openheart

Feasibility and outcomes of an automated high-alert NT-proBNP pathway

John Aaron Henry ,[1,2] Chris Brown,[1] Carolina Almeida,[1] Jack Devin,[1] Tyler Jones,[1] Marco Vidal,[1] Tim Sims,[3] Sinead O'Driscoll,[1] Aida Agostinho,[1] Brian Xiangzhi Wang,[1] Sean Pallot,[4] Elisabete Da Silva,[1] Pierre Le Page,[1] Oliver Rider,[2] Andrew Robert John Mitchell[1]

To cite: Henry JA, Brown C, Almeida C, *et al*. Feasibility and outcomes of an automated high-alert NT-proBNP pathway. *Open Heart* 2026;**13**:e004325. doi:10.1136/openhrt-2026-004325

Received 16 June 2026
Accepted 3 August 2026

Check for updates

© Author(s) (or their employer(s)) 2026. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ Group.

[1]Cardiology Department, Jersey General Hospital, Saint Helier, Jersey
[2]Division of Cardiovascular Medicine, Radcliffe Department of Medicine, University of Oxford Oxford Centre for Clinical Magnetic Resonance Research, Oxford, UK
[3]Laboratory Services, Jersey General Hospital, Saint Helier, Jersey
[4]Clinical Investigations Department, Jersey General Hospital, Saint Helier, Jersey

Correspondence to
Dr John Aaron Henry; john.henry@some.ox.ac.uk

ABSTRACT

Background NT-proBNP is a key biomarker in heart failure (HF). Patients with markedly elevated levels are at high risk of adverse outcomes but experience delays in specialist care. Evidence on the impact of an automated, high-threshold NT-proBNP referral pathway embedded in electronic patient records is limited.

Methods All NT-proBNP results >5000 pg/mL over a 12-month period triggered automatic HF team referral. Referrals were categorised as inpatients, outpatients with known HF, outpatients not suitable for follow-up or new outpatients without a diagnosis of HF who were eligible for enrolment. Eligible patients were offered echocardiography and review within 48 hours, with treatment and outcome data collected prospectively. A retrospective comparator cohort included all outpatient NT-proBNP results >5000 pg/mL from patients not known to the HF service in the 12 months before implementation.

Results Over 12 months, 889 referrals were generated: 417 (47%) inpatients, 370 (42%) known outpatients, 59 (7%) not appropriate and 43 (5%) enrolled. Median time to review was 2 days, with 70% meeting the 48-hour target. Among enrolled patients (mean age 81, 56% male, median NT-proBNP 7480 pg/mL), HF with reduced ejection fraction (HFrEF) was diagnosed in 21 (49%), HF with mildly reduced ejection fraction in seven (16%), HF with preserved ejection fraction in 10 (23%) and severe aortic stenosis or new atrial fibrillation in four each (10%). At 12 weeks, 62% of patients had improved by at least one New York Heart Association class, and mean left ventricular ejection fraction increased from 27% to 45% in those with HFrEF. At 12 weeks, admission and mortality were 36% and 8%, respectively, compared with 35% and 12% in the retrospective cohort (n=60).

Conclusion An automated high-threshold NT-proBNP pathway is feasible and identifies very high-risk patients. Enrolled patients had rapid therapy optimisation, with observed improvements in symptoms and cardiac function.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patients with very high NT-proBNP values (>5000 pg/mL) have markedly elevated short-term risks of morbidity and mortality.
⇒ Current UK pathways mandate urgent referral at lower thresholds (>2000 pg/mL), but substantial delays from testing to specialist review are common.

WHAT THIS STUDY ADDS

⇒ An automated, electronic high-alert pathway triggered by NT-proBNP >5000 pg/mL was feasible, generated a modest number of referrals and enabled most patients to be assessed within 48 hours.
⇒ Among enrolled patients, treatment changes were commonly made at the initial review, and improvements in symptoms and left ventricular function were observed.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Embedding laboratory-driven referral triggers in electronic records could provide a scalable way to fast-track patients at highest risk.
⇒ Wider implementation could improve outcomes in advanced heart failure, provided adequate echocardiography and specialist capacity is available.
⇒ Future research should evaluate long-term outcomes and assess integration of very high-risk NT-proBNP tiers into national diagnostic pathways.

