

S3 Table

Author-Date	Country of study population	Inclusion criteria	Exclusion criteria	Follow up and HRs (95% CI)	Primary outcome	Secondary outcome	Sample size	Mean age of patients (years)	Study type	Biomarker measured	Mean biomarker levels in patients (pg/ml)	Mean biomarker levels in controls (pg/ml)	QUADAS score
(Liu, Shen et al. 2013)	China	Coronary artery disease	No patients with history of cardiomyopathy, valvular heart disease, tumours, inflammatory diseases, liver/renal dysfunction, cerebral vessel diseases, peripheral angiopathy, pregnancy	None	Levels of IL-33 and IL-6	None	113	Overall: 56.5±12.54	Case control	Serum IL-33 ELISA Nanjing Jiancheng Technology Industry 5 ng/L sensitivity	Blood taken at admission ACS: 78.60±44.84 Stable angina: 102.58±37.21	130.24±10.17	15
(Liu, Shen et al. 2014)	China	Coronary heart disease	No patients with history of cardiomyopathy, valvular heart disease, severe renal disease, respiratory insufficiency, severe hepatic disease, malignancy, infection, cerebral vessel diseases	None	Levels of IL-33 and MMP-28	None	143	AMI: 58.89±12.74 Unstable angina pectoris: 56.41±7.5 Stable angina pectoris: 55.24±8.39 Excluding stable, overall mean is 57.53±10.18	Case control	Serum IL-33 ELISA Nanjing Jiancheng Technology Industry 5 ng/ml sensitivity	Blood taken at admission AMI: 71.38±6.63 Unstable angina pectoris: 83.13±17.99 Stable angina pectoris: 102.58±37.21 Overall IL-33 is 88.17±29.21 Excluding stable, overall mean is 77.84±15.15	130.24±10.17	15
(Guzel, Serin et al. 2013)	Turkey	NSTEMI	No patients with renal failure, collagen tissue disease, infection, vasculitis, depression, undergone angioplasty, bypass surgery, open heart surgery	None	Levels of IL-33 and other markers	None	80	52.36±9.4	Case control	Serum IL-33 ELISA USCN Life Science, Houston 6.4 pg/ml sensitivity	Blood collected at admission and 12, 24, 48H after percutaneous coronary intervention At admission, 94.46±32.7 At 12H: 126.82±44.5 At 24H: 119.55±32.73 At 48H: 121.74±41.38 25 patients had unstable angina: At admission, 115.36±37.16 Combined unstable angina and NSTEMI is 103.96±36.03	At admission, 122.81±47.16	15
(Zhang, Fan et al. 2020)	China	Patients undergoing coronary angiography	No patients with history of severe HF, acute infections, autoimmune diseases, malignancy, thyroid dysfunction, severe	None	Levels of ST2	Logistic regression analysis showing ST2 is	262	ACS: 66.32±12.03	Case control	Serum ST2 ELISA R&D systems	Baseline ACS: 21657±12786	16229±6564	15

		Performed for suspected CAD 97 had acute coronary syndrome (ACS), 63 had stable angina	hepatic/renal insufficiency, use of lipid lowering drugs within 3 months			independently diagnostic		Stable angina: 65.65±10.08 Total patients (N=262): 64.18±11.19			Stable angina: 17330±7232 Total ST2 level is 19953.24±11117.46		
(Demyanets, Speidl et al. 2014)	Austria	Coronary artery disease	No patients with autoimmune disease, chronic infections, hepatic/renal disorder	Mean follow up of 43 months	Levels of IL-33 and ST2	Mortality during follow up	438	Stable angina: 65.9±11.5 NSTEMI: 64.6±13.5 STEMI: 62.9±13.7	Case control	Serum ST2 ELISA R&D systems 31.3 pg/ml sensitivity	Blood taken directly before coronary angiography Stable angina: Median is 169 Mean calculated to be 169.33±135.28 NSTEMI: Median is 269 Mean calculated to be 307.33±255.11 STEMI: Median is 453 Mean calculated to be 484.67±282.16 Overall ST2 is 288.07±251.57 37 dead: Median is 415 Mean calculated to be 569.67±788.19 336 survivors: Median is 241 Mean calculated to be 265.33±221.12 Excluding stable angina, overall is 396.45±282.69	Median is 163 Mean calculated to be 179±110.69	14
(Barbarash, Gruzdeva et al. 2016)	Russia	Myocardial infarction	No patients with diabetes, anaemia, renal/hepatic failure, acute infectious/inflammation diseases, autoimmune disease, long term corticosteroid therapy, death during hospitalisation	12 day observation for unfavourable outcomes during hospital stay	Levels of ST2 and other biomarkers	Occurrence of angina, rhythm disturbance, acute HF during hospital stay	118	Median is 58 Mean age calculated to be 59±6.78	Case control	Serum ST2 Presage ST2	Blood taken at admission Median on Day 1 was 44750 Mean calculated to be 54403.33±51749.51 Median on Day 12 was 17820 Mean calculated to be 18790±5991.97 For favourable outcomes (58 patients), median on Day 1 was 35450, Day 12 was 17000 Mean calculated to be 37893.33±22312.54	Median of 18810 Mean calculated to be 18320±4600.46	13

											on Day 1, 17540±4606.95 on Day 12 For unfavourable outcomes (30 patients), median on Day 1 was 69990, Day 12 was 20200 Mean calculated to be 110686.67±132588.32 on Day 1, 25483.33±18144.98		
(Wang, Tan et al. 2018)	China	Acute myocardial infarction and acute aortic dissection	No patients with aortic trauma, pseudo aneurysm, history of heart failure, renal dysfunction, severe pulmonary diseases, cancer. Also no patients who received packed red blood cells, whole blood or platelets less than 10 days before blood sample is taken.	None	Levels of ST2 in acute aortic dissection and myocardial infarction patients	None	301	53.09±11.63	Case control	Serum ST2 DuoSet ELISA R&D systems 0.019 ng/ml sensitivity	Baseline Median is 14660 Mean calculated to be 15943.33±10047.78	Median is 6720 Mean calculated to be 6836.67±2719.95	12
(Pfetsch, Sanin et al. 2017)	Germany Part of KAROLA study cohort	Patients who were admitted within 3 months of an acute coronary event or CABG and are now stable	None	Median of 12.3 year follow up Multi-MACE HR per 1 SD log sST2: 1.01 (0.89-1.15) Adjustments: Age, gender, school education, rehabilitation clinic, smoking status, history of diabetes mellitus, PCI, left ventricular function, HDLcholesterol, LDL-cholesterol, eGFR (cystatin C based), NT-pro-BNP (log transformed), hs-CRP (log transformed), hs-TnI (log transformed)	Levels of ST2	Fatal and non-fatal cardiovascular events, total mortality and recurrent cardiovascular events during follow up	1081	58.9±8	Observational	Serum ST2 ELISA ST2 Critical Diagnostics	Blood taken at baseline during discharge from rehabilitation (average of 43 days after acute event) Median is 28980 Mean calculated to be 29306.67±8388 821 survivors: Median is 28580 Mean calculated to be 28746.67±7797.5 260 dead: Median is 31460 Mean calculated to be 31463.33±10011.69		12
(Kohli, Bonaca et al. 2012)	17 countries, part of MERLIN-TIMI 36 trial (studied Ranolazine)	Non-ST elevation acute coronary syndrome	No patients with end stage renal disease, significant hepatic disease, cardiogenic shock	1 year follow up Multi-HR all-cause mortality per log sST2: 1.26 (1.12-1.4) Multi-HR HF risk per log sST2: 1.37 (1.21-1.55) Adjustments: TIMI risk score covariates, as defined by age >65 years, known coronary artery disease, diabetes, hypertension, dyslipidemia, severe angina (≥2 episodes in 24h), ST changes	Levels of ST2	Cardiovascular disease, heart failure, all-cause mortality, during follow up	4426	Unstated	Clinical trial	Serum ST2 Presage ST2	Baseline Median is 24400 Mean calculated to be 117362.5±60469.24		12

