ONLINE SUPPLEMENTARY APPENDICES

Appendix 1: Search strategy

Database	#	Search
MEDLINE	1	Heart Failure/
	2	(heart failure or hf or chf).tw.
	3	1 or 2
	4	Natriuretic Peptide, Brain/
	5	b type natriuretic peptide*.tw.
	6	brain natriuretic peptide*.tw.
	7	brain type natriuretic peptide*.tw.
	8	bnp*.tw.
	9	probnp*.tw.
	10	pro bnp*.tw.
	11	nt probnp.tw.
	12	ntprobnp.tw.
	13	natriuretic peptide type b.tw.
	14	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
	15	Monitoring, Physiologic/
	16	Prognosis/
	17	treatment outcome/
	18	monitor*.tw.
	19	((serial or routine or longterm or long term) adj2 (measure* or test* or follow up)).tw.
	20	((guide* or target*) adj2 (therap* or treatment* or pharmacotherap* or strateg*)).tw.
	21	prognos*.tw.
	22	retest*.tw.
	23	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
	24	3 and 14 and 23
	25	randomized controlled trial.pt.
	26	controlled clinical trial.pt.
	27	randomized.ab.
	28	placebo.ab.
	29	drug therapy.fs.
	30	randomly.ab.
	31	trial.ab.
	32	groups.ab.
	33	25 or 26 or 27 or 28 or 29 or 30 or 31 or 32
	34	exp animals/ not humans.sh.
	35	33 not 34
	36	24 and 35
	37	(2016* or 2017* or 2018*).dc,dp.
	38	36 and 37
EMBASE	1	Heart Failure/
	2	Congestive Heart Failure/
	3	(heart failure or hf or chf).tw.
	4	1 or 2 or 3
	5	brain natriuretic peptide/

EMBASE (CON'D)	6	b type natriuretic peptide*.tw.
	7	brain natriuretic peptide*.tw.
	8	brain type natriuretic peptide*.tw.
	9	bnp*.tw.
	10	probnp*.tw.
	11	pro bnp*.tw.
	12	nt probnp.tw.
	13	ntprobnp.tw.
	14	natriuretic peptide type b.tw.
	15	5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14
	16	Patient monitoring/
	17	Biologic monitoring/
	18	Prognosis/
	19	treatment outcome/
	20	Follow up/
	21	monitor*.tw.
	22	((serial or routine or longterm or long term) adj2 (measure* or test* or follow up)).tw.
	23	((guide* or target*) adj2 (therap* or treatment* or pharmacotherap* or strateg*)).tw.
	24	prognos*.tw.
	25	retest*.tw.
	26	16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25
	27	4 and 15 and 26
	28	randomized controlled trial/
	29	controlled clinical trial/
	30	single blind procedure/ or double blind procedure/
	31	crossover procedure/
	32	random*.tw.
	33	placebo*.tw.
	34	((singl* or doubl*) adj (blind* or mask*)).tw.
	35	(crossover or cross over or factorial* or latin square).tw.
	36	(assign* or allocat* or volunteer*).tw.
	37	28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36
	38	27 and 37
	39	(exp animal/ or nonhuman/) not human/
	40	38 not 39
	41	(2016* or 2017* or 2018*).dc,dp.
	42	40 and 41
Cochrane Library	1	MeSH descriptor: [Heart Failure] this term only
	2	heart failure or chf or hf:ti,ab,kw (Word variations have been searched)
	3	#1 or #2
	4	MeSH descriptor: [Natriuretic Peptide, Brain] explode all trees
	5	b type natriuretic peptide*:ti,ab,kw (Word variations have been searched)
	6	brain natriuretic peptide*:ti,ab,kw (Word variations have been searched)
	7	brain type natriuretic peptide*:ti,ab,kw (Word variations have been searched)
	8	pro bnp:ti,ab,kw (Word variations have been searched)

	9	nt probnp:ti,ab,kw (Word variations have been searched)
Cochrane Library (Con'd)	10	ntpprobnp:ti,ab,kw (Word variations have been searched)
	11	natriuretic peptide type b:ti,ab,kw (Word variations have been searched)
	12	#4 or #5 or #6 or #7 or #8 or #9 or #10 or #11
	13	MeSH descriptor: [Monitoring, Physiologic] this term only
	14	MeSH descriptor: [Prognosis] this term only
	15	MeSH descriptor: [Treatment Outcome] this term only
	16	monitor*:ti,ab,kw (Word variations have been searched)
	17	((serial or routine or longterm or long term) near/2 (measure* or test* or follow up)):ti,ab,kw (Word variations have been searched)
	18	((guide* or target*) near/2 (therap* or treatment* or pharmacotherap* or strateg*)):ti,ab,kw (Word variations have been searched)
	19	prognos*:ti,ab,kw (Word variations have been searched)
	20	retest*:ti,ab,kw (Word variations have been searched)
	21	#13 or #14 or #15 or #16 or #17 or #18 or #19 or #20
	22	#3 and #12 and #21
Web of Science	1	TS=("b-type natriuretic peptide*") OR TS=(btype natriuretic peptide*) OR TS=("b type natriuretic peptide*") OR TS=("type-b natriuretic peptide*") OR TS=("natriuretic peptide* type-b") OR TS=("brain natriuretic peptide*") OR TS=("brain type natriuretic peptide*") OR TS=(bnp*) OR TS=(probnp* or "pro bnp*") OR TS=("nt probnp" or ntprobnp) OR TS=("natriuretic peptide type b")
	2	TS=(monitor*) OR TS=(((serial OR routine OR longterm OR long term) SAME (measure* or test* or follow up))) OR TS=(((serial OR routine OR longterm OR long term) SAME (measure* or test* or follow up))) OR TS=(prognos*) OR TS=(retest*)
	3	2 AND 1
	4	TS=(((random* or blind* or allocat* or assign* or trial* or placebo* or crossover* or cross-over*)))
	5	4 AND 3
	6	4 AND 3 Timespan=2016-2017
ClinicalTrials.gov	1	Title=natriuretic peptide OR bnp OR pro bnp OR probnp OR ntprobnp OR pro-bnp OR nt-probnp
	2	Intervention=natriuretic peptide OR bnp OR pro bnp OR probnp OR ntprobnp OR pro-bnp OR nt-probnp
WHO ICTRP	1	Title=natriuretic peptide OR bnp OR pro bnp OR probnp OR ntprobnp OR pro-bnp OR nt-probnp
	2	Intervention=natriuretic peptide OR bnp OR pro bnp OR probnp OR ntprobnp OR pro-bnp OR nt-probnp

