Implementation of a Sensitive Troponin I Assay and Risk of Recurrent Myocardial Infarction and Death in Patients With Suspected Acute Coronary Syndrome

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Context Although troponin assays have become increasingly more sensitive, it is unclear whether further reductions in the threshold of detection for plasma troponin concentrations will improve clinical outcomes in patients with suspected acute coronary syndrome (ACS).

Objective To determine whether lowering the diagnostic threshold for myocardial infarction (MI) with a sensitive troponin assay could improve clinical outcomes.

Design, Setting, and Patients All consecutive patients admitted with suspected ACS to the Royal Infirmary of Edinburgh, Edinburgh, Scotland, before (n = 1038; February 1-July 31, 2008, during the validation phase) and after (n = 1054; February 1-July 31, 2009, during the implementation phase) lowering the threshold of detection for myocardial necrosis from 0.20 to 0.05 ng/mL with a sensitive troponin I assay were stratified into 3 groups (<0.05 ng/mL, 0.05-0.19 ng/mL, and ≥0.20 ng/mL). During the validation phase, only concentrations above the original diagnostic threshold of 0.20 ng/mL were reported to clinicians.

Main Outcome Measure Event-free survival (recurrent MI and death) at 1 year in patients grouped by plasma troponin concentrations.

Results Plasma troponin concentrations were less than 0.05 ng/mL in 1340 patients (64%), 0.05 to 0.19 ng/mL in 170 patients (8%), and 0.20 ng/mL or more in 582 patients (28%). During the validation phase, 39% of patients with plasma troponin concentrations of 0.05 to 0.19 ng/mL were dead or had recurrent MI at 1 year compared with 7% and 24% of those patients with troponin concentrations of less than 0.05 ng/mL (P < .001) or 0.20 ng/mL or more (P = .007), respectively. During the implementation phase, lowering the diagnostic threshold to 0.05 ng/mL was associated with a lower risk of death and recurrent MI (from 39% to 21%) in patients with troponin concentrations of 0.05 to 0.19 ng/mL (odds ratio, 0.42; 95% confidence interval, 0.24-0.84; P = .01).

Conclusions In patients with suspected ACS, implementation of a sensitive troponin assay increased the diagnosis of MI and identified patients at high risk of recurrent MI and death. Lowering the diagnostic threshold of plasma troponin was associated with major reductions in morbidity and mortality.
METHODS

Study Population
We identified all consecutive patients admitted with suspected ACS to the Royal Infirmary of Edinburgh, Edinburgh, Scotland, between February 1 and July 31, 2008, during the validation phase of a sensitive plasma troponin I assay, and between February 1 and July 31, 2009, during the implementation of this assay. Patient information and clinical outcomes were obtained with permission from the Caldicott Guardian through the TrakCare software application (InterSystems Corporation, Cambridge, Massachusetts), an electronic patient record system used by the Acute Hospitals Division of Lothian National Health Service (NHS) Health Board, Scotland.

Inclusion criteria included symptoms of chest pain of suspected cardiac origin and measurement of plasma troponin I concentration on admission, 12 hours after symptom onset, or both. Exclusion criteria included noncardiac (respiratory, gastrointestinal, or musculoskeletal) chest pain, tachyarrhythmia, anemia (hemoglobin concentration <90 g/dL), severe valvular heart disease, hypertrophic cardiomyopathy, pericarditis, cocaine use, or patients resident outside the region in whom follow-up data would not be available.

Ethical Considerations
The study protocol was reviewed by the chairman and scientific advisor of the Lothian Research Ethics Committee who advised that the proposed study represented clinical audit and service evaluation; therefore, the study did not require approval by the research ethics committee. Data collection and record linkage were performed with permission from the NHS Caldicott Guardian.

Implementation of the new assay was delayed to permit an independent assessment of assay precision and repeatability, as recommended in the consensus statement,4 across all clinical laboratories in NHS Lothian. At no point were results withheld from clinicians for the purpose of the study.

Plasma Troponin I Assay
Plasma troponin I concentrations were measured by Abbott Architect assays (Abbott Laboratories, Abbott Park, Illinois). The original diagnostic threshold was 0.20 ng/mL based on within-laboratory coefficient of variation of less than 10%. This assay was reformulated by the manufacturer to achieve a greater analytical sensitivity of 0.01 ng/mL or less, with a 10% coefficient of variation of 0.032 ng/mL and a 99th percentile (male and female) of 0.012 ng/mL. During the validation phase, the reformulated assay showed a coefficient of variation of less than 10% at 0.05 ng/mL under local laboratory conditions and, as recommended by the consensus statement on the universal definition of MI,4 this was selected as the diagnostic threshold for clinical use during the implementation phase.

