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# **PROCESS AND SYSTEMS** A cohort study to evaluate the impact of service centralisation for emergency admissions with acute heart failure

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The aim of our study was to describe the impact of emergency care centralisation on unscheduled admissions with a primary discharge diagnosis of acute heart failure (HF). We carried out a retrospective cohort study of HF admissions 1 year before and 1 year after centralisation of three accident and emergency departments into one within a single large NHS trust. Outcomes included mortality, length of stay, readmissions, specialist inpatient input and follow-up, and prescription rates of stabilising medication. Baseline characteristics were similar for 211 patients before and for 307 following reconfiguration. Median length of stay decreased from 8 to 6 days (p=0.020) without an increase in readmissions (4.7% versus 4.2%, p=0.813). The proportion with specialist follow-up increased (60% to 72%, p=0.036). There was a trend towards decreased mortality (32.2% versus 27.7% at 90 days; p=0.266). Contact with the cardiology team was associated with decreased mortality. In conclusion, centralisation of specialist emergency care was associated with greater service efficiency and a trend towards reduced mortality.

**KEYWORDS:** Heart failure, service reconfiguration, centralisation, emergency care

## Introduction

Centralisation of emergency services to provide 7-day consultantled delivery is a policy priority for NHS England,<sup>1,2</sup> reflecting the evidence of higher care quality and reduced mortality for hyperacute stroke, trauma and acute coronary syndrome.<sup>3–7</sup> There is also evidence that specialist cardiology input in acute

Authors: <sup>A</sup>MPH student, Institute of Health and Society, Newcastle University, Newcastle upon Tyne, UK; <sup>B</sup>cardiology registrar, Northern Deanery, Northumbria NHS Foundation Trust, UK; <sup>C</sup>consultant cardiologist, Northumbria NHS Foundation Trust, UK; <sup>D</sup>reader in health economics, School of Health, Community and Education Studies, Northumbria University, Newcastle upon Tyne, UK; <sup>E</sup>consultant stroke physician, Northumbria NHS Foundation Trust, UK; <sup>F</sup>clinical reader, NIHR Newcastle Biomedical Research Centre and Institute of Neuroscience, Newcastle University, Newcastle upon Tyne heart failure (HF) management improves clinical outcomes.<sup>8,9</sup> Although this suggests that patients with acute HF are also likely to benefit from centralised care through earlier contact with expert clinicians, no studies have sought to demonstrate this association and confirm that outcomes are improved. A positive impact could provide further evidence for emergency care centralisation, given that patients with HF are recurrent users of hospital services and account for 5% of all emergency medical admissions.<sup>10,11</sup> Understanding the most effective ways to provide high-quality care is made more urgent by the increasing HF prevalence resulting from an ageing population and by advances in medical therapy.<sup>12–14</sup>

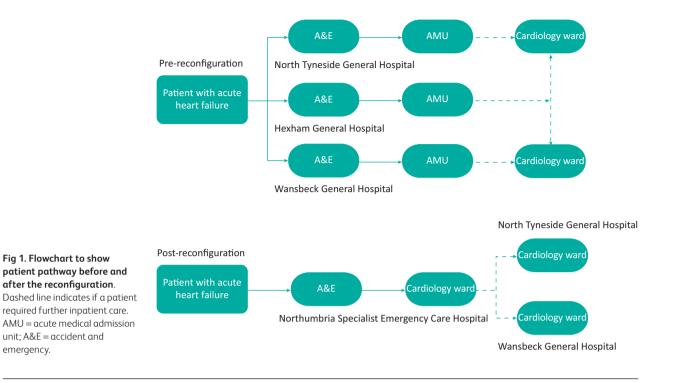
To confirm whether patients with acute HF also benefit from service centralisation, we retrospectively compared the health and care outcomes of patients admitted before and after the reconfiguration of all accident and emergency (A&E) services within a large NHS foundation trust.

