# Multimorbidity and the Risk of All-Cause 30-Day Readmission in the Setting of Multidisciplinary Management of Chronic Heart Failure

# A Retrospective Analysis of 830 Hospitalized Patients in Australia

Joshua F. Wiley, PhD; Yih-Kai Chan, PhD; Yasmin Ahamed, PhD; Jocasta Ball, PhD; Melinda J. Carrington, PhD; Barbara Riegel, PhD; Simon Stewart, PhD

Background: Multimorbidity has an adverse effect on health outcomes in hospitalized individuals with chronic heart failure (CHF), but the modulating effect of multidisciplinary management is unknown. Objective: The aim of this study was to test the hypothesis that increasing morbidity would independently predict an increasing risk of 30-day readmission despite multidisciplinary management of CHF. Methods: We studied patients hospitalized for any reason with heart failure receiving nurse-led, postdischarge multidisciplinary management. We profiled a matrix of expected comorbidities involving the most common coexisting conditions associated with CHF and examined the relationship between multimorbidity and 30-day all-cause readmission. Results: A total of 830 patients (mean age 73  $\pm$  13 years and 65% men) were assessed. Multimorbidity was common, with an average of 6.6  $\pm$  2.4 comorbid conditions with sex-based differences in prevalence of 4 of 10 conditions. Within 30 days of initial hospitalization, 216 of 830 (26%) patients were readmitted for any reason. Greater multimorbidity was associated with increasing readmission (4%-44% for those with 0-1 to 8-9 morbid conditions; adjusted odds ratio, 1.25; 95% confidence interval, 1.13–1.38) for each additional condition. Three distinct classes of patient emerged: class 1—diabetes, metabolic, and mood disorders; class 2—renal impairment; and class 3—low with relatively fewer comorbid conditions. Classes 1 and 2 had higher 30-day readmission than class 3 did (adjusted P < .01 for both comparisons). Conclusions: These data affirm that multimorbidity is common in adult CHF inpatients and in potentially distinct patterns linked to outcome. Overall, greater multimorbidity is associated with a higher risk of 30-day all-cause readmission despite high-quality multidisciplinary management. More innovative approaches to target-specific clusters of multimorbidity are required to improve health outcomes in affected individuals.

KEY WORDS: chronic heart failure, disease management, multimorbidity, premature readmission

## Joshua F. Wiley, PhD

Postdoctoral Fellow, Mary MacKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia.

#### Yih-Kai Chan, PhD

Research Fellow, Mary MacKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia.

### Yasmin Ahamed, PhD

Postdoctoral Fellow, Mary MacKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia.

#### Jocasta Ball, PhD

NHMRC/NHFA Early Career Fellow, Mary MacKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia.

#### Melinda J. Carrington, PhD

Associate Professor, Mary MacKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia.

## Barbara Riegel, PhD

Professor, University of Pennsylvania School of Nursing, Philadelphia.

#### Simon Stewart, PhD

Director, Mary MacKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia.

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#### Correspondence

Simon Stewart, PhD, Mary MacKillop Institute for Health Research, Australian Catholic University, Level 5, 215 Spring St, Melbourne, Victoria 3000, Australia (simon.stewart@acu.edu.au).

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espite an evolving armory of pharmacological agents, device-based therapies, disease management strategies, and improved outcomes, chronic heart failure (CHF) continues to be associated with premature mortality<sup>5</sup> and recurrent hospitalization.<sup>6</sup> Within the ageing populations of high-income countries, CHF-related admissions continue to rise overall because of an increasing pool of at-risk individuals (noting incident admission rates are declining)<sup>7</sup> and recurrent and often unavoidable hospitalization. The latter component of increasing hospital activity attributable to CHF is undoubtedly linked to the increasing clinical complexity of prevalent cases as reflected in the presence of CHF and multimorbidity. In this study, multimorbidity is defined as the presence of CHF and 2 or more concurrent conditions other than its antecedent hypertension and coronary artery disease. Multimorbidity represents both a challenge and an opportunity for disease management programs given recent evidence suggesting that, despite their ability to prolong days alive and out-of-hospital overall, a blanket approach to applying disease management can potentially provoke poorer health outcomes (more events) in those with multimorbidity. 10 US Medicare data show that 81% of total in-patient hospital days are accumulated by 40% of individuals with CHF who have 5 or more noncardiac comorbidities.<sup>11</sup> Increasing multimorbidity in CHF has been linked to increasing risk of 30-day readmission. 12 Whether this phenomenon persists in the setting of multidisciplinary management of CHF recommended by expert guidelines 13,14 remains unclear.