Study Phases
The study was divided into 2 phases (validation and implementation). Although plasma troponin I was measured using the reformulated sensitive assay throughout both phases, only concentrations above the original diagnostic threshold (≥0.20 ng/mL) were reported in the validation phase, and concentrations above the revised diagnostic threshold (≥0.05 ng/mL) were reported during the implementation phase. Patients were stratified into 3 groups based on declared or undeclared peak plasma troponin I assay concentration (<0.05 ng/mL, 0.05-0.19 ng/mL, and ≥0.20 ng/mL).

Clinical Characteristics and Outcome
Clinical characteristics, cardiovascular risk factors, and medication on admission were documented. Hyperlipidemia and hypertension were defined as either a documented history or the use of a lipid-lowering or antihypertensive medication, respectively. Thrombolysis in Myocardial Infarction risk scores were calculated and the presence of any electrocardiographic changes were recorded.3 Management during the index admission was assessed including referral to specialist cardiology services, coronary angiography, coronary revascularization, and use of medical therapies.

Subsequent readmission with MI or death from any cause was recorded. Myocardial infarction was defined as admission with chest pain or ST-segment deviation of at least 0.5 mm, with evidence of myocardial necrosis using plasma troponin concentrations of at least 0.05 ng/mL as the diagnostic threshold. In patients with plasma troponin assay concentrations of 0.05 to 0.19 ng/mL, all hospitalizations (excluding admission with MI) and hospitalizations due to bleeding (total bleeding, gastrointestinal bleeding, intracranial hemorrhage) were determined given the potential for reduced specificity with the sensitive assay.

Statistical Analysis
Data were analyzed using SAS version 9 (SAS Institute Inc, Cary, North Carolina) and GraphPad Prism (GraphPad, La Jolla, California). Equality of variance was assessed using Bartlett test and analyzed using 1-way analysis of variance, with Tukey post hoc analysis between pairs of groups. Categorical variables were analyzed using the χ² test, except where the frequency was less than 5 and then Fisher exact test was used. Post hoc Fisher exact testing was performed between pairs of groups. Event-free survival (recurrent MI and death) was compared using Kaplan-Meier method survival curves and log-rank tests.

Univariate analysis to identify predictors of adverse clinical outcomes at 3 and 12 months was performed by using χ² tests for categorical variables (troponin group, sex, history of ischemic heart disease, history of peripheral vascular disease, previous stroke, hypertension,
hyperlipidemia, diabetes mellitus, smoker, ex-smoker, ST-segment depression, ST-segment elevation) and a 2-sample t test for continuous variables (age). Those variables found to be related to outcomes and those that indicated significance (at the 10% level) were included in a multivariate logistic regression model.

Statistical significance was set at 2-sided P < .05, except where post hoc analysis was performed, in which it was defined as P < .0167 to account for multiple comparisons.

**RESULTS**

We identified 3434 patients who met the inclusion criteria, of whom 1342 patients had 1 of the prespecified exclusion criteria, resulting in a final study population of 2092 patients with suspected ACS. Within this population, 1340 patients (64%) had plasma troponin assay concentrations of less than 0.05 ng/mL, 170 patients (8%) had plasma troponin assay concentrations of 0.05 to 0.19 ng/mL, and 582 patients (28%) had plasma troponin assay concentrations of 0.20 ng/mL or more; a 29% increase in the rate of diagnosis of MI. During the validation and implementation phases, there were similar proportions of patients in each of these groups (Table 1) and comparable median peak troponin concentrations of 0.07 (interquartile range [IQR], 0.06-0.11) and 0.08 (IQR, 0.06-0.13) ng/mL, respectively, for patients with concentrations of 0.05 to 0.19 ng/mL (P = .44), and median peak troponin concentrations of 4.16 (IQR, 1.09-14.65) and 4.36 (IQR, 1.00-19.30) ng/mL, respectively, for patients with concentrations of 0.20 ng/mL or more (P = .91).

