

**What is already known on this topic**

People over age 60 often receive inadequate treatment for depression in primary care

Organised, multifaceted, and tailored depression treatment programmes are promising. IMPACT produced favourable results during the one year intervention

It is not known if these promising results endure

**What this study adds**

Tailored collaborative care actively engages people over age 60 in depression treatment and delivers important benefits that persist at least one year after the completion of the intervention programme

IMPACT may show the way to less depression and healthier lives for millions

We thank the patients, primary care providers, and staff at the coordinating centre, and at all of the participating study sites for their contributions and support. We would like to thank the investigators and the IMPACT study advisory board for their scientific and other contributions. We thank Christopher Langston, senior programme officer from the John A Hartford Foundation, for all of his contributions and support throughout the entire study period. We thank Sabine Oishi for her project coordination efforts. We acknowledge Diane Fraser for editorial assistance. We thank Bruce Fireman and Joe Selby for review and comments on the manuscript. We acknowledge Carla Tillman for preparation of the manuscript. We also thank Claudia Cruz and Yolanda Yarbough for their help with preparation of the manuscript.

Contributors: See [bmj.com](http://bmj.com)

**Funding:** This study is supported by grants from the John A. Hartford Foundation, the California Healthcare Foundation, the Hogg Foundation, and the Robert Wood Johnson Foundation.

**Competing interests:** EMH has received research funding from Eli Lilly and Company, Merck, Wyeth-Ayerst, Pfizer, Solvay, and GlaxoSmithKline. EMH received a consulting fee regarding women's health from Eli Lilly. JWW has received consulting fees from Wyeth-Ayerst, Pfizer, and GlaxoSmithKline for participating in advisory boards that address depression care. LH has served as a consultant to Wyeth-Ayerst and is currently employed by GlaxoSmithKline. KK has received research funding and consulting fees from Pfizer, Eli Lilly, and Wyeth-Ayerst.

**Ethical approval:** The study protocol was formulated independently by the investigators and approved by institutional review boards at all participating study sites and the UCLA study coordinating centre.

- 1 Unutzer J, Katon W, Callahan CM, Williams JW Jr, Hunkeler E, Harpole L, et al. Collaborative care management of late-life depression in the primary care setting. A randomized controlled trial. *JAMA* 2002; 288:2836-45.
- 2 Bruce ML, Ten Have TR, Reynolds CF 3rd, Katz II, Schulberg HC, Mulsant BH, et al. Reducing suicidal ideation and depressive symptoms in depressed older primary care patients. *JAMA* 2004;291:1081-91.
- 3 Unutzer J, Katon W, Williams JW, Jr., Callahan CM, Harpole L, Hunkeler EM, et al. Improving primary care for depression in late life: The design of a multicenter randomized trial. *Med Care* 2001;39:785-99.
- 4 First MD, Spitzer RL, Gibbon M, Williams JB. *Structured clinical interview for DSM-IV axis I disorders (SCID)*. Washington, DC: American Psychiatric Press, 1996.
- 5 Bartels SJ, Coakley EH, Zubritsky C, Ware JH, Miles KM, Areak PA, et al. Improving access to geriatric mental health services: A randomized trial comparing treatment engagement with integrated versus enhanced referral care for depression, anxiety, and at-risk alcohol use. *Am J Psychiatry* 2004;161:1455-62.
- 6 Hunkeler EM, Meresman JF, Hargreaves WA, Berman WH, Fireman B, Kirsch AJ, et al. Efficacy of nurse Telehealth care and peer support in augmenting treatment of depression in primary care. *Arch Fam Med* 2000;9:700-8.

