Supplementary Materials

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I. Risk scores / pathways for suspected NSTE-ACS

a. HEART-score[1,2] / HEART pathway[3,4]

Variables	Outcome	Score
History	Highly suspicious	2
	Moderately suspicious	1
	Slightly suspicious	0
ECG	Significant ST depression	2
	Nonspecific repolarization disturbance	1
	Normal	0
Age	≤65 year	2
	45-65 year	1
	≤45 year	0
Risk factors	≥ 3 risk factors or history of atherosclerotic disease	2
	1 or 2 risk factors	1
	No risk factors known	0
Troponin	>2x normal limit	2
	1-2x normal limit	1
	≤ normal limit	0

Supplementary Table 1a. Composition of the HEART score for chest pain patients in the emergency room.

Supplementary Table 1b. HEART score outcome and recommendations*

Total points	Risk of MACE**	Recommendation
0-3	Low (2.5%)	Discharge
4-6	Intermediate (20.3%)	Admission for clinical observation
≥7	High (72.7%)	Early invasive strategy

*All data is derived from the reference article Six et al.[1]

**Major adverse cardiac event (MACE) was defined as acute myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting and death.

Supplementary Table 2. HEART pathway and recommendations.[3,4] The original HEART score is used in this pathway, but the recommendations are dependent on the outcome of the (repeated) troponin values.

HEART Score	Initial troponin	Risk of 30-day MACE	Recommendation
≤3	0 points	Low (0.9-1.7%)	Repeat troponin at 3 hours and if negative, discharge home with outpatient follow-up.
	1-2 points	High (12-65%)	Cardiology consultation and admission recommended. Further testing indicated.
≥4	0 points	High (12-65%)	Admit to hospital or observation. Further testing indicated.
	1-2 points	High (12-65%)	Cardiology consultation and admission recommended. Further testing indicated.

b. EDACS / EDACS-ADP[5]

Supplementary Table 3a. Emergency department assessment of chest pain score (EDACS)

Variables	Outcome	Score
a. Age	18-45	+2
	46-50	+4
	51-55	+6
	56-60	+8
	61-65	+10
	66-70	+12
	71-75	+14
	76-80	+16
	81-85	+18
	86+	+20
b. Male sex		+6
c. Aged 18-50 years and either: Known coronary artery disease* OR ≥ 3 risk factors**		+4
d. Symptoms and signs	Diaphoresis	+3
	Radiation to arm or shoulder	+5
	Pain*** occurred or worsened with inspiration	-4
	Pain* is reproduced by palpation	-6

* Coronary artery disease (CAD) = previous acute myocardial infarction, coronary artery bypass graft or percutaneous intervention.
**Risk factors = family history of premature CAD, dyslipidemia, diabetes, hypertension, current smoker.
***pain that caused presentation to hospital

Supplementary Table 3b. EDACS-ADP and recommendation

Criteria	Risk	Recommendation
- EDACS ≤16 - No new ischemia on ECG - 0 and 2 h troponine both negative	Low	Patient safe for discharge to early outpatient follow-up investigation (or proceed to earlier inpatient testing)
- EDACS ≥ 16 - New ischemia on ECG - Either 0 or 2 h troponin positive*	Not-low	Proceed with usual care with further observation and delayed troponin

* A 2 h troponin is only required if other parameters are low risk

c. ADAPT-ADP[6]

Supplementary Table 4a. ADAPT-ADP

Variables	**0 points**	**1 points**
Abnormal troponin*	No	Yes
Abnormal EKG**	No	Yes
TIMI Risk Score for UA/NSTEMI	0	>0

*cTnI level at 0 and 2 hours above institutional cutoff for elevated troponin.
**ST-segment depression of at least 0.05 mV in ≥2 contiguous leads (including reciprocal changes), T-wave inversion of at least 0.1 mV, or Q waves ≥30 ms in width and ≥0.1 mV in depth in at least 2 contiguous leads.

Supplementary Table 4b. ADAPT-ADP and recommendation

Criteria	**Risk group**	**Risk of MACE in 30 days**
Normal troponin, normal EKG and TIMI 0	Low	0-0.3%*
Normal troponin, normal EKG and TIMI 1	Intermediate	0.8%**

Abnormal troponin or abnormal EKG and any TIMI	High	15.3%***

*Per Than 2012.