Appendix 2: Study characteristics

Study (study name)	Country	Setting	Follow-up schedule	NP target	Clinical target	Primary endpoint	Outcome data reported relevant to systematic review	Treatment algorithm (NP group)	Target duration of follow-up	Actual duration of follow-up (mean (SD), months, unless stated otherwise)	
										NP group	Control group
Anguita 2010[1]	Spain	Hospital	Minimum 4 visits in 1st quarter, 6 visits in 1st year, 7 visits overall	BNP 100 pg/ml	Framing-ham score (> or < 2)	Composite: ACM, CV admission	ACM, HFA	1. Increased dose of loop diuretic. 2. Doubling the dose of ACEi. 3. Addition of spironolactone. 4. Double dose of beta blocker. 5. Addition of an ARB. 6. Addition of chlorthalidone. 7. Addition of digoxin. 8. Add other drugs	18 months	16 (4)	16 (5)
Beck-da-Silva 2005[2]	Canada	Hospital (out-patient)	Minimum 4 visits in 1st quarter, 4 visits overall	No target set/ stated	Clinical assessment	Beta blocker titration	ACM, ACA, QoL	1. Clinically better, BNP decreasing: β blocker increased one step. 2. Clinically same or mildly worse, BNP decreasing: β blocker increased one step. 3. Clinically same or better, BNP increasing: β blocker unchanged. 4. Clinically worse, BNP increasing: β blocker decreased one step or discontinued	3 months	3 absolute	
Berger 2010[3]	Austria	Hospital & community	Minimum 6 visits in 1st quarter, 8 in 1st year, 8 to 26 visits overall	NT-proBNP <2200 pg/mL	Structured clinical assessment (multi-disciplinary care) and usual care	Survival without hospitalisation	ACM, HFM, HFA, ACA, QoL	Increase in treatment of HF medication	18 months	15 (13 - 16) median (IQR)	

Eurlings 2010 (PRIMA)[4]	Nether-lands	Hospital	Minimum 3 visits in 1stt quarter, 6 in 1st year, estimated 10 visits overall	Lowest level at dis-charge or at 2 weeks follow-up	Clinical assessment	Days alive outside the hospital	ACM, QoL	Treatment was intensified according to the ESC HF treatment guidelines	2 years	702 days (488 - 730) median (IQR)
Felker 2017 (GUIDE-IT)[5]	US and Canada	Hospital & Community	Minimum 2 visits in 1stt quarter, 5 in 1st year, 12 visits overall	NT-proBNP 1000 pg/ml	Clinical assessment	Composite: time to 1st hospitalisatio n or cardiovascular mortality	ACM, HFA	Not prescriptive but encouraged to prioritise titration of neuro-hormonal antagonists over diuretics	1 - 4 years	15 months (median)
Januzzi 2012 (PRO-TECT)[6]	USA	Hospital	Minimum 2 visits in 1st quarter, quarterly visits up to a maximum of 12 months	NT-proBNP ≤1000 pg/ml	Clinical assessment	Total cardiovascular events	HFA, Adverse events, Cost, QoL	Treatment according to ACF/AAT guidelines	6 - 12 months	10 (3)
Jourdain 2007 (STARS-BNP)[7]	France	Hospital (out-patient)	Minimum 4 visits in 1st quarter, 6 in 1st year and overall	BNP <100pg/m l	Clinical assessment	Composite: CHF-related death or CHF hospital stay	ACM, HFM, HFA, ACA	Treatment was intensified according to the ESC HF treatment guidelines	Minimum 6 months	15 median

Karlstrom 2011 (UPSTEP)[8]	Sweden & Norway	Hospital	Minimum3 visits in 1 quarter, seven in first year and overall	BNP <150 ng/L in patients <75 years, <300 ng/L in patients >75 years	Clinical assessment	Composite: ACM, hospitalisation, worsening HF	ACM, HFM, HFA, ACA, QoL	Treatment was intensified in stepwise manner whilst following guideline doses	Minimum 12 months	12
Krupicka 2010 (OPTIMA)[9]	Czech republic	Hospital (specialist HF clinic out-patients)	Minimum 2 visits in 1st quarter, 5 in 1st year, 9 overall	BNP <100 pg/ml	Clinical assessment	Composite: cardiovascular death, hospitalisation for worsening HF, outpatients episodes of worsening HF	ACM, HFM, HFA, adverse events	1. In case of either daily loop diuretic dose was increased or second diuretic was added. In patients without congestion ACEi or ARB dose was increased.2. Increase of betablocker dose. 3. Increase of MRA daily dose	Minimum 12 months	18 average
Lainchbury 2010 (BATTLE-SCAR-RED)[10]	New Zealand	Hospital and Community	Minimum 2 visits in 1st quarter, 5 in 1st year, 9 overall	NT-proBNP <150 pmol/l (approx. 1300 pg/ml)	Clinically guided and usual care	ACM, composite: ACM and HF hospitalisation	ACM, HFA, QoL	1. Algorithm for heart score >2: i) increase frusemide; ii) addition of digoxin iii) add spironolactone iv) increase frusemide v) addition of bendrofluazide or metolazone. 2. Algortihm for NT-proBNP >150 p/mol, heart score stable: i) optimisation of ACE inhibitor ii) addition or titration of beta blockade iii) addition of further therapy	2-3 years	Not reported
Li 2015[11]	China	Hospital	Minimum 5 visits in 1st month and overall	BNP 50% of the basal level or less than 300 pg/ml	Clinical assessment	No primary endpoint reported	HFM	Metoprolol succinate doubled every visit. If the BNP level did not decrease, but was elevated more than 10% then the metoprolol succinate was stopped or decrease whilst application of intravenous	1 month	1 absolute

								cardiotonic, vasodilator or diuretic drugs took place until start up BNP level achieved then the metoprolol succinate was recommenced.		
Maeder 2013[12]	Switzer-land and Germany	Hospital (out-patient)	Minimum 3 visits in 1st quarter, 5 in 1st year and 6+ overall	NT-proBNP < 400 pg/mL in patients <75 years; < 800 pg/mL in patients >75 years	Clinical assessment	18 month survival free of any hospitalisatio n	ACM, adverse events, cost, QoL	Treatment based on ESC, ACF/AHA guidelines with predefined escalation rules	18 months	18 months
Persson 2010 (SIGNAL-HF)[13]	Sweden	community	Minimum 4 visits in 1st quarter, 6 in 1st year, 6 overall	NT-proBNP At least a 50% reduction from baseline	Clinical assessment	Composite: days alive, days out of hospital, symptom score from the KCCQ	ACM, adverse events, QoL	Stepwise treatment schedule adhering to ESC guidelines for target doses.	9 months	9 months
Pfisterer 2009 (TIME-CHF)[14]	Switzerlan d & Germany	Hospital (out-patient)	Minimum 3 visits in 1st quarter, 5 in 1st year, 6 overall	NT-proBNP <400 pg/mL in patients <75 years, <800 pg/mL in patients ≥75 years	Clinical assessment	18 month survival free of any hospitalisatio n and QoL	ACM, adverse events, cost, quality of life	Treatment based on ESC, ACF/AHA guidelines with predefined escalation rules	18 months	18 months

