

Pharmacists and Medication Regimen Complexity

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Medication regimen complexity (MRC) may influence health outcomes, such as hospitalisation, hospital readmission and medication adherence. Pharmacists have been referred to as health professionals with the opportunity to act on MRC reduction.

Keywords: older adults ; medication regimen complexity ; pharmacist ; systematic review

1. Introduction

Nowadays the world faces global ageing, often associated with a high prevalence of multimorbidities. As a natural consequence, older age frequently stands out for polypharmacy and complex medication regimens ^{[1][2][3]}. When considering medication regimen complexity (MRC), there is so far no clear definition for it ^{[4][5]}. However, it has already been shown that the number of drugs is only one of the relevant factors to consider, and that, in addition, dosage form, dosage frequency and administration instructions also have to be considered ^{[6][7][8][9][10][11][12][13][14]}. Furthermore, there is also no agreement about the reference instrument for MRC determination ^{[4][5]}. Several tools have been used, with the 65-item medication regimen complexity index (MRCI), developed by George et al. ^[15], being the most common, reliable and validated tool for this purpose, which has already been translated and validated to a few languages ^{[16][17][18]} and even standardised for older adults in primary care ^[19]. It is an open-ended index, with higher total MRCI scores representing more complex medication regimens.

Interest in this subject has grown because numerous studies have associated high MRC with non-adherence ^{[4][20][21]}, higher hospitalisation rates ^[20], hospital discharge destination different than home ^[22] and low overall quality of life ^[23]. Indeed, medication management may frequently be demanding for the older population, their caregivers and healthcare professionals. In fact, older adults often present reduced manual dexterity in addition to cognitive and sensory impairment that can lead to a higher risk of medication errors and drug-related problems (DRPs) ^{[2][3][5][7][8]}. In order to reduce these negative aspects, it seems imperative to attempt medication regimen simplifications in many circumstances. Some research has already investigated its feasibility, with evidence suggesting that complexity can be reduced, and referring to pharmacists as healthcare professionals with a great potential to perform it in routine pharmaceutical dispensing or as part of medication reviews ^{[2][9][11][13][14]}. Indeed, pharmacists have a privileged access to the population's medication, both in community pharmacies and hospital settings, and awareness of this topic is needed, especially in the older population, for whom managing their daily medication may often represent a considerable challenge.

Up to the present date, to the best of our knowledge, there are no systematic reviews available about the role that pharmacists play in the older population's MRC and the effort made to simplify it. To address this gap, this study aimed to examine and describe pharmacists' role in studies on older adults' MRC.

2. Pharmacists' Role in Older Adults' Medication Regimen Complexity

Three recent systematic reviews focused on MRC: Wimmer et al. ^[20] reviewed the association of clinical outcomes with MRC in older people, Pantuzzo et al. ^[4] investigated the association between MRC and pharmacotherapy adherence and Alves-Conceição et al. ^[24] identified health outcomes related to MRC measured by MRCI.

2.1. Medication Regimen Complexity Assessment

At first, it is essential to mention the heterogeneity of instruments used to assess MRC. Several instruments were used in the different studies, including the medication complexity index (MCI) ^[25], which failed to show satisfactory reliability with complex regimens, and did not demonstrate any significant correlation with outcomes such as medication adherence ^{[15][26]}. However, most studies already use the MRCI, which already shows good evidence of classifying complexity better than a simple medication count ^[6], discriminating between regimens with an equal number of medications, resulting in

higher complexity scores for regimens with fewer drugs ^[15] and being a better overall predictor of all-cause mortality ^[27] and discharge destination ^[22] than polypharmacy. Additionally, in a few studies, the MRCI has been regarded as beneficial in targeting patients who may benefit from additional services such as domiciliary reviews and medication therapy management (MTM) services ^{[14][15][28]}. These strengths of the MRCI over other instruments should be taken into account in future investigations, especially regarding the importance of using a universal tool for MRC determination.

A greater consensus should also be achieved about the type of medication included to determine regimen complexity, which varied from prescription to non-prescription; long-term, short-term and “when required” as well as routine chronic medication. Even concerning the MRCI, there is no uniformity in the medications to be included. Although the instrument was initially developed and validated only for prescribed medications ^[15], several studies already indicate that prescription and non-prescription medications contribute to regimen complexity and should be considered ^{[14][20][22][29][28][30]}. However, even in that case, there is still no harmony in the practical applicability of the instrument: some authors ^{[22][29]} use the original MRCI, while Linnebur et al. ^[31] use the pMRCI. This aspect may be relevant to set high and low complexity scores, which has not yet been achieved despite some research in that area ^[9].

