**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 suspicious  Moderately suspicious  Slightly or non-suspicious | 2  1  0 |
| ECG | ST-segment deviation  Any abnormalities except for ST-segment deviation  Normal | 2  1  0 |
| Age, years | ≥65  45–65  ≤45 | 2  1  0 |
| Risk factors of coronary artery disease | Three and more risk factors or a history of atherosclerotic disease  One or two risk factors  No risk factor s | 2  1  0 |
| Cardiac troponin (at presentation) | ≥3x upper reference limit  1–3x upper reference limit  ≤1x upper reference limit | 2  1  0 |
| \* 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:  ECG = electrocardiogram | |

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| **Supplementary Table 4. The GRACE score.** | | |
| **Component** | **Points** | |
| Killip class | IV  III  II  I | 59  39  20  0 |
| Systolic blood pressure, mm Hg | ≤80  80–99  100–119  120–139  140–159  160–199  ≥200 | 58  53  43  34  24  10  0 |
| Heart rate, beats per minute | ≥200  150–199  110–149  90–109  70–89  50–69  ≤50 | 46  38  24  15  9  3  0 |
| Age, years | ≥90  80–89  70–79  60–69  50–59  40–49  30–39  ≤30 | 100  91  75  58  41  25  8  0 |
| Creatinine, mg/dL | >4.00  2.00–3.99  1.60–1.99  1.20–1.59  0.80–1.19  0.40–0.79  0.00–0.39 | 28  21  13  10  7  4  1 |
| Others | Cardiac arrest at presentation  Ischaemic ECG  Cardiac troponin (at presentation) > upper reference limit | 39  28  14 |
| \* 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.

**A graph of a bar chart

Description automatically generated with medium confidence**

**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

A screenshot of a medical chart

Description automatically generated

**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

A screenshot of a computer screen

Description automatically generated