INTRODUCTION

Heart failure (HF) affects over 1 million people in the UK and remains frequently diagnosed late, often during hospital admission.[1] Natriuretic peptide (NP) testing supports diagnosis and risk stratification, with higher concentrations associated with worse outcomes.[2 3] In a large UK cohort, NT-proBNP >2000 pg/mL was associated with 27% 1 year mortality and higher hospitalisation risk.[2] Local island-wide data,[4] together with international studies,[3 5] indicate that very high values (>5000 pg/mL) identify patients at especially high short-term risk.

In the UK, NICE recommends referral for specialist assessment and echocardiography within 2 weeks for NT-proBNP >2000 pg/mL, mirroring the urgency of cancer '2 week wait' pathways. However, in a national primary care diagnostic accuracy study, fewer than half of patients with NT-proBNP >2000 pg/mL received a HF diagnosis within 2 weeks

of testing.[6] There are also substantial delays from NP testing to onwards referral,[7] with one UK study finding a median time from test to HF diagnosis of 28 days in those with NT-proBNP >2000 pg/mL.[2] Furthermore, contemporary UK service evaluations report persistently high 1 year event rates among referred patients, with one study finding 38% hospitalisation and 14% all-cause mortality rates in 2-week pathway patients.[8] Together, these findings highlight the need to streamline referral processes.

Whether introducing an additional 'very high-risk' urgency tier (eg, NT-proBNP >5000 pg/mL) and automating referrals directly from the laboratory/electronic patient record (EPR) meaningfully shortens time-to-assessment and improves outcomes has not been established in routine UK practice. This short report evaluates the feasibility and clinical outcomes of an automated high-alert referral pathway for patients with NT-proBNP >5000 pg/mL across an island-wide service.

METHODS

This project received local research ethics approval (2023/HCSREC/10).

Prospective cohort

Patients were identified prospectively through an EPR linked high-alert pathway. All NT-proBNP results >5000 pg/mL island-wide over 12 months triggered automated HF referral, with the EPR inbox checked daily. To be considered eligible for pathway enrolment, individuals had to be current outpatients, without a known diagnosis of HF and not previously reviewed by the HF service. Patients were excluded if their address was a long-term residential care facility or if they were established on renal replacement therapy. For borderline cases that couldn't be resolved from test request information alone, additional information was sought from the patient's general practitioner prior to contact. Patients with clinical frailty score (CFS) ≥7 were excluded.

Eligible patients were offered echocardiography and clinical review, with a target of completion within 48 hours of referral. At the index visit, baseline medication and clinical status were documented. Data were collected at follow-up assessments at 4 and 12 weeks, and repeat echocardiography was performed at 3 months following medical optimisation as part of routine clinical care. Maximally tolerated guideline-directed therapy was defined by the treating clinician. A QUAD score was calculated for each patient at each visit, and defined as poor (<8 points), good (8–14 points) or excellent (>14 points), as previously described.[9] Outcomes recorded at 12 weeks included all-cause hospital admission, HF-related events (defined as urgent HF clinic review, rapid response team attendance for intravenous diuretics or HF-related hospital presentation) and mortality.

Retrospective cohort

For comparison, all NT-proBNP results >5000 pg/mL performed in the community during the 12 months preceding pathway implementation were identified. Patients already known to the HF service were excluded, as were those receiving renal replacement therapy and those living in a long-term residential care facility. Those who did not have an echocardiogram performed within 12 months of their NT-proBNP were excluded as it was presumed a clinical decision was made that echocardiography would not be appropriate. The remaining cohort was used to provide a retrospective comparator group.

