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SUMMARY WITH CRITICAL APPRAISAL

Multidisciplinary Medication Review in Long-Term Care: A Review of Clinical Utility, Cost-Effectiveness and Guidelines

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Context and Policy Issues

"Polypharmacy" refers to the use of two or more medications, and commonly refers to the use of five or more medications. Polypharmacy is more prevalent among those aged 65 years and over than in younger populations.[1,2] Polypharmacy occurs more frequently among those residing in long-term care facilities than those living in communities and can be due to duplicate or redundant medications for similar diseases.[2] The use of multiple medications can lead to toxicity and decrease drug compliance.[2] The adverse effects of certain medications may induce clinicians to prescribe more drugs to treat them.[2] In a 2008 survey that interviewed 3,132 Canadians aged 65 years and over, 27% of the respondents were regularly taking five or more medications and 12% of them had experienced drug-related adverse events, in comparison to 5% of Canadians taking one or two medications.[1]

To prevent inappropriate use of medications among the elderly, there are guidelines aiming at deprescribing certain classes of medications[3,4] or avoiding potentially inappropriate medications in populations with specific conditions.[5] One prominent example is the Beers criteria last updated by the American Geriatrics Society in 2019.[5] There are recommendations on the medications that should be avoided in general or specific to health conditions.[5] To put these guidelines into practice requires medication reviews to screen and deprescribe the medications among the elderly, particularly those residing in long-term care facilities.[2]

Pharmacist-led medication reviews have been implemented in countries such as the US, the UK, and Canada.[2] In a systematic review, pharmacist-led and team-based medication reviews were found to improve the quality of medication use in long-term care facilities.[2] Team-based reviews involve professionals from different disciplines and often consist of pharmacists, clinicians, and nurses.[2,6] In a 2011 Canadian Agency for Drugs and Technologies in Health report, low-quality evidence from two systematic reviews and two non-randomized studies showed that team-based medication reviews (every three months in one primary study, unspecified in others) were associated with less use of inappropriate medications and better patient health outcomes, in comparison to usual care.[6] However, it remains unclear whether more frequent medication reviews, such as every three months, can improve medication use and reduce adverse events.[2,6] This report aims to review the evidence regarding the clinical utility and cost-effectiveness of multidisciplinary medication reviews in long-term care facilities, as well as clinical guidelines on multidisciplinary medication reviews.

Research Questions

1. What is the clinical utility of multidisciplinary medication review every three months in long-term care settings?
2. What is the cost-effectiveness of multidisciplinary medication review every three months in long-term care settings?
3. What are the evidence-based guidelines regarding the use of multidisciplinary medication review in long-term care settings?

Key Findings

Two systematic reviews were included in this report, however no evidence regarding the clinical utility of different frequencies of multidisciplinary medication review was identified. No evidence for the cost-effectiveness of multidisciplinary medication review every three months among patients in long-term care settings, and no guidelines on multidisciplinary medication reviews, were identified. This report was limited by the lack of primary evidence. Further research on multidisciplinary medication reviews may help to reduce uncertainty in their clinical utility and cost-effectiveness.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE All (1946–) via Ovid, Embase (1974–) via Ovid, Cumulative Index to Nursing and Allied Health Literature (CINAHL), the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were multidisciplinary medication reviews and long-term care. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 01, 2014 and July 22, 2019.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients residing in long-term care facilities
Intervention	Multidisciplinary medication review every three months
Comparator	Q1-Q2: A different frequency of multidisciplinary medication review (e.g., annual); Medication review by a single health professional at any frequency Q3: Not applicable
Outcomes	Q1: Clinical utility (e.g., change in medication use, drug-related adverse events, mortality, quality of life) Q2: Cost-effectiveness (e.g., incremental cost per quality-adjusted life year or health benefit gained) Q3: Evidence-based guidelines
Study Designs	Health technology assessments, systematic reviews, meta-analyses, non-randomized studies, randomized controlled trials, economic evaluations, and guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2014. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

The included systematic reviews were critically appraised by one reviewer using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) 2 checklist.[7] Summary scores were not calculated for the included studies; rather, a review of the strengths and limitations of each included study was described narratively.

Summary of Evidence

Additional details regarding the characteristics of included publications are provided in Appendix 2.

