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ORIGINAL RESEARCH

Remotely Monitored Cardiac Implantable Electronic Device Data Predict All-Cause and Cardiovascular Unplanned Hospitalization

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BACKGROUND: Unplanned hospitalizations are common in patients with cardiovascular disease. The "Triage Heart Failure Risk Status" (Triage-HFRS) algorithm in patients with cardiac implantable electronic devices uses data from up to 9 device-derived physiological parameters to stratify patients as low/medium/high risk of 30-day heart failure (HF) hospitalization, but its use to predict all-cause hospitalization has not been explored. We examined the association between Triage-HFRS and risk of all-cause, cardiovascular, or HF hospitalization.

METHODS AND RESULTS: A prospective observational study of 435 adults (including patients with and without HF) with a Medtronic Triage-HFRS–enabled cardiac implantable electronic device (cardiac resynchronization therapy device, implantable cardioverter-defibrillator, or pacemaker). Cox proportional hazards models explored association between Triage-HFRS and time to hospitalization; a frailty term at the patient level accounted for repeated measures. A total of 274 of 435 patients (63.0%) transmitted ≥1 high HFRS transmission before or during the study period. The remaining 161 patients never transmitted a high HFRS. A total of 153 (32.9%) patients had ≥1 unplanned hospitalization during the study period, totaling 356 nonelective hospitalizations. A high HFRS conferred a 37.3% sensitivity and an 86.2% specificity for 30-day all-cause hospitalization; and for HF hospitalizations, these numbers were 62.5% and 85.6%, respectively. Compared with a low Triage-HFRS, a high HFRS conferred a 4.2 relative risk of 30-day all-cause hospitalization (8.5% versus 2.0%), a 5.0 relative risk of 30-day cardiovascular hospitalization (3.6% versus 0.7%), and a 7.7 relative risk of 30-day HF hospitalization (2.0% versus 0.3%).

CONCLUSIONS: In patients with cardiac implantable electronic devices, remotely monitored Triage-HFRS data discriminated between patients at high and low risk of all-cause hospitalization (cardiovascular or noncardiovascular) in real time.

Key Words: all-cause hospitalization ■ cardiac-resynchronization therapy ■ cardiovascular hospitalization ■ heart failure ■ implantable cardioverter defibrillators ■ remote monitoring ■ risk prediction

Prediction of hospitalization risk in patients with cardiovascular disease is notoriously challenging. Over the past decade, various risk tools have been proposed for the prediction of heart failure (HF) hospitalization, but few studies have prospectively examined the utility of real-time data from remotely monitored cardiac implantable electronic devices (CIEDs) for this purpose or extended prediction to all-cause hospitalization.[1,2]

Contemporary CIEDs contain multiple built-in sensors that monitor a wide range of physiological parameters (including heart rate profile, burden of atrial

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CLINICAL PERSPECTIVE

What Is New?

- This is the first real-world study to show that remotely monitored TriageHF risk data identifies ambulatory device patients with heart failure (HF) who are at significantly increased risk of unplanned all-cause and cardiovascular hospitalizations, in addition to HF hospitalizations, in the next 30 days.
- 60% of unplanned HF hospitalizations, and over one-third of cardiovascular hospitalizations, were preceded by a high-risk status in the 30 days prior, highlighting the predictive utility of a "high" risk status to identify patients who are at increased risk of imminent hospitalization to clinical teams.
- Although just 14.6% of the diagnostic episodes were evaluated as being high, they contributed to 44.8% of the overall costs for all-cause hospitalization and 69.6% of the overall costs of the HF hospitalizations.

What Are the Clinical Implications?

- Remotely monitored TriageHF risk data provides useful risk stratification for healthcare providers and may help identify patients in the community who are at increased risk of imminent hospitalization, who could benefit from targeted guideline-directed interventions.

Nonstandard Abbreviations and Acronyms

CIED	cardiac implantable electronic device
CRT	cardiac resynchronization therapy
CRTD	cardiac resynchronization therapy with defibrillator
HFH	heart failure hospitalization
SUSHRG	Secondary Uses Services Healthcare Resource Group
Triage-HFRS	Triage Heart Failure Risk Status

fibrillation, treated ventricular arrhythmias, percentage of biventricular pacing, changes in intrathoracic impedance, and physical activity), continuously and automatically. TriageHF is an integrated diagnostic algorithm that uses a Bayesian Belief Network to combine physiological data derived from compatible Medtronic CIEDs to stratify patients as low-, medium-, or high-risk of HF hospitalization (HFH) in the next 30 days.[3] A patient's risk status is presented clinically as their maximum HF Risk Status (HFRS) in the preceding 30 days.

The original development and validation of the Triage-HFRS algorithm used pooled data from various historical clinical studies, using data primarily from cardiac resynchronization therapy with defibrillator (CRTD) devices.[3] Since this time, the adoption of remote monitoring ancillary functions has expanded to other devices, such as cardiac resynchronization therapy with pacemaker devices, implantable cardioverters-defibrillators, and pacemakers. This raises the question of clinical utility in a broader population. In addition, recent research has suggested the Triage-HFRS may predict important non-cardiac acute medical events in addition to HFH, an important consideration when designing services for a (generally) older multimorbid population.

Therefore, the aim of this study was to describe the association between the Triage-HFRS and 30-day nonelective hospitalization (all cause, cardiovascular related, and HF related) in a real-world clinical cohort.

METHODS

Data Availability

The study data set will be made available to other researchers for the purpose of reproducing the results on reasonable request to the corresponding author, subject to institutional and ethical committee approvals.

Study Design, Setting, and Participants

This was a prospective observational study of patients with Triage-HFRS–enabled CIEDs (cardiac resynchronization therapy [CRT] device, implantable cardioverter-defibrillator, or pacemaker) in situ, under follow-up at Manchester Heart Centre (England, UK). Patients with at least 1 recorded Triage-HFRS transmission between December 1, 2016, and December 31, 2018, were included. Eligible patients were aged ≥18 years.

Study Outcomes

The primary outcome examined in this study was all-cause nonelective hospitalization. Secondary outcomes were nonelective cardiovascular and nonelective HFH.

Ethical Approval

The Health Research Authority's Confidentiality Advisory Group granted a confidentiality waiver (section 251) in the National Health Service (NHS) Act to link data from electronic health records, cardiac devices, and NHS Digital (as outlined below; 19/Confidentiality Advisory Group/0055). This study complies with the Declaration of Helsinki.

Data Sources and Collection

Demographic data were obtained from integrated electronic hospital care records (Chameleon) and linked primary care data for each patient in the study. Device data were collected via the One Hospital Clinical Service platform, which pulls data from the Medtronic Carelink Network for research and audit purposes. This comprised Triage-HFRS data for the duration of the study, where transmissions had been received. For the duration of the evaluation, the use of the Triage-HFRS was not formally embedded as part of the clinical care pathway, although access to summarized maximum risk status data in the last 30 days was available via the Medtronic Carelink platform.

National Health Service Digital, a centralized service that collates data for all secondary care services provided by the NHS, provided national hospitalization data for the study duration by linking each patient's NHS number. This ensured hospitalization episodes were recorded for all included patients, regardless of the location of the hospitalization. "Hospitalization" was defined as a nonelective admitted patient care episode. Data corresponding to all hospitalization episodes from January 1, 2017, to December 31, 2018, were obtained. A more detailed outline of NHS Digital data processing is available in Data S1 through S3 and Figures S1 through S3. Secondary Uses Services Healthcare Resource Group (SUSHRG) codes were used to determine if an episode was cardiovascular or HF related. Clinical coding permitting, HF admissions were presented separately to non-HF cardiovascular admissions (more information available at https://digital.nhs.uk/services/secondary-uses-service-sus). All diagnostic codes were independently reviewed by 2 clinicians (authors F.Z.A. and J.K.T.) to ensure correct clinical categorization (Tables S1 through S3).

Statistical Analysis

For descriptive analyses, continuous variables were summarized using the mean (or median for heavily skewed data), with corresponding SDs (interquartile range). Categorical variables were presented as frequencies of occurrence with relative percentages.

Patients were categorized according to the time frame of first recorded high-risk Triage-HFRS. "High at baseline" signified a patient who transmitted a high HFRS before the start of study, or whose first received transmission was "high." Conversely, patients with no "high" HRFS transmissions before, or during, study duration were categorized as "never high," and those who transmitted a "high" HFRS for the first time during the study period were categorized as "switchers." Example profiles for each of these are given in Figure 1.

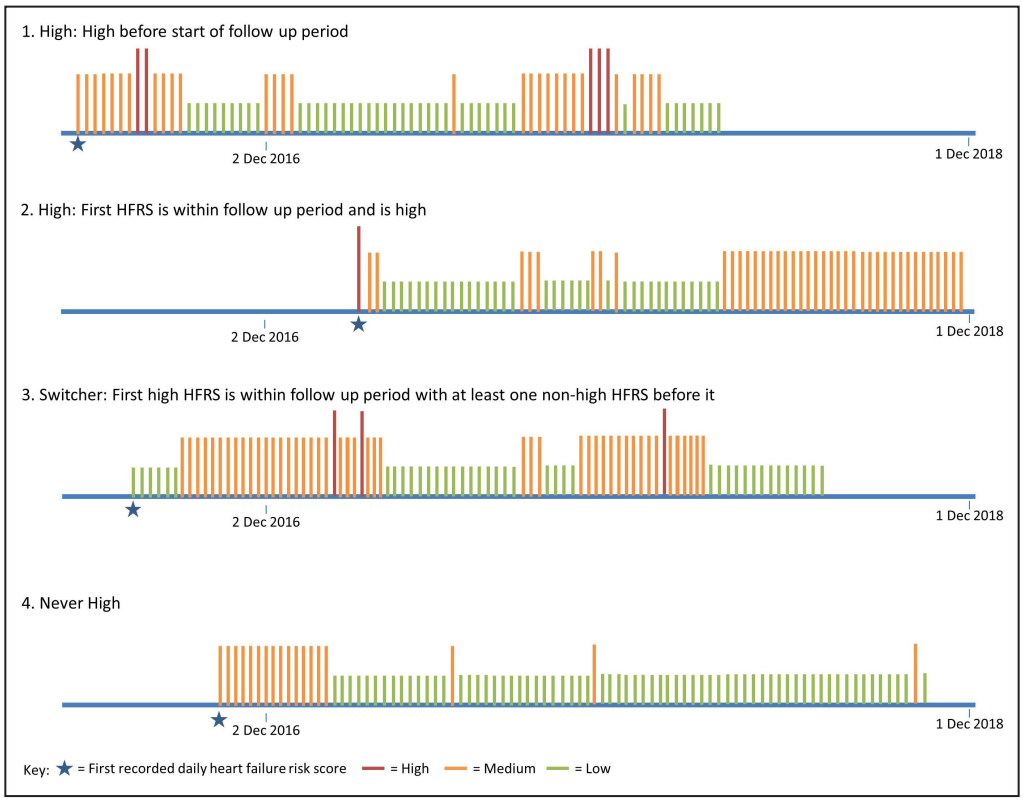

Figure 1. Example profiles for each of the patient categories: high, switcher, and never high.
HFRS indicates Heart Failure Risk Status.

