Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

- Determine the quantity of evidence available for a technology of interest.
- Identify any gaps in the evidence.
- Inform decisions on topics that warrant fuller assessment by Health Technology Wales (HTW).

Topic exploration report number:	TER430
Topic:	Percutaneous implantation of pulmonary artery pressure sensors for monitoring treatment of chronic heart failure
Summary of findings:	Heart failure (HF) occurs when the heart's pumping action is impaired due to structural or functional abnormalities. Regular monitoring is required in order to identify signs of deterioration and modify treatment, with the aim of improved quality of life and reduced hospital admissions. NICE published interventional procedures guidance (IPG711) for percutaneous implantation of pulmonary artery pressure (PAP) sensors for monitoring treatment of chronic heart failure in November 2021. It was concluded that efficacy and safety was adequate to support using this procedure provided that standard arrangements are in place for clinical governance, consent and audit. Two randomised controlled trials (RCTs) included in the IPG provided evidence of reduced hospital admissions as compared to guideline-directed standard of care management in the US and Canada, albeit this was only observed in the pre-Covid analysis in the GUIDE-HF study. No systematic reviews or RCTs were identified since the literature search for NICE IPG711 was carried out in August 2021. Two retrospective cohort studies (one based in Switzerland and the UK using CardioMEMS and Cordella devices, and one based in the US using CardioMEMS) reported reductions in hospitalisations due to heart failure. HTW researchers identified two ongoing systematic reviews and four RCTs on PAP-guided therapy in heart failure, including the use of both CardioMEMS and Cordella devices. CardioMEMS-guided HF management was found to be more effective but more costly in European healthcare systems (including in the UK) and within the US, using Markov models. It should be noted that the majority of the evidence is based on the use of CardioMEMS for PAP-guided management of HF. There is limited evidence on the use of Cordella-guided management of HF.

Introduction and aims

Heart failure (HF) occurs when the heart's pumping action is impaired due to structural or functional abnormalities. Blood flow to body tissues may subsequently be reduced, and cardiac filling pressure increased. The resulting congestion and oedema in the lungs and body causes breathlessness and swollen legs. Symptoms also include reduced exercise tolerance, fatigue and malaise. The diagnosis and management of chronic heart failure (CHF) in adults is covered by the National Institute for Health and Care Excellence (NICE) guideline NG106. Regular monitoring is required in order to identify signs of deterioration and modify treatment, with the aim of improved quality of life and reduced hospital admissions. Monitoring includes assessment of functional capacity, fluid status, blood pressure, cardiac rhythm, renal function, and cognitive and nutritional status. HF monitoring may be assisted by the percutaneous implantation of pulmonary artery pressure (PAP) sensors.

The procedure involves introducing a delivery catheter into a large vein (usually the femoral vein) under local anaesthesia. Using radiological guidance, the catheter is used to pass a pressure sensor through the heart and into a branch of the pulmonary artery where it is deployed and the delivery catheter is removed. The sensor transmits data on PAP to an external monitor in the patient's home. This data is then securely transmitted to a remote database for review by the HF team. Data may be collected and transmitted daily or as often as required.

Health Technology Wales researchers searched for evidence on clinical and cost-effectiveness of percutaneous implantation of PAP sensors for monitoring treatment of chronic heart failure. Evidence from RCTs within NICE interventional procedures guidance (IPG711) for percutaneous implantation of pulmonary artery pressure sensors for monitoring treatment of chronic heart failure has been included. Clinical-effectiveness searches focussed on evidence since the literature search was conducted for NICE IPG711 in August 2021.

Evidence overview

NICE interventional procedures guidance (IPG711)

NICE published interventional procedures guidance (IPG711) for percutaneous implantation of pulmonary artery pressure sensors for monitoring treatment of chronic heart failure in November 2021. This rapid review included evidence from two randomised controlled trials (RCTs; Abraham et al. 2016 and Lindenfeld et al. 2021). It was concluded that efficacy and safety was adequate to support using this procedure provided that standard arrangements are in place for clinical governance, consent and audit. NICE recommended that patient selection, continuing monitoring and management should be done by a multidisciplinary team. This should include healthcare professionals (both a doctor and a nurse) experienced in managing chronic heart failure, and interventional specialists experienced in rightheart catheterisation and inserting this device.

