

## Oestrogen plus progesterone decreases risk of first myocardial infarction



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Data regarding the use of hormone replacement therapy (HRT) and the risk of myocardial infarction in women with diabetes is confusing. The association between HRT and risk of coronary heart disease (CHD) in women with diabetes remains poorly studied. Meta-analyses have reported the risk of CHD to be decreased by approximately 20% in women who are currently using HRT. The HERS study, a randomised trial in women with CHD did not demonstrate a protective effect of HRT on the risk of CHD (Hulley et al, 1998). In contrast, the Women's Health Initiative study (2002) demonstrated an increased risk of primary CHD events in women assigned to oestrogen plus progesterone. Other studies have suggested an increase in other adverse events such as stroke and breast cancer.

This study from the North California Kaiser Permanente Diabetes Register examined the risk of acute myocardial infarction associated with current use of different hormone replacement regimens, oestrogen doses and the duration of HRT, in approximately 25 000 women with diabetes, aged 50 years or more.

Current HRT was associated with a reduced risk of first myocardial infarction (risk reduction 16%). The risk reduction was approximately 23% in the combined oestrogen plus progesterone HRT, but was reduced to 12% in those using unopposed oestrogen. The risk was reduced with low or medium doses of oestrogen, but not with high oestrogen doses. In this study the risk reduction appeared to have accrued after one year of HRT usage. However, as previously suggested, an increased risk of recurrent myocardial infarction was observed in current HRT users.

This large study concludes that in women without recent myocardial infarction, the use of oestrogen plus progesterone is associated with a decreased risk of myocardial infarction. However, history of recent myocardial infarction increased the risk of recurrence in patients on HRT. Clearly further studies are required to elucidate the effect of HRT in women with diabetes.

Hulley S, Grady D, Bush T et al (1998) Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in post-menopausal women: HERS Research Group. *Journal of the American Medical Association* **280**: 605–13

Writing Group for the Women's Health Initiative Investigators. (2002) Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *Journal of the American Medical Association* **288**: 321–33

### ACTA DIABETOLOGICA



## High plasma levels of homocysteine linked to CHD

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

**1** Evidence shows that increased plasma homocysteine (Hcy) levels are linked to coronary, cerebral and peripheral occlusive disease.

**2** Researchers investigated whether there was a link between raised Hcy levels and coronary heart disease (CHD) in 358 (156 men) Kuwaiti patients with type 2 diabetes.

**3** Median fasting plasma level of total Hcy in the patients was 10.2 µmol/l, and was significantly higher among men (11.3 µmol/l) than women (8.8 µmol/l).

**4** Of the 57 patients with CHD, 16% had hyperhomocysteinaemia, compared with 8.3% of patients without CHD.

**5** Multiple regression analyses showed a significant association of plasma Hcy levels with glycated haemoglobin, creatinine and apolipoprotein-B, but not with smoking, neuropathy or retinopathy.

**6** It was concluded that high plasma Hcy levels are associated with CHD, but not with microalbuminuria, neuropathy or retinopathy.

Abdella NA, Mojiminiyi OA, Akanji AO, Moussa MA (2002) Associations of plasma homocysteine concentration in subjects with type 2 diabetes mellitus. *Acta Diabetologica* **39**: 183–90

### CIRCULATION



## Current HRT use reduces risk of first MI in diabetes

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

**1** Little is known about the possible associations of hormone replacement therapy (HRT) and the risk of coronary heart disease (CHD) in women with diabetes.

**2** This 3-year follow-up observational study examined 25 000 women aged 50 years and older, identified by the Northern California Kaiser Permanente Diabetes Registry.

**3** The risk of acute myocardial infarction (MI) was examined together with different HRT regimens, oestrogen doses and time since HRT initiation.

**4** Among the 24 420 women without a recent MI, 1110 incidences of MI were identified. Current HRT was associated with reduced MI risk for oestrogen plus progesterone therapy but not for oestrogen therapy alone.

**5** Women were at reduced risk of MI if taking a low or medium dose but not a high dose of oestrogen.

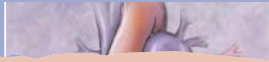
**6** HRT users of less than one year had an increased risk of MI.

**7** For women with a history of recent MI, HRT was associated with an increased risk of MI.

**8** Data from this study do not prove causality: clinical trials in women with diabetes are needed to fully understand the possible risks and benefits of HRT.

