CORONARY ARTERY DISEASE

How effective are rapid access chest pain clinics? Prognosis of incident angina and non-cardiac chest pain in 8762 consecutive patients

N Sekhri, G S Feder, C Junghans, H Hemingway, A D Timmis

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See end of article for authors' affiliations

Correspondence to: A D Timmis, London Chest Hospital, Barts and The London NHS Trust, Bonner Road, London E2 9JX, UK; timmis@lch.demon.co.uk

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Objective: To determine whether rapid access chest pain clinics are clinically effective by comparison of coronary event rates in patients diagnosed with angina with rates in patients diagnosed with non-cardiac chest pain and the general population.

Design: Multicentre cohort study of consecutive patients with chest pain attending the rapid access chest pain clinics (RACPCs) of six hospitals in England.

Participants: 8762 patients diagnosed with either non-cardiac chest pain (n = 6396) or incident angina without prior myocardial infarction (n = 2366) at first cardiological assessment, followed up for a median of 2.57 (interquartile range 1.96–4.15) years.

Main outcome measures: Primary end point—death due to coronary heart disease (International Classification of Diseases (ICD)10 I20–I25) or acute coronary syndrome (non-fatal myocardial infarction (ICD10 I21–I23), hospital admission with unstable angina (I24.0, I24.8, I24.9)). Secondary end points—all-cause mortality (ICD I20), cardiovascular death (ICD10 I00–I99), or non-fatal myocardial infarction or non-fatal stroke (I60–I69).

Results: The cumulative probability of the primary end point in patients diagnosed with angina was 16.52% (95% confidence interval (CI) 14.88% to 18.32%) after 3 years compared with 2.73% (95% CI 2.29% to 3.25%) in patients with non-cardiac chest pain. Coronary standardised mortality ratios for men and women with angina aged <65 years were 3.52 (95% CI 1.98 to 5.07) and 4.39 (95% CI 1.14 to 7.64). Of the 599 patients who had the primary end point, 194 (32.4%) had been diagnosed with non-cardiac chest pain. These patients were younger, less likely to have typical symptoms, more likely to be south Asian and more likely to have a normal resting electrocardiogram than patients with angina who had the primary end point.

Conclusion: RACPCs are successful in identifying patients with incident angina who are at high coronary risk, but there is a need to reduce misdiagnosis and improve outcomes in patients diagnosed with non-cardiac chest pain who accounted for nearly one third of cardiac events during follow-up.

Angina is the most common initial manifestation of coronary heart disease[1–3] and accounts for an estimated 1% of annual health expenditure in the UK.[4] Rapid access chest pain clinics (RACPCs) are now widely established on the basis of the assumption that one-stop cardiological assessment can successfully identify patients with angina who are considered to be at high risk of adverse cardiovascular outcomes. It is implicit in this that patients diagnosed with non-cardiac chest pain can be safely excluded from further cardiac investigation and treatment. However, the validity of this assumption is unknown because the prognosis of incident angina and non-cardiac chest pain in patients with previously undiagnosed symptoms has not been defined. Previous studies have been limited by small size and short periods of follow-up.[5–8] We have studied the prognosis of a large cohort of patients referred from primary care with chest pain, none of whom had had previous cardiological assessment. Our primary objective was to assess the clinical effectiveness of RACPCs by determining the extent to which diagnoses of angina and non-cardiac chest pain validate the prognostic assumptions that have led to their widespread introduction in the UK.

METHODS

Patients

Consecutive patients attended six RACPCs in which cardiological consultation was provided within 2 weeks of referral from primary care according to the imperatives of the UK National Service Framework for coronary heart disease.[9] The purpose of the clinics was to identify patients with angina to initiate appropriate treatment, including secondary prevention with aspirin and β-blockers, and to carry out cholesterol measurement with a view to starting statin treatment, according to contemporary guidelines.[10] Data on 11082 patients were electronically recorded from 2 January 1996 to 31 December 2002 using identical databases, details of which have been reported previously.[11] We excluded re-attendances during the study period (n = 448), patients without chest pain (n = 291), patients diagnosed with acute coronary syndromes on the day of visit (n = 246), patients who reported previously diagnosed coronary heart disease or revascularisation procedure (n = 579), patients for whom a diagnosis was either not entered (n = 132) or not identified as angina or non-cardiac chest pain (n = 83), those with undefined ethnic group (n = 134), patients with missing data (n = 367) and those who were not traced by the Office for National Statistics[12] or the NHS-wide clearing system[13] (n = 40). The remaining 8762 patients with complete data and follow-up constituted the study group.

