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Impact of medication reviews on inappropriate prescribing in aged care

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Contribution statement:

This study was designed and planned by LGK, RC, GP, TZ; LGK was responsible for data collection and writing the manuscript; RC and LGK evaluated the potentially inappropriate prescribing in the data and undertook statistical analysis; all authors assisted in the preparation of the manuscript. PJH was the provider of the RMMRs used to conduct this study.

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Abstract

Background: Inappropriate prescribing (IP) is prevalent among elderly people in aged care facilities. Little has been published on the effect of pharmacists performing residential medication management reviews (RMMRs) in aged care, on the appropriateness of prescribing. RMMRs represents a key strategy for achieving quality use of medicines, by assisting residents in aged care facilities and their carers to better manage their medicines. However, the structure of RMMR has moved from annual to every two years for each resident.

Objectives: The primary objective of this study was to investigate the impact of the effect of pharmacists performing RMMRs on medication use appropriateness, as measured by the Medication Appropriateness Index (MAI).

Methods: Retrospective analysis of RMMRs pertaining to 223 aged care residents aged ≥65 years in Sydney, Australia. The MAI was applied on two RMMR cohorts; newer cohort (n=111, 2015) i.e. following the recent changes to the RMMR funding and older cohort (n=112, 2012) at baseline, after pharmacists' recommendations (assuming all pharmacists' recommendations were accepted by the General Practitioner (GP)), and after the actual uptake of pharmacists' recommendations by the GP. Differences in the inappropriate prescribing were measured using the Wilcoxon sign rank test.

Results: Overall, all patients in study (n=223) had at least one inappropriate rating at baseline (median MAI score of 26 for the old cohort and 27 for the newer cohort). The median cumulative MAI scores were significantly lower post the RMMRs by pharmacists (15.5 and 20 for the old and new cohort respectively, $p<0.001$) and following the uptake of recommendations by the GP, indicating an increased appropriateness of drug regimen after the medication review (20 and 22 for the old and new cohort respectively, $P<0.001$).

Conclusion: This study shows that pharmacist-led medication reviews are effective in reducing inappropriate prescribing among aged care residents, as demonstrated by the reduction in MAI scores. Future studies should focus on the impact of such a decrease on patient outcomes.

Keywords: inappropriate prescribing, medication reviews, medication appropriateness index, older people, elderly, aged care, pharmacists

Introduction

As people age their organ and receptor functions change at variable rates and hence their response to medications becomes less predictable compared to that of younger patients [1]. The situation is further complicated by the presence of multiple comorbidities that require co-administration of drugs that may potentially interfere with each other or with elderly patients' medical conditions [2]. As such, the incidence of inappropriate prescribing (IP) is high amongst the elderly, resulting in increased morbidity and hospitalization, treatment failure and increased costs of care [3, 4, 5]. Hence, identifying and reducing IP in the elderly has received a great deal of attention in recent years, including the development of various validated instruments to assess IP [6].

The medication appropriateness index (MAI) is a set of implicit criteria used to evaluate drug prescribing in the elderly [7]. The MAI has been found to be a reliable, valid, standardized instrument for the evaluation of multiple elements of drug therapy prescribing for a variety of medications, clinical conditions, and settings [8, 9, 10] . The MAI, when used to assess patients' drug regimens in both hospital and community settings and prompt intervention, has been associated with safer use of medications, reduction in hospitalizations, and improved quality of life [9, 11, 12]. The MAI has also been shown to be effective in highly specialized areas, such as emergency departments, where its use has been associated with a reduction in medication misadventure [13].

Previous studies have shown that clinical interventions involving pharmacists can improve patients' care by reducing IP [14, 15]. In Australia, residential medication management reviews (RMMRs) are a government-funded service available to residents in aged care facilities once every 24 months (unless clinical need arises in the interposing period) [16, 17] and represents a key national strategy for achieving quality use of medications. It is conducted by an accredited pharmacist when requested by a resident's general practitioner (GP) and undertaken in collaboration with the resident's GP and appropriate members of the resident's healthcare team. Following GP's referral, a comprehensive assessment is undertaken by the accredited pharmacist to identify, resolve and prevent any medication-related problems and a written report is provided back to the resident's GP with suggestions for resolution of the identified medication-related problems. Accredited pharmacists providing medication reviews are pharmacists registered in Australia and have undergone specialized training, have post registration experience and have demonstrated competence to undertake medication management reviews. Pharmacists are accredited either by the Australian Association of Consultant Pharmacy (AACP) or the Society of Hospital Pharmacists of Australia (SHPA) to conduct medication management reviews.