RESULTS

Referrals

Over a 12-month period, 889 automated referrals were generated for NT-proBNP values >5000 pg/mL. Of these, 417 (47%) were current inpatients, 370 (42%) were outpatients already under the HF service and 59 (7%) were outpatients deemed not appropriate for follow-up (figure 1A). The remaining 43 (5%) were enrolled in the high-alert pathway. Median time from referral to

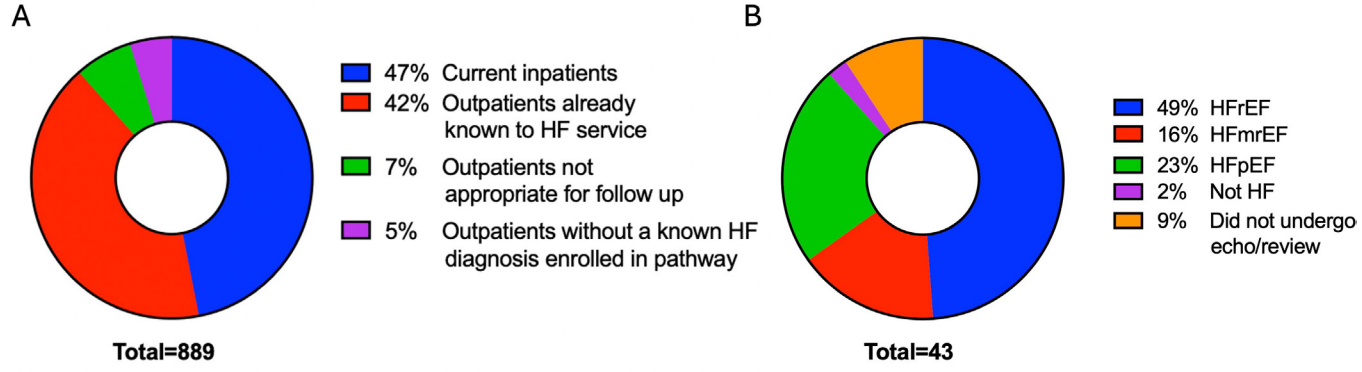


Figure 1 (A) The distribution of automated referrals triggered by NT-proBNP >5000 pg/mL over the 12-month study period. (B) The diagnostic categories among patients enrolled in the pathway, including heart failure phenotype. HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction.

Table 1 The baseline characteristic of those enrolled in the pathway who received a new diagnosis of heart failure, including demographic and clinical data, baseline medical therapy, comorbidities and heart failure aetiology. ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; MRA, mineralocorticoid receptor antagonist; SGLT2i, sodium–glucose cotransporter 2 inhibitor

Demographics and clinical, n=38	
NT-proBNP, pg/mL (median, IQR)	7590 (5988–11 150)
Age, years (mean, SD)	81 (11)
Male, n (% of total)	21 (55%)
Baseline medical therapy, n (%)	
SGLT2i	4 (11%)
ACE/ARB/ARNi	8 (21%)
Beta blocker	15 (39%)
MRA	5 (13%)
Loop diuretic	18 (47%)
Comorbidities, n (%)	
Hypertension	28 (74%)
Hypercholesterolaemia	25 (66%)
Atrial fibrillation/flutter	23 (61%)
Chronic kidney disease	18 (47%)
Ischaemic heart disease	16 (42%)
Diabetes mellitus	10 (26%)
Active malignancy	7 (18%)
COPD/asthma	3 (8%)
Stroke/TIA	3 (8%)
Heart failure aetiology, n (%)	
Arrhythmia	13 (34%)
Coronary artery disease	11 (32%)
Cardiomyopathy	8 (21%)
Valve disease	4 (11%)
Right heart disease/pulmonary hypertension	2 (5%)

echocardiography was 2 days, with 70% achieving the 48-hour target. Enrolled patients had a mean age of 81 years, 56% were male, and median NT-proBNP was 7480 pg/mL.