Two main analyses were undertaken. First, we calculated the proportion of nonelective all-cause hospitalizations, cardiovascular hospitalizations, and HFHs, according to the maximum recorded Triage-HFRS in the prior 30 days, 6 months, and 12 months of each type of hospitalization. This first analysis aims to describe the maximum transmitted risk score leading up to the hospitalization and is hereto called "retrospective analysis."

Second, the transmitted data of each patient were split into 30-day rolling-window evaluation periods, and the maximum recorded Triage-HFRS for this period was evaluated (Data S2). This second analysis, which mirrors how the Triage-HFRS would be applied in clinical practice, is hereto called "prospective analysis." Diagnostic test evaluations included sensitivity, specificity, and negative predictive value (NPV) using high versus nonhigh Triage-HFRS. We proceeded to prospective modeling with the outcome defined as time to hospitalization, starting from the end of each 30-day evaluation period until either the first hospitalization (event) or 30 days (censoring), whichever occurred first. We fitted a Cox proportional hazards model to this outcome, with a frailty (random effect) term at the patient level and the maximum Triage-HFRS in the 30-day evaluation period as a covariate. We also adjusted for age, device type, baseline HF, and baseline chronic kidney disease stage ≥3 (with these variables selected a priori). We repeated the second analysis for time-to-cardiovascular hospitalization only, where we used a cause-specific competing risk framework. Accident and Emergency department attendance data, which provide limited data about clinical diagnosis, were combined with admitted patient care episodes as a composite outcome, providing a sensitivity analysis for the study (Tables S2 through S9 and Figures S2 and S3). All analyses were undertaken in R version 3.6.0, along with the packages tidyverse, furniture, survival, and survminer.[4–8]

Cost Analysis

National tariffs linked to SUSHRG codes provided by NHS Digital for each of the hospitalizations were used to examine the relationship between Triage-HFRS status, health care use, and cost of care. The corresponding national tariffs for the relevant financial years were used to assign a cost for each of the hospitalizations. Admitted patient care episodes were costed according to the length of stay; if a patient stayed for longer than the trim point, an additional per-day cost was added to the standard nonelective tariff, otherwise the hospitalization was costed as the standard nonelective tariff. This is standard costing practice for NHS hospitalization data.

RESULTS

Patients

A total of 435 patients were included in the study, with a total follow-up of 630.1 patient-years. Most patients had a CRT device (77.2%) and New York Heart Association functional class ≥2 (68.0%) at baseline (Table 1). The mean age was 66 years, with 45.7% aged >70 years. Table 1 outlines the demographics of the studied cohort.

In total, 274 of 435 (63.0%) patients transmitted at least 1 high Triage-HFRS transmission; this group was composed of 105 patients categorized as "baseline high" (ie, a high Triage-HFRS either before the study or on first received transmission during study period) and 169 "switchers" (ie, transitioned from a lower-risk status to their first recorded high, during study period) (Figure 1). The remaining 161 patients never transmitted a high Triage-HFRS before, or during, the study (ie, "never high").

Study Outcomes

Retrospective Analysis: Triage-HFRS Preceding Hospitalization Episodes

There were 356 all-cause hospitalization episodes (128 cardiovascular and 47 HF) throughout the study period (Table 2). In the 30 days before hospitalization, maximum Triage-HFRS was high in 36.85% (131) of cases (of these, 39.1% [n=50] were cardiovascular and 59.6% [n=28] were HFHs). Seven hospitalization episodes were preceded by a 6-month period of stable low HFRS (2%), with no episodes being preceded by a 12-month period of continuous low risk. Further data are available in Data S3.

Prospective Analyses: Triage-HFRS and 30-Day Nonelective Hospitalization

There were 6819 30-day diagnostic evaluation periods (as defined in the Methods section) with complete Triage-HFRS data, from a total of 429 patients. The maximum risk was high for 996 (14.6%), medium for 3535 (51.8%), and low for 2288 (33.6%) 30-day diagnostic evaluation periods. A total of 228 (3.3%) 30-day diagnostic evaluation periods had a corresponding hospitalization in the following 30 days (from the end of each diagnostic evaluation period), of which 89 (39.0%) were cardiovascular-related admissions containing 32 HF-related admissions (Table 3). A high HFRS conferred a 37.3% sensitivity and an 86.2% specificity for 30-day all-cause hospitalization (a nonhigh score offered an NPV of 97.5%). For cardiovascular hospitalizations, sensitivity and specificity were 39.3% and 85.7%, respectively (NPV, 99.1%); and for HFHs, sensitivity and specificity were 62.5% and 85.6%, respectively (NPV,

Table 1. Baseline Patient Demographics

Demographic	Total	Baseline high	Switcher	Never high	*P* value
Patients, n	435	105	169	161	
Age, mean (SD), y	66.0 (15.5)	68.3 (14.7)	67.3 (15.5)	63.2 (15.6)	0.011
Men	276 (63.4)	62 (59)	112 (66.3)	102 (63.4)	0.482
Device type					0.161
CRTD	166 (38.2)	36 (34.3)	67 (39.6)	63 (39.1)	
CRTP	170 (39.0)	46 (43.8)	70 (41.4)	54 (33.5)	
ICD	36 (8.3)	5 (4.8)	11 (6.9)	20 (12.4)	
PPM	63 (14.5)	18 (17.1)	21 (12.4)	24 (14.9)	
NYHA class (missing data n=22)					0.055
No heart failure	62 (14.3)	13 (12.4)	19 (11.2)	30 (18.6)	
1	55 (12.6)	9 (8.6)	17 (10.1)	29 (18)	
2	151 (34.7)	39 (37.1)	61 (36.1)	51 (31.7)	
≥3	145 (33.3)	37 (35.2)	63 (37.3)	45 (28)	
LVEF <35 (missing data n=6), %	241 (56.1)	61 (58.1)	102 (60.4)	78 (48.4)	0.071
Atrial fibrillation/flutter (missing data n=3)	188 (43.2)	52 (49.5)	78 (46.2)	58 (36.0)	0.070
Diabetes (missing data n=18)	103 (23.7)	27 (25.7)	45 (26.6)	31 (19.3)	0.264
COPD (missing data n=17)	54 (12.4)	15 (14.3)	21 (12.4)	18 (11.2)	0.807
CKD stage ≥3 (missing data n=4)	134 (30.8)	35 (33.3)	53 (31.4)	46 (28.6)	0.654
At least 1 comorbidity (missing data n=10)*	388 (89.2)	98 (93.3)	156 (92.3)	134 (83.2)	<0.001
Medications					
β Blockers (missing data n=35)	319 (79.8)	74 (70.5)	132 (78.1)	113 (70.2)	0.282
ACE-I/ARB/ARNI (missing data n=37)	273 (68.6)	67 (63.8)	101 (59.8)	105 (65.2)	0.413
MRA (missing data n=38)	149 (37.5)	39 (37.1)	64 (37.9)	46 (28.6)	0.144
Diuretic (missing data n=37)	206 (51.8)	61 (58.1)	86 (50.9)	59 (36.6)	<0.001

Data are indicated as number (percentage), unless otherwise stated. ACE-I indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor and neprolysin inhibitor; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRTD, cardiac resynchronization therapy with defibrillator; CRTP, cardiac resynchronization therapy with pacemaker; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; and PPM, permanent pacemaker.

*Including heart failure, atrial fibrillation/flutter, diabetes, COPD, and CKD stage ≥3.

99.7%). Figure 2 demonstrates the cumulative probability of hospitalization (all cause and cardiovascular) following a first high risk score.

Compared with a diagnostic period with the maximum risk being low, a period evaluated as high risk conferred a 4.2 relative risk (8.5% versus 2.0%) of a 30-day all-cause hospitalization, a 5.0 relative risk (3.6% versus 0.7%) of a 30-day cardiovascular hospitalization, and a 7.7 relative risk (2.0% versus 0.3%) of a 30-day HFH (Table 3). Figure 3 illustrates the Kaplan-Meier cumulative probability of hospitalization by type, indicating clear differences between the maximum recorded risk within 30 days being high compared with medium or low. Demographics of patients who experienced hospitalizations are provided in Table S10.

Compared with low HFRS evaluations, a high HFRS evaluation was associated with significantly increased risk of subsequent 30-day all-cause and cardiovascular hospitalization. We observed a hazard ratio (HR) of 2.9 (95% CI, 1.88–4.40; *P*<0.001) for the high-HFRS evaluations compared with low-HFRS evaluations for subsequent 30-day all-cause hospitalization events, and an HR of 4.1 (95% CI, 2.08–8.01; *P*<0.001) for cardiovascular hospitalization when fitting the frailty models to the data (Table 4). The latter remained significant when adjusting the model for nonproportional hazards (Table S11) to a HR of 2.4 (95% CI, 1.65–3.51; *P*<0.001). In addition, having a non-CRT device was associated with a decreased hazard of a patient having an all-cause hospitalization (permanent pacemaker: HR, 0.40 [95% CI, 0.18–0.94]; *P*=0.03; implantable cardioverter-defibrillator: HR, 0.31 [95% CI, 0.12–0.81]; *P*=0.02) compared with those with a CRTD device (Table 4).