Although previous studies have demonstrated the benefits of RMMRs in rationalizing medications and reducing the risk of medication misadventure [16], there is a need for greater evidence of the outcomes of RMMRs, as their Federal funding has been reduced in recent years (since March 2014). Hence, the aim of this study was to evaluate the impact of RMMR service on inappropriate prescribing in aged care, as measured with the MAI.
The specific objectives of this study were to:

I. Estimate MAI scores in older patients living in Aged Care Facilities (ACFs)
II. Evaluate the potential impact of recommendations made by accredited pharmacists on reducing IP; and
III. Evaluate the potential impact of the RMMR service on IP after the acceptance of the pharmacists' recommendations by GPs.

A secondary goal was to determine the extent of IP in aged care residents before and after the reduction in funding of medication review services, by comparing two cohorts of RMMRs (conducted in 2012 vs. 2015).

Method:

Study population

This retrospective study included a random sample of de-identified RMMR reports, with general practitioner (GP, or family physician) response to pharmacists' recommendations, pertaining to aged care residents aged ≥ 65 years who received an RMMR by an accredited pharmacist. The RMMR reports were collected from a single RMMR service provider (Meditrax, Sydney, New South Wales, Australia). The first set of reviews were conducted in 2012 while the second set of reviews were conducted in 2015. A total of 911 RMMRs conducted between August 2011 and December 2012 were collected from the service provider, of which 867 were conducted in 2012. We analyzed a random sample of 112 (13%) of these RMMRs for the older cohort, whilst 111 (22%) out of 502 RMMRs conducted in 2015 were analyzed for the newer cohort.

Accredited pharmacists compiled RMMR reports, which included a comprehensive medication history, current medical diagnoses, actual medications taken, clinical pathology results, and pharmacists' findings and recommendations. GP feedback on the RMMR report and reconciled medication charts for each resident determined whether the pharmacist's recommendations to resolve any potential drug-related problems had been accepted or not. Due to the de-identified nature of data collected, the study was exempted by the local Human Research Ethics Committee.

Data collection and analyses

A comprehensive review of the RMMR reports conducted by the accredited pharmacists was performed by the primary researcher, including the collection of patient data (demographics, medical conditions, regular medications, 'as needed' medications, pathology results), pharmacists' recommendations to the GPs and GPs' responses to these recommendations. The MAI was applied retrospectively by the primary researcher to each of the RMMR reports to determine the extent of IP at baseline, following pharmacists' recommendations (with the assumption that all of the recommendations were accepted by the GPs), and following actual GP acceptance or non-acceptance of pharmacists' recommendations. The MAI scoring and categorization for each RMMR report were then reviewed for accuracy by an experienced clinical pharmacist. Several studies have shown that MAI can be applied consistently with good inter-rater reliability including retrospectively to medication reviews [8, 18].

The MAI consists of 10 criteria addressing different aspects of prescribing including indication, effectiveness, dosage, accuracy and practicality of drug administration instructions, drug-drug interactions, drug-disease interactions, avoidance of therapeutic duplication, duration of treatment

and cost [19, 20, 21]. For each of the criteria, the index has operational definitions, explicit instructions and examples. The evaluator rates the medication appropriateness as (A) appropriate, (B) marginally appropriate, (C) inappropriate or (Z) does not know. For the purpose of the analysis if information was unknown or not available it was rated as (Z). Each criterion was weighted 1-3 according to standard protocol resulting in a possible maximum of 18 for each drug. For this study, we excluded two criteria:

- **Accuracy of directions (0-2):** this criterion was excluded as it is recommended not to use this criterion for institutionalized patients.
- **Cost effectiveness (0-1):** As the first set of data was collected in 2012 it was considered not practical to compare medications prices for that period of time. For consistency, we also excluded the cost effectiveness criterion from the 2015 analysis.

Therefore, each prescribed drug could have a potential score between 0 and 15, where 0 represents appropriate prescribing and higher scores indicate a greater degree of inappropriateness [19, 20, 21]. An overall patient score was then derived by summing the MAI scores for all medications used by the individual patient at the time. Pharmacists' recommendations were divided into two categories: 1) MAI-based recommendations (those that had an impact on the MAI score) and 2) Others (recommendations that had no impact on the MAI score).

Statistical analysis:

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 20.0 (Armonk, NY: IBM Corp.). Descriptive statistics were used to describe the data. The Kolmogorov-Smirnov test was used to assess normality and subsequent selection of the statistical test.

