Major journals

Long-term obesity risk linked with future health problems

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Obesity is now firmly established as an independent risk factor for the development of coronary artery disease, type 2 diabetes and some types of cancer. The relationship between obesity and accelerated coronary artery disease was further strengthened by a recent demonstration in a large population study that obesity is a risk factor for accelerated coronary artery disease independent of both cholesterol and blood pressure (Yan et al, 2006). It is therefore important to have some idea of the future burden of obesity and its different grades.

Many estimates are based on cross-sectional studies. Vasan et al (see right) recently reported the current estimated risks of developing obesity. The report makes for sobering reading.

The investigators used the well-characterised population of white North American residents of Framingham to estimate the short- and long-term risks of developing different grades of obesity (overweight, body mass index (BMI) ≥25 kg/m^2; obesity, BMI ≥30 kg/m^2; stage II obesity, BMI ≥35 kg/m^2; stage III obesity, BMI ≥40 kg/m^2). The authors followed over 4000 non-overweight adults between the ages of 30 and 59 years; within 4 years up to 19 % of women and 30 % of men had become obese. Within 30 years these figures had risen to 33 % and 25 %, respectively. The key determinant of weight gain was baseline BMI, but of particular interest was the fact that up to 25 % of healthy, non-overweight participants became overweight or obese within 4 years. The long-term risks were similar for men and women.

With the role of obesity as an important risk factor for the development of coronary artery disease, this study by Vasan et al is a stark demonstration of how important acting now is to prevent the acceleration in the prevalence of obesity. While at present mortality from coronary artery disease is declining, these figures support the notion that the condition will soon be on the increase and in a different and possibly more dangerous form – obesity or type 2 diabetes related.

Yan LL, Daviglus ML, Liu K et al (2006) Midlife body mass index and hospitalization and mortality in older age. *Journal of the American Medical Association* **295**(2): 190–8

LANCET

Fenofibrate therapy significantly reduces CVD events

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

1 Dyslipidaemia, which has a role in the increased risk of cardiovascular disease (CVD) seen in people with type 2 diabetes, can be improved using treatment with fibrates.

2 The Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study looked at the impact of fenofibrate 200 mg/day on CVD in 4895 patients with type 2 diabetes; 4900 patients received placebo.

3 For the primary outcome measure, which was coronary events over the study's 5 years (coronary heart disease or non-fatal myocardial infarction [MI]), there was a non-significant relative reduction of 11 % in the intervention group.

4 More participants on placebo than on fenofibrate started statins during the study, which could have masked a significant effect on the primary outcome measure.

5 For the secondary outcome measure, which was total CVD events (CVD death, MI, stroke or coronary or carotid revascularisation), there was a significant relative reduction of 11 % with fenofibrate therapy.

6 Fenofibrate had a good safety profile across concomitant therapy.

Keech A, Simes RJ, Barter P et al (2005) Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study). *Lancet* **366**: 1849–61

ANNALS OF INTERNAL MEDICINE

High long-term risk for obesity in adults

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

1 The authors sought to estimate the short-term, long-term and lifetime risks for developing overweight or obesity in adults.

2 The study tracked 4117 non-overweight white adults, aged 30–59 years, who participated in the Framingham Heart Study during 1971–2001.

3 Assessment included the short-term (4 years) and long-term (10–30 years) risks for ever becoming overweight (body mass index [BMI] ≥25kg/m^2) or obese (BMI ≥30kg/m^2) for men (n=1980) and women (n=2137) at 30, 40 and 50 years of age with a normal BMI (between 18.5 and 25.0 kg/m^2).

4 Within 4 years, 14–19 % of the women and 26–30 % of the men became overweight; 5–7 % of the women and 7–9 % of the men became obese.

5 The long-term risk estimates were similar for both sexes generally, varied somewhat with age (in men, being lower for those 50 years of age), and overall exceeded 50 % for overweight or more, 25 % for obesity, and 10 % for stage II obesity (BMI ≥35 kg/m^2). The 30-year estimates correspond to the residual lifetime risk for overweight or obesity for participants 50 years of age.

6 These estimates suggest that the future burden of obesity-associated conditions may be substantial.

Vasan RS, Pencina MJ, Cobain M, Freiberg MS, D'Agostino RB (2005) Estimated risks for developing obesity in the Framingham Heart Study. *Annals of Internal Medicine* **143**: 473–80

'In patients with type 2 diabetes who are at high risk of cardiovascular events, pioglitazone treatment can reduce the composite of all-cause mortality, non-fatal myocardial infarction or stroke.'