				≥0.5 mm, and aspirin use Uni-HR all-cause mortality per log sST2: 1.56 (1.41-1.73)									
(Dieplinger, Egger et al. 2014)	Germany, part of LURIC cohort	Coronary artery disease (stable)	No patients with acute illness other than acute coronary syndrome, malignancy within 5 years	Median of 9.8 years follow up	Levels of ST2	All-cause mortality and cardiovascular mortality during follow up	1345	Median is 65 Mean calculated to be 64.67±9.65	Observational, post-hoc	Serum ST2 Presage ST2	Blood taken before angiography Median is 19400 Mean calculated to be 19900±6604.74 477 dead: Median is 21400 Mean calculated to be 22100±8699.78 868 survivors: Median is 18500 Mean calculated to be 19033.33±5791.87		14
(Jacobs, Alam et al. 2018)	USA	CAD (patients presenting for CABG), 55% was unstable angina	No patients who were not discharged alive	1 year follow up Multi-HR MACE per log sST2: 1.14 (0.95-1.36) Adjustments: The Society of Thoracic Surgeons 30-day readmission model and The Society of Thoracic Surgeons ASCERT long-term mortality risk model	Occurrence of MACE during follow up	Levels of ST2	1047	Readmitted or dead: 63.91±9.92 Not readmitted or dead: 67.8±9.98 Combined mean: 65.41±10.11	Observational	Serum ST2 Custom made multiplex ELISAs (Meso Scale Discovery)	Blood taken before CABG Median is 3800 Mean calculated to be 14912.5±8082.72		10
(Lepojarvi, Huikuri et al 2018)	Lepojarvi et al based in Finland, part of ARTEMIS trial (studied diabetes and cardiovascular issues).	Stable coronary artery disease	No patients with NYHA 4, significant valvular disease, end stage renal failure. Also no patients with permanent pacemaker, life expectancy less than 1 year, younger than 18, older than 85.	Mean follow up of 76±20 months	Levels of ST2 and other biomarkers	All-cause mortality and sudden cardiac death during follow up	1945	Survivors: 66±9 Deaths: 72±8	Observational	Serum ST2 ELISA Quantikine R&D systems	Survivors: Median is 16300 Mean calculated to be 16866.67±6454.73 Deaths: 21500 Mean calculated to be 22066.67±10377.68		13
(Dhillon, Narayan et al. 2011)	UK	NSTEMI	No patients with malignancy, renal replacement therapy, surgery in the previous month.	Mean of 532 days follow up Multi-HR all-cause mortality per log ₁₀ sST2: 2.03 (1.01-4.09) Multi-HR HF risk per log ₁₀ sST2: 1.64 (0.68-3.95) Adjustments: Age, gender, previous angina or acute myocardial infarction, HF, hypertension, diabetes, Killip class, eGFR, log ₁₀ glucose level, therapy with βblockers, or statins,	Levels of IL-33 and ST2	MACE, death, heart failure and myocardial infarction during follow up	577	70±13	Observational	Serum IL-33 and ST2 R&D systems, Abingdon	Blood collected at 3-5 days after admission Median ST2 is 638 (range of 82-18875) Mean calculated to be 5058.25±3064.19 304 patients (52.7%) had very low IL-33, below the 5.4 detection limit of the assay. In the remaining 273 patients (47.3%), levels ranged from 5.8-8966.7		10

				log10 troponin I, previous history of hypercholesterolemia, or smoking Uni-HR all-cause mortality per log ₁₀ sST2: 4.76 (2.61-8.66)									
(Dhillon, Narayan et al. 2013)	UK	STEMI	No patients with malignancy, renal replacement therapy, surgery in previous month.	Median follow up of 587 days Multi-HR all-cause mortality per log ₁₀ sST2: 3.15 (1.56-6.36) Multi-HR HF risk per log ₁₀ sST2: 2.05 (0.96-4.38) Adjustments: Age, gender, previous history of angina/AMI, hypertension, diabetes, Killip Class, eGFR, peak creatinine phosphokinase level, treatment with thrombolysis, betablockers, statins, ACE inhibitors or ARBs Uni-HR all-cause mortality per log ₁₀ sST2: 9.07 (5.15-15.99)	Levels of IL-33 and ST2	All-cause mortality, heart failure and recurrent infarction during follow up	677	64±12.2	Observational	Serum IL-33 and ST2 R&D systems 2.2 pg/ml sensitivity for ST2 5.4 pg/ml sensitivity for IL-33	Blood collected 3-5 days after admission IL-33 levels were very low in 364 patients (53.8%). These had IL-33 levels below detection limit of 5.4. The remaining 313 (46.2%) had IL-33 ranging from 6.3-17893.7 Median ST2 was 677, mean calculated to be 4677.25±2767.66 For the patients that died, median ST2 was 1125, mean calculated to be 4538.5±3404.20 For the patients that survived, median ST2 was 630, mean calculated to be 3262±1889.89		10
(Zagidullin, Motloch et al. 2020)	Russia	STEMI	No patients presenting later than 48H of symptoms, severe valvular dysfunction, stenosis in valves, atrial flutter, permanent atrial fibrillation, pacemaker, malignancy, acute pulmonary embolism, severe COPD, uncontrolled bronchial asthma, acute infection, pneumonia, kidney failure, acute bronchitis, pregnancy.	2 year follow up	Levels of ST2 and other biomarkers	Cardiovascular mortality during follow up	147	60.9±12.1	Observational	Serum ST2 Biomedica Slovakia	Blood collected at admission Median is 43800 Mean calculated to be 41700±23733.72 In the 33 patients that died (22.4%), ST2 was 93700±97100 In the 114 patients that survived (77.6%), ST2 was 51300±47300		15
(Shimpo, Morrow et al. 2004)	Part of TIMI and STEMI (ENTIRE)-TIMI 23 cohorts	Acute myocardial infarction	No patients with risk of haemorrhage, severe renal insufficiency and cardiogenic shock	30 day follow up for mortality	Levels of ST2	Mortality, recurrent MI, heart failure during follow up	810	Quartiles combined: Mean calculated to be 58±10.24	Observational	Serum ST2 ELISA Medical and Biological Laboratories	Blood taken within 24H of enrolment Dead: Median is 379 Mean calculated to be 419±268.72 Alive: Median is 233 Mean calculated to be 250.33±120.31		12
(Zhang, Zhang et al. 2013)	China	Acute myocardial infarction	None	6 month follow up	Levels of IL-33 and ST2	Recurrence of MI or mortality	95	Data not available	Case control	Serum IL-33 and ST2 R&D ELISA	Blood collected within 24H of acute attack ST2 levels read off the graph: 12000		8

						during follow up					ST2 levels read off the graph: 35000 IL-33 levels read off the graph: 450 For 25 patients, negative event occurred, their median ST2 level was 42540, mean calculated to be 48630±48778.63 Median IL-33 level was 405.24, mean calculated to be 581.38±517.49 For 34 patients, no negative event occurred, their median ST2 level was 18010, mean calculated to be 25676.67±37443.03 Median IL-33 level was 381.99, mean calculated to be 739.16±1019.30	IL-33 levels read off the graph: 440	
(Gerber, Weston et al. 2017)	USA	Myocardial infarction	Not stated	1 year follow up Multi-HR all-cause mortality per log sST2: 3.17 (2.61-3.85) Adjustments: Age, sex Uni-HR all-cause mortality per log sST2: 3.59 (3-4.31)	Mortality during follow up	Levels of ST2	1401	64.6±13.8	Observational	Serum ST2 Presage	Blood taken at index MI Median is 49000		11
(Wang, Wang et al. 2017)	China	Acute myocardial infarction	No patients with other heart disease, infection, abnormal pulmonary artery or aorta, liver/kidney dysfunction, malignancy	1 year follow up	Levels of IL-33 and ST2	MACE during follow up	180	MACE: 61.93±9.29 No MACE: 61.15±8.74 Overall mean: 61.41±8.9	Observational	Serum IL-33 and ST2 ELISA Abbott Laboratories USA	Blood taken at admission MACE: IL-33 is 433.27±95.64 ST2 is 823.47±149.25 No MACE: IL-33 is 372.25±84.25 ST2 is 601.83±125.84		12
(Yu, Oh et al. 2017)	South Korea	STEMI treated by PCI	No patients with thrombolytic therapy, MI caused by stent thrombosis, allergy to antiplatelet, history of CAD, cardiomyopathy, chronic heart failure	1 year follow up	Levels of ST2 and NT-proBNP	MACE during follow up	323	Overall: 59.1±13.1 MACE: 63.7±14.4 No MACE: 58.5±12.8	Observational	Serum ST2 R&D systems	Blood taken at admission Total: 75800±27800 MACE: 84000±29700 No MACE: 74700±27600		12

