Randomised trial of two approaches to screening for atrial fibrillation in UK general practice

Stephen Morgan and David Mant

SUMMARY

Background: *Atrial fibrillation is a common and treatable cause of stroke that often remains unrecognised. Screening has been suggested but there is very little evidence concerning the uptake of screening in the elderly population at risk, nor of the optimal method of screening in a general practice setting.*

Aim: *To compare the uptake and effectiveness of two methods of screening for atrial fibrillation in general practice — systematic nurse-led screening and prompted opportunistic case finding.*

Design of study: *Randomised controlled trial.*

Setting: *Patients aged 65 to 100 years (n = 3001) from four general practices within the MRC general practice framework.*

Method: *Each of the four study practices were selected from one quartile, after ranking all framework practices according to the small area standardised mortality ratio of the geographical area served. Patients were randomised either to nurse-led screening or to prompted opportunistic case finding. The proportion of patients assessed and the proportion found to have atrial fibrillation were compared. The sensitivity and specificity of clinical assessment of pulse are also reported.*

Results: *Substantially more patients had their pulse assessed through systematic screening by invitation (1099/1499 [73%]) than through opportunistic case finding (439/1502 [29%], difference = 44%, 95% confidence interval [CI] = 41% to 47%). Atrial fibrillation was detected in 67 (4.5%) and 19 (1.3%) patients respectively (difference = 3.2%, 95% CI = 2.0 to 4.4). Invitation to nurse-led screening achieved significantly higher assessment rates than case finding in all practices; however, the proportion of patients assessed in the case-finding arm varied markedly between practices (range = 8% to 52%). The number needed to screen to identify one additional patient with atrial fibrillation was 31 (95% CI = 23 to 50). The proportion of screened patients with atrial fibrillation receiving anticoagulation treatment was 25%, although in the majority (53/65 [82%]) atrial fibrillation had been previously recorded somewhere on their medical record. If the nurse used any irregularity of the pulse as the screening criterion, the sensitivity of screening was 91% and the specificity was 74%; sensitivity fell to 54% but specificity increased to 98% if the criterion used was continuous irregularity.*

Conclusions: *Nurse-led screening for atrial fibrillation in UK general practice is both feasible and effective and will identify a substantial number of patients who could benefit from antithrombotic therapy. Although the majority of patients detected at first screening could be identified by careful scrutiny of medical records, review of record summaries was insufficient in the practices involved in this study and screening may be a more cost-effective option.*

Keywords: *atrial fibrillation; screening; case finding; randomised controlled trial.*

S Morgan, MRCGP, Wellcome Research Training Fellow, Department of Primary Medical Care, University of Southampton, Aldermoor Health Centre, Southampton. D Mant, MA, FRCP, FRCGP, FMed Sci professor of general practice, Department of Primary Health Care, University of Oxford.

Address for correspondence

Stephen Morgan, Westbourne Medical Centre, Milburn Road, Bournemouth BH4 9HJ.

Introduction

ATRIAL fibrillation is the most common cardiac arrhythmia and increases an individual's risk of stroke fivefold.[1] The stroke risk attributable to atrial fibrillation increases with age from 9.9% at age 70 to 79 years, to 23.5% at 80 to 89 years. The strong evidence for the effectiveness of warfarin in stroke prevention[2] and the minimal impact of anticoagulation on patients' quality of life[3] has led to calls for screening for atrial fibrillation in primary care,[4] as the necessary criteria for screening may well be met.[5,6] It appears that a substantial proportion of patients who could benefit from this established treatment still do not receive it, despite the emerging consensus on treatment criteria.[7] However, the most suitable test needs to be identified and its acceptability and resource implications quantified.

The majority of United Kingdom general practices have the facility to use either clinical examination of the pulse or electrocardiogram (ECG) recordings for screening. Such screening could be undertaken systematically, or opportunistically when patients are seen for other reasons (case finding). Previous work on atrial fibrillation screening has used a single specialised nurse observer[8] or has made no comparison of different approaches to screening.[9,10] However, prior to commencing a screening programme, further evidence of the effectiveness of the possible strategies is needed. This study sought to determine whether more patients with atrial fibrillation were identified successfully using systematic nurse-led screening than prompted opportunistic case finding. It also examined the test characteristics of clinical assessment of the pulse compared with a standard limb lead ECG rhythm strip.

