

mortality was explained by the excess of suicides and deaths from malignant disease. Deaths due to malignancy were mainly linked to smoking, previously shown as common in our cohort.⁵ Given the well documented link between psychiatric disorders and a desire for cosmetic surgery, the increased risk for death from suicide may reflect a greater prevalence of psychopathology rather than a causal association between implant surgery and suicide.³ Surgeons evaluating candidates for breast implant surgery need to be vigilant for subtle signs of psychiatric problems.

Contributors: VCMK, the principal investigator, discussed the core ideas, performed the record linkages, outlined and performed analyses, and wrote most of the paper. PHMP discussed the core ideas and participated in data interpretation and writing of the paper. FG participated in discussions about the core ideas, made suggestions about analyses, and helped VCMK with the practical analysis. DEG discussed the core ideas, the design of the study, the interpretation of the data, and writing of the paper. ON initiated the research, discussed the core ideas, formulated the primary study hypothesis, made

suggestions about analyses and interpretation of the data, and supervised the writing. DEG and ON will act as guarantors for the paper.

Funding: This work was supported by a contract from the International Epidemiology Institute, Rockville, MA. VCMK was financially supported by the Netherlands Organization for Scientific Research.

Competing interests: None declared.

- 1 Angell M. Evaluating the health risks of breast implants: the interplay of medical science, the law, and public opinion. *N Engl J Med* 1996;334:1513-8.
- 2 Brinton LA, Lubin JH, Burich MC, Colton T, Hoover RN. Mortality among augmentation mammoplasty patients. *Epidemiology* 2001;12:321-6.
- 3 Hasan JS. Psychological issues in cosmetic surgery: a functional overview. *Ann Plast Surg* 2000;44:89-96.
- 4 Nyren O, Yin L, Josefsson S, McLaughlin JK, Blot WJ, Engqvist M, et al. Risk of connective tissue disease and related disorders among women with breast implants: a nation-wide retrospective cohort study in Sweden. *BMJ* 1998;316:417-22.
- 5 Fryzek JP, Weiderpass E, Signorello LB, Hakelius L, Lipworth L, Blot WJ, et al. Characteristics of women with cosmetic breast augmentation surgery compared with breast reduction surgery patients and women in the general population of Sweden. *Ann Plast Surg* 2000;45:349-56.

(Accepted 17 January 2003)

Systematic review of lipid lowering for primary prevention of coronary heart disease in diabetes

Apoor S Gami, Victor M Montori, Patricia J Erwin, Mehmood A Khan, Steven A Smith for the Evidence in Diabetes Enquiry System (EVIDENS) Research Group

Department of Internal Medicine, Mayo Clinic, 200 First Street SW, Rochester MN 55905, USA

Apoor S Gami
instructor in medicine

Division of Endocrinology, Diabetes, Metabolism, Nutrition, and Internal Medicine, Mayo Clinic

Victor M Montori
assistant professor
Mehmood A Khan
associate professor
Steven A Smith
associate professor

Mayo Medical Libraries, Mayo Clinic

Patricia J Erwin
head reference librarian

Correspondence to: S A Smith
smith.steven@mayo.edu

BMJ 2003;326:528-9



The studies included in the review are listed on bmj.com

Patients with diabetes are at high risk of coronary heart disease. Leading organisations have recommended that all diabetic patients should be treated as aggressively as patients with established coronary heart disease.¹ Randomised trials have shown the efficacy of reducing low density lipoprotein concentrations in patients without coronary heart disease. Large trials and meta-analyses of such trials would be expected to provide information on diabetic patients. We therefore systematically examined the available data on lowering low density lipoprotein concentrations in diabetic patients without coronary heart disease.

Methods and results

The review protocol is available from the authors. We searched Medline and eight other electronic databases (including five clinical trials databases) and proceedings from pertinent scientific meetings. We attempted to contact the authors of trials reporting incomplete data but received no responses. We reviewed the bibliographies of all retrieved publications.

Eligible trials randomised patients to lipid lowering interventions; included patients without coronary heart disease; and measured myocardial infarction, death from coronary heart disease, or all cause mortality. Eligible meta-analyses pooled data from similar trials. We excluded studies available only as abstracts. There were no language exclusions. We also included the Medical Research Council/British Heart Foundation heart protection study, which was pub-

lished after our search.² A list of included trials and meta-analyses is available on bmj.com

The 14 eligible trials randomised 132 977 patients without coronary heart disease, and diabetes status was stated for 1799 patients (1.3%). Three trials provided clinical endpoints for 454 diabetic patients. In addition, the heart protection study randomised 3982 diabetic patients without coronary heart disease (table).

We found 13 meta-analyses that included up to 38 trials and 146 854 patients. None presented data for diabetes subgroups. One meta-analysis postulated that diabetes might account for differences between trials, but incomplete reporting in the trials limited the analysis.

Comment

Inclusion and reporting biases in randomised controlled trials and meta-analyses limited our assessment of the efficacy of lowering low density lipoprotein concentration in diabetic patients without coronary heart disease. Most trials of lipid lowering interventions for primary prevention of coronary heart disease excluded diabetic patients by varied and ambiguous criteria. Consequently, these trials included few patients with diabetes. Those who were included were poorly characterised in terms of type and duration of diabetes, severity of complications, and metabolic control. It is therefore unclear whether the diabetes subgroups represent the general diabetic population.

