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Clinical outcomes, risk stratification and practice patterns of unstable angina and myocardial infarction without ST elevation: Prospective Registry of Acute Ischaemic Syndromes in the UK (PRAIS-UK)

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Aims To determine characteristics, outcomes, prognostic indicators and management of patients with acute coronary syndromes without ST elevation.

Methods and Results A prospective registry was carried out with follow-up for 6 months after index hospital admission. A history of acute cardiac chest pain was required plus ECG changes consistent with myocardial ischaemia and/or prior evidence of coronary heart disease. Patients with ST elevation or those receiving thrombolytic therapy were excluded. A total of 1046 patients were enrolled from 56 U.K. hospitals. The mean age was 66 ± 12 years and 39% were female. The rate of death or non-fatal myocardial infarction at 6 months was 12·2% and of death, new myocardial infarction, refractory angina or re-admission for unstable angina at 6 months was 30%. In a multivariate analysis, patients >70 years had a threefold risk of death or new myocardial infarction compared with those <60 years (P<0·01) and those with ST depression or bundle branch block on the ECG had a five-fold greater risk than those with normal ECG (P<0·001). Aspirin was given to 87% and heparin to 72% of patients in hospital. At 6 months 56% received no lipid-lowering therapy at all. The 6-month rate of coronary angiography was 27% and any revascularization 15%.

Conclusions In this cohort there was a one in eight chance of death or myocardial infarction, and a one in three chance of death, new myocardial infarction, refractory angina or re-admission for unstable angina, over 6 months. Age and baseline ECG were useful markers of risk. Aspirin, heparin and statins were not given to about one-sixth, one-third and one-half respectively. Rates of angiography and revascularization appear low. A review of treatment strategies of unstable angina and myocardial infarction without ST elevation is warranted in the U.K. to ensure that patients are receiving optimum treatments to reduce mortality and morbidity.

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Key Words: Acute coronary syndromes, risk stratification, audit, unstable angina, myocardial infarction, angiography.

See pages 1399 and 1401 for the Editorial comment on this article

Introduction

Acute coronary syndromes span the spectrum of typical acute myocardial infarction with ST elevation to unstable angina. Unstable angina and non-ST elevation myocardial infarction appear to be poorly characterized in clinical practice. In various studies 1-year death rates varied from 2 to 18% and myocardial infarction rates from 7 to 21%[1–4]. These apparently wide variations in prognosis may reflect inconsistent definitions of the syndrome. Useful treatment includes aspirin[5], heparin[6] and beta-blockers[7], as well as conventional anti-anginal treatments. Several newer antithrombotic agents have been investigated for treating these

*See Appendix for list of participating hospitals, investigators and co-ordinators.

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syndromes, including low molecular weight heparin[8], platelet glycoprotein IIb/IIIa receptor agonists[9,10] and direct antithrombin agents such as hirudin[11]. Investigation with angiography and subsequent revascularization has an important place in the management of these syndromes, although the optimal timing and frequency of these interventions is still under investigation[12]. There is very little contemporary information available about unstable angina and non-ST elevation myocardial infarction in the U.K. We undertook the Prospective Registry of Acute Ischaemic Syndromes in the U.K. (PRAIS-UK) to determine characteristics, practice patterns, outcomes and important markers of risk of patients admitted to a wide range of U.K. hospitals with acute coronary syndromes without ST elevation.

Methods

The study was designed as a prospective observational cohort registry of patients admitted to U.K. hospitals with acute coronary syndromes. A total of 56 U.K. hospitals participated. Each hospital was asked to collect data on 20 consecutive patients admitted with acute coronary syndromes without ST elevation, irrespective of admission location or consultant team. Patients had a follow-up visit at 6 months following their initial hospital admission. To select sites we constructed a random sampling framework of 69 U.K. hospitals admitting patients with acute coronary syndromes, expecting the eventual response rate to be 80% (55 hospitals) Only 50% of the original sample responded positively to our invitation to participate. The main reason for non-participation was an apparent lack of resources to complete the study. The numbers were made up to 56 by inviting other hospitals to take part.

