Supplemental material

Supplement to: Demandt JPA, Zelis JM, Koks A, et al. Prehospital risk assessment in patients suspected of Non-ST-segment elevation Acute Coronary Syndrome – A systematic review and meta-analysis

Demandt JPA, *et al. BMJ Open* 2022; 12:e057305. doi: 10.1136/bmjopen-2021-057305

eAppendix 1. Full search

Search strategy in MEDLINE:
(ambulance OR pre-hospital OR prehospital OR triage OR paramedics OR ems) AND (ecg OR troponin OR "risk scores" OR POC) AND (acute coronary syndrome OR acs OR nstemi OR "chest pain" OR (acute coronary syndrome [MeSH Terms]) OR (chest pain[MeSH Terms])).

Specific for primary care studies, we performed a second search:
("general practitioner" OR "primary care" OR outpatient) AND (ecg OR troponin OR "risk scores" OR POC) AND (acute coronary syndrome OR acs OR nstemi OR "chest pain" OR (acute coronary syndrome [MeSH Terms]) OR (chest pain[MeSH Terms]))

For our EMBASE search, we added a limitation to exclude all MEDLINE journals and we replaced the MeSH terms with the appropriate Emtree terms.
((ambulance or pre-hospital or prehospital or triage or paramedics or ems).mp. or exp ambulance/) and (ecg or troponin or risk scores or POC).mp. and ((acute coronary syndrome or ACS or NSTEMI or chest pain).mp. or exp non st segment elevation acute coronary syndrome/ or exp acute coronary syndrome/).

In EMBASE we performed a second search as well for additional primary care studies.
(general practitioner OR primary care OR outpatient OR exp general practitioner/ OR primary health care/) and (ecg or troponin or risk scores or POC) and (acute coronary syndrome or ACS or NSTEMI or chest pain or exp non st segment elevation acute coronary syndrome/ or exp acute coronary syndrome/).

eAppendix 2. Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS) Tool[1]

QUADAS tool: description

1. Was the spectrum of patients representative of the patients who will receive the test in practice?
   Patients presenting in a prehospital setting (EMS, GP) with suspected ACS = yes, retrospective=no

2. Is the reference standard likely to classify the target condition correctly?
   If reference standard in hospital adjudication of ACS, especially NSTEMI or unstable AP; if reference standard is Major Adverse Cardiac Events (MACE), including at least acute myocardial infarction (AMI) =yes

3. Is the time period between reference standard and index test short enough to be reasonably sure that the target condition did not change between the two tests?
   Adjudicated diagnosis at dismissal. MACE within 6 weeks=yes

4. Did the whole sample or a random selection of the sample, receive verification using a reference standard of diagnosis?

5. Did patients receive the same reference standard irrespective of the index test result?

6. Was the reference standard independent of the index test (i.e., the index test did not form part of the reference standard)?

7. Were the reference standard results interpreted without knowledge of the results of the index test? (Index test results blinded)

8. Were the index test results interpreted without knowledge of the results of the reference standard? (Reference standard results blinded)

9. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?
   When the test executor had as much info as in clinical practice=yes

10. Were uninterpretable/intermediate test results reported?
    Not reported, numbers are correct=yes

11. Were withdrawals from the study explained?
    Not reported, numbers are correct=yes

Did the study provide a clear definition of what was to be considered a ‘positive’ result?

QUADAS tool: judgement

Study	1	2	3	4	5	6	7	8	9	10	11	A
Van Dongen 2018	Y	Y	Y	Y	Y	N	U	Y	Y	Y	Y	Y
Van Dongen 2020	Y	Y	Y	Y	Y	N	U	Y	Y	Y	Y	Y
Ishak 2018	Y	Y	Y	Y	Y	N	U	U	Y	N	N	Y
Van Dongen 2020	Y	Y	Y	Y	Y	N	U	Y	Y	Y	Y	Y
Bruins Slot 2013	Y	Y	Y	N	Y	Y	Y	Y	Y	N	Y	Y
Andersson 2015	Y	Y	Y	Y	Y	N	Y	Y	Y	N	Y	Y
Schols 2019	Y	Y	Y	Y	U	Y	Y	Y	Y	Y	Y	U
Willemsen 2019	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Nilsson 2013	Y	Y	Y	Y	Y	N	Y	Y	Y	N	Y	Y
Anroedh 2018	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	-
Svensson 2003	Y	Y	Y	Y	Y	N	U	U	Y	N	N	Y
Stopyra 2020	Y	Y	Y	Y	Y	N	U	Y	Y	N	N	Y
Stengaard 2013	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
Sagel 2021	Y	Y	Y	Y	Y	N	U	Y	Y	N	Y	Y
Rasmussen 2019	Y	Y	U	Y	Y	N	N	Y	Y	N	Y	Y

Y = yes; N = no; U = unclear

eAppendix 3.

eAppendix 3. Study Characteristics					
Source	Study size	Incidence of ACS, No (%)	Clinical Setting	Diagnostic tests	Reference standard
Van Dongen et al.,[6] 2018	700	116 (17)	EMS	Male DM Obesity Family history of CAD Current smoker Previous AMI Previous PCI Previous CABG Previous TIA/Stroke Previous PAV POC- Troponin HEAR score HEART score	30-day MACE: ACS, death, PCI/CABG
Van Dongen et al.,[13] 2019	689	116 (17)	EMS	Core-lab PMHP score Hs-Troponin	30-day MACE: ACS, death, PCI/CABG
Ishak et al.,[14] 2016	1127	192 (17)	EMS	Modified HEART score	Final hospital diagnosis: NSTEMI or uAP
Van Dongen et al.,[15] 2018	700	96 (14)	EMS	HEART score	Final hospital diagnosis: NSTEMI or uAP
Bruins Slot et al.,[10] 2013	298	66 (22)	GP	H-FABP	Final hospital diagnosis: ACS
Andersson, et al.,[8] 2015	115	6 (5)	GP	Hs-Troponin POC-Troponin	Final hospital diagnosis: ACS
Schols et al.,[3] 2019	243	45 (19)	GP	Chest pain Duration of symptoms Worse with excercise Pressure pain Patients assumes cardiac origin of pain History of clinical vascular disease	Final hospital diagnosis: ACS

