ORIGINAL ARTICLE

Clinical characteristics of people with heart failure in Australian general practice: results from a retrospective cohort study

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Abstract

Aims Heart failure (HF) causes significant morbidity and mortality, but the rates and characteristics of people with HF in Australia are not well studied. SHAPE set out to describe the characteristics of HF patients seen in the real-world setting.

Methods We analysed anonymized patient data extracted from the clinical software of 43 participating GP clinics for the 5 year period from 1 July 2013 to 30 June 2018. Patients were stratified into 'definite' and 'probable' HF based on a hierarchy of selection criteria and analysed for their clinical characteristics. Symptoms and signs of HF and ejection fraction data were searched for within the free text of the medical notes.

Results Of the 1.12 million adults seen regularly, 20 219 were classified as having definite or probable HF. The mean age of the population was 69.8 years, 50.6% were female, and mean body mass index was 31.2 kg/m^2. Fewer than 1 in 6 had the HF diagnosis optimally recorded. Only 3.2% (650 patients) had their left ventricular ejection fraction (EF) quantified: 40.9% had an EF ≥50% and 59.1% had an EF <50%. The most common comorbidities in people with HF were hypertension (41.1%), chronic obstructive pulmonary disease/asthma (25.1%) and depression/anxiety (18.4%). Hypotension (2.3%), bradycardia (6.3%), severe renal impairment (6.4%) and hyperkalaemia (2.0%) were uncommon. Just over one-third (37.8%) had iron deficiency. Loop diuretic use was common (56.7%) but only 33.7% were on a guideline recommended beta-blockers. Use of ivabradine (1.4%) and sacubitril/valsartan (1.2%) was very low, while 39.9% had been prescribed an angiotensin-converting enzyme inhibitor, 31.6% an angiotensin receptor blocker and 16.0% spironolactone. Many patients were prescribed medications that may worsen HF or are relatively contraindicated, such as macrolide antibiotics (29.9%), corticosteroids (25.8%), nonsteroidal anti-inflammatory drugs (23.9%), and tricyclic antidepressants (9.4%).

Conclusions Heart failure is poorly documented in general practice records and may be contributing to untoward downstream effects, such as low documentation of echocardiography, poor use of guideline recommended therapies and frequent use of medications that may worsen HF.

Aims

The morbidity and mortality of chronic heart failure (HF) is significant—in Australia, it was recorded as a main or additional diagnosis in over 170 000 hospitalizations in 2015–2016 and has a 5 year survival rate of 52–63%, similar to that observed in non-haematological malignancies.[1] Despite this, few studies have established the true prevalence, incidence and characteristics of people living with HF in Australia, outside of the hospital setting. The

'Retrospective Cohort Study of Heart Failure in the Australian Primary CarE Setting' (SHAPE) set out to describe the 'real world' prevalence, incidence, demographics and clinical characteristics of the HF population being cared for by general practitioners (GPs) in Australia.

Methods

SHAPE is a retrospective cohort study that analysed secondary anonymized data from the medical records of adult patients cared for at 43 participating general practices between 1 July 2013 and 30 June 2018. We examined structured data from medical records (e.g. diagnosis, pathology and prescription fields), as well as free text entries (un-coded fields) in the consultation notes for pre-specified HF-relevant terms, to identify and describe the HF population.

The free-text notes were up to 2100 characters in length for each record. These were scanned for particular sets of characters, such as ' PND ' (note the space before and after the characters to ensure they are not part of a larger word). The text immediately before and after the word (30 characters each side) were then scanned for occurrences of 'No', 'Nil', 'Not', 'Family history', 'Nil History', 'Family Hx', 'Denies', 'Denial'. A person was classified as having PND if 'PND' was present in the absence of any of these other words. A similar approach was taken to search the free text for the various other conditions and symptoms of HF. The free-text notes were also scanned for mention of the ejection fraction (EF) (using many abbreviations). Data on drugs and other laboratory measurements were obtained from separate files where these were coded. Further details of our methods are provided in Parsons *et al*.[2]

Data were examined for the presence of a diagnosis of HF, use of HF-specific medications, HF-diagnostic investigation results (e.g. BNP/N terminal pro brain natriuretic peptide, echocardiography) and signs/symptoms of HF (typical and less typical). The population was then stratified into 'definite HF', 'probable HF' and 'possible HF' based on a hierarchy of selection criteria.[2]

The primary objective of SHAPE was to estimate the prevalence and incidence of HF. Two methods were used to obtain data for prevalence and incidence. In the primary analyses, data comprised only 'active' patients; those with at least three visits per 2 year period. The Royal Australian College of General Practitioners (RACGP) defines an 'active patient health record' as a record of a patient who has attended the practice/service three or more times in the past 2 years.[3] In the secondary analyses, both numerator and denominators were based on the total number of patients seen at the participating GP clinics during each calendar year for the period under study. These included people who were not regular patients of the medical centres.

The secondary objectives were to describe the demographics and clinical characteristics of the HF population. Separate manuscripts have been developed to describe the in-depth methodology that was used,[2] as well as the findings on prevalence, incidence and demographics.[4] The clinical profile of the collective 'definite or probable HF' group who are active patients of the centres (hereafter referred to as 'patients with HF') is described here.