A total of 223 (n=112, 2012) (n=111, 2015) residents had their MAI scores computed at three time points: baseline, post RMMR, and post-GP uptake of pharmacists' recommendations. The change in the MAI score before and after the RMMR, (i) assuming that all of the pharmacists' recommendations were accepted by the GPs and (ii) based on the actual GP acceptance or non-acceptance of pharmacists' recommendations, were compared using the 2-tailed Wilcoxon signed rank test. Differences between the two cohorts (2012 and 2015) were compared using the Mann-Whitney U-test for continuous variables and the Chi square test for categorical variables. A P value <0.05 was considered statistically significant.

Results:

The baseline characteristics of the residents in both cohorts are shown in **Table 1.** Of the 112 RMMR reports reviewed from the older cohort, the mean (SD) age of the residents was 86.0 (7.6) years; 36% were males. Similarly, of the 111 RMMR reports reviewed from the newer cohort, the mean (SD) age of the residents was 87.4 (5.9); 30% were males. At baseline, the mean number (SD) of regular medications per resident in the older cohort was 7.7 (2.9) and the mean number (SD) of medical conditions per resident was 7.4 (3.0). The corresponding values for the newer cohort were 7.2 (2.4) and 8.0 (3.4), respectively. There were no significant differences in the baseline characteristics between the two cohorts. In both cohorts' diseases of the circulatory system, followed by mental and behavioural conditions, were the most common medical conditions.

Medication appropriateness index:

Table 2 presents the MAI scores at baseline and after the RMMR service for both cohorts. The median cumulative MAI scores were significantly lower following the RMMRs by accredited pharmacists, indicating an increased appropriateness of drug regimens (P<0.001). Overall, almost all patients in the study sample had at least one inappropriate rating at baseline (new cohort, n=111; old cohort, n=112). The number of patients with a cumulative MAI score of 0 increased from 0 at baseline to 11 post-RMMR, and 6 after the GPs' uptake of the recommendations in the newer cohort, while in the older cohort the number increased from 1 to 10 post-RMMR and 7 after the GPs' uptake of the recommendations. There were no significant differences in the MAI scores between the two cohorts at all three points (p>0.05).

Number and type of recommendations from pharmacist

Table 3 presents the pharmacists' recommendations during the provision of RMMRs. Overall, there were 373 and 284 (MAI and non-MAI based) pharmacist recommendations for the two cohorts. A majority of the recommendations that impacted on the MAI score in both the cohorts included discontinuation of medications (> 50%). There was a decline in the number of recommendations concerning the initiation of new pharmacological therapy from 27.9% of the total number of recommendations in 2012 to 18.4% in 2015.

Discussion

This study demonstrates that accredited pharmacists performing medication reviews improved the appropriateness of drug therapy in Australian aged care facilities as demonstrated by a reduction in the MAI ratings post the RMMR. Overall, the appropriateness of prescribing improved significantly following pharmacists' recommendations during the RMMRs and GPs' uptake of these recommendations in both the old and new cohort of RMMRs. A median reduction of over 10 and 7 points in the overall MAI score for the old cohort and new cohorts was observed following the RMMR, respectively. Uptake of the recommendations by the GPs, resulted in a statistically significant reduction in the MAI scores from baseline for both the cohorts.

The findings are consistent with previous medication review studies in older people [9, 22, 23, 24, 25]. However, most of the studies evaluating the appropriateness of prescribing in aged care residents have used explicit criteria, such as the Beers criteria and STOPP and START criteria [26, 27, 28, 29]. Despite their potential usefulness as indicators to guide comprehensive medicines reviews, explicit criteria have multiple limitations [30]. Beers criteria does not identify all cases of IP and sometimes identify appropriate prescribing as inappropriate [31]. For example; amitriptyline may be considered to be inappropriate in the elderly according to Beers criteria whilst in some cases it may be appropriate for indications such as neuropathic pain. To our knowledge, this is the first study that has evaluated the impact of RMMRs on the appropriateness of drug therapy using an implicit criterion.

The median reduction in the MAI scores in our study was comparable to a previous medication review study which included patients living in the community [9]. The study reported a reduction of 7 and 5 points in the MAI score following the pharmacists' recommendations during the Home Medications Review (HMR) and uptake of these recommendations by the GPs, respectively [9]. The

baseline MAI scores in our study however were higher, reflecting older, institutionalized sample taking more medications.