RCTs included in IPG711

One of the RCTs considered in IPG711 was the multicentre CHAMPION study carried out in the US which included 550 patients with New York Heart Association (NYHA) class 3 HF (Abraham et al. 2016). During the 18-month randomised access period, the rate of admissions to hospital for HF was statistically significantly reduced in patients who had CardioMEMS-guided management (treatment group; n = 270) by 33% (hazard ratio [HR] 0.67 [95% confidence interval (CI) 0.55 to 0.80], p<0.0001) compared with patients who had guideline-directed standard care management (control group; n = 280). During the 13-month open access period, the rate of HF hospital admissions in the former control group (n = 170) was statistically significantly reduced by 48% (HR 0.52 [95% CI 0.40 to

0.69], p<0·0001) compared with the control group during randomised access (n = 280). The rate was not statistically significantly reduced in the open access former treatment group (n = 177) compared to the randomised treatment group (n = 177 and n = 270, respectively; HR 0.93 [95% CI 0.70 to 1.22], p = 0.58). Change in PAP was not reported. Health-related quality of life was assessed using the Minnesota living with heart failure questionnaire (MLHFQ). The mean MLHFQ scores at 12 months were 47 for the treatment group and 57 for the control group at 12-month follow up (p = 0.0267). During a 31 month follow up, the overall combined device-related or system-related complication rate was 0.02 events per patient-year.

In the treatment group, cardiac deaths accounted for 80% (n=40) of the mortality, with 20% (n=10) non-cardiac. In the control group, cardiac deaths accounted for 75% (n=48) of the mortality with 23% (n=15) non-cardiac and 2% (n=1) unknown. Mortality rate was not significantly different (HR 0.80 [95% CI 0.55 to 1.15], p = 0.23). During the first six months of the study, device-related or system related complications were observed in 1% of patients (n=8) and procedure-related adverse events were reported in 1% of patients (n=7). In the entire follow-up period, no deaths were considered to be related to the device, system or procedure.

The other RCT considered in IPG711 was a multicentre study carried out in the US and Canada which included 1,000 patients with NYHA class 2 to 4 CHF (GUIDE-HF; Lindenfeld et al. 2021). The rate of HF hospitalisations was not statistically significantly different at 1 year after CardioMEMS implantation between patients who had PAP-guided management and standard care guideline recommended medical therapy (treatment group) and patients who had standard care guideline recommended medical therapy only (control group), with 0.410 events/patient-year compared with 0.497 events/patient-year, respectively; HR 0.83, 95% CI 0.68 to 1.01, p = 0.064). However, in the pre-COVID-19 impact analysis, there was a statistically significant difference in the rate of HF hospitalisations between the treatment group and the control group (0.380 events/patient-year compared with 0.525 events/patient-year; HR 0.72, 95% CI 0.57 to 0.92, p=0.0072). The mean change in PAP was statistically significantly lower in the treatment group compared with the control group (-792.7 ± 1,767.0 mmHg-days compared with -582.9 ± 1,698.1 mmHg-days, p=0.04) at 1-year follow up from baseline. The statistically significant difference was also reported in the pre-COVID-19 impact analysis (-518.0 ± 1,327.0 mmHg-days compared with -324.2 ± 1,328.5 mmHg-days, p=0.014).

Quality of life was measured using a number of scales. There were no statistically significant differences between the treatment and control groups for any of the changes in scores observed at 1 year compared to baseline.

Death was reported in 40 patients in the treatment group and 37 patients in the control group at 1-year follow up. No statistically significant difference in the mortality rate was observed between the two groups (HR 1.09, 95% CI 0.70 to 1.70, p = 0.71). In the pre-COVID-19 impact analysis, death was described in 30 patients and 25 patients respectively (p = 0.42). The overall device-related or system-related complication rate was 1% in each group (treatment group, n=3; control group, n=5).

Systematic reviews and RCTs

No systematic reviews or RCTs were identified since the literature search was conducted for NICE IPG711 in August 2021.

Cohort studies

Dauw et al. (2022) published a retrospective multicentre cohort study in the UK and Switzerland. A total of 48 patients received a PAP sensor (29 CardioMEMS and 19 Cordella devices) with a median follow-up of 19 (13-30) months. Of those patients, 89.6% were in NYHA class 3. A numerical increase in the number of diuretic therapy changes was observed after 3 months (49 vs. 82; p = 0.284) and 6

months (82 vs. 127; p = 0.093), with a significant increase observed after 12 months (118 vs. 195; p = 0.005). For patients with a baseline mean PAP (mPAP) <25 mmHg, the area under the curve (AUC) was positive (1370 ± 2248 mmHg-days) and mPAP was similar between baseline and after 1 year (16 ± 6 mmHg vs. 19 ± 13 mmHg; p = 0.127). For patients with a baseline mPAP ≥25 mmHg the AUC was negative (-1418 ± 2541 mmHg-days) and mPAP decreased non-significantly from baseline to 1 year (40 ± 9 mmHg vs. 34 ± 11; p = 0.085). The number of HF hospitalisations was reduced for all patients after 6 months (34 vs. 17; p = 0.014) and 12 months (48 vs. 29; p = 0.032).

