The Effectiveness of Collaborative Medicine Reviews in Delaying Time to Next Hospitalization for Patients With Heart Failure in the Practice Setting

Results of a Cohort Study

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Background—Randomized controlled trials have demonstrated that collaborative medication reviews can improve outcomes for patients with heart failure. We aimed to determine whether these results translated into Australian practice, where collaborative reviews are nationally funded.

Methods and Results—This retrospective cohort study using administrative claims data included veterans 65 years and older receiving bisoprolol, carvedilol, or metoprolol succinate for which prescribing physicians indicated treatment was for heart failure. We compared those exposed to a general practitioner–pharmacist collaborative home medication review with those who did not receive the service. The service includes physician referral, a home visit by an accredited pharmacist to identify medication-related problems, and a pharmacist report with follow-up undertaken by the physician. Kaplan-Meier analyses and Cox proportional hazards models were used to compare time until next hospitalization for heart failure between the exposed and unexposed groups. There were 273 veterans exposed to a home medicines review and 5444 unexposed patients. Average age in both groups was 81.6 years (no significant difference). The median number of comorbidities was 8 in the exposed group and 7 in the unexposed ($P<0.0001$). Unadjusted results showed a 37% reduction in rate of hospitalization for heart failure at any time (hazard ratio, 0.63; 95% CI, 0.44 to 0.89). Adjusted results showed a 45% reduction (hazard ratio, 0.55; 95% CI, 0.39 to 0.77) among those who had received a home medicines review compared with the unexposed patients.

Conclusion—Medicines review in the practice setting is effective in delaying time to next hospitalization for heart failure in those treated with heart failure medicines. (Circ Heart Fail. 2009;2:424-428.)

Key Words: heart failure ■ morbidity ■ medication review ■ hospitalization

Advances in the management of patients with heart failure have led to the use of increasingly complex combinations of medicines, including angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, loop diuretics, β-blockers, and spironolactone. Despite these advances, up to 44% of patients with heart failure will be rehospitalized within 6 months of discharge due to both the progression of the condition and medication-related problems. Collaborative medicines reviews have been shown to be effective in preventing, detecting, and resolving medication-related problems. Based on this evidence, the Australian Government funded collaborative medication review services, known as Home Medicines Review (HMR), which are undertaken by accredited pharmacists and general medical practitioners. In part, this expanded role for pharmacists has been encouraged by the Australian government because of a general shortage of health professionals and a perception that pharmacists’ skills are underutilized in the health system. A 2007 systematic review and meta-analysis involving randomized controlled trials failed to find any effect of pharmacist-led reviews in older people on mortality (22 trials) or all-cause hospital admissions (17 trials). However, when limited to the population with heart failure, a 2008 systematic review of 12 randomized controlled studies involving pharmacist care of patients with heart failure found significant reductions in all-cause hospitalization (odds ratio, 0.71; 95% CI, 0.54 to 0.94) and heart failure hospitalizations (odds ratio, 0.69; 95% CI, 0.51 to 0.94). The type of medicine review...
provided seemed to have an impact with medicine reviews that involved both pharmacist and physician collaboration having the most impact, achieving a reduction in the rate of hospitalizations for people with heart failure (odds ratio, 0.42; 95% CI, 0.24 to 0.74). By comparison, pharmacist-directed care, which may not have been undertaken with physician involvement, showed no significant effect on the hospitalization rate.8 A more recent United Kingdom randomized controlled trial on the effectiveness of home visits from community pharmacists for patients with heart failure failed to show any significant difference in total hospital readmissions at 6 months after discharge.8

Australia has funded HMR services since 2001, and more than 200,000 collaborative medication reviews have been provided across the country, with approximately 40,000 provided each year.9 The Australian model is a collaborative model, where physicians refer patients to an accredited pharmacist who undertakes a home visit. The pharmacist identifies any medication-related problems, including potential underuse, overuse, adverse events, compliance and knowledge problems, or hoarding. The pharmacist provides a report, which is discussed with the physician. The physician is responsible for developing the medication management plan, communicating this with the patient and has responsibility for follow-up with the patient. The service can only be provided be a pharmacist who is accredited. The accreditation process assesses competence in clinical pharmacy, therapeutics, pharmaceutical care, and medication review. Pharmacists must be reaccredited every 3 years.10 Local area facilitators are funded across the country to support the program’s implementation.9

We aimed to determine whether the results from randomized controlled trials for the population with heart failure translated into practice as it is currently funded in Australia. This study examined the effect of the provision of a HMR for Australian war veterans and war widows with heart failure on the time to next hospitalization for heart failure. The veteran population was chosen for the study as they are an elderly, vulnerable population, who are an appropriate target population for HMR services, they are similar to the elderly Australian population, and complete data are available.