Cost Analysis

The cost of all-cause hospitalization for high-, medium-, or low-risk status events was £245 924, £209 337, and £93 604, respectively (Table S12). Over 38% of these total costs were attributed to cardiovascular hospitalizations within each risk group (high, 42.4%; medium, 38.6%; low, 41.6%). Across all-cause hospitalization, cardiovascular hospitalization, and HFH, the cost of

Table 2. Retrospective Analysis: Hospitalization Episodes by Maximum Risk Recorded Within the Previous 30 Days, 6 Months, and 12 Months

Variable	Maximum risk recorded in previous 30 d				Maximum risk recorded in previous 6 mo				Maximum risk recorded in previous 12 mo				Total
	Low	Medium	High	No transmissions received	Low	Medium	High	No transmissions received	Low	Medium	High	No transmissions received	
All-cause hospitalization	74 (20.8)	145 (40.7)	131 (36.8)	6 (1.7)	7 (2.0)	143 (40.2)	204 (57.3)	2 (0.6)	0 (0.0)	122 (34.3)	234 (65.7)	0 (0.0)	356
Cardiovascular hospitalization	21 (16.4)	54 (42.2)	50 (39.1)	3 (2.3)	3 (2.3)	48 (37.5)	76 (59.4)	1 (0.8)	0 (0.0)	43 (33.6)	85 (66.4)	0 (0.0)	128
HF hospitalization	5 (10.6)	12 (25.5)	28 (59.6)	2 (4.3)	0 (0.0)	12 (25.5)	34 (72.3)	1 (2.1)	0 (0.0)	12 (25.5)	35 (74.5)	0 (0.0)	47

Data are given as number (percentage), unless otherwise indicated. HF indicates heart failure.

hospitalization was markedly higher for high Triage-HFRS status events compared with medium- and low-risk events (Tables S12 and S13). Although just 14.6% of the diagnostic episodes were evaluated as being high, they contributed to 44.8% of the overall costs for all-cause hospitalization and 69.6% of the overall costs of the HFHs, highlighting the disproportionate impact on cost associated with a high Triage-HFRS (Figure 4). Furthermore, the cost of an all-cause hospitalization corresponding to a high Triage-HFRS was on average >£1000 more than the average cost of an all-cause hospitalization corresponding to a low Triage-HFRS (Table S12). The average cost for all-cause hospitalizations was >50% higher in those who had at least 1 day evaluated as a high HFRS compared with those who were low for the entire 30 days before the hospitalization (£3616.33 versus £2340.10).

DISCUSSION

This is the first prospective real-world study to report that remotely monitored risk data from cardiac devices, originally developed to identify patients at increased risk of HFH, can also be used to predict all-cause and cardiovascular unplanned hospitalization. The key findings were as follows: (1) experiencing any high-risk episode was associated with significantly increased risk of all-cause and cardiovascular hospitalization and (2) a nonhigh Triage-HFRS conferred a >97% NPV of all-cause and cardiovascular hospitalization. Therefore, the Triage-HFRS is a useful tool to risk stratify patients according to their risk of 30-day healthcare use.

Triage-HFRS and All-Cause Hospitalization

In contrast to previous studies, the current analysis examined noncardiovascular hospitalizations to understand the utility of Triage-HFRS to be used more broadly. A high Triage-HFRS 30-day maximum risk was associated with a 4.2 relative risk and a 2.9-fold increased hazard of 30-day all-cause hospitalization. A total of 1 in 6 patients had an unplanned admission following their first high, with most occurring within 3 months. The retrospective analysis provides additional insights; 1 in 3 patients who experienced an unplanned all-cause hospitalization had transmitted a high Triage-HFRS in the preceding 30 days. The leading diagnoses for these admissions included respiratory infections and sepsis. Given some of the nonspecific components of the Triage-HFRS algorithm (eg, heart rate and physical activity), it is not surprising that a high Triage-HFRS preceded noncardiovascular admissions. In addition, thoracic impedance measures are known to be affected by clinical states without concurrent ventricular dysfunction.[9] This highlights the

Table 3. Maximum Triage-HFRS and Associated 30-Day Hospitalizations

30-d Diagnostic evaluation period maximum Triage-HFRS	Total diagnostic evaluation periods	30-d Hospitalizations		
		All cause	Cardiovascular	Heart failure
Low	2288 (33.6)	46 (2.0)	16 (0.7)	6 (0.3)
Medium	3535 (51.8)	97 (2.7)	38 (1.1)	6 (0.2)
High	996 (14.6)	85 (8.5)	35 (3.6)	20 (2.0)
Total	6819 (100)	228 (3.3)	89 (1.3)	32 (0.5)

Data are given as number (percentage). Triage-HFRS indicates Triage Heart Failure Risk Status.

need for a high HFRS to be interpreted clinically, particularly in patients with significant comorbidities.

Triage-HFRS and Cardiovascular Hospitalization

The wider utility of Triage-HFRS to predict and identify a broader range of cardiovascular causes of hospitalization beyond HF alone is of interest to the general cardiology community. To date, only one study has previously examined the association between Triage-HFRS and cardiovascular hospitalizations; a post hoc analysis of the MORE-CARE (The Monitoring Resynchronization Devices and Cardiac Patients) Randomized Controlled Trial (patients enrolled between 2009–2014), originally designed to examine the efficacy of remote monitoring in patients with CRTD, reported that a high-risk status was associated with a 4.5 relative risk of 30-day cardiovascular hospitalization. In the current study, when all device types are considered, we report that the relative risk of a 30-day cardiovascular hospitalization was 5.0 and an associated HR of 2.4, where common non-HF cardiovascular hospitalizations included arrhythmias, chest pain, myocardial infarction, and angina. The retrospective analysis provides a different perspective; 1 in 3 patients with an unplanned cardiovascular hospitalization and 60% of those with HFH transmitted a high Triage-HFRS in the preceding 30 days.

When considering longer-term risk of hospitalization, most cardiovascular hospitalizations (over two thirds) were preceded by a high TriageHF risk status in the 12 months before admission. Of those who experienced an HFH, 87.5% had a CRT device, and 3 in 4 HFHs had a high-risk status recorded within the previous 12 months.

Triage-HFRS, Device Type, and HFH

Previous evaluations of Triage-HFRS have, for the most part, examined utility to identify patients with CRTD at

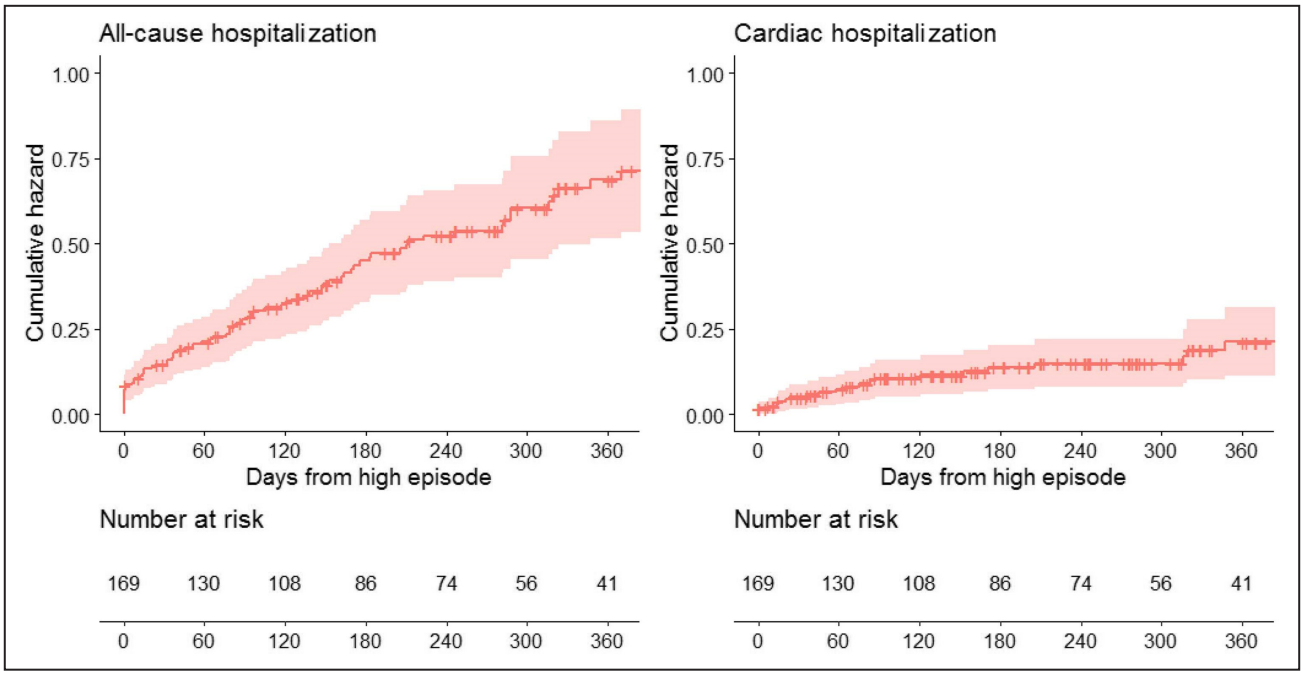

Figure 2. Kaplan-Meier cumulative incidence curves of a subsequent all-cause and cardiovascular hospitalization episode following the start of the first date a patient was recorded as being in high risk for the patients who experienced their first high Heart Failure Risk Status during the study (ie, switchers).
All-cause hospitalizations occurred more frequently within the first 180 days, but cardiovascular events occurred linearly with time.

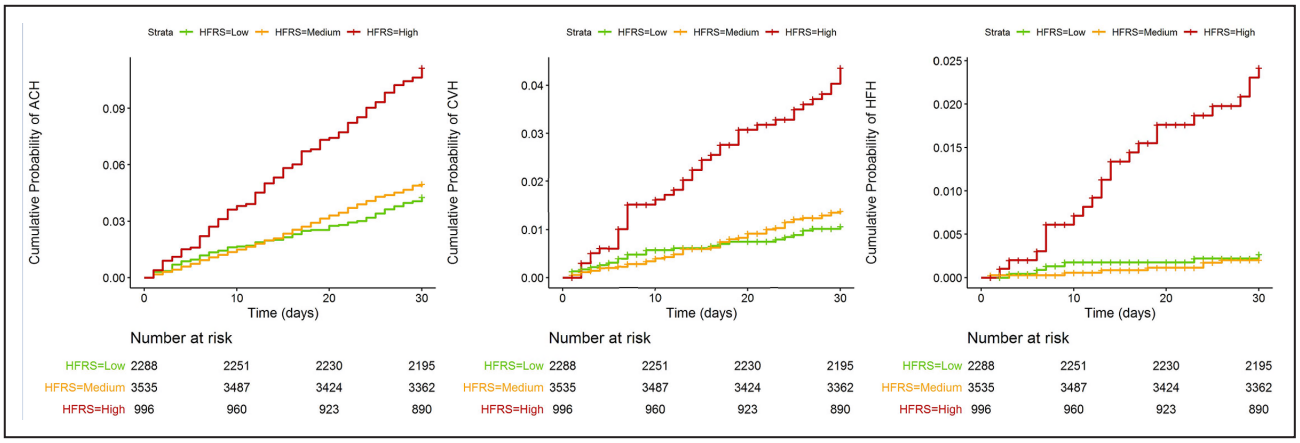

Figure 3. Kaplan-Meier cumulative incidence curves for all-cause hospitalization (ACH), cardiovascular hospitalization, and heart failure hospitalization within the 30 days following the diagnostic evaluation period, stratified by the maximum Heart Failure Risk Status (HFRS) reported in the diagnostic evaluation period.
The high-risk group had a larger incidence across all types of hospitalization compared with those who were medium or low risk after 7 days.

