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Title: Excess mortality and guideline-indicated care following non ST-elevation myocardial infarction

Authors

Tatendashe B Dondo[1], Marlous Hall[1], Adam D Timmis[2], Mark S Gilthorpe[1], Oras A Alabas[1], Phillip D Batin[3], John E Deanfield[4], Harry Hemingway[5] and Chris P Gale[1,6]

Affiliations

[1]Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, UK

[2]The National Institute for Health Biomedical Research Unit, Barts Health, UK

[3]Department of Cardiology, The Mid Yorkshire Hospitals NHS Trust, UK.

[4]National Institute for Cardiovascular Outcomes Research, University College London, UK.

[5]The Farr Institute, University College London, UK.

[6]York Teaching Hospital NHS Foundation Trust, UK.

Correspondence:

Chris P Gale

Leeds Institute of Cardiovascular and Metabolic Medicine

MRC Bioinformatics Unit, Level 11

Worsley building, Clarendon way

University of Leeds

Leeds, LS2 9JT, UK.

Email: c.p.gale@leeds.ac.uk

Abstract

Background

Adherence to guideline-indicated care for the treatment of non ST–elevation myocardial infarction (NSTEMI) is associated with improved outcomes. We investigated the extent and consequences of non–adherence to guideline-indicated care across a national health system.

Methods

Cohort study (ClinicalTrials.gov NCT02436187) using data from the Myocardial Ischaemia National Audit Project (n=389,057 NSTEMI, n=247 hospitals, England and Wales, 2003 to 2013). Accelerated failure time models were used to quantify the impact of non-adherence on survival according to dates of guideline publication.

Results

Over 1,079,044 person-years (median 2.2 years follow up), 113,586 (29.2%) NSTEMI died. Of those eligible to receive care, 337,881 (86.9%) did not receive one or more guideline-indicated intervention; the most frequently missed were dietary advice (n=254,869, 68.1%), smoking cessation advice (n=245,357, 87.9%), P2Y12 inhibitors (n=192,906, 66.3%), and coronary angiography (n=161,853, 43.4%). Missed interventions with the strongest impact on reduced survival were coronary angiography (time ratio 0.18, 95% confidence interval [CI] 0.17 to 0.18), cardiac rehabilitation (0.49, 0.48 to 0.50), smoking cessation advice (0.53, 0.51 to 0.57) and statins (0.56, 0.55 to 0.58). If all eligible patients in the study had received optimal care at the time of guideline publication, then 32,765 (28.9%) deaths (95% CI 30,531 to 33,509) may have been prevented.

Conclusion

The majority of patients hospitalised with NSTEMI missed at least one guideline-indicated intervention for which they were eligible. This was significantly associated with excess mortality. Greater attention to the provision of guideline-indicated care for the management of NSTEMI will reduce premature cardiovascular deaths.

Keywords: NSTEMI, excess mortality, National Health Service, evidence-based medicine, MINAP, electronic health records

Introduction

Cardiovascular disease is the main cause of death in Europe, with coronary heart disease accounting for 20% (1.8 million) of all deaths in Europe annually.[1] Associated productivity losses, direct health care costs and informal care, due to mortality and morbidity, cost the European Union economy €60 billion a year.[2] In America, non-ST-elevation myocardial infarction (NSTEMI) and unstable angina are the leading causes of hospitalisation.[3] Moreover, the global burden of NSTEMI persists despite substantial improvements in its treatment .[4, 5]

Among patients hospitalised with NSTEMI, survival is better for those who receive timely guideline-indicated care.[4, 6] A number of cohort studies have shown that improving adherence to evidence-based interventions reduces the risk of death after NSTEMI.[7-9] International guidelines for the management of NSTEMI advocate a series of hospital-based interventions supported by evidence from trials and observational data.[10, 11] Even so, a large proportion of patients fail to receive appropriate care. In a study of 5353 patients with acute myocardial infarction (AMI), optimal medical therapy was not provided to almost half .[12] Another study of patients with AMI found that of those who were eligible for nine evidence-based interventions 50.6% missed at least one.[13]

Thus far, however, studies concerning the relationship between mortality and care for AMI have been based on select cohorts, limited through non-contemporaneous, administrative or insurance–based databases.[7, 12, 14] None has specifically studied NSTEMI, arguably the most vulnerable of AMI phenotypes,[15] and none quantified the avoidable harm associated with sub-optimal implementation of care across a single health system. Consequently, the excess death associated with the degree of non-adherence to guideline-indicated care for NSTEMI is not

known. To address this, we used data from the UK national heart attack register (Myocardial Ischaemia National Audit Program, MINAP), which collects data from one health system (the National Health Service) including all hospitals in England and Wales.

Methods

Setting and design

The analyses were based on data from MINAP, a comprehensive registry of acute coronary syndrome hospitalisations mandated by the Department of Health.[16] The analytical cohort (n=389,057) was drawn from 441,945 patients with NSTEMI admitted to one of 247 hospitals between 1st January 2003 and 30th June 2013. Patients were eligible for the study if they were ≥18 years of age. The discharge diagnosis was used to identify patients with NSTEMI. For patients with multiple admissions the earliest record was used (to reduce potential biases from previous treatment from multiple events). We excluded 31,321 (7.1%) patients because they died in hospital (and we could not, therefore, accurately ascertain their receipt of pharmacological therapies) and 21,567 (4.9%) patients due to missing mortality data (Figure 1). Patient-level data concerning demographics, cardiovascular risk factors, medical history and clinical characteristics at the time of hospitalisation were extracted. Ethical approval for this study was not required under NHS research governance arrangements. The National Institute for Cardiovascular Outcomes Research (NICOR) which includes the Myocardial Ischaemia National Audit Project (MINAP) database (Ref: NIGB: ECC 1-06 (d)/2011) had support under section 251 of the National Health Service (NHS) Act 2006 to use patient information for medical research without consent. The study was conducted complying with the Declaration of Helsinki.

