

# Aspirin use in middle-aged men with cardiovascular disease: are opportunities being missed?

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## SUMMARY

**Background.** Since the 1980s, clinical trial evidence has supported aspirin use in the secondary prevention of cardiovascular disease (CVD).

**Aim.** To explore aspirin use among British men with known CVD in a population-based study.

**Method.** Longitudinal study (British Regional Heart Study), in which subjects have been followed up for cardiovascular morbidity and mortality since 1978–1980. Aspirin use was assessed by questionnaires to study participants in November 1992 (Q92); cardiovascular diagnoses are based on general practice notifications to October 1992. A total of 5751 men aged 52–73 years (87% of survivors) completed questions on aspirin use.

**Results.** Overall, 547 men (9.5%) were taking aspirin daily, of whom 321 (59%) had documented CVD. Among men with pre-existing disease, 153 out of 345 (44%) men with myocardial infarction, 42 out of 109 (39%) with stroke, and 75 out of 247 (29%) with angina were taking aspirin daily. Among men with angina (54% versus 26%) or myocardial infarction (59% versus 42%), those who had undergone coronary artery bypass surgery (CABG) or angioplasty were more likely to be receiving aspirin. Higher rates of aspirin use were also found in those whose last major event occurred after January 1990 (47% versus 34%). There was no association between aspirin use and social class or region of residence.

**Conclusion.** Despite strong evidence of its effectiveness, many patients with established CVD were not receiving aspirin. Daily aspirin treatment was less likely in men with less recent major CVD events and in those who had not received invasive treatment.

**Keywords:** aspirin; cardiovascular disease; longitudinal study.

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© *British Journal of General Practice*, 1997, 47, 417–421.

## Introduction

CARDIOVASCULAR disease remains the most important single cause of death in British men.<sup>1</sup> During the past two decades, the efficacy of oral aspirin treatment in the secondary prevention of CVD has been increasingly recognized. The Anti-Platelet Trialists Collaboration<sup>2–4</sup> reported that daily aspirin use reduced both fatal and non-fatal cardiovascular events in patients with previous myocardial infarction, stroke, transient ischaemic attack or unstable angina, in chronic stable angina, and following arterial graft surgery. On the basis of these studies, long-term aspirin treatment has been recommended for subjects with established CVD.<sup>3</sup>

Despite the evidence supporting aspirin treatment, few studies have examined the prevalence of aspirin use in patients with established CVD. Published reports have considered only selected groups of patients; examples include patients with acute<sup>5</sup> or recent myocardial infarction,<sup>6</sup> other major cardiological events<sup>7</sup> or stroke<sup>8</sup> managed in hospital, or those with chest pain attending cardiology outpatient clinics.<sup>9</sup> However, most patients with CVD are cared for by their general practitioner (GP), and information about these patients is required to estimate the prevalence of aspirin use in the secondary prevention of CVD.

We examined reported aspirin use in late 1992 in British middle-aged men who had a history of CVD documented by their GP during the previous 12–14 years. The influence of potential contraindications to aspirin use (including peptic ulcer and warfarin use) was also examined.

## Method

The British Regional Heart Study is a national prospective study of CVD in 7735 men, aged 40–59 years at entry in 1978–80. The criteria for selecting the towns, general practices, and subjects, and the methods of data collection, including the screening questionnaire (Q1), have been reported in detail elsewhere.<sup>10–13</sup> Men were selected from the age–sex register of one group practice in each of 24 towns in England, Scotland, and Wales (78% response rate). Since entry, participants have been followed for all-cause mortality through the National Health Service Central Registers and for cardiovascular morbidity through general practice. The practice records of all study participants were ‘tagged’. In each practice, the designated study coordinator reported major cardiovascular events, and a comprehensive biennial review was undertaken to ensure that no cases were missed. The men were also sent questionnaires enquiring about their health and treatment for CVD at five years after initial screening (Q5) and in November 1992 (Q92). The latter questionnaire included an enquiry about aspirin use and was sent to all surviving men, then aged 54–73 years. CVD status is based on general practice reports of incident cardiovascular events up to the end of September 1992. No interventions have been undertaken with the study practices.