increased risk of HFH. Using pooled data from historical studies undertaken between 2004 and 2008,[10–14] the original validation of Triage-HFRS reported that a high-risk status was associated with a 10-fold increase in risk of 30-day HFH.[3]

We present results for an unselected, real-world cohort across the entire spectrum of Triage-HFRS–compatible devices. This is important clinically as it more accurately represents the population being monitored, encompassing a broader population of patients that also includes those without an HF diagnosis and patients with cardiac resynchronization therapy with pacemaker and permanent pacemaker devices. It was anticipated this would confer a lower hospitalization rate compared with previous Triage-HFRS evaluations; however, in fact, we found that risk of 30-day HFH was similar.[15,16] We report that having a non-CRT device was associated with a decreased hazard of a patient having an all-cause hospitalization compared with those with a CRTD device, with fewest hospitalizations observed in patients with non-CRT devices. However, although >75% of the patients in our sample had CRT devices, the results found that HF and device type were not significant in relation to cardiovascular hospitalization (Table S14 compares New York Heart Association class across device types). This is reassuring in terms of the utility of HF monitoring in non-CRT devices. However, further analyses in populations with higher proportions of non-CRT devices could be warranted.

We found that when all devices are considered, experiencing at least 1 day in a high-risk status resulted in a relative risk of 7.8 for a 30-day HFH. In the current analysis, only 1 in 8 unplanned HFHs occurred in patients without CRT. Furthermore, we found that having a brady pacemaker (non-CRT) was associated with a

Table 4. Hospitalization Model Coefficients From Frailty Models Assuming Proportional Hazards

	All-cause hospitalizations within 30 d			Cardiovascular hospitalizations within 30 d		
Variable	Hazard ratio	95% CI	*P* value	Hazard ratio	95% CI	*P* value
Medium (vs low)	1.126	0.764–1.658	0.55	1.371	0.735–2.561	0.32
High (vs low)	2.874*	1.878–4.399	<0.001*	4.080*	2.077–8.012	<0.001*
No heart failure	0.961	0.423–2.180	0.92	0.975	0.293–3.247	0.97
Age	1.015*	1.000–1.031	0.05*	1.017	0.993–1.041	0.17
CRTP vs CRTD	0.668	0.428–1.042	0.08	0.559†	0.285–1.097	0.09
PPM vs CRTD	0.405*†	0.175–0.937	0.03*	0.549†	0.167–1.806	0.32
ICD vs CRTD	0.306*	0.116–0.807	0.02*	0.268	0.063–1.146	0.08
CKD stage ≥3	1.282	0.832–1.981	0.26	1.245†	0.643–2.412	0.52

CKD indicates chronic kidney disease; CRTD, cardiac resynchronization therapy with defibrillator; CRTP, cardiac resynchronization therapy with pacemaker; ICD, implantable cardioverter-defibrillator; and PPM, permanent pacemaker.
*Denotes that the comorbidities assessed include one or more of these conditions.
†Indicates a time-varying coefficient where nonproportional hazards were observed. Further analyses performed to stratify details are provided in Table S11.

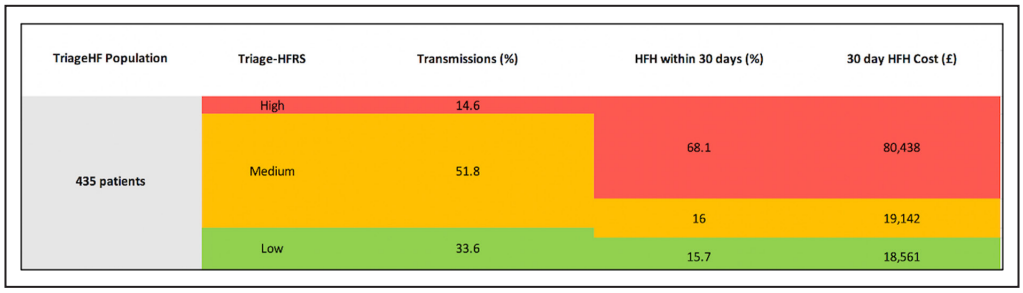

Figure 4. Visual representation of the relationship between Triage Heart Failure Risk Status (Triage-HFRS), frequency of transmission, 30-day heart failure hospitalization (HFH) cost (percentage), and total cost of HFH (£), according to Secondary Uses Services Healthcare Resource Group.

decreased hazard of all-cause hospitalization. These 2 findings suggest that remote monitoring of HF risk status is likely to be most advantageous in populations with CRT, in those in whom HF and poor functional status are more prevalent, and adds little value in patients with brady pacemakers.

Cost Perspectives

The financial cost of hospitalizations associated with a high Triage-HFRS status was significantly higher compared with those associated with a medium- or low-risk status. For the prospective analyses, even though only 14.6% of the diagnostic episodes were evaluated as being high, they contributed to 69.6% of the overall costs of the HFHs, highlighting that although high-risk episodes constituted only a small proportion of the overall follow-up, hospitalizations associated with these episodes had a disproportionate impact on cost. Furthermore, the all-cause hospitalizations corresponding to a high-risk evaluation had an average increased cost of >£1000 compared with the low-risk evaluations, largely driven by noncardiovascular hospitalizations. This indicates that there is a potential cost-benefit of targeting patients with a high Triage-HFRS to prevent both cardiovascular and noncardiovascular hospitalizations.

Clinical Perspectives

Identifying high-risk patients with HF is an important aspect of clinical care.[17] Several multivariable risk scores for the prediction of outcomes in patients with HF have been developed. However, for the most part, these focus on predicting risk of all-cause mortality rather than hospitalization.[18,19] Stratifying risk of HFH in an ambulatory population with chronic HF remains an area of primary research.[20] Another important limitation of traditional risk models is that they become out of date if there is a change in clinical circumstance (eg, the patient gets older or there is a change in medications or blood pressure). Device-based risk prediction models take a different approach to traditional risk models and are aligned to "risk" being a dynamic process that is continuously changing. Device-derived measurements are continuously monitored and automatically updated on a daily basis, enabling dynamic real-time assessment of risk of both hospitalization and mortality.[9,21–23]

The TriageHF alert-based monitoring system has been available for clinical use in the United Kingdom since 2016; however, formal monitoring has been limited to a small number of enthusiastic centers.[24,25] This study highlights the utility of the Triage-HFRS to risk stratify patients according to risk of 30-day hospitalization. Given the limited resources of HF community teams, using the Triage-HFRS to guide the prioritization of specialist care to patients at high risk of HF decompensation could be both clinically advantageous and cost saving. The best way to implement this and assess impact on clinical outcomes is an area of ongoing research (TriageHF Plus ClinicalTrials.gov Identifier: NCT04177199). In addition, an NPV of 99.7% for HFH may justify use as a screening tool to identify stable patients for whom monitoring frequency can be deescalated.

Limitations

Although hospital episode data were available from January 1, 2017, to December 31, 2018, the risk score data availability depends on the implant date of a Triage-HFRS–compatible device and contact with the home monitoring console. Consequently, the risk score may not cover the study period for all patients. Overall, the average follow-up per patient for the transmission data was 521.4 days. A small proportion of the transmission data was missing (1.9%), with most patients having no missing transmission data (n=396 [92.3%]). Of those who did have missing transmission data, the average number of days that a patient was missing transmission data was 10.1 days.

There are some periods of missing HFRS data before hospitalization. This could correspond to an

incorrect classification when evaluating the maximum risk before the event. For example, 19 of the all-cause nonelective admissions that only transmitted low-risk statuses had at least 1 day without a risk status and could have experienced a higher risk on one of these days. Similarly, we did not have information on some potentially important baseline demographic data, such as race and ethnicity.

Admitted patient care hospitalization diagnoses are based on SUSHRG codes, which differ slightly from *International Classification of Diseases* (*ICD-10*) codes. Although most codes led to consistent classification into cardiovascular HF, cardiovascular non-HF, and noncardiovascular, there were 11 of 356 (3.1%) admitted patient care episodes that were incongruent (Table S15). This could be in part because only one primary SUSHRG code per admission is recorded; therefore, concurrent diagnoses may be missed. Once hospitalized, patients often receive treatment for >1 acute medical problem. However, as only one SUSHRG code is assigned per admission, the true cost of care may be underestimated, particularly in those patients who receive treatment for multiple problems and those who develop hospital-acquired complications. Furthermore, the clinical coding for accident and emergency department admissions did not distinguish between HF and non-HF cardiovascular events. See Tables S1 through S3, S9, and S15 for more detail on SUSHRG codes.

In this analysis, it was not possible to evaluate the association between the HFRS and HFH because of the small number of episodes. Furthermore, the cohort contained relatively small numbers of patients with non-CRTS (implantable cardioverters-defibrillators in particular) because of the demographic of the population who had compatible devices. This is attributable to the way that TriageHF technology was available (according to device type) at inception. A larger study would be required to more accurately estimate the associations within this subpopulation. Finally, as is commonplace in clinical practice, a service improvement project was underway during the course of the current evaluation, whereby the Triage-HFRS data were available for review by the cardiac care team via the Carelink platform. Therefore, although the current study did not consider the impact of any downstream human interaction out with standard care, Triage-HFRS data for 1.9% of episodes (127/6819 episodes) were reviewed by the cardiac care team.[24] Because of the small numbers, this is unlikely to have had an impact on the results of the current evaluation.

CONCLUSIONS

Remotely monitored, risk-based CIED-derived data identify patients at higher risk of 30-day all-cause, cardiovascular, and HF hospitalization. Future research should focus on using the Triage-HFRS as a remote clinical management tool to facilitate rapid medical intervention, either remote or in the community, potentially avoiding need for hospitalization.