Data collection

Clinical data were systematically recorded and included age, sex, ethnicity, clinical descriptors of chest pain (duration of

Abbreviations: ECG, electrocardiogram; RACPCs, rapid access chest pain clinics; SMR, standardised mortality ratio

symptoms before attendance, character, site and radiation of chest pain, duration of an episode, precipitating factors and relief with glyceryl trinitrate), smoking status, history of hypertension, diabetes, pulse rate, systolic blood pressure, drugs and follow-up plan on discharge. Twelve-lead resting electrocardiograms (ECGs) were recorded as normal or abnormal, respectively, depending on assessment of rhythm, conduction, and the absence or presence of regional ST segment or T wave changes, left-ventricular hypertrophy and Q waves. Exercise treadmill tests were carried out at the discretion of clinicians in 58% of patients. Reasons for not carrying out an ECG treadmill test were recorded as follows: resting ECG abnormalities or other comorbidities (16%), not indicated (26%), in whom median probability of coronary artery disease was 18.6% (interquartile range (IQR) 8.4–32.4%). Diagnosis of the cause of chest pain, either angina or non-cardiac chest pain, was based on the clinical assessment of the clinician who recorded it at the end of the consultation.

Follow-up

Patients were flagged for mortality with the Office for National Statistics (to 25 April 2005), and for hospital admissions and procedures with the NHS-wide clearing system (to 23 December 2003). Successful matching was achieved in 99.5% of the cohort. Causes of death were defined by the World Health Organization *International Classification of Diseases* (ICD10 codes). Among patients undergoing hospital admission during the follow-up period, the primary discharge diagnosis was used to define events.

Main outcome measures

The primary end point was a composite of death due to coronary heart disease (ICD10 I20–I25) or acute coronary syndrome (non-fatal myocardial infarction (ICD10 I21–I23) and hospital admission with unstable angina (I24.0, I24.8, I24.9)). Secondary end points were all-cause mortality (ICD I20), cardiovascular death (ICD10 I00–I99) or non-fatal myocardial infarction (ICD10 121–123) or hospital admission with unstable angina (I24.0, I24.8, I24.9) or non-fatal stroke (I60–I69).

Ethical approval

Ethical approval was obtained from the multiregional ethics committee (MREC/02/04/095). Permission was given by the National Patient Information Advisory Group[14] to link anonymised datasets without individual patient consent.

Statistical analysis

Patients with angina and non-cardiac chest pain were compared using χ^2 and t tests for proportions and distributions, respectively. We calculated Kaplan–Meier product limits for the cumulative probability of reaching an end point and used the log rank test for evidence of a statistically significant difference between the groups. Time was measured from the first clinic visit to the outcome of interest. Cox regression analysis was used to estimate hazard ratios for the effect of angina on outcome in age-adjusted and fully adjusted models, based on covariates associated ($p<0.05$) with the outcome of interest. We used STATA V.8.0 for all the analyses.

Standardised mortality ratios

Standardised mortality ratios (SMRs) were calculated as the ratio of observed mortality within the study group to expected mortality based on data available from the Office for National Statistics. SMRs for all-cause mortality were calculated for each year of the study, taking into account the exact time each patient was in the study and using 1-year age bands. The reference death rates were for England for the same year, except for 2003 and 2004, for which the death rates were not available and the 2002 death rates were used. The reference death rates for death due to coronary heart disease and other disease groups are given in 10-year age blocks, so we used linear interpolation to derive death rates for each year of age. SMRs for coronary heart disease and other disease groups were calculated using the same method as for all-cause mortality.

RESULTS

Patients

Table 1 summarises the baseline characteristics of patients diagnosed with angina or non-cardiac chest pain.