We recently published a framework and multimorbidity matrix: Acknowledge, Routinely profile, Identify, Support, and Evaluate Heart Failure (ARISE-HF) demonstrating the complex pathways between common multimorbid conditions for systematically screening and managing this increasingly complex patient population.<sup>9</sup> We identified the top 10 cardiac and noncardiac comorbid conditions commonly affecting patients with CHF<sup>15</sup> along with recommendations for systematic screening of hospitalized patients to determine levels of multimorbidity. Our results also identified that the efficacy of existing CHF management programs would likely be eroded as the clinical/pathophysiological complexity of the patient increases. 16,17 On this basis, there is an urgent need to fully investigate the nature and impact of multimorbidity in CHF in the setting of "optimal" postdischarge multidisciplinary management.

## **Study Aims and Hypotheses**

We examined the characteristics and potential impact of multimorbidity on 30-day all-cause readmission in older patients with CHF exposed to a gold-standard, postdischarge multidisciplinary management program specifically designed to reduce recurrent hospitalization and prolong survival in the longer-term. First, we tested the hypothesis that increasing morbidity would independently predict an increasing risk of 30-day readmission despite high-quality multidisciplinary management. Consistent with the ARISE-HF framework, 9 we further hypothesized that there would be distinct patterns or clusters of multimorbidity that could inform the modification/adaptation of existing CHF management programs to enhance their ability to optimize health outcomes in this increasingly prevalent patient population.

## **Methods**

Study data were derived from 2 contiguous multicenter randomized controlled trials with equivalent baseline profiling of multimorbidity and 30-day readmissions. The Which Heart Failure Intervention is Most Costeffective & Consumer Friendly in Reducing Hospital Care (WHICH?) Trial<sup>16</sup> comprised 280 patients enrolled in a home versus clinic-based management (WHICH? Trial-Australia and New Zealand Clinical Trial Registry 12607000069459). An additional 550 patients came from an ongoing (30-day data collection completed February 2016) sequel trial of standard versus intensified and titrated home and structured telephone follow-up (WHICH? II Trial-Australia and New Zealand Clinical Trial Registry 12613000921785). These 2 closely related CHF management trials recruited equivalent patient cohorts from 5 tertiary referral hospitals and managed within the context of a subsidized Australian healthcare system. Both studies conform to the principles outlined in the Declaration of Helsinki with appropriate human ethic approvals granted by relevant governing committees.

## **Study Cohort**

The same clinical eligibility criteria and standardized protocols were applied in both trials. <sup>18</sup> Hospitalized individuals with CHF were systematically screened for eligibility to participate in either of the 2 studies and were included if they (1) were 18 years or older, (2) could provide informed consent, (3) were discharged to home with a cardiologist-confirmed diagnosis of CHF (based on symptoms and echocardiography), (4) had persistent moderate to severe functional impairment (New York Heart Association class II–IV), and (5) had a history of 1 or more admission for acute heart failure in the past 12 months (including the index admission). Those with a terminal malignancy were excluded. Nine patients participated in both studies.

## Clinical Management

Postdischarge, multidisciplinary management was explicitly guided by expert guidelines and standardized across study sites. <sup>13,18–20</sup> Although both study arms in both trials received multidisciplinary management,

there were key differences in the intervention arm that could potentially influence the pattern of recurrent readmission in the short-to-longer-term. In the WHICH? Trial, the same principles and structure of multidisciplinary management were delivered via a specialist CHF clinic or a home-based intervention. Home-based intervention was superior to specialist CHF clinic in the medium to longer-term (with respect to survival and recurrent hospital stay), 16,17 but there was no substantive difference in 30-day readmissions. 16 In the WHICH? II Trial, the same combination of nurse-led, multidisciplinary, home-based intervention with access to a specialist CHF clinic at the patient's treating hospital is applied in both study arms in the short-term. In the trial intervention arm, this standardized approach is supplemented by structured telephone support and the overall intensity of management in the longer-term is titrated to clinical need. Similar to the WHICH? Trial, we anticipate no substantive differences in the pattern of 30-day readmission according to group assignment in the WHICH? II Trial. Regardless of the management approach, following hospital discharge, all study patients had unrestricted access to specialist outpatient management, primary care physicians, subsidized pharmacological treatment and referral to allied healthcare services when required.