Kishino et al. (2022) reported results of a retrospective cohort study carried out in the US which consisted of HF patients, with (1,842 patients) or without (5,326,530 patients) CardioMEMS. After propensity matching, patient numbers for these groups were 1,839 and 1,924 patients, respectively. At 30 days, hospital readmission rates were statistically significantly lower for patients with CardioMEMS compared to without CardioMEMS (before matching: 17.3% vs. 20.9%, p = 0.021; after matching: 17.3% vs. 21.5%, p = 0.021). The 90 day and 180 day rates were also lower in the CardioMEMS group compared to the group without CardioMEMS (29.6% vs. 36.5%, p = 0.002; 39.6% vs. 46.6%, p = 0.009, respectively). In a multivariable regression model, CardioMEMS was associated with lower risk of readmissions (HR 0.75, 95% CI 0.63 to 0.89, p = 0.001).

Economic evidence

Cowie et al. (2017) developed a Markov model to estimate cost-effectiveness of CardioMEMS in European healthcare systems, including in the UK. CardioMEMS-guided HF therapy increased cost by £10,916 compared with standard care in the base case analysis over a time horizon of 10 years. The quality-adjusted life years (QALYs) per patient for CardioMEMS-guided patients was 3.14 compared to 2.57 for standard care (0.57 QALY increase with CardioMEMS-guided treatment). The incremental cost-effectiveness ratio (ICER) was £19,274 per QALY gained. Including estimated staff time resulted in an increased ICER of £22,342-£25 464 per QALY gained. The authors therefore report that CardioMEMS would be cost-effective, at a willingness-to-pay threshold of £30,000 per QALY gained.

The aforementioned retrospective multicentre cohort study carried out in the UK and Switzerland reported that HF related health care costs were reduced from €6,286 to €3,761 at 6 months (p = 0.012) and from €8,960 to €6,167 at 12 months (p = 0.032). This study included two different devices (see above; Dauw et al. 2022).

Alcaraz et al. (2021) considered the cost-effectiveness of CardioMEMS for HF compared to standard care, from the third-party payer perspective (Social Security [SS] and Private Sector) in Argentina. A Markov model was applied to a hypothetical population of patients with NYHA class 3 HF with at least one hospitalisation in the previous 12 months, using a lifetime horizon. CardioMEMS increased QALYs by 0.37 and increased costs per patient by ARS 1,081,703 for SS, as compared to standard care. The resultant ICER was ARS 2,937,756 per QALY. As there is no widely accepted willingness-to-pay threshold in Argentina, the authors have explored three alternatives, ranging from one (ARS 700,473), three (ARS 2,101,419) and five (ARS 3,502,363) Gross Domestic Product (GDP) per capita. Under these thresholds, the probability that CardioMEMS is cost-effective is 0.6, 17.9 and 64.1% for SS, respectively. Under recommendations by the World Health Organisation of a threshold of 3 times the GDP, the intervention is unlikely to be cost-effective. Translating this ICER to GBP gives an ICER of £15,470, which would be within the widely accepted threshold of cost-effectiveness in the UK; however, it should be noted that inputs within the model will be specific to an Argentinian setting and so it may not be appropriate to translate this finding.

The cost-effectiveness of CardioMEMS in the German healthcare setting was considered by Kolominsky-Rabas et al. (2016). Based on the 37% reduction of hospitalisations in persistently

symptomatic previous HF patients reported in the CHAMPION trial, an estimated 114,800 hospitalisations would be avoided. The authors reported a potential saving of an estimated €522 million.

