Supplementary material

Analytical details

The Roche Diagnostics hs-cTnT assay has a limit of blank (LoB) of 3 ng/L, a limit of detection (LoD) of 5 ng/L and a CVA of 10% or lower for concentrations >4.5 ng/L. The 99th percentile URL is 9.0 ng/L in women and 16.8 ng/L in men. The hs-TnI assay by Abbott had a LoD of 1.9 ng/L and a 10% coefficient of variation at a concentration >5.2 ng/L. The 99th percentile URL is 15.6 ng/L in women and 34.2 ng/L in men. The cTnT assay (Roche) and the cTnI assay by Abbott target capture and detection epitopes that are midmolecular and adjacent; cTnT capture epitope at aa 125-131 and a single-detection epitope at aa 136-147; cTnI Abbott capture epitope at aa 24 to 40 and a single-detection epitope at aa 41 to 49 (27, 28). The hs-cTnI assay by Siemens has a LoD of 1.6 ng/L and a 10% coefficient of variation >6 ng/L. The 99th percentile URL is 38.6 ng/L in women and 53.5 ng/L in men. The cTnI Siemens assay feature a capture antibody targeting a central epitope at amino acids (aa) 41-50 and two detection antibodies targeting a central epitope at aa 29-34 as well as a distal epitope at aa 171-190.

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| **Table S1.** Number of presumably healthy adults used to determine normal range and the identified percentiles within normal range in women/men, ng/L. Percentiles were estimated using the non-parametric method. |
| Assay | nwomen | nmen | 99th percentile | 97.5th percentile | 95th percentile | 90th percentile |
| Roche cobas | 265 | 266 | 9.0/16.8 | 8.4/13.3 | 6.9/11.3 | 6.1/9.2 |
| Abbott Architect | 765 | 766 | 15.6/34.2 | 14.1/27.0 | 8.0/13.0 | 4.8/7.6 |
| Siemens Atellica | 1007 | 994 | 38.6/53.5 | 17.8/26.3 | 10.1/15.9 | 6.3/9.2 |

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| **Table S2a.** Correlation (r) between cTn assays (0-hour samples) grouped by presence or absence of chronic myocardial injury. |
|  | CMIa | No CMI | All |
|  |  | n | r | n | r | n | r |
| cTnI Abbott vs. cTnI Siemens |  |  |  |  |
|  | Women | 111 | 0.808(0.696-0.920) | 350 | 0.716(0.643-0.790) | 461 | 0.844(0.795-0.893) |
|  | Men | 107 | 0.793(0.675-0.911) | 590 | 0.851(0.808-0.894) | 697 | 0.888(0.854-0.922) |
|  | All | 218 | 0.821(0.744-0.898) | 940 | 0.824(0.787-0.860) | 1158 | 0.876(0.849-0.904) |
| cTnT Roche vs. cTnI Abbott |  |  |  |  |
|  | Women | 111 | 0.596(0.444-0.749) | 407 | 0.643(0.568-0.718) | 518 | 0.741(0.683-0.799) |
|  | Men | 107 | 0.588(0.432-0.745) | 658 | 0.744(0.693-0.795) | 765 | 0.802(0.759-0.844) |
|  | All | 218 | 0.641(0.538-0.744) | 1065 | 0.724(0.683-0.766) | 1283 | 0.785(0.751-0.819) |
| cTnT Roche vs. cTnI Siemens |  |  |  |  |
|  | Women | 111 | 0.475(0.308-0.642) | 351 | 0.424(0.329-0.519) | 462 | 0.671(0.603-0.738) |
|  | Men | 107 | 0.428(0.253-0.603) | 593 | 0.658(0.597-0.719) | 700 | 0.742(0.692-0.792) |
|  | All | 218 | 0.510(0.395-0.626) | 944 | 0.617(0.567-0.667) | 1162 | 0.724(0.684-0.763) |
| All correlation values are significant with a p-value <0.001. cTn indicates cardiac troponin; CMI, chronic myocardial injury; n, number of patients; r, correlation measured by Pearson´s correlation test.aStable cTn concentrations with at least one value >99th percentile measured by any of the three cTn assays. |

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| **Table S2b.** Correlation (r) between cTn assays grouped by adjudicated diagnoses. |
|  | Coronary artery diseasea | Other cardiac diseasesb | Non-cardiac chest painc | All |
|  |  | n | r | n | r | n | r | n | r |