Guideline-indicated interventions

The European Society of Cardiology (ESC) guidelines for the management of NSTEMI and ESC Expert Consensus Documents were mapped to MINAP data to identify guideline-indicated interventions as they became available over the study period (supplementary section 1). Data contained information corresponding to the following 13 interventions: electrocardiogram, prescription of aspirin acutely, P2Y12 inhibitors at discharge, aspirin at discharge, beta blockers at discharge in patients with left ventricular systolic dysfunction, angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB) in patients with left ventricular systolic dysfunction, a HMG CoA reductase enzyme inhibitors (statins), in-hospital use of aldosterone antagonist in patients with left ventricular systolic dysfunction and either diabetes or heart failure without significant renal dysfunction, echocardiogram, use of early invasive procedures (coronary angiography), smoking cessation advice, dietary advice, and enrolment into a cardiac rehabilitation programme.[10] We used the adjusted mini–Global Registry of Acute Coronary Events (GRACE) risk score[17] to categorise NSTEMI as lowest (≤70), low (71 to 87), and intermediate to high risk (>88) in line with NICE guidance.[18] We quantified receipt of care only for patients who were deemed eligible for each treatment according to ESC guidelines. Patients were also classified as ineligible if a treatment was contra-indicated, not indicated, not applicable, if the patient declined treatment as recorded in MINAP or if the patient was hospitalised prior to the time the treatment was recommended by the guidelines.

Survival analysis

Multilevel accelerated failure time models were used to identify the association between missed guideline-indicated interventions and time to all-cause mortality (supplementary section 3). All models included a shared frailty term to account for clustering of patients within hospitals. Models were adjusted for case mix using the adjusted six-month mini–GRACE risk

score and for baseline patient characteristics including: previous history of AMI, angina, diabetes, hypertension, peripheral vascular disease, a family history of coronary heart disease, chronic obstructive pulmonary disease, hypercholesterolaemia and previous coronary revascularisation. Missing data were imputed using multiple imputation by chained equations for missing GRACE covariates and a default imputation strategy based on clinical expert opinion implemented for selected treatment variables (supplementary section 2). Imputation results were checked for reliability and consistency using Monte Carlo estimates and through comparison with complete case analysis (supplementary section 3). Parameter estimates were expressed as time ratios (TR) and 95% confidence intervals (CI) pooled over the 10 imputations. A TR of ≤1 indicates reduced expected survival time and, therefore, worse survival associated with the missed guideline-indicated intervention.

Excess deaths

For each patient, a score was derived by dividing the total number of interventions received by the total number of interventions that the patient was eligible for. The score was categorised into optimal care (all interventions received) or not (sub-optimal care). Using optimal care as the reference, the dichotomised score was regressed on time to death/censorship. The resultant adjusted TR was multiplied by the one year mortality rate and by the proportion of patients in the sub-optimal category. The product was then multiplied by the total number of NSTEMI between 2003 and 2013 (supplementary section 4). As a sensitivity analysis, we used latent class analysis to model the interaction of all 13 guideline-indicated interventions on survival (supplementary section 5). Briefly, latent class analysis (LCA) is a statistical method that identifies underlying subgroups of individuals based on observed characteristics. Three subgroups of care (latent classes) were identified, which represented homogenous patterns of the probability of receipt of care. The classes were then regressed on time to death/censorship

and the adjusted TRs multiplied by the one year mortality rate for the corresponding class and by the proportion of patients in that class. This figure was then multiplied by the total number of NSTEMI between 2003 and 2013.

Results

Of 389,057 patients with NSTEMI (mean age 70.9 (SD 13.3) years, 63.1% male, the majority (93.3%) were white, one third (31.5%) had angina and a quarter (24.9%) previous AMI (Table 1). Over half (71.8%) were smokers ever/ current, 48.5% had hypertension, 20.9% diabetes and 14.6% had asthma or COPD. Over 2% of patients had an admission systolic blood pressure <90 mmHg. About half (56.8%) of all electrocardiographic changes were ST-segment deviation or T-wave inversion with 15.7% of patients having no acute changes. According to the mini-GRACE risk score, eight in ten patients were intermediate or high risk.

Guideline-indicated interventions

Only 51,176 (13.2%) patients received all of the interventions for which they were eligible and 337,881 (86.9%) did not receive ≥1 guideline-indicated intervention. The most frequently missed were dietary advice (n=254,869, 68.1%), smoking cessation advice (n=245,357, 87.9%), echocardiography (n=193,483, 49.7%), P2Y12 inhibitors at discharge from hospital (n=192,906, 66.3%), coronary angiography (n=161,853, 43.4%), and in–hospital aspirin (n=106,407, 45.0%) (Table 2). Figure 2 depicts the increase, from 2003 to 2013, in all guideline-indicated interventions, except for pre-hospital use of an electrocardiogram and pre-hospital aspirin which decreased.

Patterns of Care

Using the latent class analysis, we identified three patterns of care and nominally labelled them 'high', 'intermediate', and 'low'**.** Patients in the high latent class were distinguishable from other classes by their high probabilities for receipt of P2Y12 inhibitors (0.72), echocardiography (0.60), cardiac rehabilitation (0.80), dietary advice (0.78), coronary angiography (0.69) and acute aspirin (0.65), and low receipt of ACEis/ARBs (0.01) and beta blockers (0.03) (Table 3). Whilst the use of electrocardiogram, aspirin at discharge and statins at discharge were also high in this group, these interventions were not distinguishing factors from the other latent classes. Patients in the intermediate class had a low probability of echocardiography and coronary angiography (0.43 and 0.38, respectively) and very low (<0.01) probabilities of receiving P2Y12 inhibitors, aldosterone antagonist, smoking cessation advice, and dietary advice. Patients in the low class had, in addition to the care probabilities of those in the intermediate class, very low probabilities of receiving ACEis/ARBs and beta blockers (0.01 and 0.03, respectively). Overall, there were only minor differences in baseline patients' characteristics according to the latent classes (supplementary Table S38). However, class differences were most apparent by period of hospitalisation; 99.5% of those in the high receipt of care class were hospitalised between 2009 and 2013 compared with 0.5% hospitalised between 2003 and 2008.

Survival

Over 1,079,044 person years (median 2.2 years follow up, maximum 8.4 years) there were 113,586 (29.2%) deaths, corresponding to 10.5 deaths per 100 person years. The median time to death was 1.1 (IQR 0.3 to 2.4) years. There was a significant difference in unadjusted survival between those who received optimal care and those who did not (Figure 3). After adjustment, time to death among patients who did not receive ≥1 intervention was shortened by 56% (TR 0.44, 95% CI 0.41–0.45) compared with patients who received all of the

interventions for which they were eligible (Figure 4). Time to death was 16% shorter (TR 0.84, 95% CI 0.79–0.88) for patients in the intermediate latent class and 23% shorter (TR 0.77, 95% CI 0.74–0.80) for patients in the low latent class compared with patients in the high latent class (Figure 4). Missed interventions with the strongest impact on reduced survival were coronary angiography (TR 0.18, 95% CI 0.17–0.18), cardiac rehabilitation (TR 0.49, 95% CI 0.48–0.50), smoking cessation advice (TR 0.53, 95% CI 0.51–0.57), and statins (TR 0.56, 95% CI 0.55–0.58) (Figure 4).