Schou 2013 (North-Star)[15]	Denmark	Hospital (heart failure clinics)	Minimum 2 visits in 1st quarter, 5 in 1st year, 17 overall	No target	Clinical assessment	Composite: ACM, admission for a protocol-specified CV cause	ACM, HFA, ACA, QoL	Treatment using clinical checklist. Treatment included intensification of drugs and education	6 months to 4.5 years	2.5 years
Shah 2011 (STAR-BRITE)[16]	USA	Hospital	Minimum 5 visits in 1st quarter, 6 in 1st year and overall	Discharge BNP	Congestion score (key clinical variables)	Number of days alive and not hospitalised during the 90 days	ACM, ACA	Investigators optimized ACE inhibitors, ARBs, beta-blockers, aldosterone antagonists, and other evidence-based HF medications according to their clinical judgment.	90 4 months	Not reported
Shochat 2012[17]	Israel	Hospital (out-patient)	Minimum 2 visits in 1st quarter, remainder unclear	No target	Clinical assessment	NS	ACM, (data available but not confirmed for HFM, HFA, ACA)	1. Amount of diuretics was increased. 2. ACEi, AT1 blocker and/or b-Blocker increased. Doses were determined by treating physicians	NS	16 (11)
Skvortsov 2015[18]	Russia	Hospital (out-patient)	Minimum 4 visits in 1st quarter, 8 in first year and overall	NT-proBNP <1000 pg/mL or at least 50% reduction discharge	Clinical assessment	CV events	ACM, HFM, HFA, QoL	1. Increased NT-proBNP continued without deterioration of clinical symptoms then diuretics were recommended 2. Increase in NT-proBNP with increase in clinical HF symptoms then patients immediately received diuretics. 3. Decrease in NT-proBNP plus increase in clinical symptoms then patients immediately received correction of diuretic therapy (this did effect did not happen in the study)	1 year	10.5 (2.1

Trough-ton 2000[19]	New Zealand	Hospital	Minimum 1 visits in 1st quarter, 4 in first year, visits 2 weekly until target met and then 3 monthly	NT-proBNP 200 pmol/L (IPD: <1700 pg/ml)	Clinical assessment	CV events	ACM, HFM, HFA, ACA, adverse events, QoL	Stepwise increase in treatment	17 months	9.5 median

Where NP: natriuretic peptide, BNP: B-type natriuretic peptide, NT-proBNP: N-terminal pro B-type natriuretic peptide, ACM: all-cause mortality, HF: heart failure, CHF: chronic heart failure, HFM: heart failure mortality, HFA: heart failure admission, ACA: all-cause admission, QoL: quality of life, ESC: European Society of Cardiology, CV: cardiovascular, ACF: American College of Cardiology Foundation, AAT: American Association Task Force, AHA: American Heart Association, KCCQ: Kansas City Cardiomyo-pathy Questionnaire

Appendix 3: Participant characteristics at baseline

Study (study name)	NP group (N)	Control group (N)	Age (mean (SD), unless stated)		Male (%)		LVEF (mean %, (SD), unless stated)		NYHA stage		Baseline NP biomarker (pg/ml mean (SD), unless stated)		
			NP group	Control group	NP group	Control group	NP group	Control group	NP group	Control group	Biomarker	NP group	Control group
Anguita 2010[1]	30	30	70 (8)	69 (12)	67	70	44 (18)	46 (18)	Stage III 73%, IV 27%	Stage III 63%, IV 37%	BNP	57 (77)	65 (97)
Beck-da-Silva 2005[2]	21	20	64.5 (15.2)	65.6 (13.5)	33.3	35	23.8 (8.8)	20.9 (9.2)	2.6 ± 0.7 (mean, SD)	2.4 ± 0.6 (mean, SD)	BNP	502.3 (411.3)	701.6 (409.9)
Berger 2010[3]	92	96 (multi-disciplinary care)	70 (12)	73 (11)	63	70	NS*	NS*	NS	NS	NT-proBNP	2216 (355-9649) mean (CI)	2469 (355-18487) mean (CI)
		90 (usual care)		71 (13)		69		NS*		NS			2359 (355-15603) mean (CI)
Eurlings 2010 (PRIMA)[4]	174	171	71.6 (12)	72.8 (11.7)	55	60	34.9 (13.7)	36.7 (14.8)	Stage I 11.5%, II 64.9%, III 23.6%	Stage 1 9.9%, II 70.8%, III 19.3%	NT-proBNP	2961 (1383-5144) median (IQR)	2936 (1291-5525) median (IQR)
Felker 2017 (GUIDE-IT)[5]	446	448	62 (51-70) median (IQR)	64 (54-72) median (IQR)	69	67	24 (19-30) median (IQR)	25 (20-30) median (IQR)	Stage I 8%, II 50%, II 40%, IV 2%	Stage I 5%, II 52%, III 41%, IV 2%	NT-proBNP	2632 (1462 - 5235) median (IQR)	2668 (1481 - 5604) median (IQR)
Januzzi 2012 (PROTECT)[6]	75	76	63 (14.5)	63.5 (13.5)	88.2	81.3	28 (8.7)	25.9 (8.3)	Stage II or III 85.5%	stage II or III 84.2%	NT-proBNP	2344 median	1946 median
Jourdain 2007 (STARS-BNP)[7]	110	110	65 (5)	66 (6)	59	56	29.9 (7.7)	31.8 (8.4)	2.29 (0.6) mean (SD)	2.21 (0.62) mean (SD)	BNP	352 (260)	Not measured
Karlstrom 2011 (UP-STEP)[8]	147	132	71.6 (9.7)	70.1 (10)	73	73	<30: 57%	<30: 58%	Stage II 32%, III 52%, IV 15%	stage II 27%, III 59%, IV 14%	BNP	808.2 (676.1) ng/l	898.9 (915.3) ng/l

