**Supplementary File**

**Clinical Decision Aids and Computed Tomography Coronary Angiography in Patients with Suspected Acute Coronary Syndrome**

**A secondary analysis of the RAPID-CTCA trial**

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| **Supplementary Table 1. Cardiac troponin assays and reference values.** |
|  | **Cardiac troponin assay** | **99th centile upper reference limit** |
| Royal Infirmary of Edinburgh, Edinburgh | Abbott ARCHITECT | 26 |
| Northern General Hospital, Sheffield | Roche Elecsys | 14 |
| Derriford Hospital, Plymouth | Roche Elecsys | 14 |
| Torbay Hospital, Torquay | Roche Elecsys | 14 |
| Victoria Hospital, Kirkcaldy | Roche Elecsys | 14 |
| Russells Hall Hospital, Dudley | Roche Elecsys | 14 |
| Royal Berkshire Hospital, Reading | Roche Elecsys | 14 |
| Bradford Royal Infirmary, Bradford | *Siemens ADVIA Centaur* | 40 |
| Royal Bournemouth Hospital, Bournemouth | Roche Elecsys | 14 |
| Jersey General Hospital, St Helier | *Ortho VITROS* | 34 |
| Borders General Hospital, Melrose | Abbott ARCHITECT | 26 |
| Royal Victoria Infirmary, Newcastle | Roche Elecsys | 14 |
| University Hospital Lewisham, London | Roche Elecsys (since March 2017) | 14 |
| Glasgow Royal Infirmary, Glasgow | Abbott ARCHITECT | 26 |
| Milton Keynes University Hospital, Milton Keynes | *Beckman Coulter Access* | 40 |
| Royal Stoke University Hospital, Stoke-on-Trent | *Siemens ADVIA Centaur* | 40 |
| Sandwell General Hospital, West Bromwich | Roche Elecsys | 14 |
| St Thomas' Hospital, London | Roche Elecsys | 14 |
| Rotherham Hospital, Rotherham | *Siemens ADVIA Centaur* | 40 |
| Leeds General Infirmary, Leeds | *Siemens ADVIA Centaur* | 40 |
| Queen Elizabeth Hospital Birmingham, Birmingham | Roche Elecsys | 14 |
| East Surrey Hospital, Redhill | Roche Elecsys | 14 |
| Southampton General Hospital, Southampton | *Beckman Coulter Access* | 40 |
| Wythenshawe Hospital, Manchester | Abbott ARCHITECT | 26 |
| Luton and Dunstable University Hospital, Luton | Roche Elecsys | 14 |
| Royal London Hospital, London | Roche Elecsys (laboratory assay) | 14 |
| Whipps Cross University Hospital, London | *Siemens ADVIA Centaur* | 40 |
| Worcestershire Royal Hospital, Worcester | Roche Elecsys | 14 |
| Ulster Hospital, Belfast | Roche Elecsys | 14 |
| University Hospital of North Tees, Stockton-on-Tees | *Beckman Coulter Access* | 40 |
| Ninewells Hospital, Dundee | *Siemens Dimension Vista* | 45 |
| Queen Alexandra Hospital, Portsmouth | *Beckman Coulter Access* | 40 |
| Wrexham Maelor Hospital, Wrexham | *Beckman Coulter Access* | 40 |
| Basildon University Hospital, Basildon | Roche Elecsys | 14 |
| New Cross Hospital, Wolverhampton | Abbott ARCHITECT | 26 |
| Raigmore Hospital, Inverness | Abbott ARCHITECT (since June 2017) | 26 |
| Queen Elizabeth University Hospital, Glasgow | Abbott ARCHITECT | 26 |
| \* Contemporary cardiac troponin assays are in italics.† All upper reference limits are in ng/L.‡ References are based on cardiac troponin assay analytical characteristics designated by manufacturer v052022 (<https://ifcc.org/ifcc-education-division/emd-committees/committee-on-clinical-applications-of-cardiac-bio-markers-c-cb/biomarkers-reference-tables/>, accessed on 16 June 2023). |

