#### **ORIGINAL ARTICLE**



# Mind the Gap: Mismatches Between Clinicians and Patients in Heart Failure Medication Management

Ken Lee Chin<sup>1</sup> · Marina Skiba<sup>2</sup> · Christopher M. Reid<sup>1,3</sup> · Andrew Tonkin<sup>1</sup> · Ingrid Hopper<sup>1,4</sup> · Justin A. Mariani<sup>4,5,6</sup> · Danny Liew<sup>1</sup>

Published online: 9 January 2018 © Springer Science+Business Media, LLC, part of Springer Nature 2018

#### Abstract

**Purpose** Previous studies on the 'treatment gap' in patients with heart failure (HF) have focused either on prescribing or patients' adherence to prescribed treatment. This study sought to determine whether or not recent initiatives to close the gap have also minimised any mismatches between physicians' expectation of their patients' medications, medications in the patients' possession and their actual medication use.

**Methods** A cross-sectional observational survey was conducted from December 2015 to June 2016 in The Alfred Hospital HF clinic in Melbourne, Australia. Patients were invited to participate if they had chronic HF (NYHA class II to IV), were aged  $\geq 60$  years, had no history of HF related hospitalisation within the past 6 months and were prescribed at least two HF medications.

**Results** Of 123 eligible patients, 102 were recruited into the study. Beta-blockers, mineralocorticoid receptor antagonists, loop diuretics and statins were associated with the highest rates of mismatches of drugs and doses, ranging from 10 to 17%. Discrepancy of total daily doses was the most common type of mismatch. Overall, only 23.5% of the patients were taking the right drugs at the right doses as expected by their cardiologists/HF specialists.

**Conclusions** Despite improved prescribers' adherence to guideline-directed medical therapy, there remain considerable mismatches between prescribers' expectation of patients' HF medications, medications in patients' possession and their actual medication use. Initiatives to improve this situation are urgently needed.

Keywords Chronic heart failure · Pharmacological treatment · Discrepancies · Medication therapy management

In memoriam of Henry Krum

Danny Liew danny.liew@monash.edu

- <sup>1</sup> CCRE Therapeutics, Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia
- <sup>2</sup> School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia
- <sup>3</sup> School of Public Health, Curtin University, Perth, Australia
- <sup>4</sup> Department of Cardiovascular Medicine, Alfred Hospital, Melbourne, Australia
- <sup>5</sup> Central Clinical School, Faculty of Medicine, Monash University, Melbourne, Australia
- <sup>6</sup> Heart Failure Research Group, Baker Heart and Diabetes Institute, Melbourne, Australia

## Introduction

Poor adherence to evidence-based treatment, involving both clinicians and patients, limits the effectiveness of heart failure (HF) therapies. Recent initiatives to close the 'treatment gap' have primarily focused either on prescribers' adherence to guideline-recommended treatment or patients' adherence to the prescribed therapy, under the assumption that there are no major discrepancies between prescribed medications and those in patients' possession.

To date, prescribers' adherence to guideline-recommended treatment remains suboptimal [1], with an estimated 4 to 17% of eligible chronic HF patients with reduced ejection fraction (HFrEF) not being treated with evidence-based treatment [2]. On the other hand, adherence in the community is poor: reported at about 50% at 1 year, and declining with time [3, 4]. Data suggest that poor adherers to HF therapy are more likely to be female, elderly, treated with complex medical regimens,

prescribed diuretics and have greater number of concomitant illnesses and severity [5]. Other contributing factors include polypharmacy, poor socioeconomic status, poor health literacy, low education level, problems with dexterity, lack of social support, low motivation to stay healthy and desire to preserve a good quality of life [3, 6, 7].

In Australia, a series of concerted efforts were taken, including the establishment of cardiac clinical networks nationwide, to facilitate improvement in HF care by fostering awareness, communication, partnerships and links, and by providing advice and advocacy for policy, planning and funding [8]. Despite this, prognosis of HF remains poor, with high rates of mortality and readmissions that impose a substantial burden on the healthcare system [9]. A fundamental concern here is that whether or not efforts to reduce the treatment gap in HF have also minimised any mismatches between physicians' expectation of their patients' medications, medications in the patients' possession and their actual medication use. This is an important question which requires attention since efforts to improve adherence from either end (i.e. physicians and patients) are futile if there is a break in the information chain. Our study sought to address this question. Secondary objectives were to examine prescribing pattern and patients' knowledge of their dispensed medications.