| cTnI Abbott vs. cTnI Siemens |  |  |  |  |  |  |
|  | Women | 61 | 0.835(0.691-0.978) | 19 | 0.987(0.906-1.068) | 381 | 0.801(0.741-0.862) | 461 | 0.844(0.795-0.893) |
|  | Men | 137 | 0.943(0.887-1.000) | 53 | 0.858(0.714-1.003) | 507 | 0.859(0.815-0.904) | 697 | 0.888(0.854-0.922) |
|  | All | 198 | 0.917(0.861-0.973) | 72 | 0.896(0.790-1.002) | 888 | 0.841(0.806-0.877) | 1158 | 0.876(0.849-0.904) |
| cTnT Roche vs. cTnI Abbott |  |  |  |  |  |  |  |
|  | Women | 66 | 0.625(0.431-0.820) | 20 | 0.953(0.803-1.103) | 432 | 0.689(0.620-0.757) | 518 | 0.741(0.683-0.799) |
|  | Men | 147 | 0.820(0.727-0.914) | 60 | 0.861(0.728-0.995) | 558 | 0.730(0.673-0.787) | 765 | 0.802(0.759-0.844) |
|  | All | 213 | 0.770(0.683-0.856) | 80 | 0.888(0.784-0.992) | 990 | 0.717(0.673-0.760) | 1283 | 0.785(0.751-0.819) |
| cTnT Roche vs. cTnI Siemens |  |  |  |  |  |  |
|  | Women | 61 | 0.635(0.434-0.836) | 19 | 0.941(0.767-1.114) | 382 | 0.582(0.500-0.664) | 462 | 0.671(0.603-0.738) |
|  | Men | 137 | 0.766(0.656-0.875) | 53 | 0.825(0.667-0.984) | 510 | 0.659(0.594-0.725) | 700 | 0.742(0.692-0.792) |
|  | All | 198 | 0.741(0.646-0.835) | 72 | 0.858(0.735-0.980) | 892 | 0.635(0.584-0.686) | 1162 | 0.724(0.684-0.763) |
| All correlation values are significant with a p-value <0.001. cTn indicates cardiac troponin; n, number of patients; r, correlation measured by Pearson´s correlation test.aUnstable or stable angina pectoris.bNon-coronary cardiac diseases like pericarditis, myocarditis, Takotsubo cardiomyopathy, heart failure, arrythmias or valve disorders, without dynamic change in cTn values.cMyalgia, esophageal disease, abdominal diseases, respiratory infections/diseases, pleural effusion, pulmonary embolism, and other non-cardiac conditions, without dynamic change in cTn values. |

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| **Table S3.** Clinical characteristics of patients with CMI diagnosed by any assay, the cTnT assay or a cTnI assay. |
|  | Any assay (n=218) | cTnT Roche assay only (n=152) | cTnI assay only (Abbott and/or Siemens, n=40) |
| Age, median | 76 (68-84) | 76 (71-84) | 70 (63-84) |
| Female gender (%) | 111 (50.9%) | 84 (55.3%) | 11 (27.5%)a |
| **Cardiovascular risk factors** |  |  |
| Obesityb (%) | 27 (25.7%) | 19 (23.8%) | 6 (40.0%) |
| Active smoker (%) | 32 (14.7%) | 23 (15.1%) | 4 (10.0%) |
| Former smoker (%) | 102 (46.8%) | 75 (49.3%) | 19 (47.5%) |
| Hyperlipidemia (%) | 58 (26.6%) | 45 (29.6%) | 6 (15.0%) |
| Diabetes mellitus (%) | 44 (20.2%) | 29 (19.1%) | 10 (25.0%) |
|  Insulin-dependent (%) | 19 (8.7%) | 11 (7.2%) | 5 (12.5%) |
| Hypertension (%) | 122 (56.0%) | 94 (61.8%) | 15 (37.5%)a |
| Family history of CAD (%) | 22 (10.1%) | 14 (9.2%) | 5 (12.5%) |
| **Medical history** |  |  |  |
| Previous AMI (%) | 64 (29.4%) | 44 (28.9%) | 13 (32.5%) |
| Previous PCI (%) | 55 (25.2%) | 37 (24.3%) | 14 (35.0%) |
| Previous CABG (%) | 31 (14.2%) | 21 (13.8%) | 7 (17.5%) |
| Atrial fibrillation (%) | 53 (24.3%) | 38 (25.0%) | 8 (20.0%) |
| Previous stroke (%) | 12 (5.5%) | 12 (7.9%) | 0 (0.0%) |
| Chronic kidney disease (%) | 79 (36.2%) | 54 (35.5%) | 13 (32.5%) |
| Peripheral arterial disease (%) | 10 (4.6%) | 8 (5.3%) | 2 (5.0%) |
| Known heart failure (%) | 21 (9.6%) | 10 (6.6%) | 6 (15.0%) |
| **Clinical and laboratory parameters** |  |  |
| Systolic blood pressure, mmHg | 147 (144-150) | 148 (144-151) | 143 (134-150) |
| Diastolic blood pressure, mmHg | 82 (79-85) | 82 (79-84) | 82 (77-86) |
| Pulse, bpm | 78 (75-80) | 77 (74-80) | 79 (72-85) |