Patients were eligible if they were admitted to the hospital (either through casualty or directly to the wards) with a primary clinical diagnosis of acute coronary syndromes without ST elevation (unstable angina or suspected non-Q wave myocardial infarction). ECG abnormalities consistent with myocardial ischaemia were required, but patients with a typical history and a normal ECG at the time of hospital presentation were included if they had pre-existing evidence of coronary artery disease (e.g. prior myocardial infarction, prior revascularization). Patients were required to give written informed consent. The exclusion criteria were ST elevation >1 mm in two or more contiguous leads on the ECG or planned or actual treatment with thrombolytic therapy on admission. The study was approved by the Multicentre Research Ethics Committee and the Local Research Ethics Committees of each participating hospital.

Outcomes of interest included death, new myocardial infarction, refractory angina and readmission with unstable angina. The definition of new myocardial infarction required at least two of the following: (1) new severe cardiac chest pain, (2) creatine kinase or other cardiac enzyme rise to twice the upper normal limit, (3) new ECG changes (either prolonged ST elevation or new Q waves). Refractory angina was defined as new cardiac chest pain in hospital with associated ECG changes consistent with ischaemia lasting at least 5 min despite optimal medical therapy (including intravenous nitrates) and leading to either thrombolysis for threatened myocardial infarction, insertion of an intra-aortic balloon pump or revascularization within 7 days of its onset.

Data were collected on case report forms that were sent to the co-ordinating centre at the Royal Brompton Hospital. Data checks for completeness and consistency were performed and edit queries generated. A random sample of eight centres was visited (15% of the total) for source data verification and to verify the screening methods used.

Statistical issues

A pragmatic sample size of 1000 patients was estimated to be sufficient to carry out a risk stratification analysis using the major baseline prognostic variables such as age and ECG. We estimated that for death or non-fatal myocardial infarction we would have 120 events and for the composite of death, non-fatal myocardial infarction, refractory angina and readmission for unstable angina we would have 250 events. Analysis was performed using Stata software. Comparison of proportions were made using the chi-squared test. Multiple logistic regression was used to determine whether prognostic variables were still statistically significant when corrected for other variables that were significantly associated with adverse outcomes on the univariate analysis.

Results

A total of 1046 patients were entered into the registry from 56 participating centres between 23 May 1998 and 3 February 1999. Six hospitals recruited less than 20 patients as they were unable to complete recruitment before the pre-specified termination date for the end of the screening phase of the study. One hospital apparently recruited 15 patients, but no data were received. Comparison of data from the original sample hospitals with non-sample hospitals did not show any important differences in baseline characteristics, medical history or outcomes (data not shown). Data at 6 months were unavailable for 1031 (99%) of the patients. On-site monitoring revealed no evidence of the systematic exclusion of eligible patients and less than 1% of data points were incorrectly completed.

Baseline characteristics

The mean age at presentation was 66 ± 12 years; 61% were male, 16% had diabetes, 37% treated hypertension, 23% were current smokers, 48% had had a prior

Table 1 Baseline characteristics

Characteristic	All patients (n=1046)	Number in each group
Age (years)		
Mean	66 ± 12	
<60	32·7%	342
60–70	27·2%	284
>70	40·2%	420
Time from pain onset (h)	3 (IQR 1·5–8·2)	
Admitted with chest pain	71·9%	752
Systolic BP (mmHg)	147 ± 29	
Diastolic BP (mmHg)	82 ± 16	
Heart rate (beats . min^{-1})	78 ± 19	
MI associated with admission symptoms	13·9%	145
ECG		
Normal	15·9%	166
ST depression/BBB	29·1%	304
Other changes	55·0%	576
Gender (% male)	60·7%	635
Diabetes	16·3%	170
Treated hypertension	37·1%	388
Prior stroke	7·7%	81
Heart failure	13·3%	139
Current smoker	22·9%	239
Prior angina	74·4%	778
Prior MI	48·2%	504
Prior PTCA	13·4%	140
Prior CABG	13·6%	142

IQR=interquartile range, BP=blood pressure, ECG=electrocardiogram, BBB=bundle branch block, MI=myocardial infarction, PTCA=percutaneous transluminal coronary angioplasty, CABG=coronary artery bypass grafting.