**Clinical Characteristics**

Clinical characteristics were similar in patients admitted during the validation and implementation phases (Table 1). In both cohorts, patients with troponin concentrations of 0.05 to 0.19 ng/mL were older and more likely to have a history of ischemic heart dis-

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**Table 1. Baseline Characteristics of All Patients With Suspected Acute Coronary Syndrome**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Validation Phase</th>
<th>Implementation Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All (N = 2092)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n = 657)</td>
<td>(n = 683)</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>65 (15)</td>
<td>63 (15)</td>
</tr>
<tr>
<td>Men</td>
<td>1195 (57)</td>
<td>1189 (55)</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous IHD</td>
<td>1161 (55)</td>
<td>1191 (57)</td>
</tr>
<tr>
<td>Previous revascularization</td>
<td>461 (22)</td>
<td>464 (22)</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>160 (8)</td>
<td>160 (8)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>117 (6)</td>
<td>117 (6)</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>611 (29)</td>
<td>606 (29)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>430 (21)</td>
<td>425 (21)</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>1051 (50)</td>
<td>1046 (50)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>791 (38)</td>
<td>785 (38)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1020 (49)</td>
<td>1015 (49)</td>
</tr>
<tr>
<td>Family history of IHD</td>
<td>405 (19)</td>
<td>406 (19)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>346 (17)</td>
<td>346 (17)</td>
</tr>
<tr>
<td>Electrocardiographic changes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST-segment depression</td>
<td>296 (14)</td>
<td>290 (14)</td>
</tr>
<tr>
<td>ST-segment elevation</td>
<td>244 (12)</td>
<td>247 (12)</td>
</tr>
<tr>
<td>T-wave inversion</td>
<td>305 (15)</td>
<td>306 (15)</td>
</tr>
<tr>
<td>Bundle branch block</td>
<td>219 (10)</td>
<td>219 (10)</td>
</tr>
<tr>
<td>TIMI risk score, mean (SD)</td>
<td>2.4 (1.5)</td>
<td>2.4 (1.5)</td>
</tr>
<tr>
<td>Medication on admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>1065 (51)</td>
<td>1065 (51)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>242 (12)</td>
<td>242 (12)</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>682 (33)</td>
<td>682 (33)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>741 (35)</td>
<td>743 (35)</td>
</tr>
<tr>
<td>Statins</td>
<td>1054 (50)</td>
<td>1054 (50)</td>
</tr>
</tbody>
</table>

Abbreviations: ACE, angiotensin-converting enzyme; IHD, ischemic heart disease; TIMI, Thrombolysis in Myocardial Infarction.

*A Comparisons between groups of patients within the validation or implementation phase were performed by analysis of variance for continuous and χ² test for categorical variables. Comparisons between all patients in the validation and implementation phase were performed using unpaired t tests for continuous and χ² test for categorical variables.

**Validation phase vs implementation phase.

Current smoker indicates active cigarette smoker on admission; ex-smoker, previous cigarette smoker; and nonsmoker, lifelong nonsmoker. Family history of IHD indicates a history of coronary artery disease in a first-degree relative younger than 65 years.
ease and diabetes mellitus than those who had troponin concentrations of less than 0.05 ng/mL or 0.20 ng/mL or more \((P < .02 \text{ for all comparisons})\). The majority of patients with troponin concentrations of 0.05 to 0.19 ng/mL had abnormalities on the 12-lead electrocardiogram (ST-segment elevation, ST-segment depression, T-wave inversion, or bundle branch block) during the validation (71%) and implementation (65%) phases.

**Management During Index Admission**

In the validation phase, patients admitted with troponin concentrations of 0.05 to 0.19 ng/mL were less likely to be referred to a cardiologist (44% vs 93%), receive dual-antiplatelet therapy (27% vs 80%), or undergo coronary revascularization (17% vs 59%) \((P < .001 \text{ for all comparisons})\) compared with those patients with troponin concentrations of 0.20 ng/mL or more (Table 2). Use of secondary prevention was also less prevalent in patients with troponin concentrations of 0.05 to 0.19 ng/mL compared with patients with troponin concentrations of 0.20 ng/mL or more \((P < .005 \text{ for all comparisons})\) (Table 2).