(Accepted 8 November 2005)

doi 10.1136/bmj.38683.710255.BE

## Predicting prognosis in stable angina—results from the Euro heart survey of stable angina: prospective observational study

Caroline A Daly, Bianca De Stavola, Kim M Fox, on behalf of the Euro Heart Survey Investigators

Royal Brompton Hospital, London SW3 6NP  
Caroline A Daly  
*clinical research fellow*  
Kim M Fox  
*professor of cardiology*

London School of Hygiene and Tropical Medicine, London

Bianca De Stavola  
*senior lecturer in clinical epidemiology*

Correspondence to: C A Daly  
[caroline.daly@imperial.ac.uk](mailto:caroline.daly@imperial.ac.uk)

*BMJ* 2006;332:262-5

### Abstract

**Objectives** To investigate the prognosis associated with stable angina in a contemporary population as seen in clinical practice, to identify the key prognostic features, and from this to construct a simple score to assist risk prediction.

**Design** Prospective observational cohort study.

**Setting** Pan-European survey in 156 outpatient cardiology clinics.

**Participants** 3031 patients were included on the basis of a new clinical diagnosis by a cardiologist of stable angina with follow-up at one year.

**Main outcome measure** Death or non-fatal myocardial infarction.

**Results** The rate of death and non-fatal myocardial infarction in the first year was 2.3 per 100 patient years; the rate was 3.9 per 100 patient years in the subgroup (n = 994) with angiographic confirmation of coronary disease. The clinical and investigative factors most predictive of adverse outcome were

comorbidity, diabetes, shorter duration of symptoms, increasing severity of symptoms, abnormal ventricular function, resting electrocardiographic changes, or not having any stress test done. Results of non-invasive stress tests did not significantly predict outcome in the population who had tests done. A score was constructed using the parameters predictive of outcome to estimate the probability of death or myocardial infarction within one year of presentation with stable angina.

**Conclusions** A score based on the presence of simple, objective clinical and investigative variables makes it possible to discriminate effectively between very low risk and very high risk patients and to estimate the probability of death or non-fatal myocardial infarction over one year.



See full version on [bmj.com](http://bmj.com) for complete list of authors and Appendices A and B



This is the abridged version of an article that was posted on [bmj.com](http://bmj.com) on 13 January 2006: <http://bmj.com/cgi/doi/10.1136/bmj.38695.605440.AE>

## Introduction

Stable angina is the most prevalent manifestation of coronary disease, but contemporary information on the prognosis of the condition is relatively sparse. The aims of this investigation were to ascertain the prognosis associated with a clinical diagnosis of stable angina in a contemporary setting; to determine the clinical and investigative factors predictive of death or myocardial infarction; and to construct a simple risk prediction model to assist in prognostic evaluation of stable angina.

## Methods

The Euro heart survey of stable angina is a prospective observational cohort study of patients presenting to cardiology services with stable angina—3031 patients from 156 centres in 34 countries were followed up for one year. Details of centres, data collection, and patient population have previously been described.<sup>1</sup>

**Patient population and follow-up**—Patients attending cardiology services with a new presentation of stable angina were considered for enrolment, and we included in the survey all patients with a clinical diagnosis of stable angina caused by myocardial ischaemia due to coronary disease. We followed patients up one year after initial assessment. We recorded cause of death and occurrence of cardiovascular events. We used the Canadian Cardiovascular Society classification to assess severity of angina. We defined known cardiovascular risk factors and comorbid conditions as in appendix A on [bmj.com](http://bmj.com).

**Statistical analysis**—We estimated the prevalence of risk factors, baseline clinical characteristics, and treatment at presentation. The primary outcome was death or non-fatal myocardial infarction. We defined follow-up time from study enrolment to the first event or 18 months after recruitment. We used survival analysis techniques to calculate event rates.<sup>2</sup> We determined the effects of clinical and investigative variables on the occurrence of death or non-fatal myocardial infarction. We used stepwise regression models to determine the factors predictive of death or infarction during follow-up.

## Results

From March 2002 to December 2002, 3779 patients were enrolled. Vital status during follow-up was ascertained in 3259 (86%) patients, and data were suitable for survival analysis in 3031. No substantial differences existed between the patients with and without follow-up information in terms of clinical characteristics or regional distribution. Mean age was 61 years, and 58% were male. Most patients had mild to moderate symptoms of angina for six months or less before presentation to a cardiologist.

