

WHEN LESS IS MORE: THE ROLE OF DEPRESCRIBING IN THE ELDERLY - A NARRATIVE REVIEW OF THE EVIDENCE

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Abstract

The aging population is associated with an increase in elderly individuals with multimorbidity and the consequent polypharmacy. While appropriate in some cases, this often leads to the prescription of potentially inappropriate medications. Older individuals are more susceptible to adverse events due to pharmacodynamic and pharmacokinetic changes resulting from physiological alterations typical of aging, which interfere with drug metabolism.

The aging process is complex, associated with multimorbidity, geriatric syndromes, functional and/or cognitive deficits, and, consequently, limited life expectancy. Currently, about 40% of the elderly are polymedicated. Deprescribing is an active process of

reviewing all of a patient's medications, performed by a physician, based on a risk/benefit assessment. Polypharmacy is associated with an increased risk of mortality, falls, drug interactions, and hospitalizations. The deprescribing process can lead to a reduction of about 39% in chronic medication, resulting in increased therapeutic adherence to the remaining drugs. Deprescribing is a fundamental pillar of person-centred care, and the population should be aware of its importance.

A classic review was conducted through bibliographic research of systematic reviews on Medline. This narrative review aimed to address polypharmacy and its prevalence in the elderly population, evaluate the benefits and risks of deprescribing, and identify barriers and facilitating factors in the deprescribing process.

Keywords: elderly; geriatrics; polypharmacy; deprescribing; narrative review.

Introduction

One of the biggest achievements of mankind during the last century was the increase in average life expectancy. Along with this increase, changes in the demographic pyramid occurred. This is driven mainly by a decline in fertility and mortality rates but also due to advances in public health, technology, and medicine. (Midão et al., 2018) Portugal is one of the most rapidly aging countries in the world: in 2019, 22.1% of the population was aged 65 and over. (Pereira et al., 2023)

An average European's life expectancy at birth is 80.1 years according to the 2021 statistics by Europe's official database Eurostat, with Spain being the leading country with an average life expectancy of 85,4 years. Portugal ranks 10 places behind, in 11th position, with an average life expectancy of 81.5 years. (Eurostat, 2023)

The aging process combined with the increase in life expectancy leads to higher prevalence of multimorbidity worldwide (Atella et al., 2019). Indeed, the presence of multimorbidity (defined by two or more chronic diseases) reaches approximately 40% for individuals aged 65 or more years, (Midão et al., 2018), and this prevalence is even higher with increasing age, according to (D. O'Mahony et al., 2016), currently and worldwide, 81.5% of people over 85 years of age experience multimorbidity. The presence of multiple chronic diseases, with consequent drug consumption and the risk of polypharmacy (Villén et al., 2020), makes the therapeutics difficult not only for the

patient but also for the healthcare professional. (Maher et al., 2014) To this challenge, other variables are added that contribute to the complexity of the aging process (Aging Biomarker Consortium et al., 2023), such as the presence of geriatric syndromes, functional and cognitive deficits, and limited life expectancy. (Inouye et al., 2007; Onder et al., 2011)

Quality of life is a crucial component for successful aging because low quality of life during aging is associated with low activity and physical capacity, increased chronic diseases and social isolation. (Wahrendorf & Siegrist, 2010; Wikman et al., 2011) According to (Midão et al., 2018), quality of life and well-being can be a predictor of polypharmacy, whereas lower rates of quality of life and well-being are associated with higher use of medications.

The World Health Organization (WHO) defines polypharmacy as “the administration of many drugs at the same time or the administration of an excessive number of drugs”. (WHO, 2019) While there is no consensus on the medication threshold and means of measurement, polypharmacy is often commonly defined as concomitant use of 5 or more medications. (Delara et al., 2022) Prescribing multiple medications is often clinically required (appropriate polypharmacy). However, exposure to multiple medicines may lead to harm or the ongoing use of medications no longer indicated (inappropriate polypharmacy). (Davies et al., 2020; Masnoon et al., 2017) Inappropriate polypharmacy, besides increasing health care costs, is associated with various negative health outcomes, including falls, adverse drug-related events (ADRs), decreased therapeutic adherence, decline in physical and cognitive function, frailty, and mortality (Dhalwani et al., 2017; Gnjidic et al., 2012; Maher et al., 2014; Pereira et al., 2023)

Thus, the objectives of this narrative review are to address polypharmacy and its prevalence in the elderly population, evaluate the benefits and risks of deprescribing, and identify barriers and facilitating factors in the deprescribing process.

