

Process, impact and outcomes of medication review in Australian residential aged care facilities: A systematic review

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Abstract

Objective: To systematically review literature reporting processes, impact and outcomes of medication review and reconciliation in Australian residential aged care facilities (RACFs).

Methods: PubMed/MEDLINE, EMBASE, CINAHL, Informit Health and grey literature were searched from 1995 to July 2018. Studies reporting outcomes of a stand-alone medication review or reconciliation interventions in Australian RACFs were included.

Results: Thirteen studies investigated medication review, eight of which studied Residential Medication Management Reviews (RMMRs). Five studies reported that medication reviews identified an average of 2.7–3.9 medication-related problems (MRPs) per resident. One study reported medication reviews had no impact on quality of life, hospitalisation or mortality, but was not powered to assess these. Three studies reported general practitioners' acceptance of pharmacists' recommendations to resolve MRPs, ranging between 45 and 84%.

Conclusions: Medication review may be a useful strategy to identify and prompt resolution of MRPs. However, the impact on clinical and resident-centred outcomes remains unclear.

KEYWORDS

aged care, geriatric medicine, health services, medication review, medication therapy management, pharmacist intervention

1 | INTRODUCTION

Multimorbidity, polypharmacy and age-related psychological decline mean that residents of residential aged care facilities (RACFs) are at high risk of medication-related problems (MRPs). A review of international literature reported that up to 43% of residents use one or more potentially inappropriate medications (PIMs).¹ Over three-quarters of residents in 17 Australian RACFs participating in the INvestigating Services Provided In the Residential care Environment for

people with Dementia (INSPIRED) study used anticholinergics, sedatives or PIMs in the previous 100 days.² Use of PIMs has been associated with poor health-related quality of life, poor psychological well-being, higher medication costs, hospitalisations and increased risk of mortality.^{3–6} Controlled trials of medication review in RACFs in Switzerland, the United States of America (USA) and Northern Ireland have demonstrated that rates of PIM use reduced for residents who received a medication review.^{7–9} Conversely, a recent observational study in the United States found higher medication

review completion rates were associated with improvements in four of 17 medication-related quality indicators but an increase in chronic use of atypical antipsychotic medications among Medicare Part D beneficiaries in RACFs.¹⁰ Medication reconciliation and review have been shown to identify and resolve MRPs in community and hospital settings.¹¹⁻¹⁴ Available evidence from studies in RACFs is more limited,¹² but suggests the finding may extend to the RACF setting.¹⁵ Pharmacist-led medication reconciliation was identified as the top priority for reducing polypharmacy in Australian RACFs by health professionals and consumers.¹⁶

Australia has had a national, government-funded collaborative medication review service in RACFs since 1997.¹⁷ This service, known as Residential Medication Management Review (RMMR), is similar to clinical medication review in the UK, comprehensive medication reviews provided under the medication therapy management program in the United States and MedsCheck LTC in Canada.¹⁸⁻²⁰ Residential Medication Management Reviews are conducted to optimise medication use, improve clinical outcomes and ensure the quality use of medicines (QUM; i.e. “judicious, appropriate, safe and effective use of medicines”).²¹ Medication review programs are increasingly recognised in health policy and quality standards internationally.^{18,22-24} However, although studies have reported positive impacts on MRPs and prescribing, results are conflicting for studies that investigated clinical outcomes such as decreased or no change in falls,^{9,25} decreased or no change in hospitalisations^{8,25-27} and decreased, no change, or increased in mortality.²⁵⁻²⁸ Three Australian studies were included in a recent systematic review of randomised controlled trials (RCTs) and observational studies of medication reviews in RACFs but other Australian studies were cross-sectional and, therefore, excluded.¹⁵ It is important to evaluate the evidence from these descriptive studies of “real-world” program outcomes.

The current Australian RMMR program enables residents referred by their general practitioner (GP, or family physician, the primary prescribers in RACFs in Australia) to receive a review from a clinical pharmacist every 2 years or more frequently if clinical circumstances change.²⁹ A report with recommendations from the RMMR is provided to the GP, who is responsible for implementing the recommendations in consultation with residents, carers and RACF staff.²¹ Over 1.15 million RMMRs were subsidised from 2007 to 2016, and the most recent government-funding agreement for national medication management programs allocated \$14.2 million to RMMRs.^{30,31} Although this is a well-established program, the magnitude of service provision and costs means there is a need to understand the processes, impact and outcomes of the existing and previous iterations of the program in Australia.³² Recent consultation and reviews continue to consider changes to program structure and eligibility.³³⁻³⁵ It is also important to understand impact and outcomes for residents in the light of increasing focus on the

Policy Impact

Residents of aged care facilities are often exposed to polypharmacy and high-risk medications. This review suggests that the Australian government-funded Residential Medication Management Review (RMMR) program is useful to identify and prompt resolution of medication-related problems.

Practice Impact

This review suggests that RMMRs identify 2.7-3.9 medication-related problems (MRPs) per resident and general practitioners (GPs) accept 45-84% of recommendations to resolve these MRPs. This highlights the value of pharmacists and GPs working together to optimise medication management in this setting.

need for clinical pharmacy services in RACFs.³⁶ A recent systematic review explored the process and outcomes of the corresponding Australian Home Medicines Review service and reported medication reviews are beneficial for people living in the community.¹¹ However, no systematic reviews have specifically explored the value of medication review and reconciliation in Australian RACFs.

The objective was to systematically review peer-reviewed and grey literature reporting processes, impacts and outcomes of medication review and reconciliation in Australian RACFs.

2 | METHOD

This review was conducted as per the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) statement (Figure 1).³⁷ The protocol was published prospectively on PROSPERO (CRD42016041773).³⁸

2.1 | Search strategy

PubMed, MEDLINE, EMBASE, CINAHL and Informat Health were searched using subject headings and keywords related to medication review, medication reconciliation and RACFs. The search was limited to English language articles with publication dates between January 1995 and July 2018. These publication dates were selected to include research published in the lead-in period to the RMMR program launch in 1997.²¹ Conference proceedings, relevant websites, relevant local journals, reference lists and publications of key authors in the field were manually searched to identify relevant full-text articles for inclusion (see Appendix A for full search strategy).