Results

The practices provided care to 2.3 million individual patients over the 5 year period. There were 1.93 million adults, of whom 1.12 million were active patients. Of this group, 20 219 patients satisfied predetermined criteria for definite (*n* 15 468) or probable (*n* 4751) HF. The mean age of the population was 69.8 years, 50.6% were female and mean body mass index was 31.2 kg/m^2. Only 15.0% (3026) of the combined group had HF documented in the diagnosis section of their records, *Figure* 1. Just over 40% (40.1%, 8103) had an HF term detected in the free text section of the medical notes. HF-specific medication use identified 20.4% (4132) of these patients. The presence of typical signs and symptoms of HF in combination with diuretic use identified 22.9% (4635). Other criteria accounted for the remaining 1.7%.

Of the active patients, the crude prevalence of definite or probable HF was 1.82% [95% confidence interval (CI) 1.79–1.84%, *Figure* 2], and the age-standardized prevalence was 2.20% (95% CI 2.17–2.23%). The crude annual incidence was 0.291% per year (95% CIs 0.286–0.296%), and the age-standardized annual incidence was 0.348% per year (95% CIs: 0.342–0.354%). Based on these findings, we estimate conservatively that there were at least 419 000 people

Figure 1 Different ways that patients with heart failure (HF) were identified in SHAPE. CI, confidence interval.

CRITERIA FOR IDENTIFICATION OF HF PATIENTS

- In diagnosis section 15.0%
- Free text in notes 40.1%
- HF specific medications 20.4%
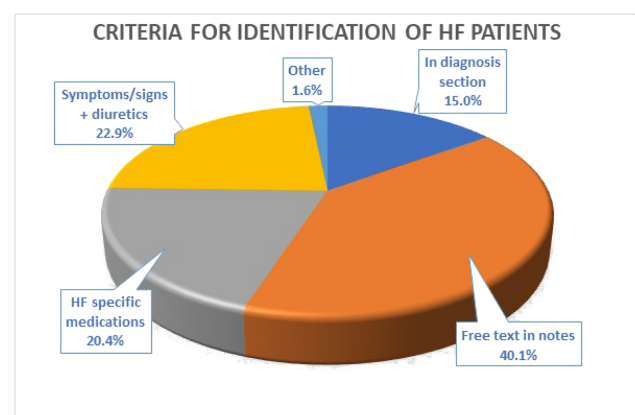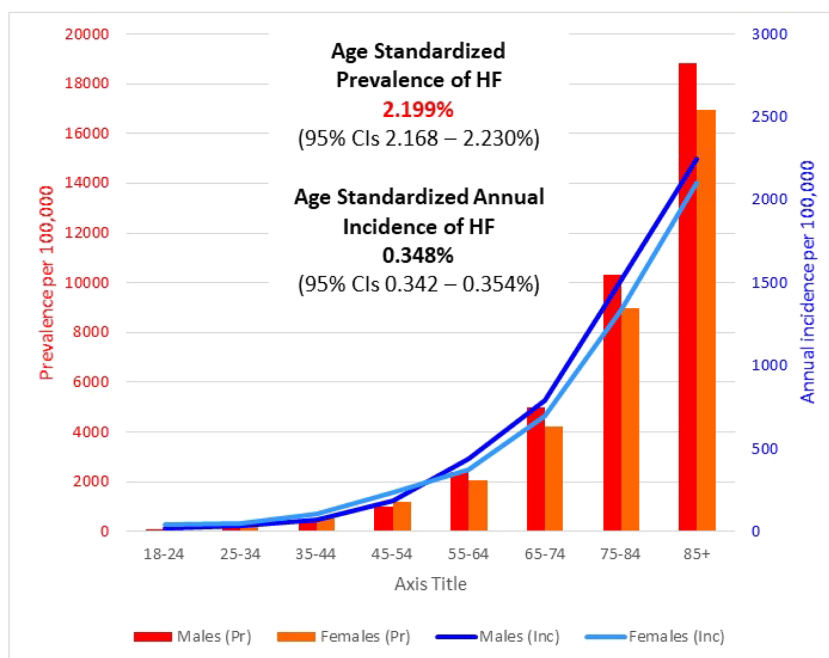- Symptoms/signs + diuretics 22.9%
- Other 1.6%

Figure 2 Prevalence and incidence of heart failure (HF).

in Australia living with HF in 2017 and more than 66 000 new cases that would have emerged over the course of 2018.

Left ventricular ejection fraction (LVEF) was mentioned in the records of 824 (4.08%) of active patients. In 21% of these (n 174), the LVEF was not quantified. Of those for whom the LVEF was quantified (n 650), 40.9% (n 266) had an LVEF ≥50% and 59.1% (n 384) had an LVEF of <50%. This latter group, which fulfilled the echocardiographic findings of HF with reduced ejection fraction (HFrEF), could be further sub-classified as 15.4% (n 100) with mildly reduced ejection fraction and 43.7% (n 284) with moderate or severely reduced ejection fraction (i.e. ejection fractions of 41–49% and ≤40%, respectively). More male patients had HFrEF compared with HF with preserved ejection fraction (HFpEF) (283 vs. 138 in active patients) but more female patients had HFpEF compared with HFrEF (128 vs. 101 in active patients). A further group (n 174) had recorded in their notes 'reduced EF' but without the EF being quantified.