				Male Pain not reproduced on palpation ECG GP immediately suspected a serious condition MHS GP probability assessment Combines MHS and GP probability assessment	
Willemsen et al.,[4] 2019	303	32 (11)	GP	H-FABP GP decision to refer CRS 1-4	Final hospital diagnosis: ACS
Nilsson et al.,[9] 2012	196	13 (7)	GP	POC-Troponin GP decision to refer GP decision to refer with POC-Troponin	Final hospital diagnosis: ACS
Anroedh et al.,[16] 2018	1421	144 (10)	EMS	ECG	Final hospital diagnosis: NSTEMI or uAP
Svensson et al.,[2] 2002	538	307 (57)	EMS	Pale Nausea Clammy AP Heart failure ECG Myoglobin CK-MB Troponin	Final hospital diagnosis: ACS
Stopyra et al.,[5] 2020	395	74 (19)	EMS	Male DM Obesity Family history of CAD Current smoker Previous AMI Previous PCI Previous CABG Previous TIA/Stroke	30-day MACE: ACS, death

				Previous PAV Hypercholesterolemia Hypertension Prior coronary disease Heart failure PMHP score Core-lab PMHP score	
Stengaard et al.,[7] 2013	985	227 (23)	EMS	Male DM Current smoker Previous AMI Previous PCI Previous CABG Previous smoker POC-Troponin	Final hospital diagnosis: ACS
Sagel et al.,[12] 2021	435	53 (12)	EMS	preHEART score HEART score	3- and 7-day MACE: ACS or death
Rasmussen et al.,[11] 2017	17938	447 (2)	EMS	POC-Troponin	Final hospital diagnosis: NSTEMI

Abbreviations: ACS, Acute Coronary Syndrome; GP, General practitioner; EMS, Emergency Medical Services; DM, diabetes mellitus; AMI, acute myocardial infarction; CABG, Coronary Artery Bypass Grafting; PCI, Percutaneous Coronary Intervention; TIA; Transient ischemic attack, PAV; Peripheral artery disease; AP, angina pectoris; CAD, Coronary artery disease; POC, Point-of-Care; HS, high sensitive; H-FABP; Heart-type Fatty Acid Binding Protein; HEART, History, ECG, Age, Risk Factors, Troponin; PMHP, prehospital modified HEART pathway; CRS, Combined Risk Scores; MHS, Marburg Heart Score; NSTEMI, non-ST-elevation myocard infarct; UAP, unstable angina pectoris; MACE, Major Adverse Cardiac Event

eAppendix 4.

eAppendix 4. Results of individual studies of symptoms

Study	Characteristic	Total no. patients	TP	FP	FN	TN
Svensson et al.,[2] 2006	Chestpain	536	294	213	13	16
	Dyspnoe	536	150	124	157	105
	Nausea	536	114	66	193	163
Schols et al.,[3] 2019	Chestpain	243	39	176	6	22
	Worse with exertion	188	17	69	19	83
	Chestpain feels like pressure pain	212	31	154	8	19
	Patients assumes cardiac origin of pain	242	28	108	17	89
	Symptoms duration <1h	243	39	176	6	22
	Symptoms duration (1-24h)	243	23	15	22	83
	Symptoms duration (>24h)	243	19	63	26	135

Abbreviations: TP, true positives; FP, false positives; FN, false negatives, TN, true negatives

eAppendix 5.

eAppendix 5. Results of individual studies of risk factors						
Study	Characteristic	Total no. patients	TP	FP	FN	TN
Stopyra et al.,[5] 2020	Prior coronary disease	389	37	76	37	239
	Previous PAV	395	4	17	70	304
Van Dongen et al.,[6] 2018	Previous PAV	700	11	20	105	564
Svensson et al.,[2] 2003	Previous AMI	536	160	80	147	149
Stopyra et al.,[5] 2020	Previous AMI	589	28	43	46	472
Van Dongen et al.,[6] 2018	Previous AMI	700	34	116	82	468
Stengaard et al.,[7] 2013	Previous AMI	985	82	206	149	548
Stopyra et al.,[5] 2020	Previous CABG	390	8	27	66	289
Van Dongen et al.,[6] 2018	Previous CABG	700	14	52	102	532
Stengaard et al.,[7] 2013	Previous CABG	985	21	13	210	721
Stopyra et al.,[5] 2020	Previous PCI	395	19	78	55	243
Van Dongen et al.,[6] 2018	Previous PCI	700	42	133	74	451
Stengaard et al.,[7] 2013	Previous PCI	985	73	179	158	575
Stopyra et al.,[5] 2020	Previous TIA/Stroke	395	7	34	67	287
Van Dongen et al.,[6] 2018	Previous TIA/Stroke	700	11	32	105	552
Svensson et al.,[2] 2003	Current smoker	700	30	126	86	458
Stopyra et al.,[5] 2020	Current smoker	395	16	87	58	234
Van Dongen et al.,[6] 2018	Current smoker	700	30	126	86	458
Stengaard et al.,[7] 2013	Current smoker	1084	80	120	151	733
Svensson et al.,[2] 2003	Male gender	536	181	128	126	101
Stopyra et al.,[5] 2020	Male gender	395	43	142	31	179
Van Dongen et al.,[6] 2018	Male gender	700	88	313	28	271
Stengaard et al.,[7] 2013	Male gender	985	170	413	61	341
Svensson et al.,[2] 2003	AP	536	196	115	111	114

