3-year scoping report

Topic: Management of chronic heart failure: SIGN 147 (2014)

Date of search: March 2019
Searched by: Lynne Smith
Prepared by: Julie Calvert, Ailsa Stein

Summary of findings

The purpose of this scoping is to identify recent secondary evidence published since of SIGN guideline 147, and whether any sections of the guideline require updating. A rapid search of the literature was conducted, using a predefined list of resources. The search focused on secondary sources of evidence (evidence-based guidelines, systematic reviews and meta-analyses). The following tables are based on information gathered from the abstracts of relevant publications. No appraisal has been carried out.

The literature search identified one NICE guideline and eight potentially relevant systematic reviews or meta-analyses. The update search did not include any new evidence likely to alter the current recommendations.

Specialist review

This topic exploration was circulated to the group responsible for developing SIGN 147, and representatives from the British Heart Foundation and Chest, Heart and Stroke Scotland, who were asked to comment primarily on the comprehensiveness and accuracy of the summary of findings and whether there is sufficient new evidence to warrant a refresh of the guideline. Guideline development group membership can be found in section 12.2 of the guideline.

Comments received are in Annex 2.

Potential areas for update identified by group members

Guideline section	Details of update	Suggested priority (Desirable or Essential)
5	Use of multiple neuroendocrine blockers versus use of one large dose of a single neuroendocrine blocker.	Desirable
5.9	Revision of B-type natriuretic peptide (BNP) guided therapy	Desirable

Decision

The Guideline Programme Advisory Group agreed on 25 September 2019 that:

This guideline was **revalidated** in 2019 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: www.sign.ac.uk

Results of the scoping search

Guidance

Guideline reference	Details	Impact on guideline
NICE guideline [NG106]. Sep 2018. Chronic heart failure in adults: diagnosis and management. https://www.nice.org.uk/guidance/ng106	(extracted verbatim) 1.10.1 Do not offer long-term home oxygen therapy for advanced heart failure. Be aware that long-term home oxygen therapy may be offered for comorbidities, such as for some people with chronic obstructive pulmonary disease (see the section on oxygen in the NICE guideline on chronic obstructive pulmonary disease in over 16s). [2018]	Section 8.3.2 Oxygen Currently states that there is no evidence available on this topic. May wish to include
	1.10.2 Do not use prognostic risk tools to determine whether to refer a person with heart failure to palliative care services. [2018]	Section 8 Palliative care May wish to include
	1.8.1 Do not routinely offer coronary revascularisation to people who have heart failure with reduced ejection fraction and coronary artery disease. [2018]	Section 6 Interventional procedures KQ11 May wish to include
	1.2.8 Perform transthoracic echocardiography to exclude important valve disease, assess the systolic (and diastolic) function of the (left) ventricle, and detect intracardiac shunts. [2003, amended 2018]	Section 3.1.5 Echocardiography May wish to include 'and detect intracardiac shunts' to the reasons for echocardiography
	1.2.9 Transthoracic echocardiography should be performed on high-resolution equipment by experienced operators trained to the relevant	Section 3.1.5 Echocardiography May wish to include

	professional standards. Need and demand for these studies should not compromise quality. [2003, amended 2018]	
	1.2.11 Consider alternative methods of imaging the heart (for example, radionuclide angiography [multigated acquisition scanning], cardiac MRI or transoesophageal echocardiography) if a poor image is produced by transthoracic echocardiography. [2003, amended 2018]	Section 3.1.5 Echocardiography May wish to include
	1.4.4 Measure serum sodium and potassium, and assess renal function, before and 1 to 2 weeks after starting an ACE inhibitor, and after each dose increment. [2010, amended 2018]	Annex 2 May wish to include
	1.4.6 Once the target or maximum tolerated dose of an ACE inhibitor is reached, monitor treatment monthly for 3 months and then at least every 6 months, and at any time the person becomes acutely unwell. [2010, amended 2018]	Annex 2 May wish to include
	1.4.8 Measure serum sodium and potassium, and assess renal function, before and after starting an ARB and after each dose increment. [2010, amended 2018]	Annex 3 May wish to include
	1.4.10 Once the target or maximum tolerated dose of an ARB is reached, monitor treatment monthly for 3 months and then at least every 6 months, and at any time the person becomes acutely unwell. [2010, amended 2018]	Annex 3 May wish to include
	1.4.13 Introduce beta-blockers in a 'start low, go slow' manner. Assess heart rate and clinical status after each titration. Measure blood pressure before and after each dose increment of a beta-blocker. [2010,amended 2018]	Annex 4 May wish to include
	1.4.16 Measure serum sodium and potassium, and assess renal function, before and after starting an MRA and after each dose increment. [2018]	Annex 5 May wish to include Annex 5