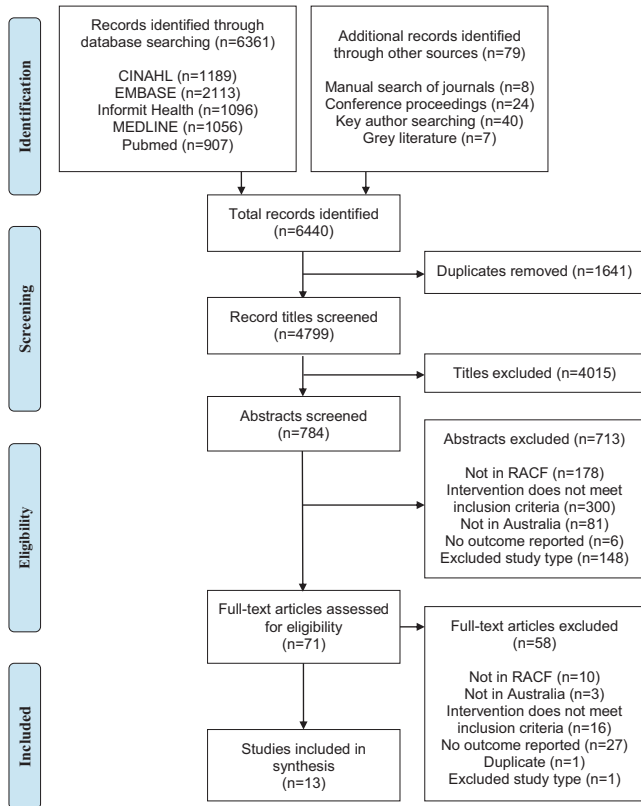


FIGURE 1 Flow chart of the literature search and study selection

2.2 | Study selection and synthesis

Studies reporting any process, impact or outcome of medication review or reconciliation for permanent residents of Australian RACFs were included. RACFs in Australia are synonymous with “nursing homes” or “long-term care facilities” in other countries and provide supported accommodation for people with care needs that can no longer be met in their own homes.¹⁷ Only stand-alone medication review or reconciliation interventions were included. Medication review was defined according to the Pharmaceutical Society of Australia's definition as “evaluation of a resident's complete medication regimen with the aims to optimise clinical outcomes, maximise benefits of medicine use and reduce risks of medicine use”.²¹ This included but was not limited to evaluation of medication reviews funded through the RMMR program.

Interventions that focused on a specific medication or single class of medications were excluded. However, studies that included a complete medication review but only reported results for a specific medication or class of medication were included. Medication reconciliation was defined according to the World Health Organization as “systematically obtaining, verifying, and documenting a best possible medication history, identifying any discrepancies between this and medication orders written at transitions of care, and resolving these

discrepancies in a timely manner”.³⁹ We searched the literature for medication reconciliation interventions completed before medication review or as part of a stand-alone intervention. Literature reviews, editorials, commentaries and case reports were excluded.

After removing duplicate records using EndNote X7.2, EYHC screened titles according to inclusion and exclusion criteria. Abstracts and full texts were screened independently by EYHC and KNW. At both stages, discrepancies were resolved through discussion and referred to a third investigator if consensus could not be reached.

Data were systematically extracted from each article using a pilot tested data extraction form. Process referred to how the program was implemented. For the purpose of the review, impact was operationally defined as an intermediary measure of change brought about by the program. Outcomes were any results that measured the success of the program against its stated aims to optimise medication use (eg, decrease in MRPs or inappropriate prescribing in a resident's therapy) and improve clinical outcomes (eg, quality of life, hospitalisations, mortality).^{29,40} Data extraction was completed independently by EYHC and KNW, with discrepancies resolved through discussion.

Studies included in the review categorised MRPs using different systems. To synthesise findings across studies, MRPs identified in each study were mapped to the DOCUMENT (Drug selection, Over or underdose, Compliance, Undertreated, Monitoring, Education, Not classifiable, Toxicity or adverse drug reaction) system.⁴¹ The DOCUMENT system was selected because it has been validated for use with Australian medication review data.^{42,43} Results from studies reporting the number of MRPs identified, recommendations made, acceptance and implementation of recommendations were extracted and pooled for analysis. Because of apparent inconsistencies with the use of the terms “acceptance” and “implementation” in the included studies, these terms were not considered to be interchangeable for the purpose of this review.

2.3 | Quality assessment

The corresponding Joanna Briggs Institute Checklist for prevalence studies, cohort studies and RCTs was used to assess the risk of bias for individual studies.⁴⁴ Methods used for the identification of outcomes were considered to be valid if based on existing definitions or widely used instruments and applied by trained professionals. Study samples were considered appropriate if the reported sample characteristics were representative of the larger RACF population. When studies did not include a sample size calculation, we calculated power to assess whether the sample size was adequate for assessing the primary outcome. Results of the checklist were reviewed when assessing and critiquing the quality of evidence. Studies were not excluded based on the quality assessment.

3 | RESULTS

Thirteen studies met the inclusion criteria (Table 1). All studies focused on medication review, and no stand-alone medication reconciliation interventions were identified. All studies involved elements of multidisciplinary collaboration but pharmacists were responsible for leading the medication review in 11 studies, geriatricians in one study⁴⁵ and a GP in one study.⁴⁶ Eight studies included medication reviews conducted under the RMMR program (Table 1).^{42,47-53} No additional studies were identified by searching the grey literature.

3.1 | Methodological quality of studies

The assessment of risk of bias is summarised in Appendix B. Nine retrospective studies analysed medication reviews conducted as part of routine clinical care. Four prospective studies analysed medication review interventions.