Quantity of Research Available

A total of 327 citations were identified in the literature search. Following screening of titles and abstracts, 313 citations were excluded and 14 potentially relevant reports from the electronic search were retrieved for full-text review. Three potentially relevant publications were retrieved from the grey literature search for full-text review. Of these potentially relevant articles, 15 publications were excluded for various reasons, and two publications met the inclusion criteria and were included in this report. These comprised two systematic reviews. Appendix 1 presents the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[8] flowchart of the study selection.

Summary of Study Characteristics

Study Design

There were two systematic reviews (SRs) identified regarding the clinical utility of multidisciplinary medication reviews.[2,9] Rankin et al. searched for randomized controlled trials (RCTs) and non-randomized studies published before May 2016 in several databases.[10] Thiruchelvam et al. searched for RCTs and observational studies published before 2015 in several databases.[2] Both systematic reviews had broader inclusion criteria than the present review (i.e., were wider in scope), and none of the included primary studies met the selection criteria for the present review. The overlap in the primary studies between the two SRs is listed in Appendix 5.

Country of Origin

The first authors of the SRs by Rankin et al. and Thiruchelvam et al. were based in the UK and Malaysia respectively.[2,10]

Patient Population

Rankin et al. synthesized the data from 28,672 people aged 65 years and over, including individuals residing in long-term care facilities.[10] Thiruchelvam et al. reviewed the data from residents in “aged care facilities”.[2]

Interventions and Comparators

Rankin et al. considered interventions that affected prescribing and aimed to improve polypharmacy in people aged 65 years and over.[10] The interventions were not limited to those in long-term care facilities.[10] There were no primary studies that examined the clinical utility of multidisciplinary medication reviews included in the SR.[10] The interventions identified by Rankin et al. were computerized decision support, and complex, multi-faceted

pharmaceutical-care based approaches (responsible provision of medicines to improve patient's outcomes).[10] These interventions were compared to usual care, as defined within each individual study.[10]

In the SR by Thiruchelvam et al., the intervention of interest was medication reviews in "aged care facilities".[2] The identified interventions were pharmacist-led medication reviews and multidisciplinary team-based reviews.[2] The frequencies of medication reviews were reported in four RCTs and not described in other studies, but different frequencies of medication reviews were not compared with one another in any study.[2] The interventions were compared with control groups and control nursing homes, but the characteristics of the control groups were not described.[2]

Outcomes

The outcomes of interest in the SR by Rankin et al. were medication appropriateness and number of potentially inappropriate medications.[10] Thiruchelvam et al. reported the number of prescribed medications, inappropriate medications, and adverse outcomes.[2]

Summary of Critical Appraisal

Systematic reviews

The characteristics of the SRs were reported clearly.[2,10] The population, intervention, comparator, and outcome components were described and included in the research questions and the inclusion criteria in the SRs by Rankin et al. and Thiruchelvam et al.[2,10] The selection of eligible study designs was explained in both SRs, however justification was not provided.[2,10] Comprehensive literature searches were conducted in both SRs.[2,10] Study selection and data extraction were conducted in duplicate.[2,10] The risk of bias in the included studies was assessed in both SRs,[2,10] and the risk of bias in the included studies was considered while interpreting the results.[2,10] The heterogeneity in the results was discussed.[2,10] There was considerable heterogeneity between the included primary studies and it was not feasible to conduct meta-analyses.[2,10] The included studies were described,[2,10] however, only Rankin et al. listed the excluded studies and the reasons for exclusion.[10] The sources of funding for the included studies were not reported.[2,10] The review protocols were not published *a priori*.[2,10]

Review authors' competing interests were reported in both SRs.[2,10] Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

Summary of Findings

Appendix 4 presents a table of the main study findings and authors' conclusions.

Clinical Utility of Multidisciplinary Medication Review Every Three Months

Systematic reviews

Two systematic reviews were identified that examined the clinical utility of interventions affecting prescribing[10] and medication reviews in "aged care facilities".[2] Rankin et al. examined the utility of interventions aimed at improving appropriate polypharmacy[10] and Thiruchelvam et al. sought evidence regarding the utility of medication reviews in aged care facilities.[2] However, no relevant evidence regarding the utility of different frequencies of multidisciplinary medication review in long-term care facilities was identified; therefore, no summary can be provided.

Cost-Effectiveness of Multidisciplinary Medication Review Every Three Months

No relevant evidence regarding the cost-effectiveness of multidisciplinary medication review every three months in long-term care facilities was identified; therefore, no summary can be provided.