#### **Methods**

#### Setting

Northumbria Healthcare NHS Foundation Trust is an acute and elective care provider to approximately 500.000 people across a large geographical area of north east England.<sup>15</sup> Before 16 June 2015, all unscheduled attendances were initially seen in the accident and emergency department (A&E) and, if required, admitted to the acute medical admission unit (AMU) (Fig 1). An A&E and AMU were available at three district general hospitals located in an approximately triangular distribution across the catchment area: North Tyneside General Hospital (North Shields), Wansbeck General Hospital (Ashington) and Hexham General Hospital (Hexham). Patients with ST-elevation myocardial infarction were triaged pre-hospital or via A&E to the Regional Cardiology Centre in Newcastle upon Tyne for consideration of urgent reperfusion; however, all other cardiology patients, including those with acute HF, were initially admitted onto an AMU at one of the three sites under the supervision of a consultant in general internal medicine. They were subsequently transferred to a cardiology ward if ongoing inpatient care was required and a specialty bed was available. There was no routine provision of cardiology specialist care at Hexham.

After service centralisation on 16 June 2015, all medical emergencies were admitted directly to a single new specialist



emergency care hospital built in-between the Wansbeck and North Tyneside sites. Patients requiring admission now passed from A&E to the most relevant specialist ward, rather than to an AMU. Those with acute HF were now directly admitted to a cardiology ward, with an on-site consultant cardiologist present for 12 hours a day, 7 days a week, and on-call availability overnight.

#### Study cohort

Patients admitted between 16 June 2014 and 16 June 2016 were included if they had an unscheduled index admission with acute HF as the primary coded diagnosis, imaging evidence of a reduced left ventricular ejection fraction (LVEF; <40% or moderate and/ or severe impairment on visual assessment) and featured in the trust HF audit database. Only patients with evidence of systolic impairment were included to ensure a clear case definition, and because there are evidence-based guidelines that define optimal medical therapy<sup>16,17</sup> and can improve prognosis.<sup>18</sup> This is not the case for patients with HF and a preserved ejection fraction; therefore, these patients were not included.<sup>19</sup> Patients recorded on the database are routinely identified by the clinical coding department using Hospital Episode Statistics (ICD10 codes I11.0 I25.5, I42.0, I42.9, I50.0, I50.1 and I50.9), and the relevant patient records are reviewed by a HF specialist nurse for inclusion to aid mandatory reporting to the National Institute for Cardiovascular Outcomes Research (NICOR).<sup>20,21</sup> Using this approach for the study cohort ensured that only patients with clinical and imaging documentation of HF in medical records were included.

#### Study variables

The primary outcome was mortality, reported as an inpatient, and 30 days, 60 days and 90 days following admission.

Secondary outcomes were the median length of stay, readmission within 30 days, proportion discharged with planned

follow-up, and proportion of patients prescribed key prognostic medication on discharge (angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), beta blockers, and/or mineralocorticoid receptor antagonists (MRA)).

Demographic data collected included place of care, postcodelevel index of multiple deprivation, and gender. Clinical data were obtained from the HF database and included past medical history of ischaemic heart disease, hypertension, diabetes mellitus, asthma and/or chronic obstructive pulmonary disease, and atrial fibrillation (AF); severity of heart failure symptoms (New York Heart Association category (NYHA)); presence of peripheral oedema; weight; and heart rate and blood pressure (BP). The Charlson co-morbidity score was calculated from Hospital Episode Statistics.<sup>22</sup> The heart failure database included in-hospital mortality only; later mortality data were obtained from the NHS Spine. Individual patient notes were only accessed to identify whether an echocardiogram had been performed and the results of this, if this information was not yet available within the HF database.

'Specialist cardiology care' was recorded on the HF database and defined by inpatient contact on at least one occasion with a consultant, specialty registrar or specialist nurse in cardiology.

#### Statistical methods

Data were assessed for normality using data histograms. The group admitted in the year before the reconfiguration (16 June 2014 to 15 June 2015) were compared with those admitted in the year following the reconfiguration (16 June 2015 to 16 June 2016). Normally distributed variables were compared using Student's t-test, non-parametric data with the Mann–Whitney U-test, and proportions with  $\chi^2$ . The association between specialist care and mortality was calculated in a multivariate logistic regression model constructed on the basis of significant factors from the univariate analysis. In the regression model, the Charlson score was

dichotomised at a threshold of >5, as in NHS Digital guidance.<sup>18</sup> The results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). Statistical analyses were performed in Stata 15.