There were no significant differences in the extent of inappropriate prescribing at all three time points between the old and new RMMR cohorts. All patients in our study had at least one inappropriate rating at baseline. These findings are important, as in Australia there has been a reduction in the funding for the provision of medication review services by pharmacists (both HMRs and RMMRs). Prior to March 2014, aged care residents were able to receive an RMMR review every 12 months, however; due to changes in funding, residents are eligible for an RMMR once every 24 months [32]. By placing restrictions on these services, there is a concern that residents in aged care facilities would be more likely to be exposed to avoidable drug-related harm and thereby potentially worse clinical outcomes. This is especially problematic in this high risk group due to the prevalence of polypharmacy and inappropriate prescribing despite the development and implementation of multiple clinical programs and interventions that aim to solve this issue [33, 34, 35, 36].

Most the pharmacists' recommendations during the RMMR that had an impact on the MAI included discontinuation of medications. This is similar to other pharmacist-led medication review studies conducted internationally [37, 38]. In the current study across both the cohorts, recommendations that led to a reduction in the MAI scores included three main drug classes: nervous system, cardiovascular system, and alimentary system and metabolism. This is not surprising, as several studies in aged care residents have shown these drug classes to be associated with adverse drug reactions and outcomes [39, 40, 41]. It is interesting to note that the GPs agreement with pharmacists' MAI recommendations increased from 46.2% in 2012 to 67% in 2015, while agreement with non-MAI recommendations dropped from 66.4% in 2012 to 44.7% in 2015.

Previous studies concerning IP suggested that implementing both explicit and implicit criteria concurrently could increase the likelihood of detecting medication-related issues [42]. Explicit criteria, such as Beers and STOPP, have been found to be effective in predicting adverse drug events and the likelihood of hospitalization, but low agreement has been detected amongst these tools; hence, it is recommended to implement them in a complementary manner [43]. The MAI, on the other hand, has demonstrated usefulness in detecting and addressing inappropriate prescribing in a patient-centered fashion; however, use of the MAI is quite time consuming [8, 9].

Our study has some limitations that should be noted. Firstly, the use of MAI as a tool has limitations. The long-term clinical significance of reducing MAI scores has not been evaluated in the literature and hence more studies are needed in this area. Secondly, the MAI scores were computed retrospectively by the research team at the three time points. The pharmacists in the study did not receive any training and would not have used the MAI when conducting their RMMRs. Additionally, there was no way of assessing the accuracy of the information recorded in the reports. However, the retrospective observational approach would have avoided the possibility of the study influencing the actual medication review practice by pharmacists. Thirdly, our study may have under or over-estimated the extent of inappropriate prescribing as we did not have information on whether the residents had previously received an RMMR service and if any changes were made to their medication regimen. Fourthly, the RMMRs for both the cohorts were collected from a single center that provides RMMR services, and were performed by approximately ten pharmacists. The

pharmacists who conducted the RMMRs may have received additional training by the service provider. Hence, the results may not be generalizable to other service providers or accredited pharmacists. Another potential limitation given the retrospective nature of this study is that it may have been hampered by missing and incomplete data.

Despite these limitations, our study demonstrates that accredited pharmacists performing RMMRs can improve the appropriateness of prescribing, as reflected by the change in MAI scores and thereby has the potential to reduce avoidable drug-related harm and adverse clinical outcomes. Our study also demonstrates that inappropriate prescribing is common among residents in aged care settings, supporting the need for pharmacists performing RMMRs.

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Table 1. Baseline characteristics of the study sample

Characteristic	**Old cohort-2012** **N=112**	**New cohort-2015** **N=111**
Age, Y, Mean (SD)	86 (7.6)	87.4 (5.9)
Sex, n, % Female Male	 72 (64.3) 40 (35.7)	 78 (70.3) 33 (29.7)
Chronic medical conditions per patient, mean (SD)	7.4 (3)	8.0 (3.4)
Major diagnosis category (ICD-10 codes), n (%)	1. Disease of circulatory system (202) 24.4% 2. Mental and behavioural disorders (172) 20.7% 3. Diseases of the musculoskeletal system and connective tissue (113) 13.6% 4. Endocrine, nutritional and metabolic diseases (62) 7.5% 5. Diseases of the digestive system (56) 6.8%	1. Disease of circulatory system (193) 21.8% 2. Mental and behavioural disorders (172) 14.4% 3. Diseases of the musculoskeletal system and connective tissue (116) 13.1% 4. Endocrine, nutritional and metabolic diseases (51) 5.8% 5. Diseases of the digestive system (50) 5.6 %
Medications per patient, mean (SD) long-term medications “as needed” medications	 7.7 (2.9) 1.8 (1.4)	 7.2 (2.4) 1.9 (1.8)
Top 5 therapeutic classes of medications, n (%)	1. Nervous system (267) 25.1 % 2. Cardiovascular system (190) 17.9% 3. Alimentary tract and metabolism (169) 15.9% 4. Blood and blood forming orangs (89) 8.4% 5. Sensory organs (56) 5.3%	1. Alimentary tract and metabolism (291) 28.5% 2. Nervous system (275) 26.9% 3. Cardiovascular system (129) 12.6% 4. Blood and blood forming orangs (51) 4.9% 5. Sensory organs (48) 4.7%

