Cardiovascular disease: major journals

Sex differences in CHD risk associated with diabetes and established CHD

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The paper by Natarajan et al is important because recent data have shown that patients with diabetes have not benefited from the improvement in mortality from cardiovascular disease seen over the last 10 years in the population as a whole. It has also been suggested that women with diabetes have a greater risk of cardiovascular death than men with diabetes – the presence of diabetes removing the protection against atherosclerosis afforded by female sex status.

This analysis, using cohort data from the Framingham Heart Study, aimed to: (1) evaluate the effect of diabetes and established coronary heart disease (CHD) on subsequent CHD mortality in men and women; (2) determine the differential sex-specific effects of diabetes on CHD mortality.

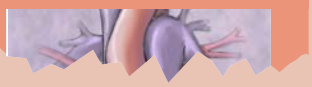
CHD was defined as myocardial infarction, coronary insufficiency or angina pectoris. Death from CHD was categorised as sudden or non-sudden. A series of analyses was performed.

The results of the study showed that men with CHD were at greater risk of subsequent death from CHD than men with diabetes and no CHD. The hazard ratio (HR) for CHD mortality in men with CHD was 4.2 (95% confidence interval [CI] 3.2–5.6); in men with diabetes alone the HR was 2.1 (95% CI 1.3–3.3). In women, the presence of CHD alone was associated with a risk of death from CHD of 1.9 (95% CI 1.1–3.4) whereas diabetes alone was associated with a risk of death from CHD of 3.8 (95% CI 2.2–6.6).

To further evaluate the effect of sex status on outcome in diabetes, regression analysis was performed, supporting the initial analysis.

In conclusion, the paper by Natarajan et al provides compelling evidence to support the notion that diabetes confers a greater risk of CHD death in women than in men. Furthermore, it demonstrates that women with diabetes have a higher risk of death from CHD than women without diabetes but with pre-existing CHD. Women with diabetes should be treated as if they have CHD until proven otherwise.

AMERICAN JOURNAL OF MEDICINE



Lipid therapy could save more lives in diabetes than in CVD

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

1 The care of patients with diabetes has not reflected current guidelines on dyslipidaemia treatment.

2 This study compared the effects of dyslipidaemia treatment in patients with diabetes but no cardiovascular disease (CVD), and those with CVD but no diabetes.

3 The authors estimated the number of adults (aged 30–74 years) requiring lipid therapy, using data from the third National Health and Nutrition Examination Survey and current guidelines.

4 The benefits of lipid therapy were estimated using the Cardiovascular Disease Life Expectancy Model.

5 The estimated mean number of life-years saved were 3–3.4 years for men with diabetes vs 2.4–2.7 for men with CVD, and 1.6–2.4 years for women with diabetes vs 1.6–2.1 years for women with CVD.

6 Overall, 25.4 million person-years of life would be saved by treating patients with diabetes compared with 16 million for those with CVD.

7 The clinical benefits of treating dyslipidaemia in patients with diabetes should be at least equal to, if not more than, those in CVD patients.

Grover SA, Coupal L, Zowall H, Weiss TW, Alexander CM (2003) Evaluating the benefits of treating dyslipidemia: the importance of diabetes as a risk factor. *American Journal of Medicine* **115**: 122–28

ARCHIVES OF INTERNAL MEDICINE

Diabetes confers greater risk of CHD death in women

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

1 The sex-specific independent effect of diabetes and established coronary heart disease (CHD) is not known.

2 This study evaluated the independent effect of diabetes and established CHD on subsequent CHD mortality, and determined the differential sex-specific effects of diabetes on CHD mortality compared with established CHD.

3 Pooled data from 5243 participants in the Framingham Heart Study and the Framingham Offspring Study were analysed.

4 Analysis was carried out using proportional hazards models, adjusting for age, hypertension, serum cholesterol, smoking and BMI.

5 Adjusted hazard ratios (HRs) for CHD death were 2.1 in men with diabetes only vs 4.2 in men with CHD only, compared with men without CHD or diabetes. In women, the HRs for CHD death were 3.8 in those with diabetes vs 1.9 in those with CHD.

4 In men, established CHD therefore signifies a higher risk for CHD death than diabetes, whereas in women diabetes is associated with a greater risk of death from CHD.

5 Limitations of the study include: participants were almost totally white, and information on potential confounders, such as family history of CHD, were not available.