ARTICLE INFORMATION

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Supplemental Material

Data S1–S3
Tables S1–S15
Figures S1–S3

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SUPPLEMENTAL MATERIAL

Data S1. NHS Digital data processing

For the admitted patient care episodes, we had only 1 episode with a missing length of stay after cleaning. However, this event occurred after the final transmitted HFRS, hence its length of stay (LoS) would not affect the validation. For the episodes which overlapped with other episodes, the earliest episode with the longest length of stay was chosen. Of those that were excluded, only 2 cardiovascular episodes were excluded in favour of a non-cardiovascular episode with a longer LoS admitted on the same date, 10 were excluded for occurring within a previous episode but none of these affected the episode type (cardiovascular vs non-cardiovascular). There were 570 A&E admissions recorded within the HFRS follow up (+30days) between 1 Jan 2017 and 31 Dec 2018. After data cleaning and removal of duplicate entries, there were a total of 554 A&E admissions. The exclusion diagrams are shown in Figure S1.

Of the 554 ED admissions, 314 were matched to an APC episode with the same date of admission (n=219) or admission the day after that of the A&E episode (n=95). Of these matched admissions, 181 were recorded as non-cardiovascular for both A&E and APC, 39 were non-cardiovascular A&E admissions but had a cardiovascular APC, 28 were a cardiovascular A&E but non-cardiovascular APC and 66 were cardiovascular for both the A&E admission and APC episode. Seven of the A&E admissions were linked to ‘elective’ or ‘other’ admission types.

Data S2. Evaluation Period Generation

For each patient,

1. Initiate the start date as the first recorded HFRS transmission within the follow up of that patient.
2. For the given start date, define a (patient-level) 30-day evaluation period to be 30 consecutive days from the start date.
3. Determine whether:
    a. the last recorded HFRS occurs after the end of the 30-day evaluation period: if not, there is not enough HFRS data for this period, move on to the next patient and restart procedure.
    b. there is HFRS data for all 30 days: if not, determine where the data is missing and reset the start date as the first date with HFRS data after the break
    c. there are no overlaps of HFRS captured: if there are overlaps, reset the start date as the first date after all overlapping periods have ended
    d. there were no non-elective hospitalisations: if there was a non-elective hospitalisation, reset the start date as the day after discharge

e. If none of (a)-(d) occurred, determine this as a suitable 30-day diagnostic evaluation period. Then reset the start date as the day following the last day of the 30-day diagnostic evaluation period. For the remaining periods, the maximum risk over the 30 days was recorded and the outcome was the time to hospitalisation within the next 30 days.

4. Repeat steps 2 and 3 using the new start date defined in step 3.

Data S3. Retrospective analyses: Maximum Triage-HFRS prior to non-elective hospitalisation

Out of the 435 patients, 153 patients (35.2%) had a non-elective all-cause hospitalisation at least once during the study period, with 76 of these patients having a cardiovascular non-elective admission. In total, there were 356 all-cause non-elective hospitalisations during the 2-year study period (median [min-max]: 0 [0–11] hospitalisations per patient) ; this corresponds to a rate of 0.565 all-cause non-elective hospitalisations per patient-year. Over one third (128/356) of these hospitalisations were cardiovascular related admissions, with HF identified as a primary diagnosis in 36.7% (47/128) of these. Common, non-HF cardiovascular admissions included; arrhythmia (n=21), chest pain (n=12), other acquired cardiac conditions (n=10), syncope/collapse (n=9), actual or suspected MI (n=6) and angina (n=6). Common, non-cardiovascular admissions included; respiratory infection or pneumonia (n=27), gastrointestinal tract disorder (n=18) and sepsis (n=10).

Of the 153 patients with at least one hospitalisation during the study period, 130 (85.0%) had a CRT device (CRT-P, 64 (41.8%); CRT-D, 66 (43.1%)), 9 (5.9%) an ICD, and 14 (9.2%) a PPM. For those who experienced a HF hospitalisation (n=31), 90.3% had a CRT device.

The majority (234/356; 65.7%) of all-cause hospitalisations took place within 1 year of a high Triage-HFRS episode and 36.8% had a high-risk status within the 30 days prior to the hospitalisation. Isolating cardiovascular hospitalisations, 85/128 (66.4%) had a high-risk status in the

preceding 12 months, 76/128 (59.4%) within the previous 6-months, and 50/128 (39.2%) in the preceding 30-days, while 34/47 (72.3%) HF hospitalisations transmitted a high HFRS status within the previous 6-months. The majority of patients with a non-elective HF hospitalisation (59.6%), transmitted a high Triage-HFRS in the preceding 30-days (Table 2).

Of the 169 'switchers', 29 (17.2%) experienced a subsequent cardiovascular hospitalisation during the study period. For these patients, the median time from the start of their first recorded high-risk episode to the cardiovascular hospitalisation was 92 days (IQR: 39 - 211). The proportion of these admissions which occurred within 30 days was modest (5/29; 17.2%) but 48.3% occurred within 3 months, 69.0% (14/29) occurred within 6 months, and nearly all occurred within 12 months (20/29; 93.1%). The Kaplan-Meier cumulative incidence curves from a patient's first high episode to subsequent hospitalisation within the study period are shown in Figure 2. The median duration of the first high episode was 6 days (IQR: 3 – 12 days) and the length of time spent in this first high was not associated with a change in hazard for non-elective cardiovascular hospitalisation (p=0.949).

Table S1. Cardiovascular SUSHRG reference (classified by FA and JKT)

SUSHRG code	HRG Name
EA03Z	Pace 1: Single Chamber or Implantable Diagnostic Device
EA05Z	Pace 2: Dual Chamber
EA07Z	Pace 3: Biventricular and all Congenital Pacemaker Procedures; Resynchronisation Therapy
EA09Z	Percutaneous Interventions: Percutaneous Transluminal ASD, VSD or PFO Closure and Valve Insertion
EA11Z	Percutaneous Interventions: Other including Septostomy, Embolisations, Non-Coronary Stents and Energy Moderated Perforation
EA12Z	Implantation of Cardioverter; Defibrillator only
EA14Z	Coronary Artery Bypass Graft (First Time)
EA17Z	Single Cardiac Valve Procedures
EA19Z	Single Cardiac Valve Procedures with Percutaneous Coronary Intervention, Pacing, EP or RFA
EA24Z	Complex Congenital Surgery
EA29Z	Percutaneous Complex Ablation, including for Atrial Fibrillation or Ventricular Tachycardia
EA31Z	Percutaneous Coronary Intervention, 0 to 2 Stents
EA36A	Catheter, 19 years and over
EA39Z	Pacemaker Procedure without Generator Implant, including Re-siting and Removal of Cardiac Pacemaker System
EA44Z	Minor Cardiac Procedures
EA45Z	Complex Echocardiogram, including Congenital, Transoesophageal and Fetal Echocardiography

EA49Z	Percutaneous Coronary Interventions with 3 or more Stents, Rotablation, IVUS or Pressure Wire
EA51Z	Coronary Artery Bypass Graft, with Valve Replacement or Repair
EA52Z	Repair or Replacement of more than one Heart Valve
EA53Z	Transcatheter Aortic Valve Implantation (TAVI)
EA54Z	Percutaneous Standard Ablation
EA56Z	Implantation of Cardiac Resynchronization Therapy Defibrillator (CRT-D)
EB01Z	Non-Interventional Acquired Cardiac Conditions
EB02A	Endocarditis with CC Score 10+
EB03A	Heart Failure or Shock, with CC Score 14+
EB03B	Heart Failure or Shock, with CC Score 11-13
EB03C	Heart Failure or Shock, with CC Score 8-10
EB03D	Heart Failure or Shock, with CC Score 4-7
EB03E	Heart Failure or Shock, with CC Score 0-3
EB03H	Heart Failure or Shock, with CC
EB03I	Heart Failure or Shock, without CC
EB05C	Cardiac Arrest with CC Score 0-4
EB06B	Cardiac Valve Disorders with CC Score 9-12
EB06D	Cardiac Valve Disorders with CC Score 0-4
EB06Z	Cardiac Valve Disorders
EB07A	Arrhythmia or Conduction Disorders, with CC Score 13+
EB07B	Arrhythmia or Conduction Disorders, with CC Score 10-12
EB07C	Arrhythmia or Conduction Disorders, with CC Score 7-9
EB07D	Arrhythmia or Conduction Disorders, with CC Score 4-6
EB07E	Arrhythmia or Conduction Disorders, with CC Score 0-3
EB07H	Arrhythmia or Conduction Disorders, with CC
EB07I	Arrhythmia or Conduction Disorders, without CC

EB08A	Syncope or Collapse, with CC Score 13+
EB08B	Syncope or Collapse, with CC Score 10-12
EB08C	Syncope or Collapse, with CC Score 7-9
EB08D	Syncope or Collapse, with CC Score 4-6
EB08E	Syncope or Collapse, with CC Score 0-3
EB08H	Syncope or Collapse, with CC
EB08I	Syncope or Collapse, without CC
EB09A	Non-Interventional Congenital Cardiac Conditions with CC Score 3+
EB10A	Actual or Suspected Myocardial Infarction, with CC Score 13+
EB10B	Actual or Suspected Myocardial Infarction, with CC Score 10-12
EB10C	Actual or Suspected Myocardial Infarction, with CC Score 7-9
EB10D	Actual or Suspected Myocardial Infarction, with CC Score 4-6
EB10Z	Actual or Suspected Myocardial Infarction
EB12A	Unspecified Chest Pain with CC Score 11+
EB12B	Unspecified Chest Pain with CC Score 5-10
EB12C	Unspecified Chest Pain with CC Score 0-4
EB13A	Angina with CC Score 12+
EB13B	Angina with CC Score 8-11
EB13C	Angina with CC Score 4-7
EB14A	Other Acquired Cardiac Conditions with CC Score 13+
EB14B	Other Acquired Cardiac Conditions with CC Score 9-12
EB14C	Other Acquired Cardiac Conditions with CC Score 6-8
EB14D	Other Acquired Cardiac Conditions with CC Score 3-5
EB14E	Other Acquired Cardiac Conditions with CC Score 0-2
EC10B	Very Complex Procedures for Congenital Heart Disease with CC Score 7-14
EC10C	Very Complex Procedures for Congenital Heart Disease with CC Score 0-6
EC11C	Complex Procedures for Congenital Heart Disease with CC Score 0-6

