Web Extra Material: Characteristics of excluded studies

Reference	Reason for exclusion
Waldo SW, Beede J, Isakson S, Villard-Saussine S, Fareh J, Clopton P et al. Pro-B-type natriuretic peptide levels in acute decompensated heart failure. Journal of the American College of Cardiology. 2008; 51(19):1874-82	Prognostic mortality study for BNP, NTproBNP and proBNP
Omland T. B-type natriuretic peptides: prognostic markers in stable coronary artery disease. Expert Review of Molecular Diagnostics. 2008; 8(2):217-25	Prognostic study for BNP in stable coronary artery disease patients
Carpenter CR, Keim SM, Worster A, Rosen P, BEEM (Best Evidence in Emergency Medicine). Brain natriuretic peptide in the evaluation of emergency department dyspnea: is there a role? Journal of Emergency Medicine. 2012; 42(2):197-205	Prognostic evidence review for BNP and NTproBNP on patient oriented outcomes
Anwaruddin S, Lloyd-Jones DM, Baggish A, Chen A, Krauser D, Tung R et al. Renal function, congestive heart failure, and amino-terminal pro-brain natriuretic peptide measurement: results from the ProBNP Investigation of Dyspnea in the Emergency Department (PRIDE) Study. Journal of the American College of Cardiology. 2006; 47(1):91-7	Post-hoc analysis of included (PRIDE) study in patients with renal insufficiency
Chen AA, Wood MJ, Krauser DG, Baggish AL, Tung R, Anwaruddin S et al. NT-proBNP levels, echocardiographic findings, and outcomes in breathless patients: results from the ProBNP Investigation of Dyspnoea in the Emergency Department (PRIDE) echocardiographic substudy. European Heart Journal. 2006; 27(7):839-45	Post-hoc analysis of included (PRIDE) study in prognostic outcomes
Studler U, Kretzschmar M, Christ M, Breidthardt T, Noveanu M, Schoetzau A et al. Accuracy of chest radiographs in the emergency diagnosis of heart failure. European Radiology. 2008; 18(8):1644-52	Post-hoc analysis of included (BASEL) study assessing diagnostic utility of chest radiographs

Reference	Reason for exclusion
Green SM, Martinez-Rumayor A, Gregory SA, Baggish AL, O'Donoghue ML, Green JA et al. Clinical uncertainty, diagnostic accuracy, and outcomes in emergency department patients presenting with dyspnea. Archives of Internal Medicine. 2008; 168(7):741-8	Post-hoc analysis of included (PRIDE) study in clinical uncertainty as a prognostic marker
Bayes-Genis A, Lloyd-Jones DM, van Kimmenade RRJ, Lainchbury JG, Richards AM, Ordonez-Llanos J et al. Effect of body mass index on diagnostic and prognostic usefulness of amino-terminal pro-brain natriuretic peptide in patients with acute dyspnea. Archives of Internal Medicine. 2007; 167(4):400-407	Post-hoc analysis of included (ICON) study in overweight and obese patients
Pahle AS, Sorli D, Omland T, Knudsen CW, Westheim A, Wu AHB et al. Impact of systemic hypertension on the diagnostic performance of B-type natriuretic peptide in patients with acute dyspnea. American Journal of Cardiology. 2009; 104(7):966-71	Post-hoc analysis of included (Breathing Not Properly) study in hypertensive patients
Daniels LB, Clopton P, Bhalla V, Krishnaswamy P, Nowak RM, McCord J et al. How obesity affects the cut-points for B-type natriuretic peptide in the diagnosis of acute heart failure. Results from the Breathing Not Properly Multinational Study. American Heart Journal. 2006; 151(5):999-1005	Post-hoc analysis of included (Breathing Not Properly) study in obese patients
Martinez-Rumayor AA, Vazquez J, Rehman SU, Januzzi JL. Relative value of amino-terminal pro-B-type natriuretic peptide testing and radiographic standards for the diagnostic evaluation of heart failure in acutely dyspneic subjects. Biomarkers. 2010; 15(2):175-82	Post-hoc analysis of included (PRIDE) study of NTproBNP versus CXR
Sakhuja R, Chen AA, Anwaruddin S, Baggish AL, Januzzi JLJ. Combined use of amino terminal-pro-brain natriuretic peptide levels and QRS duration to predict left ventricular systolic dysfunction in patients with dyspnea. American Journal of Cardiology. 2005; 96(2):263-6	Post-hoc analysis of included (PRIDE) study of combining NTproBNP and QRS duration
Boldanova T, Noveanu M, Breidthardt T, Potocki M, Reichlin T, Taegtmeyer A et al. Impact of history of heart failure on	Post hoc analysis of included (BASEL) study comparing history of heart failure with no

Reference	Reason for exclusion
diagnostic and prognostic value of BNP: results from the B-type Natriuretic Peptide for Acute Shortness of Breath Evaluation (BASEL) study. International Journal of Cardiology. 2010; 142(3):265-72	history of heart failure
Tung RH, Camargo CAJ, Krauser D, Anwaruddin S, Baggish A, Chen A et al. Amino-terminal pro-brain natriuretic peptide for the diagnosis of acute heart failure in patients with previous obstructive airway disease. Annals of Emergency Medicine. 2006; 48(1):66-74	Post-hoc analysis of included (PRIDE) study in patients with known obstructive airways disease
Chenevier-Gobeaux C, Delerme S, Allo JC, Arthaud M, Claessens YE, Ekindjian OG et al. B-type natriuretic peptides for the diagnosis of congestive heart failure in dyspneic oldest-old patients. Clinical Biochemistry. 2008; 41(13):1049-54	Post-hoc analysis of included study Chenevier-Gobeaux 2005[15] in oldest old patients
Craig, J, Bradbury, I, Cummins, E, Downie, S, Foster, L, and Stout, A. The use of B-type natriuretic peptides in the investigation of patients with suspected heart failure; Understanding our Advice: The use of B-type natriuretic peptides in the investigation of patients with suspected heart failure. NHS Quality Improvement Scotland (NHS QIS), 2005 Available from: http://www.healthcareimprovementscotland.org/previous_resources/archived/use_of_bnp_in_the_investigatio.aspx	HTA: Scotland: Cross checked for references
Mant J, Doust J, Roalfe A, Barton P, Cowie MR, Glasziou P et al. Systematic review and individual patient data meta-analysis of diagnosis of heart failure, with modelling of implications of different diagnostic strategies in primary care. Health Technology Assessment. 2009; 13(32):1-207	HTA: UK: Cross checked for references
Balion C, Santaguida PL, Hill S, Worster A, McQueen M, Oremus M et al. Testing for BNP and NT-proBNP in the diagnosis and prognosis of heart failure. Evidence Report/Technology Assessment. 2006;(142):1-147	HTA: Canada: Cross checked for references
Merlin, T, Moss, J, Brooks, A, Newton, S, Hedayati, H, and	HTA: Australia: Cross checked for references

Reference	Reason for exclusion
Hiller, J. B-type natriuretic peptide assays in the diagnosis of heart failure. Part A: in the hospital emergency setting. Part B: in the non-hospital setting. Adelaide Health Technology Assessment (AHTA), 2007	
Latour-Perez J, Coves-Orts FJ, Abad-Terrado C, Abraira V, Zamora J. Accuracy of B-type natriuretic peptide levels in the diagnosis of left ventricular dysfunction and heart failure: a systematic review. European Journal of Heart Failure. 2006; 8(4):390-9	Systematic review of BNP cross checked for references
Korenstein D, Wisnivesky JP, Wyer P, Adler R, Ponieman D, McGinn T. The utility of B-type natriuretic peptide in the diagnosis of heart failure in the emergency department: a systematic review. BMC Emergency Medicine. 2007; 7:6	Systematic review of BNP cross checked for references
Worster A, Balion CM, Hill SA, Santaguida P, Ismaila A, McKelvie R et al. Diagnostic accuracy of BNP and NT-proBNP in patients presenting to acute care settings with dyspnea: a systematic review. Clinical Biochemistry. 2008; 41(4-5):250-9	Systematic review of BNP and NTproBNP in acute care settings cross checked for references
Trinquart L, Ray P, Riou B, Teixeira A. Natriuretic peptide testing in EDs for managing acute dyspnea: a meta-analysis. American Journal of Emergency Medicine. 2011; 29(7):757-67	Systematic review of BNP or NTproBNP test versus no test on patient outcomes. No diagnostic accuracy data.
Ewald B, Ewald D, Thakkinstian A, Attia J. Meta-analysis of B type natriuretic peptide and N-terminal pro B natriuretic peptide in the diagnosis of clinical heart failure and population screening for left ventricular systolic dysfunction. Internal Medicine Journal. 2008; 38(2):101-113	Systematic review of BNP and NTproBNP. Cross referenced and all appropriate studies included
Wang CS, FitzGerald JM, Schulzer M, Mak E, Ayas NT. Does this dyspneic patient in the emergency department have congestive heart failure? JAMA. 2005; 294(15):1944-56	Systematic review of BNP or NTproBNP cross referenced and all appropriate studies included
Doust JA, Glasziou PP, Pietrzak E, Dobson AJ. A systematic review of the diagnostic accuracy of natriuretic peptides for heart failure. Archives of Internal Medicine. 2004; 164(18):1978-84	Systematic review of BNP and BNP versus NTproANP cross referenced and all appropriate studies included.
Cavallazzi R, Nair A, Vasu T, Marik PE. Natriuretic peptides in	Systematic review for RVD in patients with