Krupicka 2010 (OPTIMA)[9]	26	26	71 (36-89) mean (range)	70 (45-84) mean (range)	69	65	23 (6)	23 (7)	2.53 mean	2.34 mean	BNP	704 (228-2852) median (range)	633 (276-3756) median (range)
Lainchbury 2010 (BATTLESCAR-RED)[10]	121	121 (clinically guided)	76 (44-89) median (range)	76 (34-89) Median (range)	63	67	40 (15)	39 (15)	Stage I 12%, II 68%, III 18%, IV 2%	Stage I 7%, II 66%, III 25%, IV 2%	NT-proBNP	2012 (516-10233) median (IQR)	1996 (425-6588) median (IQR)
		122 (usual care)		75 (31-89) Median (range)		62		37 (15)		stage 1 7%, II 67%, III 25%, IV 1%			2012 (425-10571) median (IQR)
Li 2015[11]	96	99	57 (40-78) average (range)	58 (38-81) average (range)	56.3	55.4	30 (8.1)	28 (7.9)	NS	NS	BNP	1167.8 (219.9)	1145.8 (224.9)
Maeder 2013[12]	59	64	80.3 (6.8)	79.9 (7.2)	36	33	56 (6)	56 (7)	49 (83) ≥ stage III (number, %)	53 (83) ≥ III (number, %)	NT-proBNP	2210 (1514-4081) ng/L, median (IQR)	2191 (1478-4890) ng/L, median (IQR)
Persson 2010 (SIGNAL-HF)[13]	126	124	78	77	76	66	31 (9)	33 (7)	stage II 62%, III 38%	Stage II 61%, III 39%	NT-proBNP	2661 (2.1) ng/L geometric mean (coefficient of variation)	2429 (2.1) ng/L geometric mean (coefficient of variation)
Pfisterer 2009 (TIME-CHF)[14]	251	248	76	77	68.1	62.9	29.8 (7.7)	29.7(7.9)	186 ≥ stage III (number)	185 ≥ stage III (number)	NT-proBNP	3998 (2075-7220) median (IQR)	4657 (2455-7520) median (IQR)
Shah 2011 (STARBRITE)[16]	68	69	59 (50-70) median (IQR)	63 (52-74) median (IQR)	67.7	72.3	20% (15-25) median (IQR)	20% (15-25) median (IQR)	NS	NS	BNP	663(271-1560) at admission, 453 (221-1135) at discharge median(IQR)	621 (216-1175) at admission, 440 (189 - 981) at discharge median(IQR)

Schou 2013 (NorthStar)[15]	199	208	72 (56-85) mean (range)	74 (51-89) mean (range)	76	76	30 (14-45) mean (range)	30 (15-45) mean (range)	Stage I-11 86 %	Stage I-II 85 %	NT-proBNP	1884 (1033-10435) statistic not given	2042 (1023-9668) statistic not given
Shochat 2012[17]	60	60	70.2 (11)	69.4 (10.5)	88.3	83	23 (6)	23 (7)	2.53 mean	2.34 mean	NT-proBNP	5868 (2532)	5820(2434)
Skvortsov 2015[18]	35	35	63.7 (8.6)	62.5 (13.3)	61	89	29.2 (6.1)	29.4 (6.1)	Stage III 23%, IV 76%	Stage III 26%, IV 74%	NT-proBNP	3750 (2224-6613) median (IQR)	2783.0 (2021.5-4827.5) median (IQR)
Troughton 2000[19]	33	36	68	72	78	75	28	26	2.3 mean, stage II 72%	2.3 mean, stage II 67%	NT-proBNP	217 pmol/L mean	251 pmol/L mean

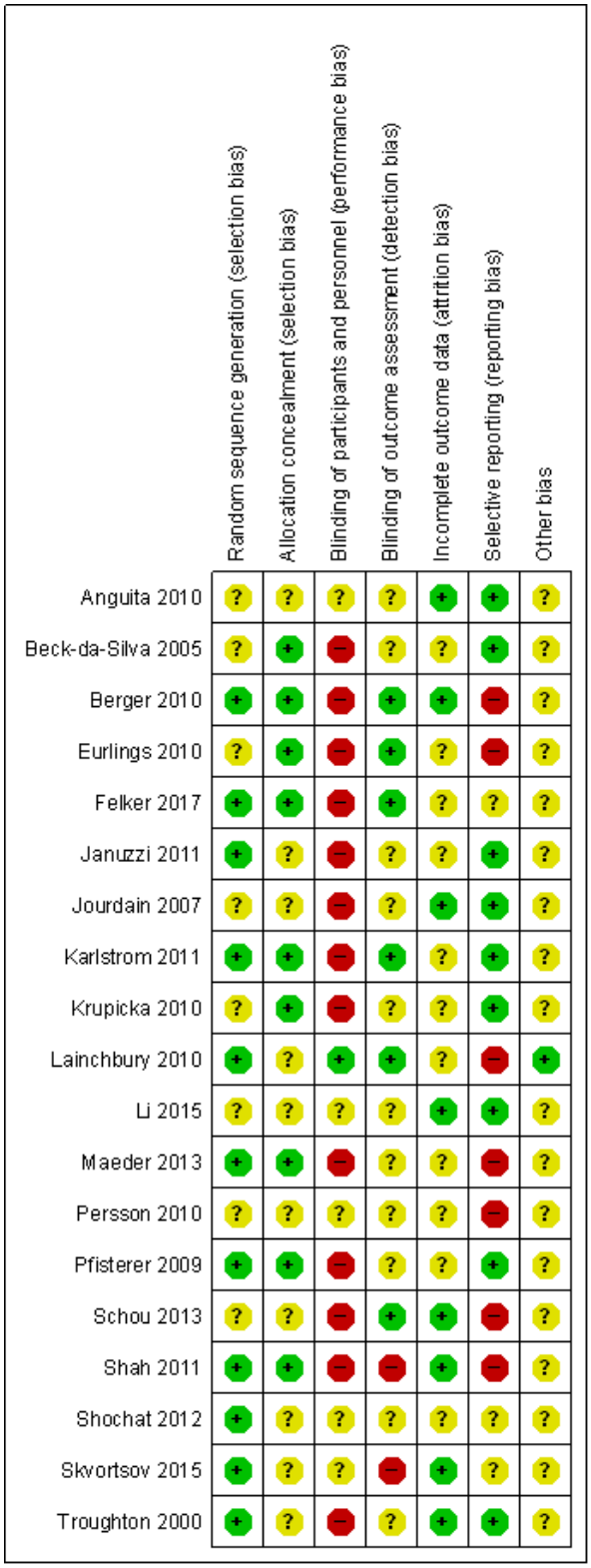
Where NP: natriuretic peptide, BNP: B-type natriuretic peptide, NT-proBNP: N-terminal pro B-type natriuretic peptide, SD: standard deviation, IQR: interquartile range, LVEF: left ventricular ejection fraction, NYHA: New York Heart Association, NS: Not stated, *: Baseline LVEF not stated, however, study inclusion criteria states 'Cardiothoracic ratio >0.5 or LVEF <40%'