**Per Cullen 2013. The study examined patients with TIMI 0 or 1, with no reported data for patients with TIMI >1 (presuming according to TIMI data, risk of MACE increases with increasing TIMI Score).

***Per Than 2012. In the original paper, 15.3% of patients studied (302 of 1,975 total) had a MACE, and only 1 patient was identified as low risk.

d. Troponin-only Manchester Acute Coronary Syndromes (T-MACS) Decision Aid[7]

Formula to calculate the probability of ACS
$\frac{1}{1+e^{-(1.713E+0.847A+0.607R+1.417V+2.058S+1.208H+0.089T-4.766)}}$

E = EKG ischemia, A = worsening or crescendo angina, R = Pain radiation to the right arm or shoulder, V = pain associated with vomiting, S=sweating observed, H = hypotension, T = hs-cTnT concentration on arrival

Supplementary Table 5a. T-MACS

Variables	**No**	**Yes**
E: EKG ischemia	0	1
A: Worsening or crescendo angina	0	1
R: Pain radiation to the right arm or shoulder	0	1
V: Pain associated with vomiting	0	1
S: Sweating observed	0	1
H: Hypotension	0	1
T: hs-cTnT concentration on arrival	hs-cTnT value	

Supplementary Table 5b. T-MACS and recommendation

Probability	**Risk**	**Interpretation**
<0.02	Very low	ACS ruled out. Consider discharge.
≥0.02 and <0.05	Low	Consider serial troponin in ED ward, e.g. 3h troponin; consider discharge if normal.
≥0.05 and <0.95	Moderate	Serial troponin in general ward and consider stress testing and/or CT coronary angiography thereafter.
≥0.95	High	ACS ruled in. Refer to cardiology, treat for ACS.

II. Risk scores during ACS admission

Mortality / ischemic risk

a. GRACE score[8–10]

For an overview of the GRACE score risk variables, see Figure 1. The GRACE-score webcalculators can be found online: https://www.outcomes-umassmed.org/risk_models_grace_orig.aspx

Supplementary Table 6a. GRACE risk score – in-hospital mortality.[8] Score outcomes and probabilities of in-hospital mortality.

Score	Probability in-hospital mortality
58	0.002
79	0.004
91	0.006
100	0.008
107	0.01
129	0.02
141	0.03
151	0.04
158	0.05
164	0.06
169	0.07
173	0.08
177	0.09
181	0.1
184	0.11
187	0.12
190	0.13
192	0.14
195	0.15
197	0.16
199	0.17
201	0.18
203	0.19
205	0.20
207	0.21
209	0.22
211	0.23
213	0.24
214	0.25
216	0.26
217	0.27
219	0.28
220	0.29
222	0.30
235	0.40
248	0.50
260	0.60
274	0.70
290	0.80
315	0.90

Supplementary Table 6b. GRACE risk score – admission-to-6-months mortality.[9] Score outcome and mortality risk from admission to 6 months.

Score Range	Mortality Risk
0-87	0-2%
88-128	3-10%
129-149	10-20%
150-173	20-30%
174-182	40%
183-190	50%
191-199	60%
200-207	70%
208-218	80%
219-284	90%
≥ 285	99%

b. TIMI risk score for STEMI[11]

Supplementary Table 7. TIMI risk score for STEMI and predicted mortality rate in 30 days

Variables	Outcome	Score
Age	<65 years	0
	65-74	+2
	≥75	+3

Diabetes, hypertension or angina	No	0
	Yes	+1
Systolic BP <100 mmHg	No	0
	Yes	+3
Heart rate >100	No	0
	Yes	+2
Killip Class II-IV	No	0
	Yes	+2
Weight <67 kg	No	0
	Yes	+1
Anterior ST Elevation or LBBB	No	0
	Yes	+1
Time to treatment >4 hours	No	0
	Yes	+1

Total score	**Mortality at 30 days (%)**
0	0.8
1	1.6
2	2.2
3	4.4
4	7.3
5	12.4
6	16.1
7	23.4
8	26.8
>8	35.9

c. <u>TIMI risk score for UA/NSTEMI</u>[12]

Supplementary Table 8. TIMI Risk score for UA/NSTEMI and the risk for combined end point of all-cause mortality, myocardial infarction and severe recurrent ischemia prompting urgent revascularization at 14 days.