Patients diagnosed with angina were older and more likely to be men than patients diagnosed with non-cardiac chest pain. Among patients with angina, 58% were referred for further outpatient cardiological assessment, with a total of 35% undergoing angiography during follow-up, of whom 43% had a revascularisation procedure. Only 18% were referred back to their primary care physician after a single clinic visit compared with 89% of patients with non-cardiac chest pain.

Prognosis of angina and non-cardiac chest pain

Figure 1 shows the Kaplan–Meier survival curves for patients with and without angina.

During a median follow-up of 2.57 (IQR 1.96–4.15) years, all outcomes were more frequent for patients with angina than for patients with non-cardiac chest pain. In patients with angina, the cumulative probability of the primary end point was 8.62% (95% CI 7.56% to 9.83%) after 1 year, rising to 16.52% (95% CI 14.88% to 18.32%) after 3 years. This compares with cumulative probabilities for the primary end point of 0.83% (95% CI 0.63% to 1.08%) after 1 year and 2.73% (95% CI 2.29% to 3.25%) after 3 years in patients with non-cardiac chest pain. In the 501 patients with missing baseline data, rates of the primary end point were not significantly different from those in the main cohort.

Predictive accuracy of diagnosis for the primary end point

Among the 599 patients with the primary end point, 194 (32.4%) had been diagnosed with non-cardiac chest pain. Compared to patients with angina who reached the primary end point ($n = 405$), those with non-cardiac chest pain ($n = 194$) were younger, a higher proportion were south Asians, >80% had normal resting electrocardiograms and a substantially lower proportion had typical symptoms and an abnormal exercise treadmill test. Multivariate associations with the primary end point in patients diagnosed with non-cardiac chest pain were age, male sex, south Asian ethnicity, diabetes, typical symptoms and abnormal ECG (table 2).

Comparison with the general population

Table 3 gives the SMRs in patients with angina and non-cardiac chest pain.

In patients with angina, coronary SMRs were increased in men (3.52 (95% CI 1.98 to 5.07)) and women (4.39 (95% CI 1.14 to 7.64)) <65 years, but not in older patients. In patients with non-cardiac chest pain, coronary SMRs were lower than in the general population in older patients, but not in men (1.15 (95% CI 0.57 to 1.73)) and women (1.96 (95% CI 0.68 to 3.24)) <65 years.

DISCUSSION

This multicentre study has shown that among patients with undifferentiated chest pain assessed in RACPCs, those diagnosed with angina have a substantially higher risk of death due to coronary heart disease or non-fatal acute coronary syndrome than patients diagnosed with non-cardiac chest pain and the

Table1 Baseline characteristics among consecutive patients diagnosed with angina or non-cardiac chest pain, in those who did and did not subsequently experience the primary end point