Appendix 4: Adverse events where reported

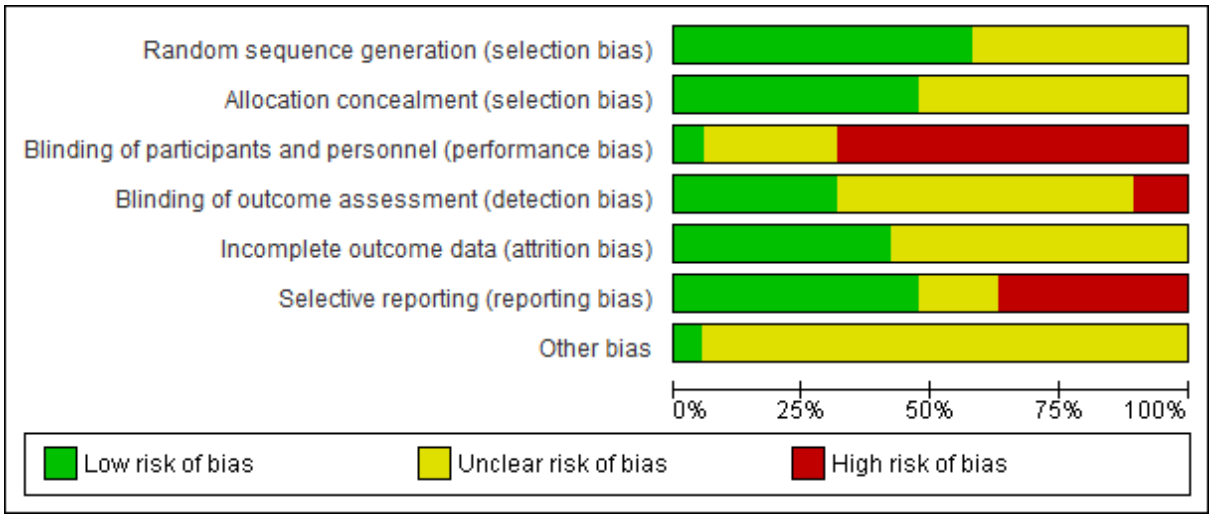
Study	Adverse events									
	Participants (N)			Missing participants (N)			Number of adverse events (definitions not consistent or not stated; not clear whether first event per participant or every event)			Additional data either from published articles or supplied by author
	NP-guided group	Control group	Total	NP-guided group	Control group	Total	NP-guided group	Control group	Total	
Felker 2017	446	448	894	49	44	93	51	36	87	Events in intervention group: Symptomatic hypotension (7); hyperkalemia (11); worsening renal function (16); other SAE's (17) Events in control group: Symptomatic hypotension (2); hyperkalemia (6); worsening renal function (9); other SAE's (19) P value between groups: Symptomatic hypotension (0.11); hyperkalemia (0.22); worsening renal function (0.15); other SAE's (0.74)
Januzzi 2012	75	76	151	6	6	12	30	23	53	No significant differences between groups. No specific event showed a significant difference between groups Events in intervention group: Abdominal pain (1); acute renal failure (4); anaemia (1); atrial fibrillation (2); cough (2); diarrhoea (2); dizziness (5); fever (1); gastrointestinal bleeding (1); hyper/hypokalaemia (3); hypotension (4); respiratory infection (2); syncope(2) Events in control group: Abdominal pain (1); acute renal failure (3); anaemia (0); atrial fibrillation (5); cough (1); diarrhoea (1); dizziness (4); fever (1); gastrointestinal bleeding (1); hyper/hypokalaemia (1); hypotension (0); respiratory infection (4); syncope(1)
Krupicka	26	26	52	0	0	0	7	0	7	Email from author 17.10.14 confirmed: Hyperkalaemia (n = 2); orthostatic hypotension (n = 2); bradycardia (n = 3)

Maeder 2013	59	64	123	12	12	24	Not reported	Not reported	66	Maeder 2013 reported: "58% of the patients in the NT-proBNP-guided and 50% in the symptom-guided group had at least one SAE (p=0.32). SAE's related to renal failure (14% versus 2%, p=0.01) were more common in the NT-proBNP-guided group, whereas hypotension tended to be less common (0% versus 8%, p=0.06)." No additional information
Persson 2010	126	124	250	8	7	15	42	39	81	No additional information provided
Pfisterer 2009	251	248	499	32	29	61	123	113	236	P = 0.47 Renal impairment: intervention group n = 4, control group n = 5 (P = 0.64) Hypotension: intervention group n = 6, control group n = 3 (P = 0.22) No other type of adverse event described. Adverse events ≥ 75 years old patients: intervention group 10.5% vs control group 5.5% (P = 0.12) Adverse events in < 75 years old patients: intervention group 3.7% vs. control group 4.9% (P = 0.74)
Troughton 2000	33	36	69	0	0	0	13	9	22	P = 0.32 No additional information provided

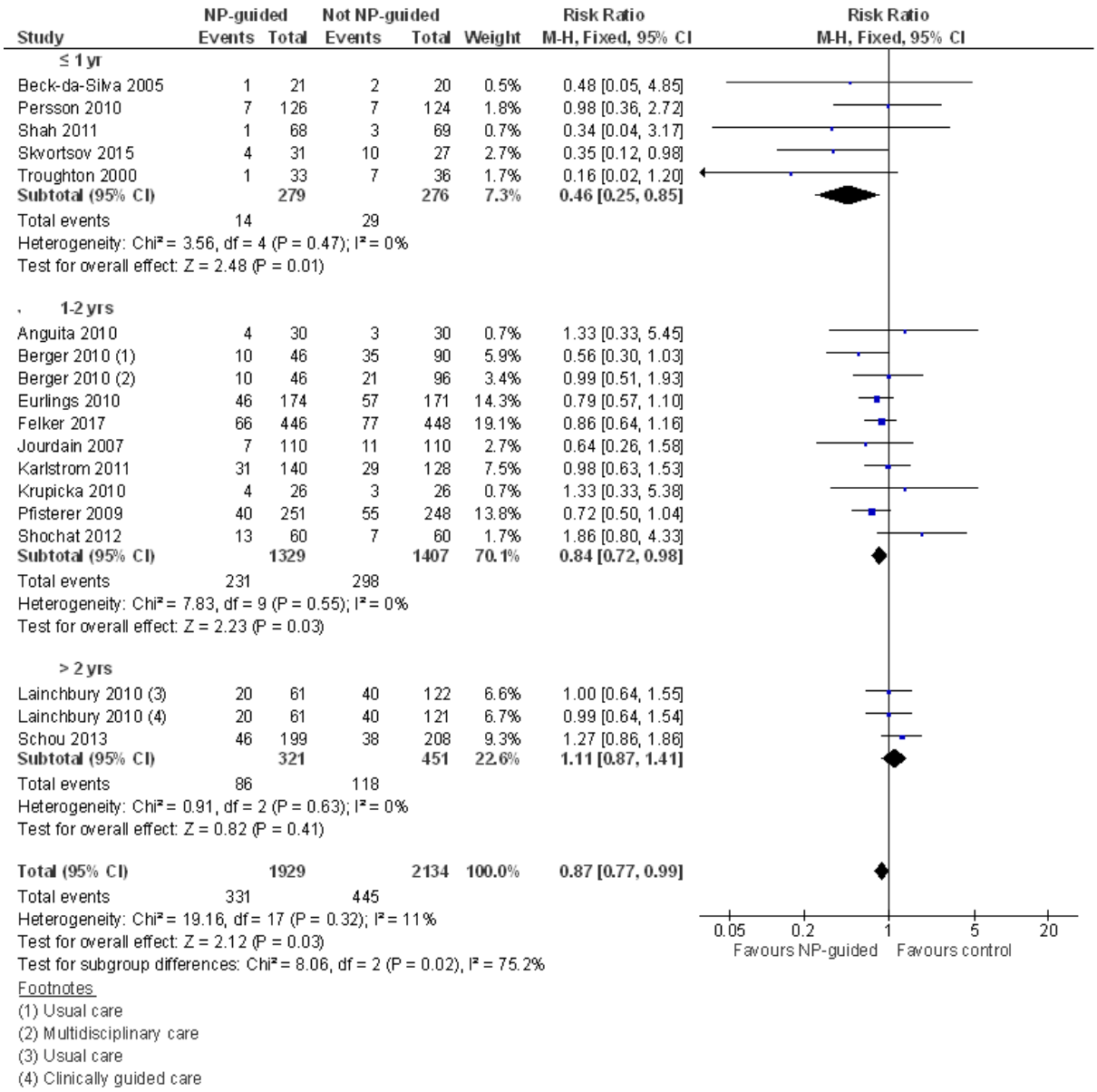
Appendix 5: Risk of bias summary for each included study