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| **Supplementary Table 2. The HEART score.** |
| **Component** | **Points** |
| History (clinical suspicion of acute coronary syndrome) | Highly suspiciousModerately suspiciousSlightly or non-suspicious | 210 |
| ECG | ST-segment deviationAny abnormalities except for ST-segment deviationNormal | 210 |
| Age, years | ≥6545–65≤45 | 210 |
| Risk factors of coronary artery disease | Three and more risk factors or a history of atherosclerotic diseaseOne or two risk factorsNo risk factor s | 210 |
| Cardiac troponin (at presentation) | ≥3x upper reference limit1–3x upper reference limit≤1x upper reference limit | 210 |
| \* History is clinical suspicion of acute coronary syndrome rated by the treating physicians.† ST-segment deviation includes ST-segment depression and transient ST-segment elevation.‡ Risk factors of coronary artery disease include diabetes mellitus, hypertension, dyslipidaemia, body mass index >30 kg/m2, current smoker, and family history of premature coronary artery disease (first-degree relative with coronary artery disease at <60 years).§ A history of atherosclerotic disease includes history of myocardial infarction, coronary revascularisation, known coronary artery disease on invasive coronary angiography, cerebrovascular disease, and peripheral vascular disease.‖ The total score is the sum of the points assigned in each component.ECG = electrocardiogram |

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| **Supplementary Table 3. The T-MCAS model.** |
| **Component** | **Measurement scale** |
| Cardiac troponin (at presentation), ng/L | Continuous |
| Ischaemic ECG | Dichotomous |
| Worsening angina | Dichotomous |
| Pain radiating to the right arm | Dichotomous |
| Sweating | Dichotomous |
| Vomiting | Dichotomous |
| Low systolic blood pressure (<100 mm Hg) at presentation | Dichotomous |
| \* Ischaemic ECG includes ST-segment depression, transient ST-segment elevation, and T-wave inversion.† Worsening angina is chest pain that is persistent or could not be relieved by rest or the use of nitrates.‡ The probability of acute coronary syndrome is estimated as follows:$$\frac{1}{1 + e^{-\left(-4.766 + 0.089 \* cardiac troponin + 1.713 \* ischaemic ECG + 0.847 \* worsening angina + 0.607 \* radiating pain + 2.058 \* sweating + 1.417 \* vomiting + 1.208 \* low systolic blood pressure\right)}}$$ECG = electrocardiogram |

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| **Supplementary Table 4. The GRACE score.** |
| **Component** | **Points** |
| Killip class | IVIIIIII | 5939200 |
| Systolic blood pressure, mm Hg | ≤8080–99100–119120–139140–159160–199≥200 | 5853433424100 |
| Heart rate, beats per minute | ≥200150–199110–14990–10970–8950–69≤50 | 46382415930 |
| Age, years | ≥9080–8970–7960–6950–5940–4930–39≤30 | 100917558412580 |
| Creatinine, mg/dL | >4.002.00–3.991.60–1.991.20–1.590.80–1.190.40–0.790.00–0.39 | 28211310741 |
| Others | Cardiac arrest at presentationIschaemic ECGCardiac troponin (at presentation) > upper reference limit | 392814 |
| \* Ischaemic ECG includes ST-segment depression and transient ST-segment elevation.† The total score is the sum of the points assigned in each component.ECG = electrocardiogram |

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| **Supplementary Table 5. Diagnostic performance for index hospital diagnosis of acute coronary syndrome by subgroup.** |
|  | **Overall** | **Subgroup** |
| Age <65 years | Age ≥65 years | Female sex | Male sex |
| HEART score | 0.74 (0.71 to 0.78) | 0.77 (0.73 to 0.82) | 0.70 (0.64 to 0.76) | 0.79 (0.74 to 0.85) | 0.72 (0.67 to 0.76) |
| T-MACS model | 0.78 (0.74 to 0.81) | 0.80 (0.76 to 0.85) | 0.75 (0.69 to 0.80) | 0.79 (0.73 to 0.85) | 0.78 (0.74 to 0.83) |
| GRACE score | 0.60 (0.55 to 0.64) | 0.60 (0.54 to 0.65) | 0.56 (0.49 to 0.62) | 0.64 (0.58 to 0.71) | 0.58 (0.52 to 0.63) |
| CTCA | 0.80 (0.77 to 0.83) | 0.85 (0.82 to 0.89) | 0.70 (0.65 to 0.76) | 0.82 (0.78 to 0.87) | 0.77 (0.73 to 0.81) |
| \* Values are *C*-statistics (95% confidence interval).CTCA = computed tomography coronary angiography |

