

# THE LANCET

## **Supplementary appendix**

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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## **High-sensitivity cardiac troponin I at presentation in patients with suspected acute coronary syndrome**

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**Table S1. Baseline characteristics of patients in the validation cohort (internal)**

	All patients (n=1,126)	<99 <sup>th</sup> centile at presentation (n=829)*
Sex (female), n (%)	504 (45)	355 (43)
Age, years	66 (16)	63 (16)
Smoker, n (%)	277 (27)	208 (27)
<b>Past medical history</b>		
Diabetes mellitus, n (%)	184 (16)	121 (15)
Hypertension, n (%)	596 (53)	420 (51)
Hyperlipidaemia, n (%)	503 (45)	375 (45)
Cerebrovascular accident, n (%)	93 (8)	61 (7)
Myocardial infarction, n (%)	292 (26)	211 (26)
Ischaemic heart disease, n (%)	466 (42)	344 (42)
<b>Previous revascularisation</b>		
Percutaneous coronary intervention, n (%)	166 (15)	139 (17)
Coronary artery bypass grafting, n (%)	86 (8)	62 (8)
<b>Haematology and biochemistry</b>		
Haemoglobin, g/dL	134 (35)	136 (38)
Creatinine, mmol/L	87 (53)	78 (23)
Urea, mmol/L	7 (5)	6 (4)
Cholesterol, mmol/L	4 (1)	5 (1)
<b>Admission drugs</b>		
Aspirin, n (%)	432 (39)	312 (38)
Clopidogrel, n (%)	133 (12)	104 (13)
Beta-blockers, n (%)	319 (29)	216 (27)
ACE-inhibitor or ARB, n (%)	366 (33)	254 (31)
Statin, n (%)	469 (42)	343 (42)
<b>Presentation observations</b>		
Systolic blood pressure, mmHg	135 (25)	135 (24)
Diastolic blood pressure, mmHg	73 (15)	72 (15)
Heart rate, beats per min	80 (21)	78 (18)
<b>Electrocardiography</b>		
ST-segment elevation, n (%)	118 (11)	48 (6)
ST-segment depression, n (%)	106 (10)	46 (6)
T-wave inversion, n (%)	221 (20)	150 (19)
<b>Outcome at 30 days</b>		
Composite of index type 1 myocardial infarction, recurrent myocardial infarction or cardiac death, n (%)	256 (23)	49 (6)

Vales are number (%) or mean (SD) or median (inter-quartile range)

Abbreviations: ACE = angiotensin converting enzyme; ARB = angiotensin receptor blockers

\*Excludes patients presenting with ST-segment elevation myocardial infarction

**Table S2. Baseline characteristics of patients in the validation cohort (external)**

	<b>All patients</b>	<b>&lt;99<sup>th</sup> centile at presentation</b>
	(n=308)	(n=232)
Sex (female), n (%)	148 (48)	101 (44)
Age, years	58 (15)	56 (15)
Smoker, n (%)	106 (34)	85 (37)
<b>Past medical history</b>		
Diabetes mellitus, n (%)	77 (25)	46 (20)
Hyperlipidaemia, n (%)	148 (48)	102 (44)
Cerebrovascular accident, n (%)	38 (12)	27 (12)
Myocardial infarction, n (%)	37 (12)	24 (10)
Ischaemic heart disease, n (%)	49 (16)	30 (13)
<b>Previous revascularisation</b>		
Percutaneous coronary intervention, n (%)	28 (9)	19 (8)
Coronary artery bypass grafting, n (%)	15 (5)	5 (2)
<b>Admission drugs</b>		
Aspirin, n (%)	163 (53)	119 (51)
Clopidogrel, n (%)	30 (10)	20 (9)
<b>Presentation observations</b>		
Systolic blood pressure, mmHg	143 (32)	140 (26)
Diastolic blood pressure, mmHg	82 (22)	82 (20)
Heart rate, beats per min	89 (25)	89 (25)
<b>Electrocardiography</b>		
ST-segment elevation, n (%)	32 (10)	24 (10)
ST-segment depression, n (%)	23 (8)	15 (6)
T-wave inversion, n (%)	36 (12)	23 (10)

**Table S3. Two-by-two tables for the derivation and validation cohorts**

		<i>Primary outcome</i>	
		<b>Yes</b>	<b>No</b>
<b>Derivation cohort (n=3,799)</b>			
<i>Troponin I on presentation &lt;5 ng/L</i>	<b>Yes</b>	9	2,302
	<b>No</b>	136	1,352
 <b>Validation cohorts (n=1,061)</b>			
<i>Troponin I on presentation &lt;5 ng/L</i>	<b>Yes</b>	3	590
	<b>No</b>	50	417

**Table S4. Patients with troponin concentration <5 ng/L meeting the primary endpoint in the derivation cohort**

Age	Gender	Peak troponin (ng/L)	Presenting symptom	Time to initial troponin (hrs)	Diagnosis	Risk factors	Initial ECG	Management
64	Male	850	Chest pain	1	NSTEMI	Previous MI and PCI Hyperlipidaemia Ex-smoker	Inferior ST-segment depression and T-wave inversion	PCI to RCA and LAD
70	Female	70	Chest pain	12	NSTEMI	Hypertension Hyperlipidaemia	Anterior ST-segment depression	PCI to LAD
48	Female	6,480	Chest pain	1	NSTEMI	Previous MI Smoker Hyperlipidaemia	Anterolateral T-wave inversion (old)	PCI to RCA
80	Male	534	Chest pain	1	NSTEMI	Angina pectoris Hypertension	Sinus rhythm	Medical
62	Male	78	Chest pain	2	NSTEMI	Hypertension Diabetes mellitus Hyperlipidaemia PVD Smoker	Sinus rhythm	PCI to RCA
69	Female	852	Chest pain	2	NSTEMI	Previous PCI Hypertension Ex-smoker	Sinus rhythm	Medical
69	Female	17	Chest pain	3	Vasospasm	Previous MI and PCI	Sinus rhythm	Medical
44	Male	14,008	Chest pain	1	NSTEMI	Hyperlipidaemia Family history of CHD Smoker	ST-segment elevation	Medical, occluded intermediate artery
56	Female	3,689	Chest pain	3	NSTEMI	Family history of CHD	Lateral T-wave inversion	PCI to LAD and circumflex

CHD = coronary heart disease; LAD = left anterior descending; MI = myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; PVD = peripheral vascular disease; RCA = right coronary artery

**Table S5. Patients with troponin concentration <5 ng/L meeting the primary endpoint in the validation cohorts**

<b>Age</b>	<b>Gender</b>	<b>Peak troponin (ng/L)</b>	<b>Presenting symptom</b>	<b>Time to initial troponin (hrs)</b>	<b>Diagnosis</b>	<b>Risk factors</b>	<b>Initial ECG</b>	<b>Management</b>
61	Male	1	Cardiac arrest	1	Cardiac arrest	None	Pulseless electrical activity	None; patient died at presentation
47	Male	3	Cardiac arrest	1	Cardiac arrest	None	Pulseless electrical activity	None; patient died at presentation
76	Male	1,094	Chest pain	8	NSTEMI	Hypertension Hyperlipidaemia Diabetes mellitus Previous CABG	Atrial fibrillation, inferolateral ST-segment depression	Medical; patent bypass grafts with occluded LAD

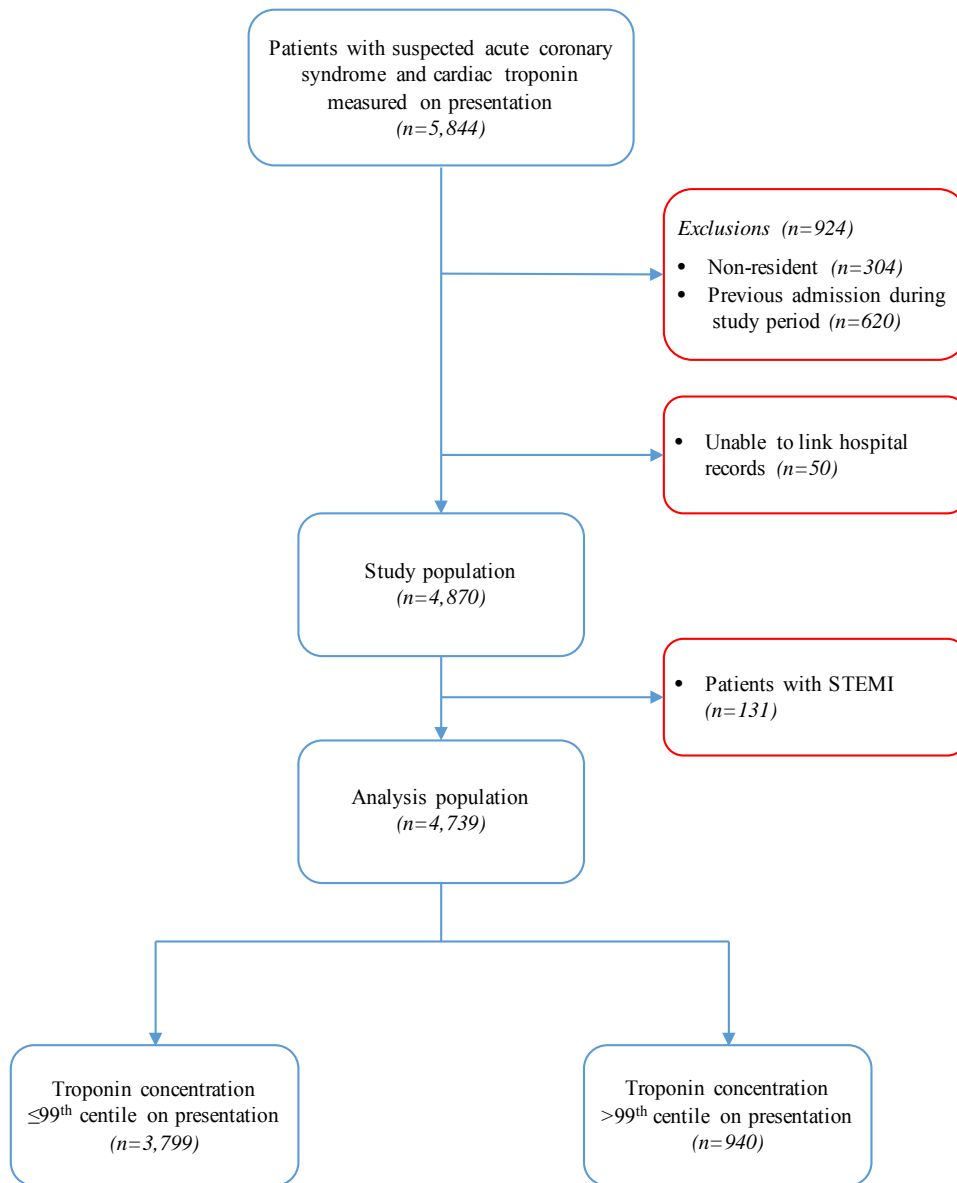
CABG = coronary artery bypass grafting; LAD = left anterior descending; NSTEMI = non-ST-segment elevation myocardial infarction;

**Table S6. Baseline characteristics of patients with suspected acute coronary syndrome and troponin concentrations <5 ng/L and 5 ng/L to 99<sup>th</sup> centile**

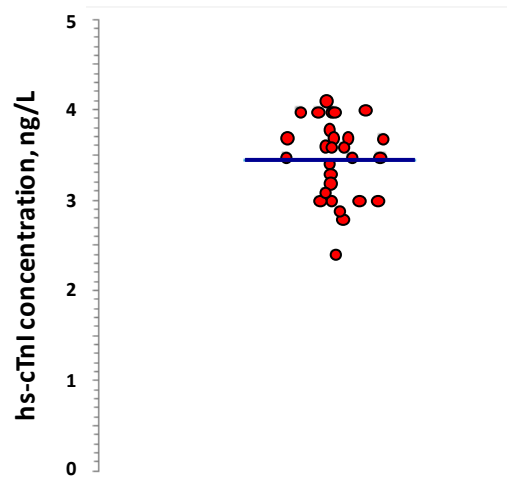
	Troponin concentration	
	<5 ng/L <i>n</i> =2,160	5 ng/L to 99 <sup>th</sup> centile <i>n</i> =1,453
Age, years	56 (15)	69 (14)
Sex (female), n (%)	1,012 (47)	502 (35)
<b>Presenting complaint</b>		
Chest pain, n (%)	1,919 (89)	1,177 (81)
Dyspnoea, n (%)	50 (2)	83 (6)
Palpitations, n (%)	61 (3)	35 (2)
Syncope, n (%)	52 (3)	78 (5)
Other, n (%)	78 (4)	80 (6)
<b>Time since onset of chest pain</b>		
<2 hours, n (%)	228 (11)	254 (16)
<b>Past medical history</b>		
Diabetes mellitus, n (%)	227 (12)	250 (20)
Hypertension, n (%)	460 (25)	493 (39)
Hyperlipidaemia, n (%)	412 (22)	378 (30)
Cerebrovascular accident, n (%)	91 (5)	129 (10)
Myocardial infarction, n (%)	229 (12)	318 (25)
Ischaemic heart disease, n (%)	402 (22)	571 (45)
<b>Previous revascularisation</b>		
Percutaneous coronary intervention, n (%)	150 (8)	178 (14)
Coronary artery bypass grafting, n (%)	35 (2)	113 (9)
<b>Admission drugs</b>		
Statin, n (%)	393 (29)	417 (47)
Aspirin, n (%)	286 (21)	372 (42)
Clopidogrel, n (%)	108 (8)	114 (13)
ACE/ARB, n (%)	329 (24)	353 (40)
Beta-blockers, n (%)	234 (17)	297 (34)
Oral anticoagulant, n (%)	39 (3)	108 (12)
<b>Electrocardiogram</b>		
Bundle branch block, n (%)	67 (4)	143 (12)
ST elevation, n (%)	40 (2)	40 (3)
ST depression, n (%)	45 (2)	68 (6)
T-wave inversion, n (%)	156 (7)	158 (11)
<b>Presentation observations</b>		
Heart rate, bpm	79 (19)	81 (23)
Systolic blood pressure, mmHg	138 (24)	138 (27)



**Figure S1. Flow diagram to illustrate study population in the derivation cohort**

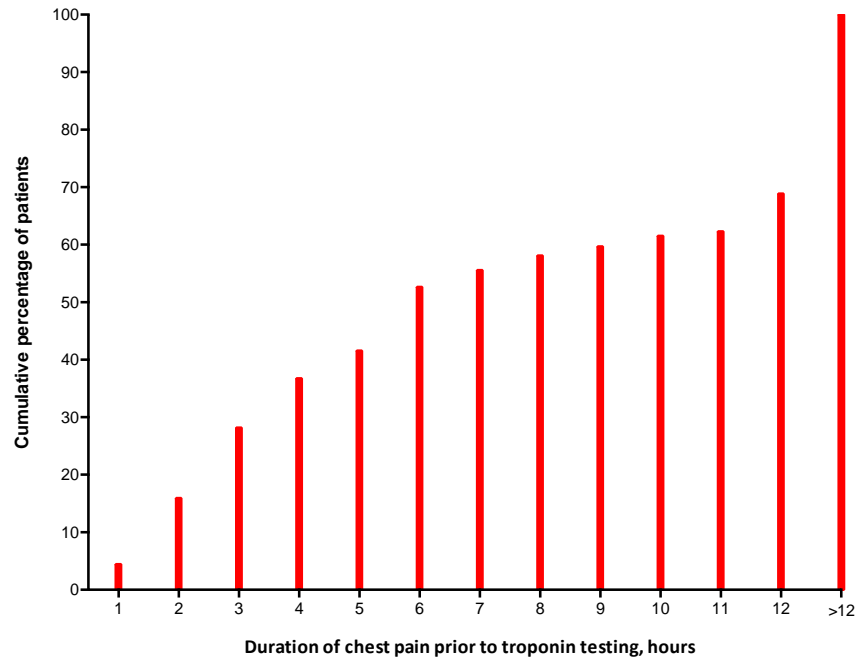


**Figure S2. Coefficient of variation derived from United Kingdom-National External Quality Assurance Scheme (UK-NEQAS) inter-laboratory reporting**



Precision analysis	n	Mean	Mean SE	Variance	SD	%CV
Pooled	33	3.45	0.076	0.19	0.44	12.6%

**Figure S3. Cumulative percentage of patients stratified by time of onset of symptoms in the derivation cohort**



**Figure S4. Histogram of time from presentation to troponin testing in the derivation cohort**