Randomised controlled trials of lipid lowering for primary prevention of coronary heart disease. Data for patients without coronary heart disease at baseline

Trial (year)*	Mean or median follow up (years)	No of patients randomised	Diabetic patients excluded	Diabetes exclusion criteria	Exclusion rationale	Baseline diabetes status published	No of diabetic patients randomised	Risk ratio (95%CI) for first coronary heart disease event	
								All patients	Diabetic patients
Diet									
MRFIT (1982) ^{w1}	7	12 866	Some	"Requiring medication"	None	No	Unknown	0.92 (0.80 to 1.05)	NR
WHO Multifactor (1983) ^{w2}	6	49 781	No	NA	NA	No	Unknown	1.08 (0.98 to 1.19)	NR
Gothenberg (1986) ^{w3}	11.8	30 000	No	NA	NA	No	Unknown	0.99 (0.91 to 1.07)	NR
Resins									
LRC-CPPT (1984) ^{w4}	7.4	3 806	All	Medical history or fasting blood glucose >130 mmol/l	None	NA	NA	0.83 (0.67 to 1.01)	NA
Fibrates									
VA Cooperative (1973) ^{w5}	4.5	532	Some	"Severe"	None	Yes	47	0.90 (0.41 to 1.97)	NR
WHO Cooperative (1979) ^{w6}	5.3	15 745	Some	"Requiring drug treatment"	None	No	Unknown	0.83 (0.68 to 1.01)	NR
Helsinki Heart Study (1987) ^{w7}	5	4 081	Some	All but "mild" or insulin use	None	Yes	135	0.66 (0.47 to 0.92)	0.32 (0.08 to 1.27)
SEDCAP (1998) ^{w8}	3	164	No	NA	NA	Yes	164	NA	0.32 (0.13 to 0.79)
DAIS (2001) ^{w9}	3	200	No	NA	NA	Yes	200	NR	NR
Statin trials									
Multination Study Group (1993) ^{w10}	0.5	1 062	All	"Significant endocrine disease"	None	NA	NA	NR	NA
Oxford (1994) ^{w11}	3.4	621	Some	Untreated	None	Yes	20	NR	NR
WOSCOPS (1995) ^{w12}	4.9	6 595	No	NA	NA	Yes	1 037	0.70 (0.58 to 0.84)	NR
ACAPS ^{w13}	2.8	919	No	NA	NA	Yes	21	0.36 (0.13 to 0.94)	NR
AFCAPS/ TexCAPS (1998) ^{w14}	5.2	6 605	Some	Uncontrolled or insulin use	None	Yes	155	0.63 (0.50 to 0.79)	0.56 (0.18 to 1.79)
Heart Protection Study (2002) ^f	5	7 150	No	NA	NA	Yes	3 982	0.77 (0.70 to 0.85)	0.74 (0.64 to 0.86)

NA=not applicable, NR=data not reported.

*Names of trials are given in full in the references, which are available on bmj.com

The meta-analyses were also affected by the limitations described above. In addition, outcome was reported for only one third of diabetic participants. Consequently, these meta-analyses cannot overcome the biases against diabetes in the original trials.

Current recommendations to manage dyslipidaemia in diabetic patients are based on observational evidence and expert judgment. The heart protection study showed that simvastatin significantly reduced the risk of major vascular events for diabetic patients without coronary heart disease at any initial low density lipoprotein concentration. It remains unclear whether the benefits of statins are mediated by lowering low density lipoprotein concentrations, whether goals of treatment should be expressed as low density lipoprotein concentrations, and whether a fixed dose of statin, increasing doses of statin, or multiple drugs can be used to achieve these goals with acceptable safety. Recommendations from policymakers and experts should reflect this uncertainty.

Contributors: ASG and VMM contributed to the design of the study, collection and assembly of data, analysis and

interpretation of data, and drafting the article. PJE participated in the design of the study and collection and assembly of data. MAK took part in the analysis and interpretation of data and drafting of the article. SAS contributed to the design of the study, analysis and interpretation of data, and drafting of the article. All authors approved the final manuscript. SAS is the guarantor.

Funding: American Diabetes Association and Mayo Foundation. The guarantor accepts full responsibility for the conduct of the study, had access to the data, and controlled the decision to publish.

Competing interests: None declared.

Ethical approval: The study did not involve human subjects or patients' records. The institutional review board of the Mayo Clinic approved the study.

- 1 Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. National cholesterol education program: executive summary of the third report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (adult treatment panel III). *JAMA* 2001;285:2486-97.
- 2 Medical Research Council/British Heart Foundation Heart Protection Study Collaborative Group. MRC/BHF heart protection study of cholesterol lowering with simvastatin in 20 536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;360:7-22.

(Accepted 17 January 2003)

An ecumenical practice?

The NHS is regularly accused of the sins of today such as institutional racism. I would like to report that in February 2002, our suburban general practice consisted of four partners, a new GP registrar, and a preregistration house officer. We all appreciated each other's worth and worked well together, even though

we comprised a Roman Catholic, a Protestant, a Hindu, an agnostic, a Muslim, and a Jew. Could this be a multifaith first?

Guy Houghton *general practitioner, Greenbank Surgery, Birmingham*