## **Study Data**

Patients were comprehensively profiled at baseline using a combination of face-to-face interview, systematic review of medical records, application of validated assessment tools, and questionnaires to measure and quantify their psychosocial and clinical profiles. Data were collected via standardized case report forms administered by trained personnel. As described in the original reports, 16,18 a detailed demographic and clinical profile (including precipitating factors, prescribed pharmacotherapy, all diagnoses, functional status and echocardiographic parameters) was collected for each patient. The criteria and recommended methods used to identify the 10 key comorbid conditions relevant to the ARISE-HF matrix are summarized in Table 1.9 Electronic health records were used to identify all recurrent hospitalization within 30 days of discharge from the index admission.

## Statistical Analyses

Assuming that 20% to 30% of patients experience a 30-day readmission, a sample size of more than 800 patients with CHF provides 80% power to detect a modest but meaningful odds ratio (OR) of 1.6 to 1.7 for morbid conditions with a prevalence of between 25% and 75% and 160 readmissions, supporting a multivariate logistic regression with up to 16 predictors, based on recommendations to have 10 events per predictor.31

Continuous and categorical data are presented as mean ± standard deviation and frequency (with percentage), respectively. A backward multiple logistic regression model (including sex, age, left ventricular ejection fraction, blood pressure, body mass index, estimated glomerular filtration rate, New York Heart Association class and Charlson Comorbidity Score), with calculation of OR and 95% confidence interval (CI) was used to identify the significant correlates of 30-day readmission.

To identify patterns of comorbidities, latent class analyses<sup>32</sup> were conducted on the 10 prespecified comorbid conditions. Latent class analysis is a statistical approach that assumes that there are distinct classes of patients and those within a class are more similar to each other than those in a different class.<sup>32</sup> It is used to describe heterogeneity in a population by finding clusters or classes that account for the observed heterogeneity and has been successfully applied to better understand other subgroups of patients with conditions such as hypertension, 33 cancer, 34 or depression. 35 We applied latent class analysis to search for distinct clusters of similar patients with CHF. 36,37 For example, in 1 class, patients may have high rates of metabolic disease, sleep disorders, and depression or anxiety, whereas in another class, patients may have high rates of renal impairment and anemia. Details on the latent class analysis are presented in the Supplementary Materials, available at http://links.lww.com/JCN/A30. All data analyses were performed using SPSS (v 22.0) except for the latent class analysis, which was performed using Mplus (v 7.3). Significance was accepted at a 2-sided  $\alpha$  of .05.

## Results

Most patients were men (65%) and mean age was 73  $\pm$ 13 years. Women were approximately 5 years older than men (P < .05), and more than half (53%) were living alone (compared with 39% of men). One in 4 patients (25%) was from a non-English-speaking background and 72% had fewer than 12 years of education (Table 2). Compared with men, women had more preserved cardiac function (left ventricular ejection fraction,  $44\% \pm 14\%$  vs  $35\% \pm 13\%$ ), higher systolic blood pressure (141  $\pm$  31 vs 131  $\pm$  26 mmHg), worse renal function (estimated glomerular filtration rate,  $51 \pm 22 \text{ vs } 57 \pm 22 \text{ mL/min/1.73 m}^2$ ), and lower serum hemoglobin (121  $\pm$  16 vs 128  $\pm$  21 g/dL) at baseline (P < .05 for all comparisons).

## Multimorbidity and 30-Day Readmission

Overall, 216 of 830 patients (26%; 95% CI, 23%–29%) were readmitted for any cause within 30 days with

TABLE 1 Definition and Methods Used to Document and Quantify Multimorbidity in Heart Failure