Table 2 Outcomes

Outcomes	In-hospital n=1046		6 months n=1033	
	%	n	%	n
Death (%)	1·5	16	7·4	76
New MI (%)	3·9	41	7·3	75
RFA/readmission with UA	3·2	36	17·0	175
Death/MI	5·0	51	12·2	136
Death/MI/RFA/UA	7·6	81	30·0	316
Stroke	0·5	5	1·5	15
Death/MI/stroke	5·3	55	14·8	152
Heart failure	8·0	83	12·6	130
Major bleed	0·8	9	1·6	17

MI=myocardial infarction, RFA=refractory angina (in-hospital), UA=unstable angina after hospital discharge.

myocardial infarction and 23% prior revascularization (either PTCA or CABG). The admission clinical diagnosis was unstable angina in 95% and myocardial infarction without ST elevation in 5% of patients. Based on cardiac enzyme elevation at hospital admission, 13·9% had myocardial infarction associated with admission symptoms. Baseline data are summarized in Table 1.

Rates of major adverse outcomes (Table 2)

Rates of death were 1·5% and 7·4% in-hospital and at 6 months respectively, and rates of myocardial infarction were 3·9% and 7·3% respectively. For the composite of death or new, non-fatal myocardial infarction, the rates were 5·0% and 12·2%. For the combination of death, myocardial infarction, refractory angina or readmission for unstable angina, rates of events were 7·6% and 30·0% respectively.

Influence of baseline variables on prognosis

In univariate analyses, age, ECG category, prior heart failure, male sex, low admission systolic blood pressure, high admission heart rate and prior PTCA were associated with an increase in death or new myocardial infarction. A multivariate analysis was performed to account for interactions between these variables. In this analysis, the odds ratios (OR) for the composite of death or non-fatal myocardial infarction for age strata 60–70 and >70 years were 2·2 (95% confidence interval [CI] 1·21–3·95, $P=0·01$) and 3·5 (95% CI 2·03–5·87, $P<0·001$), respectively, compared with <60 years. The rates for death or new myocardial infarction were 5·7%, 11·7% and 17·3% for those aged <60, 60–70 and >70 years, respectively. When baseline ECG was divided into three categories (normal, T inversion or other abnormality, ST segment depression $\geq$1 mm or any bundle branch block [BBB]), the rates of death/new myocardial infarction were 6·0%, 10·4% and 25·3%, respectively. In the multivariate analysis, the OR for death or myocardial infarction for T inversion on the ECG was 3·16 (95% CI 1·11–8·97, $P=0·03$) and for ST depression or BBB was 5·02 (95% CI 1·66–15·12, $P=0·004$) compared with normal ECG. Other significant markers of risk were gender and a history of heart failure. These data are summarized in Table 3. The rate of death or non-fatal myocardial infarction in patients >70 years and ST depression or BBB on the ECG was 31·7% (12·0 of the population), while the risk for <60 years with normal ECG was 4% (4·6 of the population). The interaction between each age stratum and the three ECG categories is shown in Fig. 1.

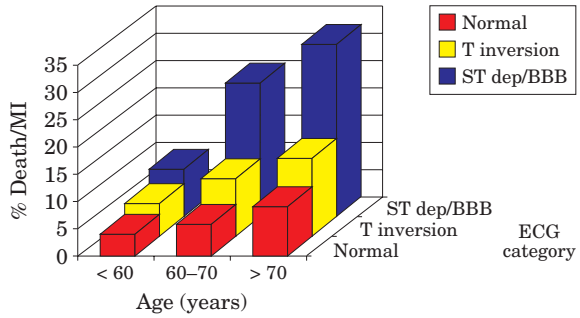
Creatine kinase measurements were available for 904 patients (86%). Analyses of baseline creatine kinase, peak creatine kinase or rise of creatine kinase were not predictive of adverse outcome. Creatine kinase-MB measurements were available in 16·7% of patients. Troponin was measured in 4·6% of patients and stress testing in 13% (1% with thallium) prior to hospital discharge.