We analysed chronic comorbidities that were pre-specified as being of interest to an HF population. The most commonly recorded comorbidities were hypertension (32.5%), chronic obstructive pulmonary disease (COPD)/asthma (19.5%) and depression (18.6%), followed by diabetes (9.0%), ischaemic heart disease (7.4%), osteoporosis (6.1%), atrial fibrillation (1.6%) and renal impairment (1.6%). However, our method of quantifying the prevalence of comorbidities may be an underestimate because we only captured comorbidities that had been entered into the 'diagnosis' field of the GPs practice software. Because of differences in recording convention, not

all comorbidities may have been entered into this field. In an attempt to control for this potential bias, we looked at comorbidities only in patients who also had their diagnosis of HF recorded in this same 'diagnosis' field (n = 3026). This resulted in only a slight increase in the rates of each comorbidity and minimal change in the relative frequencies of the comorbidities (hypertension 41.1%, COPD/asthma 25.1%, depression/anxiety 18.4%, ischaemic heart disease 12.9%, diabetes 11.9%, osteoporosis 9.5%, renal impairment 4.0% and atrial fibrillation 3.6%).

Blood pressure results were available for 17 121 patients. Mean (standard deviation, SD) systolic and diastolic blood pressure of the combined group were not low at 132.7 (19.8) mmHg and 77.3 (12.1) mmHg, respectively. The mean [SD] systolic blood pressure of the population with known EF ≥ 50% (n 266) was 133.9 [19.3] mmHg, while the mean [SD] systolic blood pressure of the population with known EF < 50% (n 397) was 127.3 [18.2] mmHg. Only 2.3% of patients with HF (n = 468) had a systolic blood pressure recording of less than 100 mmHg. Heart rate measurements were available for 15 469 patients. The mean [SD] heart rate was 74.9 [13.6] beats per minute (bpm) and 1274 (6.3%) of these patients had recorded a heart rate of <60 bpm, of whom 190 (0.9%) were less than 50 bpm.

Estimated glomerular filtration rate (eGFR) was available in 13 888 patients with HF. Of these, eGFR was <60 mL/min/ 1.73 m^2 in 32.9% (n = 4148) and <30 mL/min/1.73 m^2 in 6.4% (n = 793, severe renal impairment). Potassium levels were available for 17 405 patients. Of these, 1.24% (216)

had a potassium level of <3.5 mmol/L (hypokalaemia), 10.8% (1883) had a potassium level of 5.0 to 5.5 mmol/L and 1.9% (n 329) had a potassium level of >5.5 mmol/L (hyperkalaemia).

While anaemia was infrequent, absolute iron deficiency (defined as serum ferritin level of <100 g/L) was surprisingly common. Haemoglobin levels were available for 17 382 participants in the definite and probable HF populations. Of these, 611 (3.52%) had a documented haemoglobin level of <100 g/L. Ferritin levels were available for 13 604 patients with HF, and 6479 patients (32.0%) recorded a ferritin level of <100 ng/mL. Relative iron deficiency affected a further 7.6%, with 5205 (25.7%) recording a ferritin level in the range 100–300 ng/mL and just under a third of these (1546) also having a transferrin saturation of <20%.[1] Therefore, over a third (39.7%) of the 20 219 patients with HF had documented evidence of absolute or relative iron deficiency.

Of the active population, 6805 (33.7%) had been prescribed an HF-specific medication: bisoprolol (4335, 21.4%), carvedilol (1238, 6.1%), nebivolol (926, 4.6%), extended-release metoprolol (653, 3.2%), ivabradine (289, 1.4%), eplerenone (246, 1.2%), sacubitril/valsartan (243, 1.2%) and ethacrynic acid (40, 0.2%), *Figure* 3. Only a small proportion of those treated were on the highest doses of therapy (bisoprolol 28.4%, carvedilol 45.5%, nebivolol 24.6%, extended-release metoprolol 23.6%, ivabradine 22.5%, eplerenone 13.6%, sacubitril/valsartan 25.2%), *Table* 1.

Because taking an HF-specific medication was one of the criteria used to define HF, the medication use figures earlier may be overestimates. Consequently, the medication use was also examined within the subset of these HF cases where HF-specific drug use alone was not sufficient to classify a patient as definite or probable HF. This modified definition

of HF resulted in *n* = 16 807 cases of HF (11 427 definite and 5380 probable HF). HF-specific medication use within this subset of cases is shown as the first column in *Table* 1 and, as expected, is generally lower than in the second column that included the prescription of these medications as a method for defining a patient as having HF.

Of the active population with a recorded EF ≤ 40%, the use of an HF-specific medication was greater: bisoprolol (173, 60.9%), carvedilol (52, 18.3%), nebivolol (20, 7.0%), extended-release metoprolol (18, 6.3%), ivabradine (18, 6.3%), eplerenone (13, 4.6%), sacubitril/valsartan (243, 1.2%) ethacrynic acid (0, 0%), *Table* 2. However, the overall sample size was small (n 284), limiting interpretation.