| Hemoglobin, g/dL | 13.5 (13.3-13.7) | 13.5 (13.3-13.8) | 13.7 (13.1-14.3) |
| Glucose, mmol/L | 6.9 (6.6-7.2) | 6.7 (6.4-7.0) | 7.3 (6.4-8.1) |
| CRP, mg/L, median  | 2.0 (0.9-4.5) | 2.0 (0.6-4.0) | 2.0 (0.9-5.0) |
| proBNP, ng/L, median | 88 (32-310) | 82 (33-214) | 199 (39-984)a |
| eGFR, ml/min/1.37m2 | 65.9 (62.7-69.0) | 66.2 (63.0-69.5) | 71.7 (62.5-81.0) |
| **Ejection fraction** |  |  |  |
| >50% (%) | 66 (71.0%) | 43 (71.7%) | 15 (71.4%) |
| 30-49% (%) | 14 (15.1%) | 9 (15.0%) | 4 (19.0%) |
| <30% (%) | 13 (14.0%) | 8 (13.3%) | 2 (9.5%) |
| **Symptom triggers** |  |  |  |
| Dependent on position (%) | 14 (6.4%) | 9 (5.9%) | 5 (12.5%) |
| Dependent on respiration (%) | 21 (9.6%) | 13 (8.6%) | 4 (10.0%) |
| Dependent on palpation (%) | 22 (10.1%) | 18 (11.8%) | 1 (2.5%) |
| CMI indicates chronic myocardial injury; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention, CABG, coronary artery bypass grafting.aSignificantly different compared to patients with CMI diagnosed by the cTnT assay only; p-value <0.05.bBMI>30, measured in 48.2% of patients (105 patients in total; 80 identified with cTnT only and 15 identified with a cTnI assay only)ceGFR <60 ml/min/1.37m2dMeasured in 42.7% of patients (93 patients in total; 60 identified with cTnT only and 21 identified with a cTnI assay only) |

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| **Table S4.** Difference in area under the receiver operating characteristics (AUC-ROC) curve for the three endpoints with cTn as continuous variables.  |
|  | cTnI (Abbott) vs. cTnI (Siemens) | cTnT (Roche) vs. cTnI (Abbott) | cTnT (Roche) vs. cTnI (Siemens) |
| **Primary endpointa** |  |  |  |
| AUC women | 0.774 (0.733-0.812) vs. 0.702 (0.657-0.743)p=0.041 | 0.685 (0.640-0.727) vs. 0.774 (0.733-0.812) p=0.021 | 0.685 (0.640-0.727) vs.0.702 (0.657-0.743)p=0.757 |
| AUC men | 0.682 (0.645-0.716)vs.0.628 (0.591-0.664) p<0.001 | 0.689 (0.653-0.724) vs.0.682 (0.645-0.716)p=0.758 | 0.689 (0.653-0.724)vs.0.628 (0.591-0.664) p=0.010 |
| AUC all | 0.718 (0.691-0.744) vs. 0.662 (0.634-0.689) p<0.001 | 0.697 (0.670-0.724) vs.0.718 (0.691-0.744) p=0.316 | 0.697 (0.670-0.724)vs.0.662 (0.634-0.689) p=0.123 |
| **Secondary endpointb** |  |  |  |
| AUC women | 0.824 (0.786-0.858) vs. 0.769 (0.727-0.807)p=0.016 | 0.800 (0.761-0.836) vs.0.824 (0.786-0.858)p=0.394 | 0.800 (0.761-0.836)vs.0.769 (0.727-0.807)p=0.357 |
| AUC men | 0.720 (0.685-0.753)vs. 0.674 (0.638-0.709)p<0.001 | 0.745 (0.711-0.777) vs. 0.720 (0.685-0.753)p=0.230 | 0.745 (0.711-0.777) vs. 0.674 (0.638-0.709)p<0.001 |
| AUC all | 0.762 (0.736-0.786)vs.0.714 (0.687-0.740) p<0.001 | 0.770 (0.745-0.794)vs.0.762 (0.736-0.786)p=0.600 | 0.770 (0.745-0.794)vs.0.714 (0.687-0.740) p=0.001 |
| **Tertiary endpointc** |  |  |  |
| AUC women | 0.836 (0.798-0.868)vs.0.768 (0.726-0.806)P=0.058 | 0.880 (0.846-0.908)vs.0.836 (0.798-0.868)p=0.072 | 0.880 (0.846-0.908)vs.0.768 (0.726-0.806)p=0.002 |
| AUC men | 0.766 (0.733-0.798)vs. 0.732 (0.697-0.764)p=0.034 | 0.808 (0.776-0.836) vs.0.766 (0.733-0.798)p=0.061 | 0.808 (0.776-0.836) vs.0.732 (0.697-0.764)p=0.005 |
| AUC all | 0.796 (0.771-0.819)vs. 0.750 (0.724-0.775)p=0.005 | 0.836 (0.813-0.857) vs.0.796 (0.771-0.819)p=0.018 | 0.836 (0.813-0.857) vs.0.750 (0.724-0.775)p<0.001 |
| All differences with p-value <0.05 are highlighted. AUC indicates area under the curve; cTnT, cardiac troponin T; cTnI, cardiac troponin T, w, women; m, men, p, p-value for difference.aCardiovascular mortality, acute myocardial infarction or revascularization.bAll-cause mortality, AMI, revascularization or hospitalization due to heart failure or stroke.cAll-cause mortality. |