No studies included an a priori sample size calculation. The resident sample sizes ranged from 48 to 849. Five studies did not report the number of RACFs from which the resident samples were drawn. In the remaining studies where this was reported, the resident samples included between eight and 39 reviews per RACF.

More than one pharmacist or geriatrician delivered the medication review service in nine of the 13 included studies.^{42,45,47,49-54} This reflected “real-world” practice and increased generalisability of results.²⁰ Nine studies used a recognised classification system to categorise MRPs and/or recommendations, which facilitates more reliable comparisons.^{47-52,55,56} The lack of parallel comparison groups weakens the quality of evidence. The included studies in this review may also be subject to publication bias, where studies with positive results are more likely to be published.

3.2 | Processes

One study reported the views of GPs and nursing staff regarding medication review.⁵⁴ Of those who responded, 90% of nursing staff (n = 9/10) and 60% (n = 9/15) of prescribers found medication review to be beneficial and useful. Some prescribers had negative comments regarding having their prescribing reviewed by pharmacists.⁵⁴ No study reported resident perspectives, but six out of 15 prescribers responding to the survey reported their perception that medication reviews improved resident well-being.⁵⁴ There were no data in the included studies on resident satisfaction with the RMMR service.

One study conducted a cost analysis of the medication review intervention.⁵⁴ From a government perspective, there were overall savings in medication costs (\$29.88 per resident reviewed) but an overall increase in pathology expenditure (\$2.16 per resident reviewed).⁵⁴ The analysis was not a full

economic analysis and did not include, for example, the cost of providing the intervention.

One study evaluated PIM use in residents receiving RMMRs before and after a change in the frequency of RMMR eligibility from once a year to once every 2 years and found no significant difference in PIM use.⁵³

3.3 | Impact

An average of 2.7-3.9 MRPs was identified per review (n = 5 studies).^{42,48-50,54} Among these five studies, three different classification systems were used to categorise the MRPs and one study did not use a recognised classification system.⁵⁴

To investigate the most prevalent MRPs, 4144 MRPs from four studies with a combined resident sample size of 1374 were pooled (Figure 2).^{42,48,49,54} The most commonly reported MRPs across the four studies were undertreated conditions (23%, n = 948) (eg, untreated conditions, missing preventative treatments) and drug selection problems (22%, n = 892) (eg, duplication, drug interactions, wrong dose, strength, or form, missing indications, contraindications present). One study reported that the most common undertreatment recommendation was the addition of calcium and cholecalciferol for osteoporosis treatment.⁴⁹

Eight studies reported the types of recommendations identified during medication reviews.^{45,48-50,53-55,57} The mean number of review recommendations per resident was between 1.9 and 4.0. Results from seven studies were pooled to examine the most prevalent types of recommendations (n = 1897 residents with 5286 recommendations) (Figure 3).^{45,48,49,53-55,57} The most common recommendation made was a change in or new clinical or laboratory monitoring (27% of recommendations, n = 1416). The recommendation to add a medication to the resident's therapy, for example to address undertreated conditions, comprised 6% of recommendations (Figure 3).

Four studies reported the acceptance of recommendations by GPs.^{48,50,54,57} Acceptance of recommendations for 1177 residents across three studies was pooled,^{48,54,57} in which 45% to 84% recommendations were accepted by GPs. Recommendations related to education or counselling had a higher acceptance rate (98%, n = 186/190) (Figure 4). Recommendations that did not involve changes in therapies had a higher acceptance rate than those that did. The highest acceptance rate involving a change in therapy was to change a dose formulation (82%, n = 106/129), followed by the addition of a new medication to therapy (75%, n = 218/289). The remaining study only reported the three most frequent recommendations in the top 10 anatomic therapeutic chemical pharmacological subgroups.⁵⁰

Three studies reported the implementation of recommendations by GPs,^{45,50,55} in which 58%-72% of pharmacist recommendations were implemented. Two of the studies were

FIGURE 2 Medication-related problems (MRPs) identified by medication reviews in Australian residential aged care facilities

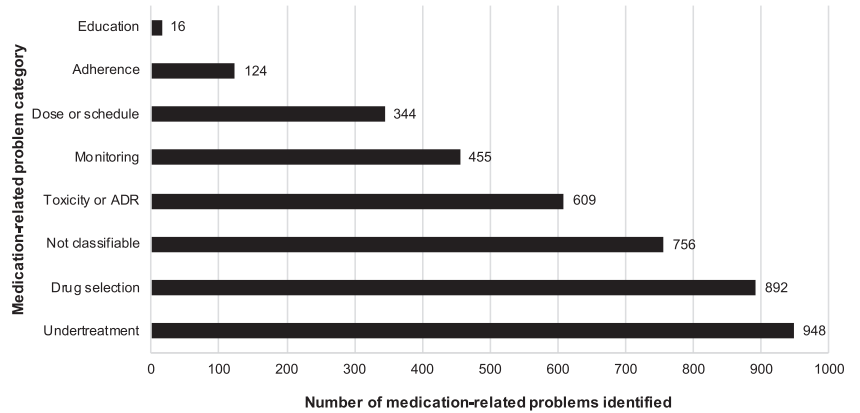


FIGURE 3 Recommendations arising from medication reviews in Australian residential aged care facilities