EC12B	Very Major Procedures for Congenital Heart Disease with CC Score 4-8
EC13B	Major Procedures for Congenital Heart Disease with CC Score 4-8
EC15A	Minor Procedures for Congenital Heart Disease with CC Score 4+
EC15B	Minor Procedures for Congenital Heart Disease with CC Score 0-3
EC20A	Diagnostic Percutaneous Intervention for Congenital Heart Disease with CC Score 4+
EC20B	Diagnostic Percutaneous Intervention for Congenital Heart Disease with CC Score 0-3
ED22B	Complex, Coronary Artery Bypass Graft with Single Heart Valve Replacement or Repair, with CC Score 6-10
ED24B	Complex, Single Heart Valve Replacement or Repair, with CC Score 6-10
ED24C	Complex, Single Heart Valve Replacement or Repair, with CC Score 0-5
ED25A	Standard, Single Heart Valve Replacement or Repair, with CC Score 11+
ED25B	Standard, Single Heart Valve Replacement or Repair, with CC Score 6-10
ED26A	Complex Coronary Artery Bypass Graft with CC Score 10+
ED26B	Complex Coronary Artery Bypass Graft with CC Score 5-9
ED27C	Major Coronary Artery Bypass Graft with CC Score 0-4
EY01A	Implantation of Cardioverter Defibrillator with Cardiac Resynchronisation Therapy, with CC Score 9+
EY01B	Implantation of Cardioverter Defibrillator with Cardiac Resynchronisation Therapy, with CC Score 0-8
EY02A	Implantation of Cardioverter Defibrillator with CC Score 9+
EY02B	Implantation of Cardioverter Defibrillator with CC Score 0-8
EY03Z	Implantation of Biventricular Pacemaker with Other Percutaneous Intervention
EY04A	Implantation of Biventricular Pacemaker with CC Score 6+
EY04B	Implantation of Biventricular Pacemaker with CC Score 0-5
EY05A	Implantation of Dual-Chamber Pacemaker with Other Percutaneous Intervention, with CC Score 6+

EY05B	Implantation of Dual-Chamber Pacemaker with Other Percutaneous Intervention, with CC Score 0-5
EY06A	Implantation of Dual-Chamber Pacemaker with CC Score 12+
EY06B	Implantation of Dual-Chamber Pacemaker with CC Score 9-11
EY06D	Implantation of Dual-Chamber Pacemaker with CC Score 3-5
EY06E	Implantation of Dual-Chamber Pacemaker with CC Score 0-2
EY07A	Implantation of Single-Chamber Pacemaker with Other Percutaneous Intervention, with CC Score 6+
EY07B	Implantation of Single-Chamber Pacemaker with Other Percutaneous Intervention, with CC Score 0-5
EY08A	Implantation of Single-Chamber Pacemaker with CC Score 12+
EY08B	Implantation of Single-Chamber Pacemaker with CC Score 9-11
EY08C	Implantation of Single-Chamber Pacemaker with CC Score 6-8
EY08D	Implantation of Single-Chamber Pacemaker with CC Score 3-5
EY08E	Implantation of Single-Chamber Pacemaker with CC Score 0-2
EY09B	Removal of Cardiac Pacemaker or Cardioverter Defibrillator, with CC Score 0-5
EY10A	Attention to Cardiac Pacemaker or Cardioverter Defibrillator, with CC Score 6+
EY10B	Attention to Cardiac Pacemaker or Cardioverter Defibrillator, with CC Score 0-5
EY11Z	Testing of Cardiac Pacemaker or Cardioverter Defibrillator
EY13Z	Removal of Electrocardiography Loop Recorder
EY20A	Transcatheter Aortic Valve Implantation (TAVI) using Other Approach, with CC Score 8+
EY20B	Transcatheter Aortic Valve Implantation (TAVI) using Other Approach, with CC Score 0-7
EY21A	Transcatheter Aortic Valve Implantation (TAVI) using Transfemoral Approach, with CC Score 8+

EY22A	Complex Other Percutaneous Transluminal Repair of Acquired Defect of Heart with CC Score 10+
EY22B	Complex Other Percutaneous Transluminal Repair of Acquired Defect of Heart with CC Score 5-9
EY30A	Complex Percutaneous Transluminal Ablation of Heart with CC Score 3+
EY30B	Complex Percutaneous Transluminal Ablation of Heart with CC Score 0-2
EY31A	Standard Percutaneous Transluminal Ablation of Heart with CC Score 3+
EY31B	Standard Percutaneous Transluminal Ablation of Heart with CC Score 0-2
EY32A	Percutaneous Diagnostic Electrophysiology Studies with CC Score 2+
EY40C	Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 4-7
EY41A	Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 12+
EY41B	Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 8-11
EY41C	Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 4-7
EY41D	Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 0-3
EY42A	Complex Cardiac Catheterisation with CC Score 7+
EY43B	Standard Cardiac Catheterisation with CC Score 10-12
EY43C	Standard Cardiac Catheterisation with CC Score 7-9
EY43D	Standard Cardiac Catheterisation with CC Score 4-6
EY43E	Standard Cardiac Catheterisation with CC Score 2-3
EY43F	Standard Cardiac Catheterisation with CC Score 0-1
EY50Z	Complex Echocardiogram
EY51Z	Electrocardiogram Monitoring or Stress Testing

CC = comorbidities score

Table S2. Non-elective hospitalisation episodes by maximum risk recorded within the previous 30 days, 6- and 12- months (APC and A&E as a joint outcome)

	Max risk recorded in previous 30 days				Max risk recorded in previous 6 months				Max risk recorded in previous 12 months				
	Low	Med	**High**	No txs received	Low	Med	**High**	No txs received	Low	Med	**High**	No txs received	Total
All-cause, n (%)	150 (24.9%)	261 (43.3%)	**184 (30.5%)**	8 (1.3%)	17 (2.8%)	277 (45.9%)	**307 (50.9%)**	2 (0.3%)	2 (0.3%)	234 (38.8%)	**367 (60.9%)**	0 (0.0%)	603
CV, n (%)	31 (16.9%)	81 (44.3%)	**67 (36.6%)**	4 (2.2%)	4 (2.2%)	70 (38.3%)	**108 (59.0%)**	1 (0.5%)	1 (0.5%)	61 (33.3%)	**121 (66.1%)**	0 (0.0%)	183
HF, n (%)	5 (10.6%)	12 (25.5%)	**28 (59.6%)**	2 (4.3%)	0 (0.0%)	12 (25.5%)	**34 (72.3%)**	1 (2.1%)	0 (0.0%)	12 (25.5%)	**35 (74.5%)**	0 (0.0%)	47

CV=Cardiovascular, HF=Heart Failure, txs=transmissions

Table S3. Maximum Triage-HFRS within 30-day diagnostic evaluation and associated non-elective hospitalisations (APC and A&E episodes)

30-day Diagnostic Evaluation Period Max Triage-HFRS	Total diagnostic evaluation periods	30-day Outcomes		
		All-cause hospitalisation (APC or A&E)	Cardiovascular hospitalisation (APC or A&E)	HF hospitalisation (APC only)
Low	2288 (33.6%)	98 (4.3%)	24 (1.0%)	6 (0.3%)
Medium	3535 (51.8%)	175 (5.0%)	48 (1.4%)	7 (0.2%)
High	996 (14.6%)	111 (11.2%)	42 (4.2%)	23 (2.3%)
Total	6819 (100%)	384 (5.6%)	114 (1.7%)	36 (0.5%)

APC = admitted patient care episode, HFRS = heart failure risk score, A&E = accident and emergency

Table S4. Demographics of patients with at least one 30-day hospitalisation outcome in prospective analysis (APC and A&E episodes)

	30-day Outcomes			All patients
	All-cause hospitalisation	Cardiovascular hospitalisation	HF hospitalisation	
Patients, n (%)	206	81	28	429
Age, mean (sd)	67.3 (16.5)	69.4 (16.7)	76.8 (9.8)	66.0 (15.5)
Male, n (%)	135 (65.5%)	60 (74.1%)	18 (64.3%)	271 (63.2%)
Device Type, n (%)				
CRT-D	82 (39.8%)	33 (40.7%)	12 (42.9%)	162 (37.8%)
CRT-P	84 (40.8%)	32 (39.5%)	13 (46.4%)	168 (39.02%)
ICD	19 (9.2%)	<5 (<5.0%)	<5 (<17.9%)	36 (8.4%)
PPM	21 (10.2%)	>11 (>13.6%)	<5 (<17.9%)	63 (14.7%)
NYHA				
No heart failure	25 (12.1%)	10 (12.3%)	<5 (<17.9%)	62 (14.5%)
1	19 (9.2%)	8 (9.9%)	<5 (<17.9%)	53 (12.4%)
2	72 (35.0%)	24 (29.6%)	5 (17.9%)	150 (35.0%)
3+	79 (38.3%)	36 (44.4%)	21 (75.0%)	142 (33.1%)
CKD stage 3 or higher	73 (35.4%)	36 (44.4%)	18 (64.3%)	132 (30.8%)

HF = heart failure, CRT-D = cardiac resynchronisation therapy device with defibrillator, CRT-P = cardiac resynchronisation therapy device with pacemaker, ICD = implanted cardiac defibrillator, PPM = pacemaker, NYHA = New York Heart Association Functional Classification, CKD = chronic kidney disease

Table S5. Coefficients of frailty model using A&E and APC episodes as a combined outcome

	All-cause hospitalisation within 30 days			Cardiovascular hospitalisation within 30 days		
Variable	Hazard Ratio	95% CI	p-value	Hazard Ratio	95% CI	p-value
Medium (vs Low)	0.986	0.748 – 1.301	0.92	1.150	0.676 – 1.959	0.61
High (vs Low)	**2.049**	1.474 - 2.846	**<0.001**	**3.320**	1.845 – 5.974	**<0.001**
No HF	1.148	0.623 - 2.113	0.66	1.012	0.343 - 2.983	0.98
Age	1.001	0.990 – 1.013	0.663	1.014	0.994 – 1.023	0.19
CRTP vs CRTD	0.699	0.487 – 1.002	0.05	0.662*	0.754 – 2.166	0.26
PPM vs CRTD	**0.478**	0.254 - 0.898	**0.02**	0.841*	0.262 - 2.698	0.77
ICD vs CRTD	0.562	0.280 - 1.124	0.10	0.169*	0.019-1.468	0.11
CKD stage 3 or higher	1.326	0.931 – 1.890	0.12	1.559*	1.054 – 2.306	0.06

HF = heart failure, CRT-D = cardiac resynchronisation therapy device with defibrillator, CRT-P = cardiac resynchronisation therapy device with pacemaker, ICD = implanted cardiac defibrillator, PPM = pacemaker, CKD = chronic kidney disease