Method

Study population

The study was based in four general practices drawn from the MRC general practice framework, each selected from one quartile after ranking all framework practices according to the small area standardised mortality ratio of the geographical area served.[11] The aggregate patient list size in the study age range (65 to 100 years) was 7493. The practices chose not to exclude any patient prior to randomisation. Approximately 750 patients from each practice list were randomly selected to give a total study sample of 3001. These patients were randomised to receive either an invitation to nurse-led systematic screening, or to opportunistic screening prompted by a reminder flag placed in their medical records (Figure 1).

The relevant local research ethics committees gave their approval to the study. Subjects attending the study nurse

HOW THIS FITS IN

What do we know?

Atrial fibrillation is a relatively common and inadequately treated condition in elderly people. Treatment by anticoagulation is effective in preventing stroke.

What does this paper add?

This paper clarifies the effectiveness of various options for the identification of patients with atrial fibrillation in general practice. It reports the likely yield from medical record review, opportunistic case finding and systematic screening. It also reports the accuracy of screening using clinical examination of the pulse by practice nurses.
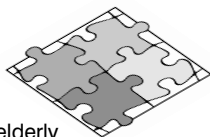
were asked to give written consent for pulse assessment and inclusion of their pulse record in the study; patient consent was not sought for randomisation nor at the point of referral of flagged patients to the study nurse.

Study design

Patients randomised to systematic screening were sent by post an explanatory leaflet and invitation to attend a specific appointment at their own general practice to see a nurse, who had received approximately two hours training in the clinical assessment of the pulse rhythm. Non-attenders were telephoned by the nurse where possible and a second invitation sent. Those unable to attend their practice were offered screening at home. Patients in the opportunistic screening arm had a large brightly coloured reminder flag inserted at the front of the continuation card of their paper medical records. In addition, if the practice did not routinely use these during consultations, a flashing reminder prompt was added to the initial summary screen of their computer record.

Nurse screening

At the screening appointment the nurse examined the radial pulse for a minimum of 20 seconds, to determine its regularity but not its rate. The rhythm was rated by the nurse as either 'regular', or 'occasional ectopics' beats, or 'frequent ectopics', or 'continuously irregular'. These categories were used to define different thresholds for defining the pulse as abnormal, namely 'continuous irregularity', 'continuous or frequent irregularity' or 'any irregularity'. Immediately after the pulse assessment was recorded a lead II rhythm strip was obtained from the patient and sent to the project co-ordinator for quality control purposes. The ECG's rhythm strips were read centrally by one of the authors (SM) to validate the clinical assessment and were not used by the nurses to assist their assessment of the cardiac rhythm.

Opportunistic screening

With the prior agreement of the practices the reminder flag was placed in the notes for a six-month period. Any doctor or nurse who made an assessment of the pulse during the routine care of the patient was asked to indicate on the flag
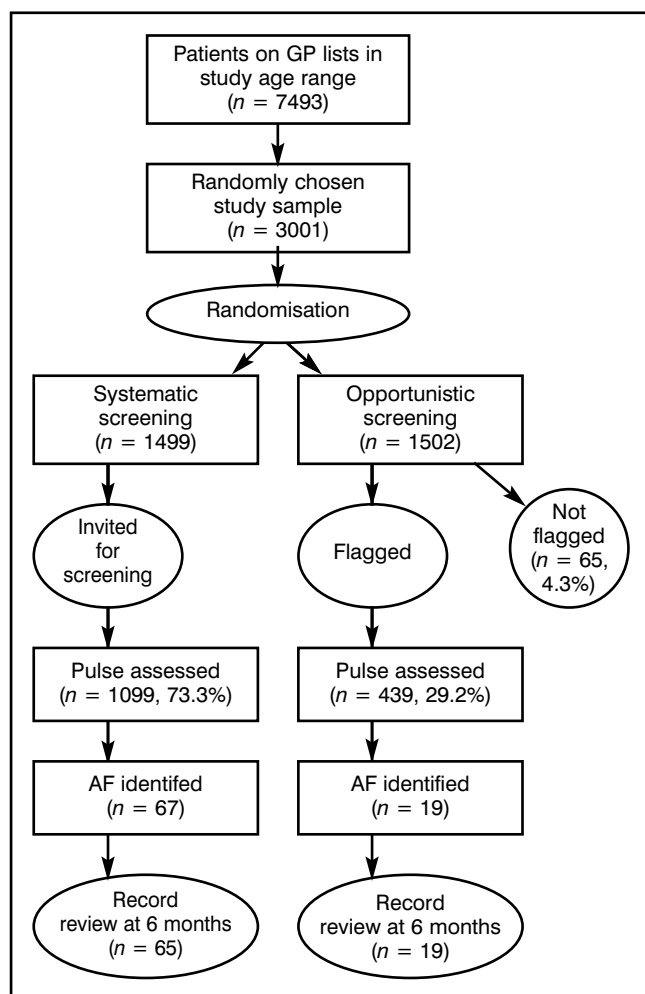
Figure 1. Flow chart of subjects' progress through the trial.