With regards to other medications that are commonly, but not exclusively, used in HF 39.9% had been prescribed an angiotensin-converting enzyme ACE inhibitor, 31.6% an angiotensin receptor blocker ARB and 16.0% spironolactone. The 5 most commonly prescribed ACE inhibitors were perindopril (22.2%) and ramipril (16.3%) followed by lisinopril (1.3%), enalapril (1.2%) and quinapril (0.7%). The five most commonly prescribed ARBs were irbesartan (11.8%), candesartan (10%) and telmisartan (8.7%) followed by olmesartan (3.1%) and valsartan (1.1%). Maximum target doses of these medications were prescribed, after the diagnosis of HF, in 36.7% for the ACE inhibitors, 47% for the ARBs and 6.1% for spironolactone, *Table* 1.

Loop diuretics (56.7%) were the most commonly prescribed HF-related medication in our cohort of primary care patients with HF, suggesting that more patients are being provided symptomatic relief rather than medications that improve HF prognosis. Over 75% of these diuretic-treated patients were on 40–160 mg of furosemide per day, *Table* 1. Oral or systemic corticosteroids, nonsteroidal anti-inflammatory drugs

Figure 3 Number of medications taken by patients with heart failure (HF).

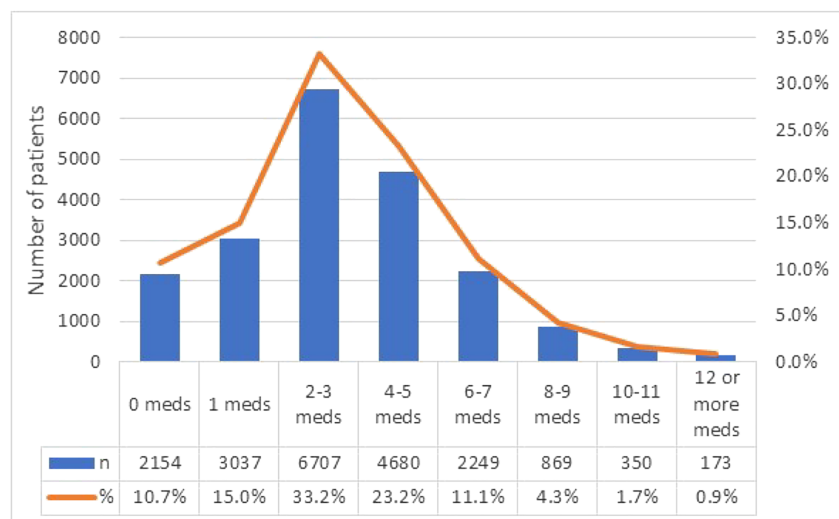|	0 meds	1 meds	2-3 meds	4-5 meds	6-7 meds	8-9 meds	10-11 meds	12 or more meds
n	2154	3037	6707	4680	2249	869	350	173
%	10.7%	15.0%	33.2%	23.2%	11.1%	4.3%	1.7%	0.9%

Table 1 Proportion of definite or probable HF active patients receiving treatment with HF therapies and the dose level for each medication/class that they had been prescribed

Medication	% of patients with HF[a] (n)	% of patients with HF (n)	Low dose N (%)	Medium dose N (%)	High dose N (%)
Medications that are only approved and reimbursed for use in HF					
HF-specific β-blocker	21.2% (3568)	33.7% (6805)	2137 (31.4%)	2549 (37.5%)	2119 (31.1%)
Bisoprolol	13.6% (2277)	21.4% (4335)	1638 (37.8%)	1466 (33.8%)	1231 (28.4%)
Carvedilol	4.3% (715)	6.1% (1238)	346 (28.0%)	329 (26.6%)	563 (45.5%)
Nebivolol	3.3% (552)	4.6% (926)	242 (26.1%)	456 (49.2%)	228 (24.6%)
Metoprolol succinate	1.7% (290)	3.2% (653)	60 (9.2%)	439 (67.2%)	154 (23.6%)
Ivabradine	0.9% (155)	1.4% (289)	0 (0%)	224 (77.5%)	65 (22.5%)
Eplerenone	0.8% (128)	1.2% (243)	210 (86.4%)	33 (13.6%)	0 (0%)
Sacubitril–valsartan	1.2% (198)	1.2% (246)	3 (1.2%)	181 (73.6%)	62 (25.2%)
Ethacrynic	0.2% (28)	0.2% (40)	36 (90%)	4 (10%)	0(0%)
Other medication commonly used in HF					
Furosemide	64.0% (10750)	56.6% (11441)	2567 (22.4%)	8763 (76.6%)	111 (1.0%)
ACE inhibitors	37.3% (6268)	39.9% (8063)	2020 (25.1%)	3081 (38.2)	2962 (36.7)
ARBs	32.2% (5416)	31.6% (6379)	983 (15.4%)	2396 (37.6%)	3000 (47.0%)
Spironolactone	16.8% (2817)	16.0% (3229)	0 (0%)	3032 (93.9%)	197 (6.1%)

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; HF, heart failure.
[a]Definition of HF excludes 'HF-specific drug' alone.