Table S6. Coefficients for time-varying covariate frailty model for cardiovascular hospitalisation within 30-days (APC and A&E as a joint outcome

	Cardiovascular hospitalisation within 30 days		
Variable	Hazard Ratio	95% CI	p-value
Medium (vs Low)	1.150	0.676 – 1.959	0.61
High (vs Low)	**3.320**	1.845 – 5.974	**<0.001**
No HF	1.012	0.343 - 2.983	0.98
Age	1.014	0.994 – 1.023	0.19
CRTP vs CRTD (0-15 days)	0.662	0.754 – 2.166	0.26
PPM vs CRTD (0-15 days)	0.841	0.262 - 2.698	0.77
ICD vs CRTD (0-15 days)	0.169	0.019-1.468	0.11
CKD stage 3 or higher (0-15 days)	1.559	1.054 – 2.306	0.06
CRTP vs CRTD (16-30 days)	0.598	0.261 - 1.369	0.22
PPM vs CRTD (16-30 days)	0.456	0.130 - 1.602	0.22

ICD vs CRTD (16-30 days)	2.277	0.220 - 23.527	0.49
CKD stage 3 or higher (16-30 days)	0.564	0.261 - 1.217	0.14

HF = heart failure, CRT-D = cardiac resynchronisation therapy device with defibrillator, CRT-P = cardiac resynchronisation therapy device with pacemaker, ICD = implanted cardiac defibrillator, PPM = pacemaker , CKD = chronic kidney disease

Table S7. Costs for hospitalisations in the retrospective analysis

	Max risk in previous 30 days											
	Low			Medium			High			No transmission		
	N	Cost	Missing	N	Cost	Missing	N	Cost	Missing	N	Cost	Missing
A&E episodes												
All-cause	78	£9,107	0	115	£14,057	1	52	£6,583	0	2	£221	0
Cardiovascular	11	£1,491	0	26	£3,671	0	17	£2,470	0	1	£130	0
Total costs (APC and A&E episodes combined)												
All-cause	151	£181,986	1	261	£389,896	4	184	£437,367	4	10	£10,312	2
Cardiovascular	31	£58,403	0	81	£139,897	0	67	£156,622	0	4	£6,250	0
HF	5	£14,676	0	12	£40,230	0	28	£94,135	0	2	£5,774	0

APC = admitted patient care episode, HFRS = heart failure risk score, A&E = accident and emergency, HF = heart failure

Table S8. Costs for A&E and APC events within the prospective analysis

30-day Diagnostic Evaluation Period Max Triage-HFRS	Total diagnostic evaluation periods	All-cause hospitalisation				Cardiovascular hospitalisation			HF hospitalisation		
		N	Total Cost	Missing	Average Cost	N	Total Cost	Average Cost	N	Total Cost	Average Cost
Low	2282 (33.6%)	98 (4.3%)	£95,133	2	£990.97	24 (1.1%)	£35,173	£1,465.55	6 (0.3%)	£18,561	£3,093.50
Medium	3530 (51.8%)	176 (5.0%)	£231,701	1	£1,324.01	48 (1.4%)	£84,819	£1,767.07	7 (0.2%)	£19,142	£2,734.58
High	993 (14.6%)	111 (11.2%)	£257,354	2	£2,361.05	42 (4.2%)	£103,832	£2,472.20	23 (2.3%)	£80,438	£3,497.31
Total	6805 (100%)	384 (5.6%)	£584,188	5	£1,541.40	114 (1.7%)	£223,824	£1,963.37	36 (0.5%)	£118,141	£3,281.70

HF = heart failure, HFRS = heart failure risk score. No missing data for cardiovascular and HF hospitalisation costs

Table S9. Cardiovascular coding according to ICD10 codes and SUSHRG codes for non-elective APC episodes (All-cause hospitalisation)

SUSHRG coding	ICD10 coding		
	Cardiovascular: HF	Cardiovascular: Non-HF	Non-Cardiovascular
Cardiovascular: HF	47	0	0
Cardiovascular: Non-HF	3	73	7
Non-Cardiovascular	0	4	229

ICD-10 = International Statistical Classification of Diseases and Related Health Problems (10th revision), SUSHRG = Secondary Uses Service generated Healthcare Resource Group code, HF = heart failure

Table S10. Demographics of patients with at least one 30-day hospitalisation outcome in prospective analysis (APC only)

	All patients	30-day Outcomes		
		All-cause hospitalisation	Cardiovascular hospitalisation	HF hospitalisation
Patients, n (%)	429	138	65	24
Age, mean (sd)	66.0 (15.5)	70.1 (14.7)	70.3 (16.2)	76.3 (10.0)
Male, n (%)	271 (63.2%)	91 (65.9%)	48 (73.8%)	14 (58.3%)
Device Type, n (%)				
CRT-D	162 (37.8%)	60 (43.5%)	26 (40.0%)	9 (37.5%)
CRT-P	168 (39.02%)	57 (41,3%)	27 (41.5%)	12 (50.0%)
ICD	36 (8.4%)	7 (5.1%)	<5 (<7.7%)	<5 (<20.8%)
PPM	63 (14.7%)	14 (10.1%)	>5 (>7.7%)	<5 (<20.8%)
NYHA				
No heart failure	62 (14.5%)	13 (9.4%)	8 (12.3%)	<5 (<20.8%)
1	53 (12.4%)	8 (5.8%)	5 (7.7%)	<5 (<20.8%)
2	150 (35.0%)	52 (37.7%)	21 (32.3%)	5 (20.8%)
3+	142 (33.1%)	59 (42.8%)	28 (43.1%)	17 (70.8%)
Missing	*22 (5.1%)*	*6 (4.3%)*	*3 (4.6%)*	*0 (0.0%)*
CKD stage 3 or higher	132 (30.8%) *Missing: 4 (0.9%)*	53 (38.4%) *Missing: 2 (1.4%)*	29 (44.6%)	16 (66.7%)

HF = heart failure, CRT-D = cardiac resynchronisation therapy device with defibrillator, CRT-P = cardiac resynchronisation therapy device with pacemaker, ICD = implanted cardiac defibrillator, PPM = pacemaker, NYHA = New York Heart Association Functional Classification, CKD = chronic kidney disease

Table S11. Coefficients for time-varying covariate frailty model for cardiovascular hospitalisation within 30-days

	Cardiovascular APC within 30 days		
Variable	Hazard Ratio	95% CI	p-value
Medium (vs Low)	1.059	0.758 – 1.481	0.74
High (vs Low)	**2.410**	1.653 – 3.512	**<0.001**
No HF	1.063	0.411 – 2.755	0.90
Age	1.015	0.998 – 1.033	0.08
CRTP vs CRTD (0-15 days)	0.653	0.373 – 1.146	0.14
PPM vs CRTD (0-15 days)	**0.352**	0.127 – 0.973	**0.04**
ICD vs CRTD (0-15 days)	**0.247**	0.080 – 0.760	**0.01**
CKD stage 3 or higher	1.379	0.800 – 2.377	0.25
CRTP vs CRTD (16-30 days)	0.789	0.484 – 1.288	0.34
PPM vs CRTD (16-30 days)	0.579	0.201 – 1.674	0.31
ICD vs CRTD (16-30 days)	0.489	0.099 – 2.440	0.38

CKD (16-30 days)	1.273	0.795 – 2.041	0.32

HF = heart failure, CRT-D = cardiac resynchronisation therapy device with defibrillator, CRT-P = cardiac resynchronisation therapy device with pacemaker, ICD = implanted cardiac defibrillator, PPM = pacemaker, CKD = chronic kidney disease

Table S12. Costs for APC hospitalisations in the prospective analysis

30-day Diagnostic Evaluation Period Max Triage-HFRS	Total diagnostic evaluation periods	All-cause hospitalisation				Cardiovascular hospitalisation				HF hospitalisation			
		N	Total Cost	Missing	Average Cost	N	Total Cost	Missing	Average Cost	N	Total Cost	Missing	Average Cost
Low	2288 (33.6%)	46 (2.0%)	£93,604	6	£2,340.10	16 (0.7%)	£38,929	0	£2,433.07	6 (0.3%)	£19,353	0	£3,225.50
Medium	3535 (51.8%)	97 (2.7%)	£209,337	18	£2,649.84	38 (1.1%)	£80,898	4	£2,379.35	6 (0.2%)	£13,055	2	£3,263.75
High	996 (14.6%)	85 (8.5%)	£245,924	17	£3,616.53	35 (3.5%)	£104,274	3	£3,258.57	20 (2.0%)	£72,703	1	£3,826.48
Total	6819 (100%)	228 (3.3%)	£548,865	41	£2,935.11	89 (1.3%)	£224,101	7	£2,732.94	32 (0.5%)	£104,481	3	£3,602.80

HF = heart failure, HFRS = Heart failure risk score, APC = admitted patient care episode

Table S13. Costs for APC hospitalisations in the retrospective analysis

	Max risk in previous 30 days											
	Low			Medium			High			No transmission		
	N	Cost	Missing	N	Cost	Missing	N	Cost	Missing	N	Cost	Missing
All-cause	72	£172,879	1	146	£375,839	3	132	£430,784	4	8	£10,091	2
Cardiovascular	20	£56,912	0	55	£136,226	0	50	£154,152	0	3	£6,120	0
HF	5	£14,676	0	12	£40,230	0	28	£94,135	0	2	£5,774	0

HF = heart failure, APC = admitted patient care episode

Table S14. Device type and NYHA class

NYHA	CRT-D	CRT-P	ICD	PPM
No HF	<5	15	>6	37
1	>23	13	6	>5
2	67	63	12	9
3+	67	72	<6	<5

HF = heart failure, CRT-D = cardiac resynchronisation therapy device with defibrillator, CRT-P = cardiac resynchronisation therapy device with pacemaker, ICD = implanted cardiac defibrillator, PPM = pacemaker, NYHA = New York Heart Association Functional Classification