Reference	Reason for exclusion
acute pulmonary embolism: a systematic review. Intensive Care Medicine. 2008; 34(12):2147-56	PE
Clerico A, Fontana M, Zyw L, Passino C, Emdin M. Comparison of the diagnostic accuracy of brain natriuretic peptide (BNP) and the N-terminal part of the propeptide of BNP immunoassays in chronic and acute heart failure: a systematic review. Clinical Chemistry. 2007; 53(5):813-22	Systematic review of BNP and NTproBNP: cross checked for all references
Hu Z, Han Z, Huang Y, Sun Y, Li B, Deng A. Diagnostic power of the mid-regional pro-atrial natriuretic peptide for heart failure patients with dyspnea: a meta-analysis. Clinical Biochemistry. 2012; 45(18):1634-9	Systematic review of MRproANP: Cross checked for all references
Gutte H, Mortensen J, Jensen CV, von der Recke P, Petersen CL, Kristoffersen US et al. ANP, BNP and D-dimer predict right ventricular dysfunction in patients with acute pulmonary embolism. Clinical Physiology and Functional Imaging. 2010; 30(6):466-72	Screening for RVD in patients with PE
Sung EK, Dae GP, Hyun HC, Duck HY, Jun HL, Kyoo RH et al. The best predictor for right ventricular dysfunction in acute pulmonary embolism: Comparison between electrocardiography and biomarkers. Korean Circulation Journal. 2009; 39(9):378-81	Screening for RVD in patients with PE
Henzler T, Roeger S, Meyer M, Schoepf UJ, Nance JWJ, Haghi D et al. Pulmonary embolism: CT signs and cardiac biomarkers for predicting right ventricular dysfunction. European Respiratory Journal. 2012; 39(4):919-26	Screening for RVD in patients with PE
Laiho MK, Harjola VP, Graner M, Piilonen A, Raade M, Mustonen P. Helical computerized tomography and NT-proBNP for screening of right ventricular overload on admission and at long term follow-up of acute pulmonary embolism. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine. 2012; 20:33	Screening for RVD in patients with PE
Ouanes I, Jalloul F, Ayed S, Dachraoui F, Ouanes-Besbes L, Fekih Hassen M et al. N-terminal proB-type natriuretic	Indirect population: Screening for LVD in patients with COPD and renal dysfunction

Reference	Reason for exclusion
peptide levels aid the diagnosis of left ventricular dysfunction in patients with severe acute exacerbations of chronic obstructive pulmonary disease and renal dysfunction. Respirology. 2012; 17(4):660-6	
Gariani K, Delabays A, Perneger TV, Agoritsas T. Use of brain natriuretic peptide to detect previously unknown left ventricular dysfunction in patients with acute exacerbation of chronic obstructive pulmonary disease. Swiss Medical Weekly. 2011; 141:w13298	Indirect population: Screening for LVD in ED patients with a final diagnosis of AECOPD
Jose JV, Gupta SN, Selvakumar D. Utility of N-terminal pro-brain natriuretic peptide for the diagnosis of heart failure. Indian Heart Journal. 2003; 55(1):35-9	Indirect population: Mixed acute and chronic shortness of breath presenting to ED and outpatient departments, no split given
Kamano C, Osawa H, Hashimoto K, Nishimura S, Saito SK, Kashiwagi T et al. N-Terminal pro-brain natriuretic peptide as a predictor of heart failure with preserved ejection fraction in hemodialysis patients without fluid overload. Blood Purification. 2012; 33(1-3):37-43	Indirect population: Screening for HFPEF in haemodialysis patients
Spevack DM, Bowers J, Banerjee A, Talreja A, Altman EJ, Friedman MA et al. Diagnostic accuracy of Doppler echocardiography for determining left ventricular diastolic pressure elevation: prospective comparison to chest radiography, serum B-type natriuretic peptide, and chest auscultation. Echocardiography. 2008; 25(9):946-54	Indirect population: Non-hospitalised patients referred for clinically indicated coronary angiography
Sonoda H, Ohte N, Goto T, Wakami K, Fukuta H, Kikuchi S et al. Plasma N-terminal pro-brain natriuretic peptide levels identifying left ventricular diastolic dysfunction in patients with preserved ejection fraction. Circulation Journal. 2012; 76(11):2599-2605	Indirect population: Patients undergoing cardiac catheterization for coronary artery disease
Lefebvre A, Kural-Menasche S, Darmon M, Thiery G, Feugeas JP, Schlemmer B et al. Use of N-terminal pro-brain natriuretic peptide to detect cardiac origin in critically ill cancer patients with acute respiratory failure. Intensive Care Medicine. 2008;	Indirect population: Any cancer patients admitted to ICU, not patients with suspected heart failure

Reference	Reason for exclusion
34(5):833-9	
Coquet I, Darmon M, Doise JM, Degres M, Blettery B, Schlemmer B et al. Performance of N-terminal-pro-B-type natriuretic peptide in critically ill patients: a prospective observational cohort study. Critical Care. 2008; 12(6):R137	Indirect population: Any patients admitted to ICU, not patients with suspected heart failure
Shuai XX, Chen YY, Lu YX, Su GH, Wang YH, Zhao HL et al. Diagnosis of heart failure with preserved ejection fraction: which parameters and diagnostic strategies are more valuable? European Journal of Heart Failure. 2011; 13(7):737-45	Indirect population: Derivation cohort consists of outpatients and inpatients with normal and hypertensive controls. Neither derivation nor validation cohort all suspected heart failure patients
Bay M, Kirk V, Parner J, Hassager C, Nielsen H, Krogsgaard K et al. NT-proBNP: a new diagnostic screening tool to differentiate between patients with normal and reduced left ventricular systolic function. Heart. 2003; 89(2):150-4	Indirect population: Screening for reduced LVEF in all patients admitted to hospital
Pfister R, Scholz M, Wielckens K, Erdmann E, Schneider CA. Use of NT-proBNP in routine testing and comparison to BNP. European Journal of Heart Failure. 2004; 6(3):289-93	Indirect population: Screening for LV dysfunction in hospitalised patients undergoing angiography
Mikkelsen KV, Bie P, Moller JE, Ryde H, Videbaek L, Haghfelt T. Diagnostic accuracy of plasma brain natriuretic peptide and aminoterminal-proBNP in mild heart failure depends on assay and introduction of therapy. Scandinavian Journal of Clinical and Laboratory Investigation. 2005; 65(8):633-47	Indirect population; patients referred by GP to HF clinic
Anjan VY, Loftus TM, Burke MA, Akhter N, Fonarow GC, Gheorghiade M et al. Prevalence, clinical phenotype, and outcomes associated with normal B-type natriuretic Peptide levels in heart failure with preserved ejection fraction. American Journal of Cardiology. 2012; 110(6):870-6	Indirect population: Stable outpatients with HFPEF
Mockel M, Muller R, Vollert JO, Muller C, Carl A, Peetz D et al. Role of N-terminal pro-B-type natriuretic peptide in risk stratification in patients presenting in the emergency room. Clinical Chemistry. 2005; 51(9):1624-31	Indirect population: Not suspected heart failure: unselected ED patients
Jefic D, Lee JW, Jefic D, Savoy-Moore RT, Rosman HS. Utility of B-type natriuretic peptide and N-terminal pro B-type	Indirect population: medical or surgical ICU patients with pulmonary artery catheter in