Stopyra et al.,[5] 2020	Hypercholesterolemia	395	26	83	48	238
Van Dongen et al.,[6] 2018	Hypercholesterolemia	700	61	214	55	370
Stengaard et al.,[7] 2013	Hypercholesterolemia	985	194	624	37	130
Svensson et al.,[2] 2003	DM	536	58	32	249	197
Stopyra et al.,[5] 2020	DM	395	29	94	45	227
Van Dongen et al.,[6] 2018	DM	700	26	87	90	497
Stengaard et al.,[7] 2013	DM	985	38	143	193	611
Svensson et al.,[2] 2003	Heart failure	536	68	57	239	172
Stopyra et al.,[5] 2020	Heart failure	389	14	40	59	276
Svensson et al.,[2] 2003	Hypertension	536	107	57	200	172
Stopyra et al.,[5] 2020	Hypertension	389	55	201	18	115
Van Dongen et al.,[6] 2018	Hypertension	700	66	306	50	278
Stengaard et al.,[7] 2013	Hypertension	985	133	405	98	349
Stopyra et al.,[5] 2020	Obesity	383	29	152	45	157
Van Dongen et al.,[6] 2018	Obesity	700	27	113	89	471
Stengaard et al.,[7] 2013	Previous smoker	985	69	208	162	546
Stopyra et al.,[5] 2020	Family history of CAD	395	19	78	55	243
Van Dongen et al.,[6] 2018	Family history of CAD	700	47	277	69	307
Schols et al.,[3] 2019	Gender	243	34	93	11	105
	History of clinical vascular disease	243	22	84	23	114

Abbreviations: 95-CI, 95% confidence interval; LR+, positive likelihood ratio; LR- negative likelihood ratio; dOR, diagnostic odds ratio; DM, diabetes mellitus; AMI, acute myocardial infarction; CABG, Coronary Artery Bypass Grafting; PCI, Percutaneous Coronary Intervention; TIA; Transient ischemic attack, PAV; Peripheral artery disease; AP, angina pectoris; CAD, Coronary artery disease; TP, true positives; FP, false positives; FN, false negatives, TN, true negatives

eAppendix 6.

eAppendix 6. Results of individual studies of electrocardiogram findings

Study	Characteristic	Total no. patients	TP	FP	FN	TN
Anroedh et al.,[16] 2018	Ischemic ECG	1421	69	457	75	820
Svensson et al.,[2] 2003	Ischemic ECG	536	52	126	255	103
Schols et al.,[3] 2019	Ischemic ECG	115	17	20	6	72
Svensson et al.,[2] 2003	Q-wave	536	33	1	274	228
	ST-depression	536	129	25	178	204
	T-wave inversion	536	55	16	252	213

Abbreviations: TP, true positives; FP, false positives; FN, false negatives, TN, true negatives

eAppendix 7.

eAppendix 7. Results of individual studies of biomarkers						
Study	Characteristic	Total no. patients	TP	FP	FN	TN
Svensson et al.,[2] 2003	POC-Troponin	536	21	2	286	227
Stengaard et al.,[7] 2013	POC-Troponin	924	73	34	146	671
Stopyra et al.,[5] 2020	POC-Troponin	395	17	11	57	310
Van Dongen et al.,[6] 2018	POC-Troponin	700	43	26	73	558
Rasmussen et al.,[11] 2019	POC-Troponin	17938	640	1175	1026	15097
Andersson et al.,[8] 2015	POC-Troponin	115	2	2	4	107
Nilsson et al.,[9] 2013	POC-Troponin	128	2	3	5	118
Willemsen et al.,[4] 2019	H-FABP	291	8	8	23	252
Bruins Slot et al.,[10] 2013	H-FABP	298	26	14	40	218
Svensson et al.,[2] 2003	CK-MB	536	37	7	270	222
	Myoglobin	536	25	9	282	220
Andersson et al.,[8] 2015	Hs-Troponin	115	5	26	1	83
Abbreviations: TP, true positives; FP, false positives; FN, false negatives, TN, true negatives; POC, Point-of-Care; H-FABP; Heart-type Fatty Acid Binding Protein; HS, high-sensitive						

eAppendix 8.

eAppendix 8. Results of individual studies of Combined Risk Scores

Study	Characteristic	Risk	TP	FP	FN	TN
Stopyra et al.,[5] 2020	Core-lab PMHP	High	50	25		
		Intermediate	24	172		
		Low	0	172		
	PMHP	High	17	11		
		Intermediate	50	193		
		Low	7	117		
Sagel et al.,[12] 2021	preHEART	High	55	56		
		Intermediate	117	797		
		Low	4	614		
	HEART	High	67	122		
		Intermediate	51	648		
		Low	5	315		
Ishak et al.,[14] 2018	Modified HEART	High	116	114		
		Intermediate	76	418		
		Low	0	403		
Willemsen et al.,[4] 2019	CRS 1	High - Low	28	130	4	141
	CRS 2	High - Low	26	130	6	141
	CRS 3	High - low	25	121	7	150
	CRS 4	High - Low	22	120	10	151
Schols et al.,[3] 2019	MHS	Cut-off value 2	27	84	9	66
	MHS	Cut- off value 1	34	126	2	24
	GP probability assessment	High - Low	36	116	6	82
	Combined MHS & GP probability assessment	High - Low	36	115	0	35

Abbreviations: TP, true positives; FP, false positives; FN, false negatives, TN, true negatives; CRS, Combined Risk Scores; HEAR, History, ECG, Age, Risk Factors; POC, Point-of-Care; H-FABP, Heart-type Fatty Acid Binding Protein; MHS, Marburg Heart Score; GP, general practitioner

eAppendix 9.