6 Findings support aggressive management of diabetes to prevent CHD, particularly in women.

Natarajan S, Liao Y, Cao G, Lipsitz SR, McGee DL. (2003) Sex differences in risk for coronary heart disease mortality associated with diabetes and established coronary heart disease. *Archives of Internal Medicine* **163**: 1735–40

THE LANCET

HPS recommends statins for high-risk diabetes patients

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

1 Most people with diabetes, apart from those with marked dyslipidaemia or CHD, do not receive cholesterol-lowering therapy, despite their increased risk of cardiovascular morbidity and mortality.

2 The Heart Protection Study (HPS) prospectively assessed the effects on vascular mortality and morbidity of a substantial LDL cholesterol reduction maintained for around 5 years in a large cohort of patients with diabetes.

3 A total of 5963 adults (aged 40–80 years) with diabetes and 14 573 with occlusive arterial disease but no diabetes were randomly allocated to 40 mg simvastatin daily or placebo.

4 Allocation to 40mg simvastatin daily reduced the rate of first major vascular event (major coronary event, stroke or revascularisation) by about a quarter in the wide range of patients with diabetes studied.

5 There were highly significant reductions of 33% in those with diabetes and no occlusive arterial disease at entry, and of 27% in those with a pretreatment LDL cholesterol of <3.0 mmol/l, indicating that cholesterol-lowering is beneficial for people with diabetes even if they do not already have coronary disease or high cholesterol levels.

6 Statin therapy should now be considered routinely for all patients with diabetes at high risk of major vascular events, irrespective of their initial cholesterol level.

Heart Protection Study Collaborative Group (2003) MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *The Lancet* **361**: 2005–15

THE LANCET

Statin therapy for all regardless of cholesterol level?

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

1 Current diabetes guidelines stress the importance of good glycaemic and blood pressure control for all patients with diabetes, but do not normally recommend statin therapy unless LDL cholesterol is >3.0 or 3.4 mmol/l.

2 Statin use is uncommon, even in those with diabetes and with hypertension and left ventricular hypertrophy taking part in clinical trials.

3 This commentary compares and contrasts the findings of five recent large-scale trials involving statin therapy in patients with diabetes, including HPS (see left), ALLHAT-LLT, ASCOT-LLA, and LIFE.

4 It goes further than HPS, suggesting that maybe *all* patients with type 2 diabetes should be given a statin, regardless of their cholesterol levels.

Lindholm LH (2003) Commentary: major benefits from cholesterol-lowering in patients with diabetes. *The Lancet* **361**: 2000–001

THE LANCET

Demographics, diabetes and chronic heart failure

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

1 Knowledge of the demography and comorbidities associated with chronic heart failure (CHF) is important for therapeutic decision making in CHF.

2 This paper presents information on the most common comorbidities in CHF (ischaemic heart disease, hypertension and diabetes mellitus) from published epidemiological studies and trials in heart failure involving more than 1000 patients during the past 10 years.

3 Diabetes is a common but overlooked comorbidity in CHF.

4 Three major factors contribute to the high prevalence of CHF in diabetes: hypertension, coronary artery disease and diabetic cardiomyopathy.

5 The presence of CHF as a comorbid disorder should be taken into account when selecting an antidiabetic drug.

Krum H, Gilbert RE (2003) Demographics and concomitant disorders in heart failure. *The Lancet* **362**: 147–58

ARCHIVES OF INTERNAL MEDICINE

Continuity of care and likelihood of disease recognition

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

1 This study examined the relationship between continuity of care and disease recognition.

2 Data from the third National Health and Nutrition Examination Survey (18162 adult non-institutionalised US residents), collected from 1988 to 1994), were analysed.

3 The proportion of unrecognised disease among all individuals with diabetes, hypertension and hypercholesterolaemia according to self-reported level of continuity of care was determined.

4 Individuals with a high level of continuity of care (a usual provider of care rather than no usual site or provider) were less likely to have unrecognised diabetes and hypertension, but not hypercholesterolaemia.

5 The benefits of continuity of care in terms of disease recognition appear to be disease-specific.

Koopman RJ, Mainous III AG, Baker R, Gill JM, Gilbert GE (2003) Continuity of care and recognition of diabetes, hypertension, and hypercholesterolemia. *Archives of Internal Medicine* **163**: 1357–61

'Statin therapy should now be considered routinely for all patients with diabetes at high risk of major vascular events, irrespective of their initial cholesterol level.'

'Individuals with a high level of continuity of care (a usual provider of care rather than no usual site or provider) were less likely to have unrecognised diabetes and hypertension.'

'Of the 35 reviews analysed, only six mentioned that tight control of blood glucose had no effect on diabetes-related or overall mortality, and seven mentioned that treatment with metformin was associated with decreased mortality.'