	Angina group (n = 2366)		Non-cardiac group (n = 6396)	
	With 1 end point*, n = 405 (17%)	Without 1 end point, n = 1961 (83%)	With 1 end point*, n = 194 (3%)	Without 1 end point*, n = 6202 (97%)
Mean (SD) age (years)	62 (11)	62 (11)	56 (11)	51 (12)
Males	240 (59%)	1114 (57%)	111 (57%)	3129 (50%)
Ethnicity, n (%)				
White	298 (74%)	1512 (77%)	97 (50%)	3878 (63%)
South Asian	90 (22%)	371 (19%)	84 (43%)	1694 (27%)
Black	17 (4%)	78 (4%)	13 (7%)	630 (10%)
Risk factor, n (%)				
Current smoker	92 (23%)	451 (23%)	52 (27%)	1500 (24%)
Hypertension	184 (45%)	930 (47%)	76 (39%)	1855 (30%)
Diabetes	78 (19%)	315 (16%)	41 (21%)	484 (8%)
Duration of chest pain†, n (%)				
<4 weeks	161 (40%)	773 (39%)	112 (58%)	3148 (51%)
1–⩽6 months	155 (38%)	769 (39%)	50 (26%)	1978 (32%)
>6–12 months	34 (8%)	132 (7%)	7 (4%)	320 (5%)
>1 year	55 (14%)	287 (15%)	25 (13%)	756 (12%)
Character of chest pain, n (%)				
Typical	304 (75%)	1390 (71%)	17 (9%)	291 (5%)
Atypical	100 (25%)	562 (29%)	128 (66%)	4289 (69%)
Non-specific	1 (0.3%)	9 (0.5%)	49 (25%)	1622 (26%)
Resting ECG, n (%)				
Normal	222 (55%)	1293 (66%)	160 (82%)	5616 (91%)
Abnormal	183 (45%)	668 (34%)	34 (18%)	586 (9%)
Exercise treadmill test, n (%)				
Positive	152 (38%)	714 (36%)	2 (1%)	23 (0.4%)
Non-diagnostic	28 (7%)	217 (11%)	4 (2%)	116 (2%)
Negative	77 (19%)	392 (20%)	99 (51%)	3257 (53%)
Not done, not indicated	5 (1%)	31 (2%)	63 (33%)	2218 (36%)
Not done, other reason	143 (35%)	607 (31%)	26 (13%)	588 (10%)
Mean (SD) systolic blood pressure (mm Hg)	148 (21)	147 (21)	143 (23)	138 (20)
Heart rate (beats/min)	77 (13)	76 (12)	77 (13)	77 (12)
Medication on discharge, n (%)				
Aspirin	347 (86%)	1650 (84%)	32 (17%)	608 (10%)
β-blockers	212 (52%)	1061 (54%)	19 (10%)	473 (8%)
Calcium blockers	167 (41%)	740 (38%)	26 (13%)	411 (7%)
Statin	113 (28%)	547 (28%)	14 (7%)	395 (6%)
Cholesterol measured‡	312 (83%)	1476 (82%)	121 (71%)	3558 (65%)
Disposal§, n (%)				
Admitted	0	0	1 (0.5%)	12 (0.2%)
Cardiac outpatients	217 (54%)	1143 (59%)	29 (15%)	670 (11%)
Angiography	115 (29%)	453 (23%)	0	2 (0.03%)
Discharged to primary care intervention	67 (17%)	342 (18%)	163 (85%)	5475 (89%)
Angiogram	237 (59%)	587 (30%)	71 (37%)	84 (1%)
PTCA	68 (17%)	134 (7%)	25 (13%)	8 (0.1%)
CABG	68 (17%)	161 (8%)	15 (8%)	5 (0.1%)
PTCA/CABG	130 (32%)	289 (15%)	39 (20%)	13 (0.2%)

CABG, coronary artery bypass graft; ECG, electrocardiogram; PTCA, percutaneous transluminal coronary angioplasty.
*1 (Primary) end point—death due to coronary heart disease or acute coronary syndrome.
†Duration of chest pain before attendance at the clinic.
‡Percentage of patients not prescribed a statin but in whom a cholesterol check was recommended (data available for 7810 patients).
§Data available for 8689 patients.

general population. The data confirm the prognostic validity of differential diagnosis within RACPCs. Our finding that 32.4% of all events during follow-up occurred in patients diagnosed with non-cardiac chest pain highlights the need to reduce misdiagnosis and identify all who might benefit from secondary prevention treatment.

This is the first large, multicentre consecutive series of ambulatory patients with new, undifferentiated chest pain, allowing estimates of prognosis in women and men. Angina was diagnosed in 27% of patients, and in this group cumulative rates of death due to coronary heart disease or acute coronary syndromes were high, estimated at 8.62% after 1 year and