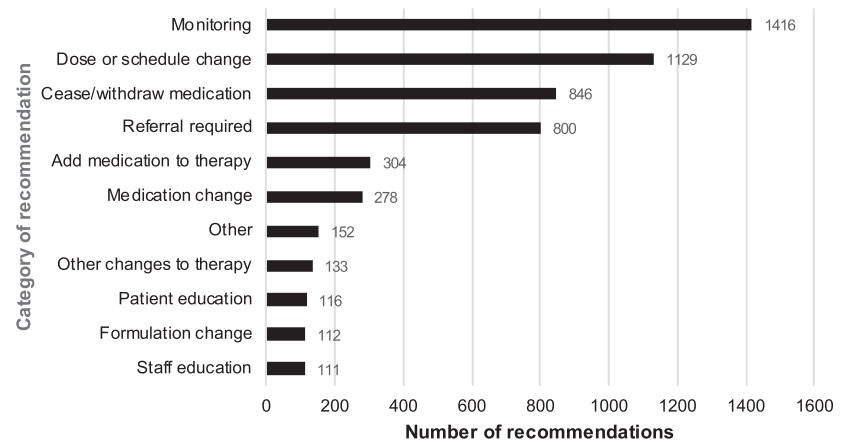
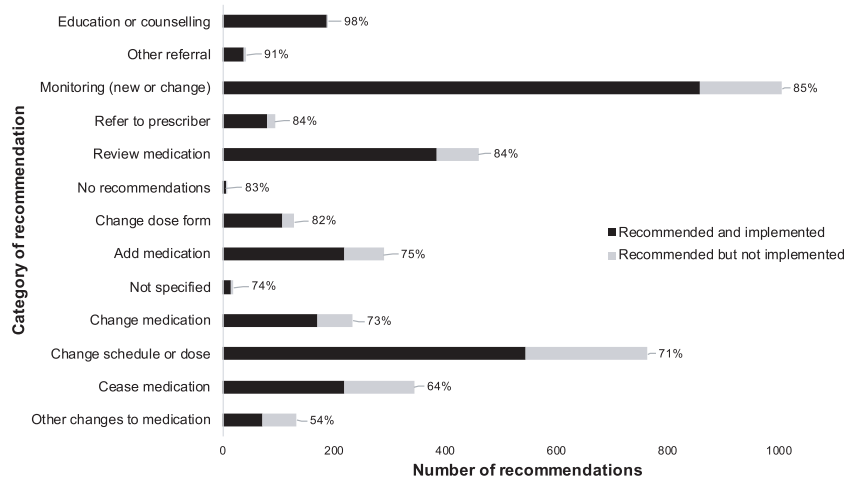


FIGURE 4 Acceptance of recommendations by general practitioners to resolve medication-related problems identified by medication reviews in Australian RACFs. “Other referral” refers to referral to health professionals other than the prescriber, for example podiatrist. “Other changes to medication” are changes to medication other than dose or schedule change, addition, cessation or change in medication, and drug formulation change



conducted retrospectively with access to medication charts and medical records,^{50,55} but only one study reported data extraction being cross-checked.⁵⁰

3.4 | Outcomes

One study reported clinical and resident-centred outcomes following medication review as secondary outcomes and was not adequately powered to assess these. Quality of life

decreased in both intervention and control groups (a mean decrease of 1.0 (SD ± 4.3 and ± 4.7 , respectively) when assessed using the Quality of Life in Alzheimer's Disease Scale ($P = 0.94$)). In the intervention group, 23/45 residents were hospitalised at least once compared with 24/48 in the control group ($P = 0.99$). After 12 months, 12/45 residents who received the intervention had died, compared to 19/48 residents in the control group (HR: 0.60, 95% CI: 0.30-1.22).⁴⁶

Medication reviews were found to significantly decrease anticholinergic and/or sedative medication burden in two studies.^{47,51} Retrospective review of RMMRs found that pharmacist recommendations effectively halved exposure to anticholinergic and sedative medications from one to half of a minimum efficacious dose (ie, the minimum daily dose approved by the United States' Food and Drug Administration⁵⁸) of an anticholinergic or sedative medication per resident, measured using the drug burden index. Overall, 61% of recommendations to reduce anticholinergic or sedative medications were implemented by GPs.⁵¹ Nervous system medications, including paracetamol, were implicated in over one-third (34%, $n = 381$) of accepted recommendations in three studies that reported by medication class.^{45,50,57}

The remaining studies investigated the impacts of comprehensive medication reviews on specific areas of therapy (Table 1). Improvements were found for the appropriateness of prescribing for older people^{45,53} and the appropriateness of prescribing of renally cleared medications.⁴⁸ There was no impact on the prevalence of use of antithrombotic medications for residents with atrial fibrillation who received a medication review.⁵²

4 | DISCUSSION

This systematic review identified a lack of research on clinical and resident-centred outcomes of medication reviews conducted. One study reported that medication reviews had no impact on quality of life, hospitalisation or mortality, but this study was underpowered to detect a significant difference in these outcomes. There was evidence that medication reviews may assist to optimise medication use by decreasing anticholinergic and/or sedative medication burden and inappropriate prescribing. Comprehensive medication reviews were successful in identifying 2.7-3.9 MRPs per resident, with up to 84% of recommendations to resolve MRPs accepted by GPs.

4.1 | RMMR program implications

Residents entering RACFs have more complex care needs, are frailer and experience more polypharmacy than when the RMMR program commenced over 20 years ago. For these reasons, access to medication review services is arguably more important than ever, as is understanding how best to target medication reviews to residents most likely to benefit and determining the clinical impact of the reviews.¹⁷ This systematic review did not identify whether specific residents benefit most from medication review, nor the optimum frequency of medication reviews. It has been estimated that only 38% of residents of Australian RACFs currently receive an RMMR annually.¹⁷ Data do not exist on the proportion of residents at risk of medication

misadventure. It was not clear from the seven studies of RMMRs included in this review whether the RMMR service is specifically being targeted to those residents at highest risk of medication-related harm.^{42,47-51,53} In Australian RACFs, 35% of residents stay <1 year.⁵⁹ Changes to the RMMR funding rules introduced in 2014 meant most residents are eligible for a RMMR every 2 years rather than every year as per the pre-2014 funding rules.⁶⁰ The implication has been that many residents now receive only one RMMR. In contrast, comparable programs in the UK, Canada and the United States permit medication reviews to be provided once per year.^{10,61,62} Evidence for the optimal frequency for medication review is sparse in both the Australian and international settings. Despite positive comments from prescribers and nursing staff regarding the value of medication review,^{54,63} one-third of directors of nursing were able to identify residents who did not receive an RMMR despite having an unmet clinical need.⁶⁴ One study compared RMMRs conducted in 2012 and 2015 before and after the funding rule changed and did not find a significant difference in PIM use.⁵³ An alternative RMMR funding model that incorporates clinical audit procedures and ensures the RMMR service is specifically targeted to residents at high risk of medication-related harm (eg, due to dementia diagnosis or frailty) has been suggested to guide RMMR referral.⁶⁰ This may also improve the cost-effectiveness of running a national medication review program, as the prevalence and cost of PIM use are high.^{1,5}