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| **Table S5.** Prognostic precision of high-sensitivity cardiac troponins at different percentile cutoff values and limit of detection provided by manufacturers for the primary endpoint of CV death, AMI or revascularization. |
|  |  | True pos | False pos | True neg | False neg | Odds ratio | NPV(95% CI) | Sens(95% CI) | PPV(95% CI) | Spes(95% CI) | >Perc.a | AUC |
| Troponin T (Roche) |
|  | 99th percentile 9.0/16.8 ng/L (w/m) | 31 | 176 | 878 | 62 | 2.5 (1.6-4.0) | 93.4(92.5-94.3) | 33.3(23.9-43.9) | 15.0(11.4-19.5) | 83.3 (80.9-85.5) | 18.0 | 0.583(0.554-0.612) |
|  | 97.5th percentile8.4/13.3 ng/L (w/m) | 45 | 221 | 833 | 48 | 3.5(2.3-5.4) | 94.6(93.4-95.5) | 48.4(37.9-59.0) | 16.9(13.8.20.5) | 79.0 (76.5-81.5) | 23.2 | 0.637 (0.609-0.665) |
|  | 95th percentile6.9/11.3 (w/m) | 51 | 291 | 763 | 42 | 3.2 (2.1-4.9) | 94.8 (93.5-95.8) | 54.8(44.2-65.2) | 14.9(12.4-17.7) | 72.4(69.6-75.1) | 29.8 | 0.636(0.608-0.664) |
|  | 90th percentile6.1/9.2 ng/L (w/m) | 58 | 334 | 720 | 35 | 3.6(2.3-5.5) | 95.4 (94.0-96.4) | 62.4(51.7-72.2) | 14.8(12.6-17.2) | 68.3(65.4-71.1) | 34.2 | 0.653(0.625-0.681) |
|  | Limit of detection5 ng/L (all) | 80 | 664 | 390 | 13 | 3.6(2.0-6.6) | 96.8 (94.7-98.0) | 86.0(77.3-92.3) | 10.7(9.9-11.7) | 37.0(34.1-40.0) | 64.9 | 0.615(0.586-0.643) |
| Troponin I (Abbott) |
|  | 99th percentile 15.6/34.2 ng/L (w/m) | 9 | 37 | 1017 | 84 | 2.9 (1.4-6.3) | 92.4 (91.9-92.8) | 9.7(4.5-17.6) | 19.6(10.8-32.8) | 96.5(95.2-97.5) | 4.0 | 0.531(0.501-0.560) |
|  | 97.5th percentile14.1/27.0 ng/L (w/m) | 11 | 49 | 1005 | 82 | 2.8(1.4-5.5) | 92.5(91.9-93.0) | 11.8(6.1-20.2) | 18.3(10.8-29.4) | 95.4(93.9-96.5) | 5.2 | 0.536(0.507-0.565) |
|  | 95th percentile8.0/13.0 ng/L (w/m) | 19 | 113 | 941 | 74 | 2.1(1.2-3.7) | 92.7(92.0-93.4) | 20.4(12.8-30.1) | 14.4(9.8-20.7) | 89.3(87.3-91.1) | 11.5 | 0.549(0.519-0.578) |
|  | 90th percentile4.8/7.6 ng/L (w/m) | 38 | 199 | 855 | 55 | 3.0(1.9-4.6) | 94.0(92.9-94.9) | 40.9(30.8-51.5) | 16.0(12.7-20.1) | 81.1(78.6-83.4) | 20.7 | 0.610(0.581-0.638) |
|  | Limit of detection1.9 ng/L (all) | 84 | 673 | 381 | 9 | 5.3(2.6-10.6) | 97.7(95.8-98.8) | 90.3(82.4-95.5) | 11.1(10.3-11.9) | 36.2(33.2-39.1) | 66.0 | 0.632(0.604-0.660) |
| Troponin I (Siemens) |
|  | 99th percentile38.6/53.5 ng/L (w/m) | 8 | 45 | 1009 | 85 | 2.1(0.97-4.6) | 92.2(91.8-92.7) | 8.6(3.8-16.3) | 15.1(8.0-26.8) | 95.7(94.3-96.9) | 4.6 | 0.522(0.492-0.551) |
|  | 97.5th percentile17.8/26.3 ng/L (w/m) | 13 | 98 | 956 | 80 | 1.6(0.85-3.0) | 92.3(91.7-92.9) | 14.0(7.7-22.7) | 11.7(7.2-18.5) | 90.7(88.8-92.4) | 9.7 | 0.524(0.494-0.553) |
|  | 95th percentile10.1/15.9 ng/L (w/m) | 25 | 165 | 889 | 68 | 2.0(1.2-3.2) | 92.9(92.0-93.7) | 26.9(18.2-37.1) | 13.2(9.5-17.9) | 84.4(82.0-86.5) | 16.6 | 0.556(0.527-0.585) |
|  | 90th percentile6.3/9.2 ng/L (w/m) | 39 | 279 | 775 | 54 | 2.0(1.3-3.1) | 93.5(92.4-94.5) | 41.9(31.8-52.6) | 12.3(9.7-15.3) | 73.6(70.8-76.2) | 27.7 | 0.577(0.548-0.606) |
|  | Limit of detection1.6 ng/L (all) | 90 | 950 | 104 | 3 | 3.3(1.0-10.6) | 97.2(91.8-99.1) | 96.8(90.9-99.3) | 8.6(8.3-9.0) | 9.9(8.1-11.8) | 90.7 | 0.533(0.504-0.562) |
| W indicates women; m, men; NPV, negative predictive value; PPV, positive predictive value; AUC, area under the receiver operator characteristics curve.aPercent of patients with high-sensitivity cardiac troponin concentration at presentation above given percentile. |

