Appendix B: stakeholder consultation comments table

4-year surveillance (2014) – Acute heart failure (2014) NICE guideline CG187

Consultation dates: 5 October 2017 to 19 October 2017

Do you agree with the proposal not to update the guideline?

Stakeholder	Overall response	Comments	NICE response
Brahms UK Limited – Thermos Fisher Scientific	No	See comments in next section	Thank you for your comment.
Roche Diagnostics Ltd	No	Although listed as in-scope for the guideline, we believe there is a lack of guidance on the management of patients with acute decompensated heart failure (ADHF) within the original guideline or within the guideline for chronic heart failure management (CG108). In particular, there is a lack of guidance around discharge planning and on-going care for patients with ADHF. Therefore, the decision not to update this guideline fails to address this gap. We believe that further evidence is available on the prognostic value of NT-proBNP testing in this population. Specifically, several studies have demonstrated that a relative NT-proBNP reduction of less than 30% at discharge is a significant predictor of readmission and mortality in patients with ADHF. A recent meta-analysis (2017) showed a reduction in all-cause mortality with natriuretic peptide-guided care compared with usual care (HR 0.62).[1] A validated risk model is now available incorporating NT-proBNP (among other criteria) to guide the hospital discharge of patients with ADHF). American[3,4] and European[5-7] Guidelines support the measurement of baseline and pre-discharge natriuretic peptide levels for post-discharge planning. There is further information on the utility of NT-proBNP testing in sub-groups of patients with ADHF. A meta-analysis concluded that NT-proBNP is useful for diagnosing ADHF in patients with renal	Thank you for your comment. The study by McQuade et al. (2017) was identified in the literature search and was excluded because of a lack of statistical data in the abstract. This study appears to have used systematic methods for searching and selecting studies for inclusion, but the synthesis of the data appeared to be a narrative description. Although meta-analysis is not always possible, the authors did not state in the abstract any reasons why the data could not be analysed in this way. Therefore, this study did not meet the criteria for inclusion in the evidence considered in surveillance. The study by Salah et al. (2014) was identified in the literature search but was initially excluded because it assessed data from cohort studies. In this surveillance review we included randomised controlled trials (RCTs) and systematic reviews that included RCTs, except for diagnostic studies. Therefore, this study looking at prognosis, did not meet the criteria for inclusion in the evidence considered in surveillance. Cohort studies would be suitable for addressing questions on prognosis, therefore it was reconsidered. For example, the guideline included prognostic studies when assessing which patients with acute heart failure would benefit or be harmed by invasive ventilation. In this example, prognostic studies were used to develop recommendations to guide the use of invasive ventilation. However,

		dysfunction with higher cut-off points and that elevated NT-proBNP confers a worse prognosis regardless of renal function.[8] Lastly, in light of newer treatment options, such as sacubitril-valsartan, further clarity may be needed on the diagnostic value of NT-proBNP testing in ADHF patients.[9] 1. McQuade CN, Mizus M, Wald JW, et al. Brain-Type Natriuretic Peptide and Amino-Terminal Pro–Brain-Type Natriuretic Peptide Discharge Thresholds for Acute Decompensated Heart Failure: A Systematic Review. Ann Intern Med. 2017;166:180–190. doi: 10.7326/M16-1468 2. Salah K, Kok W, Eurlings L, et al. A novel discharge risk model for patients hospitalised for acute decompensated heart failure incorporating N-terminal pro–B-type natriuretic peptide levels: a European coLlaboration on Acute decompeNsated Heart Failure: ELAN-HF Score. Heart. 2014; 100: 115–125 3. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. J Am Coll Cardiol 2017;Apr 28:[Epub ahead of print] 4. Chow LS et al. Role of Biomarkers for the Prevention, Assessment, and Management of Heart Failure: A Scientific Statement From the American Heart Association.Circulation. 2017;CIR.0000000000000490, originally published April 26, 2017 5. Ponikowski P, Voors A, Anker S, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur J Heart Fail, 18: 891–975. doi:10.1002/ejhf.592 6. Mebazaa A, Yilmaz M, Levy P et al. Recommendations on pre-hospital & early hospital management of acute heart failure: a consensus paper from the Heart Failure Association of the European Society of Cardiology, the European Society of Emergency Medicine and the Society	the study by Saleh et al. (2014) does not provide any information on whether NT-proBNP levels can be used to guide treatment. Therefore, this study is not eligible for consideration in surveillance at this time. Surveillance does not consider guidance from other professional organisations as a source of evidence. However, the conclusions of the following guidelines were checked in response to your comment and the evidence informing the recommendations in the publications cited was checked for eligibility. The 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure noted that predischarge NT-proBNP values 'can be useful to establish a postdischarge prognosis'. However, it additionally states: 'Although observational or retrospective studies have suggested that patients with natriuretic peptide biomarker reduction had better outcomes than those without any changes or with a biomarker rise, targeting a certain threshold, value, or relative change in these biomarker levels during hospitalization may not be practical or safe for every patient and has not been tested in a prospective large-scale trial.' The publication: Role of Biomarkers for the Prevention, Assessment, and Management of Heart Failure: A Scientific Statement From the American Heart Association cited much the same evidence as the ACC/AHA/HFSA focused update. The 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure cited another set of references around use of NT-proBNP testing at discharge. However, of 7 references, 5 had no statistical data in the abstract, and the remaining 2 were in a population with chronic heart failure, and thus are not eligible for consideration in surveillance of this guideline on acute heart failure. The Recommendations on pre-hospital & early hospital management of acute heart failure: a consensus paper from the Heart Failure Association of the European Society of Cardiology, the European Society of Emergency Medicine and the Society of Academic Emergency Medicine cited only 1 reference to support pre-discharge measurement of NT-proBNP. However, this reference was published in 2009 so was available for consideration during development of NICE CG187, and is thus not eligible for consideration in surveillance.