Reference	Reason for exclusion
natriuretic peptide in evaluation of respiratory failure in critically ill patients. Chest. 2005; 128(1):288-95	place assessing for contractile dysfunction
O'Shea P, Daly R, Kasim S, Tormey WP. B-type natriuretic peptide in the Cardiology Department. Irish Medical Journal. 2012; 105(10)	Indirect setting and population: GP referrals to cardiology outpatients
Park HJ, Baek SH, Jang SW, Kim DB, Shin DI, Shin WS et al. Direct comparison of B-type natriuretic peptide and N-terminal pro-BNP for assessment of cardiac function in a large population of symptomatic patients. International Journal of Cardiology. 2010; 140(3):336-43	Indirect setting and population: Screening for LVSD in patients with dyspnoea in daily clinical practice
Choi S, Park D, Lee S, Hong Y, Kim S, Lee J. Cut-off values of B-type natriuretic peptide for the diagnosis of congestive heart failure in patients with dyspnoea visiting emergency departments: a study on Korean patients visiting emergency departments. Emergency Medicine Journal. 2007; 24(5):343-7	Indirect reference standard: Final diagnosis of heart failure was defined by transthoracic echocardiography
Jang TB, Aubin C, Naunheim R, Lewis LM, Kaji AH. The predictive value of physical examination findings in patients with suspected acute heart failure syndrome. Internal and Emergency Medicine. 2012; 7(3):271-4	Indirect reference standard: Criterion standard was pulmonary oedema on CXR
Bal L, Thierry S, Brocas E, Van de Louw A, Pottecher J, Hours S et al. B-type natriuretic peptide (BNP) and N-terminal-proBNP for heart failure diagnosis in shock or acute respiratory distress. Acta Anaesthesiologica Scandinavica. 2006; 50(3):340-7	Indirect reference standard: Final diagnosis of heart failure was defined by echocardiography
Chien TI, Chen HH, Kao JT. Comparison of Abbott AxSYM and Roche Elecsys 2010 for measurement of BNP and NT-proBNP. Clinica Chimica Acta; International Journal of Clinical Chemistry. 2006; 369(1):95-9	Indirect reference standard: Final diagnosis of heart failure was defined by echocardiography
Zhao SQ, Hu YM, Li Q, Liu XR, Wang M, Zhang WY et al. The clinical value of rapid assay for plasma B-type natriuretic peptide in differentiating congestive heart failure from pulmonary causes of dyspnoea. International Journal of	Indirect reference standard: PCWP >12mmHg, not clinical evaluation

Reference	Reason for exclusion
Clinical Practice. 2008; 62(2):214-20	
Murray H, Cload B, Collier CP, Sivilotti MLA. Potential impact of N-terminal pro-BNP testing on the emergency department evaluation of acute dyspnea. Canadian Journal of Emergency Medicine. 2006; 8(4):251-8	Indirect reference standard: ED physician rating scale at likelihood of heart failure diagnosis and correlation with NTproBNP levels.
Levitt JE, Vinayak AG, Gehlbach BK, Pohlman A, Van Cleve W, Hall JB et al. Diagnostic utility of B-type natriuretic peptide in critically ill patients with pulmonary edema: a prospective cohort study. Critical Care. 2008; 12(1):R3	Indirect target condition: using BNP to distinguish Acute lung Injury/ARDS
Marantz PR, Kaplan MC, Alderman MH. Clinical diagnosis of congestive heart failure in patients with acute dyspnea. Chest. 1990; 97(4):776-81	Indirect index test: Physical examination manoeuvres compared to reference standard
Springfield CL, Sebat F, Johnson D, Lengle S, Sebat C. Utility of impedance cardiography to determine cardiac vs. noncardiac cause of dyspnea in the emergency department. Congestive Heart Failure. 2004; 10(2 Suppl 2):14-6	Indirect index test: Impedance cardiography versus clinical assessment
Singer AJ, Thode HCJ, Green GB, Birkhahn R, Shapiro NI, Cairns C et al. The incremental benefit of a shortness-of-breath biomarker panel in emergency department patients with dyspnea. Academic Emergency Medicine. 2009; 16(6):488-94	Indirect index test: SOB biomarker panel not broken down for individual biomarkers
Clerico A, Prontera C, Emdin M, Passino C, Storti S, Poletti R et al. Analytical performance and diagnostic accuracy of immunometric assays for the measurement of plasma B-type natriuretic peptide (BNP) and N-terminal proBNP. Clinical Chemistry. 2005; 51(2):445-7	Indirect population: Healthy subjects
Zaphiriou A, Robb S, Murray-Thomas T, Mendez G, Fox K, McDonagh T et al. The diagnostic accuracy of plasma BNP and NTproBNP in patients referred from primary care with suspected heart failure: results of the UK natriuretic peptide study. European Journal of Heart Failure. 2005; 7(4):537-41	Indirect population: Patients referred to heart failure clinics by GPs
El Mahmoud R, Alibay Y, Brun-Ney D, Boulard JC, Dubourg O, Puy H et al. [Type B natriuretic peptide (BNP) versus n-	Not in English

Reference	Reason for exclusion
terminal type B natriuretic propeptide in the diagnosis of cardiac failure in the elderly over 75 population]. Archives Des Maladies Du Coeur Et Des Vaisseaux. 2006; 99(3):201-7	
Jourdain P, Funck F, Canault E, Bellorini M, Deschamps P, Duval G et al. [Value of type B natriuretic peptide in the emergency management of patients with suspected cardiac failure. Report of 125 cases]. Archives Des Maladies Du Coeur Et Des Vaisseaux. 2002; 95(9):763-7	Not in English
Ababsa R, Jourdain P, Funck F, Deschamps P, Sadeg N. [BNP and dyspnea: proposition of a diagnostic strategy based on two cut-off]. Annales De Biologie Clinique. 2005; 63(2):213-6	Not in English
Coskun B, Kirkil G, Muz MH, Yildiz M, Ozbay Y. The diagnostic values of brain natriuretic peptide and cardiac troponin I for determining the right ventricle dysfunction in patients with submassive pulmonary thromboembolism. Turk Toraks Dergisi. 2012; 13(4):163-8	Not in English
Ray P, Chenevier-Gobeaux C, Claessens Y-E. Natriuretic peptides to diagnose acute heart failure in emergency patients. Annales Francaises De Medecine D'Urgence. 2011; 1(3):200-5	Not in English
Osca J, Quesada A, Arnau MA, Osa A, Hervas I, Almenar L et al. Brain natriuretic peptide. Diagnostic value in heart failure. Revista Espanola De Cardiologia. 2002; 55(1):7-15	Not in English
Rapid HTA on the use of natriuretic peptides for diagnosing cardiac insufficiency in patients with acute dyspnea. Department of Science and Technology - Brazilian Health Technology Assessment General Coordination (DECIT-CGATS), 2009	Not in English
Collin-Chavagnac D, Jacques D, Perrin M, Rabilloud M, Manchon M. [BNP/NT-proBNP: what is the best choice in an emergency laboratory?]. Annales De Biologie Clinique. 2006; 64(3):275-80	Not in English
Robaei D, Koe L, Bais R, Gould I, Stewart T, Tofler GH. Effect	Non diagnostic accuracy study; no reference

Reference	Reason for exclusion
of NT-proBNP testing on diagnostic certainty in patients admitted to the emergency department with possible heart failure. Annals of Clinical Biochemistry. 2011; 48(Pt 3):212-7	standard: RCT of clinicians blinded versus unblinded to BNP result in cases of suspected heart failure
Collins SP, Lindsell CJ, Yealy DM, Maron DJ, Naftilan AJ, McPherson JA et al. A comparison of criterion standard methods to diagnose acute heart failure. Congestive Heart Failure. 2012; 18(5):262-71	Non diagnostic accuracy study; no reference standard; Comparison of diagnostic strategies in ED
Paul B, Soon KH, Dunne J, De Pasquale CG. Diagnostic and prognostic significance of plasma N-terminal-pro-brain natriuretic peptide in decompensated heart failure with preserved ejection fraction. Heart, Lung and Circulation. 2008; 17(6):497-501	Non diagnostic accuracy study; studies correlation of NTproBNP with preservation of ejection fraction and correlation with outcomes.
Brenden CK, Hollander JE, Guss D, McCullough PA, Nowak R, Green G et al. Gray zone BNP levels in heart failure patients in the emergency department: results from the Rapid Emergency Department Heart Failure Outpatient Trial (REDHOT) multicenter study. American Heart Journal. 2006; 151(5):1006-11	Non diagnostic accuracy study; studies implications of BNP>100 pg/mL on outcomes in ED patients with dyspnoea
Belovicova M, Kinova S, Hrusovsky S. Brain natriuretic peptide (BNP) in differential diagnosis of dyspnea. Bratislavske Lekarske Listy. 2005; 106(6-7):203-6	Non diagnostic accuracy study; examines correlation of BNP levels with NYHA class of patients presenting to clinic.
Belagavi AC, Rao M, Pillai AY, Srihari US. Correlation between NT proBNP and left ventricular ejection fraction in elderly patients presenting to emergency department with dyspnoea. Indian Heart Journal. 2012; 64(3):302-4	Non diagnostic accuracy study; looks at correlation of NTproBNP and echo findings
Ozturk TC, Unluer E, Denizbasi A, Guneysel O, Onur O. Can NT-proBNP be used as a criterion for heart failure hospitalization in emergency room? Journal of Research in Medical Sciences. 2011; 16(12):1564-71	Non diagnostic accuracy study; compares NTproBNP levels in outpatients and those hospitalised
Karakilic E, Kepez A, Abali G, Coskun F, Kunt M, Tokgozoglu L. The relationship between B-type natriuretic peptide levels and echocardiographic parameters in patients with heart failure admitted to the emergency department. Anadolu	Non diagnostic accuracy study; looks at correlation of BNP levels with echocardiographic parameters