Table 2 Proportion of definite or probable HF active patients receiving treatment with HF therapies and the dose level for each medication/class that they had been prescribed, all reduced EF and recorded EF ≤ 40%

| Medication	% of patients with HF with a reduced EF (n)	% of patients with HF and documented EF ≤ 40% (n)
Bisoprolol	40.1% (224)	60.9% (173)
Carvedilol	11.8% (66)	18.3% (52)
Nebivolol	5.6% (31)	7.0% (20)
Metoprolol succinate	4.5% (25)	6.3% (18)
Ivabradine	3.9% (22)	6.3% (18)
Eplerenone	3.2% (18)	4.6% (13)
Sacubitril–valsartan	5.9% (33)	10.2% (29)
Ethacrynic	0% (0)	0% (0)

EF, ejection fraction; HF, heart failure.

(excluding aspirin) and tricyclic antidepressants, all of which may cause or exacerbate chronic HF,[1] had been prescribed to 25.80%, 23.9% and 9.4%, respectively. Collectively, more than 6 in every 10 patients with definite or probable HF had been prescribed at least one medication that may, according to the most recent Australian HF guidelines, cause or exacerbate HF—the 10 most common culprits here were found to be prednisolone/prednisone (23.5%), roxithromycin (17.27%), clarithromycin (12.71%), meloxicam (10.0%), amitriptyline (7.7%), celecoxib (7.1%), erythromycin (6.0%), amiodarone (4.5%), azithromycin (3.3%) and sotalol (2.0%). These prescriptions were made in the time after the diagnostic criteria for HF had been met.

Influenza vaccinations had been recorded for 2182 HF patients (10.8%) and pneumococcal vaccinations in 532 HF patients (2.7%). The majority (62.4%) of HF patients were receiving five or fewer medications (Figure 4)—3.9% on 0 medications, 6.8% on 1 medication, 24.8% on 2–3 medications, 26.97 on 4–5 medications, 18.5% on 6–7 medications, 10.6% on 8–9 medications and 8.4% on ≥10 medications. The mean (SD) number of drugs taken was 4.8 (3.1).

Discussion

SHAPE is the largest real-world evidence study into HF in Australia to date and offers important insights to help improve the primary care management of HF nationally. Our study has found that only 15% of regular or active patients with HF were clearly identified as such with more patients who have a diagnosis recorded in the history on HF-specific medication. For the remaining 85%, optimization of HF management is unlikely to be front of mind for the GP, which is a significant problem given the progressive nature of the disease and its poor prognosis. 45.9% of those (definite + probable) with a formal diagnosis of HF had been prescribed an HF drug, while 33.2% of those without did so (mainly those in whom a probable diagnosis was made on the presence of typical HF symptoms and a loop diuretic prescription, P < 0.0001). However, if this analysis is restricted only to those with a definite HF diagnosis—that is the 15 468 (active) cases classified as definite by our criteria—there is no difference in HF-specific drug prescription (both are 45.8%; P = 0.92).

Figure 4 Number of patients with heart failure (HF) receiving guideline recommended therapies for HF. ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.
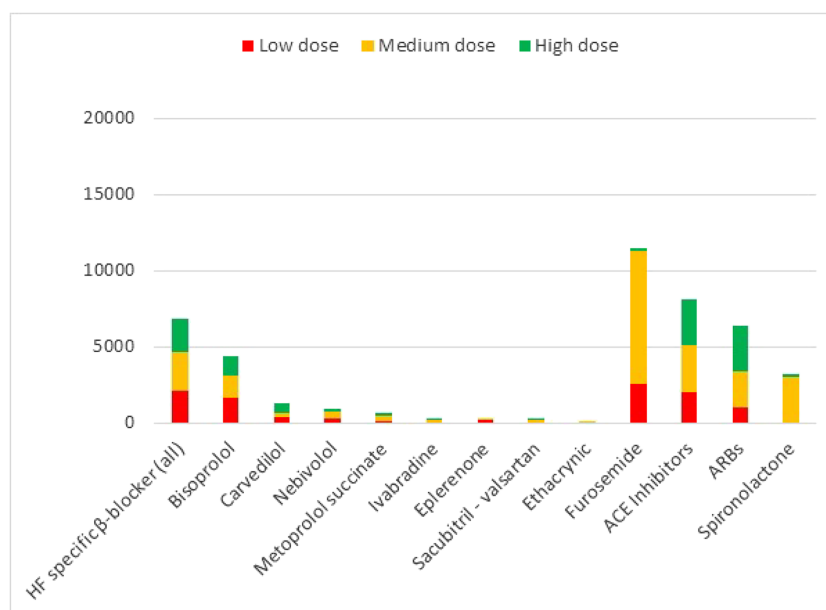
In addition, only 4.1% of patients with definite or probable HF had an ejection fraction recorded in their GPs practice software. This is a further opportunity to improve management because classification of HF into HFrEF (EF < 50%) and HFpEF (EF ≥ 50%) is integral to administering guideline recommended care.[1] While several HF pharmacotherapies have been shown to improve survival and/or reduce hospitalization in HFrEF, none have achieved their primary endpoint in HFpEF. As a result, the 2018 Australian HF guidelines recommend that patients with HFrEF but not HFpEF be treated with maximum tolerated doses of ACE inhibitors (or ARBs), beta-blockers, MRAs and ARNIs ahead of device therapy, ivabradine, nitrates, hydralazine and digoxin. Based on these findings, better identification of HF would benefit more than 8 out of 10 people living with HF in Australia while correct classification of HF is required in 9 out of 10 of these patients.