'Within a healthy diet, partial substitution of carbohydrate with either protein or mono-unsaturated fat can further reduce estimated cardiovascular risk.'

LANCET

Pioglitazone reduces vascular events in type 2 diabetes

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

1 It is well established that people with type 2 diabetes are at high risk of myocardial infarction (MI) and stroke.

2 Pioglitazone is used in the treatment of type 2 diabetes. Several of its metabolic effects suggest that it may reduce the macrovascular risk associated with the condition.

3 This prospective, randomised controlled trial assigned 5238 people with type 2 diabetes and evidence of established macrovascular disease to receive either pioglitazone (titrated up from 15 mg/day to a maximum of 45 mg/day; n=2605) or placebo (n=2633) on top of existing medications.

4 The primary end point was the time from randomisation to a composite of all-cause mortality, non-fatal MI, stroke, acute coronary syndrome or endovascular and surgical interventions; the main secondary end point was the time to the composite of all-cause mortality, stroke or non-fatal MI.

5 The proportion of patients who reached the primary end point was not significantly different between groups; the proportion of patients reaching the main secondary end point was significantly lower in the pioglitazone group (n=301/2605) than in the placebo group (n=358/2633; P=0.027).

6 In patients with type 2 diabetes who are at high risk of cardiovascular events, pioglitazone treatment can reduce the composite of all-cause mortality, non-fatal MI or stroke.

Dormandy JA, Charbonnel B, Eckland DJ et al (2005) Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events). *Lancet* **366**: 1279–89

ARCHIVES OF INTERNAL MEDICINE

Elevated HbA_{1c} is risk factor for CHD

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

1 This study tested the hypothesis that glycaemic control (HbA_{1c}) is positively associated with incident coronary heart disease (CHD) independent of other known risk factors in people with and without diabetes.

2 Using proportional hazards models, 1321 adults without diabetes and 1626 adults with diabetes were studied to assess the relationship between HbA_{1c} level and incident CHD during 8–10 years of follow-up.

3 In adults without diabetes, HbA_{1c} level was not related to CHD risk below 4.6 %, but was significantly related to risk above that level (P<0.001); in adults with diabetes, the risk of CHD increased throughout the range of HbA_{1c} levels.

4 Elevated HbA_{1c} level is an independent risk factor for CHD in people with and without diabetes.

Selvin E, Coresh J, Golden SH et al (2005) Glycemic control and coronary heart disease risk in persons with and without diabetes. *Archives of Internal Medicine* **165**: 1910–16

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

Protein and mono-unsaturated fat reduce CV risk

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

1 This study compared the effects of three healthy diets, each with reduced saturated fat intake, on blood pressure and serum lipids.

2 Participants were 164 adults with pre-hypertension or stage 1 hypertension. They were randomly assigned to a sequence of the three diets, with each feeding period lasting 6 weeks.

3 Blood pressure, low-density lipoprotein cholesterol and estimated cardiovascular (CV) risk were lower on each diet compared with baseline. Compared with the carbohydrate diet, estimated 10-year CV risk was lower and similar on the protein and unsaturated fat diets.

4 Within a healthy diet, partial substitution of carbohydrate with either protein or mono-unsaturated fat can further reduce estimated CV risk.

Appel LJ, Sacks FM, Carey VJ et al (2005) Effects of protein, monounsaturated fat and carbohydrate intake on blood pressure and serum lipids. *Journal of the American Medical Association* **294**: 2455–64

LANCET

Amlodipine reduces CV risk

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

1 The authors compared the effect of combinations of atenolol and a thiazide versus amlodipine and perindopril on non-fatal myocardial infarction and fatal coronary heart disease.

2 Using a prospective, randomised controlled trial of 19 257 patients with hypertension, aged 40–79 years, who had at least three other cardiovascular (CV) risk factors, participants were assigned either amlodipine 5–10 mg, adding perindopril 4–8 mg as required, or atenolol 50–100 mg adding a thiazide and potassium as required. The primary end point was non-fatal MI and fatal CHD.

3 The amlodipine-based regimen prevented more major CV events and induced less diabetes than the atenolol-based regimen.

Dahlof B, Sever PS, Poulter NR et al (2005) Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required vs atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial – Blood Pressure Lowering Arm (ASCOT-BPLA). *Lancet* **366**: 895–906