## Methods

#### **Study Design and Patient Population**

A cross-sectional survey was conducted in the HF clinic of the Alfred Hospital, a tertiary hospital and heart transplant centre located in Melbourne, Australia, that provides heart and lung transplantation services for the states of Victoria and Tasmania. The hospital's HF service cares for patients through a multidisciplinary approach, involving 12 HF and transplant cardiologists, 2 nurse practitioners, a pharmacist and a dietician. Medication reconciliation is primarily performed by the treating physician and the nurses and pharmacist provide ongoing regular education for patients. As required, allied health and social work services are available for patients who require additional assistance, such as the elderly, the socially disadvantaged and those with poor health literacy. Inclusion criteria were age  $\geq 60$  years; stable New York Heart Association (NYHA) Class II to IV symptoms for at least 6 months at screening; no history of HF related hospitalisation in the past 6 months at screening; prescribed at least two HF medications (angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs), beta-blockers (BBs), mineralocorticoid receptor antagonists (MRAs) and/or loop diuretics); willing and able to provide written consent and able to speak English. Patients were excluded if in the investigators' opinion, they were too ill to participate or had presented for psychiatric evaluation.

We collected information on demographics, education level, history of hospitalisation for HF within 12 months prior to interview, medical history and most recent NYHA functional class, blood pressure, heart rate, left ventricular ejection fraction (LVEF), renal function, smoking history and alcohol consumption. Physicians' expectations of the medications that patients were taking were based on what was recorded in the clinical notes at each clinical visit. We also documented any updated information obtained from general practitioner (GP) referral letters to the Alfred Hospital's cardiologists/HF specialists prior to the interview. Reasons for non-prescription or underdosing with respect to the recommended dosages by the clinical practice guidelines [10] were documented.

Patients identified from the clinic's database were invited by mail and telephone to participate. Participants were assured of anonymity and confidentiality regarding all details and answers provided. Participation was on a voluntarily basis and written informed consent was obtained before patients were interviewed at the Alfred Hospital HF clinic. All medications were reviewed, including over-the-counter medications, and information printed on the medication boxes was recorded. Participants were also asked to name the drugs, dose and frequency of use based on their actual consumption. If there was an omission of a dose or extra doses were taken, they were asked to describe the reasons and frequency for such 'deviations'. The interviews were arranged to coincide with patients' appointment in the HF clinic. Patients who had consented to participate were not excluded if they had clinical improvement or event by the time of the interview.

Patients' knowledge about indications, dosages and side effects of the medications in their possession was assessed. They were encouraged to explain the perceived purpose, dosage, frequency and side effects of each medication in their own words. Patients were also allowed to read directly from any information sheet previously provided by a pharmacist. Patients were considered knowledgeable if they could provide adequate 'correct' information about the medications. Statements such as 'atorvastatin is for cholesterol', and 'warfarin can cause bruises or bleeding' were accepted as adequate knowledge.

Information gathered from the patients regarding their medications was then compared with clinical notes obtained from the Alfred Hospital HF clinic. Medications which were newly prescribed/witheld/had doses changed on the interview day were not considered as a mismatch. Medications used on an 'as required' basis, like glyceryl trinitrate, were not considered in this analysis.

### **Statistical Analysis**

To assess the extent of patients being treated with evidencebased doses for HF drugs, patients were further categorised as receiving < 50 or  $\ge 50\%$  of target dose, based on the clinical notes and patients' self-reported medication use behaviour. Sub-groups were compared by  $\chi^2$  test for dichotomous variables and Student's *t* test for continuous variables. Simple and multiple logistic regression analyses were used to evaluate the association between overall medication mismatch and demographic and clinical characteristics. We performed univariate logistic regression by including all collected covariates for cumulative mismatches of medications and dosages. We then entered variables with P < 0.1 into a multivariate logistic regression model using a backward elimination method. Variables with P < 0.05 in the

39

multivariate model were considered to be independent predictors. Information on health literacy, cognition or health-related quality of life (HRQOL) were not available and hence not included in the analysis. Statistical analysis was performed using SPSS version 21.0 (Chicago, IL, USA).

### Results

A total of 123 patients with HF were invited to participate in this survey from December 2015 to June 2016. Twenty-one

Characteristics	Overall	Ischaemic CM	Non-ischaemic CM
N, %	102	44 (43.1)	58 (56.9)
Age, year (mean)	70.5	71.4	69.8
Male, %	73.5	88.6	62.1
Education level, %			
Secondary education and below	80.2	84.1	77.2
Tertiary education	19.8	15.9	22.8
Living arrangement, %			
Living alone	25.5	27.3	24.1
Living with family/relatives	74.5	72.7	75.9
Systolic blood pressure, mmHg	118.7	111.5	123.5
Heart rate, beats/min	71.0	71.8	70.5
NYHA, %			
Ι	17.5	11.9	21.8
Π	61.9	61.9	61.8
III	20.6	26.2	16.4
Left ventricular ejection fraction, % (mean)	38.6	30.3	44.2
< 40%	54.5	73.8	40.4
$\geq 40\%$	45.5	26.2	59.6
Estimated GFR, ml/min/1.73 m <sup>2</sup> (mean)	57.9	53.4	61.9
$\geq$ 60 ml/min.1.73 m <sup>2</sup>	49.5	38.1	58.8
30 to 59 ml/min.1.73 m <sup>2</sup>	46.2	52.4	41.2
$\leq$ 29 ml/min.1.73 m <sup>2</sup>	4.3	9.5	_
Hospitalisation for heart failure within 12 months, %	14.7	13.6	15.5
Medical history, %			
Hypertension	41.2	43.2	39.7
Atrial fibrillation or flutter	49.0	43.2	53.4
LBBB	7.8	9.1	6.9
Dyslipidaemia	30.4	36.4	25.9
Diabetes mellitus	34.3	43.2	27.6
Stroke	9.8	11.4	8.6
PCI	13.7	29.5	1.7
CABG	26.5	61.4	0.0
Device therapy, %	55.9	65.9	48.3
No. of CV drugs in the bag, median (IQR)	6(3)	7(1.8)	5(2)