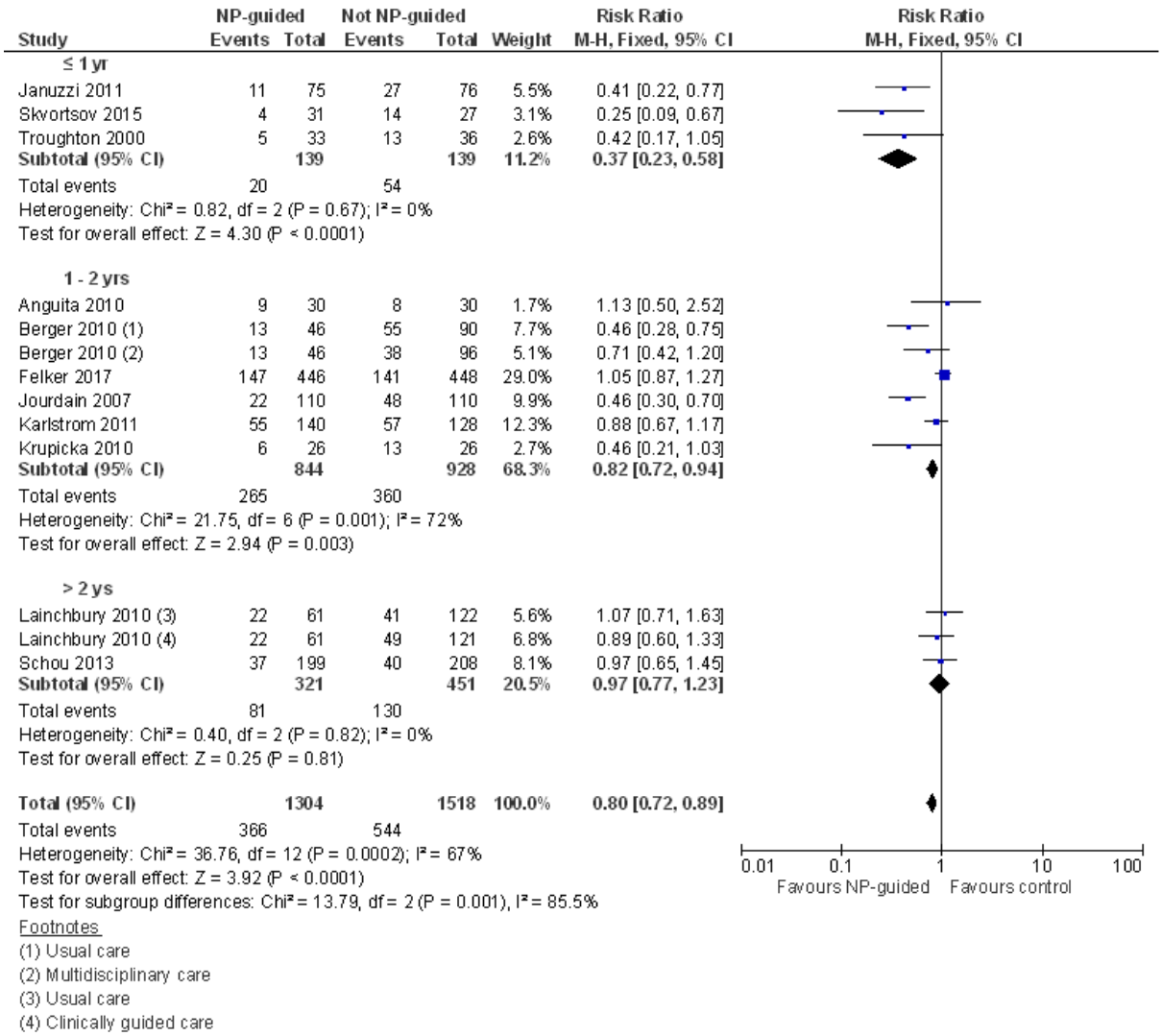
Appendix 6: Risk of bias bar chart for all studies



Appendix 7: Forest plot comparing NP-guided treatment versus control for all-cause mortality sub grouped by duration of intervention