Variables	**Outcome**	**Score**
Age	≥65	+1
Risk factors coronary artery disease (CAD)	≥3	+1
Known CAD (stenosis ≥ 50%)	Yes/No	+1
ASA use in past 7 days	Yes/No	+1
Severe angina	≥2 episodes in 24 hours	+1
EKG ST changes	≥0.5mm	+1
Positive cardiac marker	Yes/No	+1

Total score	**Combined endpoint at 14 days (%)**
0/1	4.7
2	8.3
3	13.2
4	19.9
5	26.2
6/7	40.9

d. <u>PARIS coronary thrombotic event (CTE) score</u>[13]

Supplementary Table 9. PARIS CTE score

Variables	Outcome	Score
Diabetes	None	0
	Type 2 diabetes	+1
	Type 1 diabetes	+3
Acute coronary syndrome	No	0
	Yes, troponin negative	+1
	Yes, troponin positive	+2
Current smoking	No	0
	Yes	+1
Creatinine clearance <60 ml/min	Absent	0
	Present	+2
Prior PCI	No	0
	Yes	+2
Prior CABG	No	0
	Yes	+2

PCI = percutaneous coronary intervention, CABG =coronary artery bypass graft.

Supplementary Table 9b. PARIS CTE score outcome and predicted thrombotic event rate

Points	Risk stratification	Predicted thrombotic event rate
0-2	Low	1.7%
3-4	Intermediate	4.10%
≥5	High	9.8%

Bleeding risk

e. CRUSADE score[14]

Supplementary Table 10a. Crusade score criteria, value and points.

Variables	Outcome	Score
Baseline hematocrit	<31	+9
	31-33.9	+7
	34-36.9	+3
	37-39.9	+2
	≥40	0
Creatinine clearance, mL/min	≤15	+39
	>15-30	+35
	>30-60	+28
	>60-90	+17
	>90-120	+7
	>120	0
Heart rate	≤70	0
	71-80	+1
	81-90	+3
	91-100	+6
	101-110	+8
	111-120	+10
	≥121	+11
Sex	Male	0
	Female	+8
Signs of CHF at presentation	No	0
	Yes	+7
Diabetes mellitus	No	0
	Yes	+6
Prior vascular disease	No	0
	Yes	+6
Systolic blood pressure, mm Hg	≤90	+10
	91-100	+8
	101-120	+5
	121-180	+1
	181-200	+3
	≥201	+5

Supplementary Table 10b. Crusade score and rate of major bleeding

Points	Risk stratification	Rate of major bleeding
≤20	Very low risk	3.1%
21-30	Low risk	5.5%
31-40	Moderate risk	8.6%
41-50	High risk	11.9%
>50	Very high risk	19.5%

f. PARIS Major Bleeding (MB) score[15]

Supplementary Table 11a. PARIS MB score

Variables	Outcome	Score
Age (years)	<50	0

	50-59	+1
	60-69	+2
	70-79	+3
	≥80	+4
BMI, kg/m^2	<25	+2
	25-34.9	0
	≥35	+2
Current smoking	No	0
	Yes	+2
Anemia	Absent	0
	Present	+3
Creatinine clearance <60 ml/min	Absent	0
	Present	+2
Triple therapy on discharge	No	0
	Yes	+2
Total score range 0 -15		

Supplementary Table 11b. PARIS CTE score and predicted bleeding rate

Points	Risk stratification	Rate of major bleeding
0-3	Low	1.4%
4-7	Intermediate	4.3%
≥8	High	9.5%

g. PRECISE-DAPT score[16]

For an overview of the PRECISE-DAPT variables, see Figure 1. The PRECISE-DAPT score webcalculator can be found online: http://www.precisedaptscore.com/predapt/webcalculator.html

Supplementary Table 12. PRECISE-DAPT score and recommendation

Score	Risk stratification	Recommendation
≤10	Very Low	DAPT 12-24 months
11-17	Low	DAPT 12-24 months
18-24	Moderate	DAPT 12-24 months
≥25	High	DAPT 3-6 months

h. BleeMACS score[17]