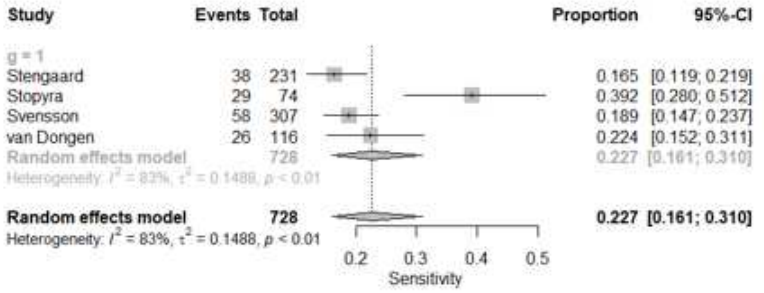
eAppendix 9. Results of individual studies of general practitioner decision making

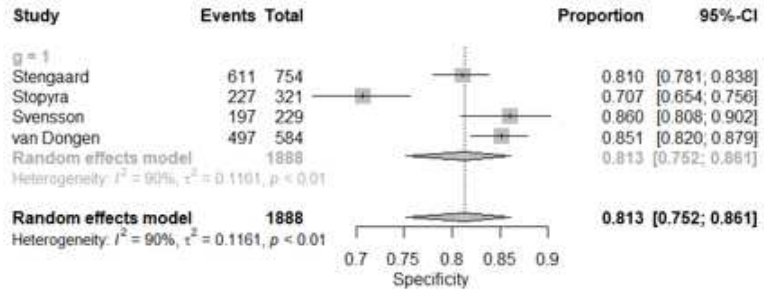
Study	Characteristic	Total no. patients	TP	FP	FN	TN
Willemsen et al.,[4] 2019	GP decision to refer	303	24	88	8	183
Nilsson et al.,[9] 2013	GP decision to refer	68	6	23	0	39
	GP decision to refer with POC-Troponin	128	5	27	2	94
Schols et al.,[3] 2019	GP immediately suspected a serious condition	243	26	94	19	104

Abbreviations: TP, true positives; FP, false positives; FN, false negatives, TN, true negatives; GP, General Practitioner; POC, Point-of-Care