2.2. Measured Outcomes

Regarding the overall measured outcomes, in pharmacy practice research, the Economic, Clinical and Humanistic Outcomes (ECHO) model should be followed, with clinically meaningful outcomes being the most desirable ^{[32][33]}. However, in the present review none of the included studies present their results entirely according to this recommendation. Despite that, most of the reported results were related to the type of regimen simplification and its feasibility, reasons for non-implementation, change in the MRCI, the effect of recommendations as well as knowledge and preference of patients, which are endpoints whose relation to better patient outcomes are unknown ^[33]. Collection and further publication of relevant outcomes should be considered in future research.

2.3. Study Setting

In contrast with what was expected, most of the included studies were conducted in hospitals or clinics, but none in community pharmacies. This can reflect different factors: on the one hand there may exist an underreporting of provided pharmaceutical services, while on the other hand, it is also possible that still little attention has been given to this subject, even though several studies already state that the MRCI may be a valuable tool to prioritise patients who could take advantage of medication reviews or drug therapy management services ^{[14][15][28]}. At that time, MRC determination tools can be included, side by side with those that identify potentially inappropriate medications (PIMs), such as Beers ^[34] and STOPP criteria ^[35], as starting points for medication reduction, which are already an onset for regimen simplification. The frequently polymedicated older population may benefit most from this proximity, as the study findings show that overcomplexity is frequent among seniors ^[36] and that regimen complexities are higher in older adults with worse socio-economic and health conditions ^[25]. Additionally, insufficient pharmacotherapy understanding was high, especially among older adults with low levels of education and dependency on medication use ^[37]. These findings reinforce the need for pharmacists' intervention regarding older peoples' medication.

2.4. Pharmacists' Role

Only four ^{[12][38][39][40]} of the 17 included studies mention pharmacists' intervention: two studies focused directly on regimen complexity simplification while the other focused on MHRPS, with MRC being one of the variables. Elliot ^[38] demonstrated that a clinical pharmacist's simplification of older inpatients' medication is feasible when previous training about simplification is provided. In addition, Elliot et al. ^[12] concluded that after an educational intervention, a pharmacist-led medication review reduced the impact of hospitalisation on the complexity of older patients' medication regimens. Furthermore, Moczygamba et al. ^[39] obtained results that show that a telephone MTM telephone program from a pharmacist reduced MHRPs. Finally, Pouranayatihosseiniabad et al. ^[40] concluded that pharmacists could use the MRCI to identify older adults with complex medication regimens, but they failed to show significant benefits of RMMRs in reducing MRC. However, other of the included studies refer to pharmacists' potential role in MRC: Elliot et al. ^[8] concluded that “most regimens had potential to be simplified by a clinical pharmacist review”; Lakey et al. ^[41] mentioned that “Educational strategies are needed to increase awareness of the pharmacist's role in facilitating medication management and the option of simplifying complex regimens” (p. 1011); Lindquist et al. ^[36] stated that “health care professionals need to be aware of how patients are taking their medications. ... another option would be to partner with pharmacists in reducing medication regimen complexity” (p.96); and Linnebur et al. ^[31] indicated that “our results suggest a need for pharmacist review of the patient's entire medication regimen ... to assess and reduce complexity to a manageable level for the patient if possible” (p. 1545).

One aspect that has to be mentioned under this topic is that the included studies were performed in many countries, where factors like national policies and culture may influence the recognition of pharmacists as a trusted profession in the community and for other health care providers, and therefore may be responsible for the differences observed in pharmacists' roles [42]. This fact may explain why Australia and the USA were the most representative countries in this review, with three of the four studies mentioning pharmacists' intervention being performed in Australia [12][38][40].

Given all the above, the present review highlights that the pharmacist's active role in improving MRC in the older population has been minimal. Nevertheless, the little evidence where pharmacists had an active role showed that medication regimen simplifications are feasible and emphasise the pharmacist's role to achieve them. However, it is also essential to bear in mind that several studies point out that previous educational sessions for pharmacists are necessary to raise awareness of this topic and give them the skills and practice to minimise regimen complexities [12][38][41]. Even so, a vital opponent to achieve regimen simplification in daily practice seems to be the lack of time of healthcare professionals [12][38]. Having this in mind, pharmacists can, however, take regimen simplifications into account in a more general way whenever they perform OTC advice in their daily routine, and more carefully when performing medication review services.