Supplementary Table 13a. BleeMACS score

Variables	**Outcome**		**Score**
Age (years)	<67		0
	67-74.9		7
	>75		9
Hypertension	Yes/No		7
Vascular disease	Yes/No		6
History of bleeding	Yes/No		19
Malignancy	Yes/No		8
Creatinine	µmol/L	g/dl	
	<88.4	<1.0	0
	88.4-131.9	1-1.49	3
	>132.0	>1.5	12
Hemoglobin	mmol/L	g/dL	
	≥6.8	<11.0	18
	6.8-8.6	11.0-13.9	9

	≥8.7	≥14	0

Table 13b. BleeMACS score outcome and risk stratification.

Points	Risk group	Bleeding events per 100 person-years
≤ 7	Very low-risk	1.48
8-16	Low-risk	2.27
17-25	Moderate-risk	3.5
≥ 26	High-risk	8.03

III. Risk scores used post-ACS

a. DAPT score[18]

Variables	Outcome	Score
Age, years	≥75	0
	65-74	-1
	<65	-2
Cigarette smoking*	Yes/No	+1
Diabetes mellitus	Yes/No	+1
MI at presentation	Yes/No	+1
Prior PCI or prior MI	Yes/No	+1
Paclitaxel-eluting stent	Yes/No	+1
Stent diameter <3 mm	Yes/No	+1
CHF or LVEF <30%	Yes/No	+2
Vein graft stent	Yes/No	+2

Supplementary Table 14a. DAPT score

*smoking within 1 year prior to index procedure.

Supplementary Table 14b. DAPT score and recommendation

DAPT Score	Net clinical benefit for extended DAPT	Recommendation
-2 to 1	No	Prolonged DAPT not recommended
≥2	Yes	Prolonged DAPT recommended

V. References used in Tables 1-3.

	Number of validation studies	Included validation studies
HEART score[1,2]	**16**[19]	Number of studies used in systematic review.
EDACS[5]	**6**[20–23]	Only studies with an end point of MACE at 30 days were included.
T-MACS[7]	**2**[7,24]	Only studies with an end point of MACE at 30 days were included.
HEART Pathway[3,4]	**7**[25–31]	Only studies with an end point of MACE at 30 days were included.
EDACS-ADP[5]	**6**[5,20,22,28,31,32]	Only studies with an end point of MACE at 30 days were included.
ADAPT-ADP[6]	**5**[26,28,33–35]	Only studies with an end point of MACE at 30 days were included.

GRACE – in-hospital[8]	**17**[8,36–51]	Only studies with an end point of in-hospital mortality were included.
GRACE – 6 months[9]	**6**[9,39,46,52–54]	Only studies with an end point of mortality at 6 months were included.
TIMI (UA/NSTEMI)[11]	**19**[12,55–72]	Only studies with a combined end point of death, MI or revascularization at 14 days were included.
TIMI (STEMI)[12]	**16**[73–86]	Only studies with an end point of mortality at 30 days were included.
PARIS CTE[15]	**6**[15,87–91]	Only studies that included MI or ST in the combined end point were included.

CRUSADE[14]	**8**[14,37,92–97]	Only studies with an end point of in-hospital bleeding were included.
PARIS MB[15]	**7**[15,87,89,90,98–100]	Only studies with an endpoint of moderate or severe bleeding were included.
PRECISE-DAPT[16]	**6**[16,90,98–101]	Only studies with an end point of moderate or severe bleeding were included.
BleeMACS[17]	**2**[17,99]	Only studies with an end point of moderate or severe bleeding were included.

DAPT score –ischemic model[18]	**2**[18,102]	Only studies that analyzed the separate ischemic model of the DAPT-score with an endpoint of MI or ST at 30 months were included.
DAPT score –bleeding model[18]	**2**[18,102]	Only studies that analyzed the separate bleeding model of the DAPT-score with an endpoint of moderate or severe bleeding at 30 months were included.
DAPT score – Final risk score – ischemic outcome[18]	**6**[87,102–106]	Studies that analyzed a long-term ischemic outcome were included.
DAPT score – Final risk score – bleeding outcome[18]	**6**[87,102–106]	Studies that analyzed a long-term bleeding outcome were included.

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