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| **Supplementary Table 6. Performance metrics for index hospital diagnosis of acute coronary syndrome using ‘high-risk’ thresholds.** |
|  | **Sensitivity (95% confidence interval)** | **Specificity (95% confidence interval)** | **Negative predictive value (95% confidence interval)** | **Positive predictive value (95% confidence interval)** | **No. considered high risk** |
| HEART score | 0.42 (0.37 to 0.47) | 0.88 (0.84 to 0.91) | 0.59 (0.55 to 0.63) | 0.78 (0.72 to 0.84) | 192 (27) |
| T-MACS model | 0.47 (0.42 to 0.53) | 0.89 (0.85 to 0.92) | 0.62 (0.57 to 0.66) | 0.81 (0.75 to 0.86) | 209 (30) |
| GRACE score | 0.15 (0.12 to 0.19) | 0.89 (0.86 to 0.92) | 0.50 (0.46 to 0.54) | 0.60 (0.49 to 0.70) | 90 (13) |
| CTCA | 0.74 (0.69 to 0.78) | 0.79 (0.74 to 0.83) | 0.74 (0.69 to 0.79) | 0.79 (0.74 to 0.83) | 336 (48) |
| \* High-risk’ thresholds are a HEART score of 6, a T-MACS estimate of 0.95, a GRACE score of 140, and obstructive coronary artery disease on CTCA.CTCA = computed tomography coronary angiography |

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| **Supplementary Table 7. Diagnostic performance for 30-day coronary revascularisation by subgroup.** |
|  | **Overall** | **Subgroup** |
| Age <65 years | Age ≥65 years | Female sex | Male sex |
| HEART score | 0.65 (0.61 to 0.70) | 0.72 (0.67 to 0.77) | 0.62 (0.56 to 0.69) | 0.77 (0.70 to 0.84) | 0.60 (0.55 to 0.66) |
| T-MACS model | 0.71 (0.67 to 0.75) | 0.73 (0.69 to 0.78) | 0.68 (0.61 to 0.75) | 0.74 (0.67 to 0.82) | 0.71 (0.66 to 0.75) |
| GRACE score | 0.49 (0.45 to 0.54) | 0.58 (0.52 to 0.64) | 0.51 (0.43 to 0.58) | 0.66 (0.58 to 0.74) | 0.55 (0.49 to 0.60) |
| CTCA | 0.80 (0.77 to 0.83) | 0.86 (0.83 to 0.89) | 0.72 (0.67 to 0.77) | 0.84 (0.79 to 0.90) | 0.75 (0.72 to 0.79) |
| \* Values are *C*-statistics (95% confidence interval).CTCA = computed tomography coronary angiography |

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| **Supplementary Table 8. Performance metrics for 30-day coronary revascularisation.** |
|  | **Sensitivity (95% confidence interval)** | **Specificity (95% confidence interval)** | **Negative predictive value (95% confidence interval)** | **Positive predictive value (95% confidence interval)** |
| **‘Low-risk’ threshold** |  |  |  |  |
| HEART score | 0.92 (0.88 to 0.96) | 0.19 (0.15 to 0.23) | 0.84 (0.76 to 0.90) | 0.35 (0.31 to 0.39) |
| T-MACS model | 0.94 (0.90 to 0.97) | 0.25 (0.21 to 0.29) | 0.89 (0.83 to 0.94) | 0.37 (0.33 to 0.41) |
| GRACE score | 0.46 (0.39 to 0.53) | 0.55 (0.50 to 0.59) | 0.68 (0.63 to 0.73) | 0.32 (0.27 to 0.38) |
| CTCA | 0.97 (0.94 to 0.99) | 0.33 (0.29 to 0.38) | 0.96 (0.92 to 0.99) | 0.41 (0.37 to 0.45) |
| **‘High-risk’ threshold** |  |  |  |  |
| HEART score | 0.40 (0.34 to 0.47) | 0.78 (0.75 to 0.82) | 0.73 (0.69 to 0.77) | 0.47 (0.40 to 0.54) |
| T-MACS model | 0.50 (0.43 to 0.56) | 0.80 (0.76 to 0.83) | 0.77 (0.73 to 0.81) | 0.54 (0.47 to 0.60) |
| GRACE score | 0.10 (0.07 to 0.15) | 0.86 (0.82 to 0.89) | 0.67 (0.63 to 0.71) | 0.26 (0.17 to 0.36) |
| CTCA | 0.87 (0.82 to 0.91) | 0.70 (0.66 to 0.75) | 0.92 (0.89 to 0.95) | 0.58 (0.53 to 0.64) |
| \* ‘Low-risk’ thresholds are a HEART score of 4, a T-MACS estimate of 0.05, a GRACE score of 109, and coronary artery disease on CTCA.† ‘High-risk’ thresholds are a HEART score of 6, a T-MACS estimate of 0.95, a GRACE score of 140, and obstructive coronary artery disease on CTCA.CTCA = computed tomography coronary angiography |