#### Ethics

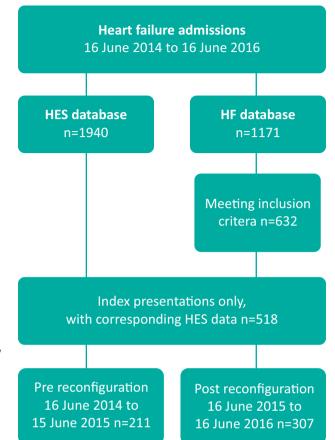
Approval from the Trust Caldicott Guardian was granted on 23 September 2016. Ethics committee approval was not required for analysis of the anonymised clinical data set.

#### Results

There were 518 index presentations over the study period of 2 years: 211 and 307 pre and post centralisation, respectively (Fig 2). Table 1 shows that the baseline characteristics of the cohorts were similar. The median age was 78 in both groups, with a similar severity of admission symptoms when classified by NYHA group. The only statistically significant difference was a greater percentage of participants with peripheral oedema at admission before the reconfiguration than after (85% versus 69%, p<0.001).

Comparing pre and post reconfiguration, there was an increase in the proportion of patients receiving specialist cardiology care (61.1% (n=129) versus 73.6% (n=226)). Overall, inpatient mortality was 17.8% and 90-day mortality was 29.5% (Table 2). Comparing mortality pre and post reconfiguration, there was a trend towards decreased mortality at each time interval that did not reach statistical significance (Fig 3). There was an absolute reduction in in-hospital, and 30-, 60- and 90-day mortality of 4.4%, 5.6%, 4.3% and 4.5%, respectively.

After adjustment for admission BP, Charlson score >5, gender, presence of oedema and AF, specialist care was associated with



**Fig 2. Flow diagram to show derivation of analytic cohort**. HF = heart failure; HES = hospital episode statistics.

Table 1. Baseline characteristics stratified by period of study: before and after reconfiguration												
Characteristic	Pre reconfiguration (total n=211)		Post reconfigu	p value								
Median age of patients, years (IQR)	78	(14)	78	(15)	0.404							
Male, n (%)	145	(69%)	192	(63%)	0.324							
Patients with oedema at admission, n ( % )	170	(85%)	189	(69%)	<0.001							
Patients with NYHA 1 or 2, n (%)	46	(23%)	76	(27%)	0.340							
Patients with NYHA 3 or 4, n ( % )	156	(77%)	210	(73%)								
Patients with ischaemic heart disease, n (%)	107	(53%)	159	(54%)	0.916							
Patients with hypertension, n (%)	98	(49%)	128	(44%)	0.296							
Patients with diabetes mellitus, n (%)	70	(34%)	102	(35%)	0.856							
Patients with asthma, n ( % )	9	(5%)	14	(5%)	0.786							
Patients with COPD, n (%)	39	(19%)	59	(21%)	0.638							
Patients with atrial fibrillation, n ( $\%$ )	85	(40%)	119	(40%)	0.878							
Median weight, kg (IQR)	78	(28.7)	80.4	(28.1)	0.214							
Median heart rate, bpm (IQR)	86	(29.0)	80	(35.0)	0.097							
Median systolic BP, mmHg (IQR)	124	(36.5)	128	(36.0)	0.174							
Median IMD, decile (IQR)	5	(4)	5	(5)	0.789							
Median Charlson index, score (IQR)	8	(10)	7	(11)	0.522							

BP = blood pressure; COPD = chronic obstructive pulmonary disease; IMD = index of multiple deprivation; IQR = interquartile range; NYHA = New York Heart Association classification

Table 2. Unadjusted mortality as inpatient, and 30-days, 60-days and 90-days post admission pre and post reconfiguration

reconfiguration									
	Mortality point	Total (n=518)		Pre reconfiguration (total n=211)		Post reconfiguration (total n=307)		p value	
		Deaths	% mortality (95% CI)	Deaths	% mortality (95% CI)	Deaths	% mortality (95% CI)		
	In-hospital	92	17.8% (14.7–21.3)	43	20.4% (15.5–26.4)	49	16.0% (12.3–20.5)	0.196	
	30 day	118	22.8% (19.4–26.6)	55	26.1% (20.6–32.4)	63	20.5% (16.4–25.4)	0.139	
	60 day	139	26.8% (23.2-30.8)	62	29.4% (23.6–35.9)	77	25.1% (20.5–30.3)	0.278	
	90 day	153	29.5% (25.8–33.6)	68	32.2% (26.2–38.9)	85	27.7% (23.0–33.0)	0.266	
	CI = confidence interv	/al.							

reduced in-hospital mortality, OR 0.44 (95% CI 0.25–0.78). This was sustained to 90 days, OR 0.55 (95% CI 0.34–0.89).