	1.4.17 Measure blood pressure before and after each dose increment of an MRA. Follow the recommendations on measuring blood pressure, including measurement in people with symptoms of postural hypotension, in the NICE guideline on hypertension in adults. [2018] 1.4.18 Once the target, or maximum tolerated, dose of an MRA is reached, monitor treatment monthly for 3 months and then at least every 6 months, and at any time the person becomes acutely unwell. [2018]	May wish to include
	1.4.22 Sacubitril valsartan is recommended as an option for treating symptomatic chronic heart failure with reduced ejection fraction, only in people: with New York Heart Association (NYHA) class II to IV symptoms and with a left ventricular ejection fraction of 35% or less and who are already taking a stable dose of angiotensin-converting enzyme (ACE) inhibitors or ARBs. [2016]	Section 5.5 SIGN recommends NYHA class 2-3 (and may be considered in class 4), LVEF 40% or less. May wish to consider changing wording
	1.4.26 Digoxin is recommended for worsening or severe heart failure with reduced ejection fraction despite first-line treatment for heart failure. Seek specialist advice before initiating.	Section 5.8 May wish to include 'seek specialist advice before initiating'.

Systematic reviews

Reference	Details	Impact on guideline
5 Pharmacological therapies		
Komajda M, Bohm M, Borer JS, Ford I, Tavazzi L, Pannaux M and Swedberg K. Incremental benefit of drug therapies for chronic heart failure with reduced ejection fraction: a network meta-analysis. European Journal of Heart Failure. 2018;20(9):1315-1322.	A network meta-analysis (NMA) of all recommended drug groups for the treatment of heart failure with reduced ejection fraction (HFrEF), including their combinations, was performed to assess the relative efficacy and incremental benefit. The included studies dated from 1991-2014, so didn't include any recent studies The relative efficacy of each treatment group (or combination) in terms of all-cause mortality, cardiovascular mortality, all-cause hospitalizations and hospitalizations for heart failure, per patient-year of follow-up, were combined in a random-effects Bayesian NMA. Combinations of drug groups showed incremental benefits on outcomes over single groups. The most effective combinations were ARNI+BB + MRA and ACEI+BB + MRA + IVA, showing reductions in all-cause mortality (vs. placebo) of 62% and 59%, respectively; hazard ratios were 0.38 [credible interval (CrI) 0.20-0.65] and 0.41 (CrI 0.21-0.70); and in all-cause hospitalizations with reductions of 42% for both. These two combinations were also the most effective for the other outcomes studied.	Section 5 SIGN may wish to consider this recent NMA which highlights specific effective combinations of treatments
5.2 ACEIs **KQ 7 In patients with heart failure and preserved left ventricular function is there any evidence of effectiveness for: a) ACE inhibitors b) beta blockers c) ARBs d) MRAs?**		
Sun W, Zhang H, Guo J, Zhang X, Zhang L, Li C and Zhang L. Comparison of the Efficacy and Safety of Different ACE Inhibitors in Patients With Chronic Heart Failure: A PRISMA-Compliant Network Meta-Analysis. Medicine. 2016;95(6):e2554.	A network meta-analysis evaluating the efficacy and safety of ACEIs (captopril, enalapril, lisinopril, ramipril, or trandolapril or combined interventions of 2 or more of these drugs) in patients with heart failure. A total of 29 studies were included. Lisinopril was associated with a higher rate of all-cause mortality compared with placebo (odds ratio 65.9, 95% credible interval 1.91 to 239.6) or ramipril (14.65, 1.23 to 49.5). Enalapril significantly reduced systolic blood pressure when compared with placebo (standardized mean differences -0.6, 95% credible interval -1.03 to -0.18). Both captopril (odds ratio 76.2, 95% credible interval 1.56 to 149.3) and enalapril (274.4, 2.4 to 512.9) were associated with a higher incidence of	Section 5.2 SIGN may wish to include this detail in Annex 2