Comorbidity	Data Source and Determination	Definition/Deficit Threshold
Anemia Atrial and ventricular arrhythmias	Full blood examination during hospital admission Review of medical notes plus review of prescribed pharmacotherapy at discharge. If high clinical suspicion of undiagnosed arrhythmia—12-lead ECG, inpatient telemetry, or extended ECG Holter monitoring	Serum Hb level <130 g/L (women)/<120 g/L (men) <sup>21</sup> Confirmation of AF, other atrial arrhythmias, second or third degree heart block, and VT/VF with prescription of antiarrhythmic therapy or pacemaker/defibrillator device <sup>22</sup>
Cognitive impairment/ dementia Depression and anxiety	Assessed via MoCA tool before hospital discharge by trained personnel Assessed via questionnaire <sup>24</sup> before hospital discharge by trained personnel plus review of medical notes and prescribed pharmacotherapy at discharge. If positive, apply more comprehensive tool (eg, HADS) <sup>25</sup>	Documented diagnosis of dementia or MoCA score <26 out of a maximal possible score of 30 <sup>23</sup> Positive response to depressive symptoms and/or confirmed diagnosis (with active antidepressive/anxiolytic) of depression or anxiety
Diabetes and metabolic disorders	Review of medical notes and prescribed pharmacotherapy at discharge. Calculation of BMI. If high clinical suspicion of underlying diabetes HbA <sub>1c</sub> and/or glucose tolerance tests.	Documented diagnosis of type 2 diabetes or obesity (BMI >30 kg/m <sup>2</sup> ) plus dyslipidemia and/or hypertension (metabolic syndrome)
Musculoskeletal disorders	Review of medical notes and prescribed pharmacotherapy at discharge. Frailty test with hand-grip manometer, gait speed, 6-minute walk test, and Short Physical Performance Battery, including static balance, gait speed, and getting in and out of a chair <sup>26</sup>	Documented diagnosis of arthritis, osteoporosis, gout, or any other musculoskeletal condition requiring active therapy (eg, anti-inflammatory or analgesia)
Renal impairment	Electrolytes and renal function obtained during hospital admission	Estimated glomerular filtration rate <sup>27</sup> <60 mL/min/1.73 m <sup>2</sup>
Respiratory disease	Review of medical notes and prescribed pharmacotherapy at discharge. If high clinical suspicion of underlying respiratory disease—formal lung function tests	Lung function confirmation of chronic airways limitation, asthma, and/or other chronic pulmonary condition requiring active treatment <sup>28</sup>
Thyroid disease	Review of medical notes and prescribed pharmacotherapy at discharge. If high clinical suspicion of or historical lack of screening, perform thyroid function tests (including thyroid stimulating hormone levels) at hospital admission.	Documented hyperthyroidism/hypothyroidism according to national standards with associated antithyroid or thyroxine replacement therapy <sup>29</sup>
Sleep disorders	Review of medical notes and prescribed sleep support device. If high clinical suspicion of sleep disordered breathing, perform formal sleep studies. Use of a screening questionnaire in hospital to identify those with sleep-disordered breathing. <sup>30</sup>	Documented diagnosis of obstructive or central sleep disordered breathing.

Abbreviations: AF, atrial fibrillation; BMI, body mass index; HADS, hospital anxiety and depression scale; Hb, hemoglobin; HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>, ECG, electrocardiogram; MoCA, Montreal Cognitive Assessment; VF, ventricular fibrillation; VT, ventricular tachycardia. From: Stewart S, Riegel B, Boyd C, et al. Establishing a pragmatic framework to optimise health outcomes in heart failure and multimorbidity (ARISE-HF): A multidisciplinary position statement. *Int J Cardiol.* 2016;212:1–10. http://dx.doi.org/10.1016/j.ijcard.2016.03.001. Under a Creative Commons license (https://creativecommons.org/licenses/by-nc-nd/4.0/).

similar proportions for men (27%) and women (25%). In an unadjusted model, the risk of 30-day readmission steadily increased with greater levels of multimorbidity (Figure 1a). Among those with 0 to 1, 2 to 3, 4 to 5, 6 to 7, and 8 to 9 comorbid conditions, 30-day readmission occurred in 1 of 27 (4%), 39 of 211 (19%), 97 of 366 (27%), 66 of 195 (34%), and 13 of 31 (42%) patients, respectively. Those readmitted within 30 days (n = 216) had significantly more comorbid conditions (5.00  $\pm$  1.62 vs 4.31  $\pm$  1.68; P < .001). In an adjusted model (independent of all key clinical and demographic variables including sex and Charlson Comorbidity Score) greater multimorbidity predicted 30-day readmission (OR, 1.25 per additional morbid condition; 95% CI, 1.13–1.38; P < .001).