Note: Values are mean  $\pm$  SD or percentage, unless otherwise specified. Device therapy includes implantable cardioverter-defibrillator (ICD) and cardiac-resynchronisation therapy (CRT)

*NYHA* New York Heart Association functional class, *GFR* glomerular filtration rate, *LBBB* left bundle branch block, *PCI* percutaneous coronary intervention, *CABG* coronary-artery bypass grafting

#### Table 1 Patient characteristics

Drug class	Clinical	Notes vs bags	ags						Notes vs behaviour	ehaviour					
	N(%)	Not found in bag,	Not in notes but present,	Different drug of the	Different dose of the same drug, $N(\%)$	lose of the $N(\%)$	0	Total mismatch	Not taking at all,	Not in notes but taking,		Different dose of same drug, $N(\%)$	Different dose of the same drug, $N(\%)$		Total mismatch according drug
		(0/,) NI	( <i>0</i> /, ) <i>N</i>	same class, N (%)	Lower dose	Higher dose	Overall	according drug class, $N(\%)^{\ddagger}$	(96) M	(0/) NI	Class, // (70)	Lower dose	Higher dose	Overall	Class, IV (70)
ACEI	62 (60.8)	3 (4.8)	2 (2.0)	1	4 (6.5)	5 (8.1)	9 (14.5)	14 (8.3)	3 (4.8)	2 (2.0)	I	4 (6.5)	5 (8.1)	9 (14.5)	14 (8.0)
ARB	35 (34.3) 1 (2.9)	1 (2.9)	1 (1.0)	I	2 (5.7)	3 (8.6)	5 (14.3)	7 (4.1)	1 (2.9)	1 (1.0)	I	2 (5.7)	2 (5.7)	4 (11.4)	6 (3.4)
BB	89 (87.3) 3 (3.4)	3 (3.4)	1 (1.0)	I			14 (15.7)	18 (10.7)	3 (3.4)	1 (1.0)	I	9 (10.1)	7 (7.9)	16 (18.0)	20 (11.4)
MRA	47 (46.1) 5 (10.6)	5 (10.6)	3 (2.9)	I	3 (6.4)	6 (12.8)	9 (19.1)	17 (10.1)	5 (10.6)	3 (2.9)	Ι	3 (6.4)	6 (12.8)	9 (19.1)	17 (9.7)
Loops diuretics	77 (75.5)	2 (2.6)	5 (4.9)	1 (1.3)	10 (13.0)	5 (6.5)	15 (19.5)	23 (13.6)	3 (3.9)	5 (4.9)	1 (1.3)	15 (19.5)	5 (6.5)	20 (26.0)	29 (16.6)
Thiazide	6 (5.9)	2 (33.3)	1 (1.0)	I	2 (33.3)	Ι	2 (33.3)	5(3.0)	2 (33.3)	1 (1.0)	Ι	2 (33.3)	1 (16.7)	3 (50.0)	6 (3.4)
Ivabradine	9 (8.8)	2 (22.2)	1 (1.0)	I	I	2 (22.2)	2 (22.2)	5(3.0)	2 (22.2)	1 (1.0)	I	Ι	2 (22.2)	2 (22.2)	5 (2.9)
Digitalis	30 (29.4)	3 (10.0)	2 (2.0)	I	3 (10.0)	2 (6.7)	5 (16.7)	10 (5.9)	3 (10.0)	2 (2.0)	Ι	2 (6.7)	2 (6.7)	4 (13.3)	9 (5.1)
CCB	6 (5.9)	1 (16.7)	1 (1.0)	I	2 (33.3)	I	2 (33.3)	4 (2.4)	1 (16.7)	1 (1.0)	I	2 (33.3)	I	2 (33.3)	4 (2.3)
Nitrates	16 (15.7)	3 (18.8)	1 (1.0)	I	1 (6.3)	I	1 (6.3)	5(3.0)	3 (18.8)	1 (1.0)	I	1 (6.3)	Ι	1 (6.3)	5 (2.9)
Anti-arrhythmic 16 (15.7) 1 (6.3)	16 (15.7)	1 (6.3)	2 (2.0)	I	1 (6.3)	5 (31.3)	6 (37.5)	9 (5.3)	2 (12.5)	2 (2.0)	I	1 (6.3)	4 (25.0)	5 (31.3)	9 (5.1)
Antiplatelet	7 (6.9)	Ι	1 (1.0)	2 (28.6)	Ι	I	I	3 (1.8)	Ι	1 (1.0)	1 (14.3)	Ι	I	I	2 (1.1)
Aspirin	56 (54.9)	5 (8.9)	4 (3.9)	1 (1.8)	1 (1.8)	2 (3.6)	3 (5.4)	13 (7.7)	6 (10.7)	5 (4.9)	1 (1.8)	Ι	2 (3.6)	2 (3.6)	14(8.0)
Warfarin	35 (34.3) 4 (11.4)	4 (11.4)	1 (1.0)	I	1 (2.9)	I	1 (2.9)	6 (3.6)	4 (11.4)	1 (1.0)	I	2 (5.7)	I	2 (5.7)	7 (4.0)
NOAC	16 (15.7) 1 (6.3)	1 (6.3)	3 (2.9)	I	I	1 (6.3)	1 (6.3)	5(3.0)	1 (6.3)	3 (2.9)	I	Ι	1 (6.3)	1 (6.3)	5 (2.9)
Statin	67 (65.7)	6(9.0)	7 (6.9)	Ι	3 (4.5)	3 (4.5)	6 (9.0)	19 (11.2)	7 (10.4)	5 (4.9)	1 (1.5)	3 (4.5)	3 (4.5)	(0.0)	19 (10.9)
Non-statin lipid	9 (8.8)	1 (11.1)	Ι	I	1 (11.1)	I	1 (11.1)	2 (1.2)	Ι	Ι	I	Ι	I	I	Ι
Other CV drugs 11 (10.8) 1 (9.1)	11 (10.8)	1 (9.1)	I	I	Ι	3 (27.3)	3 (27.3)	4 (2.4)	1 (9.1)	Ι	Ι	1 (9.1)	2 (18.2)	3 (27.3)	4 (2.3)
Total mismatch	N/A	44	36	4	42	43	85	169	47	35	4	47	42	89	175
Notes: Denominator is the number of patients prescribed according to the respective drug classes in the clinical notes, unless otherwise specified	ator is the 1	number of p	atients prescrib	ed according	to the resp	ective dr	ig classes	in the clinica	ul notes, unle	ess otherwise	specified				
$^{\dagger}$ Denominator is the total number of patients in the study (102 patients)	s the total n	number of pa	ttients in the stu	ıdy (102 pati	ents)										
<sup>‡</sup> Denominator is the cumulative total number of mismatch comparing notes vs hass and notes vs behaviour. respectively	the cumul	ative total m	mhar of miem	atch comnari	ing notes in	hoor ond	1 - atao - L		•						