Methods

We conducted a narrative review based on a literature search undertaken from September 2023 to February 2024. We searched Medline for English, Portuguese and Spanish-language systematic reviews published from January 1, 2019, to September 1, 2023. Our search strategy included the following query: “polypharmacy AND prevalence AND elderly” and

“deprescribing AND elderly”. We reviewed all titles and abstracts for relevance to determine articles for full-text review and excluded those who pertained to a specific condition or pathology, addressed the deprescribing of a particular pharmaceutical, or focused on a specific geographical area. Reference management and citation screening were performed using Zotero®.

Results

Polypharmacy and its prevalence among the elderly demographic

A total of 51 articles were identified in the Medline database (search through PubMed). Using a two-step process for study selection we screened each citation’s title and abstract to determine whether a study met the inclusion criteria, with 46 articles being excluded, based on the previously established inclusion and exclusion criteria. The complete manuscripts of all five potentially relevant articles were obtained for final evaluation, among which only Delara et al., 2022, provided a response to our research objective. The last 4 excluded articles were: (Katsimpris et al., 2019; Kok et al., 2022; Li et al., 2022; Zhou et al., 2023).

According to (Delara et al., 2022) the pooled estimated prevalence of polypharmacy was 37% (95% CI: 31 - 43%), and the subgroup analysis by age indicated that studies with a population age of ≥ 65 years were associated with a higher prevalence of polypharmacy 45% (95% CI: 37 to 54%) when compared to studies with population age of < 65 years (25, 95% CI: 15 - 35%, $P < 0.01$). The heterogeneity between the included studies was determined using the I-squared statistic: $I^2 = 100\%$.

Deprescribing and its application in the elderly population

We located a total of 56 articles in the Medline database (search through PubMed), and after screening each one’s title and abstract excluded 46 articles based on the previously established inclusion and exclusion criteria. The complete manuscripts of all 15 potentially relevant articles were obtained for final evaluation, among which 12 provided a response to our research objective (table 1), with (Ali et al., 2020; Mejías-Trueba et al., 2022; Nizet et al., 2023) being excluded.

Table 1

Systematic reviews (SRs) published about deprescribing in older patients from January 1, 2019, to September 1, 2023.

Theme within deprescribing continuum	References	Key points
Improve clinical outcome indicators for older adults	(Zhou et al., 2023)	Reduced proportions of adverse drug reactions, potentially inappropriate medication, and potentially prescription omission.
	(Omuya et al., 2023)	The reduction in patient-centred outcomes such as morbidity, mortality, patient satisfaction, and utilisation were found to be inconsistent, but the majority of studies concluded that interventions either had no significant effect or an uncertain impact. Two SRs assessing medication appropriateness found very low-quality evidence of modest improvements with polypharmacy interventions.
	(Ali et al., 2020)	Polypharmacy interventions have positive and clinically important effects on mobility outcomes demonstrated by falls incidence reductions. There is limited evidence for effects on activities of daily living or falls related mortality.
	(Pruskowski et al., 2019)	Randomized controlled trial (RCT) primary outcomes found deprescribing is safe and reduces drug number or dose. Only five RCTs found a significant deprescribing impact on health-related quality of life, cost or hospitalization.
	(Anderson et al., 2019)	Recent and high-quality SRs found evidence that polypharmacy interventions improved medication appropriateness. However, there was no consistent evidence of any impact on downstream patient-centred outcomes such as healthcare utilization, morbidity, or mortality.
Barriers to deprescribing	(Bolt et al., 2023)	Four barriers were identified: favourable perceptions of medications, fear of medication discontinuation, the complexity of the healthcare system and discouragement from healthcare professionals. Health system complexity and direct discouragement from healthcare providers were barriers uniquely identified in the older adult population.
	(M. S. O'Mahony & Parbhoo, 2020)	Conversations with individuals around rationalising treatments are time consuming and complex. They often involve families or carers, and require an understanding of the conditions being managed, and expected prognosis. Current 10-minute GP appointments do not facilitate such discussions. Delays and miscommunications between secondary and primary care may cause unintended continuation of medicines. Being unable to see the same doctor consistently can be a further barrier to building trust. It can be challenging for a generalist to discontinue medicines started by a specialist.
Attitudes Towards Deprescribing	(Oktora et al., 2022)	Populations from low-middle-income countries were less willing to stop medication than those from high-income countries. The highest average willingness scores were seen in inpatient settings. At population level, a higher average age was associated with a higher willingness but usually no associations with age were observed at individual level.
	(Weir et al., 2022)	Overall, many participants were willing to have a medication deprescribed if their doctor said it was possible (84%, 95% CI 81%–88%). Caregiver data provided a similar result, 80% (95% CI 74%–86%). However, there was significant heterogeneity ($I^2 = 95\%$ patients, 77% for carers) and no explanation for this was identified through the subgroup analyses. Consumers reported willingness to have a medication deprescribed although results should be interpreted with caution due to heterogeneity.