eAppendix 10. Forest plots

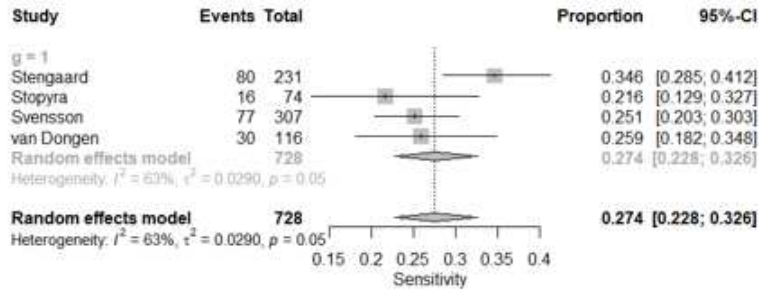
Diabetes Mellitus

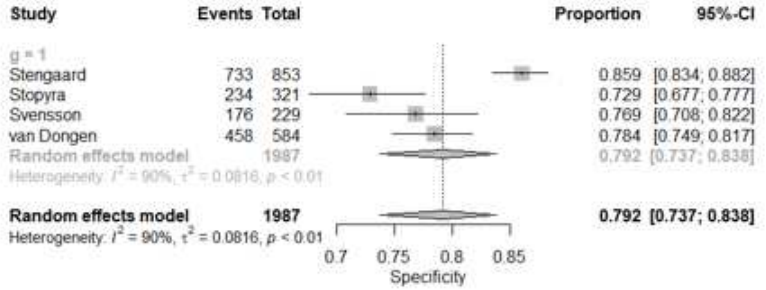




G=1 = Emergency Medical Services setting

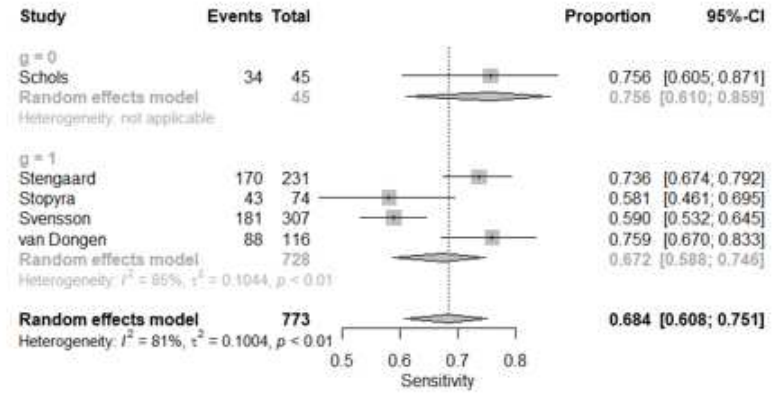
Current smoker

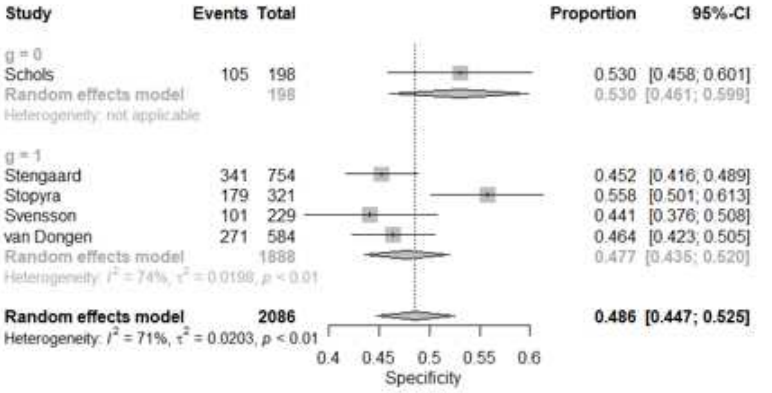




G=1 = Emergency Medical Services setting

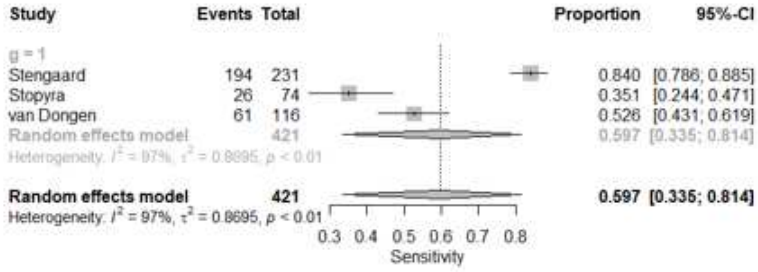
Male gender

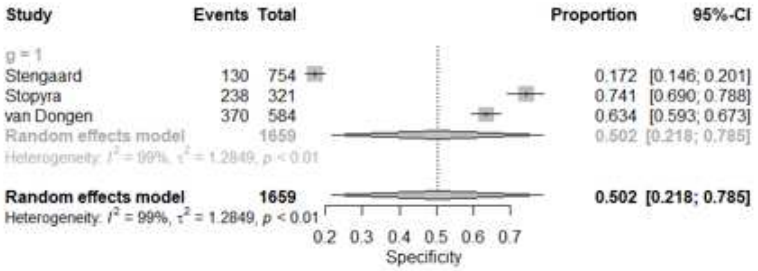




G=1 = Emergency Medical Services setting; G=-0 = General Practitioner setting

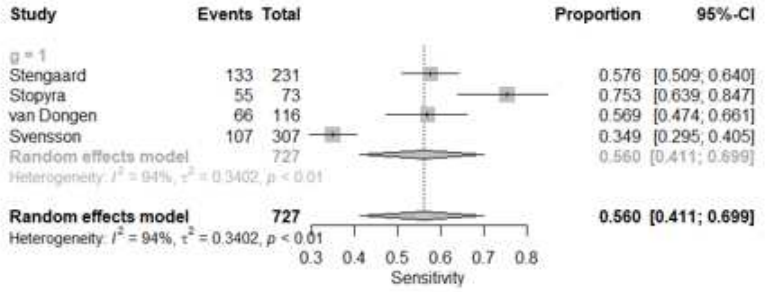
Hypercholesterolemia

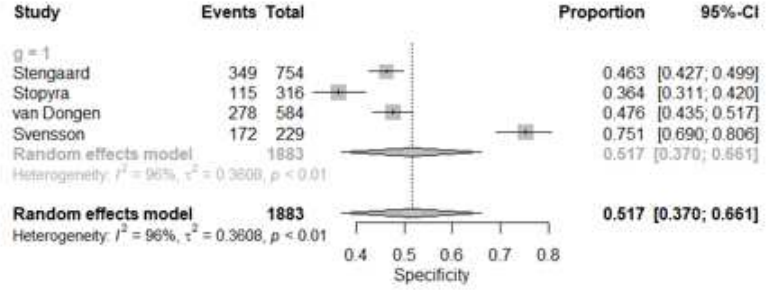




G=1 = Emergency Medical Services setting

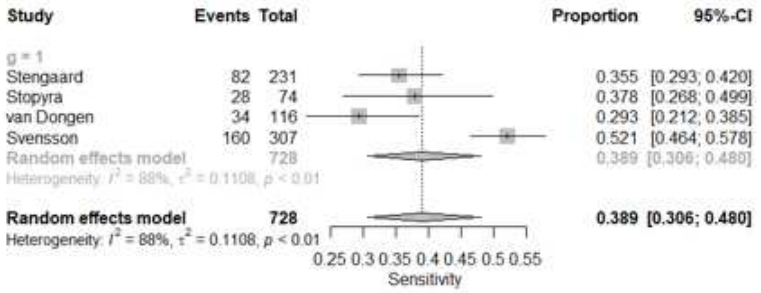
Hypertension

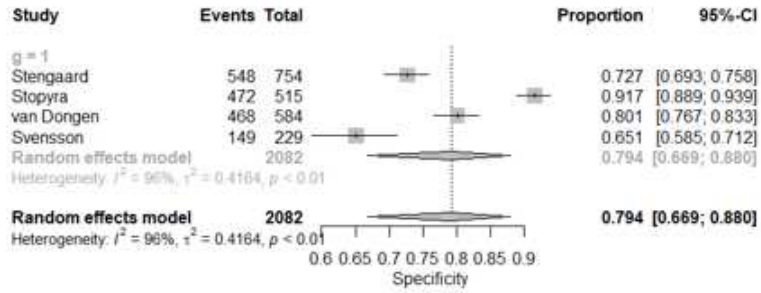




G=1 = Emergency Medical Services setting

Previous AMI

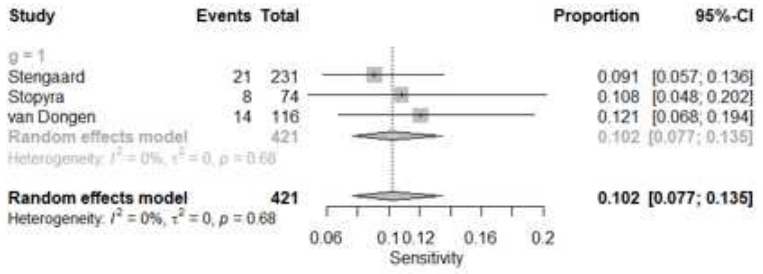


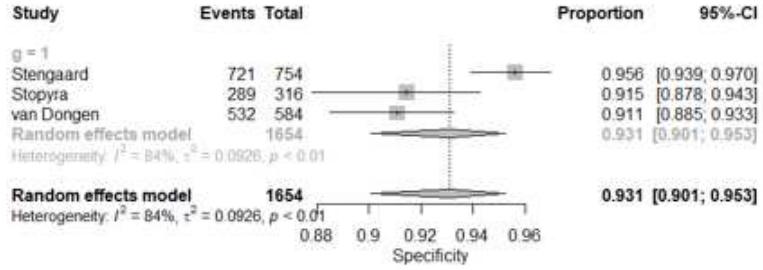


G=1 = Emergency Medical Services setting

AMI = Acute Myocardial Infarction

Previous CABG

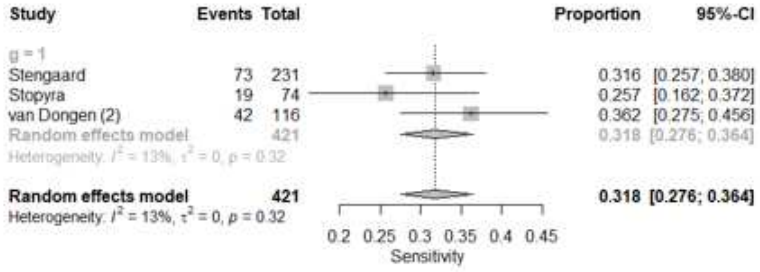


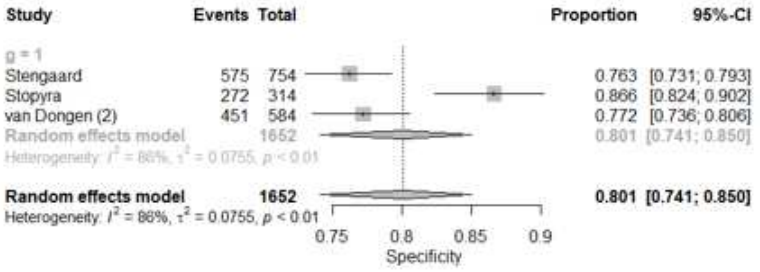


G=1 = Emergency Medical Services setting

CABG = Coronary Artery Bypass Graft

Previous PCI

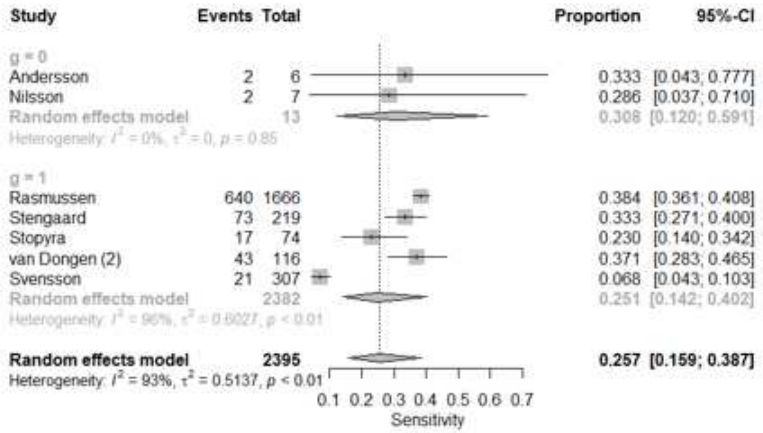


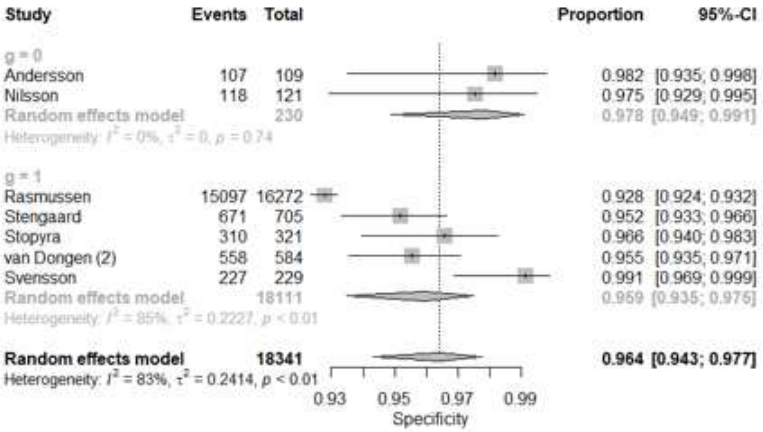


G=1 = Emergency Medical Services setting

PCI = Percutaneous Coronary Intervention

POC Troponin

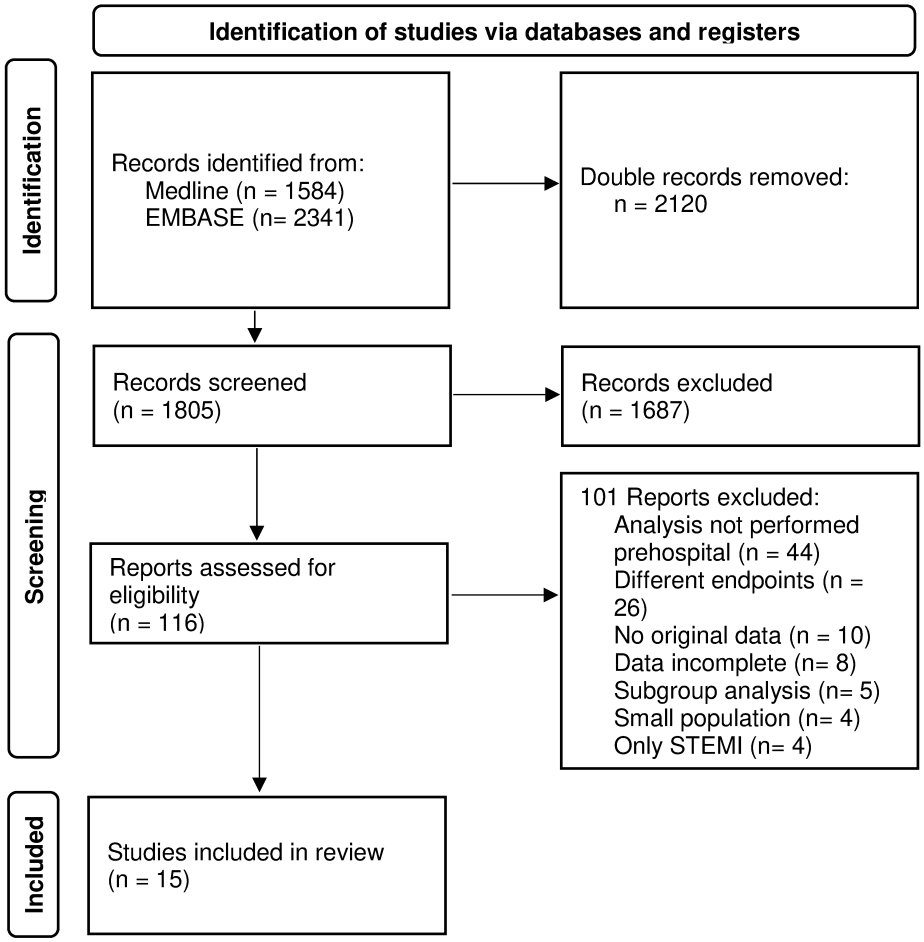