whether the pulse was suspicious of atrial fibrillation and whether they wished to investigate this further with an ECG recording, depending on previous investigations done and the clinical context. If a confirmatory ECG was requested, the diagnosis of atrial fibrillation was made as in the screening arm. If a confirmatory ECG was not requested, a patient in the opportunistic arm was included in the comparison of detection rates as a case of atrial fibrillation on the basis of the clinical diagnosis alone. Space for free text comments was also provided on the flag. When a patient had been assessed the flag was removed from the record.

Record review

The general practice medical records of the patients identified in either arm of the trial were reviewed by a single medically trained observer (SM) approximately six months after the end of the intervention for details of recorded diagnoses, investigations, and treatment, both before and after intervention. The time taken to review a patient's record was approximately 20 minutes. In two of the study practices a computer search of patients' records was undertaken to identify those individuals prescribed digoxin or any anti-arrhythmic drug from section 2.3 of the British National

Formulary[12] by their general practitioner in the six months preceding the start of the study.

Sample size

The sample size was chosen to detect a 2.5% difference between the groups in the proportion of patients with atrial fibrillation identified, with 80% power at the 5% level of significance. This assumed an atrial fibrillation prevalence of 3.4% in the flag arm patients, based on the computer records of a well organised practice,[13] and non-attendance of approximately 15% in the screened arm patients. A difference smaller than 2.5% was deemed not to be clinically significant.

Randomisation of the practice lists was done at individual patient level, using the random sample command of STATA statistical software.[14]

Data analysis

Data were also analysed at patient level. Analysis was performed on an intention-to-screen basis, including all patients initially included in the screened and opportunistic case-finding arms. All confidence intervals are at the 95% level.

Results

Uptake and yield of screening

The age and sex characteristics of people allocated to the systematic screening and flag-prompted arms of the study were very similar (Table 1). The mean age of those whose pulse was assessed (75.2 years) was also very similar to those not assessed (75.8 years) in the flag-prompted group although in the screened group those assessed were slightly younger (mean age = 74.3 versus 77.9 years, $P<0.001$). Assessment rates were 1099 (73.3%) in the systematic nurse-led screening arm and 439 (29.2%) in the opportunistic arm (difference = 44.1%, 95% CI = 40.9% to 47.3%). In excess of two-thirds of patients attended for systematic screening in all centres but the proportion of those assessed in the opportunistic screening arm was more variable (Table 2). The yield of patients found to have atrial fibrillation was 67 (4.5%) in the systematically screened arm and 19 (1.3%) in the case-finding arm (odds ratio = 3.7, 95% CI = 2.2 to 6.1). The number needed to screen to detect one additional patient with atrial fibrillation was 31 (95% CI = 23 to 50). Using a cost estimate of £6 per consultation with a practice nurse this would correspond to a cost per atrial fibrillation case detected of £186 (95% CI = £138 to £300).[15] The yield of cases with no prior evidence of atrial fibrillation in their medical records was substantially lower, with 12 (0.8%) 'new' cases in the screened arm and seven (0.5%) in the opportunistic case-finding arm.

Pulse assessment findings

Among those systematically screened, the nurses achieved high sensitivity (91%) but modest specificity (74%) using the threshold 'any irregularity' for defining a pulse as abnormal when compared with the gold standard of the concurrent ECG recording. High specificity (98.0%) but low sensitivity (54%) was achieved using the threshold 'continuously irregular' (Table 3).

Table 1. Age–sex profile of those allocated to each randomisation arm and of those within each arm in whom pulse rhythm was assessed.