Enrolment and diagnoses

Among the 43 patients enrolled, HF with reduced ejection fraction (HFrEF) was diagnosed in 21 (49%), HF with mildly reduced EF (HFmrEF) in 7 (16%) and HF with preserved EF (HFpEF) in 10 (23%) (figure 1B). One patient had no evidence of HF but did have significant pulmonary hypertension from chronic lung disease. Four patients did not undergo echocardiography (three died before assessment, one had imaging privately). New major findings included severe aortic stenosis in four patients (10%) and new atrial fibrillation in a further four (10%). Baseline characteristics of those enrolled who received a new diagnosis of HF are shown in table 1.

Management and outcomes

Of the 38 patients diagnosed with HF, three required immediate hospital admission following review: two due to hypoxia and one with atrial fibrillation and a fast ventricular response. Of the remaining 35 patients, 32 (91%) had adjustments made to their medical therapy at the initial appointment.

Among the three patients whose treatment was unchanged, one had severe aortic stenosis and was referred urgently to valve clinic; one had atrial fibrillation with HFpEF but was already established on an SGLT2 inhibitor for diabetes, and one left the department after echocardiography, prior to clinical review, due to hospital phobia.

In those diagnosed with HFrEF, over 20% were on quadruple therapy after the initial visit (figure 2A). At 4 weeks, 78% of patients were on clinician-determined maximally tolerated guideline directed therapy, rising to 89% at 12 weeks. The proportion of patients on loop diuretics fell from 74% at the initial visit to 56% at 12 weeks. The proportion of patients with a 'good' or 'excellent' QUAD score increased from 14% at baseline to 52%, 74% and 79% after the initial, 4-week and 12-week visits, respectively.

At 12 weeks, 62% of patients with follow-up data had improved by at least one New York Heart Association (NYHA) class. In those with HFrEF, mean left ventricular ejection fraction (LVEF) increased from 27% to 45% in those who had a follow-up echocardiogram (n=16/21, 76%), with 75% (n=12/16) improving above 40% (figure 2B). Of five without follow-up imaging, two died, two were deemed inappropriate, and one was lost to follow-up.

During the 12-week follow-up, all-cause admission was 36%, with 21% having a HF event. All-cause mortality at 12 weeks was 8%.

In the retrospective cohort (n=60), mean age was 83 years, 49% male and median NT-proBNP 6355 pg/mL. Overall, 80% were reviewed by the HF team, and median time from NT-proBNP test to appointment (if one occurred) was 42 days. All had evidence of HF on echocardiography (35% HFrEF, 25% HFmrEF and 40% HFpEF). The 12-week all-cause admission was 35%, and 12-week all-cause mortality was 12%.

Spotlight cases

Figure 3 highlights two illustrative cases from the pathway.

DISCUSSION

This study demonstrates that an automated high-alert NT-proBNP pathway is feasible and clinically effective. Embedding a >5000 pg/mL laboratory trigger streamlined referral, enabled rapid review and was associated with improved symptoms and cardiac function.