(Karimzadeh, Zamani et al. 2017)	Iran	Acute myocardial infarction (STEMI) Increase in TnT levels and ST elevation in anterolateral and anteroseptal leads	No patients with chronic renal failure, autoimmune disease, cardiogenic shock	None	Levels of IL-33 and ST2	Correlation of biomarker levels and ejection fraction	81	Not stated	Case control	Serum IL-33 BioLegend San Diego Serum ST2 Abcam UK	Blood taken after inclusion/exclusion criteria considered IL-33: 124.85±203.5 ST2: 419.83±285.22	IL-33: 78±41.39 ST2: 248.01±181.27	13
(Scherthaner, Lichtenauer et al. 2017) Substudy (with ST2 levels analysed) of previous study: Recruitment of circulating dendritic cell precursors into the infarcted myocardium and pro-inflammatory response in acute myocardial infarction	Germany	Myocardial infarction (STEMI and NSTEMI) Angina pectoris symptoms and elevated serum creatine kinase and cardiac Troponin I	No patients with infections, malignancies, autoimmune diseases, hyperthyroidism, immunosuppression	Total cohort mean hospital stay of 5.5 days	Levels of ST2	Correlation of biomarkers with other parameters	194	STEMI: 61.6±11 NSTEMI: 65.6±11.2 Combined: 63.53±11.23	Case control	Serum ST2 DuoSet DY523 R&D systems	Blood taken after admission STEMI (61 patients): Median is 13210.9 Mean calculated to be 37194.28±25108.68 NSTEMI (57 patients): Median is 11989.1 Mean calculated to be 33887.95±22345.13 Combined: 35597.15±23770.62	Median is 5247.7 Mean calculated to be 6853.98±2827.10	13
(Fhaid Mostafa 2019)	Egypt	Chronic heart failure	No patients with anaemia, fever, liver/renal dysfunction, diabetes, inflammatory diseases, autoimmune disease, cancer, pregnancy	3 months follow up	Levels of ST2, IL-34, BNP, TNFα	Mortality during follow up	60	55.97±8.27	Case control	Serum ST2 ELISA RayBiotech Norcross USA	Blood taken at admission 419.95±49.03 After 12 weeks standard care: 298.37±84.5 Dead: 506.19±3.87 Survived: 419.95±49.03	100.19±9.9 After 12 weeks standard care: 99.33±11.11	13
(Santhanakrishnan, Chong et al. 2012)	Singapore SHOP cohort	Heart failure	No patients with HF primarily due to severe valve disease, primary diagnosis of acute coronary syndrome that caused transient acute pulmonary edema, end-stage renal failure, rare specific cause of HF e.g. congenital, isolated right HF, life threatening comorbidity	None	Levels of ST2 and other biomarkers	None	151	HFPEF: 69±12 HFREF: 59±11	Case control	Serum ST2 Presage ST2 10.91 ng/ml sensitivity	HFPEF: Median is 31520 Mean calculated to be 36006.67±20914.55 HFREF: 35250 Mean calculated to be 39003.33±19437.81 Overall ST2 is 37519.83±20137.44	Median is 27580 Mean calculated to be 27290±8617.71	15
(Najjar, Faxen et al. 2019)	Sweden From Karolinska Rennes study	Heart failure	No patients with cardiomyopathy, pericardial constriction, clinically significant pulmonary disease, end stage renal disease requiring dialysis, bi-ventricular pacemaker, anticipated cardiac surgery, anticipated percutaneous intervention on aortic stenosis	Median follow up of 204 days Multi-HR MACE for HFpEF per log unit sST2: 6.62 (1.04-42.28) Multi-HR MACE for HFrEF per log unit	Levels of ST2	Mortality and MACE during follow up	193	Median is 63 Mean calculated to be 61±12.06	Case control	Serum ST2 Presage ST2	Blood taken at enrolment HFrEF (86 patients): Median is 35000 Mean calculated to be 36666.67±21865.95 HFpEF (86 patients): Median is 23000,	Median is 25000 Mean calculated to be 26000±8745.37	11

				<p>sST2: 3.51 (1.05-11.69)</p> <p>Multi-HR all-cause mortality for HFpEF per log sST2: 7.32 (0.35-154.27)</p> <p>Adjustments for HFpEF: Age, sex, and NYHA class</p> <p>Uni-HR HFpEF all-cause mortality per log sST2: 12.39 (0.7-218.55)</p> <p>Uni-HR HFpEF MACE per log sST2: 10.04 (1.89-53.44)</p> <p>Uni-HR HFREF MACE per log sST2: 3.28 (1.06-10.16)</p>							<p>mean calculated to be 23666.67±10555.98</p> <p>Overall mean is 30166.67±18317.96</p>		
(Aimo, Januzzi et al. 2020)	<p>Merged multiple cohorts</p> <p>Previous meta-analysis (Prognostic value of high-sensitivity troponin T in chronic heart failure: an individual patient data meta-analysis)</p> <p>PEOPLE and SHOP cohorts</p>	Heart failure	Not stated	<p>5 year follow up</p> <p>Multi-HR all-cause mortality per ln sST2: 1.61 (1.33-1.95)</p> <p>Multi-HR cardiovascular death per ln sST2: 1.51 (1.23-1.86)</p> <p>Adjustments: Age, female sex, ethnic group, ischaemic heart failure, LVEF category (heart failure with reduced, mid-range, or preserved ejection fraction), New York Heart Association class I–II vs. III–IV, body mass index, estimated glomerular filtration rate, anaemia, hypertension, atrial fibrillation, diabetes, chronic obstructive pulmonary disease, therapy with beta-blockers, angiotensin-converting enzyme inhibitor/angiotensin receptor blockers, mineralocorticoid receptor antagonists</p>	Levels of ST2 and other biomarkers	All-cause mortality, cardiac mortality and hospitalisation for heart failure during follow up	5301	<p>Median is 66</p> <p>Mean calculated to be 65.67±12.61</p>	Post-hoc	<p>Serum ST2</p> <p>Presage ST2 assay</p> <p>1.3 ng/ml sensitivity</p>	<p>Median is 29</p> <p>Mean calculated to be 31.33±15.57</p>		10
(Lupon, de Antonio et al. 2013)	Spain	Heart failure	None	Median of 41.4 months follow up	Levels of ST2 and other biomarkers	All-cause mortality during follow up	876	<p>Median is 70.3</p> <p>Mean calculated to be 69.33±12.4</p>	Observational	<p>Serum ST2</p> <p>Presage ST2</p>	<p>Blood taken at conventional hospital visits</p> <p>Median is 38.1</p>		11

											Mean calculated to be 39.93±14.92 311 dead: Median is 44.7 Mean calculated to be 46.6±20.03 565 alive: Median is 35.4 Mean calculated to be 36.73±12.04		
(Zhang, Zhang et al. 2015)	China	Heart failure (new presentation or decompensation of previously stable chronic HF)	No patients with acute coronary syndrome, cancer, acute pulmonary embolism	1 year follow up Multi-HR all-cause mortality per ln sST2: 2.09 (1.73-2.54) Adjustments: Sex, age, diabetes mellitus, ischemic heart disease, prior heart failure, systolic blood pressure, New York Heart Association functional class, left ventricular ejection fraction, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker treatment, β-blockers treatment, hemoglobin and eGFR, NT-proBNP	Levels of ST2 and galectin-3	All-cause mortality during follow up	1161	58±15	Observational	Serum ST2 Critical Diagnostics	Blood taken at admission Median is 36900 Mean calculated to be 39033.33±22118.54		13
(Dupuy, Curinier et al. 2016)	France	Heart failure	No patients with unstable angina or acute coronary syndrome in last month, cardiac surgery, chemotherapy	Median follow up of 42.3 months Uni-HR all-cause mortality per log ₁₀ sST2: 3.915 (2.31-6.635)	Levels of ST2 and CRP	All-cause mortality, cardiovascular death, HF during follow up	178	Median is 75.43 Mean calculated to be 74.34±11.06	Observational	Serum ST2 Presage ST2	Blood frozen and tested 4 years later Median is 37400 Mean calculated to be 42200±37519.64 112 Alive: Median is 28220 Mean calculated to be 31740±25685.14 66 Dead: Median is 52400 Mean calculated to be 63300±57524.46		13
(Gul, Yucel et al. 2017)	Turkey	Heart failure	No patients with cancer, sepsis, ongoing systemic inflammatory conditions, pregnancy, autoimmune disease, glucocorticoid therapy, acute MI, cardiogenic shock	Mean follow up of 12±4 months	Occurrence of cardiovascular death during follow up	Levels of ST2	130	67±11	Observational	ST2 Presage ST2 2 ng/ml lower detection limit	Assume blood taken at enrolment Survivors (107 patients): Median is 27000 Mean calculated to be 65250±37464 Deceased (23 patients): Median is 51000 Mean calculated to be 71250±36552.41		13