This systematic review found that overall 60% of medication review recommendations were accepted for all recommendation classes, except "other changes to medication" (18% acceptance rate). This rate was comparable with international observational studies on medication review (58%-68%).¹⁵ Recommendations for education and monitoring had higher acceptance rates than recommendations to change medication regimens. Higher implementation rates may have been achieved if inter-professional follow-up care were provided. A systematic review of the relationship between GP-pharmacist collaboration and recommendation implementation found medication reviews involving more intensive GP-pharmacist collaboration were more likely to result in regimen changes than reviews without intensive collaboration.⁶⁵ This was consistent with findings from a review of international systematic reviews of pharmacist-led medication review in community settings.¹⁴ Inter-professional communication pre- and postmedication review was a central component of medication review models investigated in early Australian and international research.^{28,66-68} A post-review discussion between the GP and pharmacist remains part of the program guidelines, and is mandatory unless any changes are considered minor in nature.²¹ The current Australian RMMR program does not provide specific funding to incentivise postreview collaboration as in Canada and United

TABLE 1 Summary of included studies

Author (year), study design	Intervention		Population		Results		
	Type	No of participants (No of RACFs)	Mean age (\pm SD)	Mean number of medications (\pm SD)	Measure and baseline	Impact	Outcome
Koria et al. (2018), ⁵³ retrospective cohort study	RMMR	112 from 2012 (not reported) 111 from 2015 (not reported)	2012 group: 86.0 (\pm 7.6) 2015 group: 87.4 (\pm 5.9) for 2015	2012 group: 7.7 (\pm 2.9) 2015 group: 7.2 (\pm 2.4)	MAI score, excluding 2 (accuracy of directions and cost-effectiveness) of the 10 criteria. 2012 group: MAI score before review was 26 2015 group: MAI score before review was 27	2012 group: 197 recommendations made that had an impact on MAI. After pharmacist review, MAI score would have been 15.5. 2015 group: 176 recommendations made that had an impact on MAI. After pharmacist review, MAI score would have been 20. Over 50% of recommendations that impacted MAI were to cease a medication	2012 group: After GPs' acceptance of pharmacist recommendations, MAI score was 20. 2015 group: After GPs' acceptance of pharmacist recommendations, MAI score was 22
McLarin et al. (2016), ⁴⁷ retrospective cross-sectional study	RMMR	814 (not reported)	85.6 (\pm 7.7)	11.4 (\pm 4.9)	ACB (measured using seven scales). 36-67% (depending on scale used) of residents prescribed at least one regular ACM.	Overall number of ACMs prescribed decreased following RMMR and after GP uptake of pharmacist recommendations. 103 possible anticholinergic adverse events identified by the pharmacist	Significantly lower ACB scores as measured using each of the seven scales. ~30% of recommendations pertaining to ACMs implemented. 114 dosage changes
Nishtala et al. (2016), ⁵² retrospective cross-sectional study	RMMR	146 (not reported)	88.4 (\pm 7.5)	Not reported	Use of antithrombotic therapies. 115/146 (79%) of residents prescribed antithrombotics. 7% (n = 5) of antiplatelet users were appropriately prescribed. 67 residents were not prescribed antithrombotic therapy according to guidelines	No recommendations made to prescribe antithrombotics for 10 eligible residents for antithrombotic therapy but were not prescribed any antithrombotics. No recommendations made to start antithrombotics for 30 residents eligible (without contraindications) to start guideline-recommended antithrombotics.	N/A

(Continues)

TABLE 1 (Continued)

Author (year), study design	Intervention		Population		Results		
	Type	No of participants (No of RACFs)	Mean age (\pm SD)	Mean number of medications (\pm SD)	Measure and baseline	Impact	Outcome
Potter et al. (2016), ⁴⁶ randomised controlled trial	Medication review conducted by GP	47 intervention 48 control (4)	84 (\pm 6) intervention 84 (\pm 8) control	9.6 (\pm 5.0) intervention 9.5 (\pm 3.6) control	Number of unique regular medicines at 12 months postrandomisation. Intervention: 9.6 regular medications at baseline Control: 9.5 regular medications at baseline	348 deprescribing targets identified for 45 residents.	Withdrawal of identified deprescribing targets achieved in 207 medicines (81%) in 42 people. Mean change in unique regular meds at 12 months in intervention was -1.9 ± 4.1 and in control $+0.1 \pm 3.5$.
Pouidel et al. (2015), ⁴⁵ prospective observational cohort study	Comprehensive geriatric assessment	153 (4)	83.0 (\pm 8.1)	9.6 (\pm 4.2)	Inappropriate prescribing (high-risk medications list created based on 2012 Beers Criteria, McLeod Criteria, the Laroché Criteria, the PRISCUS criteria and the Norwegian General Practice Criteria). ≥ 1 high-risk medication was prescribed to 58% of residents	Recommendations: Withdrawal of medication 10%, new medication 48%. Cease: due to ADEs (n = 66), no clear indication/medication burden (n = 63), disease cured (n = 16)	17% of high-risk medications ceased, altered dose in 3%
Gheewala et al. (2014), ⁴⁸ retrospective cross-sectional study	RMMR	847 (not reported)	84.9 (\pm 8.8)	11.2 (\pm 4.8)	MRPs (DOCUMENT classification). 2712 MRPs in 98% of residents, mean 3.2 (\pm 1.7) per resident. Inappropriate prescribing of renally cleared medications. 154 residents had CKD. 28 CKD residents were inappropriately prescribed renally cleared medications	3054 recommendations made, mean of 3.6 (\pm 1.9) per resident. Recommendations to monitor renal function were made for 94 (29%) residents with CKD. There were 28 recommendations to resolve MRPs for renally cleared medications in residents with CKD. 2560 (84%) recommendations implemented, mean 3.0 (\pm 1.9) per resident.	93% (n = 87) recommendations to monitor renal function were accepted by GPs 71% (n=20) recommendations to change treatment for residents inappropriately prescribed renally cleared medications were accepted by GPs