Table 2: Summated MAI scores before and after medication reviews

Summated MAI Scores	**Old Cohort (n=112)**			**New Cohort (n=111)**		
	Median (IQR)	P value[a]	Mean (SD)	Median (IQR)	P value[a]	Mean (SD)
Before review	26 (16-35.75)		27.7 (20.2)	27 (12.5-38)		26.6 (16.4)
After review	15.5 (9-25.75)	<0.001	18.5 (13.8)	20 (6-29.25)	<0.001	19.5 (14.6)
After GPs' acceptance of pharmacist recommendations	20 (11.25-29.75)	<0.001	21.4 (14.3)	22 (8.75-33.25)	<0.001	21.5 (15.1)

[a] *By Wilcoxon sign rank test*

Table 3: Most common recommendations made by pharmacists during the RMMR service

Recommendations that had an impact on the MAI n (%)	Old cohort: Total number of recommendations 197(100)	New cohort: total number of recommendations 176 (100)
	Cease medication 103 (52.3) Dosage change 68 (35.5) Practical directions 15 (7.6)	Cease medication 95 (53.9) Dosage change 54 (30.7) Practical directions 22 (12.5)
Recommendations that did not have an impact on the MAI score n (%)	Total number of recommendations 143 (100)	Total number of recommendations 141 (100)
	Monitoring 56 (39.2) Treatment initiation 40 (27.9) Condition management review 10 (6.9)	Monitoring 49 (34.8) Treatment initiation 26 (18.4) Condition management review 30 (21.3)

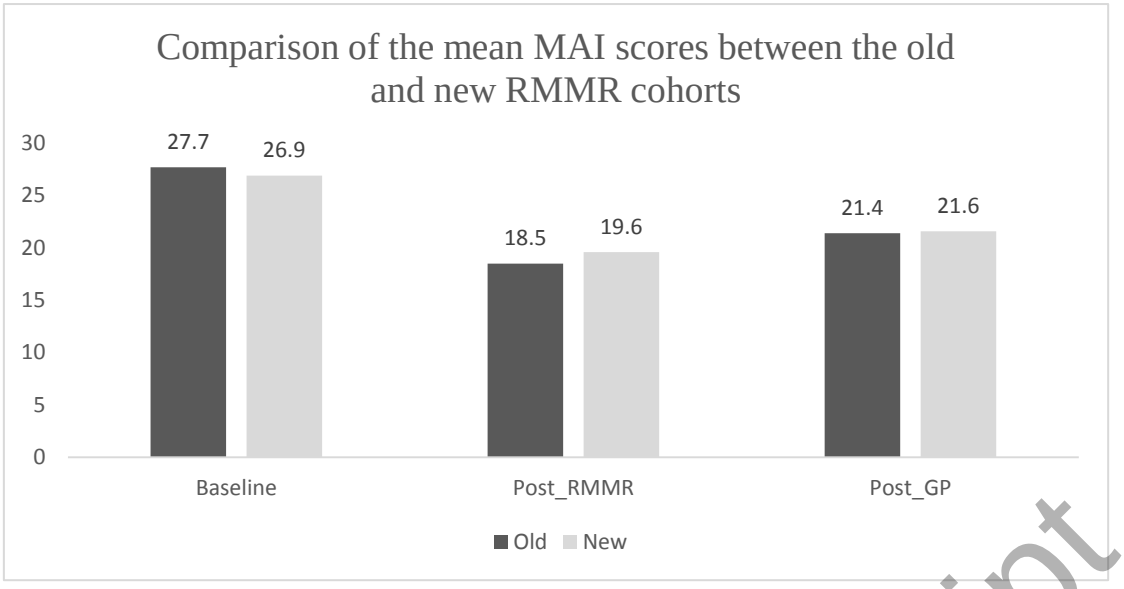

Figure 1: Comparison of the mean MAI scores between the old and new RMMR cohort at three time points