Schmier at al. (2017) and Sandhu et al. (2016) evaluated the cost-effectiveness of CardioMEMS in the US. Both applied a Markov model incorporating data from the CHAMPION trial. Schmier at al. (2017) compared outcomes over 5 years as compared to standard care patients. CardioMEMS was reportedly cost-effective, with an ICER of $44,832 per QALY. Sensitivity analysis found the model was sensitive to the device cost and to whether mortality benefits were sustained. However, the cost/QALY did not exceed $100,000 in any scenario. Sandhu et al. (2016) reported that CardioMEMS reduced lifetime hospitalisations (2.18 vs. 3.12), increased QALYs (2.74 vs. 2.46), and increased costs ($176,648 vs. $156,569), thus yielding a cost of $71,462 per QALY gained and $48,054 per life-year gained. A subgroup analysis showed that the cost per QALY gained was $82,301 in patients with reduced ejection fraction and $47,768 in those with preserved ejection fraction. An exploratory analysis in a lower-risk CHARM cohort showed that the device would need to reduce HF hospitalisations by 41% to cost <$100,000 per QALY gained. The cost-effectiveness was most sensitive to the device's durability. The generalisability of the US cost-effectiveness findings to Wales are uncertain due to the differences across the healthcare settings.

Ongoing studies

Ongoing systematic reviews on the efficacy and safety of PAP-guided therapy (Yang et al. 2021a) and CardioMEMS (Yang et al. 2021b) in HF were identified. Three ongoing RCTs were identified on the CardioMEMS-guided management of HF (Netherlands: Brugts et al. 2020; Germany: Stork et al. 2022; US/Canada: NCT03387813). A further ongoing RCT was designed to assess Cordella-guided management of HF (NCT04089059). Two additional observational studies (NCT02954341; NCT03247829) and an open-label single group study (NCT04012944) were also identified, all utilising CardioMEMS in HF (see literature search results).

Areas of uncertainty

The majority of the evidence is based on the use of CardioMEMS for PAP-guided management of HF. There is limited evidence on the use of Cordella-guided management of HF, and no evidence was identified on the use of any other PAP devices that may be available.

Most of the studies only include New York Heart Association (NYHA) class 3 HF (patients who have marked limitations in activity due to symptoms), although there is a large RCT in NYHA class 2-4 HF (mild-severe limitations).

Literature search results

Health technology assessments and guidance

Health Improvement Scotland (2016). Management of chronic heart failure. Scottish Intercollegiate Guidelines Network guideline (SIGN147). Available at: https://www.sign.ac.uk/our-guidelines/management-of-chronic-heart-failure/ [Accessed 8 November].

Knuuti J, Wijns W, Saraste A et al. (2020). 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. European Heart Journal. 41: 407-77. doi: https://doi.org/10.1093/eurheartj/ehz425.NICE. (2018). Chronic heart failure in adults: diagnosis and management. NICE guideline (NG106). National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ng106 [Accessed 8 November 2022].

NICE. (2021). Percutaneous implantation of pulmonary artery pressure sensors for monitoring treatment of chronic heart failure. NICE interventional procedures guidance (IPG711). National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ipg711 [Accessed 8 November 2022].

NIHR HSC. (2013). CardioMEMs HF System for heart failure. International HTA Database Record ID 32013000789. Available at: https://database.inahta.org/article/13778 [Accessed 8 November 2022].

NIHR HSC. (2014). CoVa™ Monitoring System for congestive heart failure. International HTA Database Record ID 32015000130. Available at: https://database.inahta.org/article/15658 [Accessed 8 November 2022].

Economic evaluations

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Dauw J, Sokolski M, Middleton JT, et al. (2022) Ambulatory haemodynamic-guided management reduces heart failure hospitalizations in a multicentre European heart failure cohort. ESC Heart Failure. doi: https://doi.org/10.1002/ehf2.14056.

Desai AS, Bhimaraj A, Bharmi R, et al. (2017). Ambulatory Hemodynamic Monitoring Reduces Heart Failure Hospitalizations in "Real-World" Clinical Practice. Journal of American College of Cardiology. 69(19): 2357-65. doi: https://doi.org/10.1016/j.jacc.2017.03.009.

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Sandhu AT, Goldhaber-Fiebert JD, Owens DK, et al. (2016). Cost-Effectiveness of Implantable Pulmonary Artery Pressure Monitoring in Chronic Heart Failure. Journal of the American College of Cardiology Heart Failure. 4(5): 368-75. doi: https://doi.org/10.1016%2Fj.jchf.2015.12.015.

Schmier JK, Ong KL, Fonarow GC. (2017). Cost-Effectiveness of Remote Cardiac Monitoring With the CardioMEMS Heart Failure System. Clinical Cardiology. 40(7): 430-6. doi: https://dx.doi.org/10.1002/clc.22696.