Guidelines

No evidence-based guidelines regarding the use of multidisciplinary medication review in long-term care settings were identified; therefore, no summary can be provided.

Limitations

The main limitation to this report was the absence of evidence for the clinical utility and cost-effectiveness of multidisciplinary medication reviews in long-term settings. No relevant primary studies were identified. No evidence-based guidelines on medication reviews in long-term care settings were identified. In the eligible SRs, the frequencies of the medication reviews were not reported in most primary studies and medication reviews of different frequencies were not compared to each other.[2,10]

Conclusions and Implications for Decision or Policy Making

Two SRs that examined the clinical utility of interventions affecting prescribing or medication reviews in long-term care facilities were included.[2,10] The inclusion criteria of two SRs[2,10] were broader than those of this report, and none of the included primary studies in the SRs were relevant to this report.[2,10] Therefore, no evidence for the clinical utility or cost-effectiveness of multidisciplinary medication reviews every three months among patients in long-term care settings was identified. Similarly, no guidelines on multidisciplinary medication reviews were identified. This report was limited by the lack of evidence. Further research on the clinical utility and cost-effectiveness of multidisciplinary medication reviews may help to reduce uncertainty.

References

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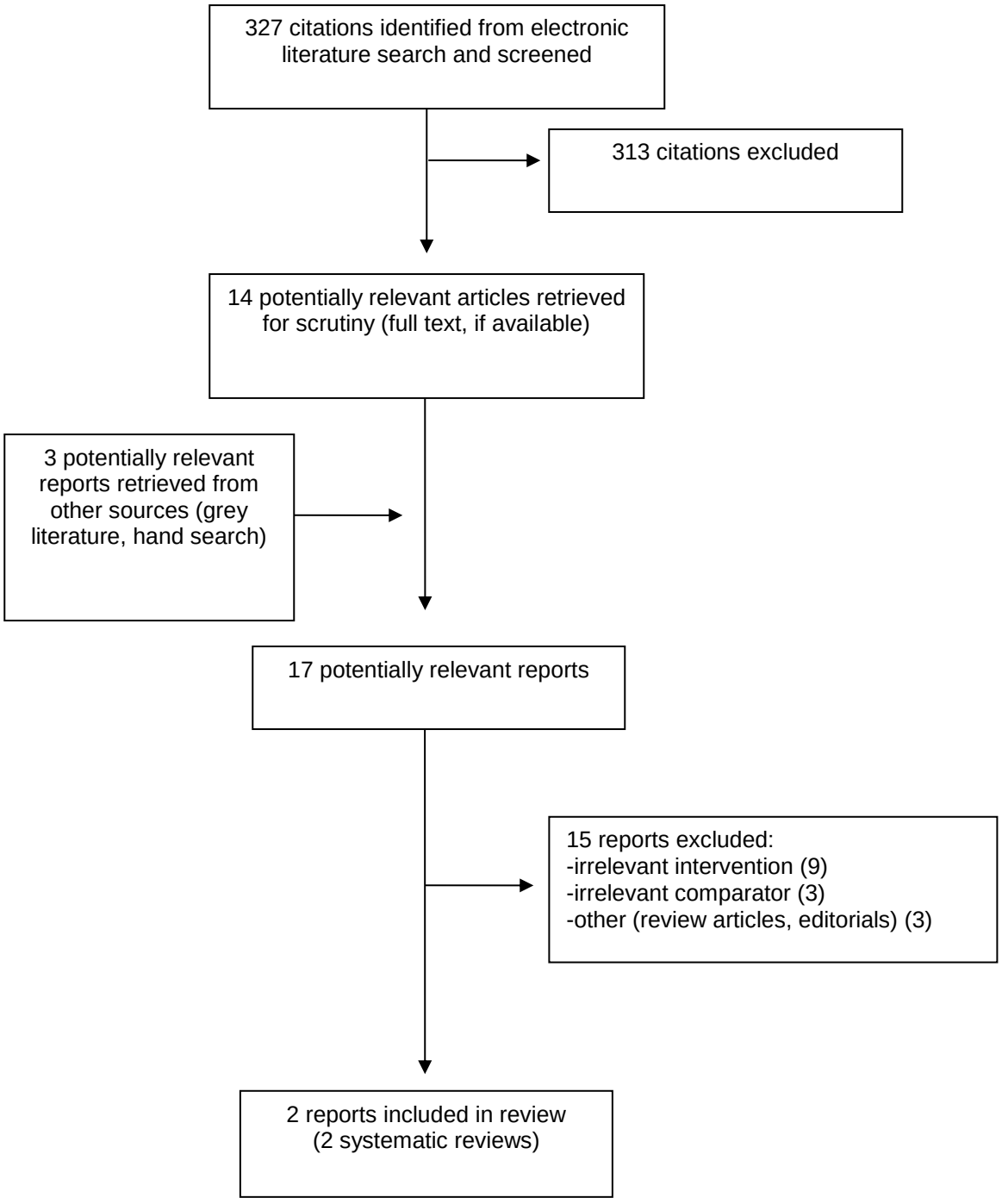
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Systematic Reviews and Meta-Analyses