Excess deaths

If all study patients with NSTEMI had received guideline recommended care for which they were eligible, then 32,765 (28.9%) (95% CI 30,531–33,509) deaths could potentially have been prevented. Similarly, 17,778 (15.7%) (95% CI 16,720–18,625) and 16,177 (14.3%) (95% CI 15,547–16,807) deaths may have been prevented had patients from the intermediate and low latent classes received similar care to those in the high class.

Discussion

This study quantified the excess mortality associated with non-adherence to international (ESC) guideline recommended care for patients hospitalised with NSTEMI across a single healthcare system (the National Health Service of England and Wales) over the last decade. We found that if all patients during the study period had received the investigations and treatments for which they were eligible, according to the time of publication of the guidelines, then around 33,000 deaths may have been prevented. This equates to over a quarter of all NSTEMI deaths or about one avoidable death per month per hospital over the last decade.

The care that was most frequently missed was dietary and smoking cessation advice, echocardiography to evaluative left ventricular systolic function, the prescription of P2Y12 inhibitors, coronary angiography and the acute prescription of aspirin. We found that all of the 13 care interventions if missed, except aldosterone antagonists, had significant and strong associations with reduced survival, in particular coronary angiography, cardiac rehabilitation, smoking cessation and the use of statins. Whilst we identified substantial improvements in care over the decade of study, in the latter years of study, a third of NSTEMI still did not receive treatments for which they were eligible. Moreover, we noted as we did in our earlier research, that patients who had low probabilities for receipt of pharmacological interventions also missed the opportunity to receive counselling interventions.[13]

The management of NSTEMI is supported by rigorous data from many randomised controlled trials.[10, 11] Advances in treatments for NSTEMI are reported in high impact publications and summarised in international guidelines, which are frequently updated as new evidence emerges.[10, 11] The underlying assumption is that this evidence is then translated into practice. Internationally, this has been summarised by several registries which report temporal improvements in care [5, 19, 20] and a global decline in mortality from cardiovascular disease. The management of patients with NSTEMI, however, is multifaceted and comprises a complex journey starting from a call for help to a range of hospital interventions and cardiac rehabilitation – hence many opportunities whereby care could be missed. Our investigation shows that national registry data allows higher resolution investigation of sequential care deficits significantly associated with premature cardiovascular death to be identified in a seemingly 'well-functioning' healthcare systems. Addressing these cumulative care gaps will save lives.

We found that many care interventions were frequently not provided subsequent to their recommendation in international guidelines. In England and Wales over 40,000 people per year are hospitalised with NSTEMI – suggesting that the opportunity to reduce death following NSTEMI is determined by supply factors and not its demand – yet the national healthcare system studied did not appear to enable all patients to have an equal chance of receiving specialist cardiac investigations and treatments. The care most frequently missed was that with the greatest potential to reduce death; not receiving coronary angiography was associated with a reduction in time to death of 82% and not receiving cardiac rehabilitation of 51%, whereas not receiving smoking cessation advice was associated with halving of the time to death, and missing P2Y12 inhibitors a 24% reduction. In part, this is likely to be due to constraints around the availability of specialists and associated equipment, but also perhaps because of the heterogenic approach to the management of patients with NSTEMI – which compares with the management of ST-elevation myocardial infarction that[10] for the NHS, is institutionally operationalised through a national primary PCI programme.[21-23] By contrast, the decision to prescribe evidence-based medications or to proceed to coronary angiography is determined at the level of the physician in a non-emergent setting.

Our labels of high, intermediate and low receipt of care aided interpretation of our latent class analysis. In reality, however, the classes were representative of more complex patient patterns of care rather than all patients receiving either high, intermediate or low levels of care. Patients in the high class had low probabilities for receipt of ACEis/ARBs and beta blockers. Whilst this seems incongruous, these patients did not have left ventricular systolic dysfunction and, therefore, these pharmacological medications were not indicated. In effect, high latent class patients were healthier and more likely to receive evidence-based care and confirm findings

from others who have shown that the patients who are most likely to receive guideline-indicated treatments tend to be the lower risk patients.[24-26]

This study has implications for international cardiovascular health. In line with the World Health Organisation Global Action Plan for non-communicable disease, we identify where in a modern healthcare system the provision of essential treatments is required to reduce premature death.[27] Our results may, therefore, be extrapolated to other developed and developing countries which lag behind Northern Europe and North America in their provision of care[28, 29] and where greater gains in cardiovascular health maybe realised. We clearly show that, across a modern healthcare system such as in the UK, there are substantial opportunities to improve outcomes through relatively simple measures: ensuring that all patients with NSTEMI receive appropriate guideline-indicated care.

Our study has strengths in that it evaluates care across a single healthcare system, is population-based and accesses a clinical registry designed specifically to evaluate quality of heart attack care. There are no other databases of comparable size, coverage and quality which include all hospitals within a country. However, our study has limitations. 1) We were reliant upon the accurate recording of data. 2) MINAP does not collect all cases of NSTEMI – our study was designed to study the impact of missed care at the level of the patient and not the numbers of NSTEMI hospitalised. We speculate that MINAP captures less than half of all NSTEMI in England and Wales; consequently, the number of preventable deaths that we report will be underestimated. 3) The deficits in care for smoking cessation and dietary advice may be inflated because advice about smoking and diet are implicit in cardiac rehabilitation programmes and there may have been preferencing by coders towards recording cardiac rehabilitation rather

than counselling. 4) Missing data could have biased our estimates. We studied the nature of missing MINAP data and used, where necessary, imputation algorithms. The corresponding sensitivity analyses confirmed consistent results irrespective of the method adopted. 5) The investigation of ESC guideline-indicated care for NSTEMI was not able to extend to all Class 1 Level A recommendations for the management of NSTEMI. Thus, it is possible that the deficits and their consequences are greater than we report. For example, we had insufficient data to study the prescription of anticoagulants. 6) It is probable that other factors beyond the hospital stay (such as drug adherence, number of cardiac rehabilitation sessions attended and primary care visits) may also have influenced survival. 7) We studied all-cause mortality, when non-cardiovascular deaths may not be attributable to missed NSTEMI care.[30] 8) Regarding the use of aldosterone antagonists, we found that application of the inclusion and exclusion criteria stated in international guidelines reduced the size of the exposed subgroup to such an extent that the resultant estimates were imprecise. 9) Although contraindication, refusal and non-applicability information was available in MINAP, additional reasons for those recorded simply as not having received care interventions were not available. 10) This observational study cannot demonstrate causation, though optimal adjustment was made for confounders based on available information in the study dataset and informed by external information from other studies.