(Segiet, Romuk et al. 2019)	Poland	Heart failure (with reduced ejection fraction) Includes stable and unstable (worsened symptoms 1 month before inclusion) heart failure	No patients with autoimmune disease, chronic or acute infection, recent immunosuppression, MI within 3 months, congenital heart disease, end stage renal failure, advanced liver cirrhosis, hyperthyroidism, acute respiratory distress syndrome, cancer, pregnancy	None	Levels of IL-33	None	215	65.39±12.75	Case control	Serum IL-33 ELISA LEGEND MAX BioLegend 4.14 pg/ml sensitivity	Blood taken at admission Median is 16.91 Mean calculated to be 32.64±60.61	Median is 92.51 Mean calculated to be 188.58±308.39	14
(Firouzabadi, Dashti et al. 2020)	Iran	Heart failure (HFrEF)	No patients with severe valvular heart disease, GFR <30 mL/min or significant comorbidities	None	Levels of IL-33 and ST2	Differences in biomarker levels in patients on beta-blockers and carvedilol	66	66±11.1	Case control	Serum IL-33 Ab119547-IL-33 ELISA Abcam company 0.2 pg/ml sensitivity Serum ST2 ST2 ELISA Elabscience Company 0.19 ng/ml sensitivity	Assume blood taken at enrolment No units given for biomarkers IL-33: 2.45±0.69 ST2: 3416.6±1089.1	No units given for biomarkers IL-33: 2.67±0.33 ST2: 2971.6±792.5	12
(Bahuleyan, Alummoottil et al. 2018)	India	Heart failure (HFrEF) Had combination of chronic and acute heart failure	No patients with recent acute coronary syndrome, coronary revascularisation within last 2 months, myocarditis, cardiogenic shock, advanced liver/renal disease, malignancy	1 year follow up Multi-HR MACE per In sST2: 2.046 (1.246-3.358) Adjustments: Age, body mass index, diabetes, dyslipidemia, creatinine clearance, smoking, NYHA functional class, use of angiotensin converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), b-blockers	Levels of ST2	Cardiovascular death, hospitalisation for HF during follow up	141	60.3±10.4	Observational	Serum ST2 Presage ST2	Blood collected at enrolment 71700±83900 57 Adverse outcome: 106600±116200 84 Non-adverse outcome: 48000±36800		12
(Zhang, Zhang et al. 2014)	China	Heart failure (de novo presentation or worsening of previous chronic HF)	No patients with acute coronary syndrome, cancer, acute pulmonary embolism	Median of 19.1 months follow up Multi-HR MACE per In sST2: 1.52 (1.3-1.78) Adjustments: Age, systolic blood pressure, body mass index, NYHA functional class, left ventricular ejection fraction, sodium, total cholesterol, blood urea nitrogen, total bilirubin, albumin, NT-proBNP and loop diuretics treatment	Levels of ST2	All-cause mortality and cardiac transplantation during follow up	1528	58±16	Observational	Serum ST2 Critical Diagnostics	Blood taken at admission Median is 37100 Mean calculated to be 39333.33±22631.27 325 adverse events: Median is 55600 Mean calculated to be 65200±50188.44 1203 no adverse events: Median is 33600		13

				Uni-HR MACE per In sST2: 2.73 (2.42-3.07)							Mean calculated to be 34966.67±17293.26	
(Xu, Su et al. 2014)	China	Heart failure (NYHA 2-4)	No patients with MI within 1 month, moderate/severe valvular disease, congenital heart disease, chronic inflammatory disease, thyroid disease, malignancy	1 year follow up Multi-HR MACE per log ₂ sST2: 2.19 (1.55-3.1) Adjustments: Age, heart rate, BMI, creatinine, NT-pro BNP, NYHA class (II versus III/IV), and history of hypertension	Levels of ST2	All-cause mortality and hospitalisation for HF during follow up	233	62±11	Observational	Serum ST2 Critical Diagnostics	Baseline Median is 35600 Mean calculated to be 37500±14993.74	12
(Bayes-Genis, Pascual-Figal et al. 2010)	Spain	Heart failure (recently destabilised)	No patients with acute coronary syndrome within 3 months, pending cardiac transplant or revascularisation, severe valvular disease, end stage pulmonary/hepatic/renal disease	1 year follow up	Levels of ST2	All-cause mortality, heart failure hospitalisation, cardiac transplantation during follow up	48	No event: 62±12 Event: 62±15	Observational	Serum ST2 ELISA Medical and Biological Laboratories, Woburn	Baseline Median is 270 Mean calculated to be 300±236.91 After 2 weeks, median is 230 Mean calculated to be 213.33±145.21 No event (22 patients): Baseline median is 310, mean calculated to be 410±396.24 Event (26 patients): Baseline median is 230, mean calculated to be 266.67±243.14	12
(Moliner, Lupon et al. 2018)	Multicentre, from well-established cohort also used in the below studies Combined use of high sensitivity ST2 and NTproBNP to improve the prediction of death in heart failure Soluble neprilysin is predictive of cardiovascular death and heart failure hospitalisation in heart failure patients Combined use of the novel biomarkers high sensitivity troponin T and	Chronic heart failure	Not stated	Mean follow up of 4.9±2.8 years Uni-HR MACE HFReEF per 1 SD log sST2: 1.45 (1.31-1.61) Uni-HR MACE HFmEF per 1 SD log sST2: 1.77 (1.32-2.36) Uni-HR MACE HFPeEF per 1 SD log sST2: 1.11 (0.86-1.43)	Levels of ST2 and other biomarkers	All-cause mortality, cardiovascular mortality, MACE during follow up	1069	HFrEF: 65.5±12.6 HFmrEF: 67±12 HFpEF: 69.6±14.4	Observational	Serum ST2 Presage ST2	Blood collected at conventional ambulatory visits HFReEF: Median is 37500 Mean calculated to be 39100±14110.42 HFmrEF: Median is 37100 Mean calculated to be 38333.33±14763.57 HFPeEF: 44400 Mean calculated to be 44666.67±18733.99 Overall mean calculated to be 39706.89±14958.45	10

	ST2 for heart failure risk stratification vs conventional assessment												
(Broch, Ueland et al. 2012)	Multicentre, 21 countries Substudy of CORONA study, which investigated the effect of Rosuvastatin in systolic HF	Heart failure (patients must be over 60 years old)	No patients with recent cardiovascular events, current/planned operations, liver disease, alanine transamine more than 2 times greater than upper limit of normal, serum creatine ≥ 2.5 mg/dL, chronic muscle disease, contraindication to statins, unexplained creatine kinase ≥ 2.5 upper limit of normal, thyroid stimulating hormone ≥ 2 upper limit of normal, any condition substantially reducing life expectancy	Median follow up of 2.6 years Multi-HR MACE per In sST2: 1.16 (0.93-1.44) Multi-HR all-cause mortality per In sST2: 1.12 (0.91-1.38) Multi-HR cardiovascular death per In sST2: 1.12 (0.89-1.41) Adjustments: Age, gender, diabetes mellitus, a history of intermittent claudication, body mass index, heart rate, left ventricular ejection fraction, and New York Heart Association class, as well as baseline estimated glomerular filtration rate and the ratio of apolipoprotein (Apo) A1 to ApoB, baseline N-terminal pro brain natriuretic peptide and C-reactive protein Uni-HR all-cause mortality per In sST2: 2.03 (1.72-2.4) Uni-HR MACE per In sST2: 1.99 (1.68-2.36)	Occurrence of MACE, CV death, all-cause mortality during follow up	Levels of ST2	1449	72 \pm 7	Observational	Serum ST2 Presage	Blood taken at baseline Median is 17800 Mean calculated to be 108950 \pm 59995.58		15
(Sanders-van Wijk, van Empel et al. 2015)	Switzerland, Germany, part of TIME-CHF study	Chronic heart failure, history of hospitalisation within last year, NT-BNP levels higher than double the normal limit	No patients with dyspnoea caused by reasons other than heart failure, valvular heart disease needing surgery, acute coronary syndrome within 10 days, angina pectoris due to document ischaemia, percutaneous coronary intervention within last month, coronary artery bypass graft surgery within last 3 months, life expectancy under 3 years for diseases other than cardiovascular	Median follow up of 540-543 days	Levels of ST2 and other biomarkers	All-cause mortality and hospitalisation for heart failure during follow up	570	HFrEF (N=458): 76 \pm 7 HFpEF (N=112): 80 \pm 7	Observational	Serum ST2	Blood collected at baseline HFrEF (N=413): Median is 35700 Mean calculated to be 37833.33 \pm 19788.37 HFpEF (N=100): Median is 37600 Mean calculated to be 40266.67 \pm 19707.77		10
(Frioies, Lourenco et al. 2015)	Portugal	Acute heart failure (including both reduced and preserved)	No patients with acute coronary syndrome, chronic renal function replacement therapy	6 month follow up	Levels of ST2 and BNP	All-cause mortality and hospital admission	195	74.8 \pm 12.3	Observational	Serum ST2 ELISA R&D systems,	Blood collected at last day of hospitalisation Patients received standard treatment,		12