G=1 = Emergency Medical Services setting; G=0 = General Practitioner setting

POC = Point-of-Care

eFigure 1. Flow diagram of study inclusion



eTable 1.

eTable 1. Performance of symptoms for risk assessment in non-ST-elevation Acute Coronary Syndrome										
Symptom	Setting	Studies	Patients	Sensitivity, % (95-CI)	I^2, %[a]	Specificity, % (95-CI)	I^2, %[a]	LR+ (95-CI)	LR- (95-CI)	dOR (95-CI)
Chestpain[2]	EMS	1	538	96 (93-98)	-	7 (4-11)	-	1.03 (0.98-1.07)	0.61 (0.58-0.63)	1.70 (0.80-3.61)
Dyspnoe [2]	EMS	1	536	49 (43-55)	-	46 (39-53)	-	0.90 (0.76-1.07)	1.12 (0.94-1.32)	0.81 (0.57-1.14)
Nausea [2]	EMS	1	536	37 (32-43)	-	71 (65-77)	-	1.29 (1.00-1.67)	0.88 (0.68-1.14)	1.46 (1.01-2.11)
Chestpain [3]	GP	1	243	87 (73-95)	-	11 (7-16)	-	0,98 (0.90-1.05)	1.29 (1.11-1.29)	0.81 (0.31-2.14)
Worse with exertion [3]	GP	1	212	47 (30-65)	-	55 (46-63)	-	1.0 (0.79-1.38)	0.97 (0.73-1.28)	1.08 (0.52-2.23)
Chestpain feels like pressure [3]	GP	1	212	79 (64-91)	-	11 (7-17)	-	0.89 (0.81-0.98)	1.87 (1.70-2.05)	0.48 (0.19-1.19)
Patient assumes cardiac origin of pain [3]	GP	1	242	62 (47-76)	-	45 (38-52)	-	1.13 (0.94-1.37)	0.84 (0.69-1.01)	1.36 (0.70-2.64)
Symptoms duration <1h [3]	GP	1	243	87 (73-95)	-	11 (7-16)	-	0.98 (0.90-1.05)	1.2 (1.11-1.29)	0.81 (0.31-2.14)

Symptoms duration (1-24h) [3]	GP	1	243	51 (36-66)	-	42 (35-49)	-	0.88 (0.72-1.08)	1.16 (0.95-1.43)	0.75 (0.39-1.44)