In a Kaplan–Meier analysis of the time to first event, most of the risk for major adverse events occurred in the first 30 days following admission. However, there was continuing risk throughout the 6-month follow-up, especially for the composite outcome of death, new

Table 3 Multivariate analysis for risk of death or non-fatal myocardial infarction at 6 months

Factor	Odds ratio	95% Confidence interval	*P*
ECG on admission			
Normal	1		
ST↓/BBB	5·02	1·66–15·12	0·004
Other	3·16	1·11–8·97	0·03
Age			
Age per 5 years increase	1·24	1·12–1·37	<0·001
<60	1		
60–70	2·2	1·21–3·94	0·01
>70	3·5	2·03–5·87	<0·001
Gender (M:F)	1·64	1·07–2·52	0·02
Heart failure	1·88	1·14–3·12	0·01
Diabetes	1·56	0·95–2·56	0·08
Prior PTCA	1·61	0·95–2·73	0·08
Systolic BP (per 10 mmHg)	0·94	0·88–1·01	0·09
Heart rate (per 5 beats . min^{-1})	1·00	1·00–1·01	0·21
Prior aspirin use	0·79	0·52–1·21	0·28
Prior MI	1·02	0·66–1·57	0·93

CI=Confidence intervals, ECG=electrocardiogram, BBB=bundle branch block, BP=blood pressure, MI=myocardial infarction, PTCA=percutaneous transluminal coronary angioplasty.



T inversion - T wave inversion; Q waves or other abnormalities; BBB - bundle branch block

Figure 1 **Six-month risk of death or new myocardial infarction (MI) stratified by age and ECG.**

myocardial infarction, refractory angina or re-admission for unstable angina (Fig. 2).

Treatments

The median time from symptom onset to hospital admission was 3 h (interquartile range [IQR] 1·5–8·2 h). First admission was to a coronary care unit in 38% of patients and to an acute admissions ward (defined as an area with cardiac monitoring facilities) in 46%. The median length of stay in hospital was 5 days (IQR 2–7 days).

Heparin (either intravenous unfractionated or low molecular weight) was used in 72% of patients. Low molecular weight heparin was used in 38% and intravenous unfractionated heparin in 28%. Both were used in 6%. Median duration of treatment for patients receiving unfractionated heparin was 2 days (IQR 1–3) and for those receiving low molecular weight heparin 3 days (IQR 2–4). The use of oral drug therapies is summarized in Fig. 3. Aspirin was used in 64% in patients on admission, 87% in-hospital and 78% at 6 months, beta-blockers were used in 32%, 50% and 41% and calcium antagonists in 40%, 54% and 41%, respectively. Intravenous nitrates were used in 31% and other nitrates (oral or buccal) in 79% of in-hospital patients.

Angiography and revascularization

The number of hospitals with cardiac catheterization facilities was 28 (50%) and cardiac surgery facilities eight (14%). The overall rate of coronary angiography, PTCA and CABG in-hospital and at 6 months was 10% and 27%, 4% and 8% and 2% and 7%, respectively. At 6 months, 3% of patients were on a waiting list for angiography and a further 3% were on a waiting list for revascularization (either PTCA or CABG). The probability of undergoing coronary angiography, PTCA and CABG during the index hospital admission to a hospital with cardiac catheterization facilities compared with a hospital without these facilities, was 17% and 3%, 7% and 1% and 4% and 0%, respectively ($P<0·01$ for all comparisons).

We performed a multivariate regression analysis to determine patient characteristics that were associated with receiving angiography. The following variables associated with increased risk of death or new myocardial infarction in this population were used: increasing age, gender, prior history of heart failure and baseline ECG. The interaction between rates of angiography at 6 months, age and admission ECG category is shown in Fig. 4. The odds ratios for angiography at 6 months for age strata 60–70 and >70 years were 0·79 (95% CI 0·57–1·11, P=NS) and 0·38 (95% CI 0·27–0·54, $P<0·0001$), respectively, compared with <60 years. The rate was 29·1% in men compared with 25·3% in women (OR 0·95, 95% 0·71–1·28, $P=0·8$) and 16·0% for those with a prior history of heart failure compared with 29·3% for those without (OR 0·60, 95% CI 0·37–098, $P=0·03$). For those with ST depression or BBB, the rate was 27·7% compared with 25·0% and 28·3% in those with a normal ECG or T inversion respectively.