Length of stay was lower post reconfiguration compared with pre reconfiguration (median 6 days (interquartile range (IQR) 12) versus 8 days (IQR 14); p=0.020) without any change in the percentage of patients readmitted within 30 days (4.7% versus 4.2%; p=0.813).

There was no significant difference in the prescription of ACEi and/or ARB (75% versus 78%; p=0.404), beta blockers (86% versus 89%; p=0.332), or MRA (28% versus 36%; p=0.104) between the two time periods. However, a greater percentage of patients had specialist follow-up arranged at discharge following reconfiguration (60% versus 72%; p=0.036).

# Discussion

This study demonstrated a trend towards a sustained decreased mortality up to 90 days for patients with acute HF following the service reconfiguration, with a shorter length of stay and no corresponding increase in readmissions. More patients were seen by a cardiology specialist, which was independently associated with reduced risk of mortality. Although this was a small study in a single NHS trust, these findings support national policy. The evidence for centralisation of emergency care has so far depended upon conditions with specific time-critical therapies, such as stroke reperfusion, trauma resuscitation care and percutaneous coronary intervention.<sup>3–7</sup> The benefits identified by this study are more likely to be related to several process changes and care decisions, in contrast to the more technical interventions in stroke, trauma and myocardial infarction, and also reflect service efficiencies gained through a whole-system reconfiguration.

Within this study, it is not possible to report the relative contribution of each component of a multi-faceted service intervention on outcomes. It is likely that improved access to echocardiography, radiography, allied health professionals and cardiology staff would have an impact. We were able to show that contact with a cardiology specialist was associated with a mortality reduction, as has been reported elsewhere,<sup>20,23</sup> but acknowledge that the availability of specialist geriatric care allowed for the appropriate triage of some older patients with complex care needs to a specialist environment for frailty rather than for HF. Therefore, it is unknown whether the same effect would be seen in other service models where a different proportion of patients with HF might be under cardiology or geriatric care.

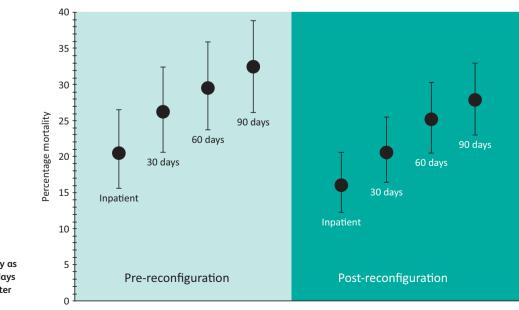


Fig 3. Unadjusted mortality as an inpatient, 30 days, 60 days and 90 days before and after reconfiguration. Estimates of inpatient mortality for HF admissions vary in the literature from 3.8% to 15%,<sup>11,24</sup> explained in part by methodological differences and case selection, thereby limiting generalisability. This study only includes the subgroup of patients with a reduced LVEF, which carries the worst prognosis,<sup>25</sup> and might explain the somewhat higher observed overall inpatient mortality rate of 17.8%. This focus allowed inclusion of patients with a more homogeneous disease state, for which there is pre-

existing evidence that specialist care can improve outcome. There is evidence that in-hospital mortality for patients with acute HF is improving across England and Wales, with the NICOR audit figures showing a 0.7% decrease between 2014–2015 and 2015–2016.<sup>20</sup> The current study showed a 4.4% decrease over a similar time interval. Nationally, it appears that mortality reduction is associated with improvements in the provision of guidelineindicated care, such as achieving optimal doses of recommended medication,<sup>18,20</sup> but we showed no significant difference in prescriptions at discharge following the reconfiguration. This could be because of the small population size and short duration of follow-up. Although dose was not recorded, it is possible that the increase in specialist care after discharge indicated plans for medication optimisation in the community, which might take longer to have an impact.