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| **Supplementary Table 9. Improvement in the diagnostic and the prognostic performance.** |
|  | **Overall** | **Improvement from clinical decision aids** | **p value** | **Improvement from CTCA** | **p value** |
| **Index hospital diagnosis of acute coronary syndrome** |  |  |  |  |  |
| HEART score *plus* CTCA | 0.85 (0.82 to 0.88) | 0.10 (0.07 to 0.13) | <0.001 | 0.05 (0.03 to 0.06) | <0.001 |
| T-MACS model *plus* CTCA | 0.88 (0.86 to 0.91) | 0.10 (0.07 to 0.13) | <0.001 | 0.08 (0.06 to 0.10) | <0.001 |
| GRACE score *plus* CTCA | 0.80 (0.77 to 0.84) | 0.21 (0.17 to 0.25) | <0.001 | 0.00 (−0.01 to 0.02) | 0.712 |
| **30-day coronary revascularisation** |  |  |  |  |  |
| HEART score *plus* CTCA | 0.82 (0.79 to 0.85) | 0.16 (0.13 to 0.20) | <0.001 | 0.02 (0.00 to 0.03) | 0.042 |
| T-MACS model *plus* CTCA | 0.85 (0.82 to 0.88) | 0.14 (0.10 to 0.17) | <0.001 | 0.05 (0.03 to 0.07) | <0.001 |
| GRACE score *plus* CTCA | 0.83 (0.80 to 0.86) | 0.34 (0.29 to 0.39) | <0.001 | 0.03 (0.01 to 0.05) | <0.001 |
| \* Values are *C*-statistics (95% confidence interval).CTCA = computed tomography coronary angiography |

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| **Supplementary Table 10. Prevalence of study outcomes by T-MACS estimate and by CTCA finding.** |
|  | **CTCA finding** |
| Normal coronary arteries | Non-obstructive coronary artery disease | Obstructive coronary artery disease |
| **Index hospital diagnosis of acute coronary syndrome** |  |  |  |  |
| **T-MACS estimate** | <0.05 | 0/41 (0) | 6/55 (11) | 16/37 (43) |
| 0.05–0.95 | 6/90 (7) | 39/103 (38) | 121/164 (74) |
| >0.95 | 11/32 (34) | 32/42 (76) | 127/135 (94) |
| **30-day coronary revascularisation** |  |  |  |  |
| **T-MACS estimate** | <0.05 | 0/41 (0) | 3/55 (5) | 11/37 (30) |
| 0.05–0.95 | 3/90 (3) | 9/103 (9) | 87/164 (53) |
| >0.95 | 3/32 (9) | 11/42 (26) | 98/135 (73) |
| CTCA = computed tomography coronary angiography |

**Supplementary Figure 1. Distribution of risk groups and coronary artery disease.**

\* The extent of coronary artery disease was based on computed tomography coronary angiography.

† Yellow bars represent normal coronary arteries.

‡ Red bars represent coronary artery disease, including both non-obstructive and obstructive coronary artery disease.

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**Supplementary Figure 2. The classification tree for index hospital diagnosis of acute coronary syndrome.**

CI = confidence interval; CTCA = computed tomography coronary angiography; NPV = negative predictive value, PPV = positive predictive value



**Supplementary Figure 3. The classification tree for 30-day coronary revascularisation.**

CI = confidence interval; CTCA = computed tomography coronary angiography; NPV = negative predictive value, PPV = positive predictive value