		ejection fraction)				for acute heart failure during follow up				Abingdon UK 0.005 ng/ml sensitivity	discharge at doctor's discretion HFpEF median is 30.5 Mean calculated to be 32.77±17.08 HFrEF median is 29.8 Mean calculated to be 30.6±13.96 Overall Median is 30.3 Mean calculated to be 31.4±15.16 Events (66 patients): Median is 33.6 Mean calculated to be 36.5±15.08 No events (129 patients): Median is 26.8 Mean calculated to be 27.63±12.22		
(Ruocco, Evangelista et al. 2019)	Italy	Acute heart failure with and without diabetes	No patients with respiratory dyspnoea due to bronchial asthma, COPD, interstitial lung disease. Also no patients with acute or recent myocardial ischaemia, severe renal insufficiency, neoplastic/haematological/immune diseases with systemic involvement.	6 months follow up	Levels of ST2 and BNP	Hospitalisation and deaths during follow up	121	HFrEF: Median is 82 HFpEF: Median is 83	Observational	Serum ST2 Presage ST2	HFrEF: Median is 63000 Mean calculated to be 66333.33±62285.77 HFpEF: Median is 48000 Mean calculated to be 59666.67±52390.21		13
(Zhang, Meng et al. 2018)	China	Acute heart failure (446 ischaemic heart failure, 574 non-ischaemic heart failure)	No patients with acute coronary syndrome (including unstable angina pectoris and acute MI), cancer, acute pulmonary embolism, unclear primary aetiology of HF	1 year follow up Multi-HR ischaemic all-cause mortality per log sST2: 2.38 (1.64-3.47) Multi-HR Non-ischaemic all-cause mortality per log sST2: 2.16 (1.7-2.76) Adjustments: Age, sex, diabetes mellitus, systolic blood pressure, New York Heart Association functional class, left ventricular ejection fraction, hemoglobin, sodium, C-reactive protein, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker treatment, -blockers and estimated	Levels of ST2 and other biomarkers	All-cause mortality during follow up	1020	57.5±15.7	Observational	Serum ST2 ELISA Critical Diagnostics	Blood collected within 12 hours of admission (also says obtained day after admission) Median is 37700 Mean calculated to be 40066.67±22790.5 All patients received intravenous loop diuretics during first 24H of admission		13

				glomerular filtration rate (GFR)									
(Tang, Wu et al. 2016)	Multinational (in this substudy, mostly from N. America) Analysis of ASCEND-HF trial, which looked at Nesiritide in decompensated heart failure	Acute decompensated heart failure	Not stated, refers to ASCEND-HF trial for criteria	180 days follow up Multi-HR all-cause mortality per log sST2: 1.35 (0.9-2.03) Adjustments: ASCEND-HF (Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure) trial risk model according to endpoints, NT-proBNP Uni-HR all-cause mortality per log sST2: 2.21 (1.57-3.13)	All-cause mortality during follow up	Levels of ST2	858	65.5±15.2	Post-hoc	Serum ST2 Presage	Blood taken at baseline Median is 71200 Mean calculated to be 76833.33±46707.15		11
(Jin, Wei et al. 2017)	China	Acute heart failure (including acute exacerbation of chronic heart failure)	No patients with malignancies, cognitive deficit, severe mental illness, uncontrolled systemic disease.	1 year follow up Multi-HR all-cause mortality per ln sST2: 1.542 (1.001-2.375) Adjustments: age, sex, hypertension, diabetes mellitus, renal insufficiency, hemoglobin, serum sodium, ln-transformed NT-proBNP, and NYHA	Levels of ST2 and other biomarkers	All-cause mortality during follow up	270	60.5±16.4	Observational	Serum ST2 ELISA R&D systems, Abingdon UK 3.1 ng/ml sensitivity	Blood collected at admission or morning after Median is 31760 Mean calculated to be 35476.67±28523.29 223 survivors, 47 deaths in 1 year Survivors: Median is 29070 Mean calculated to be 31396.67±23101.33 Deaths: Median is 55640 Mean calculated to be 70086.67±71441.64		13
(van Vark, Lesman-Leegte et al. 2017)	Netherlands (part of TRIUMPH study)	Acute heart failure (including decompensated chronic heart failure)	No patients with HF caused by non-cardiac reason, severe valvular dysfunction without sustained left ventricular dysfunction, acute STEMI, scheduled for coronary revascularisation, severe renal failure	Median of 325 days follow up Multi-HR MACE per 1 SD increase of log ₂ scale sST2: 1.3 (1.08-1.56) Multi-HR all-cause mortality per 1 SD increase of log ₂ scale sST2: 1.43 (1.11-1.86) Adjustments: Age, sex, systolic blood pressure, diabetes mellitus, left ventricular ejection fraction, previous hospitalization for HF during the last 6 months, ischemic heart failure, body	Levels of ST2	All-cause mortality and readmission for heart failure during follow up	475	Median is 74 Mean calculated to be 73±11.15	Observational	Serum ST2 Presage ST2 assay	Blood taken at admission, then days 2-4, discharge, until 12 months after discharge Median is 71000 Mean calculated 73000±41640.52		11

				<p>mass index, estimated glomerular filtration rate, and baseline NT-proBNP</p> <p>Uni-HR all-cause mortality per 1 SD log₂ sST2: 1.8 (1.41-2.29)</p> <p>Uni-HR MACE per 1 SD log₂ sST2: 1.49 (1.26-1.77)</p>									
(Pascual-Figal, Manzano-Fernandez et al. 2011)	Spain	Acute decompensated heart failure	Not stated	<p>Followed up for median of 739 days</p> <p>Multi-HR all-cause mortality per log sST2 (back transformed to show clinical relevance): 1.09 (1.03-1.15)</p> <p>Adjustments: Sex, body mass index, and left ventricular ejection fraction</p> <p>Uni-HR all-cause mortality per log sST2 (back transformed to show clinical relevance): 1.09 (1.04-1.13)</p>	All-cause mortality during follow up	Levels of ST2 and other biomarkers	107	72±13	Observational	Serum ST2 Presage ST2	<p>Blood taken at admission</p> <p>Median is 62960 Mean calculated to be 69853.33±49598.05</p> <p>Data for survival seems incorrect, the median is lower than the 25th percentile</p>		12
(Pascual-Figal, Bayes-Genis et al. 2019)	Spain	Acute decompensated heart failure (including decompensated chronic HF)	Not stated	<p>1 year follow up</p> <p>Multi-HR all-cause mortality per 1 SD of ln sST2: 1.39 (1.05-1.84)</p> <p>Adjustments: Gender; Age; Body mass index; Diabetes mellitus; Cerebrovascular disease; Coronary disease; Prior myocardial infarction; Prior heart failure hospitalization; New York Heart Association class; Beta-blockers; Mineralocorticoid receptor antagonists; Systolic blood pressure; Diastolic blood pressure; Creatinine; Urea; Sodium; Potassium; N-terminal pro-B-Type natriuretic peptide; high sensitivity Troponin T; Left ventricular ejection</p>	All-cause mortality during follow up	Levels of ST2 and other biomarkers	316	71.8±11.7	Observational	Serum ST2 Presage ST2	<p>Blood taken at admission</p> <p>58130±38830</p>		11