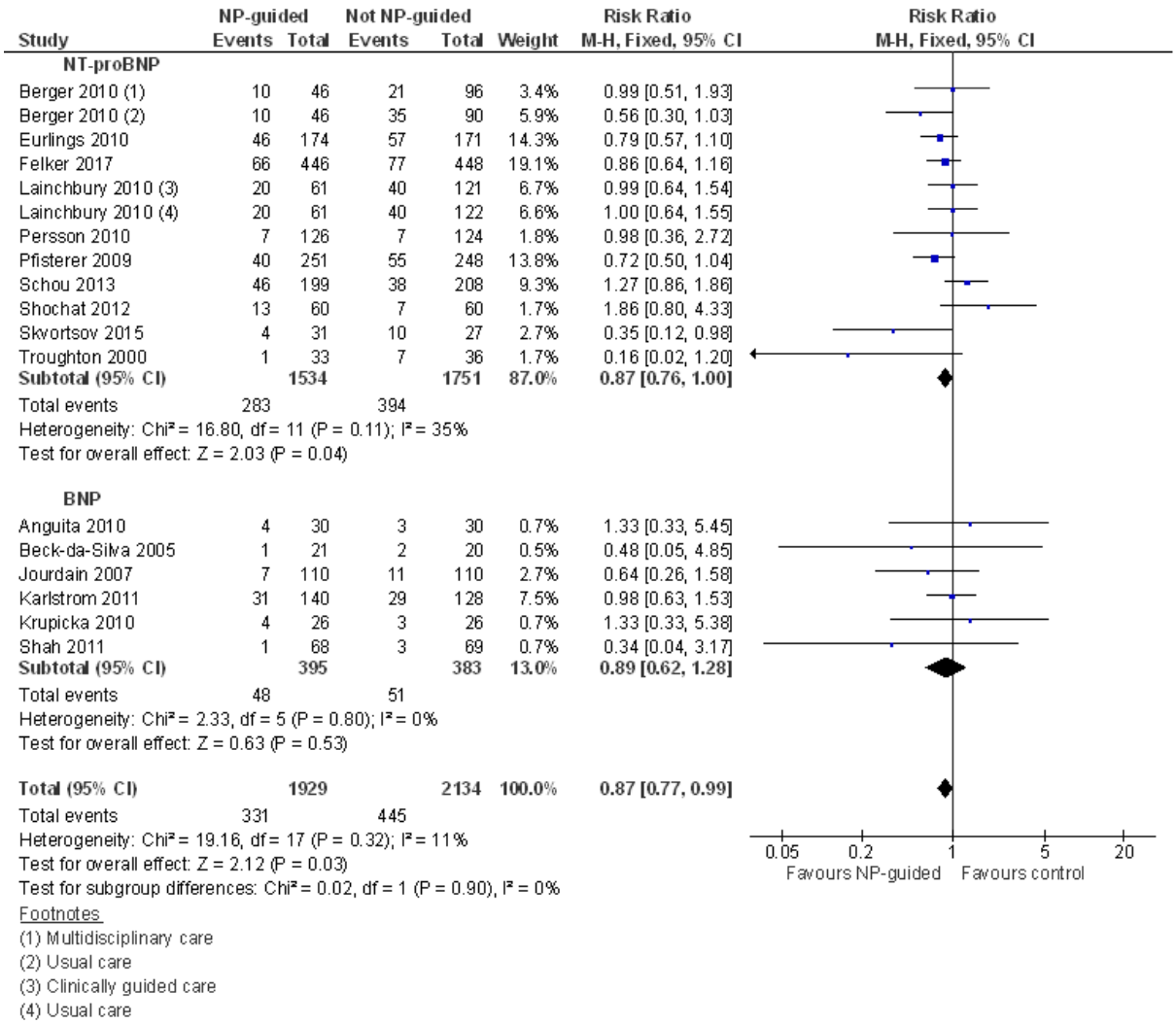


Appendix 8: Forest plot comparing NP-guided treatment versus control for heart failure admission sub grouped by duration of intervention

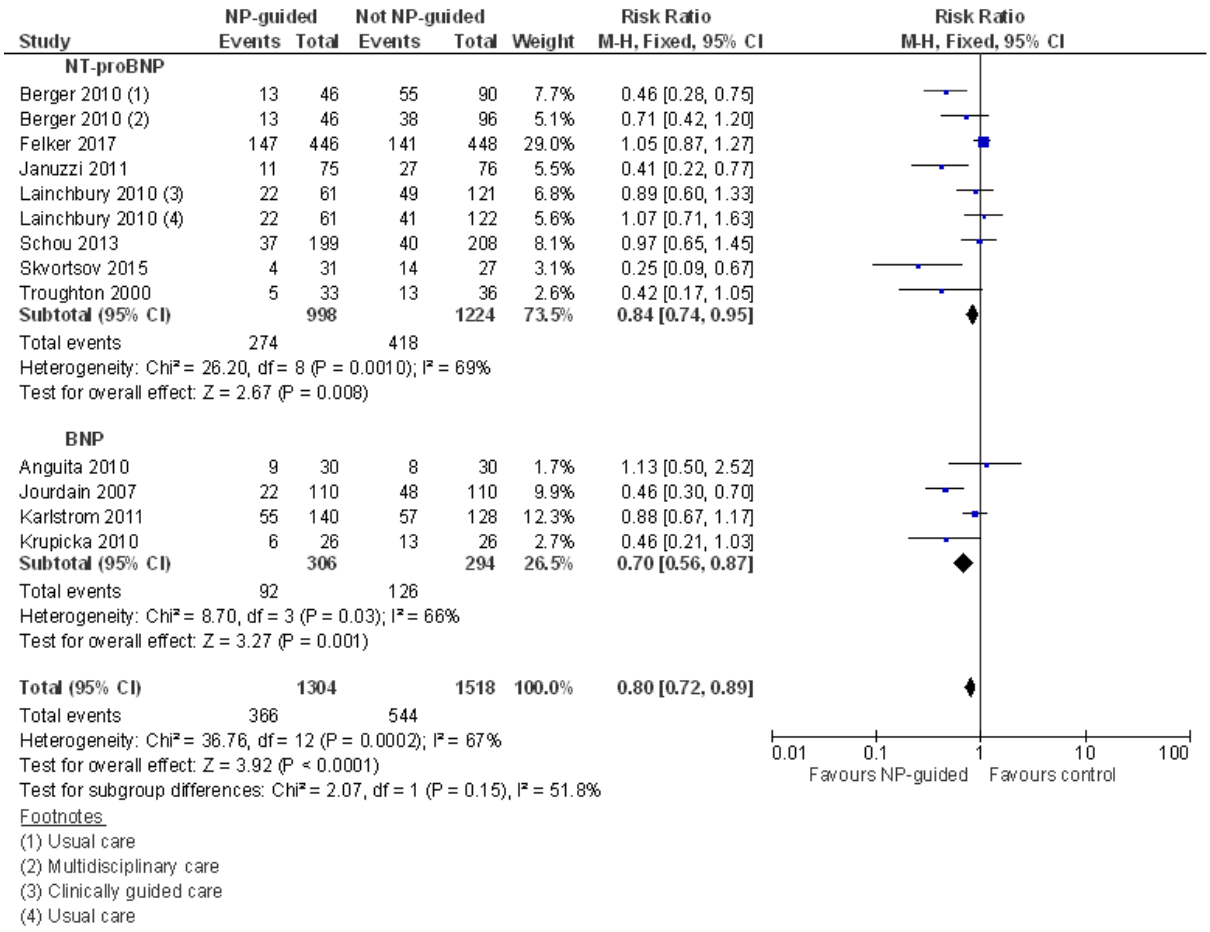


Footnotes
(1) Usual care
(2) Multidisciplinary care
(3) Usual care
(4) Clinically guided care

Appendix 9: Forest plot comparing NP-guided treatment versus control for all-cause mortality sub grouped by NP biomarker used



Appendix 10: Forest plot comparing NP-guided treatment versus control for heart failure admission sub grouped by NP biomarker used



Footnotes
(1) Usual care
(2) Multidisciplinary care
(3) Clinically guided care
(4) Usual care