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| **Table S6.** Prognostic precision of high-sensitivity cardiac troponins at different percentile cutoff values and limit of detection provided by manufacturers for the secondary endpoint of all-cause mortality, AMI, revascularization, or hospitalization due to heart failure or stroke. |
|  |  | True pos | False pos | True neg | False neg | Odds ratio | NPV(95% CI) | Sens(95% CI) | PPV(95% CI) | Spes(95% CI) | >Perc.a | AUC |
| Troponin T (Roche) |
|  | 99th percentile 9.0/16.8 ng/L (w/m) | 74 | 133 | 852 | 88 | 5.4(3.8-7.7) | 90.6(89.4-91.8) | 45.7(37.8-53.7) | 35.8(30.6-41.2) | 86.5(84.2-88.6) | 18.0 | 0.661(0.633-0.688) |
|  | 97.5th percentile8.4/13.3 ng/L (w/m) | 90 | 176 | 809 | 72 | 5.7(4.0-8.1) | 91.8(90.4-93.1) | 55.6(47.6-63.4) | 33.8(29.7.38.3) | 82.1(79.6-84.5) | 23.2 | 0.688(0.661-0.715) |
|  | 95th percentile6.9/11.3 (w/m) | 102 | 240 | 745 | 60 | 5.3(3.7-7.5) | 92.6(91.0-93.8) | 63.0(55.0-70.4) | 29.8(26.6-33.3) | 75.6(72.8-78.3) | 29.8 | 0.693(0.665-0.720) |
|  | 90th percentile6.1/9.2 ng/L (w/m) | 115 | 277 | 708 | 47 | 6.2(4.3-9.0) | 93.8(92.2-95.1) | 71.0(63.4-77.8) | 29.3(26.5-32.3) | 71.9(69.0-74.7) | 34.2 | 0.714(0.687-0.740) |
|  | Limit of detection5 ng/L (all) | 145 | 599 | 386 | 17 | 5.5(3.3-9.2) | 95.8(93.5-97.3) | 89.5(83.7-93.8) | 19.4(18.3-20.6) | 39.2(36.1-42.3) | 64.9 | 0.643(0.615-0.671) |
| Troponin I (Abbott) |
|  | 99th percentile 15.6/34.2 ng/L (w/m) | 15 | 31 | 954 | 147 | 3.2(1.7-6.0) | 86.7(86.1-87.3) | 9.3(5.3-14.8) | 32.6(21.1-46.7) | 96.9(95.6-97.9) | 4.0 | 0.531(0.501-0.560) |
|  | 97.5th percentile14.1/27.0 ng/L (w/m) | 19 | 41 | 944 | 143 | 3.1(1.7-5.4) | 86.9(86.2-87.5) | 11.7(7.2-17.7) | 31.7(21.6-43.8) | 95.9(94.4-97.0) | 5.2 | 0.538(0.509-0.567) |
|  | 95th percentile8.0/13.0 ng/L (w/m) | 44 | 88 | 897 | 118 | 3.8(2.5-5.7) | 88.4(87.4-89.4) | 27.2(20.5-34.7) | 33.3(26.6-40.8) | 91.1(89.1-92.8) | 11.5 | 0.591(0.562-0.620) |
|  | 90th percentile4.8/7.6 ng/L (w/m) | 73 | 164 | 821 | 89 | 4.1(2.9-5.9) | 90.3(88.9-91.4) | 45.1(37.3-53.1) | 30.8(26.3-35.7) | 83.4(80.9-85.7) | 20.7 | 0.642(0.614-0.670) |
|  | Limit of detection1.9 ng/L (all) | 150 | 607 | 378 | 12 | 7.8(4.2-14.2) | 96.9(94.8-98.2) | 92.6(87.4-96.1) | 19.8(18.7-20.8) | 38.4(35.3-41.5) | 66.0 | 0.655(0.627-0.682) |
| Troponin I (Siemens) |
|  | 99th percentile38.6/53.5 ng/L (w/m) | 17 | 36 | 949 | 145 | 3.1(1.7-5.7) | 86.8(86.2-87.4) | 10.5(6.2-16.3) | 32.1(21.4-45.1) | 96.4(95.0-97.4) | 4.6 | 0.534(0.505-0.563) |
|  | 97.5th percentile17.8/26.3 ng/L (w/m) | 30  | 81 | 904 | 132 | 2.5(1.6-4.0) | 87.3(86.4-88.1) | 18.5(12.9-25.4) | 27.0(20.1-35.2) | 91.8(89.9-93.4) | 9.7 | 0.551(0.522-0.581) |
|  | 95th percentile10.1/15.9 ng/L (w/m) | 55 | 135 | 850 | 107 | 3.2(2.2-4.7) | 88.9(87.7-89.9) | 34.0(26.7-41.8) | 29.0(23.8-34.7) | 86.3(84.0-88.4) | 16.6 | 0.601(0.572-0.630) |
|  | 90th percentile6.3/9.2 ng/L (w/m) | 83 | 235 | 750 | 79 | 3.4(2.4-4.7) | 90.5(89.0-91.8) | 51.2(43.3-59.2) | 26.1(22.7-29.9) | 76.1(73.4-78.8) | 27.7 | 0.637(0.608-0.665) |
|  | Limit of detection1.6 ng/L (all) | 157 | 883 | 102 | 5 | 3.6(1.5-9.0) | 95.3(89.5-98.0) | 96.9(92.9-99.0) | 15.1(14.6-15.5) | 10.4(8.6-12.5) | 90.7 | 0.536(0.507-0.566) |
| W indicates women; m, men; NPV, negative predictive value; PPV, positive predictive value; AUC, area under the receiver operator characteristics curve.aPercent of patients with high-sensitivity cardiac troponin concentration at presentation above given percentile. |