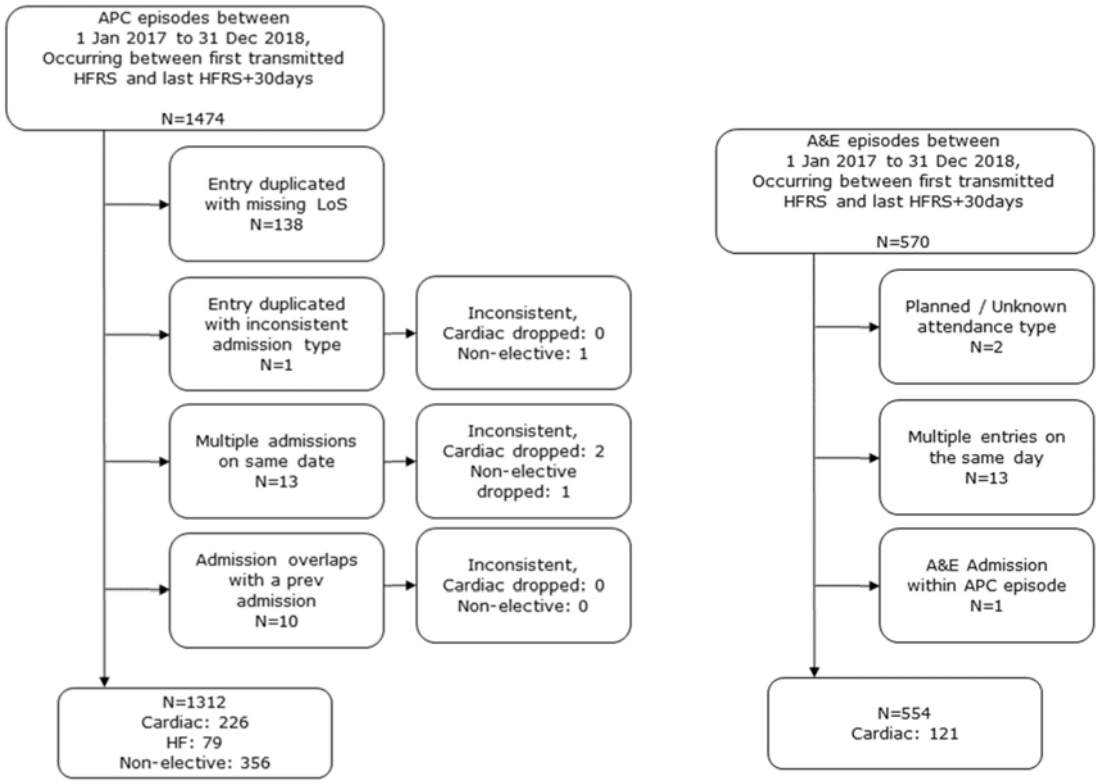
Table S15. Diagnosis codes which led to incongruent cardiovascular classification for non-elective APC episodes (ACH)

ICD10 code	ICD10 Rubric	ICD10 categorisation	SUSHRG code	SUSHRG Rubric	SUSHRG categorisation
K59.0	Constipation	Non-cardiovascular	EB10	Actual or suspected Myocardial infarction	Cardiovascular
I95.9	Hypotension, unspecified	Non-cardiovascular	EB14	Other acquired cardiovascular conditions	Cardiovascular
I95.1	Orthostatic hypotension	Cardiovascular	DZ65	COPD	Non-cardiovascular
T82.7	Infection and inflammatory reaction due to other cardiovascular and vascular devices, implants and grafts	Cardiovascular	YR44	Removal of central venous catheter	Non-cardiovascular
I25.1	Atherosclerotic heart disease	Cardiovascular	YF01	Radiological insertion of gastronomy tube	Non-cardiovascular
I42.0*	Dilated cardiomyopathy	Cardiovascular	UZ01	Data invalid for grouping	Non-cardiovascular
R05*	Cough	Non-cardiovascular	EB12	Unspecified chest pain	Cardiovascular

R06.0*	Dyspnoea	Non-cardiovascular			
J45.9*	Asthma, unspecified	Non-cardiovascular			
C79.5*	Secondary malignant neoplasm of bone and bone marrow	Non-cardiovascular			
J44.9*	Chronic obstructive pulmonary disease, unspecified	Non-cardiovascular			
I50.0*	Congestive heart failure	Cardiovascular: HF			

ICD-10 = International Statistical Classification of Diseases and Related Health Problems (10th revision), SUSHRG = Secondary Uses Service generated Healthcare Resource Group code, HF = heart failure
**second ICD-10 code as first code was not categorisable.*

Figure S1. Selection process for (left:) APC episodes between 1 Jan 2017 and 31 Dec 2018 and (right:) A&E attendances between 1 Jan 2017 and 31 Dec 2018



HF = heart failure, APC = admitted patient care, HFRS = heart failure risk score

Figure S2. Cumulative event rates for hospitalisation after first high, where hospitalisation can be an A&E attendance or an APC episode. Following their first high, a substantial number of patients experienced an all-cause hospitalisation within days, but this was not observed for the first cardiovascular hospitalisations following the first high episode.

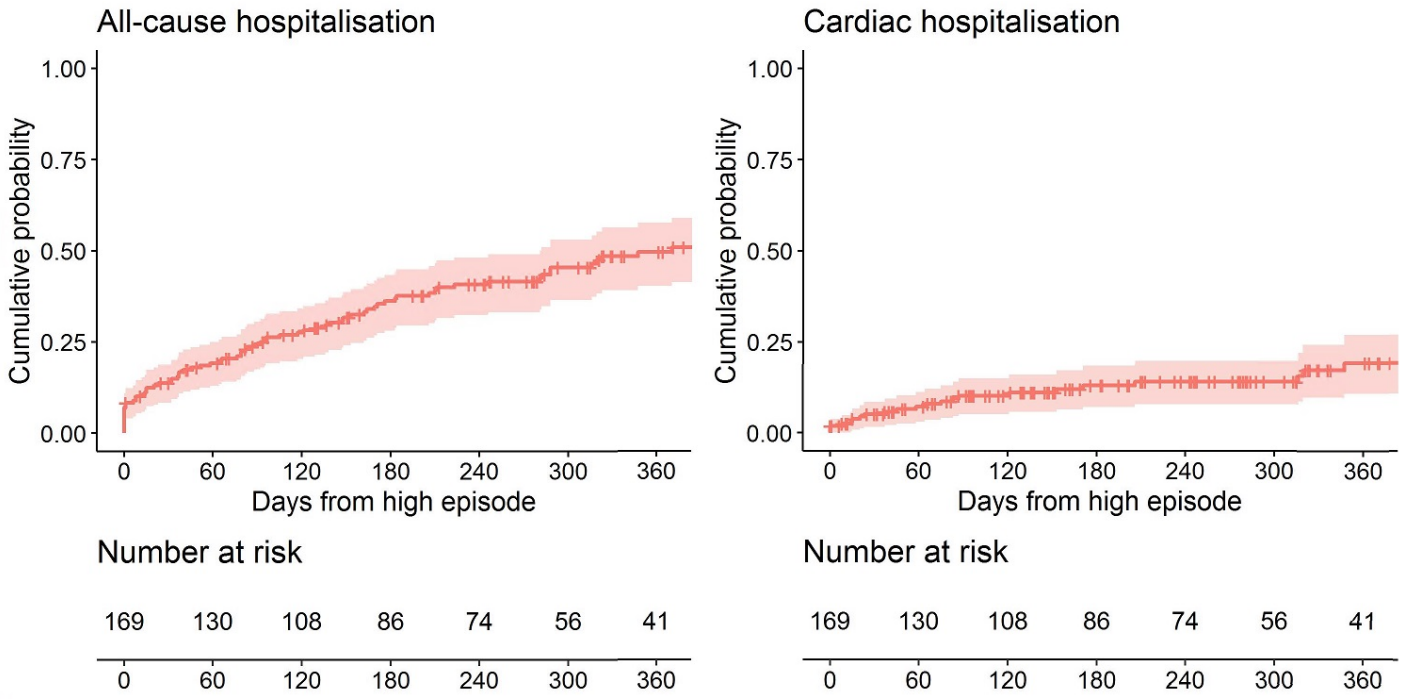
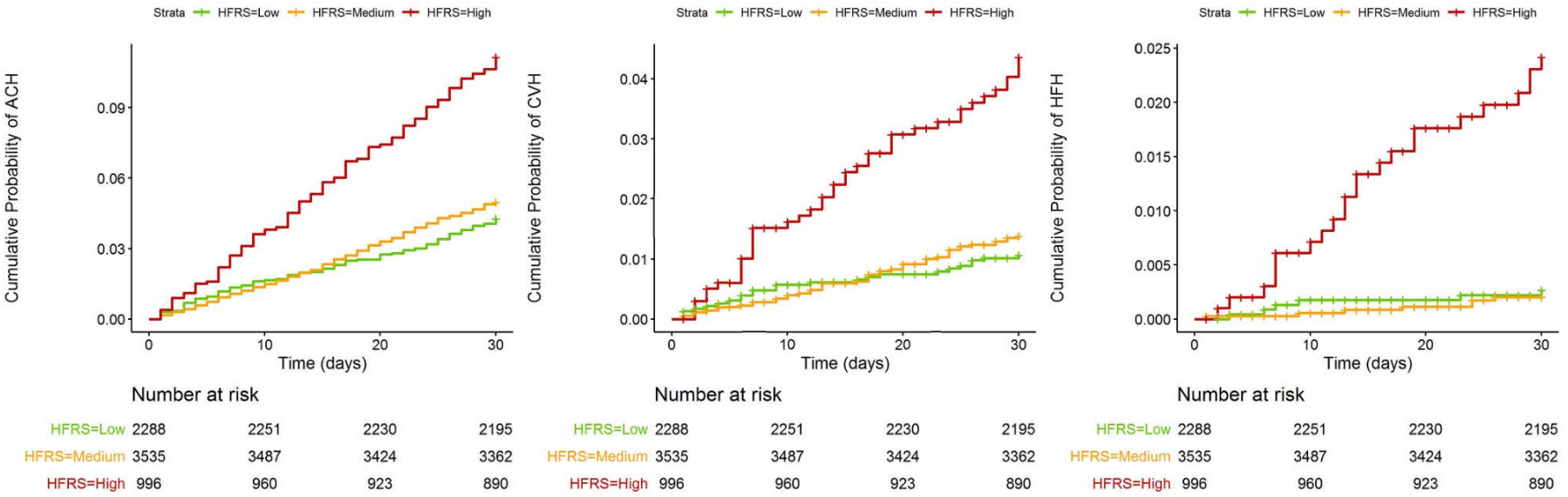


Figure S3. Cumulative probability curves for hospitalisation in prospective analysis, where hospitalisation can be an A&E attendance or an APC episode. The high-risk group had higher incidence rates beyond 3 days compared with medium- and low-risk groups.



ACH = all-cause hospitalisation, CVH = cardiovascular hospitalisation, HFH = heart failure hospitalisation