Reference	Reason for exclusion
Kardiyoloji Dergisi. 2010; 10(2):143-9	
van der Burg-de Graauw, Cobbaert CM, Middelhoff CJFM, Bantje TA, van Guldener C. The additive value of N-terminal pro-B-type natriuretic peptide testing at the emergency department in patients with acute dyspnoea. European Journal of Internal Medicine. 2009; 20(3):301-6	No extractable diagnostic accuracy data; examines additive value of NTproBNP in certain groups
Cinar O, Cevik E, Acar A, Kaya C, Ardic S, Comert B et al. Evaluation of mid-regional pro-atrial natriuretic peptide, procalcitonin, and mid-regional pro-adrenomedullin for the diagnosis and risk stratification of dyspneic ED patients. American Journal of Emergency Medicine. 2012; 30(9):1915-20	Comparison of initial diagnosis; marker aided diagnosis and final diagnosis as a process.
Jungbauer CG, Buchner S, Birner C, Resch M, Heinicke N, Debl K et al. N-terminal pro-brain natriuretic peptide from fresh urine for the biochemical detection of heart failure and left ventricular dysfunction. European Journal of Heart Failure. 2010; 12(4):331-7	Urinary BNP study
Sabatasso S, Vaucher P, Augsburger M, Donze N, Mangin P, Michaud K. Sensitivity and specificity of NT-proBNP to detect heart failure at post mortem examination. International Journal of Legal Medicine. 2011; 125(6):849-56	Forensic study of death with heart failure
Collins SP, Lindsell CJ, Peacock WF, Hedger VD, Askew J, Eckert DC et al. The combined utility of an S3 heart sound and B-type natriuretic peptide levels in emergency department patients with dyspnea. Journal of Cardiac Failure. 2006; 12(4):286-92	Diagnostic accuracy of S3 auscultation + BNP. No individually extractable data for BNP alone
Diercks DB, Miller CD. Natriuretic peptide testing: a useful diagnostic test. Annals of Emergency Medicine. 2009; 53(3):386-7	Letter to editor
Golabchi A. Can atrial natriuretic peptides measurement diagnose heart failure at different age groups? Journal of Research in Medical Sciences. 2012; 17(1):116-7	Letter to editor
McCullough PA, Nowak RM, McCord J, Hollander JE,	Subgroup analysis of included (Breathing

Reference	Reason for exclusion
Herrmann HC, Steg PG et al. B-type natriuretic peptide and clinical judgment in emergency diagnosis of heart failure: analysis from Breathing Not Properly (BNP) Multinational Study. Circulation. 2002; 106(4):416-22	Not Properly) study with information recorded for ED physician assessment of probability of heart failure
Coste J, Jourdain P, Pouchot J. A gray zone assigned to inconclusive results of quantitative diagnostic tests: Application to the use of brain natriuretic peptide for diagnosis of heart failure in acute dyspneic patients. Clinical Chemistry. 2006; 52(12):2229-35	No extractable diagnostic accuracy data; calculation of grey zone likelihood ratios on the basis of history of heart failure
Liteplo AS, Marill KA, Villen T, Miller RM, Murray AF, Croft PE et al. Emergency thoracic ultrasound in the differentiation of the etiology of shortness of breath (ETUDES): sonographic B-lines and N-terminal pro-brain-type natriuretic peptide in diagnosing congestive heart failure. Academic Emergency Medicine. 2009; 16(3):201-210	No extractable diagnostic accuracy data. Threshold of NTproBNP not reported alongside sensitivity and specificity. No AUC value given.
Dieplinger B, Gegenhuber A, Haltmayer M, Mueller T. Evaluation of novel biomarkers for the diagnosis of acute destabilised heart failure in patients with shortness of breath. Heart. 2009; 95(18):1508-13	Duplicate data: Previously presented in included study Gegenuber 2006[18]
Shaikh K, Hanif B, Siddique AA, Shaikh MY, Khan MN. Pro-brain natriuretic peptide plasma levels, left ventricular dimensions and ejection fraction in acute dyspnoea. Journal of the College of Physicians and Surgeons--Pakistan. 2012; 22(12):751-5	Duplicate data: From included study Shaikh 2011[42]
Kevin Rogers R, Stehlik J, Stoddard GJ, Greene T, Collins SP, Peacock WF et al. Adjusting for clinical covariates improves the ability of B-type natriuretic peptide to distinguish cardiac from non-cardiac dyspnoea: a sub-study of HEARD-IT. European Journal of Heart Failure. 2009; 11(11):1043-9	Duplicate data: From included substudy (HEARD-IT) trial
Steg PG, Joubin L, McCord J, Abraham WT, Hollander JE, Omland T et al. B-type natriuretic peptide and echocardiographic determination of ejection fraction in the diagnosis of congestive heart failure in patients with acute	Duplicate data: From included study (Breathing Not Properly) data

Reference	Reason for exclusion
dyspnea. Chest. 2005; 128(1):21-9	
Knudsen CW, Riis JS, Finsen AV, Eikvar L, Muller C, Westheim A et al. Diagnostic value of a rapid test for B-type natriuretic peptide in patients presenting with acute dyspnoe: effect of age and gender. European Journal of Heart Failure. 2004; 6(1):55-62	Duplicate data: Norwegian data from included study (Breathing Not Properly) data
Morrison LK, Harrison A, Krishnaswamy P, Kazanegra R, Clopton P, Maisel A. Utility of a rapid B-natriuretic peptide assay in differentiating congestive heart failure from lung disease in patients presenting with dyspnea. Journal of the American College of Cardiology. 2002; 39(2):202-9	Duplicate data: San Diego data from included study (Breathing Not Properly) data
Pang PS, Xue Y, DeFilippi C, Silver M, Januzzi J, Maisel A. The role of natriuretic peptides: from the emergency department throughout hospitalization. Congestive Heart Failure. 2012; 18 Suppl 1:S5-S8	Review article
Januzzi JLJ, Chen-Tournoux AA, Moe G. Amino-terminal pro-B-type natriuretic peptide testing for the diagnosis or exclusion of heart failure in patients with acute symptoms. American Journal of Cardiology. 2008; 101(3A):29-38	Review article
Michaels AD, Rogers R, Stoddard G, Green T, Collins SP, Peacock WF et al. Adjusting for clinical covariates improves the ability of BNP to distinguish cardiac from non-cardiac dyspnea. European Heart Journal. 2009; 30(Suppl 1):131-2	Conference abstract of included study (HEARD-IT)
Shetty K, Garber A. B type natriuretic peptide testing was more cast effective than conventional diagnosis in patients with acute dyspnoea: Commentary. Evidence-Based Medicine. 2007; 12(1):28	Economic comment article on included (BASEL) study
Jones DJL, Willingale R, Quinn PA, Lamb JH, Farmer PB, Davies JE et al. Improving the diagnostic accuracy of N-terminal B-type natriuretic peptide in human systolic heart failure by plasma profiling using mass spectrometry. Journal of Proteome Research. 2007; 6(8):3329-34	Case-control study: Population consists of known CHF patients and healthy controls not suspected heart failure.
Sultana P, Hoque M, Shafiullah S. Plasma BNP (B-type	Case-control study: Population consists of

Reference	Reason for exclusion
natriuretic peptide) and heart failure: A case-control study. Journal of Medicine. 2010; 11(1):46-50	known CHF patients and healthy controls not suspected heart failure.
Michielsen ECHJ, Bakker JA, Kimmenade RRJV, Pinto YM, Dieijen-Visser MPV. The diagnostic value of serum and urinary NT-proBNP for heart failure. Annals of Clinical Biochemistry. 2008; 45(Pt 4):389-94	Case-control study: Population consists of known CHF patients and healthy controls not suspected heart failure.
Ajuluchukwu JNA, Ekure EN, Mbakwem AC, Okoromah CN, Oladipo OO. Reliability and accuracy of point-of-care amino-terminal probrain natriuretic peptide in congestive heart failure patients. International Journal of Cardiology. 2010; 9(2):2	Case-control study: Population consists of known CHF patients and healthy controls not suspected heart failure.
Shah RV, Truong QA, Gaggin HK, Pfannkuche J, Hartmann O, Januzzi JLJ. Mid-regional pro-atrial natriuretic peptide and pro-adrenomedullin testing for the diagnostic and prognostic evaluation of patients with acute dyspnoea. European Heart Journal. 2012; 33(17):2197-2205	Did not present sufficient data to allow us to extract or calculate age-independent absolute numbers of true positives, false positives, false negatives, and true negatives
Gruson D, Ketelslegers JM, Verschuren F, Thys F. Head-to-head comparison of the prohormone proBNP1-108 with BNP and Nt-proBNP in patients admitted to emergency department. Clinical Biochemistry. 2012; 45(3):249-52	Did not present sufficient data to allow us to extract or calculate absolute numbers of true positives, false positives, false negatives, and true negatives
Fabbian F, De Giorgi A, Pala M, Tiseo R, Portaluppi F. Elevated NT-proBNP levels should be interpreted in elderly patients presenting with dyspnea. European Journal of Internal Medicine. 2011; 22(1):108-11	Did not present sufficient data to allow us to extract or calculate absolute numbers of true positives, false positives, false negatives, and true negatives
Havelka EG, Rzechula KH, Bryant TO, Anneken SM, Kulstad EB. Correlation between impedance cardiography and B-type natriuretic peptide levels in dyspneic patients. Journal of Emergency Medicine. 2011; 40(2):146-150	Did not present sufficient data to allow us to extract or calculate absolute numbers of true positives, false positives, false negatives, and true negatives
Afaq MA, Shoraki A, Ivanov O, Srinivasan J, Bernstein L, Zarich SW. Validity of Amino Terminal pro-Brain Natriuretic Peptide in a Medically Complex Elderly Population. Journal of Clinical Medicine Research. 2011; 3(4):156-163	Did not present sufficient data to allow us to extract or calculate absolute numbers of true positives, false positives, false negatives, and true negatives
deFilippi CR, Seliger SL, Maynard S, Christenson RH. Impact of	Did not present sufficient data to allow us