## Aspirin use

In Q92, subjects were asked whether they took aspirin on a regular or daily basis and the number of aspirin tablets taken each

**Table 1.** Use of aspirin in middle-aged British men with documented evidence of previous CVD.

Diagnosis	Number with condition	Daily aspirin use 7+ tablets per week		All regular aspirin use	
		Number (%)	95% CI	Number (%)	95% CI
Myocardial infarction	345	153 (44)	39–49	200 (58)	53–63
Angina	247	75 (30)	24–36	97 (39)	33–45
Stroke	109	42 (39)	30–48	58 (53)	43–63
Transient ischaemic attack	89	38 (43)	32–54	49 (55)	44–66
None of these conditions	4961	239 (5)	4–6	413 (8)	8–9
Men who underwent invasive treatment					
*CABG	92	48 (52)	41–63	64 (69)	59–79
*Angioplasty	13	10 (77)	46–95	10 (77)	46–95

Based on 5751 subjects with complete data on aspirin use. \*There were 790 subjects with a diagnosis of myocardial infarction, angina, stroke or transient ischaemic attack. Patients who underwent CABG or angioplasty are also recorded under the appropriate CVD category.

**Table 2.** Daily aspirin use in patients with a history of angina or myocardial infarction: influence of invasive treatment.

Diagnosis	Received CABG or angioplasty		Received neither CABG nor angioplasty		Difference in proportion taking aspirin between those who did and did not undergo CABG or angioplasty		
	Number	Number (%) taking daily aspirin	Number	Number (%) taking daily aspirin	Difference in proportions	95% CI on difference in proportions	P value
Myocardial infarction	41	24 (59)	304	129 (42)	17%	0–32%	0.05
Angina	35	19 (54)	212	56 (26)	28%	10–45%	0.0009

This table excludes men who underwent CABG in whom stroke or transient ischaemic attack was recorded as the most serious cardiovascular event.

**Table 3.** Daily aspirin use in patients with CVD by date of most recent documented episode of CVD

Diagnosis	Number with condition	Men in whom last event occurred before 1 January 1990		Men in whom last event occurred after 1 January 1990		P value (no difference between periods)
		Number of men affected	Number (%) taking daily aspirin	Number of men affected	Number (%) taking daily aspirin	
Myocardial infarction	345	216	75 (35)	129	78 (61)	< 0.0001
Stroke	109	65	26 (40)	44	16 (36)	0.7
Transient ischaemic attack	89	55	23 (42)	34	15 (44)	0.8
Angina	247	153	43 (28)	94	32 (34)	0.3
All	790	489	167 (34)	301	141 (47)	0.0004

week. They were not asked to specify the dosage of aspirin or whether it was taken on prescription.

#### Ascertainment of CVD

The presence or absence of new major cardiovascular diagnoses (myocardial infarction, stroke, transient ischaemic attack or angi-

na) and invasive treatment (CABG or angioplasty) were ascertained from general practice reports to October 1992.<sup>12,13</sup> All diagnoses of myocardial infarction were based on at least two of the following: (i) a history of severe prolonged chest pain; (ii) cardiac enzyme changes; and (iii) electrocardiographic changes. The diagnosis of stroke was based on a neurological deficit of

presumed vascular origin lasting over 24 hours; a diagnosis of transient ischaemic attack required a similar deficit of no more than 24 hours' duration. The diagnosis of angina required a history of effort or stress-related chest pain in the preceding four weeks.

#### *Ascertainment of other conditions*

Information on arthritis and peptic ulcer was based on participants' recall of diagnosis by a doctor recorded at Q92. Respondents were asked to record all current medications; warfarin and other oral anticoagulants were extracted from the responses.

#### *Definition of social class and region of residence*

Social class was defined by the longest held occupation at Q1. Region of residence was classified as north or south, depending on whether the town of residence at Q1 was north or south of a line joining Bristol and the Wash.

#### *Statistical methods*

Prevalences of aspirin use have been expressed as percentages, with 95% confidence intervals, where appropriate, using the Confidence Interval Analysis programme.<sup>14</sup> Frequency differences have been analysed using chi-squared tests. The influence of social class (manual/non-manual), region of residence at screening (north/south), and age at which the last major event occurred (under or over 60 years) on the prevalence of aspirin use were examined simultaneously using multiple logistic regression analysis.

### **Results**

Of the 7735 men originally examined in 1978–80, 37 had emigrated or were lost to follow up and 1116 had died by October 1992. Questionnaires (Q92) were therefore mailed to 6582 men. The overall response rate was 91%, and 5751 men (87%) completed the questions on aspirin use. Overall, 547 men (9.5%) reported taking aspirin at least daily; an additional 270 men (4.7%) reported regular but less frequent aspirin use. Among those taking aspirin daily, 321 (59%) had evidence of previous CVD.