 Table 2
 Cumulative mismatches of medications and dosages according to drug classes at individual level

 $\underline{\textcircled{O}}$  Springer

ACEI angiotensin-converting enzyme inhibitors, ARB angiotensin-receptor blockers, BB beta-blockers, MRA mineralocorticoid receptor antagonists, CCB calcium channel blockers, NOAC new oral anticoagulants, N/A not applicable

patients declined (n = 18) or died (n = 3) before the interview, leaving 102 (82.9%) who completed the survey.

Table 1 summarises patient characteristics. Patients had a mean age of 70.5 years, 73.5% were male, 43.1% had ischaemic aetiology and mean LVEF of 38.6%. Nearly 15% of the participants had been hospitalised for heart failure within the year prior to the interview day. Of note, we did not recruit patients with NYHA class IV because all these patients experienced heart failure-related hospitalisation or died within 6 months of screening.

#### **Prescribing Pattern**

Ninety percent of the patients were prescribed ACE inhibitors/ ARB and BB. In addition, MRA, loops diuretics and statins were prescribed to 46, 76 and 66% of the patients, respectively (Table 2). More than 70% of the patients were prescribed with  $\geq$  50% of the target doses for ACE inhibitors/ARB and BB, and over 90% for MRA (Table 3). The proportion of patients claiming to be taking these medications at  $\geq$  50% of the target doses were similar to those prescribed.

#### Mismatches at Individual Level

The cumulative mismatches of the cardiovascular (CV) medications and/or dosages between clinical notes, medications found in the patients' bags and self-reported medication use behaviour were high (Fig. 1). When CV medications listed in the notes were compared with those found in patients' bags, there were mismatches in the medications (49%) and dosages (57.8%). When the medications found in the bag were compared with self-reported medication use, 2 and 21.6% had mismatches in the medications and dosages, respectively. Patients with LVEF  $\geq$  40% had lower number of mismatches in medications and dosages compared to those with LVEF < 40% (Fig. 2). Overall, only 23.5% of the patients were taking the correct medications at the correct total daily doses as expected by their HF clinic's physicians.