Ferrara A, Quesenberry CP, Karter AJ et al (2003) Current use of unopposed estrogen and estrogen plus progestin and the risk of acute myocardial infarction among women with diabetes. *Circulation* **107**: 43–8

## JOURNAL OF HUMAN HYPERTENSION



### Trend to improved hypertension control

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

- 1 Levels of hypertension control are often far from optimal in people with diabetes.
- 2 This study examined people with type 1 diabetes or type 2 diabetes included in four surveys from 1996-1999 in Sweden. Data were obtained from repeated surveys or from repeated measures in the same individual.
- 3 A decreasing trend in mean and median blood pressure levels was seen during the 4-year period for both type 1 diabetes and type 2 diabetes.
- 4 The proportion of hypertensive patients with acceptable blood pressure control increased in type 1 and type 2 diabetes.
- 5 If sustained, an increasing trend towards improved blood pressure control could lead to substantial clinical benefits in cardiovascular and diabetes-related morbidity.

Nilsson PM, Gudbjornsdottir S, Eliasson B, Cederholm J (2003) Hypertension in diabetes: trends in clinical control in repeated large-scale national surveys from Sweden. *Journal of Human Hypertension* 17: 37-44

## DIABETIC MEDICINE



### Microalbuminuria more prevalent in UK South Asians

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

- 1 This study compared levels of urinary albumin excretion and microalbuminuria in UK South Asians and Europeans.
- 2 Microalbuminuria was measured by albumin-creatinine ratio (ACR) in 825 European, 259 Indian, 305 Pakistani and 120 Bangladeshi UK adults.
- 3 Urinary albumin excretion levels were higher in South Asians (mean ACR: 0.83) than in Europeans (0.55) and were independent of the risk factors of old age, hypertension and diabetes.
- 4 High urinary albumin excretion levels in UK South Asians may partly explain the high levels of cardiovascular mortality and renal failure in this population.

Fischbacher CM, Bhopal R, Rutter MK et al (2003) Microalbuminuria is more frequent in South Asian than in European origin populations: a comparative study in Newcastle, UK. *Diabetic Medicine* 20: 31-6

fatty acids (Mediterranean diet), may have several advantages over high-carbohydrate diets.

- 3 This seems to be particularly the case for populations such as the US, which have a high prevalence of insulin resistance due mainly to obesity and lack of exercise.
- 4 If these populations were to modify their behaviour towards better weight control and increased exercise, they might be better able to tolerate higher levels of carbohydrate. In healthier populations, diets high in unsaturated fats are well tolerated.

Grundy SM, Abate N, Chandalia M (2002) Diet composition and the metabolic syndrome: what is the optimal fat intake? *American Journal of Medicine* 113(9B): 25S-29S

## EUROPEAN JOURNAL OF CLINICAL PHARMACOLOGY



### Better outcomes not linked to drug prescription

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

- 1 Guidelines to achieve a good quality of life for patients with diabetes were drawn up in 1999 by The National Swedish Board of Health and Welfare.
- 2 This study describes and compares the distribution of prescribed drugs in patients with diabetes between 1995 and 2001. It is interesting to speculate whether the new guidelines have influenced medical diabetes care in Swedish primary health care.
- 3 Two cross-sectional surveys of the medical records of type 2 patients with diabetes were carried out in two primary healthcare centres in 1995 and 2001. Subjects comprised 59 men and 43 women in 1995 and 80 men and 80 women in 2001 (aged 35-64).
- 4 Between 1995 and 2001 fewer subjects were treated with insulin (15% vs 3%), while more were treated with tablets and insulin (13% vs 23%). Sulphonylurea use decreased (54% vs 41%) while metformin use increased (34% vs 48%). More lipid-lowering agents were used (14% vs 37%).
- 5 Mean HbA<sub>1c</sub> (7.6% vs 6.5%) and mean cholesterol level (5.9 mmol/l vs 5.3 mmol/l) decreased. Macrovascular complications decreased in men (39% vs 21%) and women (26% vs 6%).
- 6 Metabolic control and complications improved but these changes were not associated with prescription pattern changes.

Wandell PE, Gafvels C (2002) Drug prescription in men and women with type-2 diabetes in Stockholm in 1995 and 2001: change over time. *European Journal of Clinical Pharmacology* 58: 547-53

**'If sustained, an increasing trend towards improved blood pressure control could lead to substantial clinical benefits in cardiovascular and diabetes-related morbidity.'**

## AMERICAN JOURNAL OF MEDICINE



### Unsaturated fat diet better than high-carbohydrate diet

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

- 1 This article considers whether diet affects the risk factors of the metabolic syndrome and insulin resistance independently of obesity.
- 2 Recent evidence suggests that diets high in unsaturated fatty acids, particularly monounsaturated

**'Recent evidence suggests that diets high in unsaturated fatty acids, particularly monounsaturated fatty acids, may have several advantages over high-carbohydrate diets.'**

**'In short-term diabetes, mortality was attributed largely to other risk factors, while in long-term diabetes, it was due to the diabetes itself.'**

## EUROPEAN JOURNAL OF CLINICAL INVESTIGATION



### Mortality risk rises with increasing duration of diabetes

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

**1** This research examined mortality in relation to diabetes duration and other cardiovascular risk factors.

**2** Subjects ( $n=174$ ) had type 2 diabetes; 95 were diagnosed by

screening. They were assessed for cardiovascular risk factors and mortality over a 10-year period.