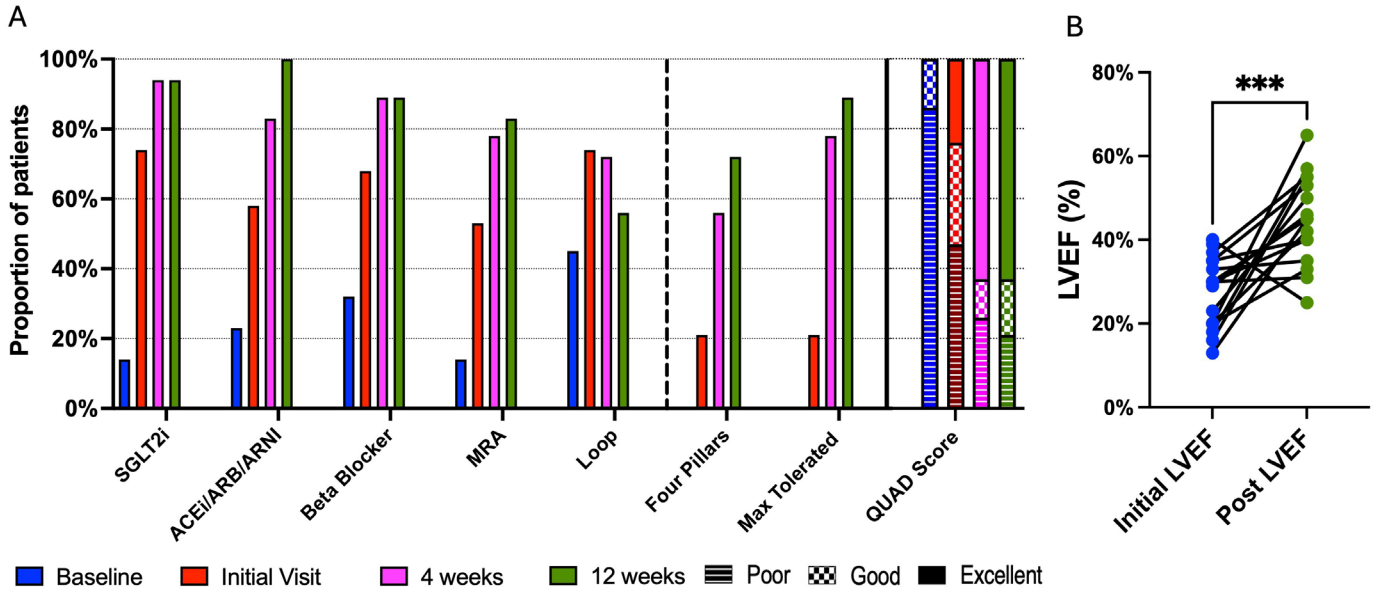


Figure 2 (A) The proportion of patients with HFrEF receiving each class of guideline-directed medical therapy at baseline, after initial visit, 4 weeks and 12 weeks, including the proportion receiving four-pillar therapy (ACEi/ARB/ARNI, beta-blocker, MRA and SGLT2 inhibitor), clinician-determined maximally tolerated therapy and QUAD score (poor <8, good 8-14, excellent >14). (B) Left ventricular ejection fraction at baseline and 3-month follow-up in patients with HFrEF who underwent repeat echocardiography. ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; SGLT2i, sodium–glucose cotransporter 2 inhibitor; ***p<0.0001, paired t test.

Our findings highlight several important points. First, very high NT-proBNP values consistently identified patients with advanced cardiac disease and a high short-term event risk, consistent with previous epidemiological evidence.[2 3] The rapid review facilitated not only early optimisation of HF therapy but also detection of other clinically significant conditions, including severe valvular disease and atrial fibrillation.

Second, the pathway substantially reduced time-to-assessment compared with routine care, where delays of over a month were typical. Patients enrolled in the pathway had earlier initiation and titration of guideline-directed medical