(Seewoodharry et al., 2022)

Most older adults and their caregivers were willing to have medication deprescribed if told to do so by a healthcare professional. Other factors that increased willingness to deprescribing included trust in the health care professional, side effects and inconvenience from medications as well as the prospect of follow-up and monitoring during deprescribing. In contrast, perceived effectiveness, unawareness of lack of benefit, negative expectations of ageing and fear were factors preventing deprescribing.

(Chock et al., 2021)

Overall, 87.6% (95% CI: 83.3 to 91.4%) patients were willing to deprescribe their medication, based upon the doctors' suggestions. This was lower among caregivers, with only 74.8% (49.8% to 93.8%) willing to deprescribe their care recipients' medications. Patients' or caregivers' willingness to deprescribe were not influenced by study location, study population, or the number of medications they took. Most patients and their caregivers were willing to deprescribe their medications, whenever possible and thus should be offered a trial of deprescribing. Nevertheless, as these tools have a poor predictive ability, patients and their caregivers should be engaged during the deprescribing process to ensure that the values and opinions are heard, which would ultimately improve patient safety.

Discussion

Our review indicates that polypharmacy is common with an estimated prevalence of 37%, and in the subgroup of population with ≥ 65 years the prevalence rises to 45%. However, the prevalence estimates in (Delara et al., 2022) were based mainly on dispensing data and adherence to prescribed medications was not available in the studies included by these authors. Besides, the included studies did not use a homogenous study populations or polypharmacy definition which contributed to variability observed across studies. Therefore, this meta-analysis does not allow us to draw conclusions, due to the high heterogeneity of the study ($I^2 = 100\%$).

There is large diversity in the definition of polypharmacy; ranging from numerical counts only, numerical counts for a given duration of therapy or setting or descriptive, which included terms such as minor, moderate, major, and excessive polypharmacy. While (Delara et al., 2022) did not observe any difference in the estimated prevalence of polypharmacy using continuous or simultaneous approaches to defining polypharmacy, the lack of a clear and universal definition of polypharmacy as well as terms such as minor, moderate and major polypharmacy makes it challenging for healthcare professionals to assess and consider efficacy and safety issues within the clinical setting. (Masnoon et al., 2017; Monégat, 2014)

It is our view that it would be important for organisations to reach a consensus on this matter so that in the future, the aggregation of results might be facilitated, thereby enabling more reliable scientific evidence.

Additionally, we have decided to limit our search to systematic reviews, since they are the studies with a higher level of evidence. This search strategy, however, reduced the number of articles found (only one for our first objective) and may be considered a limitation of this review.

The word “deprescribing” first appeared in the literature only 11 years ago, in 2003, (Woodward, 2003), with the World Health Organization considering today that the process should be as robust as that of prescribing, with considerations for cessation of medication being an important part of all medication reviews. (WHO, 2019). Theoretical benefits to patients and healthcare systems include reduced ADRs (Garfinkel, 2018

Garfinkel & Mangin, 2010; Iyer et al., 2008; Johansson et al., 2016; Page et al., 2016; Reeve et al., 2014), with (Gurwitz et al., 2000) saying that 51% of the reported ADRs were presumable preventable, improved medication adherence (Reeve & Wiese, 2014) and cost savings (Garfinkel et al., 2007; Thompson et al., 2016).

Also, potentially inappropriate medication (PIM), defined as drugs that are ineffective or with a poor benefit/risk ratio, (American Geriatrics Society Beers Criteria® Update Expert Panel, 2023) should be a concern when it comes to polypharmacy in the elderly, (Khezrian et al., 2020; Santana et al., 2016; Simões et al., 2019; Zechmann et al., 2019). Our findings align with and support some of these data, with (Zhou et al., 2023) demonstrating a degree of efficacy in reducing the occurrence of ADRs and PIM, and (Anderson et al., 2019) showing that polypharmacy interventions improved medication appropriateness. Thus, the implementation of simple and effective action projects for drug therapy management is essential to avoid ADRs and control PIM prescription, and thereby improve older adults' life quality (Lenander et al., 2018; Mekdad & Alsayed, 2019)

Concerning patient-centred outcomes, such as morbidity, mortality, healthcare utilization and patient satisfaction, the data were found to be inconsistent, with interventions either having no significant effect or an uncertain impact by (Omuya et al., 2023) and (Anderson et al., 2019). On the other hand, (Ali et al., 2020) showed positive and clinically important effects on mobility outcomes demonstrated by falls incidence reductions while (Pruskowski et al., 2019) found that not only deprescribing is safe but also that it may have a significant deprescribing impact on health-related quality of life, cost or hospitalization.

