Table 1: **Studies showing the predictive effect of adrenomedullin on all-cause mortality in patients with heart failure.**

Author	Year	Sample size	Number of Deaths	HR (95% CI)	AUC (95% CI or p-value)	Duration follow-up	Measure of Adrenomedullin	Primary endpoint	Modelled adrenomedullin
Pousset(6)	2000	117	14	1.56 (1.05-2.32)	NA	237 days	Mature ADM	Death, cardiac transplant	1 SD increase, pg/ml
Richards(7)	2001	297	35	3.92 (1.76-8.70)	NA	300 days	Mature ADM	Death, HF hospitalization	Above median, pmol/l
Gegenhuber(8)	2007	137	41	2.11 (0.93-4.77)	0.71 (0.63-0.79)	365 days	MRproADM	Death	Upper tertile > 1.23, nmol/l
Adlbrecht(16)	2009	786	233	1.77 (1.41-2.22)	NA	24 Months	MRproADM	Death	Continuous, 1 nmol/l
Potocki(23)	2009	287 acute dyspnoea 54% AHF	77	10.46 (1.26-80.50)	0.75 (0.69-0.81)	1 year	MRproADM	Death	Log10 MRproADM, nmol/l
Masson(17)	2010	1237	332	1.91 (1.29-2.82)	0.70 (0.67-0.74)	3.9 yrs	MRproADM	Death	Upper tertile >/= 0.88 ,nmom/l
Neuhold(18)	2010	181	36	2.79 (1.29-5.95)	NA	24 months	MRproADM	Death	Continuous, 1 nmol/l
Haehling(12)	2010	501	70	1.82 (1.24-2.66)	0.72 (0.67-0.76)	1 year	MRproADM	Death	Log10 MRproADM, nmol/l
Maisel(14)	2011	568 AHF	65	2.4 (1.40-4.40)	0.67 (NA)	90 days	MRproADM	Death	Log10 MRproADM, nmol/l
Shah(15)	2012	560 acute dyspnoea 180 AHF	189	1.51 (1.03-2.20)	0.77 (p<0.001)	4 years	MRproADM	Death	ROC curve optimal cut-off value of 0.77, nmol/l
Cinar(13)	2012	154 acute dyspnoea 42.2 % AHF	15	8.5 (2.50-28.50)	0.81 (0.71-0.91)	30 days	MRproADM	Death	Cut-off 1.5, nmol/l
Bosselmann(22)	2013	424	252	2.37 (1.66-3.38)	NA	4.9 years	MRproADM	Death	Continuous 1 nmol/l

Xue(19)	2013	724	195	2.307 (P<0.001)	0.68 (P<0.00001)	6 years	MRproADM	Death	ROC curve optimal cut-off value of 0.72, nmol/l
Travaglino(20)	2014	441 acute dyspnoea 162 AHF	21	NA	0.66 (p<0.001)	90 days	MRproADM	Death	AUC for baseline MRproADM, nmol/l

HR: Hazard ratio; CI: Confidence interval; AUC: Area under the curve; NA: Not applicable; ADM: Adrenomedullin; MRproADM: Mid-regional adrenomedullin; HF: Heart failure; AHF: Acute heart failure; SD: Standard deviation; ROC curve: Receiver operator characteristic curve.