The proportion of patients with anaemia (3.5% had haemoglobin below 100 g/L) was low compared with the proportion with iron deficiency (39.7%, with either ferritin below 100 ng/mL or ferritin 100–300 ng/mL and transferrin saturation below 20%). This is likely to be a function of only a partial correlation between anaemia and iron deficiency. Many patients with iron deficiency are not anaemic.[5] Patients included in this study are from the primary care setting, with fewer comorbidities and less advanced HF, hence it is plausible that they will have a lower prevalence of both iron deficiency and of anaemia. Only 2.6% (*n* 516) of patients with HF had been prescribed intravenous iron by their GP, which has been shown to improve symptoms[3] and reduce hospitalizations[6] in patients with HF. The low use of IV iron

is likely due to a lack of awareness on the part of the GPs of the benefits of IV iron and the lack of benefits of oral iron in patients with HF, along with the lack of awareness of the 'heart failure definition of iron deficiency'.

The findings from SHAPE suggest that there may be an opportunity for earlier and more aggressive management of HF in the primary care setting. Through SHAPE, we have uncovered that the HF patients seen in general practice have fewer comorbidities recorded compared with those seen in hospital settings[7] or clinical trials,[8,9] and this may reflect a lower risk of hospitalization and mortality or perhaps patients who are earlier in their disease trajectory.[9–11] For example, in the SNAPSHOT study, Newton *et al.* documented rates of ischaemic heart disease (56%), renal disease (55%) and diabetes (38%) that were far higher than those see in our primary care population (12.9%, 4.0% and 11.9%, respectively).[9] Other possible explanations for this difference could include a lower impetus by GPs to record past medical history (e.g. not relevant to presenting complaint, not prompted by practice software) or low health literacy of patients (i.e. they may not be aware of all their comorbidities to report them to their GP). SHAPE has also shown that the rates of the four clinical features which most commonly impede the initiation and up-titration of HF therapies is relatively low in primary care (bradycardia 6.3%, eGFR<30 mL/min/1.73 m^2 6.38%, hypotension 2.3% and hyperkalaemia 2.0%) suggesting that the large majority of people with HF in the primary care setting could have guideline recommended therapies safely initiated or up-titrated provided this is accompanied by close monitoring.

There are other explanations for the lower prevalence of comorbidities noted in the HF population. We did not specifically search the database for an elevated HbA1c result, for example, as confirmation of diabetes, nor the use of inhalers for COPD. There would also have been a lot of omitted diagnosis coding, as is a well-known phenomenon in such electronic records. Also, although some of the patients with fewer comorbidities may have been because of lack of confirmation of the comorbidities, some may be because a proportion of the patients did not have true HF and a proportion may have been earlier in their disease, particularly if they were younger. Our clinical experience suggests that younger patients are referred for a cardiology opinion later, with other diagnosis being considered before HF.

While SHAPE is a new study, its findings replicate in part those of Krum et al. who also found that diuretics were the most commonly used therapy in HF patients identified in primary care (56.6%) and that few patients were on treatments which improve HF outcomes (i.e. beta-blockers and spironolactone).[12] Diuretics are effective at providing symptomatic relief from fluid overload in HF but their effect on morbidity and mortality in chronic HF has not been studied.[1,13] In patients who are at low risk for developing worsening congestion, the use of diuretics might result in further neuro-hormonal stimulation of the sympathetic nervous system and the renin-angiotensin system, which contributes to the pathophysiology of HF. More importantly in this primary care context, overuse of diuretics which carry the risks of worsening renal function, hypotension and electrolyte abnormalities may impede a GPs willingness to initiate and up-titrate guideline recommended therapies such as beta-blockers, ACE inhibitors (or ARBs or ARNIs) and MRAs. Given our findings of their widespread use among people with HF in the primary care setting, diuretics could flag to GPs patients who are at risk of HF but have not yet been conclusively diagnosed, classified and documented as having HFrEF or HFpEF.

SHAPE has also uncovered that people with definite or probable HF are at real risk of a 'double whammy' when it comes to their medications. First, the vast majority are not receiving guideline recommended therapies that have been proven to reduce mortality, lower their risk of hospitalization and improve quality of life—when they do, only a small proportion are up-titrated to high dose levels. The scope for improvement here is highest for ARNI (sacubitril/valsartan) followed by MRAs with only 1.2% and 15.3% of people with definite or probable HF receiving these treatments (as of 30 June 2018). Similarly, relatively few had received immunizations and intravenous iron (despite the high rates of iron deficiency we uncovered). Second, most (64.2%) have been prescribed at least one medication that may worsen their HF. Most importantly, 23.9% had been prescribed an NSAID. Other medications of note were macrolide antibiotics (most commonly prescribed and may prolong QT interval) and tricyclic antidepressants.