(Continues)

TABLE 1 (Continued)

Author (year), study design	Intervention		Population		Results		
	Type	No of participants (No of RACFs)	Mean age (\pm SD)	Mean number of medications (\pm SD)	Measure and baseline	Impact	Outcome
Kaur et al. (2012), ⁴⁹ retrospective cross-sectional study	RMMR	296 (6)	82.0 (\pm 11.1)	11.3 (\pm 4.8)	MRPs (Strand et al. 1990 definition) ⁸⁴ . 802 MRPs total 2.7 (range 0-12) per review	741 recommendations made. 37 recommendations implemented (49% of known outcomes, n = 75).	N/A
Khalil et al. (2011), ⁵⁵ retrospective cross-sectional study	Medication review by pharmacist as part of routine clinical care	48 (1)	86.0 (\pm not reported)	9.0 (\pm not reported)	MRPs (PNCE V5.01, 2006 classification). Number of MRPs not reported.	196 recommendations made, mean 4 (range 1-7) per resident. ~70% of recommendations implemented.	N/A
Nishtala et al. (2011), ⁵⁰ retrospective cross-sectional study	RMMR	500 (62)	84.0 (\pm 9.0)	7.4 (\pm 3.5)	MRPs (Bergen District Nursing Home study classification). 1433 MRPs identified in 96% of residents (mean of 3.0 per resident).	Number of recommendations not reported. 73% recommendations accepted. 58% recommendations implemented	N/A
Nishtala et al. (2009), ⁵¹ retrospective cross-sectional study	RMMR	500 (62)	84.0 (\pm 9.0)	7.4 (\pm 3.5)	DBI, a measure of exposure to medications with anticholinergic and sedative properties. Mean DBI before review: 0.59 (SD \pm 0.60)	Mean DBI after pharmacist recommendations would have been 0.47 (SD \pm 0.53), a 20% decrease (n = 0.12) from baseline.	Mean DBI after GP uptake of recommendations was 0.52 (SD \pm 0.58).
Stafford et al. (2009), ⁴² retrospective cross-sectional study	RMMR	96 (not reported)	83.9 (\pm 9.3)	9.7 (\pm 3.8)	MRPs (DOCUMENT classification). Mean of 3.9 (\pm 2.0) MRPs identified per resident.	Number of recommendations not reported. Acceptance of recommendations not reported.	N/A
Smith et al. (2002), ⁵⁷ prospective observational cohort study	Medication review by pharmacists	202 (14)	86.4 (\pm not reported)	3.9 (\pm 2.8)	MRPs (no formal definition). Number of MRPs not reported.	409 recommendations made, frequently cease therapy (n = 160), then change to dose regimen (n = 79), and biochemical tests (n = 56). 141 changes were made in 69 (51% of 135 residents whose medications were discussed with GP) residents.	N/A

(Continues)

TABLE 1 (Continued)

Author (year), study design	Intervention		Population		Results		Outcome
	Type	No of participants (No of RACFs)	Mean age (\pm SD)	Mean number of medications (\pm SD)	Measure and baseline	Impact	
Elliott and Thomson (1999), ⁵⁴ prospective observational cohort study	Medication review by pharmacists	128 (4)	82 (\pm 8.9)	7.4 (\pm 3.4)	MRPs (actual or potential problems, no formal definition). 254 MRPs identified at baseline.	247 recommendations made. 149 (60%) recommendations implemented.	N/A

Abbreviations: ACB: anticholinergic burden; ACM: anticholinergic medication; ADEs: adverse drug events; CKD: chronic kidney disease; DBI: drug burden index; GP: general practitioner; MAI: medication appropriateness index; MRP: medication-related problem; RACF: residential aged care facility; SD: standard deviation.

States,¹⁹ or remuneration for case conferencing as suggested by a previous evaluation of the RMMR program.⁶⁰ Lack of opportunity for collaboration in resident follow-up has been identified as a barrier to clinical decision-making and deprescribing in the RACF setting.^{60,69} There is increasing focus on integrating clinical pharmacists within RACFs which would support inter-professional communication.³⁶

4.2 | Clinical implications

One of the included studies reported clinical outcomes of medication review as secondary outcomes and was not adequately powered to assess these.⁴⁶ Small sample size was also identified as a factor that limited interpretation of the findings from the three Australian studies included in the recent international systematic review of medication reconciliation and review in RACFs.¹² Earlier Australian studies have reported medication review improved pain and mobility but were not associated with changes in morbidity or survival, although measuring improvements in these outcome measures is difficult.^{26,28} It is also inherently difficult to compare outcomes among residents who did and did not receive RMMRs, given that residents who were unwell, had more complex medication regimens or were at higher risk of medication-related harm may be more likely to receive RMMRs. Although the RMMR program has existed for over 20 years, there is a lack of Australian research into clinical and resident-centred outcomes in the RACF setting.