Lipid management

Overall, 28%, 43% and 44% were taking a statin on admission, at discharge and at the 6-month follow-up respectively. Total cholesterol was measured in 63% of patients. When total cholesterol was divided into four strata (total cholesterol <5·0, 5·0–<6·0, 6·0–<7·0, $\geq$7·0 mmol . l^{-1}), 50% of those already taking statins had a total cholesterol <5·0 mmol . l^{-1} compared with

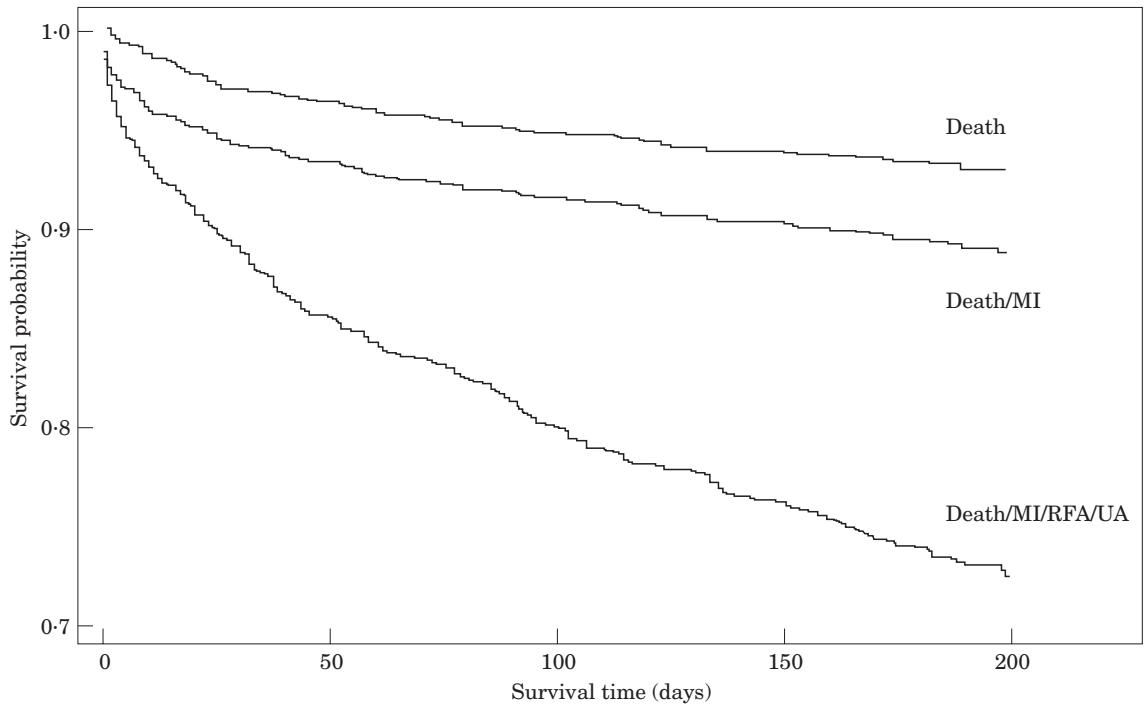


Figure 2 **Kaplan–Meier curves for events from index admission. Death/MI=death or new myocardial infarction; Death/MI/RFA/UA=death, new myocardial infarction, refractory angina or readmission for unstable angina.**