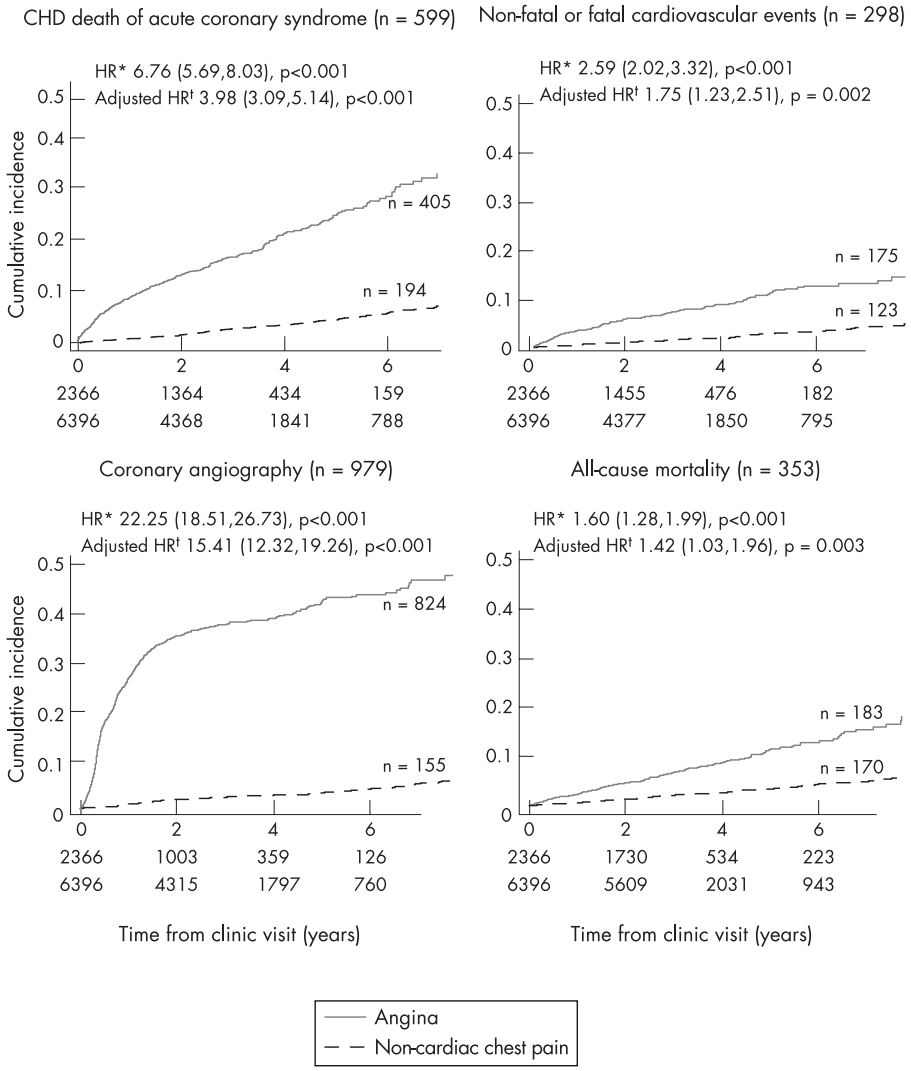

Figure 1 Kaplan–Meier survival curves for patients with and without angina. Numbers at risk at beginning of each year of follow-up are displayed at the bottom of each graph. *Hazard ratio (HR) adjusted for age only. †HR adjusted for sex, age, ethnicity, diabetes, smoking status, heart rate, character of chest pain and resting ECG. CHD, coronary heart disease.

16.52% after 3 years. Our finding of a poor prognosis for patients with incident angina, none of whom had a history of myocardial infarction, emphasises the importance of early diagnosis within RACPCs and contrasts with findings in recent trials of chronic stable angina, ACTION (A CHF Trial Investigating Outcomes of Exercise Training)[15] and PEACE (Prevention of Events with Angiotensin-converting Enzyme Inhibition)[16] reporting annual mortalities of 1.5% (95% CI 1.4% to 1.7%) and 1.7% (95% CI 1.5% to 1.9%) compared with 3.1% (95% CI 2.6% to 3.5%) in our registry population. The trialists' conclusions that angina has a good prognosis,[15] with risk reduced to normal levels with contemporary treatment,[17] may partly reflect the selection bias in the patients they recruited, which comprised stable patients in secondary or tertiary care settings. Similarly, 75% of patients in the Euro Heart survey[18] of stable angina had had symptoms for >6 months before their first cardiological assessment and are different from the patients in our study with incident angina, many of whom were within 4 weeks and most within 6 months of symptom onset, suggesting recent plaque instability and predisposition to ischaemic events.[19 20] Underuse of secondary prevention drugs may also have contributed to the high event rates we observed, and although rates of aspirin and β-blocker treatment in patients in our study diagnosed with angina were similar to those reported in the Euro Heart Survey, only 28% were prescribed statins at this first cardiological consultation. This is lower than the entry treatment rates for angina trial participants, many of whom had had prior myocardial infarction and full cardiological investigation over many visits, but exceeds the treatment rates reported for patients with ischaemic heart disease in primary care settings.[21] More than 80% of our patients with angina did undergo further cardiological follow-up and although most probably came to receive statins, it is a limitation of our study that we do not know what proportion remained untreated.