## Pattern of Multimorbidity According to Sex

As expected, beyond hypertension (77% women vs 68% men; P < .05) and coronary artery disease (66% men vs 48% women; P < .05), multimorbidity was common at index presentation and was closely aligned with the 10 conditions prespecified in the ARISE-HF matrix (ie, there were no other significant comorbid conditions identified, Supplementary Appendix I, http://links.lww.com/JCN/A30). Figure 1b shows the broad distribution of comorbid conditions according to sex. These conditions were normally distributed in both genders (the most common frequencies at  $\geq 3$  and  $\leq 5$  comorbid conditions), with similar means seen in

TABLE 2 Demographic and Clinical Profile				
	All (n = 830)	Men (n = 539)	Women (n = 291)	
Demographic profile				
Mean age at admission, y	73 ± 13	71 ± 13	76 ± 12 <sup>a</sup>	
Living alone	364 (44)	210 (39)	154 (53) <sup>a</sup>	
<12 y of education	592 (72)	350 (65)	242 (84) <sup>a</sup>	
English not first language	206 (25)	139 (26)	67 (23)	
Clinical profile				
Left ventricular ejection fraction, %	38 ± 14	35 ± 13	44 ± 14 <sup>a</sup>	
Heart rate, bpm	87 ± 24	87 ± 24	87 ± 24	
Systolic blood pressure, mm Hg	135 ± 28	131 ± 26	141 ± 31 <sup>a</sup>	
Diastolic blood pressure, mm Hg	77 ± 17	77 ± 16	77 ± 19	
Body mass index, kg/m <sup>2</sup>	29 ± 7	29 ± 6	29 ± 8	
Current smoker	259 (43)	199 (49)	60 (30)	
eGFR, mL/min/1.73 m <sup>2</sup>	55 ± 23	57 ± 23 <sup>a</sup>	51 ± 22	
Hemoglobin, g/dL	125 ± 20	128 ± 21 <sup>a</sup>	121 ± 16	
Comorbid profile				
Charlson comorbidity score	$6.6 \pm 2.4$	$6.5 \pm 2.6$	$6.8 \pm 2.1$	
History of hypertension	590 (71)	366 (68)	224 (77) <sup>a</sup>	
Coronary artery disease	494 (60)	354 (66) <sup>a</sup>	140 (48)	
Arrhythmias	583 (70)	387 (72)	196 (67)	
Renal impairment	517 (62)	321 (60)	196 (67) <sup>a</sup>	
Diabetes and metabolic disorders	510 (61)	334 (62)	176 (61)	
Respiratory disease	409 (49)	261 (48)	148 (51)	
Anemia	411 (50)	273 (51)	138 (47)	
Depression and anxiety	472 (57)	290 (54)	182 (63) <sup>a</sup>	
Mild cognitive impairment	289 (35)	190 (35)	99 (34)	
Musculoskeletal disorders	257 (31)	173 (32)	84 (29)	
Sleep disorders	178 (21)	129 (24) <sup>a</sup>	49 (17)	
Thyroid disease	103 (12)	41 (8)	62 (21) <sup>a</sup>	

Data are presented as n (%) or mean ± SD.

Abbreviation: eGFR, estimated glomerular filtration rate.

women and men overall  $(4.57 \pm 1.68 \text{ vs } 4.45 \pm 1.70;$ P = .323) and among those 65 years or older (4.65 ± 1.65 versus  $4.71 \pm 1.66$ , P = .686). However, there were key differentials according to sex on an age-adjusted basis, including more thyroid disease, depression and anxiety and moderate-to-severe renal dysfunction in women and more sleep disorders in men (all comparisons P < .05). Reflecting the high prevalence of multimorbidity, the majority of patients received extensive concomitant pharmacotherapies (data not shown) most commonly including angiotensin converting enzyme inhibitors, beta-blockers and diuretics (all >90% where indicated and tolerated).