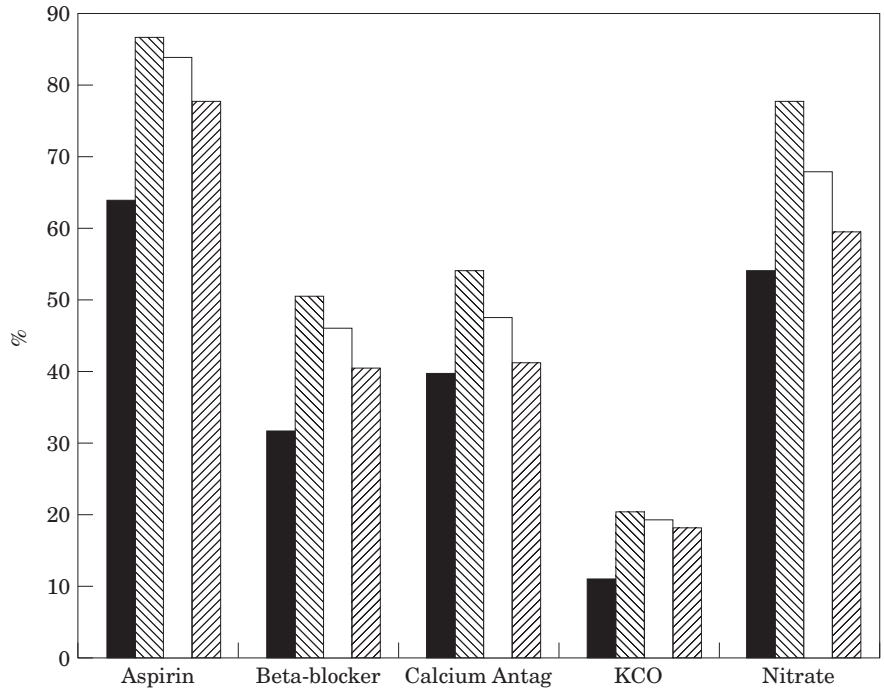
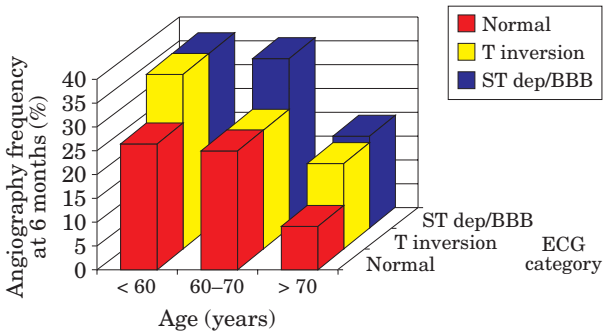


Figure 3 **Oral drug treatments. Calcium antag=calcium channel blockers; KCO=potassium channel openers; Nitrate=oral, buccal or tropical nitrates. ■=admission, ▧=in-hospital, □=at discharge, ▨=at 6 months.**

20% of those not taking a statin ($P<0{\cdot}001$) and 12% and 47%, respectively, had a total cholesterol $\geq 6{\cdot}0$ mmol . l^{-1} ($P<0{\cdot}001$). There was a strong positive relationship between measured total cholesterol and the probability of receiving a statin at discharge and 6 months ($P<0{\cdot}001$ for trend). Patients with total



T inversion - T wave inversion; Q waves or other abnormalities; BBB - bundle branch block

Figure 4 **Six-month angiography rates stratified by age and admission ECG.**

cholesterol 6·0–7·0 and $\geq$7·0 mmol . l^{-1} had a 52% and 47% probability respectively of not receiving a statin over a 6-month follow-up.

Discussion

Our study enrolled a very high proportion of patients with acute coronary syndromes and documented coronary artery disease. Death, new myocardial infarction, refractory angina or readmission for unstable angina at 6 months occurred in about one-third of patients. Thus PRAIS-UK found that acute coronary syndromes without ST elevation carry a substantial burden of mortality and morbidity with continuing risk at 6 months. Age and baseline ECG provide much of the prognostic information. About 30% of patients did not receive an effective heparin regimen in hospital and, by 6 months, nearly one-quarter of patients were not taking aspirin. Angiography was performed in about one-quarter of patients at 6 months and revascularization in about one-sixth. Angiography rates were lower in some higher risk categories including older patients or those with prior heart failure. The majority of patients were not treated with a statin, including about half of those with high cholesterol and established coronary artery disease.