	cough compared to placebo.Some important outcomes such as rehospitalization and cardiac death were not included. The sample size and the number of studies were limited, especially for ramipril. Our results suggest that enalapril might be the best option when considering factors such as increased ejection fraction, stroke volume, and decreased mean arterial pressure. However, enalapril was associated with the highest incidence of cough, gastrointestinal discomfort, and greater deterioration in renal function. Trandolapril ranked first in reducing systolic and diastolic blood pressure. Ramipril was associated with the lowest incidence of all-cause mortality. Lisinopril was the least effective in lowering systolic and diastolic blood pressure and was associated with the highest incidence of all-cause mortality.	
5.4 Mineralocorticoid receptor antagonists **KQ4 What are the benefits and harms of mineralocorticoid receptor antagonists (MRAs) in patients with HF-REF? Consider cost effectiveness**		
Vukadinovic D, Lavall D, Vukadinovic AN, Pitt B, Wagenpfeil S and Bohm M. True rate of mineralocorticoid receptor antagonists-related hyperkalemia in placebo-controlled trials: A meta-analysis. American Heart Journal. 2017;188(99-108.	A meta-analysis of RCTs aimed to determine the truly MRA-related rate of hyperkalemia, corrected for hyperkalemia on placebo (Pla), according to the equation: True MRA (%)=(MRA (%) - Pla (%))/MRA (%). A total number of 16,065 patients from 7 trials were analyzed. Hyperkalemia was more frequently observed on MRA (9.3%) vs placebo (4.3%) (risk ratio 2.17, 95% CI 1.92-2.45, P<.0001). Truly MRA-related hyperkalemia was 54%, whereas 46% were non-MRA related. In trials using eplerenone, hyperkalemia was documented in 5.0% on eplerenone and in 2.6% on placebo (P<.0001). In spironolactone trials, hyperkalemia was documented in 17.5% and in 7.5% of patients on placebo (P=.0001). Hypokalemia occurred less frequently in patients on MRA (9.3%) compared with placebo (14.8%) (risk ratio 0.58, CI 0.47-0.72, P<.0001).	Section 5.4/ Annex 5 Relevant to KQ 4 but doesn't change recommendation. May wish to include in Annex 5
Pei H, Wang W, Zhao D, Wang L, Su G-H and Zhao Z. The use of a novel non-steroidal mineralocorticoid receptor antagonist finerenone for the treatment of chronic heart failure: A systematic review and meta-analysis. Medicine. 2018;97(16):e0254.	A systematic review of finerenone versus spironolactone or eplerenone in patients with chronic heart failure. There were 3 trials with 1520 CHF patients. In terms of anti-ventricular remodeling, we calculated the effective number of cases with a 30% reduction in NT-proBNP. Finerenone was equivalent to the existing steroidal mineralocorticoid antagonist (P < .05). However, the efficacy of finerenone appeared to be dose-dependent. At a dose of 10 mg/d finerenone was found to be marginally better than that of steroidal mineralocorticoid receptor antagonists (MRAs) (RR = 1.18, 95% confidence interval [CI] 0.88, 1.57, P > .05). The incidence of treatment-related adverse events (TEAEs) of finerenone at 10 mg/d	Section 5.4/ Annex 5 Relevant to KQ but doesn't change recommendation.