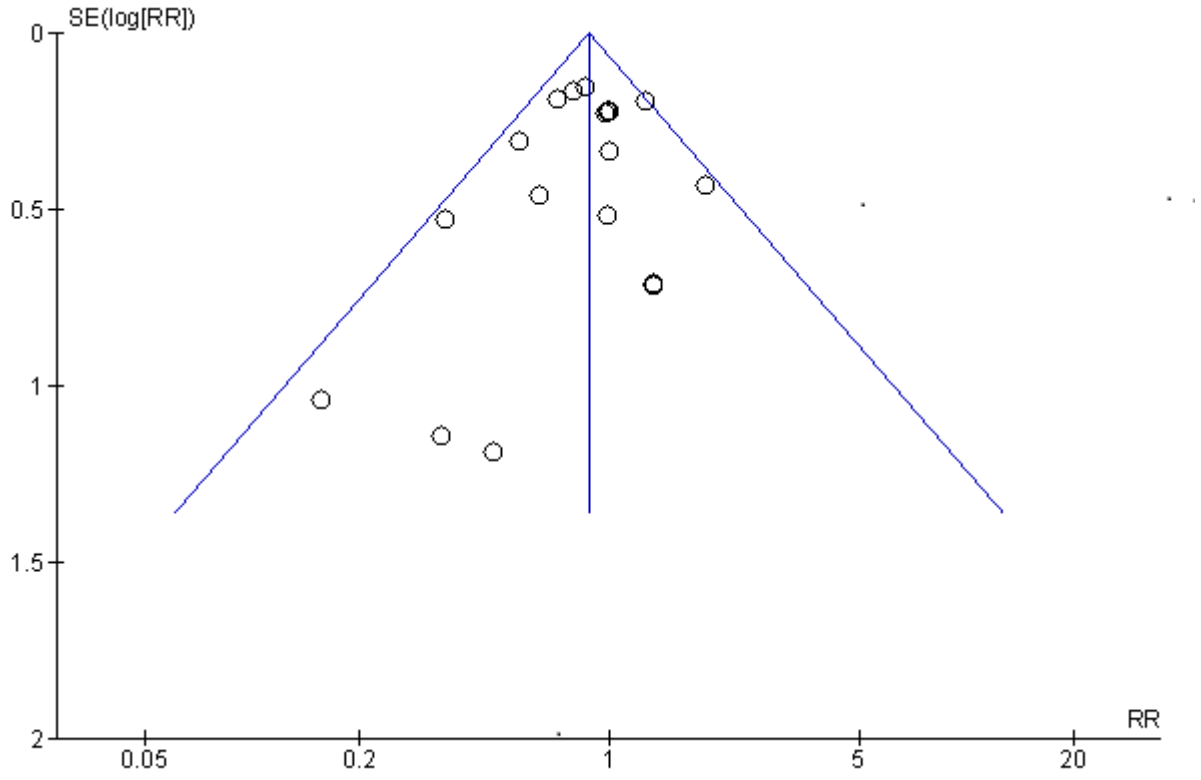
Appendix 11: Table to show agreements and disagreements with other systematic reviews and meta-analyses

Outcome	Review	Number of RCTs	N	Summary measure		95% Confidence intervals	p-value	Hetero-geneity (I^2)
All-cause mortality (all patients)	Felker 2009[20]	6	1627	HR	0.69	0.55 to 0.86	NR	NR
	Porapakkham 2010[21]	8	1726	RR	0.76	0.63 to 0.91	0.003*	NR
	Li 2013[22]	11	2414	RR	0.83	0.69 to 0.99	0.035*	0%
	Savarese 2013[23]	12	2686	OR	0.74	0.6 to 0.91	0.005*	0%
	Li 2014[24]	NR	NR	RR	0.79	0.67 to 0.92	0.004*	NR
	Troughton 2014[25]	10	2280	HR	0.82	0.67 to 1.00	0.05	0%
	Xin 2015[26]	14	3004	RR	0.94	0.81 to 1.08	0.39	3%
	McLellan 2016[27]	15	3169	RR	0.87	0.76 to 1.01	0.06	16%
	Purfulete 2017[28]	11	2919	HR	0.87	0.73 to 1.04	0.423	2.4%
	This review	**16**	**4063**	**RR**	**0.87**	**0.77 to 0.99**	**0.03***	**11%**
Heart failure admission	Li 2013[22]	7	1190	RR	0.65	0.5 to 0.84	0.001*	52.30%
	Savarese 2013[23]	8	1920	OR	0.55	0.4 to 0.77	<0.0001*	58.20%
	Li 2014[24]	NR	NR	RR	0.67	0.46 to 0.97	0.03*	NR
	Troughton 2014[25]	11	2431	HR	0.74	0.60 to 0.90	0.002*	24.00%
	Xin 2015[26]	11	2572	RR	0.79	0.63 to 0.98	0.03*	67.00%
	McLellan 2016[27]	10	1928	RR	0.70	0.61 to 0.80	<0.0001*	60%
	Purfulete 2017[28]	12	2939	HR	0.78	0.65 to 0.95	0.064	40.4%
	This review	**11**	**2822**	**RR**	**0.8**	**0.72 to 0.89**	**<0.0001***	**67.00%**
All-cause admission	Porapakkham 2010[21]	3	330	RR	0.82	0.64 to 1.05	0.12	NR
	Savarese 2013[23]	5	1108	OR	0.8	0.63- 1.02	0.077	0%
	Xin 2015[26]	7	1627	RR	0.97	0.89 to 1.07	0.56	8%
	Purfulete 2017[28]	6	1606	HR	0.97	0.85 to 1.10	0.651	0%
	McLellan 2016[27]	6	1142	RR	0.93	0.84 to 1.03	0.15	0%
Adverse events	Li 2014[24]	NR	NR	RR	1.15	0.99 to 1.34	0.69	NR
Adverse events (symptomatic hypotension)	Xin 2015[26]	4	838	RR	1.72	0.59 to 5.05	0.32	43%

Adverse events (hyper/hypo-kalemia)	Xin 2015[26]	2	354	RR	1.34	0.42 to 4.34	0.62	0%
Adverse events (renal dysfunction)	Xin 2015[26]	3	769	RR	1.46	0.34 to 6.24	0.21	0%
Adverse events (severe cough)	Xin 2015[26]	2	220	RR	1.93	0.69 to 5.37	0.21	0%
Quality of life	Xin 2015[26]	5	1172	WMD	-1.29	-3.81 to 1.22	0.31	49%
	McLellan 2016[27]	8	1812	WMD	-0.03	-1.18 to 1.13	0.97	75%

Where RCT – randomised control trial, HR - hazard ratio, RR - risk ratio, OR - odds ratio, WMD - weighted mean difference, NR - not reported, * - statistically significant result

Appendix 12: Funnel plot comparing NP-guided versus control for all-cause mortality



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