There are many reasons why GPs do not initiate or upgrade the medical treatment of the patients with HF. First, the identification of patients with HF may be difficult in general practice. Second, GPs may be reluctant to 'interfere' with the cardiologist's management plan. Also, as the management of HF has changed dramatically in the past 20 years, many GPs find it to be a very complex and confusing area with frequently updated recommendations with which it may be difficult to keep up to date.

Some of these issues can be addressed through strategies designed to systematically identify, recall, diagnose, classify and treat the at-risk patients. This study has also identified that there is a requirement for more upskilling of GPs in the management of HF through continuing medical education programmes, clinical audits and clinical placements such as 'preceptorships' in HF clinics to keep them abreast of the changes in management. And a quality improvement initiative such as this on its own stands to make huge improvements in the prognosis of people living with HF in Australia without the need for any new high-cost technology or innovation.

Strengths and limitations

The major strength of SHAPE lies in its size and involvement of a large number of general practices from across Australia. Also, it is the first study of HF involving data directly drawn from the general Australian community.

It is well-known that observational studies are susceptible to confounding, information bias and selection bias.[14] In terms of potential information bias, population-level databases often do not include details regarding comorbidities, disease severity status and specific treatment plans.[15] Furthermore, although medical record systems in the primary care setting can be well-structured, provider compliance with populating the records in accordance with the systems intended structure is variable and often incomplete. Some data in the records are not available for electronic assessment as they are contained in scanned attachments in the systems (e.g. discharge summaries and echocardiogram reports) which reduced our ability to identify severity of HF and outcome (e.g. rehospitalization and death). As the point of diagnosis, treatment initiation and performance of key investigations may occur in the hospital setting, some patients may have been reclassified if the full hospital data had been available.

While some of the data were extracted as coded entries to specific files (formal diagnoses, drugs prescribed, BNP, and management items), symptoms and signs of HF, and ejection fraction data were searched for within the free text of the medical notes. The use of programming methods to search free text for specific keywords is an inexact science. However,

the search criteria were refined by reviewing records manually and to confirm that commonly appearing miss-spellings of words were correctly identified. Although it was not feasible to review all the patient notes (there were over 8 million records in total), we believe that misclassification errors would have occurred infrequently so that the final results should be a good representation of the epidemiology in the Australian community setting.

In terms of comorbidities, the diagnostic fields of GP records are not always completely nor accurately filled, but the issue is of random data misclassification rather than information bias. It is unlikely that reporting of conditions will differ, especially if they have obvious symptoms. Specifically, it is unlikely that GPs would have been less likely to record conditions like diabetes, ischaemic heart disease and atrial fibrillation when HF is also recorded.

A further limitation of this study would be the possibility of over diagnosing patients with HF based on medications alone, it is possible that we are under diagnosing patients as the patients symptoms are being treated as another condition and so not on appropriate therapy. Three quarters of the included patients were assigned an HF diagnosis using a strong categorization method: history, reason for visit and HF-specific medications. Of the remaining 25% who were on a diuretic with symptoms, or signs of HF, it is possible that some would not have HF. Hence overall, we believe that the impact from over-diagnosis of HF would be small.

And if some of the cohort did not have true HF, then they may not have had iron deficiency due to this chronic condition. However, it still is important to note that iron deficiency is under diagnosed and is a relatively simple way to improve outcomes for patients with HF.

For the calculation of incidence rates, we assumed that new cases were those that appeared in the database from July 2014 onwards (excluding those that were diagnosed in the first year of the data extract). This assumes that patients were being treated by the same general practice during the whole period, so that any mention of HF-specific terms would have appeared during that first year. In other words, it assumes that participating practices did not inherit new patients with existing HF during the subsequent years. This may not be valid for a patient with established HF who commences their interaction with the participating general practice at some point after July 2014. This may mean that our estimated incidence rates may be slightly high (as these cases would be considered 'new' by mistake). However, with the large numbers of patients involved, we expect this to have a small influence on the final estimates.

This study is limited to patients in a single primary care network (albeit a large one). However, we are confident that the results are representative of the epidemiology in the Australian community setting. The key word search was conducted on the medical records of 1.93 million adult Australians—over 10% of the adult population. The skewness

of the sample towards areas of higher socioeconomic status may have led to a slight underestimation of the population rates of HF (as rates of HF appear to be slightly higher in areas of lower SES), so in this sense, our final estimates of prevalence and incidence may be conservative.

Conclusions

SHAPE is the largest real-world evidence study of HF in Australia. Mindful of the well-known limitations stemming from real-world medical records, the study suggests that about five out of every six patients with definite or probable HF do not have this diagnosis clearly documented in their primary care medical records and fewer still have their condition adequately categorized to allow for management as per guideline recommendations. Perhaps because of this lack of diagnosis and classification, fewer than 4 out of every 10 in this combined group are being treated with HF-specific guideline recommended therapies such as beta-blockers, MRA and ARNI, while over 6 in every 10 are prescribed medications that may worsen their condition, such as macrolide antibiotics, nonsteroidal anti-inflammatory drugs and tricyclic antidepressants. Loop diuretics are the most commonly prescribed therapy in this combined group, which may serve as a prompt to help GPs identify, diagnose, classify and therefore treat these at-risk patients more optimally. Our data suggest an opportunity to better identify and manage HF in primary care.