In the implementation phase, the management of patients with troponin concentrations of 0.05 to 0.19 ng/mL improved (Table 2). Compared with those patients admitted during the validation phase, more patients were referred to a cardiologist (74% vs 44%), received dual-antiplatelet therapy (58% vs 27%), and underwent coronary angiography (46% vs 20%) \((P < .001 \text{ for all comparisons})\) (Table 2). In general, the management of patients with troponin assay concentrations of less than 0.05 ng/mL and 0.20 ng/mL or more was unchanged following the reduction in diagnostic threshold.

**Clinical Outcomes During the Validation Phase**

Patients admitted during the validation phase were followed up for a median of 453 (range, 366-540) days. Patients with troponin assay concentrations of 0.05 to 0.19 ng/mL were more likely to have died (25%) or been readmitted with an MI (31%) compared with those with troponin assay concentrations of less than 0.05 ng/mL (4% and 5%, respectively) or with troponin assay concentrations of 0.20 ng/mL or more (13% and 18%, respectively) (Table 3). Differences in outcome appeared early with the survival

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**Table 2. Management of Patients With Suspected Acute Coronary Syndrome Before (Validation Phase) and After (Implementation Phase) the Introduction of a Sensitive Troponin Assay**

<table>
<thead>
<tr>
<th>No. (%) of Patients</th>
<th>Post Hoc Analysis P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
</tr>
<tr>
<td><strong>Validation phase</strong></td>
<td>(N = 1038)</td>
</tr>
<tr>
<td>Cardiology referral</td>
<td>508 (49)</td>
</tr>
<tr>
<td>PCI</td>
<td>187 (18)</td>
</tr>
<tr>
<td>CABG surgery</td>
<td>16 (2)</td>
</tr>
<tr>
<td>Medication on discharge</td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>712 (69)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>393 (38)</td>
</tr>
<tr>
<td>Dual-antiplatelet therapy</td>
<td>336 (32)</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>473 (46)</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>477 (46)</td>
</tr>
<tr>
<td>Statins</td>
<td>685 (66)</td>
</tr>
</tbody>
</table>

| Implementation phase | (N = 1054) | n = (683) | n = (80) | n = (291) | | | |
| Cardiology referral | 573 (54) | 242 (35) | 59 (74) | 272 (93) | <.001 | <.001 | <.001 | <.001 |
| PCI | 302 (29) | 44 (6) | 37 (46) | 221 (76) | <.001 | <.001 | <.001 | <.001 |
| CABG surgery | 21 (2) | 3 (0) | 3 (4) | 15 (5) | <.001 | .02 | <.001 | .77 |
| Medication on discharge | | | | | | | | |
| Aspirin | 707 (67) | 376 (55) | 66 (83) | 265 (91) | <.001 | <.001 | <.001 | <.001 |
| Clopidogrel | 403 (38) | 89 (13) | 49 (61) | 265 (91) | <.001 | <.001 | <.001 | <.001 |
| Dual-antiplatelet therapy | 348 (33) | 55 (8) | 46 (58) | 247 (85) | <.001 | <.001 | <.001 | <.001 |
| β-Blockers | 468 (44) | 232 (34) | 50 (62) | 186 (64) | <.001 | <.001 | <.001 | .90 |
| ACE inhibitors | 514 (49) | 246 (36) | 47 (59) | 221 (76) | <.001 | <.001 | <.001 | .03 |
| Statins | 695 (66) | 369 (54) | 64 (80) | 262 (90) | <.001 | <.001 | <.001 | .02 |

Abbreviations: ACE, angiotensin-converting enzyme; CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention.

*a*Variables analyzed using χ² test with post hoc Fisher exact testing between individual groups.

*b*P < .05 for validation phase vs implementation phase.

*c*P < .001 for validation phase vs implementation phase.
curves separating within 3 months of the index admission. At 3 months, a greater proportion of patients with troponin assay concentrations of 0.05 to 0.19 ng/mL had died or been readmitted with an MI (27%) compared with those patients with troponin assay concentrations of less than 0.05 ng/mL (3%) or 0.20 ng/mL or more (14%; P < .001) (Table 3). Similarly at 12 months, a greater proportion of patients with troponin assay concentrations of 0.05 to 0.19 ng/mL had died or been readmitted with an MI (39%) compared with those with troponin assay concentrations of less than 0.05 ng/mL (7%) or 0.20 ng/mL or more (24%; P < .001) (FIGURE). These findings were similar using either 0.05 ng/mL or 0.20 ng/mL as the diagnostic threshold.

