Low prevalence of lipid lowering drug use in older men with established coronary heart disease

P H Whincup, J R Emberson, L Lennon, M Walker, O Papacosta, A Thomson

Objective: To determine the prevalence and correlates of lipid lowering drug use among older British men with established coronary heart disease (CHD).

Design: Cross sectional survey within a cohort study (British regional heart study) carried out at 20 years of follow up in 1998–2000.

Setting: General practices in 24 British towns.

Participants: 3689 men aged 60–75 years (response rate 76%).

Main outcome measures: Diagnoses of myocardial infarction and angina based on detailed review of general practice records. Lipid lowering drug use and blood cholesterol concentrations ascertained at 20 year follow up examination.

Results: Among 286 men with definite myocardial infarction, 102 (36%) were taking a lipid lowering drug (93 [33%] a statin); among 360 men with definite angina without myocardial infarction, 84 (23%) were taking a lipid lowering drug (78 [21%] a statin). Most men with documented CHD who were not receiving a lipid lowering drug had a total cholesterol concentration of 5.0 mmol/l or more (87% of those with myocardial infarction, 82% with angina). Fewer than half of men with CHD receiving a statin had a total cholesterol concentration below 5.0 mmol/l (45% of those with myocardial infarction and 47% of those with angina). Only one third of the men taking a statin were receiving trial validated dosages. Among men with CHD, a history of revascularisation, more recent diagnosis, and younger age at diagnosis were associated with a higher probability of receiving lipid lowering drug treatment.

Conclusion: Among patients with established CHD, the prevalence of lipid lowering drug use remains low and statin regimens suboptimal. Major improvements in secondary prevention are essential if the benefits of statins are to be realised.

Despite the clear efficacy of statin treatment, previous reports have suggested that lipid lowering drugs are not being widely used in Britain. A recent report from the Health Survey for England suggested that these drugs were being underused in both primary and secondary prevention. However, the Health Survey for England report was based only on doctors’ diagnoses recalled by patients, could not identify types of lipid lowering drugs or dosages, and did not examine characteristics of patients receiving and not receiving lipid lowering treatment. We have used a population based study of cardiovascular disease carried out between 1998 and 2000 to examine the use of lipid lowering drugs among men aged 60–75 years, particularly those with a CHD diagnosis confirmed by a doctor, and to examine factors related to the use of lipid lowering drugs in this context.

METHODS
The British Regional Heart Study is a national prospective study of cardiovascular disease in one general practice in each of 24 British towns, representing all major British regions. Participants were enrolled in 1978–80, aged 40–59 years, and have been followed up for all cause mortality using the National Health Service (NHS) central registers and for cardiovascular morbidity through regular biennial reviews of
general practice records. Fewer than 1% of participants have
been lost to follow up.16,17
Between February 1998 and February 2000, all surviving
men were invited to attend for a 20 year follow up at 60–79
years of age. Men who were still living in the same town as in
1978–1980 were invited to return to their original practice for
reassessment; men who had moved from the original study
town were given a choice of returning to their original town,
or travelling to a London assessment centre. Men were asked to
attend for screening after a minimum six hour fast and with
all their medications. At screening, men completed a study
questionnaire, which was checked by research nurses. All cur-
current medications were recorded and verified either against the
medication container or (if the container was not available)
against a prescription record; any participant in whom the
completeness of the medication record was uncertain was
excluded from this analysis. Diabetes diagnosed by a doctor
and percutaneous transluminal coronary angioplasty,
including dates, that had occurred up to the time of examina-
tion. Before a practice diagnosis of myocardial infarction was
accepted as definite, additional clinical information on stand-
World Health Organization criteria (requiring two of the
following: (a) a history of severe chest pain, (b) changes in
cardiac enzymes, and (c) characteristic electrocardiographic
changes) was obtained from the general practitioner.17 Among
patients without CHD diagnosed, absolute CHD risk was
calculated by the standard Framingham equation, using age,
diabetic status, systolic pressure, smoking status, total and
high density lipoprotein cholesterol, and left ventricular
hypertrophy.19

### RESULTS

In all, 3689 men aged 60–75 years participated in the 20 year
follow up examination and provided a full medication history
(76% of those invited). Almost all (3495, 95%) had a study
total cholesterol measurement. A total of 294 men (8.0%) were
taking lipid lowering medication; of these 259 (88%) were
taking statins, 31 (11%) fibrates, and 4 (1%) ion exchange res-
in. Of these 294 men, 208 (71%) had cardiovascular disease
documented in their general practice records and a further 48
(16%) recalled a cardiovascular diagnosis.