Method

Setting

The Australian Government’s Department of Veterans’ Affairs (DVA) claims databases contain details of all prescription medicines, medical and allied health services, and hospitalizations provided to veterans for which DVA pay a subsidy. The data file contains 140 million pharmacy records, 200 million medical and allied health service records, and more than 6 million hospital records for a treatment population of 310,000 veterans. The DVA maintain a client file, which includes data on gender, date of birth, date of death, and family status. Medicines are coded in the dataset according to the World Health Organization anatomic and therapeutic chemical classification,14 and the Schedule of Pharmaceutical Benefits item codes.12 Hospitalizations are coded according to the International classification of diseases classification, version 10, Australian modification.15

Study Design

A cohort study was undertaken during the period January 1, 2004, until July 1, 2006. The exposed group were veterans who had received an HMR and had all health services fully subsidized by DVA, were dispensed a β-blocker subsidized for heart failure in the 6 months before the HMR, and aged 65 years or older at the time of the review. The unexposed group were veterans who had all health services fully subsidized by DVA and were aged 65 years and older and who had been dispensed a β-blocker subsidized for heart failure but had not had an HMR. The eligibility of the veterans for the unexposed group was determined each month throughout the study period. Eligible veterans were then randomly allocated to an index month in the study period to match the time of an HMR in the exposed group. The allocation of unexposed to exposed was approximately 20 to 1. Unexposed veterans were only matched once in the study period. The β-blockers included bisoprolol, carvedilol, and metoprolol succinate, which throughout the study period, were only available under a prior authorization process where the prescribing physician had to indicate at the time of prescription that the patients had heart failure. It is considered unlikely that these would have been prescribed for other indications as alternative β-blockers are available for other indications with no requirement for prior authorization.

Subjects were followed up until time to first hospitalization for heart failure (ICD codes11 1500, 1501, and 1509) post the index month for the unexposed group or post the HMR in the exposed group, or until death or study end, whichever was the earliest. Subjects who were resident in aged-care facilities were excluded, as HMRs are only funded for the community dwelling elderly.

Demographics were compared between the exposed and unexposed groups using the following methods. t-tests were used for normally distributed continuous variables; the nonparametric Kruskal-Wallis test was used to analyze nonnormal data. Discrete categorical variables were analyzed using the χ2 statistic and for ordinal categorical variables the Cochran-Mantel-Haenszel statistic was used.

Kaplan-Meier analyses were used to compare time to next hospitalization for heart failure between the HMR exposed and unexposed groups. Cox-proportional hazards models were used to determine hazard ratios. The models were adjusted at the time of HMR or index month for age, gender, and comorbidity as measured in the 6 months before the HMR by the Australian adaption of Rx-Risk-V.14 socioeconomic index based on socioeconomic indexes for areas,15 season, number of prescriptions in the previous year, number of prescribers in the previous year, number of pharmacies in the previous year, number of medications change over a 6-month period in the previous year, number of hospitalizations in the previous year, number of occupational therapy visits in the previous year, number of speech therapy visits in the previous year, and region of residence (remote, outer regional, inner regional, and major city).16 All analyses were undertaken using SAS version 9.1.3. (SAS Institute Inc, Cary, NC). Statistical significance was set a priori at P<0.05. Ethics approval for the study was obtained from the Department of Veterans’ Affairs Human Research Ethics Committee and the University of South Australia Ethics Committee. The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

There were 273 persons included in the HMR exposed group and 5444 in the unexposed group. Demographics of the groups are presented in Table 1. Although of similar ages and gender, the exposed group had more comorbidities, more prescriptions, more changes in their medications before the HMR, more prescribers, and more hospitalizations. The unexposed groups were more likely to have high socioeconomic disadvantage scores.

The Figure shows the Kaplan-Meier analysis for time to hospitalization for heart failure is significantly delayed in the group that had received a HMR.

The adjusted results show that for those who received a HMR there was a 45% reduction in the rate of hospitalization

The Figure shows the Kaplan-Meier analysis for time to hospitalization for heart failure is significantly delayed in the group that had received a HMR.

The adjusted results show that for those who received a HMR there was a 45% reduction in the rate of hospitalization
for heart failure at any time (hazard ratio, 0.55; 95% CI, 0.39 to 0.77; Table 2). The model shows that 5.5% of the exposed group compared to 12% of the unexposed group were hospitalized within 365 days.