Table 3 Proportion of patients being prescribed or self-reported to be taking  $\geq$  50% of target doses

Drug class	Clinical notes, $(\%)^{\ddagger}$	Behaviour, $(\%)^{\ddagger}$	P value <sup>¶</sup>
ACEI	77.4	75.4	0.48
ARB	54.3	57.6	0.57
ACEI/ARB	69.1	68.1	0.77
BB	77.3	69.8	0.08
MRA	91.5	97.8	0.57

<sup>‡</sup> Number of patients being prescribed with  $\geq$  50% of target doses over total number of patients being prescribed with the drug

<sup>¶</sup>Comparison of clinical notes and patients' medication use behaviour

Table 2 summarises cumulative mismatches of medications and dosages according to drug classes. When information in the clinical notes were compared with medications found in the bags, loop diuretics, BB, MRA and statins were mismatched in 13.6, 10.7, 10.1 and 11.2%, respectively, of cases. Discrepancy of total daily doses was the most common type of mismatch, where 14.5, 14.3, 15.7, 19.1 and 19.5% mismatches were recorded in ACE inhibitors, ARB, BB, MRA and loops diuretics, respectively. When information in the notes was compared with self-reported medication use, the rate of mismatches was similar. Figure 3 depicts the type of mismatches in ACE inhibitors, ARB, BB, MRA and loops diuretics. A total of 16.7% of participants said that they had deliberately skipped doses on occasional/regular basis, mainly for loop diuretics and drugs to be taken in the afternoon and evening.

On multivariate analysis, ischaemic cardiomyopathy, history of myocardial infarction and percutaneous coronary intervention were the most significant predictors of mismatches.

#### Pill Burden and Patients' Knowledge

The median (interquartile range, IQR) number of cardiovascular and HF drugs found in the medication bags were 6(3)and 3(2), respectively (Table 4). Figure 4 illustrates the number of CV and HF drugs by LVEF category. Patients' knowledge of their cardiovascular drugs was poor, where the median (IQR) number of indications, dose and side effects correctly identified were 4(4), 6(3) and 0(1), respectively. When only HF medications were considered, the median (IQR) number of indications, dose and side effects correctly identified were 2.5(2), 3(2) and 0(1), respectively.

## Discussion

In this study, we found that the majority of HF patients attending the Alfred Hospital HF clinic were treated in accordance to guideline-recommended treatments. Despite this, only a quarter of them were taking HF medications at the doses expected by their physicians. A significantly high proportion of the mismatches involved medications known to be life-saving: ACE inhibitors, ARB, BB and MRA. The number of mismatches increased with the number of prescribed medications. With the exception of drug doses, patients' knowledge of their HF drugs was generally poor regarding indications and side effects. Ischemic cardiomyopathy, history of myocardial infarction and percutaneous coronary intervention were the most significant predictors of mismatches. Although important factors, health literacy and HRQOL are not routinely measured in our hospital. Cognitive capacity is frequently assessed, but not routinely; it is measured only among patients suspected or known to have cognitive impairment.

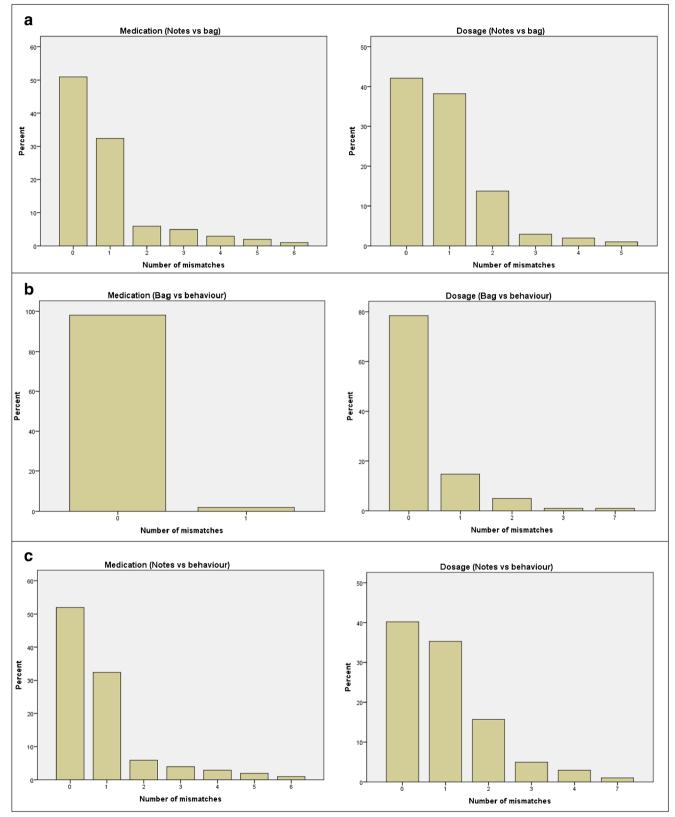
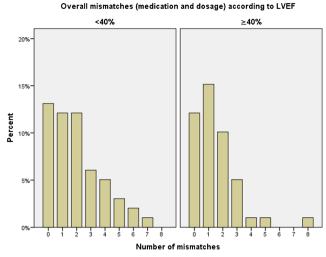