	was significantly lower than 25 to 50 mg/d of steroidal MRAs (RR = 0.81, 95% CI = 0.66-0.99, P = .04). Moreover, the serum potassium levels in the finerenone 10 mg/d group were lower than those in the 25 to 50 mg/d steroidal MRAs group (MD = -0.14, 95% CI -0.30-0.02, P = .09), whereas the estimated glomerular filtration rate (eGFR) was higher in finerenone versus steroidal MRAs treated patients (MD = 2.07, 95% CI -0.04-4.17, P = .05).	
5.9 Natriuretic peptide-guided treatment		
Xin W, Lin Z, Mi S. Does B-type natriuretic peptide-guided therapy improve outcomes in patients with chronic heart failure? A systematic review and meta-analysis of randomized controlled trials. Heart Failure Reviews. 2015;20(1):69-80.	Meta-analysis to evaluate the effect of BNP-guided therapy in CHF. Fourteen studies with 3,004 CHF patients were included. This meta-analysis included a 3 additional studies (Anguita et al. 2010, Schou et al. 2013, Maeder et al. 2013) that were not included in the meta-analysis used in SIGN 147 (Li et al. 2013). Compared with clinical group, BNP-guided treatment significantly decreased the risk of heart failure-related hospitalization (RR 0.79, 95 % CI 0.63–0.98, p = 0.03), although did not significantly affect the risk of all-cause mortality (RR 0.94, 95 % CI 0.81–1.08, p = 0.39) or all-cause hospitalization (RR 0.97, 95 % CI 0.89–1.07, p = 0.56). Furthermore, between group BNP changes seemed to be a significant modifier to the effects of BNP-guided therapy on clinical outcomes, and BNP-guided therapy may improve the clinical outcomes of CHF patients if substantial reduction of BNP can be achieved. In addition, BNP-guided therapy was not associated with increased risk for serious adverse events. BNP-guided therapy may improve the clinical outcomes of CHF patients if substantial reduction of BNP can be achieved. BNP-guided therapy seemed to be safe and promising for CHF patients, and future studies with well-designed BNP-guided medication up-titration strategies are needed to confirm these results.	Section 5.9 Confirms previous studies showing a benefit to HF patients. However, unlike the Li et al. 2013 meta-analysis reported in SIGN 147, this meta-analysis indicated no effect on all-cause mortality or all-cause hospitalization (while reducing the risk of HF related hospitalization). Doesn't change recommendation.
6 Interventional procedures		
Use of Cardiac Resynchronization Therapy in the Medicare Population Rickard J, Michtalik H, Sharma R, Berger Z, Iyoha E, Green AR*, et al.* Use of cardiac	Objectives: To assess the benefits and harms of cardiac resynchronization with (CRT-D) and compared to an ICD alone, CRT without a defibrillator (CRT-P) compared with optimal medical therapy and CRT-D compared with CRT-P in patients with an EF ≤35% and a QRS duration ≥120 ms. We also sought to assess predictors of response to CRT-D and CRT-P. CRT-D was found to be effective in reducing heart failure hospitalizations, inducing ventricular reverse remodeling,	Section 6.1 SIGN may wish to consider this in relation to Table 5, ICD vs. CRT-D when QRS