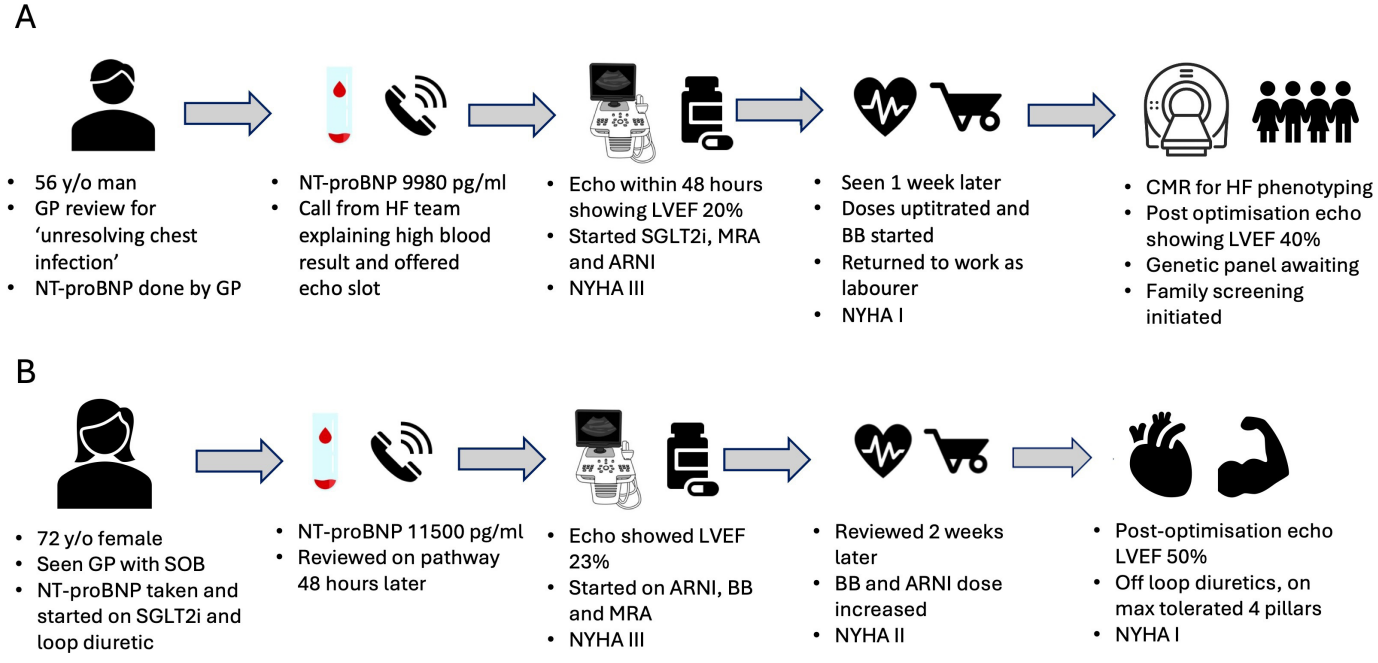


Figure 3 Two illustrative cases identified through the automated high-alert NT-proBNP pathway. ARNI, angiotensin receptor–neprilysin inhibitor; BB, beta blocker; CMR, cardiovascular magnetic resonance; HF, heart failure; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NYHA, New York heart association; SGLT2i, sodium–glucose cotransporter 2 inhibitor.

therapy, with a high proportion of HFrEF patients achieving quadruple therapy by 12 weeks. An improvement in LVEF was observed among patients with HFrEF who underwent paired follow-up echocardiography; however, causality cannot be inferred from this non-randomised study, and no direct comparison of LVEF change with the retrospective cohort was performed.

Third, feasibility was supported by the relatively small number of eligible patients (5% of all alerts), which limited service burden while targeting those at highest risk. However, implementation requires adequate echocardiography capacity and dedicated HF team input, which may not be available in all healthcare systems. Scalability to larger populations will therefore need careful evaluation.

The expected clinical value of this pathway lies primarily in automated identification, rapid assessment and early treatment optimisation of a small but very high-risk outpatient group, rather than in proving improved clinical outcomes within this feasibility study. Twelve-week all-cause admission rates were similar in the prospective and retrospective cohorts; however, three patients in the prospective cohort were admitted immediately following initial pathway review, suggesting that some early admissions may have reflected appropriate escalation of care after rapid clinical assessment. Similarly, although 12-week all-cause mortality was numerically lower in the prospective cohort, the modest sample size and non-randomised design preclude any inference of clinical effectiveness on hard outcomes such as mortality. The main benefit demonstrated is therefore operational: the pathway generated a manageable number of eligible referrals, enabled most patients to receive echocardiography and specialist review within 48 hours, identified actionable pathology including severe aortic stenosis and new atrial fibrillation and facilitated early initiation or optimisation of guideline-directed medical therapy. Whether this approach translates into improved longer-term outcomes requires prospective evaluation in larger, adequately powered studies.