Fig. 1 Cumulative mismatches of drugs and their respective total daily doses at individual level

A lower age limit of 60 years was chosen because younger patients with heart failure tend to have different etiological bases to their disease (such as viral cardiomyopathy) and less stable disease. In patients with non-stable disease, mismatches



**Fig. 2** Overall mismatches for cardiovascular drugs between clinical notes and medication use behaviour at individual level by ejection fraction

tend to be more common as medication regimens undergo frequent change, but these mismatches may also be transient. It was for this reason that patients hospitalised within 6 months were also excluded. Inclusion of younger patients and those with unstable disease would have made the study population heterogeneous and likely over-estimated medication mismatch.

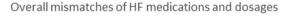
HF affects primarily elderly patients, and its prevalence rises with age [11, 12]. Despite advances in prevention, diagnosis and management, HF remains a major public health burden. Contemporary treatment for HF has been shown to be costeffective and has a significant impact on mortality and hospitalisation rates [13, 14]. Hence, it is important that prescribers adhere to guideline-recommended treatment whenever possible and patients use the right drugs at the right doses, as instructed by their physicians, to obtain the desired outcomes. 43

Previous studies have largely focused either on physicians prescribing patterns or HF patients' adherence to prescribed pharmacological treatment [1, 15–17]. Both prescribers and patients' adherence to guideline-recommended treatment are associated with improved outcomes [18, 19]. In Germany, a study of patients with HF showed that they have on average 13 different drug packs per day at home, of which 18% was not taken. Twenty-eight percent of the medications not taken as prescribed were for HF indications and 56% of the unused medications were prescribed by GPs [20]. Mattila et al. reported that discrepancies between self-reported medications and medical record data are common, and a large proportion of HF patients used non-prescription medications, often unknown to healthcare providers [21]. To date, no consistent predictors of patients' non-adherence have been identified [22].

Our study differs from previous studies in that we provide new information on the specific characteristics of mismatches between physicians' expectation of their HF patients' medications, medications in the patients' possession and their actual medication use. Our study also extends current knowledge of treatment gap in the Australian context. The findings suggest that recent initiatives have improved prescribers' adherence to guideline-directed medical therapy but discrepancies persist in terms of recorded data, medications in possession and actual use of medications. There is a break in the information chain between cardiologists/HF specialists and patients, and possibly also GPs and pharmacists, potentially contributing to poor outcomes in patients with HF. This impedes any initiatives to improve drug distribution, utilisation of evidence-based treatment and importantly, patients' outcomes.

The comparison of downstream clinical outcomes between compliant and non-compliant patients would indeed be interesting, these were not pre-specified outcomes in our study and hence we did not seek ethical approval to capture these. Adherence to HF medications is known to be associated with

**Fig. 3** Type of mismatches in ACE inhibitors, ARB, BB, MRA and loops diuretics. Abbreviation: ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor blockers; BB, beta-blockers; MRA, mineralocorticoid receptor antagonists; NTAA, patient is not taking at all; NNBT, not in the notes but patient is taking; DDSC, different medication but of the same drug class; LD, lower dose; HD, higher dose



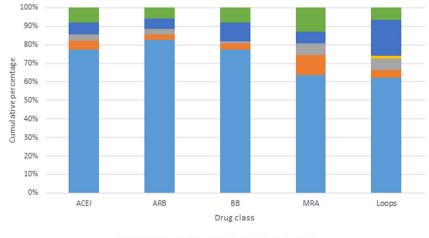




Table 4	Patients'	knowledge of
their me	dications'	indications,
dosages	and side e	effects

Knowledge	Overall	Ischaemic CM	Non-ischaemic CM	P value <sup>‡</sup>
No. of CV drugs in the bag, median (IQR)	6(3)	7(1.8)	5(2)	0.004
No. of correct indications	4(4)	5(4)	4(3)	0.04
No. of correct doses	6(3)	6(2)	5(2)	0.02
No. of correct side effects	0(1)	0(1.8)	0(1)	0.33
No. of HF drugs in the bag, median (IQR)	3(2)	3(1)	3(1)	0.04
No. of correct indications	2.5(2)	3(3)	2(2)	0.84
No. of correct doses	3(2)	3(1.8)	3(1)	0.08
No. of correct side effects	0(1)	0(1)	0(0)	0.29

HF drugs is defined as ACEI, ARB, BB, MRA and loops diuretics

CM cardiomyopathy, IQR interquartile range, CV cardiovascular, HF heart failure

<sup>‡</sup> Comparison of patients with ischemic cardiomyopathy and non-ischemic cardiomyopathy

improved outcomes in patients with HF, partly because it serves as a surrogate for adherence to medications in general [19]. Poor adherence is associated with higher mortality and hospitalisation rates [3, 19]. Hence, it would be interesting to see if clinical outcomes differed between sub-groups of patients in our study defined by levels of mismatch, and this will be the focus of further research.