The GUSTO IIb study enrolled 12 142 patients with acute coronary syndromes and an abnormal ECG[13]. Early mortality was higher in those presenting with ST elevation than ST depression. By 20 days the mortality curves had crossed and at 6 months mortality in patients with ST elevation was 6·8% compared with 8·9% in those with ST depression. The combined end-point of death or myocardial infarction was 12·3% and 15·4%, respectively. The OASIS registry enrolled similar patients to PRAIS-UK from six countries (U.S.A., Australia, Brazil, Canada, Poland, Hungary)[14]. The rate of death was 4·7% at 6 months in the 7987 OASIS registry patients compared with 7·4% in PRAIS-UK. The combination of death or non-fatal myocardial infarction occurred in 11% versus 12·2% respectively. A smaller American registry of 393 patients[15] also identified age and ST depression as important predictors of adverse outcomes, but PRAIS-UK provides stronger correlation with clear gradation of risk in the important subgroups (Fig. 1). Troponin measurement[16] and stress testing[3] have been shown to be useful in identifying high-risk patients who may benefit from more intensive management but both strategies were used infrequently in our cohort. In addition, the use of specialized chest pain units may allow more appropriate risk stratification[17].

The benefits of antithrombotic treatments with heparin and aspirin for acute coronary syndromes without ST elevation are well established[18]. Intravenous unfractionated heparin has been standard treatment, but the use of low molecular weight heparins was higher in our study[19]. The use of aspirin, heparin and beta-blockers in our study was lower than in the OASIS registry. For secondary prevention of acute coronary syndromes without ST elevation, European[20] and U.K. guidelines[21] state that total cholesterol should be measured on admission in all patients, and statin treatment started immediately if total cholesterol is $\geq$6·0 mmol . l^{-1}. Our data suggest that in spite of these guidelines only a minority of eligible patients receive statins and that a sizeable proportion of those who do receive treatment still have an elevated total cholesterol. The use of statins for similar patients recruited in the 4S[22], LIPID[23] and CARE[24] was associated with about one-quarter to one-third relative risk reduction for death and major cardiovascular events.

Overall rates of angiography and revascularization at 6 months in the U.K. were comparable to those seen in Poland and Hungary (the lowest tertile in the OASIS registry). The European Society of Cardiology Working Group reported that rates of coronary angiography and PTCA in the U.K., corrected for population, were about one-third of those in Germany, about half of those in France and about the same as those in Italy[25]. The ENACT Registry (in this issue, page 1440) confirms these observations. The U.K. has high rates of coronary artery disease and there are concerns that revascularization rates may be inappropriately low. However, no optimal rate or timing for these interventions in acute coronary syndromes without ST elevation has yet been established[12,26]. The TIMI III registry of patients with unstable angina found that women were treated less intensely than men and that there was less angiography performed in the elderly[27], but overall rates of angiography were higher in all TIMI groups than in our study. The Fragmin during Instability in Coronary Artery Disease (FRISC) 2 study supports a strategy of routine angiography and subsequent revascularization for patients with acute coronary syndrome without ST elevation[28].

Although a representative sample of U.K. hospitals was planned, the final sample was achieved by inviting a broad range of hospitals. The hospitals involved serve about 14 million people, or one-quarter of the U.K. population. In addition, there were no discernible

differences in the patients and outcomes between hospitals included in the original sample and those that were not. For these reasons, we believe that the results are generalizable to the U.K. as a whole.

Based on our findings, an increase in the use of existing effective treatments like aspirin, heparin, beta-blockers and statins, and optimization of angiography and revascularization, are needed in the U.K. The introduction of newer effective treatments like glycoprotein IIb/IIIa receptor antagonists is likely to be important especially for higher risk patients[9,10]. Our experience demonstrates that contemporary observational registries identify potential deficiencies in treatment strategies, and can help to guide improvements.