| Table 1 | Prevalence and correlates of lipid lowering drug use in men with documented myocardial infarction (MI) or angina |

<table>
<thead>
<tr>
<th>Definite MI (n=286)</th>
<th>Definite angina, no MI (n=360)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>n</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Overall prevalence</td>
<td>Any lipid lowering drug</td>
</tr>
<tr>
<td></td>
<td>Statins</td>
</tr>
<tr>
<td>p value</td>
<td>0.018</td>
</tr>
<tr>
<td>Previous revascularisation</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>No</td>
</tr>
<tr>
<td>p value</td>
<td>0.001</td>
</tr>
<tr>
<td>Year of last diagnosis</td>
<td>Pre 1994</td>
</tr>
<tr>
<td></td>
<td>1994–1997</td>
</tr>
<tr>
<td></td>
<td>Post 1997</td>
</tr>
<tr>
<td>p value</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Age at last diagnosis [years]</td>
<td>&lt; 60</td>
</tr>
<tr>
<td></td>
<td>60–69</td>
</tr>
<tr>
<td></td>
<td>≥ 70</td>
</tr>
<tr>
<td>p value</td>
<td>0.55</td>
</tr>
<tr>
<td>Social class*</td>
<td>Non-manual</td>
</tr>
<tr>
<td></td>
<td>Manual</td>
</tr>
<tr>
<td>p value</td>
<td>0.31</td>
</tr>
<tr>
<td>Geographic residence</td>
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</tr>
<tr>
<td></td>
<td>Scotland</td>
</tr>
<tr>
<td></td>
<td>North, Midlands, and Wales</td>
</tr>
<tr>
<td>p Value</td>
<td>0.018</td>
</tr>
<tr>
<td>Cigarette smoking status†</td>
<td>Current</td>
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<tr>
<td></td>
<td>Former</td>
</tr>
<tr>
<td></td>
<td>Never</td>
</tr>
<tr>
<td>p value</td>
<td>0.56</td>
</tr>
</tbody>
</table>

N, total in category; n, number within the category taking lipid lowering drugs.
*Social class not available for 16 subjects in the MI group and 20 in the angina group; †Smoking status not available for 11 subjects in the MI group and
in the angina group.

In all, 3689 men aged 60–75 years participated in the 20 year
follow up examination and provided a full medication history
(76% of those invited). Almost all (3495, 95%) had a study
total cholesterol measurement. A total of 294 men (8.0%) were
taking lipid lowering medication; of these 259 (88%) were
taking statins, 31 (11%) fibrates, and 4 (1%) ion exchange res-
in. Of these 294 men, 208 (71%) had cardiovascular disease
documented in their general practice records and a further 48
(16%) recalled a cardiovascular diagnosis.

Lipid lowering drug use in men with documented CHD

In all, 286 patients (7.8%) had definite myocardial infarction
diagnosed, of which 33 (12%) were recurrent. Three hundred
and sixty patients (9.8%) had angina diagnosed, of which 117
(33%) were recurrent. Men who had both of these conditions
diagnosed were included in the myocardial infarction group.

Table 1 shows the prevalences of lipid lowering drug use

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among these groups. Approximately one third of patients with a history of myocardial infarction and one fifth of those with angina were receiving lipid lowering drugs; most of these were statins. The overall prevalence of lipid lowering drug use among patients with documented CHD was 186 of 646 (29%). Among men with myocardial infarction not being treated, 87% had a total cholesterol concentration of 5 mmol/l or more and 91% had one above 4.8 mmol/l. Among men with angina who were not receiving treatment, 82% had a total cholesterol concentration of 5 mmol/l or more and 60% had one above 5.5 mmol/l.