resynchronization therapy in the Medicare population. Rockville: Agency for Healthcare Research and Quality (AHRQ). Technology Assessment Report. 2015.	improving quality of life, and increasing six-minute hall walk distances compared to an ICD alone with a high strength of evidence. In a meta-analysis of minimally symptomatic patients, CRT-D reduced LVESV (ml) (mean difference -22.55, 95% CI -40.66 to -9.56). This analysis was comprised primarily on NYHA class II patients; therefore, the applicability to NYHA class I patients is unclear. In a meta-analysis of patients with advanced heart failure (NYHA class III-IV), CRT-D improved quality of life scores (as measured by the Minnesota Living with Heart Failure Questionnaire) (mean difference -10.91, 95% CI -12.03 to - 7.27) compared to an ICD alone. CRT-P was found to be effective in improving all-cause survival and reducing heart failure hospitalizations compared to optimal medal therapy alone with a moderate level of evidence. CRT-P was also found to induce reverse ventricular remodeling and increase six-minute hall walk distances compared to optimal medical therapy alone. These findings were primarily noted in NYHA class III-IV patients. The applicability of these findings to NYHA class I-II patients is unclear. Determining predictors of response to CRT was limited by the likely presence of reporting bias. Nevertheless, a left bundle branch (LBBB) morphology, non-ischemic cardiomyopathy (NICM), and female gender were generally associated with improved outcomes following CRT-D. Sinus rhythm (as compared to atrial fibrillation) and a wider QRS duration were associated with improved outcomes following CRTD albeit with a lower strength of evidence. There is insufficient evidence to determine predictors of outcomes in patients undergoing CRT-P. There is insufficient evidence to determine the effectiveness of CRT-D versus CRT-P. Compared to CRT-P, device infection was slightly more common in patients receiving CRT-D. Conclusions: There is convincing evidence that CRT-D is effective with regard to improvements in multiple clinical outcomes compared to an ICD alone in patients with an LVEF≤35% and a QRS duration ≥120ms. Similarly, there is convincing evidence that CRT-P is effective in improving multiple clinical endpoints compared to optimal medical therapy alone in the same population. The certainty of these findings varies based on NYHA class. Female gender, LBBB, a wider QRS duration, sinus rhythm, and non-ischemic cardiomyopathy are associated with improved outcomes following CRT although the likely presence of reporting bias qualifies these results. More data are needed for several questions including the efficacy of CRT in patients with a non-LBBB morphology or atrial fibrillation and the comparison of outcomes in patients receiving a CRT-D vs. CRT-P device.	interval is >120ms.

6.2 Assisted ventilation **KQ 20 In patients with sleep apnoea and heart failure, is adaptive servoventilation more effective than non-invasive ventilation/continuous positive airway pressure?**		
Nakamura S, Asai K, Kubota Y, Murai K, Takano H, Tsukada YT and Shimizu W. Impact of sleep-disordered breathing and efficacy of positive airway pressure on mortality in patients with chronic heart failure and sleep-disordered breathing: a meta-analysis. Clinical Research in Cardiology. 2015;104(3):208-16.	A meta-analysis on the effects of positive airway pressure (PAP) on mortality in patients with chronic heart failure (HF). Five randomized controlled studies (395 participants) that assessed the effect of PAP in chronic HF patients with SDB were analyzed. ASV was used in three trials, and CPAP was used in two trials. ASV significantly reduced all-cause mortality in chronic HF patients with SDB [RR 0.13 (0.02-0.95)], whereas continuous PAP did not significantly reduce all-cause mortality [RR 0.71 (0.32-1.57)].	Section 6.2 SIGN recommend that ASV should not be used in patients with HF and CSA. However, the 3 studies in this meta-analysis were small with low event numbers (there were 0 events in the ASV groups and 7 events in the control groups) and the study used in SIGN was large (n=1325 patients).

Annex 1: Search results

Date range: 2015-2019	Management of Chronic Heart Failure 3-year scoping search
Resource	**Results**
Previous HIS projects on this topic *Check if any team within HIS has conducted/ is conducting work on this topic.*	Nothing published after the current SIGN guideline (SIGN 147 March 2016)
UK guidelines and guidance	
SIGN	Current guideline: SIGN 147 https://www.sign.ac.uk/sign-147-management-of-chronic-heart-failure.html
NICE *Check for guidelines, technology appraisals, diagnostics, interventional procedures, and medical technologies guidance*	Chronic heart failure in adults: diagnosis and management. NICE guideline [NG106]. Sep 2018 https://www.nice.org.uk/guidance/ng106 Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction. Technology appraisal guidance [TA388]. April 2016. https://www.nice.org.uk/guidance/ta388 ENDURALIFE powered CRT-D devices for treating heart failure. Medical technologies guidance [MTG33]. March 2017. https://www.nice.org.uk/guidance/mtg33 Artificial heart implantation as a bridge to transplantation for end-stage refractory biventricular heart failure. Interventional procedures guidance [IPG602]. December 2017. https://www.nice.org.uk/guidance/ipg602 Implantation of a left ventricular assist device for destination therapy in people ineligible for heart transplantation. Interventional procedures guidance [IPG516]. March 2015 https://www.nice.org.uk/guidance/ipg516