Undertreatment was the most common MRP identified in this systematic review, although only one study described the specific health conditions that were undertreated. This is counter-intuitive because medication review is often advocated as a method to decrease polypharmacy.^{70,71} In the present review, 16% (n = 846/5286) of all recommendations were to cease a medication. Planned and supervised medication cessation, known as deprescribing, is an area of increasing interest in RACFs. Deprescribing may include the conscious decision to withhold guideline-recommended therapies in accordance with the residents' goals of care. For this reason, apparent undertreatment may actually reflect an intentional prescribing decision informed by discussions with the resident and their family members. In a survey of residents in South Australia, 41% of residents wanted to decrease their number of regular medications and 79% of residents indicated a willingness to have medications deprescribed if recommended by their doctor.⁷² Lack of information on goals of care in RMMR referrals has been identified as a barrier for deprescribing.⁶⁹ No studies investigated to what extent residents' goals of care were considered in medication review recommendations, so it is unknown to what extent the MRPs identified by pharmacists reflected intentional and unintentional undertreatment. Another factor contributing to this finding may be that people with dementia are less likely

to be prescribed guideline-recommended medications for chronic conditions.⁷³ Clinicians may perceive the benefits and risks of medicines are different among older people with and without dementia. More than half of all residents in Australian RACFs are living with dementia.⁷³

The most common recommendation related to the need for additional tests or monitoring (27% of recommendations, $n = 1416/5286$). This finding was consistent with common recommendations in international studies of similar interventions.^{8,25,74} Although close monitoring is often necessary in older people due to physiological changes that occur with ageing, there may also be inconsistent understanding of the role and value of routine laboratory monitoring in this setting.^{57,75} For example, intensive management of type 2 diabetes is no longer recommended for residents of RACFs. Care should instead be individualised to maximise the residents' quality of life.⁷⁶ While monitoring may detect and prevent adverse drug events (ADEs), in some cases the rate of detection may not justify invasive testing.^{77,78} Where laboratory tests have occurred, results may not have been well documented or communicated to allied health professionals involved in the resident's care. Over half of all residents included in an Australian study did not have serum creatinine values recorded in clinical notes, despite 61% of residents receiving one or more renally cleared medications.⁴⁸ Careful consideration of what monitoring is necessary may avoid the cost, time and burden to residents in the RACF setting.⁷⁹

4.3 | Strengths and limitations

A strength of this review was the inclusion of a range of prospective and retrospective studies including medication reviews delivered as part of research studies and as part of routine clinical care. This allowed a comprehensive and robust evaluation of all aspects of the medication review intervention.

A limitation of this review was that studies that included medication reviews as part of complex multifactorial interventions were excluded. This included medication reviews conducted in conjunction with multidisciplinary case conferences.^{26,28} Other complementary interventions include QUM activities that are independently subsidised by the Australian government. The QUM program is a complementary service whereby pharmacists work with local stakeholders to deliver interventions at a facility level to improve medication management.¹⁷ Interventions specifically addressing particular classes of medications were also excluded by our criteria. The processes for assessing single medication classes may be similar to a complete medication review and may be relevant in reducing MRPs and risk of ADEs.

The use of different MRP classification systems limited comparison between studies included in this review. For

example, we were unable to separate medication dose increases from decreases, while the implications may be quite different. Similar categories from three different classification systems were re-classified into the DOCUMENT system to facilitate comparisons between studies.⁴¹ However, there were inherent limitations with this approach because each classification system differs in terms of definitions, structure and approach. These factors can influence the apparent number of MRPs identified.⁸⁰ The terminology of MRPs identified, recommendations made, acceptance and implementation of recommendations were not consistently applied to differentiate between the four categories, despite having different clinical implications. Therefore, our pooled analyses may not be a true reflection of MRPs. Additionally, the sensitivity and specificity of MRPs identified could not be evaluated.

To investigate the uptake of recommendations, the included studies used the terms “acceptance” and/or “implementation,” but no study provided definitions. In our pooled analysis of “acceptance” and “implementation,” we used the author terms and did not consider the terms interchangeable. Therefore, our results for “acceptance” and “implementation” are not directly comparable. In general, the difference between acceptance and implementation may be that the resident did not accept the recommendation, in which case the GP would agree with the recommendation but not change the therapy due to resident preference. The difference between “recommendation” and “acceptance” may also be due to a difference in information available to the pharmacist and the GP. The GP may accept the recommendation in principle but not implement the recommendation due to having access to clinical information that was not available to or considered by the pharmacist at the time of medication review.

4.4 | Future directions

While the high rate of acceptance of recommendations found in this systematic review may translate to resident benefit, there was minimal published evidence to support this. Hospitalisations, pain, cognitive function or resident-reported outcomes were only reported in one study, which was not powered to assess these outcomes. Evidence from international studies with similar interventions is mixed. While one US study found that medication review reduced hospitalisations,⁸¹ a RCT in the UK showed a reduction in the number of falls, but no impact on GP visits, hospitalisations or mortality.²⁵ Further longitudinal studies with parallel comparison groups are needed to investigate these and other resident-reported outcomes. Given the small sample sizes of existing studies, the increasing availability of “big data” for recipients of aged care services could play a role in understanding the impacts and outcomes of medication reviews on a wider population

level.⁸² The need for a core outcome set for medication review intervention studies, including standard measurement instruments, has been suggested.⁸³ This evidence would inform targeting of medication reviews and may allow medication review data to be used at policy level to manage medication-related risk.

5 | CONCLUSIONS

Collaborative medication reviews are a useful strategy to identify and resolve MRPs in RACFs and may improve the optimal use of medicines. However, there were no adequately powered data on the impact of medication review on clinical and resident-centred outcomes. It was unclear what proportion of residents at high risk of MRPs receive a medication review. There were no studies that focused on stand-alone medication reconciliation. Future studies of medication interventions in RACFs which assess clinical and resident-centred outcomes are needed.