Conclusion

This first national study of the pathway of care for NSTEMI has identified substantial gaps in the provision of guideline-indicated interventions as recommended by the ESC. Such deficits in care, cumulatively, were significantly associated with many premature cardiovascular deaths when compared with patients who were eligible for and received guideline-indicated care – about a third of the deaths may have been preventable. Whilst cardiovascular care has

substantially improved in modern healthcare systems with the resultant reductions in mortality, only though higher resolution investigations using whole healthcare system clinical registries can modifiable deficits of care be identified and, therefore, addressed.

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medical research without consent.

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Conflicts of interest: The authors have no conflicts of interest.

Contributorship: TBD analysed the data. CPG, OAA and MH provided scientific input. CPG, AT, HH, JED, and PDB provided expert clinical opinion and interpretation of the data. MSG provided advice on latent class analysis. All authors made critical revisions and provided intellectual content to the manuscript, approved the final version to be published and agreed to be accountable for all aspects of the work. CPG is the guarantor for this study.

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Figure Legends

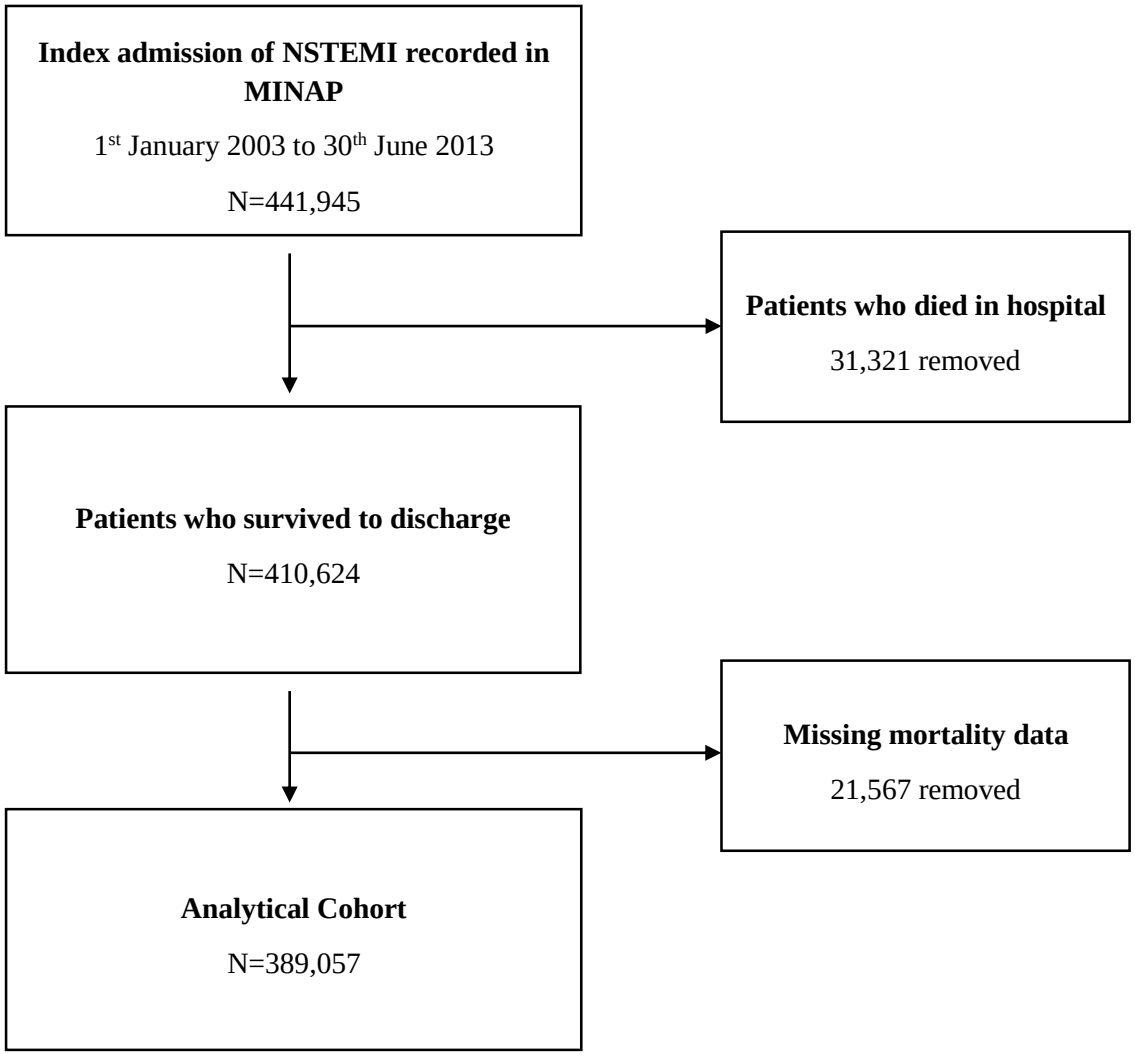
Figure 1. STROBE diagram showing the derivation of the analytical cohort from the Myocardial Ischaemia National Audit Project (MINAP) dataset