Individual studies

Abraham WT, Stevenson LW, Bourge RC et al. (2016) Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: complete follow-up results from the CHAMPION randomised trial. Lancet 387: 453-61. doi: https://doi.org/10.1016/S0140-6736(15)00723-0.
RCT included in IPG711 and discussed in TER.

Dauw J, Sokolski M, Middleton JT, et al. (2022) Ambulatory haemodynamic-guided management reduces heart failure hospitalizations in a multicentre European heart failure cohort. ESC Heart Failure. doi: https://doi.org/10.1002/ehf2.14056. Epub ahead of print.

Kishino Y, Kuno T, Malik AH, et al. (2022) Effect of pulmonary artery pressure-guided therapy on heart failure readmission in a nationally representative cohort. ESC Heart Failure. 9(4): 2511-7. doi: https://doi.org/10.1002/ehf2.13956.

Lindenfeld J, Zile MR, Desai AD et al. (2021) Haemodynamic-guided management of heart failure (GUIDE-HF): a randomised controlled trial. The Lancet. 398(10304): 991-1001. doi: https://doi.org/10.1016/S0140-6736(21)01754-2
RCT included in IPG711 and discussed in TER.

Ongoing research

Brugts JJ, Veenis JF, Radhoe SP, et al. (2020). A randomised comparison of the effect of haemodynamic monitoring with CardioMEMS in addition to standard care on quality of life and hospitalisations in patients with chronic heart failure: Design and rationale of the MONITOR HF multicentre randomised clinical trial. Netherlands Heart Journal. 28(1): 16-26. doi: https://doi.org/10.1007/s12471-019-01341-9.
Multicentre RCT (NCT7672) CardioMEMS; Netherlands, estimated enrollment, n=340.

CardioMEMS HF system OUS post market study (NCT02954341). Available at: https://clinicaltrials.gov/ct2/show/NCT02954341 [Accessed 16 November 2022].
Observational, cohort study; Australia, Belgium, Denmark, France and UK; estimated enrollment, n=800; estimated primary completion date: December 2023.

Hemodynamic-guided management of heart failure (GUIDE-HF; NCT03387813). Available at: https://clinicaltrials.gov/ct2/show/NCT03387813 [Accessed 16 November 2022].
Single-blinded, multicentre, RCT, CardioMEMS; US and Canada; estimated enrollment, n=3,600; estimated primary completion date: May 2023.

Investigation to optimize hemodynamic management of left ventricular assist devices using the CardioMEMS™ (Intellect2; NCT03247829). Available at: https://clinicaltrials.gov/ct2/show/NCT03247829 [Accessed 16 November 2022].
Observational, single group, multicentre study; US, actual enrollment, n=101; actual completion date: June 2020.

PROACTIVE-HF IDE trial heart failure NYHA class 3 (NCT04089059). Available at: https://clinicaltrials.gov/ct2/show/NCT04089059 [Accessed 16 November 2022].
Multicentre, RCT, Cordella; US, estimated enrollment, n=970; estimated primary completion date: November 2022.

SIRONA 2 trial heart failure NYHA class 3 (NCT04012944). Available at: https://clinicaltrials.gov/ct2/show/NCT04398654 [Accessed 16 November 2022].
Open-label, multicentre, single group study; Belgium, Germany and Ireland, estimated enrollment, n=60; estimated primary completion date: May 2022.

Störk S, Bernhardt A, Böhm M, et al. (2022) Pulmonary artery sensor system pressure monitoring to improve heart failure outcomes (PASSPORT-HF): rationale and design of the PASSPORT-HF multicenter randomized clinical trial. Clinical Research in Cardiology. 111(11): 1245-55. doi: https://doi.org/10.1007/s00392-022-01987-3.
Multicentre, RCT (NCT04398654) CardioMEMS; Germany, estimated enrollment, n=554; estimated primary completion date: May 2022.

Yang L, Du S, Shu T, et al. Efficacy and safety of Pulmonary Artery Pressure-Guided Therapy in the management of heart failure patients. PROSPERO 2021 CRD42021275914 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021275914 [Accessed 14 November 2022].
Ongoing; anticipated completion date: 31 December 2021.

Yang L, Du S, Shu T and Chen H. Efficacy and safety of CARDIOMEMS™ HF SYSTEM in the management of heart failure patients. PROSPERO 2021 CRD42021275774 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021275774 [Accessed 14 November 2022].
Ongoing; anticipated completion date: 30 November 2021.

Date of search:	November 2022
Concepts used:	CardioMEMS; chronic heart failure; Cordella; congestive heart failure; heart failure; monitor; pressure; sensor.