CONFLICT OF INTEREST

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APPENDIX A**Search strategy****MEDLINE VIA OVID**

- 1 exp Aged/
- 2 Homes for the aged/
- 3 exp Nursing Homes/
- 4 Long-term care/
- 5 Assisted Living Facilities/
- 6 residential aged care facilit*.mp.
- 7 Aged care hom*.mp.
- 8 care home\$1.mp.
- 9 (long-term adj2 facilit\$3).mp.
- 10 Nursing home\$1.mp.
- 11 (Residential\$1 adj2 facilit\$3).mp.
- 12 ((Residential\$1 or home\$1 or house\$1) adj2 (old or elderly or aged or geriatric\$1)).mp.
- 13 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12
- 14 exp Medication errors/
- 15 exp Utilization Review/
- 16 Medication Therapy Management/
- 17 Pharmacists/
- 18 medicat* use\$.mp.
- 19 medica* reconciliation.mp.
- 20 (medicat* review\$ OR medicine* review\$).mp.
- 21 (medica* adj3 management).mp.
- 22 pharmaci*.mp.
- 23 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
- 24 exp Australia/
- 25 Australia*.mp.
- 26 (New South Wales or NSW or Victoria or VIC or South Australia or SA or Western Australia or WA or Northern Territory or NT or Queensland or QLD or Tasmania or TAS or Australian Capital Territory or ACT).mp.
- 27 (Sydney or Melbourne or Adelaide or Hobart or Brisbane or Perth or Darwin or Canberra).mp.
- 28 24 or 25 or 26 or 27
- 29 13 and 23 and 28
- 30 RMMR*.mp.
- 31 Residential medication management review*.mp.
- 32 30 or 31
- 33 29 or 32
- 34 limit 33 to (yr="1995 -Current" and english)
- 35 limit 34 to (addresses or autobiography or biography or comment or dictionary or directory or editorial or festschrift or letter or portraits)
- 36 34 not 35

PUBMED

((((((((((Homes for the aged) OR Nursing homes) OR Long-term care) OR Residential aged care facilit*) OR Aged care hom*)) AND (((((((Medication reconciliation) OR Utilization review) OR Medication therapy management) OR Medication review) OR Medicine review) OR Medicines review) OR Medication management) OR Pharmacist)) AND Australia[Affiliation])) OR (((RMMR) OR RMMRs) OR Residential medication management review*) OR Residential medication management review)

Publication date from 1995/01/01 to 2018/07/31.

EMBASE VIA OVID

- 1 exp Aged/
- 2 exp Very elderly/
- 3 exp Frail elderly/
- 4 exp Nursing home/
- 5 exp Home for the aged/
- 6 Residential care/
- 7 Residential aged care facilit*.mp.
- 8 Aged care hom*.mp.
- 9 (long-term adj2 facilit\$3).mp.
- 10 Nursing home\$1.mp.
- 11 ((Residential\$1 or home\$1 or house\$1) adj2 (old or elderly or aged or geriatric\$1)).mp.
- 12 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
- 13 exp Medication therapy management/
- 14 exp "Drug use"/
- 15 exp Inappropriate prescribing/
- 16 Pharmacist/
- 17 Medicat* use\$.mp.
- 18 Medica* reconciliation.mp.
- 19 Medicat* review\$.mp.
- 20 (medicat* adj3 management).mp.
- 21 Pharmaci*.mp.
- 22 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21
- 23 exp Australia/
- 24 Australia*.mp.
- 25 (New South Wales or NSW or Victoria or VIC or South Australia or SA or Western Australia or WA or Northern Territory or NT or Queensland or QLD or Tasmania or TAS or Australian Capital Territory or ACT).mp.
- 26 (Sydney or Melbourne or Adelaide or Hobart or Brisbane or Perth or Darwin or Canberra).mp.
- 27 23 or 24 or 25 or 26
- 28 12 and 22 and 27
- 29 RMMR*.mp.
- 30 Residential medication management review*.mp.
- 31 29 or 30
- 32 28 or 31
- 33 limit 32 to (yr="1995 -Current" and english)

CINAHL

S1 (MH “Aged+”)
 S2 (MH “Nursing Homes+”)
 S3 (MH “Nursing Home Patients”)
 S4 (MH “Long Term Care”)
 S5 Residential Aged Care Facilit*
 S6 Aged Care Hom*
 S7 Long-term N2 Facilit*
 S8 “Nursing Hom*”
 S9 ((Residential# or home# or house#) N2 (old or elderly or aged or geriatric#))
 S10 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9
 S11 (MH “Medication Reconciliation”)
 S12 (MH “Record Review”)
 S13 (MH “Medication History”)
 S14 (MH “Medication Compliance”)
 S15 (MH “Medication Errors+”)
 S16 (MH “Drug Utilization”)
 S17 (MH “Utilization Review+”)
 S18 (MH “Pharmacists”)
 S19 Medicat* Use*
 S20 Medica* Reconciliation
 S21 Medicat* Review*
 S22 Medicine* Review*

S23 Medicat* N3 Management
 S24 S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 or S23
 S25 AF Australia
 S26 S10 AND S24 AND S25
 S27 RMMR*
 S28 Residential medication management review*
 S29 S27 OR S28
 S30 S26 OR S29
 S31 Limit S30 to Publication Year: 1995-2018
 S32 Narrow S31 by Language: English
 S33 Narrow S32 by SubjectAge: -aged, 80 and over, and—middle aged: 45-64 years

INFORMIT HEALTH COLLECTION

(SUBJECT:Aged OR (SUBJECT:”Older people”) OR (SUBJECT:”Old age homes”) OR (SUBJECT:”Long-term care”) OR (SUBJECT:Nursing ! SUBJECT:hom*) OR (ID:residential ID:aged ID:care ID:facility) OR (Aged % care % hom*) OR (Residential ! aged ! care ! facility*)) AND (SUBJECT:Drugs OR (Medicat* % management) OR (Medica* %2 reconciliation) OR (Medicat* % review*) OR (Medicine* % review*) OR (Pharmacis*)) limit to date 1995-2018.