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Appendix

Participating hospitals and investigators

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Hospital, Birmingham, P. Ludman, J. Pitt; *Borders General Hospital, Melrose*, P. Broadhurst, D. Edgar; *Bradford Royal Infirmary, Bradford*, C. Morley, T. Kurdziel; *City Hospital, Dudley*, T. Millane, L. Cadd; *Cumberland Infirmary, Carlisle*, R. H. Robson, M. Weston, A. Graham; *Dryburn Hospital, Durham*, G. Terry, J. Close; *Ealing Hospital, London*, J. Kooner, N. Smith; *East Surrey Hospital, Redhill*, J. P. Lyons, M. Sopher, E. Behr; *University Hospital Aintree, Liverpool*, E. A. Rodrigues, A. Robinson; *Glasgow Royal Infirmary, Glasgow*, S. Cobbe, H. Young; *Hammersith Hospital, London*, R. Hall, C. Shilling; *Hillingdon Hospital, London*, G. C. Sutton, H. Penston, S. McDonagh; *Hull Royal Infirmary, Hull*, J. L. Caplin, A. Beasty; *Ipswich Hospital, Ipswich*, N. Irvine, J. Greenfield; *John Radcliffe Hospital, Oxford*, Y. Bashir, A. Dury; *Kettering General Hospital, Kettering*, P. S. Astridge; *King George Hospital, Ilford*, A. Deaner, D. Mulvey; *Leicester General Hospital, Leicester*, A. Scriven, K. Tordoff; *Lewisham Hospital, London*, S. Lewis, K. Marshall, P. Marley; *Nevill Hall Hospital, Abergavenny*, S. J. Hutchison, J. Austin, J. Hillman; *North Devon District Hospital, Barnstaple*, T. L. Roberts; *North Tees General Hospital, Stockton-on-Tees*, R. H. Smith, J. Wardle; *Northampton General Hospital, Northampton*, D. C. Sprigings, J. O'Callaghan; *Nottingham City Hospital NHS Trust, Nottingham*, G. K. Morris, A. Ahsan, K. Knowles; *Pinderfields General Hospital, Wakefield*, P. Batin, C. Taylor, J. I. Wilson; *Queen Margaret Hospital NHS Trust, Dunfermline*, D. C. Macleod, P. Rodger; *Royal Alexandra Hospital, Paisley*, I. Findlay, K. Mowat; *Royal Cornwall Hospital, Truro*, A. J. Mourant, A. Mitchell; *Royal Gwent Hospital, Newport*, J. Davies, M. Williams, T. Watton; *Royal Hallamshire Hospital, Sheffield*, K. S. Channe, M. Ferrar, A. Birchall, H. Parry; *Royal Infirmary of Edinburgh, Edinburgh*, K. A. A. Fox, K. Carruthers, L. Smythe; *Royal Sussex County Hospital, Brighton*, C. Davidson, N. Morris, E. Joyce; *Royal United Hospital NHS Trust, Bath*, W. N. Hubbard, J. Wallace; *Royal Victoria Hospital, Belfast*, J. Adgey, L. Hill; *Royal Victoria Infirmary NHS Trust, Newcastle*, P. C. Adams, C. Albers, M. Thompson; *Sandwell District General Hospital, West Bromwich*, R. A. S. Ahmad, M. Pritchard; *Scunthorpe General Hospital, Scunthorpe*, J. Dhawan, M. Webb, D. Remington; *Stirling Royal Infirmary, Stirling*, A. Bridges, C. Mondoa; *Stobhill Hospital, Glasgow*, F. G. Dunn, A. Wright; *Sunderland Royal Hospital, Sunderland*, S. Pugh, Z. Htet, M. Farrer; *Tameside and Glossop Acute Services NHS Trust, Ashton-under-Lyne*, M. H. Husaini, S. Horner, A. Saha; *Torbay Hospital, Torquay*, P. J. Keeling, D. Hughes; *University Hospital, Nottingham*, J. R. Hampton, M. Melville; *Victoria Hospital, Blackpool*, M. J. Brack, L. Radford; *Walsgrave Hospital, Coventry*, R. Mattu, W. K. Lee; *West Suffolk Hospital, Bury St Edmunds*, D. L. Stone, S. Reader, A. Mortimer; *Whipps Cross Hospital, London*, J. Hogan, B. Coleman; *Whiston Hospital, Prescot*, J. Ball, S. Houghton; *Wycombe General Hospital, Wycombe*, W. G. Hendry, J. Wiltshire; *York District Hospital, York*, R. M. Boyle, S. Wiseman.

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