At last, one of the biggest challenges seems to be multidisciplinary collaboration. Among the findings of the studies, non-acceptance of recommendations by the prescribers is mentioned as one of the most common reasons for noncompliance with suggested regimen changes. As difficulties in the relationship between pharmacists/physicians are well known, we think it is also imperative to sensitise physicians to this subject and make clear that the ultimate goal of this collaboration is health gain, including optimising patients' health care.

Based on the present review findings, it seems that, until now, pharmacists have not played a relevant role in older people's MRC. For this reason, future high-quality research should focus on this subject, and in particular should include community pharmacists' interventions and the resulting possible benefits, not only for patients, e.g., in terms of safety, clinical outcomes and quality of life, but also for the healthcare system, in particular in terms of cost reductions.

3. Conclusions

Old age is often synonymous with multiple comorbidities and consequently polypharmacy and complex medication regimens. As the latter has been associated with several negative outcomes, particularly in the older population, an effort should be made to reduce MRC whenever possible. Pharmacists may play a relevant role at this point after previous training, which has, however, been underexplored. There is almost no research on pharmacists' intervention on older people's MRC; that which does exist is of moderate quality. This aspect leaves an open door for future high-quality evidence investigations on pharmacists' interventions and their relation to better outcomes. Therefore, pharmacists should be provided with the necessary skills, either during graduation or in post-graduate education and training programs, and encouraged to assess the possibility of simplifying the medication regimen in their daily routine or even on a service-based remuneration model.

References

1. World Health Organization. World Report on Ageing and Health; World Health Organization Press: Geneva, Switzerland, 2015.
2. Advinha, A.M.; De Oliveira-Martins, S.; Mateus, V.; Pajote, S.G.; Lopes, M.J. Medication regimen complexity in institutionalized elderly people in an aging society. *Int. J. Clin. Pharm.* 2014, 36, 750–756.
3. Silva, C.; Ramalho, C.; Luz, I.; Monteiro, J.; Fresco, P. Drug-related problems in institutionalized, polymedicated elderly patients: Opportunities for pharmacist intervention. *Int. J. Clin. Pharm.* 2015, 37, 327–334.
4. Pantuzza, L.L.N.; Ceccato, M.D.G.B.; Silveira, M.R.; Junqueira, L.M.R.; Reis, A. Association between medication regimen complexity and pharmacotherapy adherence: A systematic review. *Eur. J. Clin. Pharmacol.* 2017, 73, 1475–1489.
5. Paquin, A.M.; Zimmerman, K.M.; Kostas, T.R.; Pelletier, L.; Hwang, A.; Simone, M.; Skarf, L.M.; Rudolph, J.L. Complexity perplexity: A systematic review to describe the measurement of medication regimen complexity. *Expert Opin. Drug Saf.* 2013, 12, 829–840.
6. Advinha, A.M.; Lopes, M.; De Oliveira-Martins, S. Assessment of the elderly's functional ability to manage their medication: A systematic literature review. *Int. J. Clin. Pharm.* 2016, 39, 1–15.