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Rankin et al. 2018, UK[10]	32 studies (28 RCTs, 2 non-randomised trials and 2 controlled before-after studies No primary studies relevant to the present review All conducted in high-income countries Search date: May 2016	28,672 participants aged 65 years and over Female: 64.4% Mean age: 72.8 years	Eligible interventions: those "*affecting prescribing aimed at improving appropriate polypharmacy in people aged 65 years and older, prescribed polypharmacy (four or more medicines), which used a validated tool to assess prescribing appropriateness. These tools can be classified as either implicit tools (judgement-based/based on expert professional judgement) or explicit tools (criterion-based, comprising lists of drugs to be avoided in older people).*" (p. 1) None of the identified interventions were relevant to this report Computerised decision support (1 study) Complex, multi-faceted pharmaceutical-care based approaches (responsible provision of medicines to improve patient's outcomes, 31 studies) All interventions delivered by healthcare professionals such as general physicians, pharmacists and geriatricians Comparator: usual care defined by each study	Medication appropriateness, number of potentially inappropriate medications Follow-up: 6 to 12 months

Table 2: Characteristics of Included Systematic Reviews and Meta-Analyses

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Thiruchelvam et al. 2017, Malasia[2]	22 studies (10 observational studies and 12 controlled trials) No primary studies relevant to the present review RCTs and observational studies English articles only Databases searched: PubMed, CINAHL, IPA, TRiP, and the Cochrane Library Search date: December 2015	Ranges of sample sizes: 148 to 1854 Residents in aged care facilities	Medication review in aged care facilities searched Pharmacist-led medication reviews (8 studies) and multidisciplinary team-based reviews (4 studies) Frequency: weekly (1 RCT), monthly (1 RCT), and 6 months (2 RCTs); not reported in other studies Comparators: control groups or control nursing homes (details not described)	Number of prescribed medications, inappropriate medications, and adverse outcomes (including number of deaths, frequency of hospitalizations) Follow-up: 1 to 12 months

CINAHL = Cumulative Index to Nursing and Allied Health Literature; IPA = International Pharmaceutical Abstracts; RCT = randomized controlled trial.

Appendix 3: Critical Appraisal of Included Publications

Table 3: Strengths and Limitations of Systematic Reviews and Meta-Analyses using the Amstar 2 checklist[7]

Strengths	Limitations
Rankin et al., 2018[10]	
- PICO components included in the research questions and inclusion criteria - Selection of eligible study designs explained - Comprehensive literature searches - Study selection in duplicate - Data extraction in duplicate - List of excluded studies with reasons for exclusion provided - Included studies described - Risk of bias in the included studies assessed with published tools - Appropriate statistical tests planned for meta-analysis (not conducted for heterogeneity) - Risk of bias in the included studies considered while interpreting the results - Heterogeneity in the results discussed - Review authors' competing interests declared	- Review protocol not published *a priori* - Sources of funding for the included studies not reported
Thiruchelvam et al., 2017[2]	
- PICO components included in the research questions and inclusion criteria - Selection of eligible study designs explained - Comprehensive literature searches - Study selection in duplicate - Data extraction in duplicate - Included studies described - Risk of bias in the included studies assessed with published tools - Risk of bias in the included studies considered while interpreting the results - Heterogeneity in the results discussed - Review authors' competing interests declared	- Review protocol not published *a priori* - Sources of funding for the included studies not reported - List of excluded studies not provided

PICO = population, intervention, comparator, and outcome.