Reference	Reason for exclusion
renal disease on natriuretic peptide testing for diagnosing decompensated heart failure and predicting mortality. Clinical Chemistry. 2007; 53(8):1511-9	to extract or calculate absolute numbers of true positives, false positives, false negatives, and true negatives
Moe GW, Howlett J, Januzzi JL, Zowall H. N-terminal pro-B-type natriuretic peptide testing improves the management of patients with suspected acute heart failure: primary results of the Canadian prospective randomized multicenter IMPROVE-CHF study. Circulation. 2007; 115(24):3103-10	Did not present sufficient data to allow us to extract or calculate absolute numbers of true positives, false positives, false negatives, and true negatives

Web Extra Material: Data extraction table

Reference	Study type	Number of patients	Patient characteristics	Index test(s) and reference standard + target condition	Outcome measures		Effect sizes		Comments
Name of author; Year of study	Natriuretic peptide/s (assay): Threshold/s available Study design: Setting: Country:	N = Inclusion criteria: Exclusion criteria:	Mean age: Male/Female (n):	Index test: Reference standard: Target condition:		Ref std +	Ref std -	Total	Source of funding: Limitations: Additional data:
					Natriuretic peptide (threshold) +	TP	FP		
					Natriuretic peptide (threshold) -	FN	TN		
					Total				
					Sensitivity [95%CI]: Specificity[95%CI]: AUC[95%CI]:				

1 **Web Extra Material:**

2 **CENTRAL on The Cochrane Library**

#1	MeSH descriptor: [Heart Failure] explode all trees
#2	MeSH descriptor: [Cardiomyopathy, Dilated] explode all trees
#3	MeSH descriptor: [Shock, Cardiogenic] explode all trees
#4	MeSH descriptor: [Ventricular Dysfunction] explode all trees
#5	MeSH descriptor: [Cardiac Output, Low] explode all trees
#6	(heart or cardiac or myocardial) near/2 (failure or decompensation):ti
#7	((congestive or acute or decompensat*) near/2 "heart failure"):ti,ab
#8	(dilated or congestive) near/2 cardiomyopath*:ti
#9	cardiogenic shock:ti
#10	(ventricular or ventricle*) near/2 (failure or insufficien* or dysfunction*):ti
#11	(("left ventricle" or "left ventricular") near/2 (failure or insufficienc* or dysfunction*)):ti,ab
#12	lvsd:ti,ab
#13	MeSH descriptor: [Pulmonary Edema] this term only
#14	cardiogenic near/2 ("pulmonary edema" or "pulmonary oedema" or "lung edema" or "lung oedema"):ti,ab
#15	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14
#16	MeSH descriptor: [Natriuretic Peptides] explode all trees
#17	(natriuretic near/2 peptide*):ti,ab
#18	(natriuretic near/2 factor*):ti,ab
#19	(BNP or ANP or pro-BNP or pro-ANP or pro BNP or pro ANP):ti,ab
#20	#16 or #17 or #18 or #19
#21	#15 and #20

3

4 **Medline (on Ovid)**

5 1   exp Heart Failure/

6 2   Cardiomyopathy, Dilated/

7 3   Shock, Cardiogenic/

8 4   exp Ventricular Dysfunction/

9 5   Cardiac Output, Low/

10 6   ((heart or cardiac or myocardial) adj2 (failure or decompensation)).ti.

11 7   ((congestive or acute or decompensat$) adj2 " heart failure").ti,ab.

12 8   ((dilated or congestive) adj2 cardiomyopath$).ti.

13 9   "cardiogenic shock".ti.

14 10   ((ventricular or ventricle$) adj2 (failure or insufficien$ or dysfunction$)).ti.

15 11   (("left ventricular" or "left ventricle") adj2 (failure or insufficien$ or

16 dysfunction$)).ti,ab.

17 12   lvsd.ti,ab.

18 13   or/1-12

19 14   letter/

20 15   editorial/

21 16   news/

22 17   exp historical article/

23 18   Anecdotes as Topic/

24 19   comment/

25 20   case report/

26 21   (letter or comment*).ti.

27	22	or/14-21
28	23	randomized controlled trial/ or random*.ti,ab.
29	24	22 not 23
30	25	animals/ not humans/
31	26	exp Animals, Laboratory/
32	27	exp Animal Experimentation/
33	28	exp Models, Animal/
34	29	exp Rodentia/
35	30	(rat or rats or mouse or mice).ti.
36	31	or/24-30
37	32	13 not 31
38	33	limit 32 to english language
39	34	Epidemiologic studies/
40	35	exp Case control studies/
41	36	exp Cohort studies/
42	37	Cross-sectional studies/
43	38	case control.ti,ab.
44	39	(cohort adj (study or studies or analys*)).ti,ab.
45	40	((follow up or observational or uncontrolled or non randomi#ed or
46		nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
47	41	((longitudinal or retrospective or prospective or cross sectional) and (study or
48		studies or review or analys* or cohort*)).ti,ab.
49	42	or/34-41
50	43	33 and 42
51	44	exp *Natriuretic Peptides/
52	45	(natriuretic adj2 peptide$).ti,ab.
53	46	(natriuretic adj2 factor*).ti,ab.
54	47	(BNP or ANP or pro-BNP or pro-ANP or pro BNP or pro ANP).ti,ab.
55	48	44 or 45 or 46 or 47
56	49	43 and 48
57	50	33 and 48
58		
59	**Embase (on Ovid)**	
60	1	*heart failure/ or acute heart failure/ or *cardiogenic shock/ or *diastolic
61		dysfunction/ or *forward heart failure/ or *high output heart failure/ or
62		*systolic dysfunction/
63	2	*Congestive Cardiomyopathy/ or exp *Congestive Heart Failure/
64	3	exp *Heart Ventricle Failure/
65	4	((heart or cardiac or myocardial) adj2 (failure or decompensation)).ti.
66	5	((congestive or acute or decompensat$) adj2 " heart failure").ti,ab.
67	6	((dilated or congestive) adj2 cardiomyopath$).ti.
68	7	"cardiogenic shock".ti.
69	8	((ventricular or ventricle$) adj2 (failure or insufficien$ or dysfunction$)).ti.