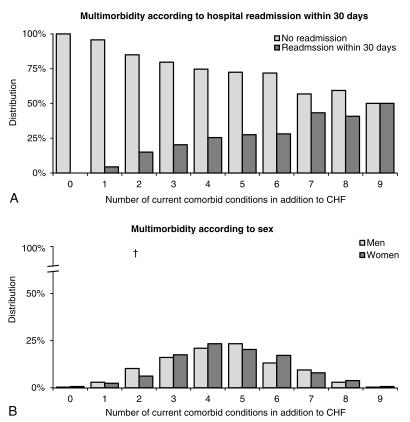
## **Clusters of Multimorbidity**

There were distinct patterns of multimorbidity that centered on the 4 most common comorbidities of arrhythmias (predominantly atrial fibrillation), renal impairment, respiratory disease, and diabetes and metabolic disease, with slightly different patterns seen in men and women. Results from the latent class analysis determined that grouping patients into 3 classes provided the best empirical fit to the data (Supplementary Appendix II, http://links.lww.com/JCN/A30). The classes identified were characterized by distinct patterns of comorbid conditions (Figure 2). Class 1 comprised 148 of 830 (17.8%) patients with a high prevalence of comorbid diabetes and metabolic disorders (88.7%), depression and anxiety (83.8%), sleep disorders (74.9%), and respiratory disease (74.5%). Class 2 comprised 362 of 830 (43.7%) patients who had comorbid renal impairment (100%) and to a lesser extent elevated musculoskeletal disorders (41.0%) compared with Class 3 (17.0%). Class 3 comprised 320 of 830 (38.6%) patients with the lowest rates of comorbid conditions. In addition to providing an empirically based approach to grouping similar patients, the latent class analysis showed a downward gradient in 30-day readmissions, with 38.6%, 27.2%, and 18.0% readmitted for classes 1, 2, and 3, respectively. Classes 1 and 2 had significantly higher readmission rates than class 3 did (P < .001 and P = .006, respectively). The difference between class 1 and 3 remained significant (P = .016) adjusting for sex, age, living alone, education, history of hypertension and coronary artery disease, Charlson Comorbidity Score, and all clinical profile factors from Table 2.

## **Discussion**

To the best of our knowledge, this represents the first study to comprehensively assess the impact of multimorbidity

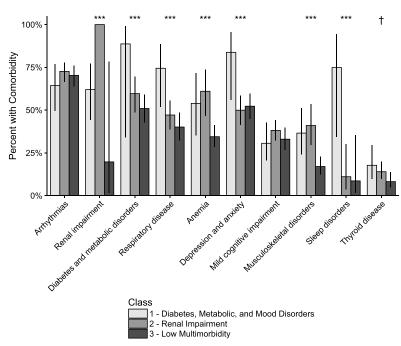
 $<sup>^{</sup>a}P < .05$  men versus women.



**FIGURE 1.** Distribution of multimorbidity in addition to chronic heart failure (CHF) according to (a) hospital readmission within 30 days and (b) sex. Prevalence differences of each morbid condition by sex were tested using  $\chi^2$  tests.  $^{\dagger}P = .054$ .

on 30-day all-cause readmission in the context of high levels of otherwise effective (at least in the longer-term) postdischarge multidisciplinary management of CHF.

These data demonstrated that even in the setting of a multidisciplinary management of CHF program, 26% of patients experienced a recurrent hospital admission



**FIGURE 2.** Distribution of morbid conditions by latent class with 95% confidence intervals. Prevalence differences of each morbid condition by class were tested using  $\chi^2$  tests. \*\*\*P < .001,  $^{\dagger}P = .051$ .

within 30 days. Moreover, the risk of 30-day readmission progressively increased with greater multimorbidity, ranging from 4% in those with a single condition to 42% in those with 8 to 9 comorbid conditions. There are also potentially important differences in the pattern of multimorbidity and risk of 30-day allcause readmission according to sex, even though the risk of readmission was similar in an adjusted model. Importantly, in the current cohort of older individuals with CHF, beyond the typical antecedents of hypertension and coronary artery disease, CHF in isolation is rare, with most patients having 3 or more additional comorbid conditions, which complicates their clinical management and increases their risk for poorer health outcomes.

Our data are consistent with previous reports of increased hospitalization risk in the setting of CHF and multimorbidity, 11,38 with 30-day readmission more likely with increasing comorbidity despite being discharged as (presumed) clinically stable and being exposed to gold standard, postdischarge multidisciplinary management of CHF. As is reported in the United States, CHF in isolation is rare and extremely rare among older patients.<sup>39</sup> As such, multimorbidity in CHF represents a global phenomenon that reflects the population dynamic of increased risk and exposure to chronic disease with increasing survival from previously fatal events and greater longevity overall. 40,41