Guidelines International Network (GIN)	Only SIGN and NICE guidelines which are already noted above.
TRIP (UK guidelines)	Only SIGN and NICE guidelines which are already noted above.
Royal Colleges	Nothing
International Guidelines	2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). European Heart Journal, Volume 37, Issue 27, 14 July 2016, Pages 2129–2200. Avail: https://academic.oup.com/eurheartj/article/37/27/2129/1748921
Secondary literature and economic evaluations	
ECRI *Logins are available from KMT. Use the search option to identify relevant content. Evidence reports and special HTA reports are the most applicable products.*	Nothing found for heart failure
Cochrane library *Check for Cochrane reviews*	Driscoll, A., J. Currey, et al. (2015). "Nurse-led titration of angiotensin converting enzyme inhibitors, beta-adrenergic blocking agents, and angiotensin receptor blockers for people with heart failure with reduced ejection fraction." Cochrane Database of Systematic Reviews(12). Fisher, S. A., C. Doree, et al. (2016). "Stem cell therapy for chronic ischaemic heart disease and congestive heart failure." Cochrane Database of Systematic Reviews(12). Inglis, S. C., R. A. Clark, et al. (2015). "Structured telephone support or non-invasive telemonitoring for patients with heart failure." Cochrane Database of Systematic Reviews(10). Martin, N., K. Manoharan, et al. (2018). "Beta-blockers and inhibitors of the renin-angiotensin aldosterone system for chronic heart failure with preserved ejection fraction." Cochrane Database of Systematic Reviews(6). McLellan, J., C. J. Heneghan, et al. (2016). "B-type natriuretic peptide-guided treatment for heart failure." Cochrane Database of Systematic Reviews(12).

	Shantsila, E. and G. Y. H. Lip (2016). "Antiplatelet versus anticoagulation treatment for patients with heart failure in sinus rhythm." Cochrane Database of Systematic Reviews(9). Takeda, A., N. Martin, et al. (2019). "Disease management interventions for heart failure." Cochrane Database of Systematic Reviews(1).
HTA database *Limit results to published HTAs using the options on the right of the screen.*	Clark AL, Johnson M, Fairhurst C, Torgerson D, Cockayne S, Rodgers S, Griffin S, Allgar V, Jones L, Nabb S, Harvey I, Squire I, Murphy J, Greenstone M. Does home oxygen therapy (HOT) in addition to standard care reduce disease severity and improve symptoms in people with chronic heart failure? A randomised trial of home oxygen therapy for patients with chronic heart failure. Health Technology Assessment 2015; 19(75) https://www.journalslibrary.nihr.ac.uk/hta/hta19750/#/abstract Rickard J, Michtalik H, Sharma R, Berger Z, Iyoha E, Green AR, Haq N, Robinson KA. Use of cardiac resynchronization therapy in the Medicare population. Rockville: Agency for Healthcare Research and Quality (AHRQ). Technology Assessment Report. 2015 https://www.cms.gov/Medicare/Coverage/DeterminationProcess/Downloads/id100TA.pdf Pufulete M, Maishman R, Dabner L, Mohiuddin S, Hollingworth W, Rogers C A, Higgins J, Dayer M, Macleod J, Purdy S, McDonagh T, Nightingale A, Williams R & Reeves B C. Effectiveness and cost-effectiveness of serum B-type natriuretic peptide testing and monitoring in patients with heart failure in primary and secondary care: an evidence synthesis, cohort study and cost-effectiveness model. Health Technology Assessment 2017; 21(40) https://www.journalslibrary.nihr.ac.uk/hta/hta21400/#/abstract Suarthana E, Almeida N, Dendukuri N.. Cardiac resynchronization therapy in heart failure. Montreal: Technology Assessment Unit of the McGill University Health Centre (MUHC). 2016 Gillespie F, Abraha I, Amicosante AMV, Caimmi P, Chiarolla E, Corio M, Paone S, Jefferson T, Cerbo M. Implantable Left Ventricular Assist Device (LVAD) in addition to guideline directed medical therapy (GDMT) in end stage heart failure. Rome: Agenzia nazionale per i servizi sanitari regionali. 2016 http://www.salute.gov.it/imgs/C_17_pagineAree_1202_listaFile_itemName_10_file.pdf