Logistic regression confirmed that troponin assay concentration, history of ischemic heart disease, and age were independent predictors of outcome (P < .05). Compared with those patients with troponin assay concentrations of less than 0.05 ng/mL, the adjusted odds ratio (OR) for death or recurrent MI at 3 months was 9.4 (95% confidence interval [CI], 4.7-18.8) and 5.3 (95% CI, 2.9-9.6) in patients with troponin assay concentrations of 0.05 to 0.19 ng/mL and 0.20 ng/mL or more, respectively (eTable, available at http://www.jama.com).

**Clinical Outcomes During the Implementation Phase**

Patients admitted after the sensitive troponin assay had been introduced into clinical practice were followed up for a median of 451 (range, 364-579) days. The proportion of patients who died or were readmitted with MI at 12 months was unchanged for patients with troponin assay concentrations of less than 0.05 ng/mL (7% vs 5%; OR, 0.69; 95% CI, 0.44-1.10; P = .11) or 0.20 ng/mL or more (24% vs 24%; OR, 0.98; 95% CI, 0.67-1.44; P = .92) (Table 3). Reducing the diagnostic threshold to 0.05 ng/mL improved clinical outcomes in patients with troponin assay concentrations of 0.05 to 0.19 ng/mL (39% vs 21%; OR, 0.42; 95% CI, 0.24-0.84; P = .01).

In patients with troponin assay concentrations of 0.05 to 0.19 ng/mL admitted during the validation and implementation phases, recurrent hospitalization for unrelated illness was common (36/90 and 32/80, respectively; P > .99), but there were few admissions due to bleeding (1/90 and 2/80, respectively; P = .44) and only 1 inappropriate diagnosis of ACS during the implementation phase in a patient who was subsequently readmitted with similar symptoms and a confirmed pulmonary embolism.

**COMMENT**

In patients presenting with suspected ACS, the use of a sensitive troponin I assay increased the detection of MI by 29% and identified patients who were at the highest risk of recurrent MI and death. Implementation of this assay and the diagnostic reclassification of these patients was associated with improved clinical management, fewer deaths, and fewer admissions with recurrent MI.

One of the main strengths of our study is that both clinicians and investigators were unaware of the sensitive troponin assay concentration result during the validation phase, which allowed assessment of the potential effect of lowering the diagnostic threshold for...
detection of myocardial necrosis on the management and outcomes of patients with suspected ACS. To our knowledge, this study design is unique and was only possible because of the need to validate independently the sensitive assay, thereby delaying the introduction of a lower diagnostic threshold into the clinic.

Adopting a lower threshold for the detection of myocardial necrosis will inevitably result in an increased incidence of MI. In our study, adopting a diagnostic threshold of at least 0.05 ng/mL increased the number of patients diagnosed with MI by 29%. This percentage may increase further with future improvements in assay performance allowing the 99th percentile to be used as the diagnostic threshold. This greater diagnostic performance will have implications for public health targets, government statistics, health care resources, and on the employment prospects and insurance policies of our patients.

Previous studies have identified a linear association between peak troponin assay concentration and outcome in patients with ACS.7-12 In the study by Antman et al,12 the lowest quintile of troponin included concentrations of less than 0.40 ng/mL. In our validation cohort, patients with troponin assay concentrations of 0.20 ng/mL or more had better clinical outcomes than those with undisclosed increases in plasma troponin assay concentrations of 0.05 to 0.19 ng/mL. These latter patients were 2 to 3 times more likely to have an adverse outcome in comparison with those with more marked elevation in troponin concentrations. This observation appears counterintuitive and requires further discussion.

There are several reasons why the prognosis of patients with small undisclosed elevations in plasma troponin assay concentrations (0.05-0.19 ng/mL) was much worse than those with more substantial increases (≥0.20 ng/mL). First, in previous studies assessing the use of plasma troponin assays, the attending clinicians were unaware of the plasma troponin assay concentration because assays were performed following recruitment of a cohort of patients with ACS.2,13

The intention of these studies was to assess prognosis rather than diagnosis, and as such there was no opportunity for the clinician to modify patient management in the knowledge of the plasma troponin assay concentration. Second, these studies included a homogeneous population of patients recruited into randomized controlled trials that, unlike our “real world” population, were uniformly treated for an ACS. In our study, patients with suspected ACS and an undisclosed small troponin elevation had a worse outcome. This poorer outcome may be explained by the fact that many of these patients did not receive treatment for acute MI because of inadequate diagnostic information. These patients were less likely to be referred to a cardiologist, prescribed dual-antiplatelet therapy, considered for revascularization, or commenced on secondary preventative therapies. These differences occurred despite the majority of these patients having evidence of myocardial ischemia on the electrocardiogram and underlining the heavy reliance placed by clinicians on the plasma troponin assay concentration in the modern management of patients with suspected ACS.