70	9	(("left ventricular" or "left ventricle") adj2 (failure or insufficien$ or
71		dysfunction$)).ti,ab.
72	10	lvsd.ti,ab.
73	11	or/1-10
74	12	letter.pt. or letter/
75	13	note.pt.
76	14	editorial.pt.
77	15	case report/ or case study/
78	16	(letter or comment*).ti.
79	17	or/12-16
80	18	randomized controlled trial/ or random*.ti,ab.
81	19	17 not 18
82	20	animal/ not human/
83	21	nonhuman/
84	22	exp Animal Experiment/
85	23	exp Experimental Animal/
86	24	animal model/
87	25	exp Rodent/
88	26	(rat or rats or mouse or mice).ti.
89	27	or/19-26
90	28	11 not 27
91	29	limit 28 to english language
92	30	exp *natriuretic factor/
93	31	(natriuretic adj2 peptide$).ti,ab.
94	32	(natriuretic adj2 factor*).ti,ab.
95	33	(BNP or ANP or pro-BNP or pro-ANP or pro BNP or pro ANP).ti,ab.
96	34	or/30-33
97	35	29 and 33
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124 **Web Extra Material: PRISMA Flowchart**
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┌─────────────────────────────────┐     ┌─────────────────────────────────┐
│ Records identified through       │     │ Additional records identified    │
│ database searching, n = 7713     │     │ through other sources, n = 2     │
└─────────────────────────────────┘     └─────────────────────────────────┘
                    │                                    │
                    └────────────────┬───────────────────┘
                                     ▼
              ┌─────────────────────────────────┐
              │ Records screened in 1ˢᵗ sift,    │
              │ n = 7715                         │
              └─────────────────────────────────┘
                    │                              ┌─────────────────────────────────┐