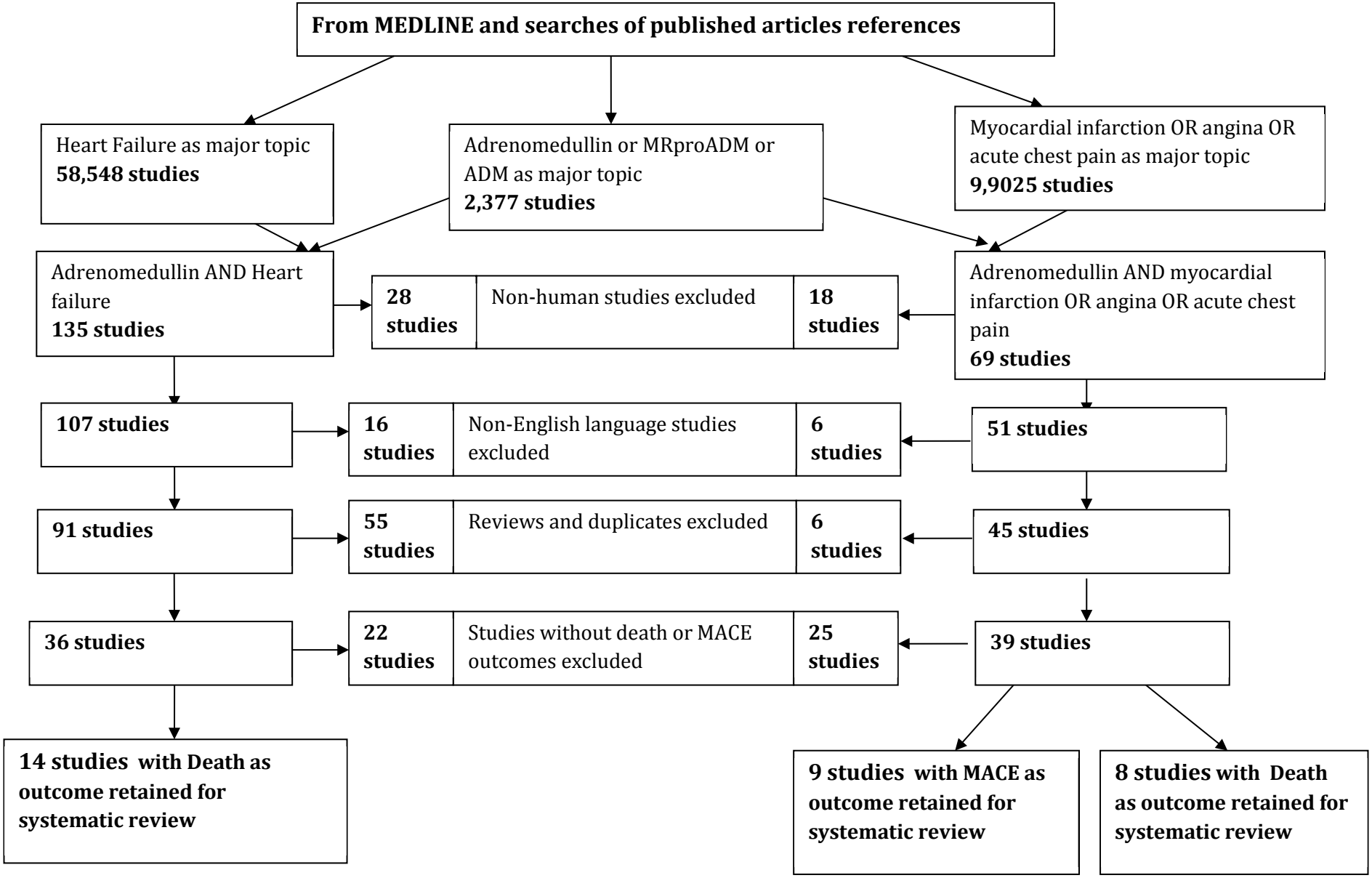
<u>Table 2:</u> Studies showing the predictive effect of adrenomedullin on major adverse cardiovascular events (MACE) in acute myocardial infarction patients.