Symptoms duration (>24h)[3]	GP	1	243	42 (28 58)	-	68 (61-75)	-	1.33 (0.97-1.82)	0.85 (0.62-1.16)	1.57 (0.81-3.04)

Abbreviations: 95-CI, 95% confidence interval; LR+, positive likelihood ratio; LR- negative likelihood ratio; dOR, diagnostic odds ratio

[a] When the summary measure was from less than 3 studies, I^2 was not calculated

eTable 2

eTable 2. Performance of physical examination for risk assessment in non-ST-elevation Acute Coronary Syndrome

Test	Setting	Studies	Patients	Sensitivity, % (95-CI)	I^2, %[a]	Specificity, % (95-CI)	I^2, %[a]	LR+ (95-CI)	LR- (95-CI)	dOR (95-CI)
Pale [2]	EMS	1	536	60 (54-65)	-	49 (42-56)	-	1.17 (1.00-1.38)	0.82 (0.70-0.96)	1.43 (1.01-2.02)
Clammy [2]	EMS	1	536	37 (32-43)	-	68 (62-74)	-	1.16 (0.21-1.49)	0.92 (0.72-1.18)	1.26 (0.88-1.81)
Pain not reproducible by palpation [3]	GP	1	210	92 (79-98)	-	16 (11-23)	-	1.10 (1.02-1.20)	0.47 (0.43-0.51)	2.35 (0.68-8.16)
Cardiac murmur [4]	GP	1	250	4 (0-19)	-	91 (86-94)	-	0.41 (0.08-1.91)	1.06 (0.23-4.89)	0.39 (0.05-3.03)

Abbreviations: 95-CI, 95% confidence interval; LR+, positive likelihood ratio; LR- negative likelihood ratio; dOR, diagnostic odds ratio

[a] When the summary measure was from less than 3 studies, I^2 was not calculated

eTable 3

eTable 3. Performance of risk factors in EMS setting for risk assessment in non-ST-elevation Acute Coronary Syndrome