Appendix 4: Main Study Findings and Authors' Conclusions

Table 4: Summary of Findings Included Systematic Reviews and Meta-Analyses

Main Study Findings	Authors' Conclusion
Rankin et al., 2018[10]	
- No studies were included that compared medication reviews of different frequencies	- "*It is uncertain whether pharmaceutical care improves medication appropriateness*" (p. 1) - "*It is uncertain whether pharmaceutical care reduces the number of potentially inappropriate medications*" (p. 1) - "*It is uncertain whether pharmaceutical care reduces the proportion of patients with one or more PIMs*" (p. 1) - "*Pharmaceutical care may slightly reduce the number of potential prescribing omissions*" (p. 1) - "*it is uncertain whether pharmaceutical care reduces the proportion of patients with one or more PPOs*" (p. 1) - "*Pharmaceutical care may make little or no difference in hospital admissions*" (p. 1) - "*Pharmaceutical care may make little or no difference in quality of life*" (p. 1)
Thiruchelvam et al., 2017[2]	
No studies were included that compared medication reviews of different frequencies Studies regarding the following types of medication reviews were identified (none of which compared different frequencies): - Prescription reviews (n = 8 trials) and clinical medication reviews (n = 4 trials) - Pharmacist-led medication reviews (8/12 observational studies) and multidisciplinary team-based reviews (2 observational studies) - Prescription reviews (6 observational studies) and clinical medication reviews (4 observational studies) Clinical effectiveness - "*The number of prescribed medications, inappropriate medications, and adverse outcomes (eg, number of deaths, frequency of hospitalizations) were reduced in the intervention group*" (p. 87.e1) The intervention group received medication reviews.	- "*Medication reviews conducted by pharmacists, either working independently or with other health care professionals, appear to improve the quality of medication use in aged care settings*" (p. 87.e1) - "*However, robust conclusions cannot be drawn because of significant heterogeneity in measurements and potential risk for biases*" (p. 87.e1)

CI = confidence interval; PIM = potentially inappropriate medication; PPO = potential prescribing omission; RR = risk ratio; SMD = standardized mean difference.

Appendix 5: Overlap between Included Systematic Reviews

Table 5: Primary Study Overlap between Included Systematic Reviews

Primary Study Citation	Systematic Review Citation	
	Rankin 2018[10] (n = 32)	Thiruchelvam 2017[2] (n = 22)
Alldred 2007		X
Baqir 2014		X
Basger 2015	X	
Bladh 2011	X	
Briesacher 2005		X
Brulhart 2011		X
Bucci 2003	X	
Campins 2017	X	
Chia 2015		X
Chiu 2018	X	
Christensen 2004		X
sswClaesson 1998		X
Clyne 2015	X	
Crotty 2004a	X	X
Crotty 2004b	X	
Dalleur 2014	X	
Dilles 2013		X
Finkers 2007		X
Franchi 2016	X	
Frankenthal 2014	X	
Fried 2017	X	
Furniss 2000		X
Gallagher 2011	X	
Garcia-Gollarte 2014	X	
Haag 2016	X	
Hanlon 1996	X	
Houghton 2014		X
King 2001		X
Koberlein-Neu 2016	X	
Lapane 2011		X

Table 5: Primary Study Overlap between Included Systematic Reviews

Primary Study Citation	Systematic Review Citation	
	Rankin 2018[10] (n = 32)	Thiruchelvam 2017[2] (n = 22)
Mestres 2015		X
Michalek 2014	X	
Milos 2013	X	X
Muth 2016	X	
Muth 2018	X	
Olsson 2012	X	
Patterson 2010		X
Pitkala 2014	X	
Roberts 2001		X
Schmader 2004	X	
Spinewine 2007	X	
Stuijt 2008		X
Tamblyn 2003	X	
Taylor 2003	X	
Thyrian 2017	X	
Trygstad 2005	X	
Trygstad 2009	X	
Van der Linden 2017	X	
Verrue 2012		X
Wehling 2016	X	
Zarowitz 2012		X
Zermansky 2006		X

Appendix 6: Additional References of Potential Interest

Deprescribing guidelines

Bjerre LM, Farrell B, Hogel M, et al. Deprescribing antipsychotics for behavioural and psychological symptoms of dementia and insomnia: evidence-based clinical practice guideline. *Can Family Physician.* 2018;64(1):17-27.
PubMed: PM29358245

2019 Beers criteria updated by the American Geriatrics Society

American Geriatrics Society Beers Criteria® Update Expert P, Fick DM, Semla TP, et al. American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2019;67(4):674-694.
PubMed: PM 30693946