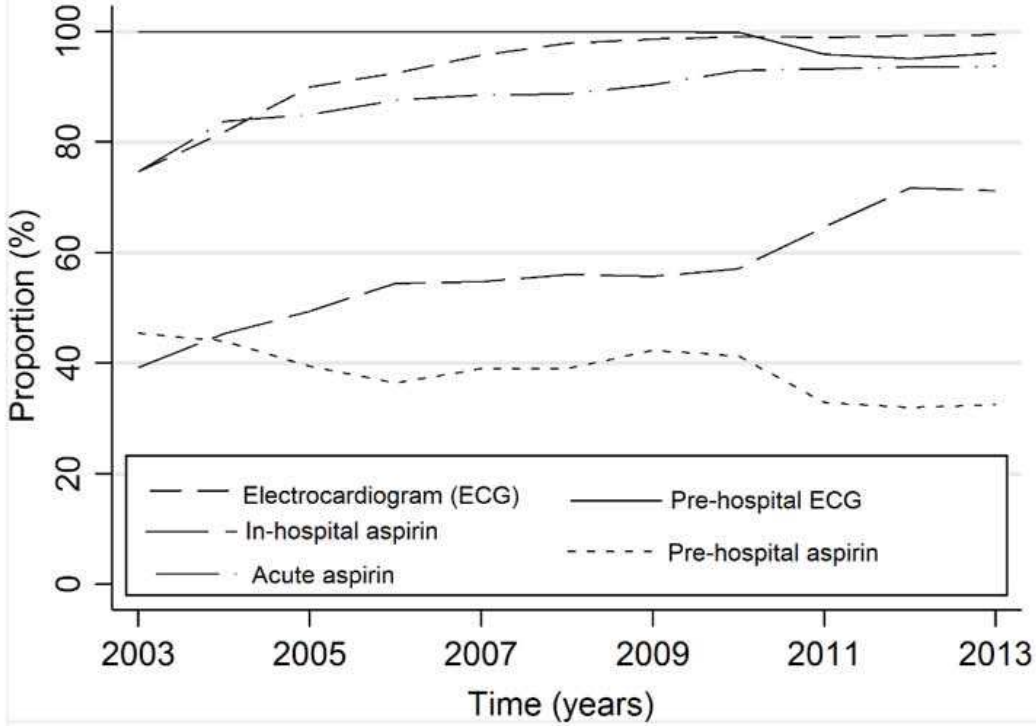
Figure 2. Temporal trends in guideline-indicated interventions by year of publication of ESC guidelines

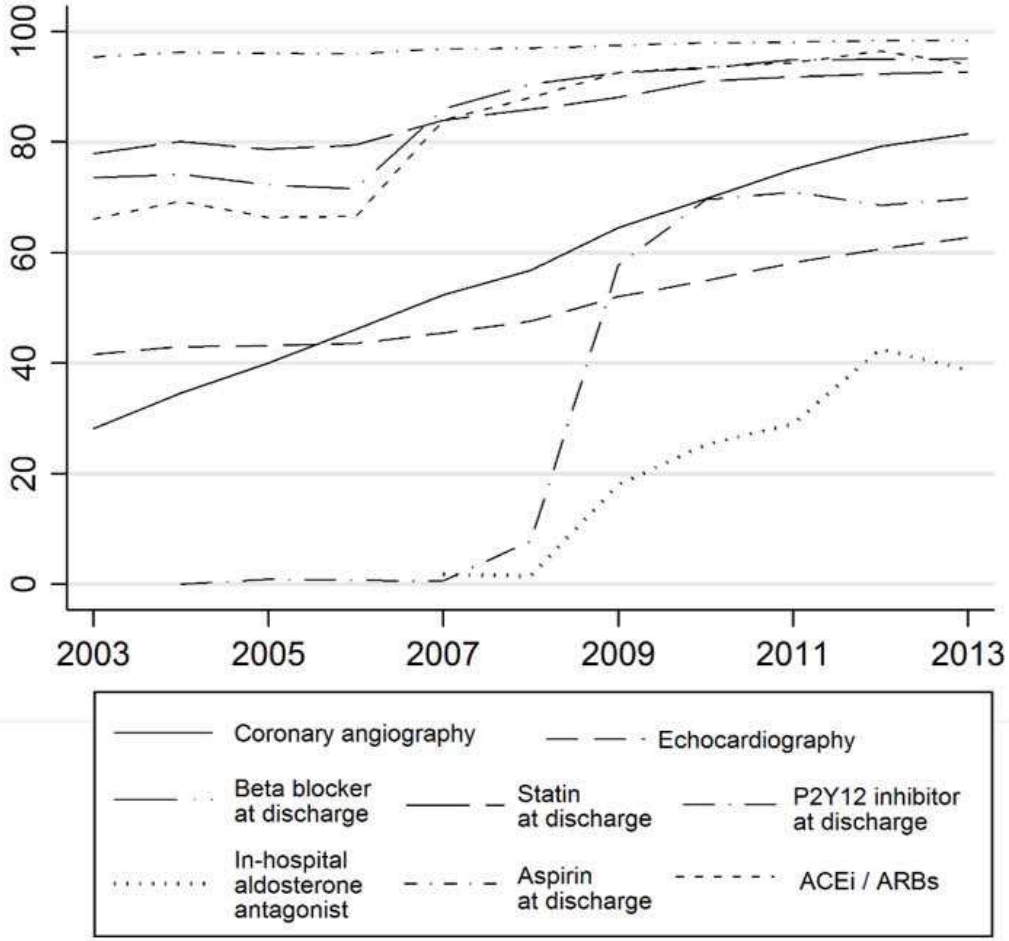
Figure 3. Unadjusted Kaplan-Meier survival estimates

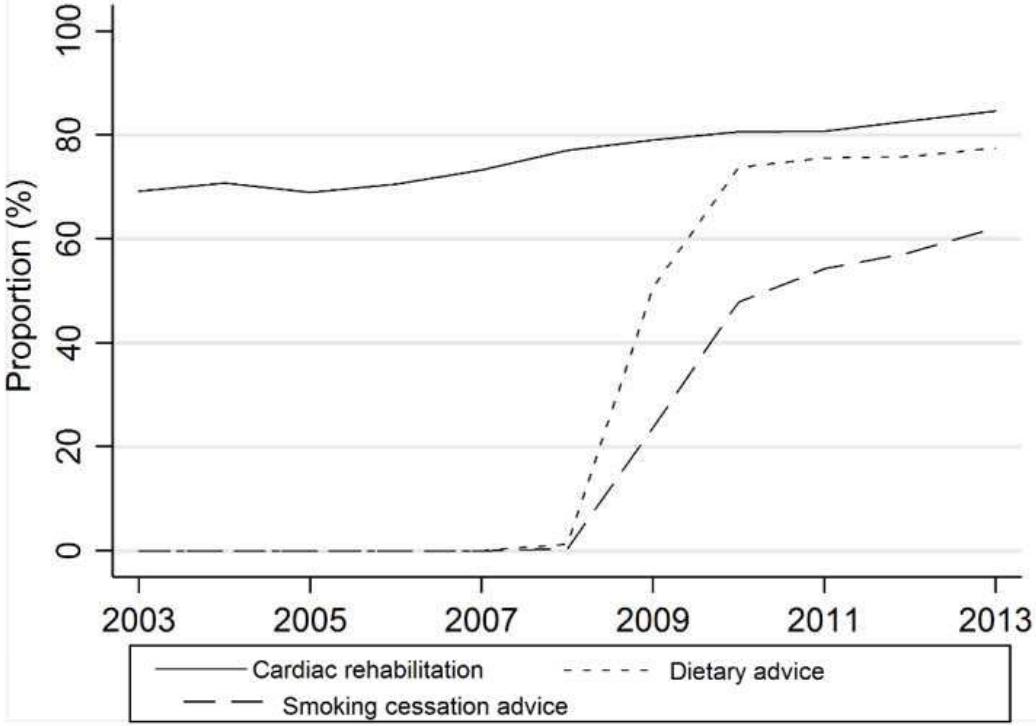
Figure 4. Impact of missing specific guideline-indicated interventions, sub-optimal care, and intermediate and low receipt of care on survival