7. Wimmer, B.C.; Johnell, K.; Fastbom, J.; Wiese, M.; Bell, J.S. Factors associated with medication regimen complexity in older people: A cross-sectional population-based study. *Eur. J. Clin. Pharmacol.* 2015, 71, 1099–1108.
8. Herson, M.; Bell, J.; Tan, E.; Emery, T.; Robson, L.; Wimmer, B. Factors associated with medication regimen complexity in residents of long-term care facilities. *Eur. Geriatr. Med.* 2015, 6, 561–564.
9. Ferreira, J.M.; Galato, D.; Melo, A.C. Medication regimen complexity in adults and the elderly in a primary healthcare setting: Determination of high and low complexities. *Pharm. Pr.* 2015, 13, 659.
10. Elliott, R.A.; O'Callaghan, C.J. Impact of Hospitalisation on the Complexity of Older Patients' Medication Regimens and Potential for Regimen Simplification. *J. Pharm. Pr. Res.* 2011, 41, 21–25.
11. Witticke, D.; Seidling, H.M.; Lohmann, K.; Send, A.F.J.; Haefeli, W.E. Opportunities to Reduce Medication Regimen Complexity: A retrospective analysis of patients discharged from a university hospital in Germany. *Drug Saf.* 2012, 36, 31–41.
12. Elliott, R.A.; O'Callaghan, C.; Paul, E.; George, J. Impact of an intervention to reduce medication regimen complexity for older hospital inpatients. *Int. J. Clin. Pharm.* 2013, 35, 217–224.
13. Stange, D.; Kriston, L.; Von-Wolff, A.; Baehr, M.; Dartsch, D.C. Reducing Cardiovascular Medication Complexity in a German University Hospital: Effects of a Structured Pharmaceutical Management Intervention on Adherence. *J. Manag. Care Pharm.* 2013, 19, 396–407.
14. Rettig, S.M.; Wood, Y.; Hirsch, J.D. Medication regimen complexity in patients with uncontrolled hypertension and/or diabetes. *J. Am. Pharm. Assoc.* 2013, 53, 427–431.
15. George, J.; Phun, Y.-T.; Bailey, M.J.; Kong, D.C.; Stewart, K. Development and Validation of the Medication Regimen Complexity Index. *Ann. Pharmacother.* 2004, 38, 1369–1376.
16. Melchior, A.C.; Correr, C.J.; Fernandez-Llimos, F. Tradução e validação para o português do Medication Regimen Complexity Index. *Arq. Bras. Cardiol.* 2007, 89, 210–218.
17. Stange, D.; Kriston, L.; Langebrake, C.; Cameron, L.K.; Wollacott, J.D.; Baehr, M.; Dartsch, D.C. Development and psychometric evaluation of the German version of the Medication Regimen Complexity Index (MRCI-D). *J. Eval. Clin. Pr.* 2011, 18, 515–522.
18. De La Fuente, J.S.; Díaz, A.S.; Cañamares, I.; Ramila, E.; Izquierdo-Garcia, E.; Esteban, C.; Escobar-Rodríguez, I. Cross-cultural Adaptation and Validation of the Medication Regimen Complexity Index Adapted to Spanish. *Ann. Pharmacother.* 2016, 50, 918–925.
19. Pantuzza, L.L.N.; Ceccato, M.D.G.B.; Silveira, M.R.; Pinto, I.V.; Reis, A. Validation and standardization of the Brazilian version of the Medication Regimen Complexity Index for older adults in primary care. *Geriatr. Gerontol. Int.* 2018, 18, 853–859.
20. Wimmer, B.C.; Cross, A.J.; Jokanovic, N.; Wiese, M.; George, J.; Johnell, K.; Diug, B.; Bell, J.S. Clinical Outcomes Associated with Medication Regimen Complexity in Older People: A Systematic Review. *J. Am. Geriatr. Soc.* 2016, 65, 747–753.
21. De Vries, S.T.; Keers, J.C.; Visser, R.; De Zeeuw, D.; Haaijer-Ruskamp, F.M.; Voorham, J.; Denig, P. Medication beliefs, treatment complexity, and non-adherence to different drug classes in patients with type 2 diabetes. *J. Psychosom. Res.* 2014, 76, 134–138.
22. Wimmer, B.C.; Dent, E.; Visvanathan, R.; Wiese, M.; Johnell, K.; Chapman, I.; Bell, J.S. Polypharmacy and Medication Regimen Complexity as Factors Associated with Hospital Discharge Destination Among Older People: A Prospective Cohort Study. *Drugs Aging* 2014, 31, 623–630.
23. Fröhlich, S.E.; Zaccolo, A.V.; Da Silva, S.L.C.; Mengue, S.S. Association between drug prescribing and quality of life in primary care. *Pharm. World Sci.* 2010, 32, 744–751.
24. Alves-Conceição, V.; Rocha, K.S.S.; Silva, F.V.N.; Silva, R.O.S.; Da Silva, D.T.; De Lyra, D.P., Jr. Medication Regimen Complexity Measured by MRCI: A Systematic Review to Identify Health Outcomes. *Ann. Pharmacother.* 2018, 52, 1117–1134.
25. Acurcio, F.A.; Silva, A.L.; Ribeiro, A.Q.; Rocha, N.P.; Silveira, M.R.; Klein, C.H.; Rozenfeld, S. Complexidade do regime terapêutico prescrito para idosos. *Rev. Assoc. Med. Bras.* 2009, 55, 468–474.
26. Conn, V.S.; Taylor, S.G.; Kelley, S. Medication Regimen Complexity and Adherence Among Older Adults. *Image J. Nurs. Sch.* 1991, 23, 231–236.
27. Wimmer, B.C.; Bell, J.S.; Fastbom, J.; Wiese, M.; Johnell, K. Medication Regimen Complexity and Polypharmacy as Factors Associated With All-Cause Mortality in Older People: A population-based cohort study. *Ann. Pharmacother.* 2015, 50, 89–95.