	Prompted opportunistic case finding	Systematic screening
Randomised (*n*)	1502	1499
Mean age (years)	75.6	75.3
65–74 years (%)	51.5	53.4
75–84 years (%)	35.8	35.1
85+ years (%)	12.7	11.5
Female (%)	58.9	58.6
Rhythm assessed (*n*)	439	1099
Mean age (years)	75.2	74.3
Female (%)	59.5	56.5

*Table 2. Comparison of uptake and yield of pulse assessment between prompted opportunistic case finding (n = 1502) and nurse-led systematic screening by invitation (*n = 1499).*

	Prompted opportunistic case finding *n* (%)	Systematic screening *n* (%)	Percentage difference in proportion (95% CI)	Significance
Rhythm assessed				
Overall	439 (29.2)	1099 (73.3)	44.1 (40.9–47.3)	χ^2 = 584, 1 df, $P<0.001$
Practice 1 (*n* = 751)	196 (52.1)	289 (77.1)	24.9 (18.3–31.5)	χ^2 =51, 1 df, $P<0.001$
Practice 2 (*n* = 750)	37 (9.9)	278 (74.1)	64.3 (58.9–69.6)	χ^2 = 318, 1 df, $P<0.001$
Practice 3 (*n* = 750)	30 (8.0)	251 (66.9)	58.9 (53.4–64.4)	χ^2 = 278, 1 df, $P<0.001$
Practice 4 (n = 750)	176 (46.8)	281 (75.1)	28.3 (21.6–35.0)	χ^2 = 63, 1 df, $P<0.001$
Atrial fibrillation identified				
Overall	19 (1.26)	67 (4.47)	3.2 (2.0–4.4)	χ^2 = 27.7, 1 df, $P<0.001$
Practice 1 (*n* = 751)	9 (2.4)	20 (5.3)	2.9 (0.2–5.7)	P = 0.039[a]
Practice 2 (*n* = 750)	1 (0.3)	18 (4.8)	4.5 (2.3–6.8)	$P<0.001$[a]
Practice 3 (*n* = 750)	4 (1.1)	13 (3.5)	2.4 (0.3–4.5)	P = 0.047[a]
Practice 4 (*n* = 750)	5 (1.3)	16 (4.28)	3.0 (0.06–5.3)	P = 0.015[a]

[a]Fisher's exact test.

*Table 3. The test characteristics of clinical pulse assessment by the nurses in those systematically screened using different thresholds to define an abnormal pulse rhythm. Values are percentages (*n = 1099) (95% confidence intervals).*

	Threshold of nurse pulse assessment					
	n	Percentage with any irregularity (95% CI)	*n*	Percentage with frequent or continuous irregularity (95% CI)	*n*	Percentage with continuous irregularity (95% CI)
Sensitivity	61/67	91 (82–97)	48/67	72 (59–82)	36/67	54 (41–66)
Specificity	767/1032	74 (72–77)	972/1032	94 (93–96)	1009/1032	98 (97–99)
Positive predictive value	61/326	19 (15–23)	48/108	44 (35–54)	36/59	61 (47–73)
Negative predictive value	767/773	99 (98–100)	972/991	98 (97–99)	1009/1040	97 (96–98)
Positive likelihood ratio	–	3.6 (3.1–4.0)	–	12 (9.2–16)	–	24 (15–38)
Negative likelihood ratio	–	0.12 (0.06–0.26)	–	0.30 (0.28–0.32)	–	0.47 (0.36–0.62)

Characteristics of cases

Among the cases identified, the proportion reporting awareness of having previously been told about a pulse rhythm abnormality was high, reaching 49% in the screened arm (Table 4). A prior diagnosis of atrial fibrillation was found in the notes of 53/65 (82%) of the screen-detected patients but only 10/17 (59%) of the opportunistically-detected patients (χ^2 test, P = 0.048). The proportions who had the diagnosis recorded in their notes summary was much lower, 28/65 (43%) and 4/17(26%) respectively.

The computer search of digoxin prescribing data identified the patients found to have atrial fibrillation in the screened arm with a sensitivity of 47.4% (18/38) and a specificity of 52.9% (18/34). The inclusion of all anti-arrhythmic drugs only detected two more of the patients.

The suitability of the patients for treatment was generally high, with 70% (47/67) of patients who were identified as having atrial fibrillation from systematic screening having an additional risk factor for stroke. Twenty-five per cent had a contraindication to such treatment but, for most of these, sub-optimally controlled hypertension and current non-steroidal anti-inflammatory drug use were the only contraindications, leaving only 5% (3/64) who had an irreversible contraindication to antithrombotic therapy.

Discussion

A high rate of uptake of the invitation to atrial fibrillation screening in this study (73.3%) was found from a 'raw' sample of patients registered with practices, with no attempt to remove patients who had moved away, changed doctor or died without their practice being informed. The accuracy of

Table 4. Characteristics of patients identified by systematic screening as having atrial fibrillation.