### Confirmation of coronary disease

Coronary angiography was done during follow-up in 1253 (41%) patients. At the end of the follow-up period, approximately one third ( $n=994$ ) of patients had had coronary disease confirmed angiographically and a further third ( $n=1023$ ) had negative investigations. One sixth of patients had no definitive diagnostic test.

### Clinical events during follow-up

The incidence of death or infarction was significantly greater ( $P<0.001$ ) in patients with confirmed coronary disease than in those with negative investigations or positive non-invasive tests without angiographic confirmation. Patients who had no investigation, or inconclusive results on non-invasive investigation, had a rate of death or infarction (4.1/100 patient years, 95% confidence interval 2.7 to 6.0) similar to that in the population with confirmed coronary disease.

### Clinical and investigative factors predictive of adverse outcome

Previous myocardial infarction, signs of heart failure, or a history of diabetes, hypertension, or any comorbidity were significant predictors of adverse outcome, as were increasing severity of symptoms and shorter duration of symptoms. Resting electrocardiographic abnormalities were associated with approximately double the risk of death or myocardial infarction, but positive non-invasive stress test results were not significantly associated with adverse outcome. Not having had any functional assessment was an indicator of substantially increased risk, as was abnormal left ventricular function assessed by echocardiography (see [bmj.com](http://bmj.com)).

Stepwise regression selected comorbidity, diabetes, recent onset of symptoms, more severe symptoms, ST or T wave abnormalities on the resting electrocardiogram, not having any stress test done, and abnormal ventricular function as most predictive of outcome (table 1). Age and sex were not significant predictors

**Table 1** Clinical and investigative parameters independently predictive of death or myocardial infarction, determined by using stepwise selection procedures in general population with stable angina

	Hazard ratio (95% CI)	P value*
<b>Clinical variables (n=2183)</b>		
Comorbidity	2.41 (1.49 to 3.91)	<0.001
Signs of heart failure	1.62 (0.85 to 3.07)	0.14
Previous myocardial infarction	2.19 (1.08 to 4.42)	0.03
Diabetes	2.03 (1.25 to 3.31)	0.004
Symptom duration >6 months	0.54 (0.33 to 0.87)	0.01
Symptom severity:		
Class II versus class I	1.95 (1.07 to 3.54)	0.005
Class III versus class I	2.65 (1.29 to 5.50)	
<b>Investigative variables (n=2963)</b>		
Stress testing:		
Positive test	1.43 (0.76 to 2.70)	0.0001
No stress test done	3.78 (2.04 to 7.00)	
Echocardiography:		
Abnormal left ventricular function	2.57 (1.62 to 4.08)	<0.0001
Electrocardiography:		
ST or T wave changes	1.63 (1.06 to 2.50)	0.03
<b>Combined clinical and investigative variables (n=2528)</b>		
Comorbidity	2.25 (1.43 to 3.56)	0.0008
Diabetes	1.95 (1.22 to 3.11)	0.007
Previous myocardial infarction	—	
Symptoms >6 months	0.48 (0.30 to 0.77)	0.002
Symptom severity:		
Class II versus class I	1.76 (1.00 to 3.09)	0.05
Class III versus class I	2.18 (1.10 to 4.33)	
ST or T wave changes	1.56 (0.99 to 2.45)	0.05
Stress test:		
Positive stress test result	1.29 (0.63 to 2.67)	<0.0001
No stress test done	3.48 (1.71 to 7.07)	
Abnormal left ventricular function	2.11 (1.29 to 3.46)	0.004

\*Likelihood ratio test for heterogeneity among category specific rates (hazards) for variables categories.

when forced into the model. Although age had a linear effect that was significant when examined on its own, its strong association with most other variables led to its lack of significance in the multivariate model.