**Control of blood total cholesterol among men with documented CHD receiving lipid lowering treatment**

Among 186 men with CHD diagnosed who were on any lipid lowering treatment, 44% had a total cholesterol concentration below 5 mmol/l; this proportion was similar both among men with myocardial infarction and angina. When this analysis was restricted to 171 men with CHD diagnosed who were receiving statin treatment, 46% had a total cholesterol concentration below 5 mmol/l (45% of those with myocardial infarction, 47% of those with angina). Of patients with documented CHD and a presumed baseline total cholesterol of 5 mmol/l or above (that is, those with a current total cholesterol $\geq$ 5.0 mmol/l and/or receiving lipid lowering drug treatment), 75 of 630 (12%) had a total cholesterol concentration below 5 mmol/l. Of 171 men with CHD receiving a statin, 104 (61%) were taking simvastatin and 19 (11%) pravastatin (the drugs used in the secondary prevention trials\(^2\)); 26 (15%) were taking atorvastatin. Of the patients taking simvastatin, only 41% were taking a daily dose similar to that used in the 4S (Scandinavian simvastatin survival study) (20–40 mg daily); most (59%) were taking a smaller dose (10 mg daily). All the patients receiving pravastatin were taking either 10 or 20 mg daily; none was taking the 40 mg daily dose used in the CARE (cholesterol and recurrent events) and LIPID (long-term intervention with pravastatin in ischaemic disease) trials.\(^3\) Most (85%) of the patients receiving atorvastatin were taking a daily dose of 10 mg. These dosage patterns did not vary greatly when men whose myocardial infarction or angina had been diagnosed in the last year were excluded, or when men with total cholesterol concentrations below 5 mmol/l were excluded.

**Factors related to use of lipid lowering drug treatment in men with CHD**

Table 1 presents factors related to the use of lipid lowering drug treatment in men with myocardial infarction or angina. A history of coronary revascularisation was related to increased lipid lowering drug use in both groups of men. Year of last diagnosis was strongly related to drug use in men with myocardial infarction, with prevalence of treatment being much higher among recently diagnosed cases; results of the year of first diagnosis (data not presented) were similar. Prevalence of lipid lowering drug use appearance to be slightly (though not significantly) higher in patients who were younger at last diagnosis, in patients who were of non-manual social class, and among men studied in Scotland and southern England compared with those in the Midlands and the north of England. Men who were cigarette smokers were slightly though not significantly less likely than non-smokers to receive lipid lowering drugs. Table 2 shows odds ratios after adjustment for these interrelated factors. For patients with either myocardial infarction or angina, a history of previous coronary revascularisation, younger age at last diagnosis, and more recent date of last diagnosis were strongly related to increased lipid lowering drug use. The weak and non-significant relation between social class, region, cigarette smoking, and lipid lowering drug use were little altered by adjustment for these other factors.

**Lipid lowering drug use among men at high risk of CHD**

Among 2868 men with no CHD diagnosis in whom a Framingham risk score could be calculated, 578 (20%) had a Framingham risk score consistent with an absolute CHD risk of 3.0% per year or more. However, of these men only 19 (3%) were receiving lipid lowering drug treatment of any kind.

**DISCUSSION**

These results suggest that most older men with established CHD are not receiving lipid lowering drug treatment, and that even those who receive treatment are in many cases receiving inadequate drug doses. The CHD ascertainment methods in this investigation were used specifically to avoid falsely low prevalence estimates of lipid lowering drug use. Cases in which there was any doubt about the completeness of the medication record were excluded. The CHD diagnoses on
which analyses were based were all known to the general practitioners and did not depend on patient recall, which is less specific than a diagnosis based on general practice records.25 Although the long term involvement of participating practices in the British regional heart study could have affected lipid lowering drug use in this study population, participation might have been expected to increase (rather than decrease) preventive activities, including prescription of lipid lowering drugs. However, the study has maintained a low profile in the participating practices and avoided making any specific recommendations about treatment practices to the general practitioners involved in the study.

The prevalence of lipid lowering drug use in patients with established CHD (29%) is very similar to the estimates provided by Primastena and Poulter in men aged 65–75 years in the Health Survey for England (25%) and from general practice statistics in men aged 65–74 years (29%).16 15 The overall proportion of patients with increased blood cholesterol concentrations controlled by lipid lowering drugs is also very similar to the estimate of 16% in the Health Survey for England.16 The present results show clearly that a large proportion of patients are taking inadequate doses of statins, in most cases well below the dosages shown to be effective in the randomised controlled trials of secondary prevention.5 26 Although these findings are only for men, recent studies suggest that the extent of secondary prevention in women is even less complete.14 15 The lower rates of lipid lowering drug use in older patients in the present study (a group at particularly high CHD risk and who, up to 75 years of age, are known to benefit from statins) are also consistent with earlier reports.14 15 Our findings that the prevalence of lipid lowering drug use is lower among patients with angina than those with myocardial infarction, among those who have not undergone revascularisation, and among those whose condition was diagnosed less recently, are consistent with our earlier report on the use of aspirin in the secondary prevention of cardiovascular disease11 and with European experience.25 Our results are also consistent with the possibility of an adverse social gradient in lipid lowering drug use, though they also suggest that there is a particularly high prevalence of lipid lowering drug use in Scotland; this may result from the high local profile of the West of Scotland coronary prevention study (WOSCOPS).5