**3** Relative risks of mortality were 2.06 for those with short-term and 3.19 for those with long-term diabetes compared with newly screened subjects with diabetes.

**4** Mortality risk increased with increasing diabetes duration.

In short-term diabetes, mortality was attributed largely to other risk factors, while in long-term diabetes it was due to the diabetes.

Spijkerman AMW, Dekker JM, Nijpels G et al (2002) Impact of diabetes duration and cardiovascular risk factors on mortality in type 2 diabetes: the Hoorn Study. *European Journal of Clinical Investigation* **32**: 924–30

## DIABETIC MEDICINE



### Further evidence for heterogeneity of type 2 diabetes

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

**1** Variability in insulin sensitivity and  $\beta$ -cell function were investigated in 54 patients with type 2 diabetes referred to hospital because of poor glycaemic control.

**2** Insulin sensitivity varied 18-fold and 6-fold between subjects using two different methods.

**3** Beta-cell function varied 4-fold and 8-fold between subjects using two different methods.

**4** The wide variations in insulin sensitivity and  $\beta$ -cell function in patients with type 2 diabetes support the notion that the disorder is highly heterogeneous. Reduced insulin sensitivity was related to the metabolic syndrome and increased risk of CHD.

Birkeland KI, Kilhovd B, Thorsby P et al (2003) Heterogeneity of non-insulin-dependent diabetes expressed as variability in insulin sensitivity,  $\beta$ -cell function and cardiovascular risk profile. *Diabetic Medicine* **20**: 37–45

## JOURNAL OF CARDIOVASCULAR RISK



### Obesity and diabetes cause CHD in women

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

**1** This review examines epidemiological data on the impact of obesity and diabetes on cardiovascular health in women.

**2** Women have a high prevalence of obesity, which is associated with a number of coronary risk factors,

including hypertension, dyslipidaemia, insulin resistance, glucose intolerance and type II diabetes.

**3** Coronary disease in women is closely associated with adiposity.

**4** By age 40, CHD is the leading cause of death in subjects with diabetes, but women with diabetes are at greater risk than men with diabetes.

**5** Women with diabetes aged 45–74 years are at greater risk of cardiovascular mortality than non-diabetic women.

**6** Obesity prevention and treatment should be part of cardiovascular risk modification in women.

Pradhan AD, Skerrett PJ, Manson JE (2002) Obesity, diabetes, and coronary risk in women. *Journal of Cardiovascular Risk* **9**: 323–30

## NEW ENGLAND JOURNAL OF MEDICINE



### Cardiovascular events reduced by intensive treatment

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

**1** Cardiovascular morbidity is a major problem for people with type 2 diabetes.

**2** The Steno-2 Study evaluated the effect of a targeted, intensive, multifactorial intervention comprising behaviour modification and polypharmacological therapy on modifiable risk factors in patients with type 2 diabetes and microalbuminuria.

**3** Subjects (mean age 55.1 years) were randomly assigned to either conventional treatment (80) or intensive treatment (80) that targeted hyperglycaemia, hypertension, dyslipidaemia and microalbuminuria, along with secondary prevention of cardiovascular disease with aspirin. Subjects were followed up for a mean of 7.8 years.

**4** Glycosylated haemoglobin, blood pressure, serum cholesterol and triglyceride levels measured after an overnight fast, and urinary albumin excretion were all significantly reduced in the intensive therapy group.

**5** Patients in this group also had a significantly lower risk of cardiovascular disease, nephropathy, retinopathy and autonomic neuropathy than those on conventional treatment.

**6** Intensive treatment targeted at multiple risk factors in patients with type 2 diabetes and microalbuminuria reduced the risk of cardiovascular and microvascular events by about 50%.

Gaede P, Vedel P, Larsen N et al (2003) Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *New England Journal of Medicine* **348**: 383–93

**'Wide variations in insulin sensitivity and  $\beta$ -cell function in patients with type 2 diabetes support the notion that the disorder is highly heterogeneous.'**