                    │──────────────────────────────▶│ Records excluded in 1ˢᵗ sift,   │
                    │                              │ n = 7560                         │
                    ▼                              └─────────────────────────────────┘
              ┌─────────────────────────────────┐
              │ Full-text articles assessed for  │
              │ eligibility, n = 155             │
              └─────────────────────────────────┘
                    │
        ┌───────────┴───────────────────────────────┐
        ▼                                            ▼
┌───────────────────────┐         ┌───────────────────────────────────┐
│ Studies included in    │         │ Studies excluded from review,     │
│ review, n = 42         │         │ n = 113                           │
│                        │         │                                   │
│                        │         │ Reasons for exclusion: (see       │
│                        │         │ exclusion lists)                  │
│                        │         │                                   │
└───────────────────────┘         └───────────────────────────────────┘
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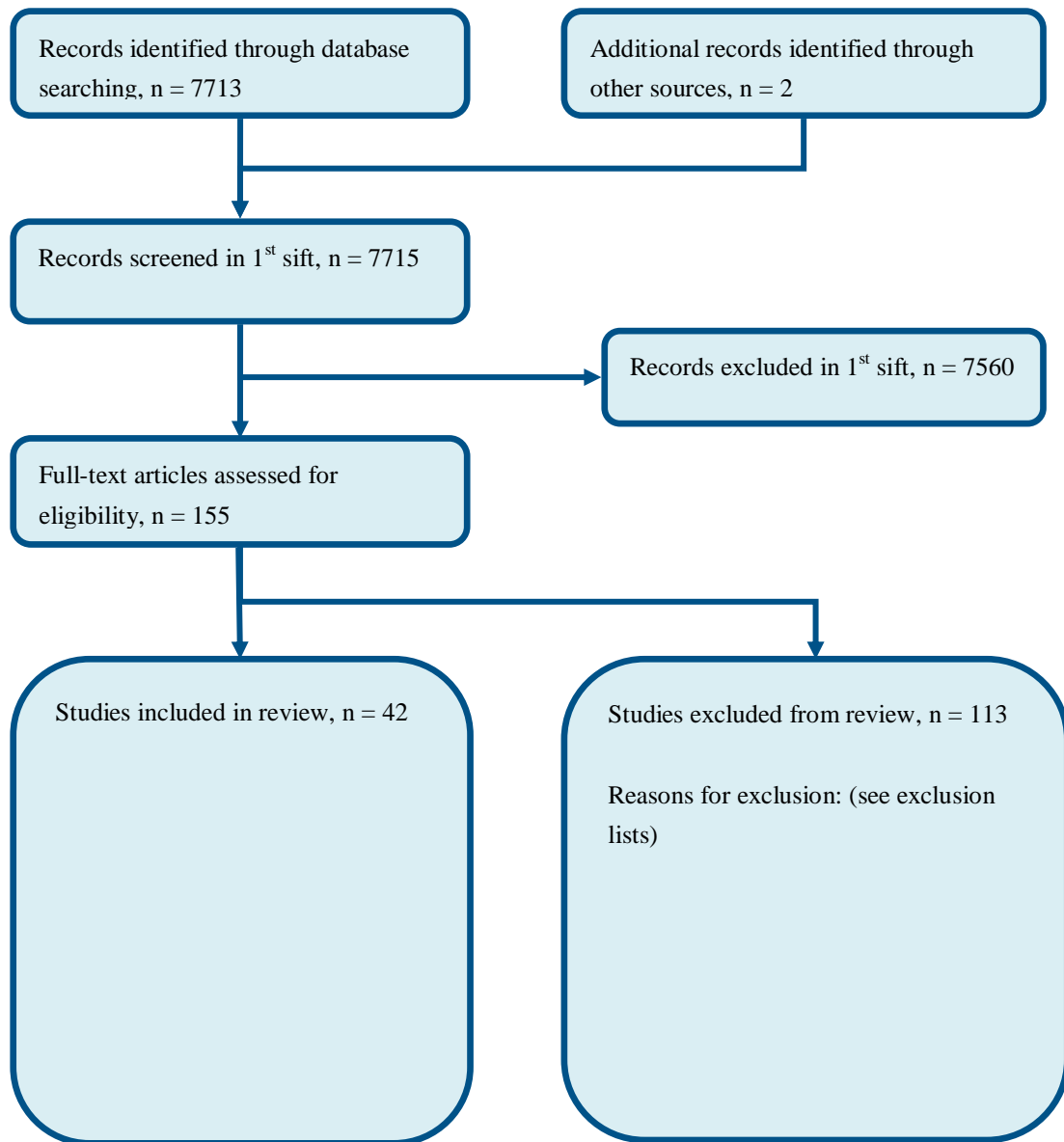
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133 **Web Extra Material: Deeks Funnel Plots**
134
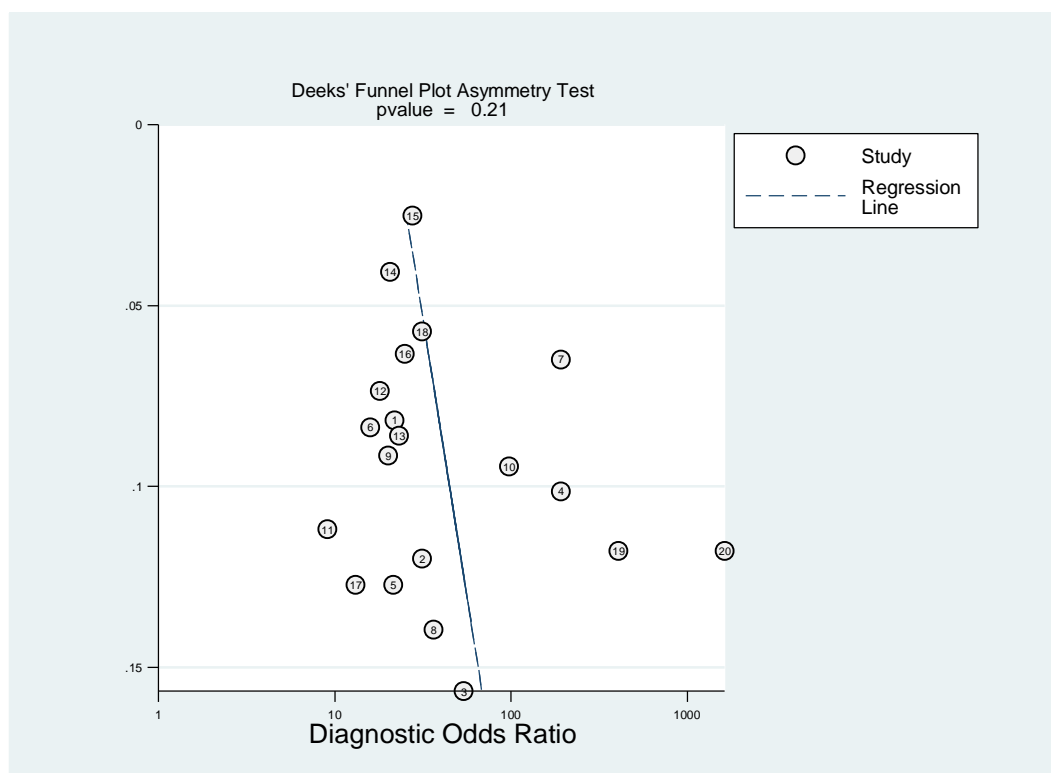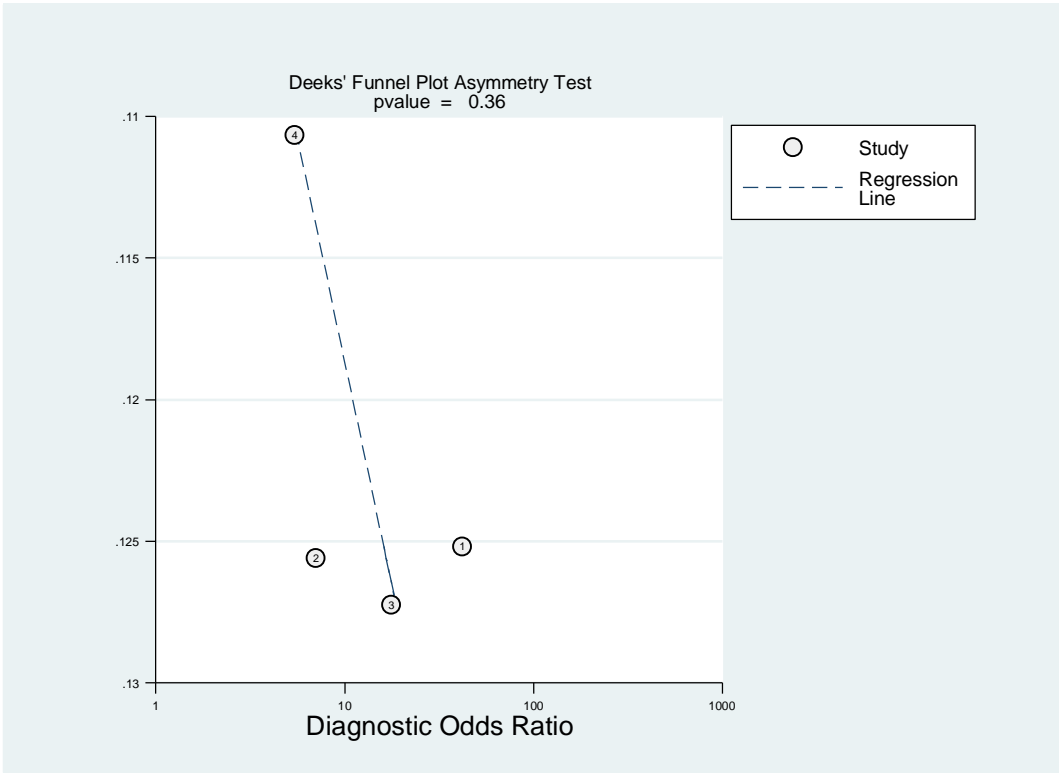
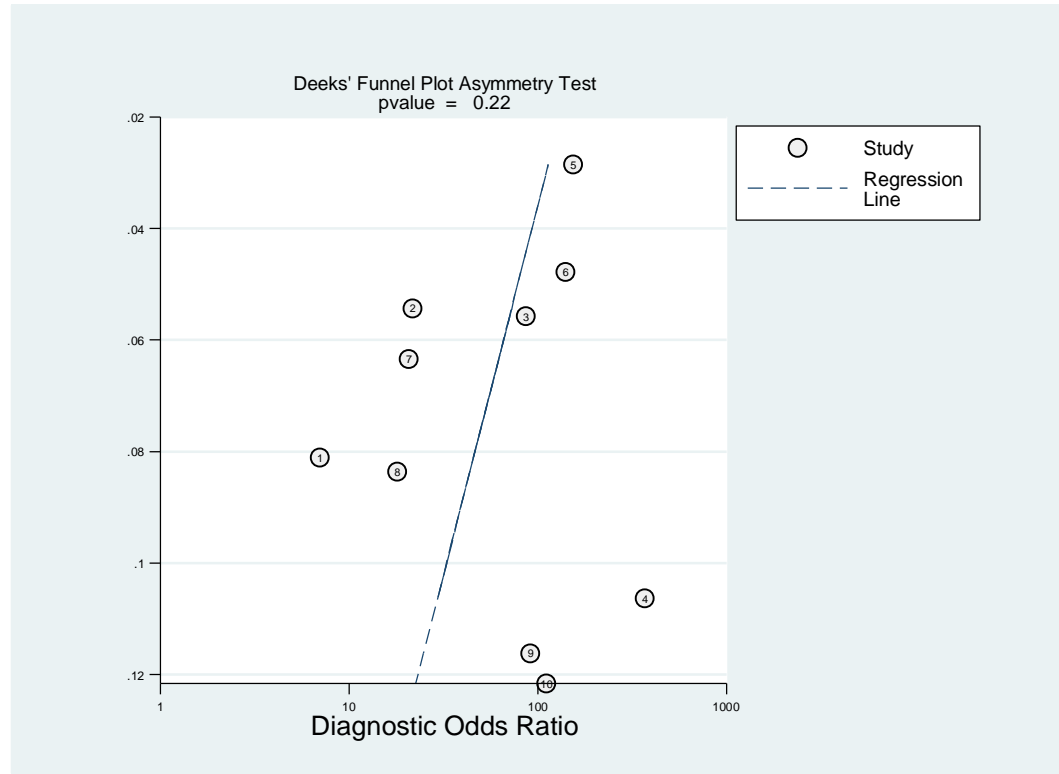135   BNP ≤ 100 ng/L
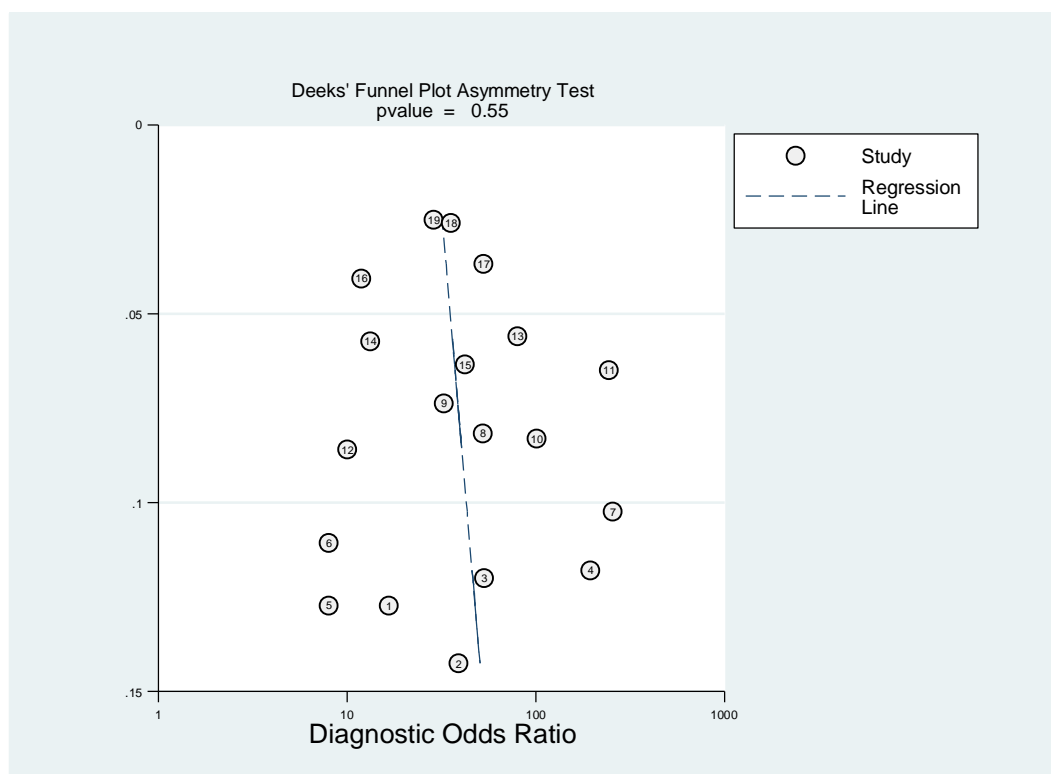
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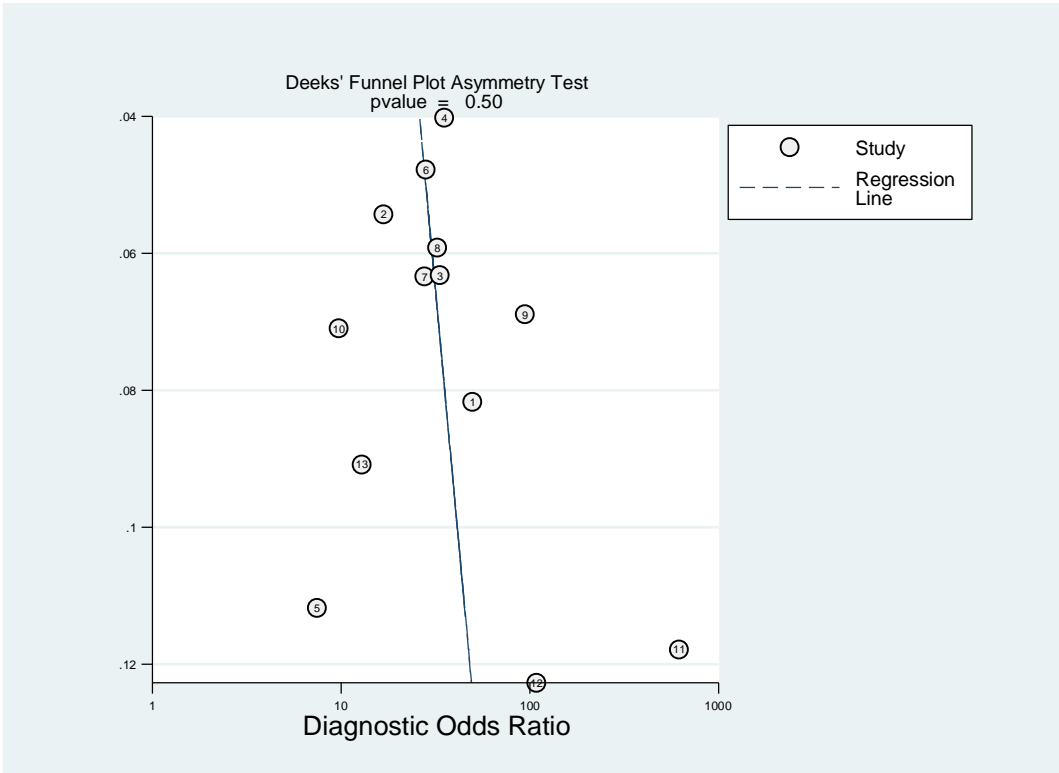138   BNP 100-500 ng/L