**Discussion**

The study demonstrates that research outcomes from randomized controlled trials of the effectiveness of collaborative medication reviews in the population with heart failure can translate into practice. Our results showed HMR in the population with heart failure was effective in delaying time to hospitalization for heart failure with a 45% reduction in the rate of hospitalization for heart failure at any time. Although not directly comparable with intervention studies, our results are not dissimilar to the results from the systematic review that reported a 31% reduction in hospitalization for heart failure in those who had participated in collaborative medication reviews; involving both physician and pharmacist input. These findings are also in keeping with expectations that the service would be effective for heart failure, as medication problems have been found to be a common contributor to hospitalization for heart failure. A Spanish study of 293 cases found poor medication compliance was a precipitating factor for heart failure hospitalizations in 12.5% of cases, use of harmful medications in 6.5% of cases and withdrawal of beneficial medications in 1.4%. The results are also consistent with findings demonstrating medication-related problems are contributors to admissions for heart failure. With hospitalizations in Australia for heart failure estimated to cost $140 million per annum, these delays to next hospitalization could contribute to significant cost savings to the health system.

Despite groups being similar, in that both groups were 65 years of age or older and dispensed a β-blocker listed for heart failure, the demographic analysis shows that those who received a HMR had more comorbidities, more prescriptions

**Table 1. Demographics of Study Participants**

<table>
<thead>
<tr>
<th></th>
<th>Exposed (n=273)</th>
<th>Unexposed (n=5444)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>70</td>
<td>74</td>
<td>0.11</td>
</tr>
<tr>
<td>Age, y</td>
<td>81.6 (4.8)</td>
<td>81.6 (4.8)</td>
<td>0.87</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>8 (2)</td>
<td>7 (2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prescriptions in previous year</td>
<td>95 (69 to 123)</td>
<td>76 (54 to 104)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Changes in medicines during 6-mo period in the previous year</td>
<td>3 (2 to 6)</td>
<td>3 (1 to 5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Prescribers in the previous year</td>
<td>5 (3 to 6)</td>
<td>4 (3 to 6)</td>
<td>0.002</td>
</tr>
<tr>
<td>Pharmacies in the previous year</td>
<td>2 (1 to 3)</td>
<td>2 (1 to 3)</td>
<td>0.43</td>
</tr>
<tr>
<td>Socioeconomic index of disadvantage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowest disadvantage</td>
<td>31</td>
<td>25</td>
<td>0.01</td>
</tr>
<tr>
<td>Medium/low disadvantage</td>
<td>25</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Medium/high disadvantage</td>
<td>24</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Highest disadvantage</td>
<td>20</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Hospitalizations in the previous year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>27</td>
<td>34</td>
<td>0.03</td>
</tr>
<tr>
<td>1</td>
<td>23</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>&gt;2</td>
<td>28</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remote</td>
<td>0</td>
<td>1</td>
<td>0.86</td>
</tr>
<tr>
<td>Outer regional</td>
<td>12</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Inner regional</td>
<td>29</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Major city</td>
<td>59</td>
<td>59</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as %, median (SD), or n (range).

![Figure](http://circheartfailure.ahajournals.org/)
dispensed, more changes to their medicines before the review, and more prior hospitalizations. This suggests the population receiving a HMR had a higher burden of illness than those who did not, potentially indicating the exposed group were more likely to receive the service because of more severe diseases; representing confounding by indication or selection bias.\(^{20}\) This is likely to bias the study toward the null effect, suggesting the study is unlikely to have overestimated the effect.

Our study was limited to veterans dispensed \(\beta\)-blockers for heart failure, and it is possible that some of the effect observed is related to better patient management due to pharmacist involvement after \(\beta\)-blocker initiation. However, we did not limit our study to patients newly initiated on \(\beta\)-blockers. Patients may have been on \(\beta\)-blockers for variable lengths of time. Given that many medications contribute to problems in the population with heart failure, including suboptimal use of \(\beta\)-blockers or angiotensin-converting enzyme inhibitors, poor compliance and concurrent use of nonsteroidal anti-inflammatory drugs, verapamil or diltiazem, as well as lack of early recognition of signs of deterioration,\(^ {21}\) it is likely that the effect observed was related to the HMR, not just better patient management while on \(\beta\)-blockers.

A study limitation is the low numbers of veterans who have received a HMR. Overall, only 5% of veterans with heart failure have received a HMR, despite all veterans in this treatment population being eligible for the service. The focus of this study on war veterans may also be seen as a limitation. In Australia, however, war veterans are treated in the same way as nonveteran patients in both the primary and tertiary care sectors. The health services they receive are the same, and they are delivered by the same practitioners as those visited by nonveterans. The veteran population have slightly more general practice visits (rate ratio, 1.17; \(P<0.05\)) and hospitalizations (rate ratio, 1.21; \(P<0.05\)) per year than other Australians aged 40 years and older.\(^ {22}\) Veterans with no service related disability have similar levels of use.\(^ {22}\) Similar numbers of prescriptions per general practitioner visit are observed between the veteran population and the Australian population; however, because of the higher rate of general practitioner visits, veterans receive slightly more prescriptions annually than other Australians (rate ratio, 1.13; \(P<0.05\)).\(^ {22}\)