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| **Table S7.** Prognostic precision of high-sensitivity cardiac troponins at different percentile cutoff values and limit of detection provided by manufacturers for the tertiary endpoint of all-cause mortality. |
|  |  | True pos | False pos | True neg | False neg | Odds ratio | NPV(95% CI) | Sens(95% CI) | PPV(95% CI) | Spes(95% CI) | >Perc.a | AUC |
| Troponin T (Roche) |
|  | 99th percentile 9.0/16.8 ng/L (w/m) | 52 | 155 | 901 | 39 | 7.8(4.9-12.1) | 95.9(94.4-97.0) | 57.1(46.3-67.5) | 25.1(19.4-31.6) | 85.3(83.0-87.4) | 18.0 | 0.712(0.685-0.738) |
|  | 97.5th percentile8.4/13.3 ng/L (w/m) | 61 | 204 | 852 | 29 | 8.9(5.6-14.2) | 96.7(95.3-97.8) | 68.1(57.5-77.5) | 23.3(18.4.28.9) | 80.7(78.2-83.0) | 23.2 | 0.744(0.718-0.769) |
|  | 95th percentile6.9/11.3 (w/m) | 69 | 273 | 783 | 22 | 9.0(5.5-14.8) | 97.3(95.9-98.3) | 75.8(65.7-84.2) | 20.2(16.1-24.8) | 74.2(71.4-76.8) | 29.8 | 0.750(0.724-0.775) |
|  | 90th percentile6.1/9.2 ng/L (w/m) | 76 | 316 | 740 | 15 | 11.9(6.7-21.0) | 98.0(96.7-98.9) | 83.5(74.3-90.5) | 19.4(15.6-23.7) | 70.1(67.2-72.8) | 34.2 | 0.768(0.742-0.792) |
|  | Limit of detection5 ng/L (all) | 86 | 658 | 398 | 5 | 10.5(4.2-25.9) | 98.8(97.1-99.6) | 94.5(87.6-98.2) | 11.6(9.4-14.1) | 37.7(34.8-40.7) | 64.9 | 0.661(0.633-0.688) |
| Troponin I (Abbott) |
|  | 99th percentile 15.6/34.2 ng/L (w/m) | 13 | 33 | 1023 | 78 | 5.2(2.6-10.2) | 92.9(91.2-94.4) | 14.3(7.8-23.2) | 28.3(16.0-43.5) | 96.9(95.6-97.8) | 4.0 | 0.556(0.527-0.585) |
|  | 97.5th percentile14.1/27.0 ng/L (w/m) | 16 | 44 | 1012 | 75 | 4.9(2.6-9.1) | 93.1(91.4-94.5) | 17.6(10.4-27.0) | 26.7(16.1-39.7) | 95.8(94.5-97.0) | 5.2 | 0.567(0.538-0.596) |
|  | 95th percentile8.0/13.0 ng/L (w/m) | 32 | 100 | 956 | 59 | 5.2(3.2-8.4) | 94.2(92.6-95.6) | 35.2(25.4-45.9) | 24.2(17.2-32.5) | 90.5(88.6-92.2) | 11.5 | 0.628(0.600-0.657) |
|  | 90th percentile4.8/7.6 ng/L (w/m) | 47 | 190 | 866 | 44 | 4.9(3.1-7.6) | 95.2(93.6-96.5) | 51.7(40.9-62.3) | 19.8(15.0-25.5) | 82.0(79.6-84.3) | 20.7 | 0.668(0.640-0.696) |
|  | Limit of detection1.9 ng/L (all) | 88 | 669 | 387 | 3 | 17.0(5.3-54.0) | 99.2(97.8-99.8) | 96.7(90.7-99.3) | 11.6(9.4-14.1) | 36.7(33.7-39.6) | 66.0 | 0.667(0.639-0.694) |
| Troponin I (Siemens) |
|  | 99th percentile38.6/53.5 ng/L (w/m) | 14 | 39 | 1017 | 77 | 4.7(2.5-9.1) | 93.0(91.3-94.4) | 15.4(8.7-24.5) | 26.4(15.3-40.3) | 96.3(95.0-97.4) | 4.6 | 0.558(0.529-0.587) |
|  | 97.5th percentile17.8/26.3 ng/L (w/m) | 25  | 86 | 970 | 66 | 4.3(2.6-7.1) | 93.6(92.0-95.0) | 27.5(18.6-37.8) | 22.5(15.1-31.4) | 91.9(90.0-93.4) | 9.7 | 0.597(0.568-0.625) |
|  | 95th percentile10.1/15.9 ng/L (w/m) | 36 | 154 | 902 | 55 | 3.8(2.4-6.0) | 94.3(92.6-95.6) | 39.6(29.5-50.4) | 19.0(13.6-25.3) | 85.4(83.1-87.5) | 16.6 | 0.625(0.596-0.653) |
|  | 90th percentile6.3/9.2 ng/L (w/m) | 56 | 262 | 794 | 35 | 4.8(3.1-7.6) | 95.8(94.2-97.0) | 61.5(50.8-71.6) | 17.6(13.6-22.3) | 75.2(72.5-77.8) | 27.7 | 0.684(0.656-0.710) |
|  | Limit of detection1.6 ng/L (all) | 87 | 953 | 103 | 4 | 2.4(0.8-6.5) | 96.3(90.7-99.0) | 95.6(89.1-98.8) | 8.4(6.8-10.2) | 9.8(8.0-11.7) | 90.7 | 0.527(0.497-0.556) |
| W indicates women; m, men; NPV, negative predictive value; PPV, positive predictive value; AUC, area under the receiver operator characteristics curve.aPercent of patients with high-sensitivity cardiac troponin concentration at presentation above given percentile. |

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| **Table S8.** Prognostic precision for high-sensitivity cardiac troponin I using biologic equivalent cutoff values compared to high-sensitivity cardiac troponin T for the primary endpoint of CV death, AMI, or revascularization. |