				fraction; C-reactive protein. Uni-HR all-cause mortality per 1 SD In sST2: 1.56 (1.2-2.03)									
(Manzano-Fernandez, Mueller et al. 2011)	Multicentre, based on 3 similar previous study populations Diagnostic accuracy of B type natriuretic peptide and amino terminal proBNP in the emergency diagnosis of heart failure The N-terminal pro-BNP investigation of dyspnea in the emergency department (PRIDE) study Complementary prognostic value of cystatin C, N-terminal pro-B-type natriuretic peptide and cardiac troponin T in patients with acute heart failure	Acutely decompensated heart failure	Not stated	1 year follow up Multi-HR all-cause mortality per log sST2 (back transformed to show clinical relevance): 1.23 (1.13-1.34) Adjustments: Age, Body mass index, Systolic blood pressure, Diastolic blood pressure, Previous heart failure, New York Heart Association functional class, β Blocker, Angiotensin-converting enzyme inhibitor, Hemoglobin (g/dl), Leukocytes, Creatinine, Estimated glomerular filtration rate, Blood urea nitrogen, C-reactive protein, Plasma amino terminal B-type natriuretic peptide Uni-HR all-cause mortality per log sST2 (back transformed to show clinical relevance): 1.74 (1.43-2.12)	Levels of ST2	Mortality during follow up	447	73 \pm 13	Observational	Serum ST2 ELISA Medical and Biological Laboratories, Woburn	Measurements made using frozen blood samples Median is 470 Mean calculated to be 563.33 \pm 490.86 117 died: Median is 800 Mean calculated to be 1016.67 \pm 1058.36 330 survivors: Median is 380 Mean calculated to be 446.67 \pm 357.4		10
(Jackson, Haig et al. 2016)	Scotland, multicentre Profile of microvolt T-wave alternans testing in 1003 patients hospitalized with heart failure	Decompensated heart failure (but studied 1 month post-hospitalisation so considered stable)	No patients with primary presentation with MI, concurrent systemic disease that reduces life expectancy	Mean follow up of 3.2 \pm 1.5 years Multi-HR all-cause mortality per log sST2: 1.31 (1.04-1.65) Adjustments: LVEF, BMI per unit decrease, Age, Sex, Diabetes, HF, NYHA, SBP, Peripheral edema, Previous MI, Current smoker, PAD, Lymphocytes, COPD, Creatinine, Hemoglobin, Bilirubin, log BNP Uni-HR all-cause mortality per log sST2: 1.53 (1.23-1.9)	All-cause mortality during follow up	Levels of ST2 and other biomarkers	628	70.8 \pm 10.6	Observational	Serum ST2 ELISA R&D systems, Abingdon UK 0.1 ng/ml sensitivity	Blood taken at 1 month post hospitalisation Median is 19900 Mean calculated to be 20300 \pm 7727.46		11

(Sugano, Seo et al. 2019)	Japan	Acute decompensated heart failure (HFpEF)	No patients with malignancy, acute coronary syndrome, severe valvular heart disease, hypertrophic cardiomyopathy, end stage renal disease	Median follow up of 445 days Multi-HR all-cause mortality per log sST2 (back transformed for clinical significance): 1.02 (1.009-1.04) Adjustments: Age, BMI, glomerular filtration rate, Haemoglobin, BNP, CRP, Noradrenaline Uni-HR all-cause mortality per log sST2 (back transformed for clinical significance): 1.02 (1.01-1.03)	Levels of ST2	Cardiovascular death, all-cause mortality during follow up	191	76.4±11.9	Observational	Serum ST2 ELISA R&D systems	Blood taken before discharge in stable condition Median is 18 Mean calculated to be 18.7±10.68		11
(Pacho, Domingo et al. 2018)	Part of STOP-HF cohort	Acute decompensated heart failure	Not stated	1 year follow up Multi-HR MACE per 1 SD of log transformed sST2: 1.41 (1.21-1.63) Multi-HR all-cause mortality per 1 SD of log transformed sST2: 1.45 (1.21-1.74) Adjustments: Age, sex, NYHA, Charlson comorbidity index, Barthel index, urea, Hb, NT-proBNP, CA125, Hs-Tnl Uni-HR all-cause mortality per 1 SD of log sST2: 1.86 (1.59-2.18) Uni-HR MACE per 1 SD log sST2: 1.63 (1.44-1.85)	All-cause mortality and hospitalisation for heart failure during follow up	Levels of ST2 and other biomarkers	522	82.1±8.7	Observational	Serum ST2 Presage ST2	Blood taken 4.9±2 days after discharge Median is 42700 Mean calculated to be 45800±24457.04		10
(Wang, Yang et al. 2016)	Taiwan (China)	Acute heart failure and decompensated chronic HF	No patients with disorder other than HF that could compromise survival for next 6 months, bedridden for more than 3 months, dialysis in last 2 weeks, severe coronary artery disease without complete revascularisation therapy, pregnancy	Follow up of 3.7±1.3 years Uni-HR all-cause mortality per log sST2: 2.652 (1.473-4.773) Uni-HR MACE per log sST2: 2.156 (1.489-4.249)	Levels of ST2 and Gal-3	Mortality and hospitalisation for heart failure during follow up	344 (288 acute heart failure)	60.6±13.4	Observational	Serum ST2 Presage ST2 assay Critical Diagnostics 1.8 ng/ml sensitivity	Blood collected at enrolment 48300±46100		12
(Llibre, Zamora et al. 2016)	Spain	Acute heart failure	Not stated	1 year follow up Uni-HR all-cause mortality per 1 SD log sST2: 1.58 (1.12-2.24) Uni-HR MACE per 1 SD log sST2: 1.44 (1.08-1.92)	All-cause mortality and hospitalisation for heart failure during follow up	Levels of ST2	182	69.2±12.8	Observational	Serum ST2 Presage ST2	Blood taken at admission Median is 59100 Mean calculated to be 62800±41174.49		11

(Breidhardt, Balmelli et al. 2013)	Switzerland	Acute heart failure	No patients undergoing haemodialysis	Median of 368 days follow up	Levels of ST2	Mortality during follow up	207	Median is 80 Mean calculated to be 79.67±8.21	Observational	Serum ST2 Presage ST2	Blood taken at presentation Median is 78000 Mean calculated to be 81666.67±55990.85 138 Survivors: Median is 65000 Mean calculated to be 67666.67±41954.26 Died: Median is 120000 Mean calculated to be 128666.67±81774.05		12
(Ky, French et al. 2011)	Multicentre, USA (Penn Heart Failure Study) Comparison of MMP-9 and BNP as clinical biomarkers in chronic heart failure Neuregulin-1beta is Associated with Disease Severity and Adverse Outcomes in Chronic Heart Failure	Chronic heart failure	No patients with non-cardiac condition resulting in mortality within 6 months	Median follow up of 2.8 years Multi-HR MACE per log ₂ sST2: 1.4 (1.2-1.7) Adjustments: Age, gender, and race, cardiomyopathy etiology (ischemic versus nonischemic), tobacco use, body mass index, systolic blood pressure, creatinine, ejection fraction, biventricular pacemaker, cardioverter-defibrillator, ACE inhibitor/angiotensin receptor blocker, aldosterone antagonist, beta blocker therapy, and clinical site, NT-proBNP Uni-HR MACE per log ₂ sST2: 1.7 (1.5-1.9)	Levels of ST2	All-cause mortality and cardiac transplantation	1141	56.3±14	Observational	Serum ST2 Presage ST2	Blood taken at admission Median is 27500 Mean calculated to be 30033.33±17665.53		11
(Wojtczak-Soska, Sakowicz et al. 2014)	Poland Prognostic value of ST2 in short term follow up for chronic HF	Chronic systolic heart failure	No patients with NYHA 4, acute HF, acute coronary syndrome, inflammatory states, thyroid dysfunction	1 year follow up	Composite endpoint is death or hospitalisation for HF during follow up	Levels of ST2	167	62.92±11.58	Observational	Serum ST2 ELISA Medical and Biological Laboratories	Blood collected at admission 650±700 Composite endpoint (93 patients): 820±860 No composite endpoint (74 patients): 440±300		11
(Sobczak, Wojtczak-Soska et al. 2014)	Poland Prognostic value of ST2 in chronic HF	Chronic heart failure	No patients with acute HF, acute coronary syndrome, autoimmune disease, inflammatory states	1 year follow up	Composite endpoint is cardiova	Levels of ST2	145	62.16±11.25	Observational	Serum ST2 ELISA Medical and	Blood taken at admission Median is 515		11