Outcome measure	n/Total	Percentage	95% CI
Identification and treatment before study			
History of AF[a]	33/67	49	37–62
AF in GP records	53/65	82	70–90
AF on record summary	28/65	43	31–56
Anticoagulation[a]	17/67	25	16–37
Aspirin[a]	26/67	39	27–51
Risk factors and contraindications to treatment			
CVA/TIA	14/67	21	12–33
Hypertension[b]	38/67	57	44–69
Diabetes	6/67	12	5–22
At least one additional risk factor for stroke[c]	47/67	70	58–81
Any contraindication[d]	16/64	25	15–37
Any irreversible contraindication[e]	3/64	5	1–13

[a]Self reported by subject to researcher. [b]History of hypertension or mean of most recent three blood pressure readings >160mmHg systolic or 90mmHg diastolic, based on self report or record review. [c]History of hypertension, stroke or TIA or diabetes based on self report or record review. [d]History of gastrointestinal or genitourinary bleeding in the preceding six months, or injurious fall in last year, or excess alcohol consumption (>28 units per week for men and 21 units per week for women), uncontrolled hypertension or use of non-steroidal anti inflammatory drugs (NSAIDs), or inability to comply with medication. [e]As above, except excluding NSAID use and uncontrolled hypertension.

a nurse assessment of the pulse demonstrates that a characteristic pulse of atrial fibrillation is identified in only half of atrial fibrillation sufferers in this age group; however, 90% have a pulse that can be identified as in some way irregular. The yield of cases of atrial fibrillation identified by systematic screening was almost three times that identified by the opportunistic case-finding method used in this study, and double the number identified from a computerised record search for patients prescribed digoxin. Although most of the cases identified had some record of atrial fibrillation in the past; this was only apparent on exhaustive record searching.

Strengths and shortcomings

This was a pragmatic trial using widely generalisable interventions in representative UK general practices. While the systematic screening had a similar effect in all practices, the impact of the prompt flag on opportunistic case-finding behaviour varied between practitioners. This was despite efforts to standardise the guidance given. Such variability is likely to reflect differing degrees of enthusiasm and other constraints that would inevitably occur in any similar approach to case finding. The level of identification in the case-finding arm of this study is likely to be higher than that which would be achieved in unprompted normal care, although some patients in the opportunistic arm may not have consulted during the six-month study period (although consultation rates in this age group are high — mean = six consultations/year — some patients seldom consult; approximately 25% of those aged 65 years and over do not consult at all in a one-year period).[16]

In the case-finding arm, confirmation of atrial fibrillation by ECG was at the discretion of the GP, depending on the clinical context. In the few cases where an ECG was not done, the GP's clinical diagnosis was accepted. This may have slightly increased the apparent effectiveness of opportunistic case finding.

Although this study did not use the clinical endpoints of stroke and death, the evidence for the effectiveness of preventive antithrombotic therapy in the majority of patients with atrial fibrillation is strong and such treatment is highly cost effective[17]. No formal economic evaluation was included in this study and this would be required before screening could be recommended more widely. However, our cost estimate based on the practice nurse time suggests that the cost of screening could be relatively small.

Comparison with other studies

The uptake of screening was in line with the 74% attendance for a prevalence study from Northumberland[8] and an uncontrolled study of ECG screening in a single Sheffield practice, where recruitment of 85% was obtained with the assistance of GP visits to non-responders.[9] Although response to any invitation varies with the presentation of potential benefit,[18] it suggests that this older group of adults are receptive to interventions to prevent stroke. The accuracy of clinical diagnosis in this study was lower than was obtained by the more experienced single observer used in the Northumberland study. The level of accuracy in this study is likely better to reflect what would be achieved in a screening programme using trained practice nurses.

High level of prior diagnosis.

Most patients identified by screening had, at some stage in the past, had a diagnosis of atrial fibrillation made. This suggests that record review, rather than screening, could have promise as a method for identifying cases. However, the time-consuming nature of the full record review and the far poorer recording on the computerised record summary implies that, at present, such an approach might fail to identify a substantial proportion of patients. However, computerised searching of primary care records based on prescribing and diagnosis may be an effective first step for some practices.