Several limitations should be acknowledged. The study was observational and non-randomised, with modest numbers. Follow-up was limited to 12 weeks, so longer-term durability of benefit remains uncertain. Furthermore, exclusion of patients with advanced frailty or long-term residential care residence means that findings may not generalise to all individuals with very high NT-proBNP. While every effort was taken to match the retrospective comparator, there may have been a small number of individuals who would have been excluded from the prospective arm on grounds of having a CFS ≥7 which could not be captured in the retrospective data. Exclusion of retrospective patients without echocardiography may have introduced survivor bias, as those who died early or were too unwell for investigation may have been missed. This limits direct comparison with the prospective cohort, which had a much shorter interval from NT-proBNP testing to echocardiography. Follow-up echocardiograms were performed as part of routine clinical care. We therefore cannot exclude the possibility that sonographers recognised some patients as being enrolled in the high-alert pathway.

CONCLUSION

An automated NT-proBNP-driven high-alert pathway was feasible within routine clinical practice and enabled rapid specialist assessment of a small group of high-risk outpatients. The pathway identified patients with a high burden of cardiac disease and facilitated early treatment review. Observed improvements in symptoms and LVEF, particularly among patients with HFrEF, are encouraging but hypothesis-generating. Larger prospective studies are required to determine whether this approach improves clinical outcomes and is generalisable across healthcare systems.

Social media John Aaron Henry, X @johnaaronhenry; Andrew Robert John Mitchell, X @mitcharj

Contributors JAH, TS, PLP and ARJM conceptualised and designed the project. Data were collected by JAH, CB, CA, JD, TJ, MV, SOD, AA, BW, SP and EDS. Data analysis was conducted by JAH and CB. JAH, CB, PLP, OJR and ARJM contributed to data interpretation. The manuscript was written by JAH. All authors contributed to the article and approved the submitted version. JAH acts as guarantor.

Competing interests None declared.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer-reviewed.

Data availability statement Data are available upon reasonable request.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: https://creativecommons.org/licenses/by-nc/4.0/.

ORCID iD

John Aaron Henry https://orcid.org/0000-0002-7650-0963

REFERENCES

1 Bottle A, Kim D, Aylin P, *et al*. Routes to diagnosis of heart failure: observational study using linked data in England. *Heart* 2018;104:600–5.
2 Taylor CJ, Lay-Flurrie SL, Ordóñez-Mena JM, *et al*. Natriuretic peptide level at heart failure diagnosis and risk of hospitalisation and death in England 2004-2018. *Heart* 2022;108:543–9.
3 Januzzi JL, van Kimmenade R, Lainchbury J, *et al*. NT-proBNP testing for diagnosis and short-term prognosis in acute destabilized heart failure: an international pooled analysis of 1256 patients: the International Collaborative of NT-proBNP Study. *Eur Heart J* 2006;27:330–7.
4 Brown C, Wang B, Almeida C, *et al*. Evaluating early cardiology involvement and survival outcomes across NT-proBNP levels: An island-wide retrospective cohort study. *Eur J Heart Fail* 2025;27:2935–7.
5 Golcuk Y, Golcuk B, Velibey Y, *et al*. Predictive cutoff point of admission N-terminal pro-B-type natriuretic peptide testing in the ED for prognosis of patients with acute heart failure. *Am J Emerg Med* 2013;31:1191–5.
6 Taylor CJ, Ordóñez-Mena JM, Lay-Flurrie SL, *et al*. Natriuretic peptide testing and heart failure diagnosis in primary care: diagnostic accuracy study. *Br J Gen Pract* 2023;73:e1–8.
7 Hayhoe B, Kim D, Aylin PP, *et al*. Adherence to guidelines in management of symptoms suggestive of heart failure in primary care. *Heart* 2019;105:678–85.
8 Zheng A, Cowan E, Mach L, *et al*. Characteristics and outcomes of patients with suspected heart failure referred in line with National Institute for Health and Care Excellence guidance. *Heart* 2020;106:1579–85.
9 Savage HO, Dungu JN, Dimarco A, *et al*. A novel treatment score (QUAD score) to promote treatment optimization in heart failure with a reduced ejection fraction. *ESC Heart Fail* 2025;12:4150–9.