Several factors may be responsible for the low use of lipid lowering drugs observed in this study. There is always a lag period before research findings influence clinical practice. Concern, initially about the benefits of cholesterol reduction, and latterly about the extent to which statins should be used in primary CHD prevention,22 27 may have delayed widespread use of statin drugs in secondary prevention. The costs of statin treatment have been an additional concern. However, with the strong evidence that statin use is cost effective, particularly in secondary prevention of CHD,28 it is important that priority is given to meeting these prescribing costs.

Although this study cannot establish the relative contribution of primary and secondary care in the underprovision of lipid lowering treatment, the results emphasise that active primary care is particularly important if comprehensive and effective secondary prevention of CHD is to be achieved. Several categories of patients at risk of not receiving lipid lowering treatment in this study (older patients, those with relatively longstanding CHD, particularly angina, and those not receiving invasive treatment) are likely to receive most or all of their clinical care in the primary care setting and will only be identified by systematic retrospective identification and management. The low current levels of lipid lowering drug use suggest that a strongly proactive approach to implementation of secondary prevention, both prospectively and retrospectively, will be essential.29 This will need to build on the framework of CHD registers now being established under National Service Framework directives.11 Such an approach will need to be based on clear guidance, giving appropriate priority to secondary prevention in relation to primary prevention, and providing clear recommendations on treatment regimens to ensure that patients receive optimal benefit.29 However, since the cost effectiveness of statin treatment for secondary prevention of CHD is greater than that of many procedures currently performed under the NHS,27 such action would be amply justified.

ACKNOWLEDGMENTS

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**IMAGES IN CARDIOLOGY**

Intercoronary communication between the circumflex and right coronary arteries: distinct from coronary collaterals

A 49 year old man presented with atypical chest pain for five months. He had no risk factors for atherosclerosis. Exercise electrocardiography was stopped prematurely because of leg cramp. Coronary angiography was performed and revealed normal left ventricular function. Left and right coronary angiography did not show any evidence of luminal narrowing or occlusion of either coronary artery (below left). However, with the selective injection of the right coronary artery (RCA) in a left anterior oblique view, the RCA and distal and mid portion of left circumflex artery (CX) were simultaneously visualised. An intercoronary connection was also seen near the crux (below centre). The RCA and CX were then catheterised at the same time. There was no pressure damping during selective placement of the catheter tip in either coronary ostium. In the left anterior oblique view with cranial angulation, simultaneous injection of contrast material into both coronary ostia revealed interarterial continuity between the RCA and CX (below right: arrowheads show both antegrade and retrograde filling of CX lumen).

Intercoronary artery continuity or “coronary cascade” is a rare variant of the coronary circulation. Two types have been described: communication between the CX and the RCA in the posterior atrioventricular groove (as in this patient), and communication between left anterior descending and posterior descending artery in the distal interventricular groove. Compared with collaterals, intercoronary arterial connections are larger in diameter (≥1 mm), extramural, and straight. Furthermore, the structure of an intercoronary arterial connection is typical of an epicardial coronary artery, with a well defined muscular layer. Intercoronary arterial connections are thought to be congenital in origin. It is suggested that faulty embryological development allows the existing intercoronary channel to remain prominent and maintain a large calibre.

In our case selective injection of the left coronary artery did not demonstrate retrograde filling of the distal RCA. One may propose that both the force of injection and the velocity of flow in the left coronary artery would account for this discrepancy.

True prevalence of this entity is unknown but we identified only one patient among the 7066 angiograms performed at our laboratory during the last 10 years. The functional significance of this large anastomotic connection between normal coronary arteries is unclear but one may speculate that they have a potential role in protecting the myocardium should significant atherosclerosis develop in either of the parent arteries.

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