					scular death, hospitalisation for HF exacerbation during follow up					Biological Laboratories	Mean calculated to be 740.33±849.14		
										0.032 ng/ml sensitivity	For composite endpoint: Median is 670 Mean calculated to be 905.33±1081.9		
											For no composite endpoint: Median is 377 Mean calculated to be 550.33±551.02		
(Rienstra, Yin et al. 2014)	USA, part of Framingham cohort, from the 6 th examination	Community population	No atrial fibrillation	10 year follow up Multi-HR AF risk per 1 SD In sST2: 1 (0.87-1.15) Adjustments: Sex, age, smoking status, height, weight, systolic and diastolic blood pressure, hypertension treatment, diabetes status, heart failure and myocardial infarction, In CRP, In BNP	Levels of ST2	Occurrence of atrial fibrillation during follow up	3217	Controls: 59±10	Observational	Serum ST2 Presage ST2 Critical Diagnostics 2 ng/ml sensitivity		Median is 20800 Mean calculated to be 21066.67±6823.06	14
(Eggers, Kempf et al. 2016)	Sweden, part of PIVUS cohort	Community population	No cardiovascular disease	10 years follow up Multi-HR all-cause mortality per 1 SD In sST2: 0.95 (0.81-1.12) Multi-HR CV events per 1 SD In sST2: 0.95 (0.81-1.12) Adjustments: Sex, hypertension, diabetes, HDL cholesterol, LDL cholesterol, current smoking, body mass index, previous CV disease (if applicable), CRP, eGFR and each investigated biomarker	Levels of ST2	All-cause mortality and cardiovascular events during follow up	864	Controls: 70	Observational	Serum ST2 Presage ST2 assay Critical Diagnostics		Baseline Median is 21300 Mean calculated to be 21633.33±6534.47	15
(AbouEzzeddine, McKie et al. 2016)	USA, part of Olmsted country cohort	Community population	No HF or systolic dysfunction	Median of 12 years follow up Multi-HR HF risk per 1 SD In sST2: 1.19 (1.02-1.4) Adjustments: Age, sex, BMI, eGFR, hypertension, systolic blood pressure, CAD and diabetes mellitus Multi-HR MACE per 1 SD In sST2: 1.09 (0.97-1.21)	Levels of ST2 and other biomarkers	Occurrence of heart failure and MACE during follow up	1824	Median is 61 Mean calculated to be 61.33±12.61	Observational	Serum ST2	Baseline Median is 26200 Mean calculated to be 26400±9199.48		14

				Adjustments: Age, sex, BMI, eGFR, hypertension, systolic blood pressure, CAD, diabetes mellitus, total cholesterol, HDL and smoking history Uni-HR HF risk per 1 SD In sST2: 1.26 (1.07-1.48)									
(Parikh, Seliger et al. 2016)	USA Part of Cardiovascular Health Study (CHS)	Community population	No patients with past or current HF	Median of 13.7 years follow up Multi-HR HF risk per In sST2: 1.12 (0.93-1.35) Multi-HR CV death per In sST2: 1.18 (0.95-1.48) Adjustments: demographics and history of coronary heart disease, smoking status, systolic blood pressure, heart rate, serum glucose, creatinine, albumin levels, and left ventricular hypertrophy by electrocardiogram, NTproBNP, hsTnT Uni-HR HF risk per In sST2: 2.06 (1.75-2.43)	Levels of ST2	Occurrence of heart failure and cardiovascular death during follow up	3915	72.7±5.5 (no heart failure cohort)	Observational, post-hoc	Serum ST2 Presage ST2		Blood collected at initial admission in the 1990s Median is 23500 Mean calculated to be 57700±24283.54	14
(Hughes, Appelbaum et al. 2014)	Finland (FINRISK97 cohort, selected from national register)	Community population	Not stated	Mean follow up of 15 years Multi-HR all-cause mortality per 1 SD In sST2: 1.09 (1.01-1.19) Multi-HR MACE per 1 SD In sST2: 1.02 (0.96-1.09) Multi-HR CVD per 1 SD In sST2: 1.01 (0.94-1.08) Multi-HR CHD per 1 SD In sST2: 1.004 (0.92-1.09) Multi-HR MI per 1 SD In sST2: 0.97 (0.86-1.1) Adjustments: Framingham risk factors (HDL and nonHDL cholesterol, systolic blood	Levels of ST2 and other biomarkers	Occurrence of cardiovascular event and MACE during follow up	8444	48.79±22.08 (control)	Observational	Serum ST2 Presage ST2 2.35 ng/ml sensitivity		Blood taken at enrolment, in 1997 890 values were missing, data presented is imputed, as imputed and complete case analysis were similar Median is 26950 Mean could not be calculated, as IQR provided as a single figure rather than quartiles.	13

				pressure (BP), smoking, prevalent diabetes) and geographic area, r NT-proBNP (N-terminal Pro-Brain Natriuretic Peptide), eGFR (estimated glomerular filtration rate) and prevalent valvular heart disease Multi-HR HF risk per 1 SD In sST2: 1.06 (0.96-1.16) Adjustments: Framingham risk factors (HDL and nonHDL cholesterol, systolic blood pressure (BP), smoking, prevalent diabetes) and geographic area, r NT-proBNP (N-terminal Pro-Brain Natriuretic Peptide), eGFR (estimated glomerular filtration rate) and prevalent valvular heart disease, hsTroponin I									
(Andersson, Preis et al. 2015)	USA (Framingham 6 th cycle)	Community population	No patients with prevalent stroke, dementia, neurological conditions	Follow up over mean of 11.8±3 years	Levels of ST2 and GDF-15	Occurrence of stroke during follow up	3374	59±9.7	Observational	Serum ST2 Presage ST2		Median ST2 of controls is 20900 Mean calculated to be 21166.67±6971.24	14
(Alkhiary, Abdalaal et al. 2015)	Saudi Arabia	Atrial fibrillation (persistent)	No patients with congenital heart disease, ACS, cardiomyopathy, concomitant valvular heart disease, previous cardiac surgery, heart failure, renal insufficiency, thyroid dysfunction, chronic inflammation, autoimmune disease, sepsis, malignancy, liver disease, haematological disease, bronchial asthma	None	Levels of IL-33 and ST2	None	160	60.2±6.4	Case control	Serum IL-33 RayBio Human IL-33 ELISA kit Serum ST2 ELISA RayBio Minimum detection of 2pg/ml for both	Blood taken when sinus heart rate measured IL-33: Median is 155.2 Mean calculated to be 148.63±40.9 ST2: 970.5±98.6	IL-33: Median is 92.6 Mean calculated to be 96.93±34.39 ST2: 361.4±44.8	15
(Ma, Yuan et al. 2018)	China	Atrial fibrillation	No patients with cancer, acute infection, immunological diseases	None	Levels of ST2 in AF patients	None	254	61±11	Case control	Serum ST2 ELISA (Presage ST2 Critical Diagnostics) 2 ng/ml sensitivity	Blood taken at admission Median is 21690 Mean calculated to be 22733.33±10030.83	Median is 17040 Mean calculated to be 17650±6038.68	13
(Chen, Qu et al. 2018)	China	Non-valvular atrial fibrillation	No patients with acute MI, stroke, congenital heart disease, significant HF, chronic pulmonary heart disease, dilated or hypertrophic cardiomyopathy, inflammatory	Median follow up of 6 months	Levels of ST2 in AF patients	Occurrence of HF during follow up	290	Paroxysmal atrial fibrillation: 65.8±10.9 Persistent atrial	Case control	Serum ST2 ELISA by Boyun	Blood taken at admission Paroxysmal atrial fibrillation: Median is 276.4	Median is 222.4 Mean calculated to be 225.63±112.98	13