Author	Year	Sample size	MACE	HR MACE (95% CI)	AUC (95 % CI)	Duration of follow-up	Measure of Adrenomedullin	Primary endpoint	Modelled adrenomedullin
Khan(30)	2007	983	150	3.63 (1.48-8.90)	0.77 (0.72-0.81)	2.1 years	MRproADM	Death, HF	Log Base10 MRproADM, nmol/l
Behnes(32)	2008	30	11	2.80 (1.20-6.90)	0.71 (0.51-0.86)	10 months	MRproADM	Death, HF, PCI, CABG	Continuous 1, nmol/l
Dhillon(10)	2010	745	262	9.75 (3.60-26.16)	0.72 (0.67-0.77)	2 years	MRproADM	Death, HF, AMI	Log Base10 MRproADM, nmol/l
Walter(33)	2010	30	11	2.80 (1.20-6.90)	0.71 (0.51-0.86)	10 months	MRproADM	Death, HF, PCI, CABG	Continuous, 1 nmol/l
Klip(9)	2011	214	61	1.78 (0.94-3.35)	0.66 (0.58-0.75)	2.5 years	MRproADM	Death, AMI, Stroke, resuscitated CA	Doubling of MRproADM, nmol/l
Dzielinska(34)	2011	127	12	2.12 (1.18-3.81)	NA	6 months	Mature ADM	Death, AMI, Stroke	Every 10 pmol/l increase
Wild(25)	2012	1355 stable angina	90	3.40 (1.06-10.92)	0.64 (0.57-0.71)	3.6 years	MRproADM	Nonfatal AMI or CVD death	Continuous, 1 nmol/l
Wild(25)	2012	885 ACS	102	4.10 (1.66-10.12)	0.64 (0.57-0.70)	3.6 years	MRproADM	Nonfatal AMI or CVD death	Continuous 1 nmol/l
Meune(37)	2012	1247 acute chest pain	21	8.70 (1.10-69.4) 3rd quartile to 1st & 10.90 (1.40-85.4) 4th quartile to 1st	0.71 (0.62-0.81)	22 Months	MRproADM	Death, AMI	3rd quartile compared to 1st, nmol/l & 4th quartile compared to 1st, nmol/l
Tzikas(35)	2013	1386 acute chest pain	132	1.26 (1.06-1.49)	0.80 (0.73-0.87)	6 months	MRProADM	Death, AMI, Revascularization, Stroke, HF	1 SD log-tranformed MRproADM, nmol/l

HR: Hazard ratio; CI: Confidence interval; AUC: Area under the curve; NA: Not applicable; ACS: Acute coronary syndrome; MACE: Major adverse cardiovascular eventes; ADM: Adrenomedullin; MRproADM: Mid-regional adrenomedullin; HF: Heart failure; AMI: Acute myocardial infarction; CVD: Cardiovascular diseases; CABG: Coronary artery bypass grafting; PCI: Percutaneous coronary intervention; SD: Standard deviation; CA: Cardiac arrest.

<u>Table 3:</u> Studies showing the predictive effect of adrenomedullin on all-cause mortality in acute myocardial infarction patients.

Author	Year	Sample size	Number of Deaths	HR Death (95% CI or P value)	AUC (95% CI)	Duration follow-up	Measure of Adrenomedullin	Primary endpoint	Modelled adrenomedullin
Richards(11)	1998	121	27	1.21 (not significant)	NA	2 4 month	Mature ADM	Death, HF	Conitinous, 1 pmol/l
Richards(7)	2001	297	35	3.92 (1.76-8.70)	NA	18 months	Mature ADM	Death, HF	Above median, pmol/l
Nagaya(31)	1999	113	16	1.04 (1.01-1.08)	NA	25 months	Mature ADM	Cardiovascular death	Continuous, 1 pmol/l
Katayama(29)	2005	124	9	10.63 (1.06-107.06)	NA	90 days	Mature ADM	Death	Continuous 1, fmol/l
Khan(30)	2007	983	101	4.86 (p=0.001)	NA	2.1 years	MRproADM	Death, HF	Log Base10 MRproADM, nmol/l
Dhillon(10)	2010	745	120	16.68 (4.56-60.99)	0.79 (0.74-0.84)	2 years	MRproADM	Death, HF, AMI	Log Base10 MRproADM, nmol/l
Klip(9)	2011	214	31	3.51 (1.38-5.49)	0.81 (0.73-0.90)	2.5 years	MRproADM	Death, AMI, Stroke, resuscitated CA	Doubling of MRproADM, nmol/l
Haaf(36)	2013	1179 Acute chest pain	79	2.79 (1.81-4.33)	0.84 (0.81-0.86)	2 years	MRproADM	Death	Continuous, 1 nmol/l

HR: Hazard ratio; CI: Confidence interval; AUC: Area under the curve; NA: Not applicable; ADM: Adrenomedullin; MRproADM: Mid-regional adrenomedullin; HF: Heart failure; AMI: Acute myocardial infarction; CA: Cardiac arrest.

<u>Figure 1:</u> Flow chart of literature search and identification of relevant English language studies on of adrenomedullin and death in heart failure patients and adrenomedullin and major adverse cardiovascular events (MACE) and death in myocardial infarction patients(1st January 1993 to 30th of June 2014)