Patients diagnosed with non-cardiac chest pain in our study had a lower event rate, but accounted for almost one third of all primary end points. This is a cause for concern, because these patients had been assessed for coronary disease in the RACPCs and might therefore be expected to exhibit a distinctly lower coronary mortality than the general population. We found evidence for this in older patients diagnosed with non-cardiac chest pain, but not in patients aged <65 years for whom SMRs were not significantly different from the general population.

Table 2 Predictors of death due to coronary heart disease or acute coronary syndrome in 6396 patients diagnosed with non-cardiac chest pain

	CHD death or acute coronary syndrome (n = 194)			
Covariates	Age-adjusted* HR (95% CI)	p Value	Adjusted† HR (95% CI)	p Value
Male sex	1.41 (1.06 to 1.87)	0.018	1.36 (1.02 to 1.81)	0.033
Age/10-year increase*	1.47 (1.32 to 1.65)	<0.000	1.46 (1.29 to 1.64)	<0.000
Ethnicity				
Black *v* white	0.63 (0.35 to 1.12)	0.000	0.58 (0.32 to 1.04)	0.001
SA *v* white	1.73 (1.27 to 2.35)		1.51 (1.10 to 2.08)	
History of hypertension	1.22 (0.91 to 1.65)	0.189	NA	NA
Systolic blood pressure	1.00 (0.99 to 1.01)	0.747	NA	NA
Current smoking	1.30 (0.95 to 1.80)	0.111	NA	NA
Diabetes *v* none	2.49 (1.76 to 3.52)	<0.000	2.14 (1.49 to 3.09)	0.000
Symptoms				
Typical *v* non-specific	2.03 (1.17 to 3.54)	0.050	2.12 (1.21 to 3.70)	0.040
Atypical *v* non-specific	1.04 (0.75 to 1.45)		1.07 (0.76 to 1.49)	
Duration of symptoms >1 month *v* ⩽1 month	1.01 (0.76 to 1.35)	0.931	NA	NA
Heart rate, 10 beats/min	0.97 (0.86 to 1.09)	0.550	NA	NA
Abnormal ECG result	1.66 (1.14 to 2.42)	0.012	1.62 (1.10 to 2.36)	0.0188

CHD, coronary heart disease; ECG, electrocardiogram; SA, South Asians.
*Age is univariable.
†Adjusted for all variables in the table apart from history of hypertension, systolic blood pressure, current smoking, duration of symptoms and heart rate.

Probably most of these patients, who were told they did not have angina, but then had a coronary event, were misdiagnosed at the initial assessment, perhaps because they were younger than patients diagnosed with angina, fewer had typical symptoms and most had normal resting ECGs. Among patients diagnosed with non-cardiac chest pain, coronary event rates fell below current thresholds for secondary prevention treatment,[10] but we identified subgroups in whom hazard ratios for the primary end point were increased by ⩾50%. These included patients with diabetes, for whom secondary prevention treatment is already recommended,[22] but also south Asians and patients with ECG abnormalities who might benefit from more aggressive preventive strategies in RACPCs. Although clinical factors signal a heightened risk among subgroups diagnosed with non-cardiac chest pain, there is now a need for research to identify the methods for improving diagnostic precision. This may entail a better understanding of existing measures—for example, by development and validation of risk scores in this population, as well as consideration of the incremental prognostic or diagnostic value of serological testing[23] and non-invasive coronary imaging.[24 25] Unlike myocardial infarction,[26] there is no internationally agreed standard for defining the presence or absence of angina.