#### *Aspirin use in patients with specific forms of CVD*

The proportions of patients in each category who reported daily aspirin use are shown in Table 1. Myocardial infarction, angina, stroke, and transient ischaemic attack have been defined so that patients with multiple diagnoses appear only once, in the highest category in Table 1. Of the 790 subjects with these four diagnoses, overall, 39% (95% CI: 36–42%) of subjects were taking daily aspirin; the proportion was lowest for those with angina. However, of those with a history of CABG or angioplasty (defined separately from the above disease categories), over half reported taking aspirin daily. When aspirin use on a less than daily basis was included, this increased the proportions of subjects taking aspirin in the four main diagnoses by about a quarter (23.8%), an extra 96 subjects overall.

Patterns of daily aspirin use in subjects with angina and myocardial infarction were examined separately in those with and without CABG or angioplasty. The prevalence of daily aspirin use increased from 42% to 59% in men with myocardial infarction and from 26% to 54% in men with angina (Table 2).

#### *Influence of other conditions on daily aspirin use*

The influence of other circumstances that might contraindicate

aspirin use (history of peptic ulcer, use of warfarin or other oral anticoagulant) or increase it (such as the use of aspirin for pain relief by those who reported a history of arthritis) was examined. There were 673 subjects with a history of peptic ulcer, of whom 60 (9%) were also taking aspirin daily. The exclusion of all subjects with a history of peptic ulcer made little difference to the prevalence of daily aspirin use in the four main disease categories (41% with peptic ulcer cases excluded versus 39% when peptic ulcer cases were included). Similarly, the exclusion of 53 men taking oral anticoagulants, of whom five (9%) were also taking aspirin, had little effect on aspirin use in the four main disease categories (41% with exclusion versus 39% without). In 1486 subjects with recall of arthritis, 160 (11%) were receiving regular aspirin. Excluding men with a history of arthritis did not affect the proportions of subjects in the four CVD categories receiving aspirin daily (40% versus 39%).

#### *Influence of social class, residence at time of screening, age and date of most recent cardiovascular event on daily aspirin use*

The prevalence of aspirin use was similar in men in manual (39%) and non-manual (39%) occupations, and for men screened in the south (38%) and in the north (39%), but was greater among those aged over 60 years at the time of their event (43%) compared with those aged under 60 years (35%) ( $P = 0.04$ ). The influence of the date of the most recent major cardiovascular event recorded in the general practice records on the prevalence of daily aspirin use was examined in men with myocardial infarction, stroke, transient ischaemic attack, and angina (Table 3). Men whose most recent major cardiovascular event had occurred on or after 1 January 1990 were more likely to be receiving aspirin than those in whom it had occurred before that date. The change was marked for men with a diagnosis of myocardial infarction but not for those with transient ischaemic attack, stroke or angina.

In those whose most recent event occurred after January 1990, an increase in aspirin use was observed both in those aged under 60 years and in those aged over 60 years at the time of the event. The increase in aspirin use was broadly similar in both social class groups (non-manual from 33% to 50%, manual from 35% to 45%) ( $P = 0.3$ ). The increase in aspirin use in those whose last event occurred after 1990 appeared to be slightly more marked in the south (from 29% to 52%) than in the north (from 36% to 45%), but this increase was not statistically significant ( $P = 0.10$ ). Among men who underwent CABG and angioplasty, however, aspirin use was similar (54% versus 59%) whether the procedure was undertaken before or after 1990.

### **Discussion**

In this study of middle-aged men, less than half of those with a previous GP diagnosis of myocardial infarction, stroke, transient ischaemic attack or angina reported daily aspirin use. The inclusion of patients taking aspirin less than daily had little effect on the results. Daily aspirin was used more widely in patients with a history of coronary artery surgery or coronary angioplasty and in patients whose last major cardiovascular event was more recent. Levels of aspirin use in those who underwent CABG or angioplasty were similar, whether the intervention was undertaken before or after January 1990. The prevalence of aspirin use in subjects with established CVD was unaffected by excluding patients with peptic ulcer or those taking warfarin.