Risk factor	Setting	Studies	Patients	Sensitivity % (95-CI)	I^2, %[a]	Specificity % (95-CI)	I^2, %[a]	LR+ (95-CI)	LR- (95-CI)	dOR (95-CI)
Prior coronary disease [5]	EMS	1	389	50 (38-62)	-	76 (71-80)	-	2.07 (1.58-2.71)	0.66 (0.50-0.86)	3.14 (1.86-5.31)
Previous PAV [5 6]	EMS	2	1095	8 (1-16)	-	96 (92-98)	-	1.93 (0.38-5.53)	0.96 (0.37-2.70)	2.01 (0.33-6.35)
Previous AMI [2 5-7]	EMS	4	2618	39 (31-48)	88%	79 (69-88)	96%	1.84 (1.21-2.80)	0.80 (0.71-0.91)	2.32 (1.34-4.00)
Previous CABG [5-7]	EMS	3	2080	10 (8-14)	0%	93 (90-95)	84%	1.60 (1.14-2.24)	0.96 (0.93-0.99)	1.67 (1.15-2.44)
Previous PCI [5-7]	EMS	3	2080	32 (28-36)	13%	80 (74-85)	86%	1.49 (1.24-1.78)	0.87 (0.81-0.93)	1.71 (1.35-2.17)
Previous TIA/Stroke [5 6]	EMS	2	1095	9 (4-19)	-	93 (86-96)	-	1.30 (0.45-3.21)	0.98 (0.52-2.00)	1.33 (0.37-3.7)
Current smoker [2 5-7]	EMS	4	2618	27 (23-33)	63%	79 (74-84)	90%	1.29 (0.78-2.14)	0.93 (0.80-1.07)	1.39 (0.72-2.68)
Male gender [2 5-7]	EMS	4	2618	67 (59-75)	85%	48 (44-52)	74%	1.28 (1.12-1.45)	0.69 (0.53-0.90)	1.86 (1.39-2.80)

AP [2]	EMS	1	536	64 (58-69)	-	50 (43-56)	-	1.27 (1.08-1.49)	0.73 (0.62-0.85)	1.75 (1.24-2.48)
Hypercholesterolemia [5-7]	EMS	3	2080	60 (34-81)	97%	50 (22-79)	99%	1.23 (0.93-1.61)	0.83 (0.73-0.94)	1.47 (1.04-2.10)
DM [2 5-7]	EMS	4	2618	23 (16-31)	83%	81 (75-86)	90%	1.22 (0.95-1.57)	0.96 (0.89-1.03)	1.29 (0.93-1.80)
Heart failure [2 5]	EMS	2	933	22 (11-30)	-	82 (69-91)	-	1.21 (0.65-2.49)	0.95 (0.56-1.52)	1.27 (0.57-3.2)
Hypertension [2 5-7]	EMS	4	2618	56 (41-70)	94%	52 (37-66)	96%	1.14 (1.04-1.25)	0.88 (0.81-0.95)	1.33 (1.10-1.61)
Obesity [5 6]	EMS	2	1095	29 (16-51)	-	70 (45-84)	-	0.99 (0.65-1.62)	1.00 (0.70-1.47)	0.99 (0.40-2.04)
Previous smoker [7]	EMS	1	985	30 (24-36)	-	72 (69-76)	-	1.08 (0.89-1.31)	0.97 (0.80-1.18)	1.12 (0.81-1.55)
Family history of CAD [5 6]	EMS	2	1095	35 (16-50)	-	61 (48-80)	-	0.89 (0.73-1.50)	1.07 (0.69-1.39)	0.82 (0.50-1.92)

Abbreviations: 95-CI, 95% confidence interval; LR+, positive likelihood ratio; LR- negative likelihood ratio; dOR, diagnostic odds ratio; DM, diabetes mellitus; AMI, acute myocardial infarction; CABG, Coronary Artery Bypass Grafting; PCI, Percutaneous Coronary Intervention; TIA; Transient ischemic attack, PAV; Peripheral artery disease; AP, angina pectoris; CAD, Coronary artery disease

[a] When the summary measure was from less than 3 studies, I^2 was not calculated

eTable 4

eTable 4. Performance of risk factors in primary care for risk assessment in non-ST-elevation Acute Coronary Syndrome

Risk factor	Setting	Studies	Patients	Sensitivity, % (95-CI)	I^2, %[a]	Specificity, % (95-CI)	I^2, %[a]	LR+ (95-CI)	LR- (95-CI)	dOR (95-CI)
Male gender [3]	GP	1	243	77 (61-86)	-	53 (46-60)	-	1.61 (1.34-1.93)	0.46 (0.38-0.55)	3.49 (1.67-7.23)
History of clinical vascular disease [3]	GP	1	243	49 (34-64)	-	58 (50-65)	-	1.15 (0.90-1.48)	0.89 (0.69-1.14)	1.30 (0.68-2.48)

Abbreviations: 95-CI, 95% confidence interval; LR+, positive likelihood ratio; LR- negative likelihood ratio; dOR, diagnostic odds ratio

[a] When the summary measure was from less than 3 studies, I^2 was not calculated

eTable 5.

eTable 5. Additional information about Point-of-Care (POC) analyzers							
Study	Setting	Manufacturer	Assay	Median duration (minutes)	Test result (minutes)	Succes rate (%)	Positive threshold
Van Dongen[6]	EMS	Roche Diagnostics	Troponin T	150	8 – 12	90	0.04 µg/L
Andersson [8]	GP	Roche Diagnostics	Troponin T	600	14	-	0.03 µg/L
Willemsen [4]	GP	FABPulous BV	H-FABP	-	-	-	4 µg/L
Nilsson [9]	GP	Roche Diagnostics	Troponin T	600	14	-	0.03 µg/L
Bruins Slot [10]	GP	Cardiodetect Rennesens GmbH	H-FABP	180	15	89	7 µg/L
Stopyra [5]	EMS	Abbott	Troponin I	-	8-10	-	0.08 µg/L
Svensson [2]	EMS	Cardiac Status Spectral Diagnostics Tests	Myoglobin CK-MB Troponin I	90	15	-	2.91 nmol/L 5 µg/L 0.1 µg/L
Stengaard [7]	EMS	Roche Diagnostics	Troponin T	70	12	90%	0.05 µg/L

Rasmussen [11]	EMS	Roche Diagnostics	Troponin T	55	12	-	0.05 µg/L
Sage[12]	EMS	Abbott	Troponin I	294	8-10	-	0.34 µg/L
Abbreviations: POC, Point-of-Care; HS, high sensitive; GP, General practitioner; EMS, Emergency Medical Services							

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