Lowering the diagnostic threshold for MI was associated with an increase in the use of evidence-based therapies and a 50% reduction in the rate of death or recurrent MI in the subgroup of patients with small increases in plasma troponin assay concentration (0.05-0.19 ng/mL) below the diagnostic threshold of the previous generation of assay. This group stands to gain most benefit from the introduction of this assay. However, among all patients with suspected ACS irrespective of troponin level, a halving in the rate of recurrent MI was observed, although this was not associated with a reduction in overall mortality. The composite of mod-
ern treatments for ACS may have achieved major clinical benefits in this unselected “real world” population of patients.

The appropriateness of continuing to lower the threshold of plasma troponin assay concentration to define increasing numbers of patients with MI may be questioned. This concern relates to the potential to reduce specificity and increase false-positive diagnoses of MI. Our study supports the contention that this is not the case, rather the concern relates to the potential for misclassification of high-risk patients through the use of outdated diagnostic thresholds. Moreover, the universal definition uses an arbitrary cutoff of 10% coefficient of variation for assay performance.4 This appears to be an empirical distinction and does raise the question of where higher coefficients of variation should be tolerated to identify patients who may benefit from intervention. The next generation of assays may define progressively lower thresholds for detection of plasma troponin that ultimately may lead to the definition of a normal reference range. These assays are necessary to assess whether further reductions in the diagnostic threshold are indicated.

Our study has some potential limitations. Although an increased troponin concentration has previously been identified as an important prognostic factor independent of age,14 we observed significant differences in age and the prevalence of cardiovascular risk factors among each of the groups in our cohort. Patients with a troponin assay concentration of less than 0.05 ng/mL were younger and more likely to have non-ischemic chest pain. Patients with troponin assay concentrations of 0.20 ng/mL or more were more likely to have presented with ST-segment elevation MI. These patients are typically younger than patients presenting with non-ST-segment elevation MI and are known to have better long-term clinical outcomes.15 However, having an undisclosed troponin increase remained a major and independent predictor of outcome, even after adjusting for age, history of ischemic heart disease, cardiovascular risk factors, and the presence of ST-segment deviation. Furthermore, the age and clinical characteristics of patients with plasma troponin assay concentrations of 0.05 to 0.19 ng/mL were similar before and after the introduction of a high-sensitivity assay to the clinic. Consistent with this, the event rates in these patients improved and were similar to those with plasma troponin assay concentrations of 0.20 ng/mL or more following implementation of the lower diagnostic threshold. In addition, our observations were derived from a single regional cardiac center and further studies are required to confirm these findings in larger cohorts from different healthcare settings.

In conclusion, the use of a sensitive troponin assay in patients with suspected ACS increased the rate of diagnosis of MI and identified a high-risk group of patients. Lowering the diagnostic threshold for MI was associated with an immediate and substantial improvement in the clinical management and outcome of patients with suspected ACS.

Author Contributions: Dr Mills had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Mills, Walker, Denvir, Fox, Newby. Acquisition of data: Churchouse, Lee, Anand, Gamble, Shah, Paterson, MacLeod.

Analysis and interpretation of data: Mills, Churchouse, Lee, Anand, Graham, Walker, Denvir, Fox, Newby. Drafting of the manuscript: Mills, Churchouse, Newby.

Critical revision of the manuscript for important intellectual content: Mills, Churchouse, Lee, Anand, Gamble, Shah, Paterson, MacLeod, Graham, Walker, Denvir, Fox, Newby. Statistical analysis: Mills, Churchouse, Lee, Graham. Obtained funding: Mills, Newby. Administrative, technical, or material support: Walker, Newby.

Study supervision: Mills, Denvir, Newby.

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Online-Only Material: An eTable is available at http://www.jama.com.

Additional Contributions: Mary Stoddart (Department of Clinical Biochemistry, Royal Infirmary of Edinburgh, Edinburgh, Scotland), performed the assessment of assay precision. No compensation was received for her contribution.

REFERENCES