**Development of a clinical risk score for patients with stable angina**

We used a further stepwise selection process to consider only the results of non-invasive investigations. A positive versus negative or inclusive non-invasive stress test result was not selected as a significant predictor when combined with information from echocardiography and resting electrocardiography. Thus in the model developed to derive the clinical risk score the final predictors of death or myocardial infarction were comorbidity, diabetes, severity of symptoms, duration of symptoms, resting electrocardiogram abnormalities, and abnormal ventricular function. Using these parameters a risk score can be calculated according to the weighted scores shown in table 2. This score can then be used to estimate visually the probability of death or myocardial infarction from the plot in the figure or (using the closest rounded figure) to read the estimated probability from table 7 on bmj.com.

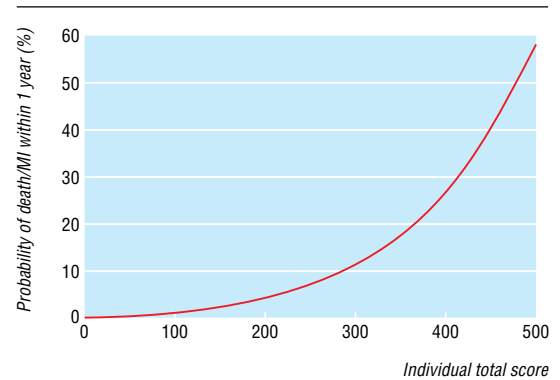
**Discussion**

The Euro heart survey of stable angina population differs from a general selection of people with angina in the community and from the overall primary care angina population in that they have been selected for

**Table 2** Score sheet to calculate risk score for patients presenting with stable angina

Risk factor	Score contribution	Individual's score
<b>Comorbidity*</b>		
No	0	
Yes	86	
<b>Diabetes</b>		
No	0	
Yes	57	
<b>Angina score</b>		
Class I	0	
Class II	54	
Class III	91	
<b>Duration of symptoms</b>		
≥6 months	0	
<6 months	80	
<b>Abnormal ventricular function</b>		
No	0	
Yes	114	
<b>ST depression or T wave inversion on resting electrocardiogram</b>		
No	0	
Yes	34	
		Total=

\*One or more of previous cerebrovascular event; hepatic disease defined as chronic hepatitis or cirrhosis, or other hepatic disease causing elevation of transaminases more than three times upper limit of normal; peripheral vascular disease defined as claudication either at rest or on exertion, amputation for arterial vascular insufficiency, vascular surgery (reconstruction or bypass) or angioplasty to the extremities, documented aortic aneurysm, or non-invasive evidence of impaired arterial flow; chronic renal failure defined as chronic dialysis or renal transplantation or serum creatinine greater than 200 μmol/l; chronic respiratory disease defined as a diagnosis previously made by physician or patient receiving bronchodilators or FEV<sub>1</sub><75%, arterial pO<sub>2</sub><60%, or arterial pCO<sub>2</sub>>50% predicted in previous studies; chronic inflammatory conditions defined as a diagnosis of rheumatoid arthritis, systemic lupus erythematosus or other connective tissue diseases, polymyalgia rheumatica, and so on; malignancy defined as a diagnosis of malignancy within a year or active malignancy.



Plot to assign estimated probability of death or non-fatal myocardial infarction within one year of presentation according to combination of clinical and investigative features in patients with stable angina (corresponding to scoring system in table 7 on bmj.com). MI=myocardial infarction

specialist assessment. However, the population is comparatively less selected than those in randomised controlled trials or angiographic registries.

**Comparisons with clinical trial populations with stable angina**

The annual incidence of death in the survey was 1.5%, and the incidence of non-fatal myocardial infarction was 1.4%. In the subgroup with proved coronary disease these rates were 1.8% and 3.2%. Estimates of annual mortality from modern clinical trials range from 0.9% to 1.7%.<sup>3-6</sup> Reported annual incidences of non-fatal myocardial infarction range from 1.1% to 1.5%.<sup>4,5</sup>

**Determining prognosis in an individual**

The features identified in this study as predicting adverse outcome in the population with stable angina are in keeping with previous observations in registry data.<sup>7,8</sup> Importantly, negative investigations, either invasive or non-invasive, identify a low risk population. The prognostic importance of comorbidity is substantial, of the same order as abnormal ventricular function. This has also recently been shown in a study from the Duke database.<sup>9</sup> A further important finding is that, in this population with largely uncomplicated stable angina, the severity of angina was a useful prognostic indicator.