As predicted, most (97%) patients in our study were diagnosed with more than 2 chronic conditions and more than two-thirds (71%) with more than 4 chronic conditions (predominately noncardiac). Noncardiac comorbidities in older adults with CHF are highly prevalent and are strongly associated with adverse clinical outcomes, including premature death. 11 It has been previously reported that patients with a high burden of multimorbidity and living in low-income areas have an elevated risk of rehospitalization or death, 42 suggesting that illness burden influences the association between income and health outcomes in these individuals. Critically, we also identified 3 main patterns of multimorbidity. Two of these clusters (classes 1 and 2) were at high risk of 30-day readmission. Class 1 was characterized by high prevalence of diabetes and metabolic disorders, depression and anxiety, sleep disorders, and respiratory disease, and class 2, by renal impairment. Combined, these 2 high-risk clusters accounted for just more than 60% of cases. These data both confirm and extend previous reports that particular clusters of comorbidity in CHF are associated with increasing levels of hospital stay, cost, and death.<sup>43</sup> Unfortunately, expert guidelines are yet to articulate strategies that specifically address the issue of CHF and multimorbidity.44

This study does not provide causal evidence that increasing multimorbidity is associated with poorer

health outcomes in the longer-term (ie, beyond 30 days). However, it still strongly indicates the potential to improve the efficacy of current CHF management programs in the setting of multimorbidity. In a recent composite analysis of trials focusing on the overall benefits of multidisciplinary, home-based intervention in the setting of CHF, 16,17 chronic atrial fibrillation, 45 and chronic heart disease overall, 46 there was clear evidence of a differential effect of this intervention on survival (and perhaps recurrent hospitalization) according to multimorbidity. Higher levels of multimorbidity were associated with worse outcomes. 10 In the current study, it is difficult to determine if we are observing (a) the early stages of the same phenomenon (ie, a deleterious response to proactive home-based, CHF management), (b) triggering of early readmissions that are therapeutic (by proactively addressing critical clinical issues) in the longer-term, or (c) a combination of the both. Certainly, this is an important area for further scrutiny and research.

Consistent with the idea of adopting a goal-orientated approach that identifies multimorbidity as a distinct clinical entity,<sup>47</sup> our mapping of the potentially complex matrix of multimorbidity in CHF reveals multiple intervention points to improve health outcomes. Although it is challenging to develop interventions that optimally adapt to all possible combinations of comorbid conditions, the 3 empirical clusters of patients we identified in this study may be a pragmatic starting point. Tailoring interventions to a CHF patient-centric disease profile may well improve outcomes compared to a "one size fits all" approach. Interventions derived from disease profiles may be more feasible as they are strategic management plans based on the most common patterns of disease rather than trying to respond to every possible combination of multimorbidity. For the training heart failure nurses, there are practical implications for widening curricular to incorporate a wider spectrum of clinical management skills directed toward complex patients with CHF and multimorbidity. This is particularly true when considering that 2 clusters were associated with worse outcomes. Building upon these data and with ongoing validation of the ARISE-HF matrix, our group is currently mapping out the best way to address multimorbidity in CHF as part of an attempt to develop and test a cost-effective intervention for affected individuals.

## Limitations

This was a retrospective cohort study from and included an ethnically diverse cohort (many with English as a second language) reflecting the multicultural diversity of Australia. We have combined outcome data from contiguous trials with equivalent baseline profiling of multimorbidity but some differences between the

## **What's New and Important**

- Multimorbidity is common among adult CHF patients and demonstrates distinct patterns linked to readmissions
- Greater multimorbidity is associated with higher risk of 30-day all-cause readmission despite high-quality multidisciplinary management.
- Developing innovative, cost-effective and patient-centric interventions targeting specific clusters of multimorbidity may be a key direction for future clinical research.

adjudication of multimorbidity may have occurred. Moreover, at this time, we are unable to consider the role of treatment adherence and self-care behaviors in determining the risk of 30-day readmission. We also did not specifically account for visual and hearing deficits and health literacy issues (these are routinely assessed but not formally documented at baseline) that should be factored into future analyses of this kind. Pending formal assessment of all trial events, we have only examined 30-day readmissions on an "all-cause" basis. Lastly, we have yet to examine the impact of multimorbidity on long-term outcomes.

#### Conclusion

Our findings confirm that multimorbidity is common among hospitalized patients with CHF. Moreover, we found that even in those exposed to multidisciplinary CHF management (with minimum standards of care applied), increasing multimorbidity per se was associated with a parallel increase in all-cause 30-day readmissions. This is a major issue for individuals and the healthcare system as a whole. In light of our evidence of common clusters of comorbid conditions in CHF, developing and testing novel interventions tailored to patients in each of these clusters may be a key direction for future clinical research and trials.

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