This is the first large multicentre study to evaluate the effectiveness of RACPCs by examining coronary outcomes in relationship to clinical diagnosis and mortality in the general population. There have been no previous outcome studies of other models of ambulatory chest pain assessment, particularly conventional cardiology outpatient clinics or chest pain assessment units. Our conclusions about the adverse prognosis of angina are consistent with those of a large population-based outcome study from Finland,[27] but are limited to those patients selected for referral by their primary care physicians, and generalisation to chest pain in the community requires caution. Additional limitations relate to ethical constraints that prohibited the documentation of ongoing secondary prevention treatment during follow-up, and also the inevitable restriction imposed on baseline covariates by the data that was recorded. For example, a reliable history of hyperlipidaemia was unavailable, and we excluded from analysis family history of coronary disease as it was not clear whether it related to history of premature death in first-degree relatives.

Table 3 Standardised mortality ratios (to April 2004) in patients diagnosed with angina and non-cardiac chest pain (n = 8762)

	Angina group				Non-cardiac group			
	Male		Female		Male		Female	
	O/E	SMR (95% CI)	O/E	SMR (95% CI)	O/E	SMR (95% CI)	O/E	SMR (95% CI)
All-cause mortality								
< 65	40/23	1.83 (1.26 to 2.39)	20/11	1.78 (1.00 to 2.56)	54/54	1.00 (0.73 to 1.26)	44/36	1.21 (0.85 to 1.57)
⩾65	79/91	0.87 (0.68 to 1.05)	45/53	0.85 (0.60 to 1.09)	46/63	0.73 (0.52 to 0.94)	26/51	0.51 (0.32 to 0.71)
All ages	119/113	1.05 (0.86 to 1.24)	65/64	1.01 (0.76 to 1.25)	100/117	0.85 (0.68 to 1.02)	70/88	0.80 (0.61 to 0.98)
CHD (ICD 10 I20–I25)								
<65	20/6	3.52 (1.98 to 5.07)	7/2	4.39 (1.14 to 7.64)	15/13	1.15 (0.57 to 1.73)	9/5	1.96 (0.68 to 3.24)
⩾65	35/27	1.62 (1.09 to 2.16)	18/10	1.76 (0.95 to 2.58)	11/16	0.71 (0.29 to 1.12)	3/10	0.31 (0.00 to 0.65)
All ages	55/28	2.03 (1.49 to 2.56)	25/12	2.13 (1.29 to 2.96)	26/26	0.92 (0.57 to 1.28)	12/15	0.85 (0.37 to 1.32)
Non-cardiovascular causes								
<65	15/14	1.04 (0.77 to 1.31)	10/8	1.19 (0.81 to 1.57)	31/35	0.88 (0.72 to 0.83)	26/28	0.92 (0.74 to 1.10)
⩾65	33/53	0.62 (0.51 to 0.73)	22/34	0.64 (0.50 to 0.78)	30/36	0.83 (0.68 to 0.98)	18/32	0.56 (0.43 to 0. 69)
All ages	48/68	0.70 (0.60 to 0.80)	32/40	0.79 (0.65 to 0.93)	61/75	0.81 (0.71 to 0.91)	48/63	0.76 (0.65 to 0.87)

O, observed mortality; CHD, coronary heart disease; E, expected mortality; ICD, International Classification of Diseases; SMR, standardised mortality rate.

Conclusion

One-stop cardiological assessment in RACPCs successfully identifies patients with incident angina who are at substantially higher coronary risk than those patients with non-cardiac chest pain and the general population. However, >70% of patients attending these clinics were diagnosed with non-cardiac chest pain, and our data have exposed misdiagnosis in a minority who were not appropriately treated. We need to improve the diagnosis and treatment of ambulatory patients when they first present with chest pain, to reduce coronary event rates.

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Authors' affiliations

N Sekhri, Newham University Hospital, London, UK
G S Feder, A D Timmis, Barts and The London Queen Mary's School of Medicine and Dentistry, London, UK
C Junghans, H Hemingway, Department of Epidemiology and Public Health, UCL Medical School, London, UK

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ADT, GSF, HH and NS were responsible for the design and management of this study. NS and CJ were responsible for the statistical analysis. All the authors participated in the preparation of the manuscript.

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