Figure 1. STROBE diagram showing the derivation of the analytical cohort from the Myocardial Ischaemia National Audit Project (MINAP) dataset

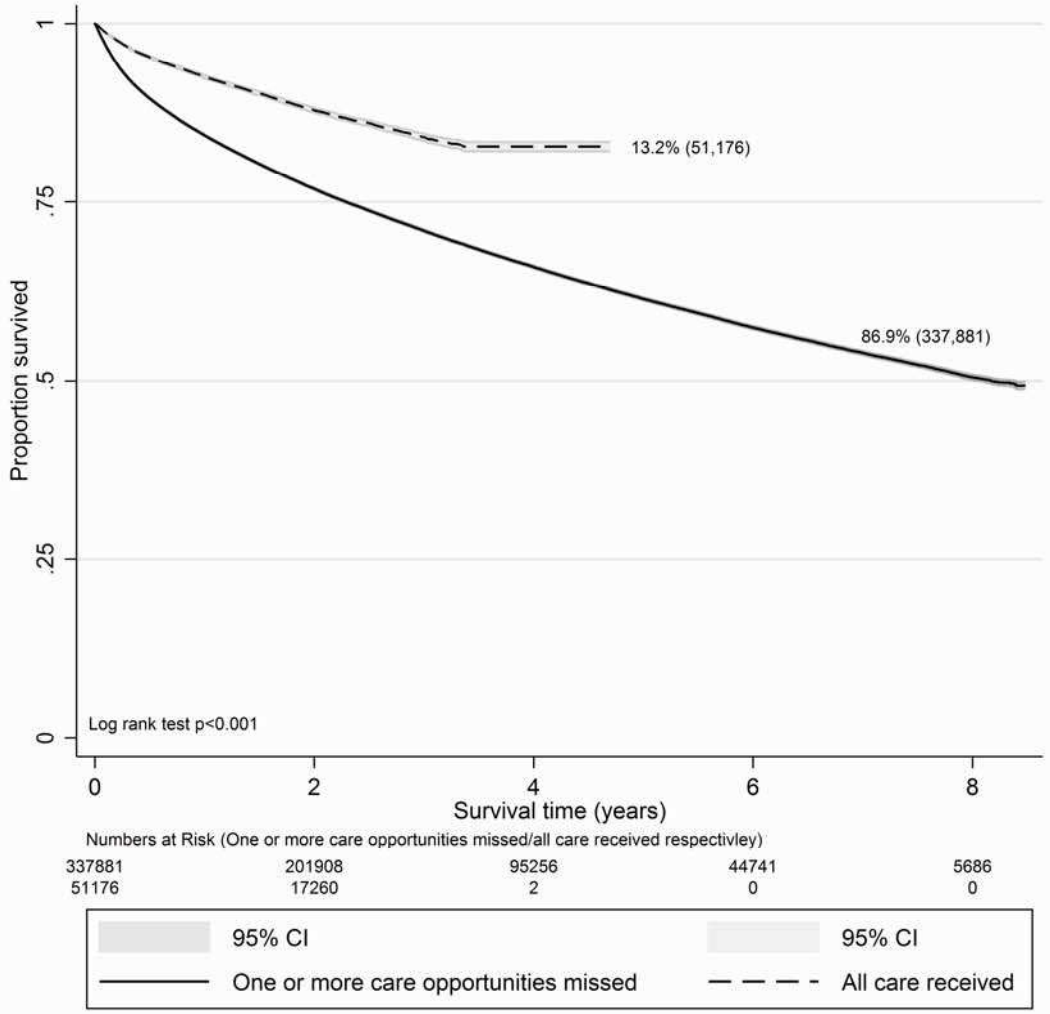


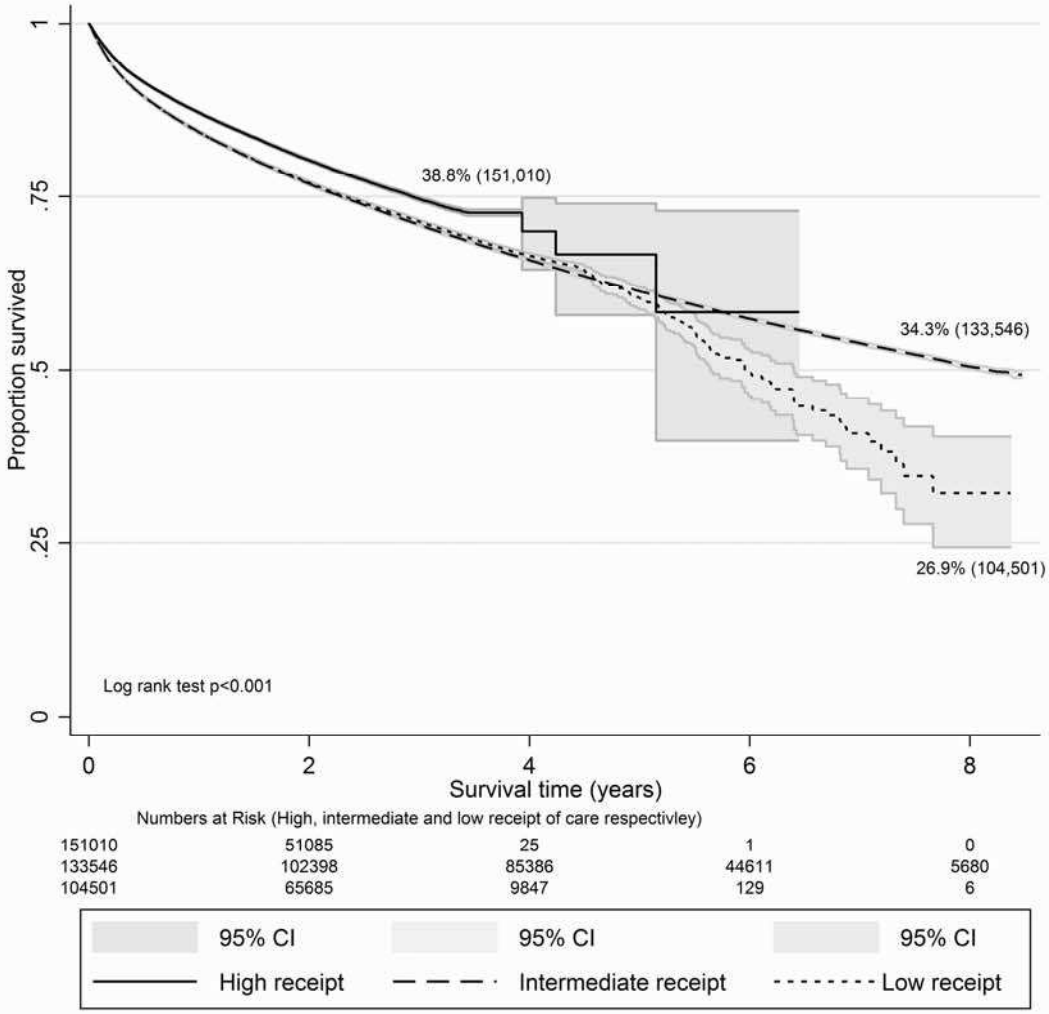


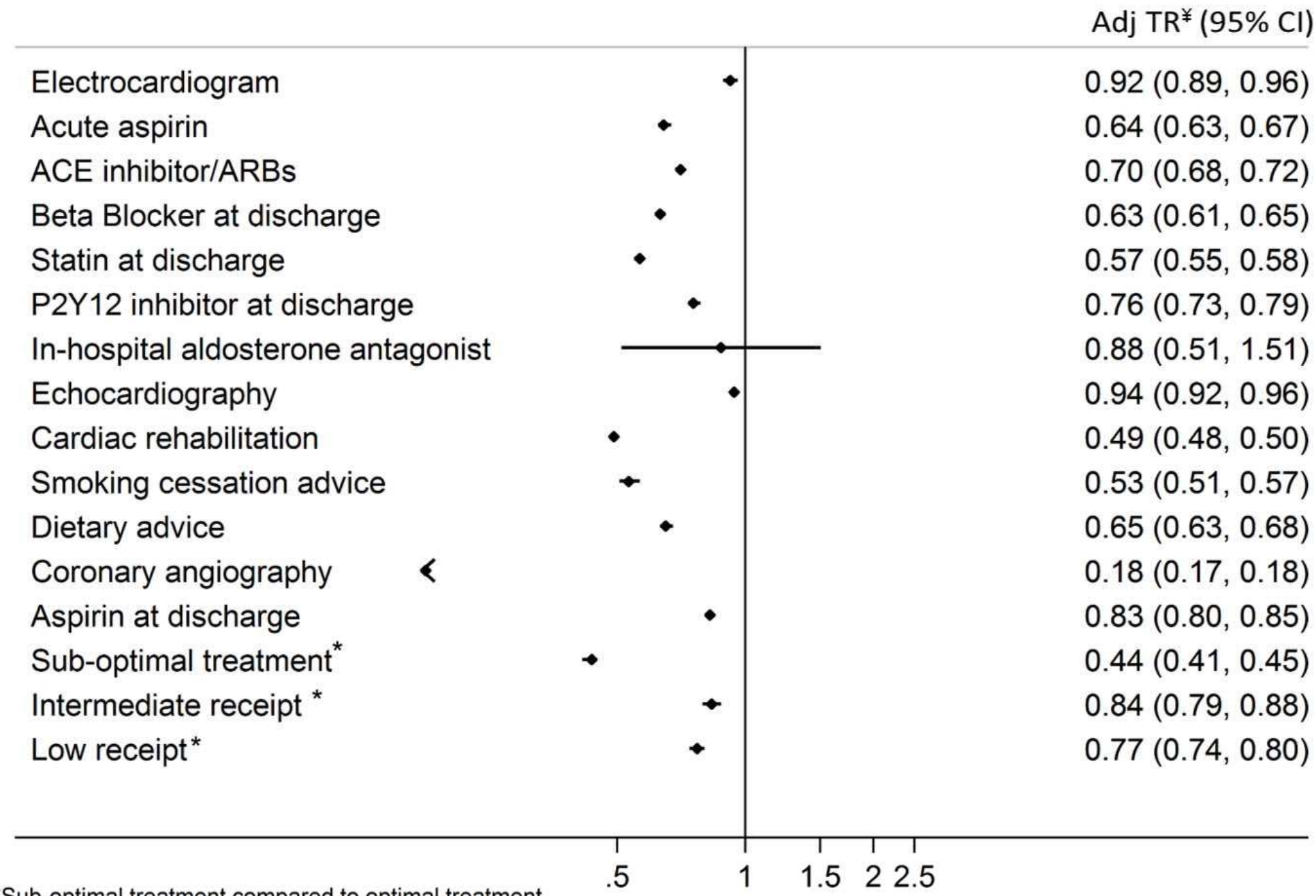




	2000	2002	2004	2007	2011
Electrocardiogram	✓	✓	✓	✓	✓
Acute aspirin	✓	✓	✓	✓	✓
ACEi /ARBs	✓	✓	✓	✓	✓
Beta blocker at discharge	✓	✓	✓	✓	✓
Statin at discharge	✓	✓	✓	✓	✓
P2Y12 inhibitor at discharge	x	x	✓	✓	✓
In-hospital aldosterone antagonist	x	x	x	✓	✓
Echocardiography	✓	✓	✓	✓	✓
Cardiac rehabilitation	✓	✓	✓	✓	✓
Smoking cessation advice	✓	✓	✓	✓	✓
Dietary advice	✓	✓	✓	✓	✓
Aspirin at discharge	✓	✓	✓	✓	✓
Coronary angiography	✓	✓	✓	✓	✓


Proportion survived
1
.75
.5
.25
0
13.2% (51,176)
86.9% (337,881)
Log rank test p<0.001
0
2
4
6
8
Survival time (years)
Numbers at Risk (One or more care opportunities missed/all care received respectivley)
337881 201908 95256 44741 5686
51176 17260 2 0 0
95% CI
95% CI
One or more care opportunities missed
All care received


Proportion survived
1
.75
.5
.25
0
38.8% (151,010)
34.3% (133,546)
26.9% (104,501)
Log rank test p<0.001
0
2
4
6
8
Survival time (years)
Numbers at Risk (High, intermediate and low receipt of care respectivley)
151010 51085 25 1 0
133546 102398 85386 44611 5680
104501 65685 9847 129 6
95% CI
95% CI
95% CI
High receipt
Intermediate receipt
Low receipt



*Sub-optimal treatment compared to optimal treatment

*Intermediate and low receipt of care compared to high receipt of care

Table 1. Baseline demographic and clinical characteristics for the 2003-2013 NSTEMI cohort.