Our study highlights the importance of all stakeholders maintaining the correct and up-to-date medication list for every patient through multiple levels of reconciliation, which is often challenging and laborious due to gaps in electronic medical record interoperability [23]. Any changes to the treatment plan need to be relayed quickly and accurately to other healthcare providers. Also, deprescribing medications which are no longer necessary, simplifying medication regimens and minimising out-of-pocket expenses for unnecessarily expensive drugs should be attempted whenever possible. Efforts to increase the provision of, as well as patients' interest in, home medication review should be revisited, as there is evidence that these programs improve safe medication use and optimal use of evidence-based HF treatment [24, 25]. In Australia, home medication review programs are run under the Domiciliary Medication Management Review program for people in the community and Residential Medication Review program for residents of aged care facilities [26]. Patients' willingness to utilise such services has been shown to be strongly influenced by their perception of the program's ability in improving knowledge, medicines management capability and reducing medication-related concerns [27].

Provision of personalised medication information sheets to all HF patients may be a convenient way to improve patients' knowledge retention about their current medications, as observed in our study.

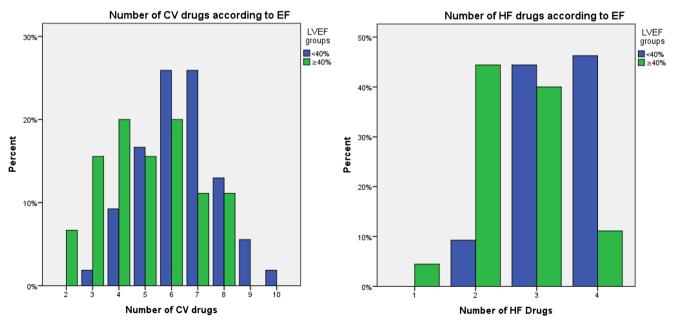


Fig. 4 Number of cardiovascular and heart failure drugs by ejection fraction category

#### Limitations

Our findings may have been affected by selection bias as the patients in our study were enrolled from a single study site and may not have been representative of the general population. Data misclassification may also have been present, as in any observational study, but the extent to which this may have caused bias, both in terms of direction and magnitude, was unknown.

## Conclusions

There are considerable mismatches between prescribers' expectation of their HF patients' daily heart medications, medications in patients' possession and their actual medication use. Future efforts should focus on ways to streamline information sharing processes to minimise mismatches between physicians' expectation, dispensed medications and medication use.

Acknowledgements KLC receives a PhD scholarship from the Ministry of Education, Malaysia. CMR is supported by a Research Fellowship from the National Health and Medical Research Council of Australia (NHMRC APP 1045826). The late Professor Henry Krum had made substantial contribution to the study design before he passed away.

#### **Compliance with Ethical Standards**

**Conflict of Interest** All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

**Ethical Approval** This study was approved by the Alfred Hospital Ethics Committee (233/15) and Monash University Human Research Ethics Committee (CF15/2335-2015000940).

**Informed Consent** Informed consent was obtained from all individual participants included in the study.

#### References

- Komajda M. How well are we implementing evidence-based care? Eur J Heart Fail Suppl. 2009;8(Supplement 1):i39–44.
- Chin KL, Skiba M, Tonkin A, Reid CM, Liew D, Krum H, et al. The treatment gap in patients with chronic systolic heart failure: a systematic review of evidence-based prescribing in practice. Heart Fail Rev. 2016;21(6):675–97.
- van der Wal MHL, Jaarsma T. Adherence in heart failure in the elderly: problem and possible solutions. Int J Cardiol. 2008;125(2):203–8.
- Wu J-R, Corley DJ, Lennie TA, Moser DK. Effect of a medicationtaking behavior feedback theory-based intervention on outcomes in patients with heart failure. J Card Fail. 2012;18(1):1–9.
- Bradi B, Granger, Ekman I, Granger CB, Ostergren J, Olofsson B, et al. Adherence to medication according to sex and age in the CHARM programme. Eur J Heart Fail. 2009;11:1092–8.