Angina scores incorporating the pattern of occurrence of angina and the severity of symptoms unresponsive to medical treatment or recurrent symptoms after revascularisation have previously been shown to predict prognosis in the stable angina population,<sup>10,11</sup> but the predictive value lessens with longer follow-up and is greatest in patients with preserved ventricular function. The strength of angina symptoms in predicting prognosis in this population may be related to the low prevalence of pronounced ventricular dysfunction and the short duration of follow-up.

**Risk prediction score**

Several widely available multiple risk factors equations exist to calculate the absolute risk of developing coronary or cardiovascular disease in patients without established disease.<sup>12,13</sup> However, such risk scores do not apply to a population with symptoms. Although several scores have been developed to predict the

### What is already known on this topic

Contemporary data on clinical outcome in stable angina outside randomised controlled trials are lacking, and in recent clinical trials the annual mortality ranges from 0.9% to 2.9%

Previous reports of the factors of prognostic importance in stable coronary disease were drawn from highly selected populations and predate modern drug management

### What this study adds

In this contemporary evaluation of the prognosis associated with stable angina, the incidence of death and myocardial infarction was 2.3/100 patient years

Comorbidity, diabetes, severity of angina, shorter duration of symptoms, left ventricular dysfunction, and ST changes on the resting electrocardiogram independently predicted outcome

A simple score involving these six characteristics can be used to estimate the probability of death or myocardial infarction in the year after presentation with stable angina

presence of coronary disease by using clinical or exercise variables,<sup>14 15</sup> applicability is limited to those who can exercise.<sup>16 17</sup> Cumulative data from single institution databases, such as the Duke database, have also been used as predictive tools.<sup>18</sup> However, these tools were developed in populations assessed up to 30 years ago and are not specific to a stable angina population.

The Euro heart angina score allows discrimination between low risk and high risk groups over a one year period, in a population with a clinical diagnosis of stable angina. The predictive accuracy of this score is comparable to that of older predictive models but is more relevant to a contemporary population.<sup>19</sup>

### Conclusions

In patients presenting with stable angina, simple clinical features are strongly predictive of prognosis. A low risk population may be effectively identified by negative investigations, and those who are not investigated constitute a high risk group. By identifying the features most predictive of adverse outcome we have been able to construct a simple scoring system to calculate an estimate of the one year probability of death or non-fatal myocardial infarction in patients with stable angina.

We are indebted to the Euro heart survey investigators who collect and submit data on a voluntary basis and the Euro heart survey team members who have contributed to this survey.

Contributors: See bmj.com.

Funding: Servier Laboratories was the principal financial sponsor for the study. The funding source had no role in study design, data collection, analysis, or interpretation.

Competing interests: None declared.

Ethical approval: Ethical approval was sought in each country in accordance with local practice. In the UK multicentre research ethics committee was granted; in other countries the local ethics committee or relevant authority granted approval.