There were 96 more patients in the post-centralisation than pre-centralisation group, which might indicate the more effective direction of HF cases into the correct specialty and/or greater attention to case finding for the HF database. This could influence the case mix and subsequent mortality if milder cases of HF were more easily identified after centralisation. However, all patients had echocardiographic evidence of at least moderate LV systolic impairment, and the baseline characteristics of the two groups were similar. Centralising admissions from the three hospitals into a single site led to an overall increase in patient volume at the new hospital, which has in itself been associated with improved outcomes for HF.<sup>26,27</sup>

The readmission rate for patients in this study was low compared with the those reported elsewhere,  $^{28-30}$  and should be interpreted cautiously, because previous work has shown that discharge codes tend to underestimate hospital events related to HF.<sup>31,32</sup> It is possible that the true 30-day readmission rate is somewhat higher.

This study has several strengths. It used a clinical database compiled by specialist staff and subject to routine data-quality checks. During the study period, there were no significant changes to National Institute for Health and Care Excellence recommended therapy<sup>10,16</sup> or to coding practice within the Trust that might have influenced the observed findings. We were able to report mortality up to 90 days following admission, including deaths in the community. This reduced discharge bias, whereby an early death following early discharge gives an apparent improvement in inpatient mortality. However, there are limitations that must be considered. It is possible that not all cases of HF were identified, although there should not be a differential effect between the two groups studied because coding and HF database processes did not change. Second, it was only possible to observe the impact of the overall change, rather than each component; therefore, a mechanism supporting causation cannot be demonstrated. Third, because of data limitations, we were only able to report all-cause mortality, rather than cardiovascular-specific mortality. Fourth, the different geographical location of the hospitals might have altered the case mix of emergency admissions, although

this was not intended by the reconfiguration. Finally, this was not a whole-service evaluation, but instead provided short-term evidence regarding a selected cohort of patients. This study used the first year of data post reconfiguration, and it is unclear whether wider system effects of the whole-system change would result in our findings being sustained. Further data collection over several years, including an economic evaluation and more patient-centred outcomes, such as satisfaction, waiting times and differences in accessibility, are required to form a broader assessment of centralisation impact.

In conclusion, we observed a trend towards decreased mortality in the context of a shorter length of stay and no corresponding increase in readmissions following centralisation of specialist services for acute HF, which are consistent with evidence for other conditions. Documentation of specialist input was associated with a mortality benefit, but case-mix biases could not be fully accounted for. Further research is needed to confirm these findings in different settings with a study design that minimises the potential influence of population and external healthcare delivery changes.

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#### References

- 1 Imison C. The reconfiguration of hospital services: is there evidence to guide us? *Fut Hosp J* 2015;2:137–41.
- 2 NHS England. NHS Five Year Forward View. London: NHS, 2014.
- 3 Morris S, Hunter RM, Ramsay AIG et al. Impact of centralising acute stroke services in English metropolitan areas on mortality and length of hospital stay: difference-in-differences analysis. BMJ 2014;349: q4757
- 4 Department of Health. Treatment of heart attack national guidance: final report of the National Infarct Angioplasty Project (NIAP). London: DoH, 2008.
- 5 Kanakaris NK, Giannoudis PV. Trauma networks: present and future challenges. *BMC Med* 2011;9:121.
- 6 Xian Y, Holloway RG, Chan PS *et al*. Association between stroke center hospitalization for acute ischemic stroke and mortality. *JAMA* 2011;305:373–80.
- 7 MacKenzie EJ, Rivara FP, Jurkovich GJ *et al*. A national evaluation of the effect of trauma-center care on mortality. *N Engl J Med* 2006;354:366–78.
- 8 Selim AM, Mazurek JA, Iqbal M et al. Mortality and readmission rates in patients hospitalized for acute decompensated heart failure: a comparison between cardiology and general-medicine service outcomes in an underserved population. *Clin Cardiol* 2015;38:131–8.
- 9 Uthamalingam S, Kandala J, Selvaraj V *et al.* Outcomes of patients with acute decompensated heart failure managed by cardiologists versus noncardiologists. *Am J Cardiol* 2015;115:466–71.
- 10 National Institute for Health and Care Excellence. National costing report: chronic heart failure. In: *Clinical guideline [CG108]*. London: NICE, 2010.
- 11 Bottle A, Goudie R, Bell D, Aylin P, Cowie MR. Use of hospital services by age and comorbidity after an index heart failure admission in England: an observational study. *BMJ Open* 2016;6:e010669
- 12 Cowie MR, Anker SD, Cleland JGF *et al.* Improving care for patients with acute heart failure: before, during and after hospitalization. *ESC Heart Fail* 2014;1:110–45.

