular disease Clinica DIGEST

<sup>L</sup> Presence of psychosocial stressors is associated with increased risk of acute myocardial infarction. suggesting that approaches aimed at modifying these factors should be developed. <sup>5</sup>

<sup>L</sup>Thiazolidinediones have similar effects on glycemic control and body weight. <sup>5</sup>

#### **ARCHIVES OF INTERNAL** MEDICINE VICE

#### **TZDs** have similar effects on HbA1c and weight but differing effects on lipids

Readability 1111 Applicability to practice 🗸 WOW! factor

- The effect of rosiglitazone and pioglitazone on glycaemic control, blood pressure, lipids and weight in patients with type 2 diabetes was analysed in this meta-analysis.
- Twenty-three randomised controlled trials that had run for 12 weeks comparing patients on rosiglitazone or pioglitazone with placebo were included.
- Analysis compared thiazolidinediones with placebo and outcomes of rosiglitazone compared to pioglitazone.
- Decreases in HbA<sub>1c</sub> and increases in body weight were similar between the thiazolidinediones.
- Triglyceride level was significantly lowered, HDL-cholesterol significantly increased and LDL- and total cholesterol levels were unaffected by pioglitazone.
- HDL-cholesterol was significantly increased but LDL-cholesterol and total cholesterol levels were also increased, and triglyceride levels were unaffected by rosiglitazone.
- Rosiglitazone had a neutral effect on blood pressure, and no data were available on pioglitazone.
- Similar effects on body weight and glycaemic control occur with thiazolidinediones, however, pioglitazone gave a more favourable lipid profile than rosiglitazone. To determine long-term cardiovascular outcomes in patients with type 2 diabetes, head-to-head trials are needed.

Chiquette E. Ramirez G. DeFronzo R (2004) A metaanalysis comparing the effect of thiazolidinediones on cardiovascular risk factors. Archives of Internal Medicine 164: 2097-104

#### LANCET

#### **Increased MI risk with** psychosocial stress

Readability Applicability to practice 🗸 🗸 WOW! factor

- This study across 52 countries investigated the relation of psychosocial risk factors to myocardial infarction (MI) risk.
- Four questions were used to assess psychosocial stress (work, home, financial and major life events in the past year) in 11 119 patients with first MI and 13 648 age- and sex-matched controls.

#### **JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION** W Ble

#### Mediterranean diet reduces metabolic syndrome

Readability 1111 Applicability to practice 🗸 🗸 🗸 WOW! factor

- This trial of 180 patients with the metabolic syndrome assessed the effects of a Mediterranean-style diet on vascular inflammatory markers and endothelial function.
- The intervention group (n=90) were instructed to follow a Mediterranean-style diet and given advice. The control group (n=90) followed a prudent diet.

#### **NEW ENGLAND JOURNAL OF MEDICINE** W MAR

#### **ACE inhibitors not** beneficial in those with stable CAD

Readability Applicability to practice //// WOW! factor

The benefits of addition of angiotensinconverting enzyme (ACE) inhibitors to conventional therapy in people with coronary artery disease (CAD) and normal or slightly reduced left ventricular function was evaluated in the Prevention of Events with Angiotensin Converting Enzyme inhibition (PEACE) trial.

- There was a significantly higher prevalence of all four stress factors reported in people with MI (p<0.0001).
- These differences were seen irrespective of gender, ethnicity or country.
- Additional questions on depression and locus of control showed that depression was more frequent in people with MI than those without.
- There is an increased risk of MI when psychosocial stressors are present.

Rosengren A, Hawken S, Ôunpuu S et al (2004) Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13 648 controls from 52 countries (the INTERHEART study: case-control study. Lancet 364: 953-62

- Monosaturated and polyunsaturated at, fibre, fruit, vegetable, whole grain, nuts and olive oil consumption were higher in the intervention group after two years.
- Compared to the control group, mean body weight, insulin resistance and levels of C-reactive protein decreased more in the intervention group.
- Endothelial function score remained stable in the control group and improved in the intervention group.
- Follow-up at two years showed 40 intervention patients and 78 control patients still had features of the metabolic syndrome.