|  |  | True pos | False pos | True neg | False neg | Odds ratio | NPV(95% CI) | Sens(95% CI) | PPV(95% CI) | Spes(95% CI) | >Perc.a | AUC |
| Troponin I (Abbott) |
|  | 99th percentile 4.1/8.7 ng/L (w/m) | 36 | 204 | 850 | 57 | 2.6 (1.7-4.1) | 93.7(92.7-94.6) | 38.7(28.8-49.4) | 15.0(11.7-19.0) | 80.7(78.1-83.0) | 20.9 | 0.597c(0.568-0.625) |
|  | 97.5th percentile3.8/6.8 ng/L (w/m) | 41 | 244 | 810 | 52 | 2.6 (1.7-4.0) | 94.0(92.9-95.0) | 44.1(33.8-54.8) | 14.4(11.5-17.8) | 76.9(74.2-79.4) | 24.8 | 0.605c(0.576-0.633) |
|  | 95th percentile3.1/5.7 ng/L (w/m) | 49 | 290 | 764 | 44 | 2.9(1.9-4.5) | 94.6(93.3-95.6) | 52.7(42.1-63.1) | 14.5(12.0-17.3) | 72.5(69.7-75.2) | 29.6 | 0.626c(0.597-0.654) |
|  | 90th percentile2.8/4.6 ng/L (w/m) | 58 | 354 | 700 | 35 | 3.3(2.1-5.1) | 95.2(93.9-96.3) | 62.4(51.7-72.2) | 14.1(12.1-16.4) | 66.4(63.5-69.3) | 35.9 | 0.644(0.615-0.672) |
| Troponin I (Siemens) |
|  | 99th percentile6.9/16.5 ng/L (w/m) | 27 | 198 | 856 | 66 | 1.8(1.1-2.9) | 92.8(91.9-93.7) | 29.0(20.1-39.4) | 12.0(8.8-16.1) | 81.2(78.7-83.5) | 19.6 | 0.551(0.522-0.580) |
|  | 97.5th percentile6.3/12.5 ng/L (w/m) | 33 | 232 | 822 | 60 | 1.9(1.2-3.1) | 93.2(92.2-94.1) | 35.5(25.8-46.1) | 12.5(9.6-16.1) | 78.0(75.4-80.5) | 23.1 | 0.567b(0.538-0.596) |
|  | 95th percentile5.0/10.3 ng/L (w/m) | 40 | 298 | 756 | 53 | 1.9(1.2-2.9) | 93.5(92.3-94.5) | 43.0(32.8-53.7) | 11.8(9.4-14.7) | 71.7(68.9-74.4) | 29.5 | 0.574(0.544-0.603) |
|  | 90th percentile4.3/8.1 ng/L (w/m) | 48 | 364 | 690 | 45 | 2.0(1.3-3.1) | 93.9(92.5-95.0) | 51.6(41.0-62.1) | 11.7(9.6-14.0) | 65.6(62.5-68.3) | 35.9 | 0.585(0.556-0.614) |
| W indicates women; m, men; NPV, negative predictive value; PPV, positive predictive value; AUC, area under the receiver operator characteristics curve.aPercent of patients with high-sensitivity cardiac troponin concentration at presentation above given percentile.bSignificantly different compared to percentile provided by manufacturer, p<0.05cSignificantly different compared to percentile provided by manufacturer, p<0.01 |

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| **Table S9.** Prognostic precision of high-sensitivity cardiac troponin I using biologic equivalent cutoff values compared to high-sensitivity cardiac troponin T for the secondary endpoint of all-cause mortality, AMI, revascularization, or hospitalization due to heart failure or stroke. |
|  |  | True pos | False pos | True neg | False neg | Odds ratio(95% CI) | NPV(95% CI) | Sens (95% CI) | PPV(95% CI) | Spes(95% CI) | >Perc.a | AUC |
| Troponin I (Abbott) |
|  | 99th percentile 4.1/8.7 ng/L (w/m) | 71 | 169 | 816 | 91 | 3.8(2.7-5.4) | 90.0(88.6-91.2) | 43.8(36.1-51.8) | 29.6(25.2-34.4) | 82.8(80.3-85.2) | 20.9 | 0.633c(0.605-0.661) |
|  | 97.5th percentile3.8/6.8 ng/L (w/m) | 81 | 204 | 781 | 81 | 3.8(2.7-5.4) | 90.6(89.2-91.9) | 50.0(42.1-58.0) | 28.4(24.6-32.6) | 79.3(76.6-81.8) | 24.8 | 0.646c(0.618-0.674) |
|  | 95th percentile3.1/5.7 ng/L (w/m) | 95 | 244 | 741 | 67 | 4.3(3.1-6.1) | 91.7(90.2-93.0) | 58.6(50.7-66.3) | 28.0(24.7-31.6) | 75.2(72.4-77.9) | 29.6 | 0.669c(0.641-0.697) |
|  | 90th percentile2.8/4.6 ng/L (w/m) | 110 | 302 | 683 | 52 | 4.8(3.3-6.8) | 92.9(91.3-94.3) | 67.9(60.1-75.0) | 26.7(24.0-29.6) | 69.3(66.4-72.2) | 35.9 | 0.686b(0.658-0.713) |
| Troponin I (Siemens) |
|  | 99th percentile6.9/16.5 ng/L (w/m) | 60 | 165 | 820 | 102 | 2.9(2.0-4.2) | 88.9(87.7-90.1) | 37.0(29.6-45.0) | 26.7(22.2-31.7) | 83.3(80.8-85.5) | 19.6 | 0.601c(0.572-0.630) |