- 13 Driscoll A, Meagher S, Kennedy R *et al.* What is the impact of systems of care for heart failure on patients diagnosed with heart failure: a systematic review. *BMC Cardiovasc Disord* 2016;16:195.
- 14 Anon. Crunch time for heart failure care in England and Wales. *Lancet* 2010;376:2041.
- 15 Northumbria NHS Foundation Trust. *Trust in us: corporate prospectus*. North Shields: Northumbria NHS Foundation Trust, 2015.
- 16 National Institute for Health and Care Excellence. Acute heart failure: diagnosis and management. In: *Clinical guideline [CG187]* London: NICE, 2014.
- 17 Ponikowski P, Voors AA, Anker SD *et al.* 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) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016;37:2129–200.
- 18 De Blois J, Fagerland MW, Grundtvig M *et al.* ESC guidelines adherence is associated with improved survival in patients from the Norwegian Heart Failure Registry. *Eur Heart J Cardiovasc Pharmacother* 2015;1:31–6.
- 19 Roh J, Houstis N, Rosenzweig A. Why don't we have proven treatments for HFpEF? *Circ Res* 2017;120:1243–5.
- 20 National Institute for Cardiovascular Outcomes Research. National Heart Failure Audit, April 2014–March 2015. London: University College London, 2017.
- 21 National Institute for Cardiovascular Outcomes Research (NICOR). Data collection 2018 [31 March 2018]. www.ucl.ac.uk/nicor/data [Accessed 19 December 2018].
- 22 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.
- 23 Parmar KR, Xiu PY, Chowdhury MR, Patel E, Cohen M. In-hospital treatment and outcomes of heart failure in specialist and non-specialist services: a retrospective cohort study in the elderly. *Open Heart* 2015;2:e000095.

- 24 Maggioni AP, Dahlstrom U, Filippatos G *et al.* EURObservational Research Programme: the Heart Failure Pilot Survey (ESC-HF Pilot). *Eur J Heart Fail* 2010;12:1076–84.
- 25 Bello NA, Claggett B, Desai AS *et al.* Influence of previous heart failure hospitalization on cardiovascular events in patients with reduced and preserved ejection fraction. *Circ Heart Fail* 2014;7:590–5.
- 26 Joynt KE, Orav EJ, Jha AK. Physician volume, specialty, and outcomes of care for patients with heart failure. *Circ Heart Fail* 2013;6:890–7.
- 27 Ross JS, Normand SL, Wang Y *et al*. Hospital volume and 30-day mortality for three common medical conditions. *N Engl J Med* 2010;362:1110–8.
- 28 Davison BA, Metra M, Senger S *et al*. Patient journey after admission for acute heart failure: length of stay, 30-day readmission and 90-day mortality. *Eur J Heart Fail* 2016;18:1041–50.
- 29 McIlvennan CK, Allen LA. Outcomes in acute heart failure: 30-day readmission versus death. *Curr Heart Fail Rep* 2014;11:445–52.
- 30 Shah M, Patnaik S, Patel B *et al.* The day of the week and acute heart failure admissions: relationship with acute myocardial infarction, 30-day readmission rate and in-hospital mortality. *Int J Cardiol* 2017;249:292–300.
- 31 Horvitz-Lennon M, Braun D, Normand SL. Challenges in the use of administrative data for heart failure services research. J Cardiac Fail 2016;22:61–3.
- 32 Khand AU, Shaw M, Gemmel I, Cleland JG. Do discharge codes underestimate hospitalisation due to heart failure? Validation study of hospital discharge coding for heart failure. *Eur J Heart Fail* 2005;7:792–7.

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