In the future, more systematic recording of the diagnosis of atrial fibrillation in a form that could be identified by a computerised search would reduce the need for population screening. If the task of systematic screening was to detect

only cases in whom no prior diagnosis of fibrillation had ever been recorded in the medical record, the number needed to screen to detect an additional case would increase to 91 and the minimum cost estimate per case identified based on practice nurse time would increase to £550. However, at present it seems likely that a single round of screening could be expected to identify a substantial pool of untreated older patients who would benefit from antithrombotic therapy in many practices, and would achieve much more complete case ascertainment than record review or case finding using reminder prompts.

Service implications

Screening and effective treatment could substantially reduce the burden of stroke, particularly in areas where high stroke morbidity and low level of atrial fibrillation identification and anticoagulation use co-exist. However, it is misleading to assume that clinical screening could be introduced with little extra resource, even if the pulse assessments were conducted alongside other screening procedures that are already in place, such as influenza vaccination for those over 65 years old. The low specificity of nurse assessment means that ECG confirmation of diagnosis is both essential and a substantial component of screening. Moreover, anticoagulation and its ongoing monitoring also have significant workload implications and significant resources would be required for primary care to introduce such a programme.[19,20] The cost-effectiveness of screening in an NHS setting therefore needs careful assessment and needs to take account of the reduced yield of further (non-prevalent) screening rounds, the completeness of morbidity recording in medical records, and the potential for emerging new technologies to simplify and improve the diagnostic accuracy.

References

1. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: The Framingham study. *Stroke* 1991; **22:** 983-988.
2. Atrial Fibrillation Investigators. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. *Arch Intern Med* 1994; **154:** 1449-1457.
3. Lancaster TR, Singer DE, Sheehan MA, *et al*. The impact of long-term warfarin therapy on quality of life. *Arch Intern Med* 1991; **151:** 1944-1949.
4. Ramsay LE. Warfarin in chronic atrial fibrillation. *Lancet* 1993; **341:** 1376-1377.
5. Wilson JMG, Junger G. *Principles and practice of screening for disease*. Geneva: WHO, 1968.
6. National Screening Committee. *First report of the National Screening Committee. 1*. Milton Keynes: Department of Health, 1998.
7. Royal College of Physicians of Edinburgh. Consensus conference on medical management of stroke: consensus statement. *Proc R Coll Physicians Edinb*, 1999.
8. Sudlow M, Rodgers H, Kenny RA, Thomson R. Identification of patients with atrial fibrillation in general practice: a study of screening methods. *BMJ* 1998; **317:** 327-328.
9. Wheeldon NM, Tayler DI, Anagnostou E, *et al*. Screening for atrial fibrillation in primary care. *Heart* 1998; **79:** 50-55.
10. Somerville S, Somerville J, Croft P, Lewis M. Atrial fibrillation: a comparison of methods to identify cases in general practice. *Br J Gen Pract* 2000; **50:** 727-729.
11. Bajekal, M. Small area standardised mortality ratios. 1996. [Personal communication.]
12. *British National Formulary*. London: British Medical Association & Royal Pharmaceutical Society of Great Britain, 1997.
13. Lip GY, Beevers DG. ABC of atrial fibrillation. History, epidemiology, and importance of atrial fibrillation. *BMJ* 1995; **311:** 1361-1363.
14. Statacorp. *Stata Statistical Software: Release 6.0*. College Station, TX: Stata Corporation, 1999.
15. Netten A, Dennett J. *Unit costs of health and social care. 5*. Canterbury: Personal Social Services Research Unit, 1997.
16. Fleming DM. Consultation rates in English general practice. *J R Coll Gen Pract* 1989; **39:** 68-72.
17. Gage BF, Cardinalli AB, Albers GW, Owens DK. Cost-effectiveness of warfarin and aspirin for prophylaxis of stroke in patients with non-valvular atrial fibrillation. *JAMA* 1995; **274:** 1839-1845.
18. Sarfati D, Howden-Chapman P, Woodward A, Salmond C. Does the frame affect the picture? A study into how attitudes to screening for cancer are affected by the way benefits are expressed. *J Med Screen* 1998; **5:** 137-140.
19. Rodgers H, Sudlow M, Dobson R, *et al*. Warfarin anticoagulation in primary care: a regional survey of present practice and clinician's views. *Br J Gen Pract* 1997; **47:** 309-310.
20. Sudlow CM, Rodgers H, Kenny RA, Thomson RG. Service provision and use of anticoagulants in atrial fibrillation. *BMJ* 1995; **311:** 558-560.