The low rates of daily aspirin use reported here are unlikely to be an artefact of the study design. Previous studies indicate that patient recall of daily aspirin treatment is reliable and that, when

doctor initiated, over 80% of patients comply with treatment.<sup>15,16</sup> Our estimates of the prevalence of aspirin use are not deflated by the inclusion of men with previously undiagnosed CVD, those in whom there has been no opportunity to initiate aspirin therapy. All cases of CVD reported here were known to the GP before the survey of aspirin use.

In patients with a previous myocardial infarction, the prevalence of aspirin use reported here is lower than the 80% reported in patients discharged following myocardial infarction in 1991,<sup>6</sup> or the 76% reported in patients attending cardiology outpatient clinics in 1994.<sup>9</sup> However, the ranking of prevalence of aspirin use in the outpatient study, from the lowest (patients with suspected angina) to the highest category (patients with a history of coronary revascularization)<sup>9</sup> is similar, both to that observed in a random sample of patients following major cardiac events<sup>7</sup> and to that observed here. Our reported prevalence of aspirin use after stroke is also lower than the prescription rate reported at discharge after stroke (50%) in a single hospital study conducted in 1989–90.<sup>8</sup>

This study examines aspirin use beyond the immediate discharge period, upon which hospital case series concentrate. Aspirin taken only in the acute setting and then discontinued; for example, immediately following myocardial infarction, would not be included in this study of patients with established CVD. It is also difficult to establish the extent to which the differences in the prevalence of aspirin use between our study and those of earlier investigators reflect differences in the initiation of aspirin therapy rather than its duration. We have no direct information on the duration of aspirin therapy, on discontinuation of treatment either by the patient or his doctor, or on the failure of the hospital to communicate the need for treatment.<sup>17</sup> Whitford and Southern<sup>17</sup> found that the proportion of patients receiving aspirin declined from 95% in hospital to 88% one year later. However, they were unable to identify whether this decline reflected the use of aspirin in the acute situation only, the failure of the hospital to communicate the need for aspirin, the discontinuation of the treatment by the patient or his GP, or a combination of these factors. Deeks *et al*<sup>18</sup> consider that the primary responsibility of the GP is to ensure that patients with established CVD continue to take aspirin therapy; initiation should only be necessary for those with newly confirmed diagnoses and for those in whom it has been overlooked during an acute episode. However, GPs may be unlikely to commence medication that the specialist has not recommended,<sup>17</sup> particularly when the specialist has initiated treatment. The strong case for long-term aspirin treatment in patients with established CVD<sup>3,19</sup> means that strategies to increase both the initiation and the continuation of aspirin treatment must be pursued.

Daily aspirin use may have become more widespread since this survey was conducted. Our results suggest that the prevalence of aspirin use associated with more recent events may have increased, particularly in patients with myocardial infarction. However, the present study has identified groups at risk of not receiving aspirin treatment. This risk of exclusion from potentially beneficial treatment remains important, particularly for patients who have not undergone coronary revascularization, patients with chronic stable angina, and those whose most recent cardiovascular episode occurred before 1990. These findings have implications for the steps necessary to improve this situation.

While it is important that patients with new episodes of CVD receive aspirin, our results suggest that this approach may be insufficient. Specific efforts may be necessary to ensure that patients with established CVD are offered and maintained on aspirin treatment. Since many of those at risk may not be in con-

tact with hospital services, these efforts should be focused in primary care. First, efforts to identify patients with established CVD and to monitor long-term compliance will be assisted by accurate disease registers. Secondly, compliance may be improved by a greater involvement of patients in discussions about symptoms, treatment options and the benefits expected, prognosis, and the specific benefits of aspirin treatment. These approaches would be consistent with recent studies of CVD prevention in primary care, which emphasize the cost-effectiveness of targeting prevention towards subjects with pre-existing CVD.<sup>20</sup>

The results of the Anti-Platelet Trialists Collaboration overviews<sup>2-4</sup> suggest that the dividends of such an approach could be substantial; the high absolute risk of future events in those with established CVD means that the number who require treatment with aspirin to prevent one event is low (30 patients treated for two years). Using the absolute benefits reported in the Anti-Platelet Trialists Collaboration overviews,<sup>2-4</sup> one can estimate that by increasing the prevalence of aspirin use from the 39% observed in BRHS participants to a figure of 80% over a two-year period,<sup>3</sup> approximately 7900 major cardiovascular events and 3400 cardiovascular deaths in men aged 55–74 years in England and Wales could be postponed.

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#### **Acknowledgements**

The British Regional Heart Study is a British Heart Foundation Research Group and also receives support from the Department of Health and the Stroke Association.

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