- Daly CA, Clemens F, Lopez Sendon JL, Tavazzi L, Boersma E, Danchin N, et al. The clinical characteristics and investigations planned in patients with stable angina presenting to cardiologists in Europe, from the Euro heart survey of stable angina. *Eur Heart J* 2005;26:996-1010.
- Collett D. *Modelling survival data in medical research*. London: Chapman and Hall, 1994.
- IONA Study Group. Effect of nicorandil on coronary events in patients with stable angina: the impact of nicorandil in angina (IONA) randomised trial. *Lancet* 2002;359:1269-75.
- Fox KM. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study). *Lancet* 2003;362:782-8.
- Braunwald E, Domanski MJ, Fowler SE, Geller NL, Gersh BJ, Hsia J, et al. Angiotensin-converting-enzyme inhibition in stable coronary artery disease. *N Engl J Med* 2004;351:2058-68.
- Henderson RA, Pocock SJ, Clayton TC, Knight R, Fox KA, Julian DG, et al. Seven-year outcome in the RITA-2 trial: coronary angioplasty versus medical therapy. *J Am Coll Cardiol* 2003;42:1161-70.
- Mock MB, Rinqvist I, Fisher L, Davis K, Chaitman B, Kouchoukos N, et al. Survival of medically treated patients in the coronary artery surgery study (CASS) registry. *Circulation* 1982;66:562-8.
- Hammermeister KE, De Rouen TA, Dodge HT. Variables predictive of survival in patients with coronary disease: selection by univariate and multivariate analysis from the clinical, exercise arteriographic, and quantitative angiographic evaluations. *Circulation* 1979;59:421-30.
- Sachdev M, Sun JL, Tsiatis AA, Nelson CL, Mark DB, Jollis JG. The prognostic importance of comorbidity for mortality in patients with stable coronary artery disease. *J Am Coll Cardiol* 2004;43:576-82.
- Califf RM, Mark DB, Harrell FE Jr, Hlatky MA, Lee KL, Rosati RA, et al. Importance of clinical measures of ischemia in the prognosis of patients with documented coronary artery disease. *J Am Coll Cardiol* 1988;11:20-6.
- Hultgren HN, Peduzzi P. Relation of severity of symptoms to prognosis in stable angina pectoris. *Am J Cardiol* 1984;54:988-93.
- Grundy SM, Pasternak R, Greenland P, Smith S Jr, Fuster V. Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation* 1999;100:1481-92.
- Hense HW. Risk factor scoring for coronary heart disease. *BMJ* 2003;327:1238-9.
- Pryor DB, Shaw L, Harrell FE Jr, Lee KL, Hlatky MA, Mark DB, et al. Estimating the likelihood of severe coronary artery disease. *Am J Med* 1991;90:553-62.
- Yamada H, Do D, Morise A, Atwood JE, Froelicher V. Review of studies using multivariable analysis of clinical and exercise test data to predict angiographic coronary artery disease. *Prog Cardiovasc Dis* 1997;39:457-81.
- Mark DB, Hlatky MA, Harrell FE, Lee KL, Califf RM, Pryor DB. Exercise treadmill score for predicting prognosis in coronary disease. *Ann Intern Med* 1987;106:793-800.
- Prakash M, Myers J, Froelicher VF, Marcus R, Do D, Kalisetti D, et al. Clinical and exercise test predictors of all-cause mortality: results from >6,000 consecutive referred male patients. *Chest* 2001;120:1003-13.
- Califf RM, Armstrong PW, Carver JR, D'Agostino RB, Strauss WE. 27th Bethesda Conference: matching the intensity of risk factor management with the hazard for coronary disease events. Task Force 5: stratification of patients into high, medium and low risk subgroups for purposes of risk factor management. *J Am Coll Cardiol* 1996;27:1007-19.
- Pryor DB, Shaw L, McCants CB, Lee KL, Mark DB, Harrell FE, et al. Value of the history and physical in identifying patients at increased risk for coronary artery disease. *Ann Intern Med* 1993;118:81-90.

(Accepted 8 November 2005)

doi 10.1136/bmj.38695.605440.AE

### Endpiece

#### Fashionable successions and popular rages

Naples is not the only place that has its fashionable successions and popular rages; a much larger city than it, is at one time full of liver complaints, at another of digestive organ disturbances; now the talk of medical men is about spasm—now about inflammation. Excitement is the order of the day at one time, and mucous membrane irritations at another. Purgatives are to do everything at this period; blue pill is the catholicon of that. Portland powder has been the mustard seed of a preceding era; mustard seed is its substitute at a succeeding one; and so on. Whether Dr Heinemann [Hahnemann], with his billionth part of a grain dose, will, in his turn, take his footing among us, remains to be seen.

Unwinds D. *A Treatise on those Diseases which are either Directly or Indirectly, Connected with Indigestion: Comprising a General view of Sympathetic Affections*. London: Thomas and George Underwood, 1827:268

Submitted by Jeremy Hugh Baron, honorary professorial lecturer, Mount Sinai School of Medicine, New York