Characteristics N=389,057	Cases	Missing
Age, years*	70.9 (13.3)	638 (0.2)
Male	244,837 (63.1)	832 (0.2)
Deprivation (IMD score)		
Least deprived (1)	61,697 (17.2)	
2	70,526 (19.7)	
3	75,459 (21.0)	30,417 (7.8)
4	72,539 (20.2)	
Most deprived (5)	78,419 (21.8)	
Year of admission		
2003-2005	102,207 (26.3)	
2006-2008	102,324 (26.3)	0
2009-2011	127,877 (32.9)	
2012-2013	56,649 (14.6)	
Ethnicity		
White	327,625 (93.3)	
Black	2,560 (0.7)	
Asian	15,422 (4.4)	37,922 (9.8)
Mixed	424 (0.1)	
Other	5,104 (1.5)	
Cardiovascular history		
Myocardial infarction	97,002 (24.9)	0¥
Congestive cardiac failure	24,529 (6.3)	0¥
PCI	32,663 (8.4)	0¥
CABG	27,637 (7.1)	0¥
Angina	122,566 (31.5)	0¥
Cerebrovascular disease	34,146 (8.9)	0¥
Peripheral vascular disease	18,324 (4.7)	0¥
Cardiovascular risk factors		
Diabetes	81,469 (20.9)	0¥
Chronic renal failure	21,938 (5.6)	0¥

Hypercholesterolaemia	121,243 (31.2)	0[¥]
Hypertension	188,503 (48.5)	0[¥]
Smoker ever / current	279,178 (71.8)	0[¥]
Asthma or COPD	56,708 (14.6)	0[¥]
Family history of CHD	77,288 (19.9)	0[¥]
Presenting characteristics		
Systolic blood pressure, mmHg*	142.5 (28.4)	66,688 (17.1)
Systolic blood pressure, <90 mmHg	6,483 (2.0)	66,688 (17.1)
Heart rate*	80 (67-95)	65,863 (16.9)
Heart rate >110 bpm	177,810 (55.0)	65,863 (16.9)
Creatinine*	92 (76-114)	165,622 (42.6)
Creatinine >200 (μmol/l)	9,546 (4.3)	165,622 (42.6)
Peak troponin[§*]	1.2 (0.3-8.2)	19,114 (4.9)
Peak troponin ≥ 0.06[§]	350,368 (94.7)	19,114 (4.9)
Cardiac arrest	6,740 (1.8)	22,901 (5.9)
Electrocardiographic characteristics		
No acute changes	55,498 (15.7)	
ST-segment elevation	15,962 (4.5)	
Left bundle branch block	23,066 (6.5)	35,699 (9.2)
ST segment depression	92,227 (26.1)	
T wave changes only	92,716 (26.2)	
Other acute abnormality	73,889 (20.9)	
Use of a loop diuretic	97,972 (30.5)	67,556 (17.4)
Grace risk score classification		
Lowest (≤70)	16,657 (9.1)	
Low (71-87)	20,483 (11.2)	205.461 (52.8)
Intermediate to high (>88)	146,456 (79.8)	

*All are numbers (%), unless normally distributed continuous data (mean (SD)), or non-normally distributed continuous data (median (IQR)).

Abbreviations: IMD, Index of multiple deprivation; CABG, coronary artery bypass graft; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; PCI,

percutaneous coronary intervention; SD, standard deviation; IQR, interquartile range; ¥ missing data default imputed to “No”, § peak troponin values truncated at 50.

Table 2. Eligibility and receipt of guideline-indicated care for NSTEMI between 2003 and 2013.

Treatment	Patients receiving treatment N (%)	Patients eligible
Pre-hospital electrocardiogram	115,702 (96.2)	120,270
Pre-hospital aspirin	49,682 (55.0)	90,304
Electrocardiogram	364,760 (93.75)	389,057
Acute aspirin	230,822 (88.7)	260,384
In-hospital aspirin	130,185 (55.0)	236,592
Echocardiography	195,537 (50.3)	389,020
Coronary angiography	211,267 (56.6)	373,120
Coronary angiography in high risk patients	29,274 (53.9)	54,325
Aspirin at discharge	301,639 (88.5)	340,982
P2Y12 inhibitor at discharge	126,995 (39.7)	319,901
ACE inhibitor or ARBs	91,159 (67.5)	135,131
Beta Blocker at discharge	90,185 (74.5)	121,094
Statin at discharge	297,045 (85.4)	347,701
In-hospital aldosterone antagonist	144 (24.3)	592
Dietary advice	119,321 (31.9)	374,190
Smoking cessation advice	33,821 (12.1)	279,178
Cardiac rehabilitation	279,027 (76.0)	366,938
Care by a Cardiologist	220,208 (56.6)	389,057

Abbreviation: ARB, angiotensin receptor blocker; ACE, angiotensin converting enzyme.

Table 3. Latent classes according to probabilities of receipt of guideline-indicated interventions for NSTEMI.

Care Opportunity	Latent Class Structure (probabilities)		
	Class1	**Class 2**	**Class 3**
	High receipt of care	**Intermediate receipt of care**	**Low receipt of care**
Electrocardiogram	0.994	0.847	0.970
Acute aspirin	0.647	0.545	0.577
ACE inhibitor or ARBs	0.006	0.670	0.014
Beta blocker at discharge	0.039	0.614	0.029
Statin at discharge	0.779	0.769	0.733
P2Y12 inhibitor at discharge	0.715	0.004	0.175
In-hospital aldosterone antagonist	0.001	0.000	0.000
Echocardiography	0.600	0.430	0.455
Cardiac rehabilitation	0.795	0.686	0.645
Smoking cessation advice	0.221	0.000	0.004
Dietary advice	0.780	0.000	0.014
Coronary angiography	0.688	0.377	0.544
Aspirin at discharge	0.781	0.798	0.739

Abbreviation: ARB, angiotensin receptor blocker; ACE, angiotensin converting enzyme.