	Neyt M, Leroy R, Devos C, Van Brabandt H. Left ventricular assist devices in the treatment of end-stage heart failure. Brussels: Belgian Health Care Knowledge Centre (KCE). KCE Reports 264. 2016
Medline *Check for systematic reviews, meta-analyses, economic evaluations. Use the SIGN search filters for these study designs.*	Original Heart Failure stem search strategy combined with the SIGN systematic review filter and the economic search filter; limited to humans, English, date range 2015-2019 (date of search 08/03/19): SRs: 1392 Economics: 1110 "Chronic heart failure" (in title or abstract) combined with filters and limits (human, English, date 2015-2019): SRs: 129 Economics: 92
Primary studies (only if insufficient secondary evidence found)	
Medline RCTs *Use the SIGN search filters for individual study designs.*	Heart Failure stem search strategy and RCT filter = 34882 (applying limits: 6847) "chronic heart failure".ti,ab. And RCT filter = 3723 (applying limits: 613)
Cochrane library *Check for RCTs in the trials database*	Central database: Heart failure stem strategy with date limit 2015-2019: 14042 "Chronic heart failure". ti, ab, kw. and date limit 2015-2019: 6948
Ongoing secondary research	
EUnetHTA Planned & Ongoing Projects database *Check for any planned projects by EUnetHTA members on similar topics. You will need to register for an EUnetHTA login to access this resource.* This can be obtained from the SHTG administrative officer.	1 ref: NICE. Furosemide micro-pump for treating oedema associated with heart failure (ID1061) In development [GID-TA10179] Expected publication date: TBC

PROSPERO database *Check for recent systematic review protocols.*	"chronic heart failure" and Health Area of Review: cardiovascular
Ongoing research (only if insufficient secondary evidence and primary studies found)	
Clinicaltrials.gov *Check for ongoing studies that have recently closed or are due to complete in the next 6-12 months.*	Chronic heart failure, interventional studies, closure dates 01/01/2019 to 01/01/2020: 336 studies

Annex 2: Consultation feedback

Former members of the SIGN 147 guideline development group, representatives from Chest, Heart and Stroke Scotland and the British Heart Foundation were invited to comment on the report and the proposed areas for update.

Reviewer	Comments
Professor Allan Struthers	Areas to consider: • The new analysis on using two classes of drugs rather than one class (section 5, pharmacological treatment).It gives an evidence base to the practical idea of trying to use as many neuroendocrine blockers as possible. Often this is a practical issue as blood pressure is too low on a big dose of one neuroendocrine blocker. The advice here is to try to use lower doses of two drugs rather than a big dose of one. • BNP guided therapy may be worth considering. The other reviews would not change the guideline. Other things are really guidance from experts which are helpful but not evidence based.
Richard Forsyth (on behalf of the British Heart Foundation)	The BHF are happy with the content and have no further issues to raise.
Dr Pardeep Jhund	I don't see any data that would change the guidelines currently. There are two big trials of drugs in heart failure about to report that may change things. However, they would still need to go through licensing with the European Medicines Agency etc before they could be used in patients and recommended in guidelines. If they are positive then it would be next year before I think we could even use the drugs other than in an off licence way. So if the aim is to draw the line in the sand as of this search, then I don't see any need to update.
Dr John Sharp	No secondary evidence has been identified within the summary relating to psychological wellbeing. There have been recent systematic reviews and meta-analyses on both cognitive behavioural therapy

	and anti-depressants but these are consistent with previous reviews and would not meaningfully change the current guidance.