			states, autoimmune disease, thyroid dysfunction					fibrillation: 65.4±9.9			Mean calculated to be 288.77±156.46 Persistent atrial fibrillation: Median is 285 Mean calculated to be 303.77±115.06 Overall ST2 is 297.13±134.75		
(Wolcott, Batra et al. 2017)	USA	Acute ischaemic stroke	No patients without baseline plasma samples	90 days	Levels of ST2	Mortality and favourable/unfavourable outcomes during follow up	646	69±15	Observational	Serum ST2 Presage ST2 3.1 ng/ml sensitivity	Plasma samples collected at 7.1±3.3 hours after stroke. Median ST2 level is 35000 Mean calculated to be 36833.33±17905.73 At 48H post stroke, 210 patients had their ST2 levels measured again, median ST2 level is 37400 At 90 days, poor outcome patients had median ST2 of 38200, good outcome patients had 32600 Patients who died had median ST2 of 51000, patients who survived had 33700		9
(Jiang, Liu et al. 2018)	China	Acute ischaemic stroke	Not stated	None	Levels of IL-33	None	120	62.2±8.2	Case control	Serum IL-33 ELISA Sen-Xiong Company	283±54.8 (blood taken within 24H of event)	165±25.6	11
(Liu, Xing et al. 2014)	China	Acute cerebral infarction	None had liver/kidney dysfunction, heart failure, severe infection, malignancy, potential infection symptoms, surgical/trauma history, aspirin/statin/anti-hypertensive drug consumption within 2 weeks	None	Levels of IL-33	None	90	51.2±6.8	Case control	Serum IL-33 R&D systems	22 patients Large infarct (>10cm ³): 447.94±274.65 20 patients Medium infarct (5-10cm ³): 281.74±105.36 20 patients Small infarct (<5cm ³): 176.56±100.27 Overall mean and pooled standard deviation: 306.79±213.33 Blood taken within 48H of event	186.71±89.69	12
(Qian, Yuanshao et al. 2016)	China	Acute ischaemic stroke	No patients with heart failure, surgery/trauma within 2 months, renal dysfunction, liver insufficiency, serious infections, Th2 related diseases such as asthma/dermatitis/anaphylaxis	3 months follow up	Levels of IL-33	Barthel Index score during follow up	287	61.2±10.4	Case control	Serum IL-33 ELISA Boyun Biotech Shanghai	Median is 57.68 (measured the morning after admission) Using (Wan, Wang et al. 2014), mean	Median is 47.48 Mean calculated to be 46.64±11.40	12

										0.5 ng/L sensitivity	<p>calculated to be 59.79±23.73</p> <p>Median is 62.53 for favourable outcome, mean calculated to be 63.69±25.57</p> <p>Median is 49.83 for unfavourable outcome, mean calculated to be 49.08±19.17</p> <p>Small infarct (<5cm³): Median is 59.36 (134 patients) Large infarct: 55.72 (41 patients)</p> <p>Mild stroke is NIHSS score of <6, moderate to severe stroke is ≥6. For mild stroke (153 patients), median IL-33 is 60.32. For moderate to severe stroke (53 patients), median IL-33 is 52.77</p>		
(Chen, Lin et al. 2018)	China	Acute ischaemic stroke	No patients with cerebral haemorrhage, subdural haematoma, intracranial space occupying lesions, cerebrovascular damage caused by trauma, heart failure, malignancy, autoimmune disease, severe infection, pregnancy.	None	Levels of IL-33 and ST2	MRI scans for infarct volume	190	67.3±10.9	Case control	<p>Serum IL-33 and ST2</p> <p>Westang Biotech ELISA, Shanghai</p> <p>15 pg/ml sensitivity for IL-33</p> <p>30 pg/ml sensitivity for ST2</p>	<p>Measurements made within 48H of symptoms</p> <p>Median IL-33 is 29.8 Mean calculated to be 30.4±22.23</p> <p>Median ST2 is 103 Mean calculated to be 102.33±61.58</p> <p>Mild stroke is NIHSS score of <6, severe stroke is ≥6</p> <p>Mild stroke (73 patients) had ST2 median of 820, severe stroke (39 patients) had ST2 median of 118</p>	<p>Median IL-33 is 26.7 Mean calculated to be 27.63±22.06 Median ST2 is 27 Mean calculated to be 28±18.88</p>	12
(Stankovic, Lujic et al. 2019)	Serbia	Patients recruited before carotid endarterectomy	Not stated	None	Levels of IL-33 and ST2	None	221	~60s	Case control	<p>Serum IL-33 and ST2</p> <p>ELISA R&D systems</p> <p>0.069-1.51 pg/ml sensitivity for IL-33</p> <p>2.45-13.5 pg/ml sensitivity for ST2</p>	<p>Blood taken before surgery</p> <p>IL-33: 35.86±7.93 ST2: 183±8.03</p>	<p>IL-33: 12.29±1.8 ST2: 122.31±15.89</p>	10

(Li, Wang et al. 2019)	China	Acute ischaemic stroke	No patients with hydrocephalus, dementia, traumatic brain injury, Parkinson's, schizophrenia, active infection, haematological disease, history of cancer, liver/renal insufficiency, autoimmune disease	1 year	Levels of IL-33	Barthel Index score during follow up	259	63.14±10.02	Observational	Serum IL-33	Blood taken within 24H of admission. 58760±20670 Favourable outcome patients had 62450±20500 after admission, unfavourable outcomes had 51580±19160 after admission. Infarct considered small if less than 5 cm ³ . The infarct volume of all patients was small. Follow up after 2.17±0.57 years, 35 patients (13.5%) had recurrent ischaemic stroke, 224 didn't. Patients with recurrent stroke had IL-33 levels of 50680±17260 after admission, those that didn't had 60060±20910		11
(Dieplinger, Bocksruck 2017)	Austria	Acute ischaemic stroke	No patients with transient ischemic attack, non-stroke, haemorrhagic stroke. Also no patients without blood taken with 24H of admission.	90 days follow up	All-cause mortality	Functional outcome	721	Median of 76 Mean calculated to be 75.33±13.37	Observational	ST2 Presage ST2	Overall median is 35000 Mean calculated to be 37666.67±16341.64 Deceased (81 patients): Median is 55000 Mean calculated to be 70333.33±63402.42 Survivors (640 patients): Median is 34000 Mean calculated to be 35666.67±14116.85		13
(Yin, Cao et al. 2019)	China	Essential hypertension (same as primary hypertension)	No patients with secondary hypertension, coronary artery disease, heart failure, stroke, valvular heart disease, collagen disease, diabetes, advanced liver disease, renal failure, malignancy, sepsis, inflammatory disease, recent trauma, mental disorder, autoimmune disease	None	Levels of IL-33 and ST2	None	472	54.29±9.31	Case control	Serum IL-33 and ST2 IL-33: Human Pre-Mixed Multi—nalyte kit R&D systems ST2: DST200	Does not say when blood is collected, assumed to be on hospital visit. IL-33 median was 108340 Mean calculated to be 107660±18726.08 ST2 median was 663840	IL-33 median was 109650 Mean calculated to be 109720±16289.72 ST2 median was 549050 Mean calculated to be 565530±219207.38	11

										R&D systems	Mean calculated to be 665700±227853.9 Systolic pressure: 153.13±13.38mmHg Diastolic pressure: 92.61±10.32mmHg		
(Ates, Ozkayar et al. 2016)	Turkey	Primary hypertension	No patients with cardiovascular/cerebrovascular/peripheral artery disease, diabetes, kidney disease, liver disease, infection, rheumatic inflammatory disease	None	Levels of IL-33 and ST2	Carotid intima media thickness	172	46±12	Case control	Serum IL-33 and ST2 IL-33: ELISA Affymetix Company Vienna, 0.2 pg/L sensitivity ST2: ELISA RayBiotech, 2 pg/L sensitivity	Blood taken at admission, after 8H fasting IL-33 level is 0.0025±0.0002 ST2 median level is 0.08 (could not calculate mean)	IL-33 level is 0.0026±0.0003 ST2 median level is 0.046 (could not calculate mean)	10
(Yavuzer, Cengiz et al. 2016)	Turkey	Hypertension (untreated)	No patients with metabolic syndrome, diabetes, atherosclerosis, endocrine disease, malignancy, connective tissue disease, on blood pressure medication within 12 months	None	Levels of IL-33	None	66	46.3±5.8	Case control	Serum IL-33 ELISA eBioscience	5.85±1.02	5.34±0.67	11