This study used prescription data for identifying the population with heart failure; however, the \(\beta\)-blockers used as indicators of heart failure were only subsidized for heart failure under a prior authorization policy. Similarly to what has been observed in the United States,\(^ {23}\) prior authorization policies restrict physicians using medicines for unspecified purposes, but unlike the United States, Australia does not provide exemptions, thus the medicines are not subsidized for other indications. Given that the \(\beta\)-blockers in our study all required prior authorization which required physicians to apply in writing or by telephone and indicate the medicine was for heart failure, it is unlikely that the use of these \(\beta\)-blockers was for other indications as alternative \(\beta\)-blockers are available with no requirement for prior authorization.

Diagnostic data are not available in Australia’s primary health care administrative data sets, thus we were neither able to adjust for severity of illness nor able to adjust for other potential confounders such as quality of care administered by attending physicians. This study assumes consistent implementation of the reviews across the country. No data are available to confirm this; however, the program is implemented nationally in a structured manner with consistent rates of uptake per capita in all states and territories.\(^ {9}\) Furthermore, all areas have locally used facilitators to assist program implementation and all pharmacists and pharmacies must be accredited with competencies in clinical pharmacy, therapeutics, pharmaceutical care, and medication review before they can provide the service.\(^ {10}\)

Despite these limitations, this study shows that randomized controlled trial results do translate into practice and that positive results are measurable in practice from the nationally funded program. From a health services research perspective, this study provides evidence that the service as currently administered provides health gain for Australian consumers with heart failure. The program is a consumer-focused structured service requiring collaboration between general medical practitioner, pharmacist, and patient. The funding and business rules that have been established for the Australian program differentiates claims for the service from both pharmacists and medical practitioners. The statistics highlight that both parties are active participants in the provision of the service; as of June 2008, 180 000 claims had been received from pharmacists with just less than 170 000 claims from general practitioners.\(^ {9}\)

This study adds to the available literature on the effectiveness of pharmacists’ collaborative contribution to the care of complex older patients. A systematic review conducted to clarify the role of pharmacists in the care of patients with heart failure found a significant decrease in hospitalization for patients who had received pharmacists collaborative care; however, no effect of pharmacist-directed care.\(^ {7}\) The results observed in our study are consistent with those reported in the systematic review finding collaborative medicines review is

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Table 2. Cox Proportional Hazards Model Results for Time to Hospitalization for Heart Failure

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Parameter Estimate</th>
<th>SE</th>
<th>( \chi^2 )</th>
<th>( P )</th>
<th>Hazard Ratio*</th>
<th>95% Hazard Ratio Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted: exposed to home medicines review</td>
<td>-0.47</td>
<td>0.18</td>
<td>7.0035</td>
<td>0.008</td>
<td>0.63</td>
<td>0.44 0.89</td>
</tr>
<tr>
<td>Adjusted: exposed to home medicines review</td>
<td>-0.61</td>
<td>0.18</td>
<td>11.61</td>
<td>0.0007</td>
<td>0.55</td>
<td>0.39 0.77</td>
</tr>
</tbody>
</table>

\*Adjusted for age, gender, comorbidity, socioeconomic index of disadvantage, season, region of residence, and number of prescriptions, prescribers, pharmacies, changes in medications, hospitalizations, occupational therapy visits, and speech therapy visits.
effective in the population with heart failure. Similar programs offering home-based visits to patients with heart failure in collaboration with health professionals other than pharmacists, including nurse practitioners, have also been shown to be effective. The white paper on Pharmacy in England identifies pharmacists as an underutilized resource in the health system, and the United Kingdom government is encouraging such role extension. If the findings of this study are replicated in other patient groups who are at high risk of medication misadventure and consequent rehospitalization, there will be an even stronger case to require pharmacists to be involved in this extension of their role in collaboration with physicians.

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Mr Peck and Dr Killer are employees of the DVA, the funder of the research.

References

Clinical Perspective
Hospitalization for heart failure is commonly identified as preventable, with medication related problems found to be a causal factor. Randomized controlled trial evidence has shown that collaborative medication reviews are effective in improving health outcomes in those with heart failure. This research demonstrates that these results translate to the practice setting. Collaborative medication review services, where physicians and pharmacists collaborate to improve medication management in the population with heart failure, are funded nationally in Australia. This research shows that the service as currently administered provides health gain for Australian consumers with heart failure, with a 45% reduction in rate of hospitalization for heart failure at any time.
The Effectiveness of Collaborative Medicine Reviews in Delaying Time to Next Hospitalization for Patients With Heart Failure in the Practice Setting: Results of a Cohort Study

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