'Insulin response to an oral glucose load was significantly improved by both diets. (None of the participants had diabetes, but some were probably insulin-resistant because of their obesity.) Further studies are needed to evaluate this issue more thoroughly.'

ARCHIVES OF INTERNAL MEDICINE

Adverse effect of aspirin may be dose-related

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

1 This study explored the possibility that giving aspirin and ACE inhibitors (ACEIs) concurrently to patients with CHF affects mortality and that the interaction may be related to the dose of aspirin.

2 A total of 344 patients with CHF taking ACEIs were analysed.

3 They were divided into three groups: group 1 (235; no aspirin); group 2 (45; ≤160 mg aspirin daily); group 3 (64; ≥325 mg aspirin daily).

4 Survival was similar in groups 1 and 2 (36% and 33%, respectively), but significantly worse in group 3 (55%). The combination of high-dose aspirin with ACEI was independently associated with risk of death, but low-dose aspirin with ACEI was not.

5 Aspirin may have a dose-related effect in some patients with CHF taking an ACEI, adversely affecting survival.

Guazzi M, Brambilla R, Reina G, Tumminello G, Guazzi MD (2003) Aspirin–angiotensin–converting enzyme inhibitor coadministration and mortality in patients with heart failure. *Archives of Internal Medicine* **163**: 1574–9

NEW ENGLAND JOURNAL OF MEDICINE

Cardiovascular events predicted by ambulatory BP

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

1 The prospective multicentre Office versus Ambulatory Blood Pressure Study investigated whether ambulatory BP monitoring in patients with treated hypertension could predict cardiovascular events and death, even after adjusting for classic risk factors, including office BP measurement.

2 Of the 1963 patients with hypertension enrolled in the study, 157 had a new cardiovascular event.

3 Results showed that after adjusting for confounding factors, including routine BP measurement, higher mean values for 24-hour ambulatory systolic and diastolic BP were independent risk factors for cardiovascular events.

Clement DL, De Buyzere ML, De Bacquer DA et al, for the Office versus Ambulatory Pressure Study Investigators (2003) Prognostic value of ambulatory blood-pressure recordings in patients with treated hypertension. *New England Journal of Medicine* **348**: 2407–15

NEW ENGLAND JOURNAL OF MEDICINE

Evaluation of the low-carbohydrate (Atkins) diet

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

1 This 1 year, multicentre trial evaluated the efficacy of the low-carbohydrate, high-protein, high-fat (Atkins) diet.

2 Sixty-three obese men and women were randomly allocated to either the Atkins diet or a low-calorie, high-carbohydrate, low-fat (conventional) diet. Professional contact was minimal to simulate dieters' usual approach.

3 The Atkins diet produced greater weight loss over the first 6 months, but the difference was not maintained at 1 year.

4 Diastolic blood pressure was significantly improved by both diets.

5 Insulin response to an oral glucose load was significantly improved by both diets. (None of the participants had diabetes, but some were probably insulin-resistant because of their obesity.) Further studies are needed to evaluate this issue more thoroughly.

Foster GD, Wyatt HR, Hill JO, McGuckin BG, Brill C, Mohammed BS et al (2003) A randomised trial of a low-carbohydrate diet for obesity. *New England Journal of Medicine* **348**: 2082–90

BRITISH MEDICAL JOURNAL

Review articles do not effectively transmit research

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

1 The UKPDS presented vital information that should be used to guide patient care, and contained both patient-oriented and disease-oriented outcomes.

2 This study evaluated how the findings of the UKPDS have been transmitted.

3 An inception cohort analysed 35 review articles on treatment of type 2 diabetes that had been written 2 years or more after the publication of the major findings of the UKPDS.

4 Of the 35 reviews analysed, only six mentioned that tight control of blood glucose had no effect on diabetes-related or overall mortality, and seven mentioned that treatment with metformin was associated with decreased mortality.

5 Most reviews (30) did not report that people with diabetes and hypertension benefit more from good blood pressure control than from good blood glucose control.

6 None of the reviews stated that treatment of overweight people with type 2 diabetes with insulin or sulphonylurea drugs had no effect on microvascular or macrovascular outcomes; 13 reviews recommended drugs as first-line treatment for which we do not have patient-oriented outcomes data.

7 The mean validity score for the 35 papers was 1.3 from a possible 15.

8 The current system of transmitting new research about type 2 diabetes to clinicians by review articles is less than optimal.

Shaughnessy AF, Slawson DC (2003) What happened to the valid POEMs? A survey of review articles on the treatment of type 2 diabetes. *British Medical Journal* **327**: 266–72