Eposito K, Marfella R, Ciotola M et al (2004) Effect of a Mediterranean-style diet on endothelial markers of vascular inflammation in the metabolic syndrome. Journal of the American Medical Association 292: 1440-46

- Patients received intensive treatment and were assigned to either trandolapril 4 mg daily (n=4158) or placebo (n=4132).
- Over a mean follow-up of 4.8 years, 21.9 % of patients on trandolapril and 22.5 % on placebo died from cardiovascular causes. MI or coronary revascularisation.
- There is no evidence that there is additional benefit in adding an ACE inhibitor to intensive treatment in patients with stable CAD and preserved left ventricular function.

The PEACE Trial Investigators (2004) Angiotensinconverting-enzyme inhibition in stable coronary artery disease. New England Journal of Medicine **351**: 2058-68

### Cardiovascular disease



#### Statins reduce stroke risk in those with or without CHD

Readability
WOW! factor

J J J

In many countries, stroke is a major cause of death and the leading cause of disability.

This study aimed to examine whether lipid-lowering therapies such as statins, resins, fibrates, n-3 fatty acids and diet can reduce the risk of stroke in people with and without coronary heart disease (CHD).

The investigators carried out a meta-analysis of all randomised contolled trials available in the literature prior to August 2002. The aim was to determine whether the effects of lipid-lowering therapies differed according to therapy type and whether patients had CHD or not.

Sixity-five trials incorporating 200 607 patients were retrieved in the literature search.

Compared with control, the risk ratio for patients having nonfatal or fatal while on statin therapy was 0.82 (95 % CI: 0.76–0.90). For patients with CHD, this ratio was 0.75 (95 % CI: 0.65–0.87), and 0.77 (95 % CI: 0.62–0.95) for those without CHD.

For patients treated with non-statin lipid-lowering interventions, the risk ratio was 0.98 (95 % CI: 0.90–1.07). The difference between the statin and non-statin intervention risk ratios was significant (p=0.0002).

Thus, it is suggested that patients treated with statin therapy are less likely to suffer from fatal or nonfatal stroke compared with those treated with other lipid-lowering interventions.

Briel M, Studer M, Glass TR, Bucher HC (2004) Effects of statins on stroke prevention in patients with and without coronary heart disease: A meta-analysis of randomized controlled trials. *American Journal of Medicine* **117**: 595–606

ARCHIVES OF INTERNAL MEDICINE

## Diabetes increases risk in those who survive MI with

Readability

11

WOW! factor

- Little is known about the subsequent morbidity and mortality of patients with diabetes after surviving myocardial infarction (MI).
- This study aimed to examine the effect of diabetes on cardiovascular events and death in those patients surviving MI and having left ventricular dysfunction (LVD).
- This randomised, double-blind, placebo-controlled trial (SAVE; The Survival And Ventricular Enlargement trial) investigated the effects of captopril in over 2230 diabetes patients following acute MI with LVD (categorised as an ejection fraction ≤40 %).

Participants were randomised to receive either captopril or placebo three to 16 days after acute MI. Patients were followed up for a mean of 3.5 years.

Twenty-two-point-two per cent of patients had a history of diabetes. Just over one-third of these were taking insulin.

After adjusting for all significant baseline differences between patients with diabetes and those without, those with the condition had 39 % greater total mortality (p=0.001) and 49 % more cardiovascular events (p=0.001).

The presence of diabetes in patients who survived MI with LVD was associated with increased risk of death.

Murcia AM, Hennekens CH, Lamas GA et al (2004) Impact of diabetes on mortality in patients with myocardial infarction and left ventricular dysfunction. *Archives of Internal Medicine* **164**: