Point-of-Care (POC) Testing for a panel of Cardiac Markers

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Clinical Question:

1. In patients presenting to Primary Care and the Emergency Department with acute chest pain, what is the accuracy and utility of a POC panel of cardiac markers compared to standard practice in diagnosing myocardial infarction?
2. In patients presenting to Primary Care and the Emergency Department with acute chest pain, what is the prognostic value of a POC panel of cardiac markers compared to standard practice in predicting short-term (up to six-month) future cardiac events?

Background, Current Practice and Advantages over Existing Technology:

Myocardial infarction (MI), 'a heart attack', is caused by myocardial ischaemia[(1)]. Upon myocardial ischaemia, components of cardiac muscle are released into the blood stream[(1)]. The detection of these biomarkers - cardiac troponin (cTn), myoglobin and creatine kinase MB isoenzyme (CK-MB) - form the foundation of MI diagnosis[(2, 3)].

Due to its high cardiac specificity[(2)], the National Institute for Health and Clinical Excellence (NICE) currently recommends testing of troponin I or T on initial presentation to hospital and again 10-12 hours after the onset of symptoms[(4)]. One limitation of this current protocol is troponin levels do not increase to a detectable level until 6 hours after the onset of symptoms[(1)], although limits of detection of troponin are diminishing with newer assays[(5)] (see concluding comments below). Myoglobin, however, is detectable within 1-2 hours of symptom onset[(6)], and generally returns back to normal levels within 24 hours of symptom onset[(6)]. CK-MB, like troponin, is elevated approximately 6 hours after symptom onset, however, unlike troponin remains elevated for only 24-36 hours (troponin remains elevated for 7-10 days[(6)]). Therefore, it has been proposed that myoglobin could be useful for early detection of MI and both myoglobin and CK-MB could be useful for monitoring re-infarction[(7)].

Mortality risk has been strongly linked to time until treatment[(8)], with evidence showing a 1% mortality rate when treatment is implemented within 1 hour of an acute event, compared to 10-12% at 6 hours[(8)]. It has been suggested that POC testing could facilitate more rapid treatment decisions.

However, it must be noted that the improved detection limit and functional sensitivity has led to some literature suggesting highly sensitive troponins alone may soon be sufficient to rule in or out MI within an hour[5].

Chest pain accounts for 700,000 attendances to Emergency Departments (ED) in England and Wales annually[9]. Studies have suggested that up to 85% of these patients are not actually suffering from MI[6, 10, 11]. Much time and money is spent stratifying these 700,000 patients[12]. POC panels of all three cardiac markers could provide a result (predictive for actual risk of having an MI) more rapidly after onset of symptoms and thus confidently rule in or out MI. This ability to rule out in particular would allow patients who do not have an MI to be discharged, easing the financial burden and time pressure of current practice.

Details of Technology:

The available products that measure multiple cardiac markers are shown in the tables below. Qualitative devices only indicate if the specific biomarker is present in the sample at increased levels, whereas quantitative devices give a numerical value for each biomarker.

For the qualitative devices, the sample is applied to the cassette and results can be read directly. The quantitative devices consist of one or more cassettes, where the sample is applied and then inserted into a bench-top analyser to obtain the results. The Nano-ditech and Anibiotech can be read as an individual cassette (qualitatively) or with a reader (quantitatively).

Qualitative POC devices:

	Tn	**CK-MB**	**Myo**	**Type of sample**			**Volume**	**Time (min)**	**FDA/CE approved**	**Individual cassette**
				WB	**P**	**S**				
Decision point **(**EU)/ Cardiac STATus (US) **(**Nexus Dx, Inc, USA)	✓	✓	✓	✓	✓	✓	~6 drops	15	Decision point: CE Cardiac STATus: FDA	Yes
MI CK-MB/Myo/TnI (US) (LifeSign LCC, USA)	✓	✓	✓	✓	✓	✓	120 µL (3 drops)	15	CE	Yes
Instant view (Alfa Scientific. Inc, USA)	✓	✓	✓	✓		✓	4 drops	10	CE	Yes
Cardiac STATus (Spectral Diagnostics Inc, Canada)	✓	✓	✓	✓	✓	✓	~6 drops	15	N/A	No

Quantitative POC devices

	Tn	CK-MB	Myo	Type of sample			Volume	Time (min)	FDA/CE approved	Individual cassette
				WB	P	S				
Triage Cardiac panel (Alere, UK) (*Alere acquired Biosite)	✓	✓	✓	✓	✓		250 µL (~6 drops)	15	CE	Yes
RAMP (Response Biomedical, Canada)	✓	✓	✓	✓			~6 drops	15	Both	No
Cobas h 232 system (Roche Diagnostics Ltd., UK)	✓ (T)	✓	✓	✓			150 µL (~4 drops)	8-12	CE	No
Stratus CS Acute Care Diagnostic System (Siemens AG, Germany) *Formerly, Dade-Behring	✓	✓	✓	✓			~6 drops	14	FDA	No
AQT90 FLEX analyser (Radiometer Ltd, England)	✓ (T+ I)	✓	✓	✓	✓		~6 drops	10-20	N/A	Yes
Vidas Emergency Panel (BioMerieux Ltd, UK)	✓	✓	✓	✓	✓	✓	250 µL (~6 drops)	30	N/A	No
Pathfast (Mitsubishi, Tokyo)	✓	✓	✓	✓	✓	✓	100 µL (~3 drops)	16	N/A	No

Qualitative and Quantitative

	Tn	CK-MB	Myo	Type of sample			Volume	Time (min)	FDA/CE	Individual cassette
				WB	P	S				
Nano-Check AMI Cardiac Markers (Nano-Ditech Corp.,USA)	✓	✓	✓	✓	✓	✓	~6 drops	10-15	FDA	Yes
Cardiac marker tests (Anibiotech, Finland)	✓		✓	✓		✓	100 µL (~3 drops)	15	CE	No

Tn: Troponin; CK-MB: Creatine Kinase MB; Myo: Myoglobin; Where no indication, troponin represents troponin I.
WB = Whole blood; P = Plasma; S = Serum; N/A: Not available

Patient Group and Use:

Patients presenting to General Practice or Emergency Departments with acute chest pain suspicious of myocardial infarction

Importance:

Although identification and management of risk factors and improved medication has resulted in a declining incidence of coronary heart disease (CHD), it remains the most common cause of death in the UK[(12)]. Annually 1 in 5 male deaths and 1 in 10 female deaths can be attributed to CHD[(12)]. It is estimated that CHD cost £1.8 billion in 2009[(12)]. Of this, 56% is estimated to be due to inpatient

hospital care[12]. Additional cost, not included in the above estimation, can be attributed to lost working days (over £3 billion annually) and the burden of informal care (£1.7 billion in 2009)[12]. Accumulatively, in 2009, the financial burden of CHD on the UK economy was estimated to be £6.7 billion[12]. In the US, it is estimated to be "in excess of $10 billion"[10]. Much of this cost, morbidity and mortality can be off-set by early diagnosis, and consequential, early treatment. As well as accurate exclusion of patients presenting with chest pain, but not suffering a MI[8]. In addition to management of patients with confirmed MI, there is also a considerable burden and cost of managing patients presenting to primary care, emergency ambulance services and emergency departments with chest pain[12]. This is an extremely common clinical presentation, and requires usually immediate access to clinical services and the ability to safely risk stratify patients. By far the largest proportion of patients presenting in such settings will not have acute ischaemia as the cause of their chest pain[6], but clinical assessment alone, without the use of biomarkers, is not sufficient to make safe diagnostic decisions in the majority of patients.

Previous Research:

A total of 23 studies were identified of which 12 examined the Biosite/Alere Triage Cardiac Panel, 3 the Siemens Stratus CS Acute Care diagnostic system, 4 the Spectral Cardiac STATus and 1 each for the Response Biomedical RAMP, Radiometer AQT90 FLEX analyser and Nexus Cardiac STATus. All were based in the ED except one, which was based in an ambulance setting (Leshem-Rubinow et al 2011).

We present the results grouped by POC device, and for each of these present existing research on diagnostic accuracy for MI, clinical utility, and prediction of future cardiac risk (at up to six months after initial chest pain event). Clinical utility is a broad term used to incorporate 'practical' aspects of Point-of-care testing (POCT). These practical outcomes vary between studies and can include Emergency Department length of stay (ED LOS), acceptance of POCT by ED staff, turnaround time (the time between blood sample taken and results returning) etc.

The term 'diagnostic study' refers to the ability of the experimental POCT Multi-marker panel (MMP) protocol to acutely diagnose (rule in or rule out) an MI compared with the control protocol. Both the intervention protocol (POCT MMP protocol) and the control protocol (generally hospital-based laboratory) varied amongst studies. The term 'prognostic study' refers to the experimental POCT MMP protocol to predict risk of short-term future cardiac events. Studies used varying follow up periods, but none more than 6 months.

Biosite/Alere Triage Cardiac Panel

The table below shows the studies that assessed the Biosite/Alere Triage Cardiac Panel. Together, these 12 studies examined 13 148 patients.

All studies included all three cardiac biomarkers (cTn, CK-MB, Myoglobin) except one, which examined only cTnI and Myoglobin[6]. The table shows diagnostic, prognostic and performance studies as indicated.

Study	Control: Central lab	No. of patients	Cut-off (µg/L)			Protocol	Sen % (95%CI)	Spec % (95%CI)	PPV % (95%CI)	NPV % (95%CI)
			TnI	CK-MB	Myo					
Than et al 2011[13] Prognostic	Varied (Architect, Access Accu, Vidas Ultra, Vitros ECi ES, E170, Elecsys (2010), Centaur Ultra)	3582	0.05	4.3	108	Prognostic at 30 days	82.9% (79-86.2)	56% (54.3-57.7)	20.1% (18.2-22.0)	96.1% (95-96.9)
Aldous et al 2012[14] Prognostic + Clinical utility	Architect	1000	0.05	4.3	108	Prognostic at 30 days	90.9% (86.7-94.0)	52.2 (50.9-53.2)	37.8 (36.1-39.1)	94.7% (92.3-96.5)
Birkhahn et al 2011[15] Diagnostic + Clinical Utility	Hitachi Modular Analytics system	151	0.1	4.3	150	Diagnostic at 2 hours	100% (74-100)	65% (57-73)	20% (11-32)	100% (96-100)
Meek et al 2012[16] Diagnostic + Clinical utility	Access Accu	258	0.08	6	107	Diagnostic at 2 hours	92.6% (74.2-98.7) N=25/27	98.7% (95.9-99.7) N=228/231	89.3% (70.6-97.2) N = 25/28	99.1% (96.6-99.8) N=228/230
Lee-Lewandrowski et al 2011[17] Diagnostic	E170, i-STAT (POC)	204	MMP: 0.05*	7.4	170	Diagnostic at present-ation (0 hours)	83%	78%	34%	97%
			MMP: 0.39*	7.4	170		55%	80%	25%	94%
			cTnI alone (Abbott): 0.08				63%	94%	58%	95%
			cTnT (Roche)< 0.03				88%	87%	48%	98%
Macdonald et al 2008[18] Diagnostic +Prognostic	Elecsys	100	0.05	4.3	107	Diagnostic at 2 hours	100%	86%	33%	100%
						Prognostic at 30 days	86%	88%	38%	97%
Straface et al 2008[7] Diagnostic	Dimension RxL	5201	0.4	50% increase	Doubling	Diagnostic at 3 hours	98.0% (95.7-100.2)	99.8% (99.6-99.9)	92.4% (88.2-96.5)	99.9% (99.9-100.0)
Ng et al 2001[19] Diagnostic + Clinical utility	Opus	1285	0.4	8.9	170	Diagnostic at 90mins	100%(CI not stated)	94% (CI not stated)	47%(CI not stated)	100%(CI not stated)

McCord et al 2001[6] Diagnostic + clinical utility	AxSYM analyzer	817	0.4 (CV:12%)	6 (CV:12%)	200 (CV:11%)	Diagnostic at 90mins cTn and Myo only	96.7% (89-100)	53.1%(49-57)	15.2%(12-19)	99.6% (98-100)
Apple et al 1999[20] Diagnostic	Stratus, Access, Opus	192	0.4	4.3	107	0-<6h	52.5(37-68)	100(100-100)		
						6-<12h	53.1(35.8-70.4)	98.5(95.5-100)		
						12-<24h	61.4(47-75.8)	97.8(94.7-100)		
						>24-72h	60.4(50.4-70.5)	98.6(95.9-100)		
Rathore et al 2008[21] Prognostic	Not available	325	0.1	4.1	150	Prognostic at 6 months	85.7%(not stated)	96.5%(not stated)	92.3%(not stated)	
Di Serio et al 2003[22] Clinical utility	Dimensions RxL	33	0.19	4.3	107	*Clinical utility study				

*The manufacturer's recommended cut-off point is 0.39. However, the CV at this concentration of troponin is greater than 10% and thus does not meet with current acceptable guidelines. For this reason, this study used both cut off points (manufacturer's: 0.39 and cut-off that meets guidelines: 0.05)[17].

Architect: Abbott Diagnostics; Access: Beckman Coulter, Inc. ; Vidas Ultra: bioMerieux; Vitros ECi ES: Ortho Clinical Diagnostics; E170: Hitachi Modular Analytics system, Roche Diagnostics; Elecsys (2010): Hitachi Modular Analytics system, Roche Diagnostics; Centaur Ultra: Siemens; i-STAT: Abbott diagnostics (POC device: cTnI only); Dimension RxL: Formerly Dade-Behring, now Siemens; AxSYM analyzer: Abbott Diagnostics; Stratus: Dade-Behring; Opus: Dade-Behring

The consistently high sensitivity and NPV supports the notion of using POCT as a 'rule out' device. 8 of the 9 diagnostic studies showed a sensitivity of greater than 82% (with 8 above 90%) and the NPV ranged from 94 to 100%. Conversely, the highly variable specificity and PPV (from 52.2 to 100% and 15.2 to 92.3%, respectively), helps confirm the minimal use for a POC device in 'ruling in' MI.

Four prognostic studies[13, 14, 18, 21] examined the ability of cardiac biomarkers to predict future cardiac risk. Three of these used cardiac biomarker results to stratify chest pain patients into risk groups and assess major adverse cardiac events (MACE) over the following 30 days[13, 14], another study used the same methodology, however assessed over 6 months[21]. All studies used all three cardiac biomarkers (cTn, CK-MB, Myoglobin) except one, which examined only cTnI and Myoglobin[6]. The consistently high negative predictive value found across studies supports the notion that this device could be potentially employed as a risk stratification and rule out tool.

Clinical utility

The measures of clinical utility predominantly revolved around time saved from POCT in comparison to routine practice. The savings from sampling to receiving results ranged from 47-59 minutes[6, 16, 22]. Emergency Department Length of Stay (ED LOS) (median) was also decreased for both patients who were discharged (248 minutes saved) and admitted (124 minutes saved)[16] and an estimated 172[14] and 13650[15] bed days and patient care hours could be saved, respectively.

One study also estimated that 22.8% of stress tests, 3% of angiography, and 4.6% of antiplatelet drugs currently used would be unnecessary under a POCT protocol[14]. Two studies showed the predictive value of POCT stratification, with only 1%[21] and 4%[13] of patients deemed low risk by POCT suffering a Major Adverse Cardiac Event (MACE) in the following 6 months and 30 days respectively. Importantly, POCT was well accepted by ED staff, with 90% supporting its on-going use[16].

Siemens Stratus CS Acute Care Diagnostic System (Formerly Dade-Behring)

A small number of studies (3) were identified that examined the Siemens Stratus CS Acute Care POC MMP. Collectively, 3453 patients in total were assessed. The types of studies are indicated in the table below.

Study	**Control: Central lab**	**No. of patients**	**Cut-off µg/L**			**Sen % (95%CI)**	**Spec % (95%CI)**	**PPV % (95%CI)**	**NPV % (95%CI)**	**Odds ratio (95%CI)**
			TnI	**CK-MB**	**Myo**					
Caragher et al 2002[8] Diagnostic at 24 hours	Stratus, Hitachi, Axsym analyzer	205	0.1	5.6	85	100% (CI not stated)	100% (CI not stated)	97% (CI not stated)	100% (CI not stated)	
Newby et al 2001[23] Prognostic at 30 days	Varied (individually not reported)	1005	0.1	4	105					Mortality: 5.4 (2.8-10.4, p=0.0001) MI: 9.6(4.9-19, p=0.0001)
Goodacre et al 2011[9] Diagnostic at 4 hours + Prognostic at 3 months + Clinical utility	Centaur Ultra, Elecsys, iSTAT, Access Accu,	2243	0.03	5	2nd sample 25% higher	Diagnostic at 4 hours: Odds ratio: 3.81 (3.01 to 4.82, p < 0.001)				
						Prognostic at 3 months: adjusted OR 1.31; 95% CI 0.78 to 2.20, p = 0.313).				

One prognostic study showed the value of POCT in predicting future cardiac risk (assessed at 30 days) with an odds ratio of 5.4 (95% CI: 2.8-10.4, p=0.0001) and 9.6 (95% CI: 4.9-19, p=0.0001) for death and myocardial infarction after a positive POC result[23]. The diagnostic accuracy appears strong, with the one diagnostic accuracy study showing exceptionally high sensitivity, specificity, PPV and NPV (100% for sensitivity, specificity and NPV, and 97% PPV)[8]. However, since no confidence intervals were presented, this data should be interpreted with caution.

Clinical utility

One study of clinical utility found that patients in the POC group were successfully discharged at a higher rate compared to standard-care group (358/1125 (32%) vs. 146/1118 (13%))[9]. Further, the same investigators found a decrease in both median and mean LOS ($p < 0.001$ and $p = 0.462$ respectively) and a higher percentage of patients that had no inpatient days ($p < 0.001$) for the POC group[9]. The other clinical utility study compared the POC 'time-to-result' to standard care and found a 48 minute and 52 minute decrease for mean and median, respectively[8].

Spectral Cardiac STATus

A total of 4 studies were identified that compared the Spectral Cardiac STATus POC MMP with standard care; 2 studies focused on clinical utility, 2 on diagnosis.

Study	**Control: Central lab**	**No. patients**	**Cut-off µg/L**			**Sen % (95%CI)**	**Spec % (95%CI)**	**PPV % (95%CI)**	**NPV % (95%CI)**
			TnI	**CK-MB**	**Myo**				
Kratz et al 2002[24] Diagnostic at 0 hours.	Elecsys	3369	1.5	5	50	Not reported	Not reported	76% (CI not stated)	Not reported
Hillis et al 1999[25] (*This study also included myosin light chain (MLC)) Diagnostic at 0, 4 and 8 hours.	Stratus	208	0.2	5	100	4hr: 88.0 (82.4 to 92.1)	57.7 (50.4 to 64.7)	23.7 (16.1 to 33.3)	97.0 (90.8 to 99.2)
						8hr: 92.9 (88.2 to 95.8)	54.0 (46.9 to 61.0)	24.5 (17.3 to 33.6)	97.9 (92.0 to 99.6)
						16hr: 92.9 (88.1 to 95.9)	51.5 (44.3 to 58.5)	23.6 (16.6 to 32.5)	97.8 (91.5 to 99.6)
						24hr: 92.9 (88.0 to 95.9)	46.6 (39.4 to 54.0)	23.2 (16.3 to 31.9)	97.4 (90.9 to 99.5)
Mutrie 1999[26] Clinical utility	Not reported	100	Not reported	Not reported	Not reported	*Clinical utility study only			
Lee-Lewandrowski et al 2003[27] Clinical utility	Not reported	369	Not reported	Not reported	Not reported	*Clinical utility study only			

The strong NPV and sensitivity in the one diagnostic study (which these figures were reported in), support the other (above) research that POCT could work as an effective rule out tool. The PPV varied significantly between the two diagnostic studies (~23% vs. 76%). The contradictory cut-off levels used, year of study, the number of patients used in each study and/or the potentially variable methodological quality of each study could have influence these results.

Clinical Utility

Two clinical utility studies[26, 27] found a decreased turnaround time of 45 minutes[27] and 30%[26] respectively. Further, both found that POCT was well accepted by ED staff[26, 27]. Other notable findings include a 30 minute decrease in ED LOS[27] and 60% fewer "non-MI, non-unstable angina" patients admitted[26].

Radiometer AQT90 FLEX Analyser

One study was identified that assessed the Radiometer AQT90 FLEX Analyser. This Australian prognostic study stratified patients into risk groups according to their POC cardiac biomarker results and followed each group over 30 days to observe for MACE. The Radiometer POC MMP was outperformed by both the Radiometer POC cTnI and Beckman central laboratory.

Study	**Control: Central lab**	**No. patients**	**Cut-off µg/L**			**Sen % (95%CI)**	**Spec % (95%CI)**	**PPV % (95%CI)**	**NPV % (95%CI)**	**Area under ROC curve (95%CI)**
			TnI	**CKM B**	**Myo**					
Cullen et al 2012[28] Prognostic at 30 days	Access Accu, Radiometer cTnI (POC)	704	0.023	4.3	108	Not available	Not available	Not available	Not available	POC MMP: 0.67 (0.61-0.72)
										POC cTnI: 0.73 (0.68-0.78)
										Central lab: 0.77 (0.72-0.82)

Nexus Decision Point (EU)/Cardiac STATus

One study was identified that assessed the Nexus Decision Point POC MMP. This study explored the use of POC MMP in a pre-hospital (ambulance) setting. Only 15 of the 641 negative POC patients suffered an MI in the following three days[29]. The sensitivity (86.6%) and NPV (97.6%) supports the idea that POCT can be used as a 'rule out' tool[29].

Study	Control: Central lab	No. of patients	Cut-off µg/L			Sen % (95%CI)	Spec % (95%CI)	PPV % (95%CI)	NPV % (95%CI)
			TnI	CKMB	Myo				
Leshem-Rubinow et al 2011[29] Prognostic at 3 days	Not available	821	Not available	Not available	Not available	86.6% (CI not specified)	83.3%(CI not specified)	53.8%(CI not specified)	97.6% (CI not specified)

Guidelines and Recommendations

The European Society of Cardiology (ESC) and the American College of Cardiology (ACC) recently re-defined the diagnostic criteria for myocardial infarction[2, 3] – see appendix 1. The British Cardiovascular Society (BCS), ESC, ACC, American Heart Association (AHA) and the National Academy of Clinical Biochemistry (NACB) recognize cTn (I or T) as the preferred biomarker for detection of MI[30, 31].

In accordance to the ESC/ACC definition, NICE recommends testing of troponin I or T on initial presentation to hospital and again 10-12 hours after the onset of symptoms[4]. The AHA guidelines and National Academy of Clinical Biochemistry (NACB) have similar recommendations (presentation and 8-12 hours after symptom onset, and 0-6h and 6-9 respectively)[32]. Clinical settings in the UK and worldwide use different strategies to try ensure the most efficient and safe management of patients presenting with acute chest pain, given the need for two tests separated by several hours. As alternatives to simply keeping patients in the emergency department, some centres use short stay wards, dedicated chest pain units, or admit patients to the inpatient wards.

Further, there is recent and building evidence to suggest that single marker (troponin) rule out protocols are as effective as multi-marker protocols and will, most likely, become the standard(5, 33-35).

According to the ACC/AHA, 60 minutes is the maximum acceptable turnaround time (for cardiac biomarker results to be returned), with 30 minutes the preferred[36, 37]. Further, studies have recommended that “if standard laboratory testing exceeds a maximum 60-minute turn-around time (the average being 65–128 min) or 25% of decision time, then a POC device (with an average turn-around time of 15–26.5min) should be implemented”[32].

Research Questions:

1. In primary care, emergency ambulance and ED settings, what is the role of panels of (and single) POC cardiac biomarkers in the management of patients presenting with acute or subacute chest pain? This research needs to focus on accuracy, clinical utility, cost effectiveness and comparison with existing clinical pathways. Particular issues include low prevalence of acute ischaemia among patients presenting with chest pain (particularly in primary care).
2. Given the above, what is the role of emerging diagnostic cardiac biomarkers in the above settings? Highly sensitive troponins, Heart-type fatty acid binding protein (H-FABP), Brain natriuretic Peptide/N-terminal prohormone of brain natriuretic peptide (BNP/NT-proBNP), ischaemia modified albumin (IMA), Myeloperioxidase (MPO), soluble CD40 ligand (sCD40L) etc.
3. To what extent will increasingly sensitive Troponin assays replace the need for panels of biomarkers for the above indications and above settings?

Suggested next step:

- There is a building amount of evidence to suggest that single-marker protocols – highly sensitive troponins – are as effective as any multi-marker strategy(5, 33-35). Because of this, future research attention should be directed towards highly sensitive troponin protocols.
- Systematic review on the diagnostic accuracy and utility of POC panel of and single cardiac markers in patients presenting to ED and Primary care with acute chest pain.

Expected outcomes:

- Acute chest pain is a common presentation in primary care, ambulance and ED settings, and typically requires biomarkers to safely and accurately rule in and rule out acute ischaemia. The main limitation in primary care settings is the need to have two tests taken several hours apart, which is generally not feasible in primary care. This could be transformed either by the use of single tests or panels with sufficiently high rule out value on single samples, or by incorporating biomarker results with clinical information (typically available in primary care), to enhance prediction.
- For the ED setting, where chest pain is also a common presentation, POCT could improve management of acute chest pain by reducing time to obtain results and offer one, rather than two tests separate by at least 6 hours. These two advantages could improve patient management via more rapid rule in/out protocols and potentially offer a more cost effective protocol.

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Appendix

1. ESC/ACC definition of Myocardial Infarction[(2)]: Detection of rise and/or fall of cardiac biomarker values (preferably cTn) with at least one value above 99th percentile and with at least one of the following
    a. Symptoms of ischaemia
    b. New or presumed new significant ST segment T waves changes or new LBBB
    c. Pathological Q wave on ECG
    d. Imaging evidence of new loss viable myocardium
    e. Identification of intracoronary thrombus by angiography or autopsy.

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