Acknowledgements

Conflict of interest

DL has received honoraria from Amgen, AZ, Bayer, BI, BMS, Novartis, Pfizer, Sanofi and Shire. PP has sat on advisory boards and/or spoken at, facilitated or chaired at meetings for and/or received travel and accommodation costs from AbbVie, Amgen, AZ, Bayer, BI, BMS, CSL, Eli Lilly, GSK, Janssen, Menarini, MSD, Novartis, Novo Nordisk, Pfizer, Sanofi and Seqirus. RA served as a member of several advisory boards and conducted paid presentations for AZ, Novartis and Sanofi in the past 2 years, and Abbott, BMS, Eli Lilly, Novo Nordisk, Servier and Takeda prior to this. DH has given talks for AZ,

Funding

Patient and public involvement

This is a retrospective cohort study based on analysis of existing medical records of patients aged 18 years or more cared for at participating general practices. The study utilized techniques to identify potential heart failure patients who would not have been identified using standard search processes. A list of the relevant unique study specific codes was sent back to the medical centre groups Chief Medical Officer to allow HF patients to be identified at the centres and then to manage patients as was deemed clinically appropriate.

References

1. Atherton J, Sindone A, De Pasquale C, Driscoll A, MacDonald PS, Hopper I, Kistler PM, Briffa T, Wong J, Abhayaratna W, Thomas L, Audehm R, Newton P, O'Loughlin J, Branagan M, Connell C. National heart foundation of australia and cardiac society of ustralia and New Zealand: guideline for the prevention detection and management of heart failure in Australia 2018. *Heart Lung Circ* 2018; **27**: 1123–1208.
2. Parsons R, Liew D, Neville AM, Audehm RG, Haikerwal D, Piazza P, Lim K, Sindone AP. Study of Heart Failure in the Australian Primary carE setting (SHAPE): methods. *BMC Public Health.* 2020; **20**: 648.
3. Royal Australian College of General Practitioners. *Standards for general practices (5th edition)* 2017.
4. Liew D, Audehm RG, Haikerwal D, Piazza P, Neville AM, Lim K, Parsons RW, Sindone AP. Epidemiology of heart failure: study of Heart failure in the Australian Primary carE setting. *ESC Heart Failure* 2020; **7**: 3871–3880.
5. Boyko EJ. Observational research opportunities and limitations. *J Diabetes Complications* 2013; **27**: 642–648.
6. Australia Population. 2020; www.population.net.au/ (accessed on 24 Jul 2019)
7. Anker S, Comin-ColetJ FG, Willenheimer R, Dickstein K, Drexler H, Lüscher TF, Bart B, Banasiak W, Niegowska J, Kirwan BA. Ferric carboxymaltose in patients with heart failure and iron deficiency (FAIR HF study). *N Engl J Med* 2009; **361**: 2436–2448.
8. Anker SD, Kirwan BA, van Veldhuisen DJ, Filippatos G, Comin-Colet J, Ruschitzka F, Lüscher TF, Arutyunov GP, Motro M, Mori C, Roubert B. Effects of ferric carboxymaltose on hospitalisations and mortality rates in iron-deficient heart failure patients: an individual patient data meta-analysis. *Eur J Heart Fail.* 2018; **20**: 125–133.
9. Newton PJ, Davidson PM, Reid CM, Krum H, Hayward C, Sibbritt DW, Banks E, MacDonald PS. Acute heart failure admissions in New South Wales and the Australian Capital Territory: the NSW HF snapshot study. *Med J Australia.* 2016; **204**: 113.e1–113.e8.
10. McMurray JJ, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, Rouleau JL, Shi VC, Solomon SD, Swedberg K, Zile MR. Angiotensin–neprilysin inhibition versus enalapril in heart failure. *N Engl J Med.* 2014; **371**: 993–1004.
11. Solomon SD, Rizkala AR, Lefkowitz MP, Shi VC, Gong J, Anavekar N, Anker SD, Arango JL, Arenas JL, Atar D, Ben-Gal T. Baseline characteristics of patients with heart failure and preserved ejection fraction in the PARAGON-HF trial. Circulation. *Heart Fail.* 2018; **11**: e004962.
12. Krum H, Tonkin AM, Currie R, Djundjek R, Johnston CI. Chronic heart failure in australian general practice. *Med J Aust* 2001; **174**: 439–444.
13. Mullens W, Damman K, Harjola VP, Mebazaa A, Brunner-La Rocca HP, Martens P, Testani JM, Tang WW, Orso F, Rossignol P, Metra M. The use of diuretics in heart failure with congestion – a position statement from the heart failure Association of the European Society of cardiology. *Eur J of Heart Fail* 2019; **21**: 137–155.
14. Booth CM, Tannock IF. Randomised controlled trials and population-based observational research: partners in the evolution of medical evidence. *Br J Cancer* 2014; **110**: 551–555.
15. Klip IT, Comin-Colet J, Voors AA, Ponikowski P, Enjuanes C, Banasiak W, Lok DJ, Rosentryt P, Torrens A, Polonski L, van Veldhuisen D, van der Meer P, Jankowska EA. Iron deficiency in chronic heart failure: an international pooled analysis. *Am Heart J.* 2013; **165**: 575–582.