28. Hirsch, J.D.; Metz, K.R.; Hosokawa, P.W.; Libby, A. Validation of a Patient-Level Medication Regimen Complexity Index as a Possible Tool to Identify Patients for Medication Therapy Management Intervention. *Pharmacother. J. Hum. Pharmacol. Drug Ther.* 2014, 34, 826–835.
29. Wimmer, B.C.; Dent, E.; Bell, J.S.; Wiese, M.D.; Chapman, I.; Johnell, K.; Visvanathan, R. Medication Regimen Complexity and Unplanned Hospital Readmissions in Older People. *Ann. Pharmacother.* 2014, 48, 1120–1128.
30. Libby, A.M.; Fish, D.N.; Hosokawa, P.W.; Linnebur, S.A.; Metz, K.R.; Nair, K.V.; Saseen, J.; Griend, J.P.V.; Vu, S.P.; Hirsch, J.D. Patient-Level Medication Regimen Complexity Across Populations With Chronic Disease. *Clin. Ther.* 2013, 35, 385–398.
31. Linnebur, S.A.; Griend, J.P.V.; Metz, K.R.; Hosokawa, P.W.; Hirsch, J.D.; Libby, A.M. Patient-level Medication Regimen Complexity in Older Adults with Depression. *Clin. Ther.* 2014, 36, 1538–1546.e1.
32. Kozma, C.M.; Reeder, C.E.; Schultz, R.M. Economic, clinical, and humanistic outcomes: A planning model for pharmaco-economic research. *Clin. Ther.* 1993, 15, 1121–1132.
33. Charrois, T.L.; Durec, T.; Tsuyuki, R.T. Systematic Reviews of Pharmacy Practice Research: Methodologic Issues in Searching, Evaluating, Interpreting, and Disseminating Results. *Ann. Pharmacother.* 2009, 43, 118–122.
34. American Geriatrics Society. American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J. Am. Geriatr. Soc.* 2019, 67, 674–694.
35. O'Mahony, D.; O'Sullivan, D.; Byrne, S.; O'Connor, M.N.; Ryan, C.; Gallagher, P. STOPP/START criteria for potentially inappropriate prescribing in older people: Version 2. *Age Ageing* 2014, 44, 213–218.
36. Lindquist, L.A.; Lindquist, L.M.; Zickuhr, L.; Friesema, E.; Wolf, M.S. Unnecessary complexity of home medication regimens among seniors. *Patient Educ. Couns.* 2014, 96, 93–97.
37. Pinto, I.V.L.; Reis, A.; Almeida-Brasil, C.C.; Da Silveira, M.R.; Lima, M.G.; Ceccato, M.D.G.B. Avaliação da compreensão da farmacoterapia entre idosos atendidos na Atenção Primária à Saúde de Belo Horizonte, MG, Brasil. *Cien. Saude Colet.* 2016, 21, 3469–3481.
38. Elliott, R.A. Reducing medication regimen complexity for older patients prior to discharge from hospital: Feasibility and barriers. *J. Clin. Pharm. Ther.* 2012, 37, 637–642.
39. Moczygamba, L.R.; Barner, J.C.; Gabrillo, E.R. Outcomes of a Medicare Part D telephone medication therapy management program. *J. Am. Pharm. Assoc.* 2012, 52, e144–e152.
40. Pouranayati Hosseinabad, M.; Zaidi, S.T.R.; Peterson, G.; Nishtala, P.S.; Hannan, P.; Castelino, R. The impact of residential medication management reviews (RMMRs) on medication regimen complexity. *Postgrad. Med.* 2018, 130, 575–579.
41. Lakey, S.L.; Gray, S.L.; Borson, S. Assessment of Older Adults' Knowledge of and Preferences for Medication Management Tools and Support Systems. *Ann. Pharmacother.* 2009, 43, 1011–1019.
42. Anderson, S. The state of the world's pharmacy: A portrait of the pharmacy profession. *J. Interprofessional Care* 2002, 16, 391–404.