		of Academic Emergency Medicine. Eur J Heart Fail 2015, 17: 544–558. doi:10.1002/ejhf.289 7. Aspromonte N, Gulizia M, Clerico A. ANMCO/ELAS/SIBioC Consensus Document: biomarkers in heart failure. Eur Heart J Suppl 2017; 19 (suppl_D): D102-D112. doi: 10.1093/eurheartj/sux027 8. Schaub J, Coca S, Moledina D, et al.Amino-Terminal Pro-B-Type Natriuretic Peptide for Diagnosis and Prognosis in Patients With Renal Dysfunction, JACC: Heart Failure, Volume 3, Issue 12, 2015, Pages 977-989, ISSN 2213-1779, http://dx.doi.org/10.1016/j.jchf.2015.07.014 9. Mair J, Lindahl B, Giannitsis E, et al. Will sacubitril-valsartan diminish the clinical utility of B-type natriuretic peptide testing in acute cardiac care? European Heart Journal: Acute Cardiovascular Care, 2016. Available from: DOI: 10.1177/2048872615626355	The references cited in the ANMCO/ELAS/SIBioC Consensus Document: biomarkers in heart failure were all published before NICE's guideline on acute heart failure and were available for consideration in developing the guideline. These publications had consistent conclusions, generally, that although pre-discharge measurement of NT-proBNP may provide prognostic information, it cannot yet guide treatment decisions. This is supported by the findings of the ACC/AHA/HFSA focused update (page 10), the AHA scientific statement (page e1072), the 2016 ESC guidelines (p 951), and the ANMCO/ELAS/SIBioC Consensus Document (p D106). The study by Schaub et al (2015) was identified in the literature search but was excluded because the study population listed in the title, people with renal dysfunction, would not be applicable to this guideline. However, in reviewing the abstract again, this has now been included in the summary of evidence. However, it was not considered to indicate a need to update the guideline because measurement of NT-proBNP is only one part of establishing a diagnosis of heart failure, and people with renal dysfunction would be included in the overall cut-off for ruling out acute heart failure. The study by Mair et al. (2016) has no information to suggest a systematic search and selection process for systematic reviewing of the evidence and has no data to indicate an impact on the guideline. Therefore, this study did not meet the criteria for inclusion in the evidence considered in surveillance. Overall, we cannot consider adding recommendations on measurement of NT-proBNP before discharge from hospital at this time, because of insufficient evidence showing that NT-proBNP levels can be used to guide management and improve patients' outcomes.
Royal Devon & Exeter NHS Foundation Trust	Yes		Thank you for your response.
Elcena Jeffers Foundation	No	Research is a lifetime activity	Thank you for your comment.
Royal College of Nursing	Yes	A clear indication that a systematic review process has been followed and the recommendations remain unchanged due to no significant new evidence.	Thank you for your comment.