- Wu J-R, Moser DK, Lennie TA, Peden AR, Chen Y-C, Heo S. Factors influencing medication adherence in patients with heart failure. Heart Lung. 2008;37(1):8–16.
- Modig S, Kristensson J, Ekwall AK, Hallberg IR, Midlöv P. Frail elderly patients in primary care—their medication knowledge and beliefs about prescribed medicines. Eur J Clin Pharmacol. 2009;65(2):151–5.
- Page K, Marwick TH, Lee R, Grenfell R, Abhayaratna WP, Aggarwal A, et al. A systematic approach to chronic heart failure care: a consensus statement. Med J Aust. 2014;201(3):146–50.
- Chan Y-K, Tuttle C, Ball J. Teng T-HK, Ahamed Y, Carrington MJ, Stewart S. Current and projected burden of heart failure in the Australian adult population: a substantive but still ill-defined major health issue. BMC Health Serv Res. 2016;16(1):501.
- McMurray JJV, Adamopoulos S, Anker SD, Auricchio A, Böhm M, Dickstein K, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The task force for the diagnosis and treatment of acute and chronic heart failure 2012 of the European Society of Cardiology. Developed in collaboration with the heart failure association (HFA) of the ESC. Eur Heart J. 2012;33:1787–847.
- 11. Braunwald E. Heart failure. J Am Coll Cardiol. 2013;1:1-20.
- Norton C, Georgiopoulou VV, Kalogeropoulos AP, Butler J. Epidemiology and cost of advanced heart failure. Prog Cardiovasc Dis. 2011;54(2):78–85.
- Rohde LE, Bertoldi EG, Goldraich L, Polanczyk CA. Costeffectiveness of heart failure therapies. Nat Rev Cardiol. 2013;10(6):338-54.
- Banka G, Heidenreich PA, Fonarow GC. Incremental costeffectiveness of guideline-directed medical therapies for heart failure. J Am Coll Cardiol. 2013;61(13):1440–6.
- Cline C, Björck-Linné A, Israelsson B, Willenheimer R, Erhardt L. Non-compliance and knowledge of prescribed medication in elderly patients with heart failure. Eur J Heart Fail. 1999;1(2):145–9.
- Dunlay SM, Eveleth JM, Shah ND, McNallan SM, Roger VL. Medication adherence among community-dwelling patients with heart failure. Mayo Clin Proc. 2011;86(4):273–81.
- Komajda M, Anker SD, Cowie MR, Filippatos GS, Mengelle B, Ponikowski P, et al. Physicians' adherence to guidelinerecommended medications in heart failure with reduced ejection fraction: data from the QUALIFY global survey. Eur J Heart Fail. 2016;18(5):514–22.
- Komajda M, Lapuerta P, Hermans N, Gonzalez-Juanatey JR, van Veldhuisen DJ, Erdmann E, et al. Adherence to guidelines is a predictor of outcome in chronic heart failure: the MAHLER survey. Eur Heart J. 2005;26(16):1653–9.
- Granger BB, Swedberg K, Ekman I, Granger CB, Olofsson B, McMurray JJV, et al. Adherence to candesartan and placebo and outcomes in chronic heart failure in the CHARM programme: doubleblind, randomised, controlled clinical trial. Lancet. 2005;366(9502):2005–11.
- Ewen S, Baumgarten T, Rettig-Ewen V, Mahfoud F, Griese-Mammen N, Schulz M, et al. Analyses of drugs stored at home by elderly patients with chronic heart failure. Clin Res Cardiol. 2015;104(4):320–7.
- Mattila M, Boehm L, Burke S, Kashyap A, Holschbach L, Miller T, et al. Nonprescription medication use in patients with heart failure: assessment methods, utilization patterns, and discrepancies with medical records. J Card Fail. 2013;19(12):811–5.
- Vermeire E, Hearnshaw H, Van Royen P, Denekens J. Patient adherence to treatment: three decades of research. A comprehensive review. J Clin Pharm Ther. 2001;26(5):331–42.
- Rose AJ, Fischer SH, Paasche-Orlow MK. Beyond medication reconciliation: the correct medication list. JAMA. 2017;317(20): 2057–8.

- 24. Milfred-Laforest SK, Chow SL, DiDomenico RJ, Dracup K, Ensor CR, Gattis-Stough W, et al. Clinical pharmacy services in heart failure: an opinion paper from the Heart Failure Society of America and American College of Clinical Pharmacy Cardiology Practice and Research Network. J Card Fail. 2013;19(5):354–69.
- Warden BA, Freels JP, Furuno JP, Mackay J. Pharmacy-managed program for providing education and discharge instructions for patients with heart failure. Am J Health Syst Pharm. 2014;71(2):134–9.
- 26. The Department of Health Australia. Medication management reviews. In, 2017.
- Carter SR, Moles R, White L, Chen TF. Patients' willingness to use a pharmacist-provided medication management service: the influence of outcome expectancies and communication efficacy. Res Soc Adm Pharm. 2012;8(6):487–98.