|  | 97.5th percentile6.3/12.5 ng/L (w/m) | 73 | 192 | 793 | 89 | 3.3(2.4-4.8) | 89.9(88.5-91.1) | 45.1(37.3-53.1) | 27.6(23.5-32.0) | 80.5(77.9-82.9) | 23.1 | 0.628c(0.599-0.656) |
|  | 95th percentile5.0/10.3 ng/L (w/m) | 83 | 255 | 730 | 79 | 3.0(2.1-4.2) | 90.2(88.7-91.6) | 51.2(43.3-59.2) | 24.6(21.3-28.1) | 74.1(71.3-76.8) | 29.5 | 0.627 (0.598-0.655) |
|  | 90th percentile4.3/8.1 ng/L (w/m) | 96 | 316 | 669 | 66 | 3.1(2.2-4.3) | 91.0(89.3-92.5) | 59.3(51.3-66.9) | 23.3(20.6-26.2) | 67.9(64.9-70.8) | 35.9 | 0.636 (0.607-0.664) |
| Tn cutoff values are for women and men respectively. NPV indicates negative predictive value; PPV, positive predictive value; AUC, area under the receiver operator characteristics curve.aPercent of patients with high-sensitivity cardiac troponin concentration at presentation above given percentile.bSignificantly different compared to percentile provided by manufacturer, p<0.05cSignificantly different compared to percentile provided by manufacturer, p<0.001 |

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| **Table S10.** Prognostic precision of high-sensitivity cardiac troponin I using biologic equivalent cutoff values compared to high-sensitivity cardiac troponin T for the tertiary endpoint of all-cause mortality. |
|  |  | True pos | False pos | True neg | False neg | Odds ratio(95% CI) | NPV(95% CI) | Sens (95% CI) | PPV(95% CI) | Spes(95% CI) | >Perc.a | AUC |
| Troponin I (Abbott) |
|  | 99th percentile 4.1/8.7 ng/L (w/m) | 46 | 194 | 862 | 45 | 4.5(2.9-7.0) | 95.0(93.4-96.4) | 50.6(39.9-61.2) | 19.2(14.4-24.7) | 81.6(79.2-83.9) | 20.9 | 0.661d(0.633-0.688) |
|  | 97.5th percentile3.8/6.8 ng/L (w/m) | 54 | 231 | 825 | 37 | 5.2(3.3-8.1) | 95.7(94.1-97.0) | 59.3(48.5-69.5) | 19.0(14.6-24.0) | 78.1(75.5-80.6) | 24.8 | 0.687d(0.660-0.714) |
|  | 95th percentile3.1/5.7 ng/L (w/m) | 62 | 277 | 779 | 29 | 6.0(3.8-9.5) | 96.4(94.9-97.6) | 68.1(57.5-77.5) | 18.3(14.3-22.8) | 73.8(71.0-76.4) | 29.6 | 0.710c(0.682-0.736) |
|  | 90th percentile2.8/4.6 ng/L (w/m) | 69 | 343 | 713 | 22 | 6.5(4.0-10.7) | 97.0(95.5-98.1) | 75.8(65.7-84.2) | 16.8(13.3-20.7) | 67.5(64.6-70.3) | 35.9 | 0.717b(0.690-0.743) |
| Troponin I (Siemens) |
|  | 99th percentile6.9/16.5 ng/L (w/m) | 39 | 186 | 870 | 52 | 3.5(2.3-5.5) | 94.4(92.7-95.8) | 42.9(32.5-53.7) | 17.3(12.6-22.9) | 82.4(80.0-84.6) | 19.6 | 0.626c(0.597-0.654) |
|  | 97.5th percentile6.3/12.5 ng/L (w/m) | 51 | 214 | 842 | 40 | 5.0(3.2-7.8) | 95.5(93.9-96.7) | 56.0(45.3-66.4) | 19.3(14.7-24.5) | 79.7(77.2-82.1) | 23.1 | 0.679d(0.651-0.706) |
|  | 95th percentile5.0/10.3 ng/L (w/m) | 56 | 282 | 774 | 35 | 4.4(2.8-6.8) | 95.7(94.0-97.0) | 61.5(50.8-71.6) | 16.6(12.8-21.0) | 73.3(70.5-75.9) | 29.5 | 0.674b(0.646-0.701) |
|  | 90th percentile4.3/8.1 ng/L (w/m) | 61 | 351 | 705 | 30 | 4.1(2.6-6.4) | 95.9(94.2-97.2) | 67.0(56.4-76.5) | 14.8(11.5-18.6) | 66.8(63.8-69.6) | 35.9 | 0.669(0.641-0.696) |
| Tn cutoff values are for women and men respectively. NPV indicates negative predictive value; PPV, positive predictive value; AUC, area under the receiver operator characteristics curve.aPercent of patients with high-sensitivity cardiac troponin concentration at presentation above given percentile.bSignificantly different compared to percentile provided by manufacturer, p<0.05cSignificantly different compared to percentile provided by manufacturer, p<0.01dSignificantly different compared to percentile provided by manufacturer, p<0.001 |