Do you have any comments on areas excluded from the scope of the guideline?

Stakeholder	Overall response	Comments	NICE response
Brahms UK Limited – thermos Fisher Scientific	Yes	In the 'Diagnosis, Assessment and Monitoring' Procalcitonin should be included in patients with suspicion of infection. It can lead to improved outcomes and plays an important role in stewardship of antibiotics with obvious implications around Antimicrobial resistance and healthcare associated infections. The European Society of Cardiology (ESC) has recommended "Assessment of procalcitonin levels may be considered in patients with AHF with suspected coexisting infection, particularly for the differential diagnosis of pneumonia and to guide antibiotic therapy, if considered." European Heart Journal (2016) 37, 2129–2200. Infection is a leading cause of AHF admission, patients with pneumonia have a higher in-hospital mortality (M. Arrigo et al. European Journal of Heart Failure (2016)). Diagnosis of pneumonia in HF is difficult due to overlapping clinical features. Procalcitonin can identify HF patients with pneumonia who therefore need antibiotics. The BACH study – Maisel et al., EurJ Heart Fail 2012; 14: 278-86. Demonstrated Procalcitonin could identify AHF patients in need of antibiotics and safely withhold antibiotics in those with dyspneoa who don't have infection. There are important mortality benefits demonstrated by the authors. Subgroup analysis of the proHOSP study (Schuetz et al., Int J Cardiol 2014; 175: 464-72) found that AHF patients who follow a PCT algorithm had lower antibiotic exposure (-2.8 days) and 30 day adverse outcome was significantly reduced (-16%).	Thank you for your comment. The ESC guidelines (2016) are not eligible for consideration as a source of evidence for surveillance. However their recommendation was based on the BACH study by Maisel et al (2012), which you have also highlighted. This study, published in 2012, was available for consideration during the development of the guideline on acute heart failure (NICE CG187). This study is thus not eligible for consideration in surveillance. The study by Arrigo et al. (2016) is an observational study; the study by Schuetz et al. (2014) does not clearly include a population with acute heart failure; and the study by Moekel et al. (2017) has no evidence of systematic search and selection of included studies and has no data in the abstract. Therefore, these studies are not eligible for consideration in surveillance at this time. Additionally, procalcitonin testing appears to be more relevant to NICE's guideline on diagnosis and assessment of pneumonia in adults (NICE CG191). During development of NICE CG191, both procalcitonin and C-reactive protein testing were considered, but procalcitonin testing was not recommended. C-reactive protein testing was recommended to help guide antibiotic prescribing in situations in which a diagnosis of pneumonia is uncertain. NICE has also published diagnostics guidance on Procalcitonin testing for diagnosing and monitoring sepsis (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay) (NICE DG18). This guidance recommended that there was insufficient evidence to recommend the routine adoption of procalcitonin tests in the NHS. However, centres currently using procalcitonin tests to guide decisions on antibiotic use were encouraged to participate in research and data collection. Although the diagnostics guidance addressed sepsis, rather than pneumonia, when considered alongside the findings of the guideline on diagnosis and assessment of pneumonia, the evidence for procalcitonin testing does not appear to be sufficient at this time.

		Recent Procalcitonin in HF mini-review is relevant – Moeckel et al - ESC Heart Failure 2017; 4: 203–208	Moekel et al. (2017) highlighted the ongoing IMPACT-EU study, which is an RCT in people with suspected acute heart failure assessing antibiotic prescribing according to procalcitonin levels compared with standard care. We will check regularly for publication of results from this study and consider the impact of the results on the guideline.
Roche Diagnostics Ltd	No		Thank you for your response.
Royal Devon & Exeter NHS Foundation Trust	No		Thank you for your response.
Elcena Jeffers Foundation	Why exclude any one?	Life is life	Thank you for your comment.
Royal College of Nursing	No		Thank you for your response.

Do you have any comments on equalities issues?

Stakeholder	Overall response	Comments	NICE response
Brahms UK Limited – thermos Fisher Scientific	No		Thank you for your response.
Roche Diagnostics Ltd	No		Thank you for your response.
Royal Devon & Exeter NHS Foundation Trust	No		Thank you for your response.
Elcena Jeffers Foundation	Equalities is for every one		Thank you for your response.
Royal College of Nursing	No		Thank you for your response.