139

140   BNP ≥500 ng/L
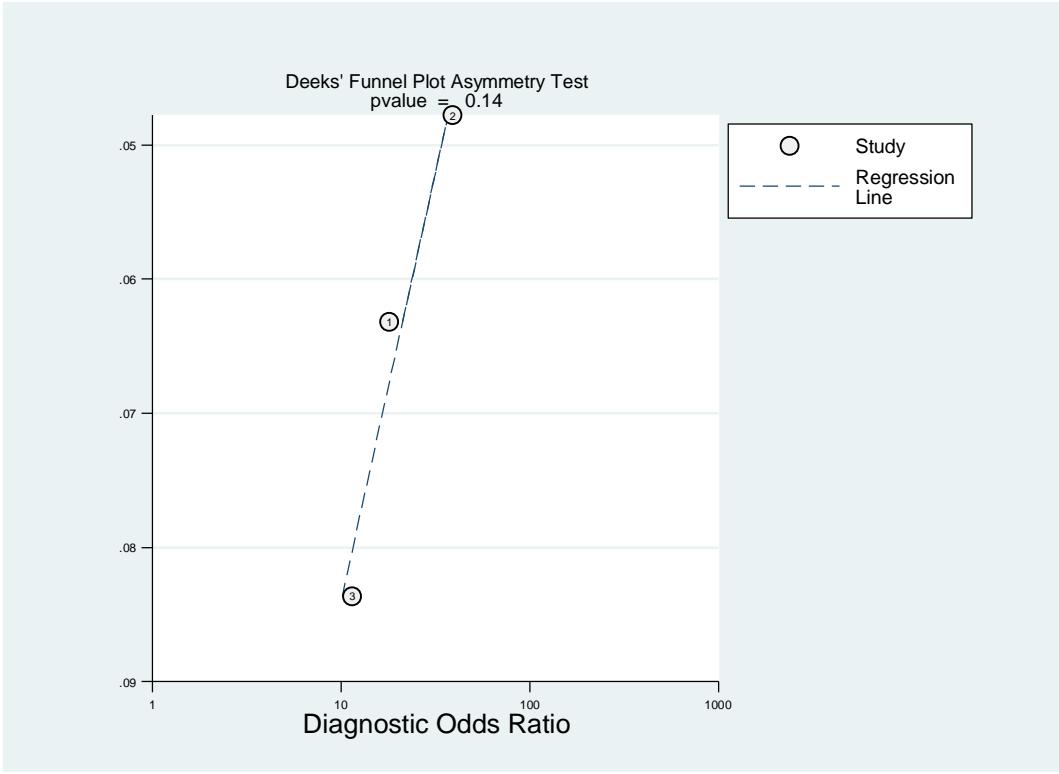
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143   NTproBNP ≤ 300ng/L

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146   NTproBNP 300-1800 ng/L

Deeks' Funnel Plot Asymmetry Test
pvalue = 0.50

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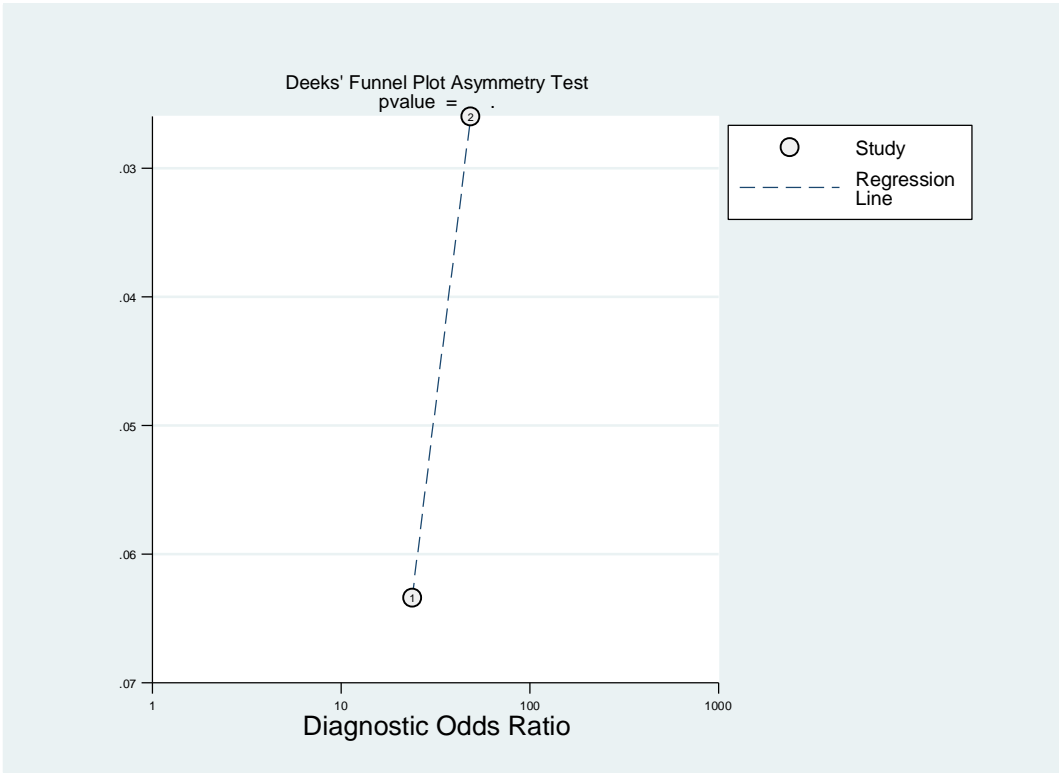149   NTproBNP ≥1800 ng/L

Deeks' Funnel Plot Asymmetry Test
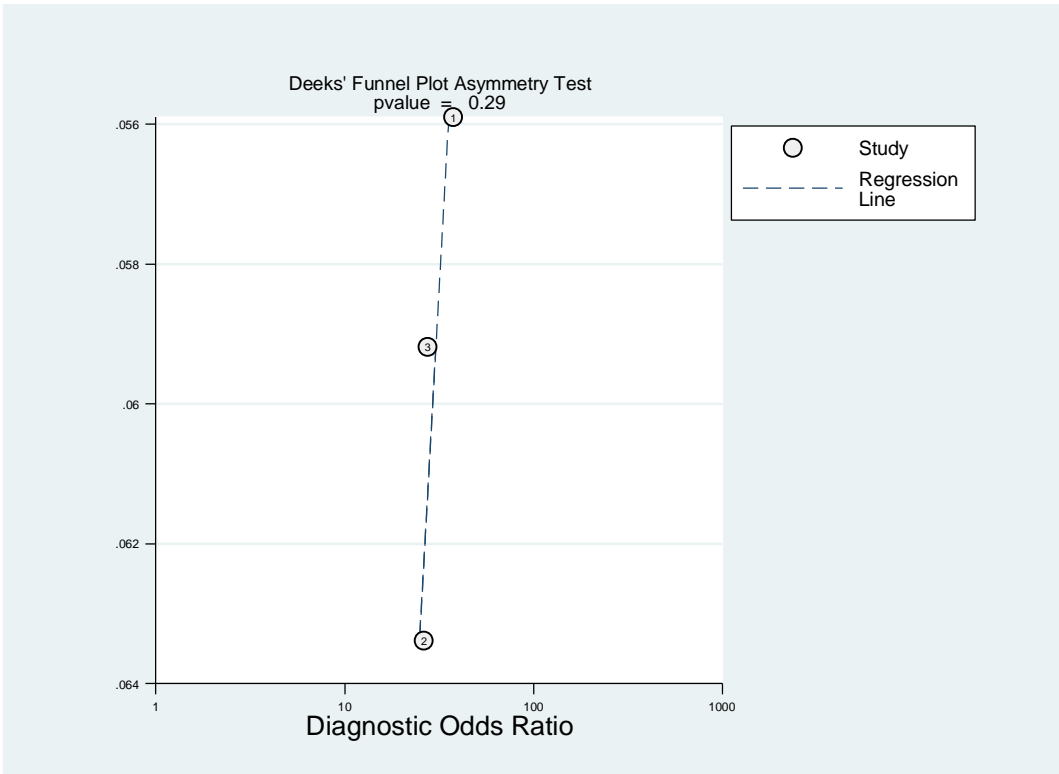pvalue = 0.14

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151   MRproANP ≤120 pmol/L

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154   MRproANP >120 pmol/L

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