To date, most clinical studies have failed to consistently demonstrate an effect of deprescribing interventions on clinical outcomes such as hospitalization, cognitive and physical function decline. This is partly because most deprescribing studies have relatively small sample sizes and have residual confounding by factors that are not accounted for in the analysis. (Wu et al., 2021)

Our research demonstrates considerable attention towards interventions designed to optimize polypharmacy, with the existing literature exploring an extensive range of patient outcomes, but the benefits and sustainability of these interventions on long-term quality of life, morbidity and geriatric outcomes remain unclear. (Wu et al., 2021)

It could be argued that establishing a solid benefit (e.g. reduction in mortality) of deprescribing is not necessary. If an intervention enables identification and withdrawal or dose reduction of medications deemed to be inappropriate in the individual, without worsening in outcomes, then this should be seen as a benefit itself. (Reeve et al., 2017) Further high-quality studies are needed to assess the impact of efforts of reduce polypharmacy on patient care, especially among older adults.

In addition to the unclear benefits, there are also numerous barriers to this process. (Bolt et al., 2023) identified four main barriers, such as favourable perceptions of medications, fear of medication discontinuation, the complexity of the healthcare system and discouragement from healthcare professionals. (M. S. O'Mahony & Parbhoo, 2020) similarly assert that the process is complex and time-consuming, involving family members and carers, and requires an understanding of the conditions being managed and expected prognosis.

Patient education and improvement in health literacy are potential strategies to help patient develop realistic expectations about their health treatment, and these strategies are likely to be more effective if delivered using a patient-centred approach. (Wu et al., 2021) Shared, informed decision making is central to delivering patient-centred care and can be an effective method of reaching agreement in regard to treatment of chronic illness. (Reeve et al., 2017) According to (Jansen et al., 2016) the process of deprescribing begin with creating awareness that options exist and exploring patient preferences for the different options. It is important that treating physicians understand patient's preferences and goals of care, and how they can contribute to improving clinical outcomes through goal-directed medication reviews. (Wu et al., 2021)

(M. S. O'Mahony & Parbhoo, 2020) also advise of delays and miscommunications between secondary and primary care, which can lead to the unintended continuation of medications. Taking patient-, provider-, and system-level factors into consideration is important given that patients frequently receive care from different providers and healthcare settings. (Zimmerman & Linsky, 2021) Researchers, healthcare professionals and policymakers have a great responsibility to promote quality use of medication in older people by overcoming these challenges. This will help deprescribing find its place in routine prescribing, under the umbrella of personalized medicine. (Wu et al., 2021) When it comes to facilitating factors in the deprescribing process the majority of the

SRs, (Chock et al., 2021; Seewoodharry et al., 2022; Weir et al., 2022) found that many participants (patients and carers) were willing to have a medication deprescribed if their doctor said it was possible. Meaning whenever possible should be offered a trial of deprescribing. (Chock et al., 2021). Other factors that increased willingness to deprescribing included trust in the health care professional, side effects and inconvenience from medications as well as the prospect of follow-up and monitoring during deprescribing. (Seewoodharry et al., 2022)

Older people's willingness to either tolerate polypharmacy or discontinue a medicine seems to be influenced by the communication skills, (Jansen et al., 2016), thereby making the language used by clinicians when starting a medicine very important. For example, if patients have been told that they would need the medicines for the "rest of their lives," discussion of possible discontinuation can make them anxious. (Linsky et al., 2015) This involves ensuring that the patient knows what options are available (including the option to continue medicines) and understands the process of deprescribing, the expected benefits and harms of each option, and how likely they are to occur. (Jansen et al., 2016)

Deciding whether to deprescribe requires integrating the patient's preferences and priorities with information on benefits and harms. Decisions may be made by the patient, made collaboratively, or deferred to the clinician. Algorithms exist to guide the process of deciding which medicines to stop first. (Declercq et al., 2013; Scott et al., 2015)

Both STOPP and Beers criteria are widely used worldwide, to define which medications to target, and although they do not provide a list of prohibited medications, they are an important tool for physicians due to their evidence-based rationale and constant updating. (Monteiro et al., 2019) The STOPP/START criteria (Screening Tool of Older Persons' Prescriptions—STOPP; Screening Tool to Alert to Right Treatment—START) were found to be significantly associated with detecting adverse events in acutely ill older people. (Monteiro et al., 2022) For this reason were translated and adapted from English into several languages such as Czech, French (Lang et al., 2015), Dutch (Knol et al., 2015), Italian, Spanish (Delgado Silveira et al., 2015), and Portuguese (Monteiro et al., 2022) to facilitate the local application of the criteria worldwide and have had a positive impact on patient evaluation.

Conclusions

There is large heterogeneity in the definition of polypharmacy and study populations, therefore, this review does not allow us to draw conclusions. It is our view that it would be important for organisations to reach a consensus on this matter so that in the future, the aggregation of results might be facilitated, thereby enabling more reliable scientific evidence.

While the data on the benefits is inconsistent, deprescribing appears to be safe. Nonetheless, its implementation encounters notable challenges. Future research should focus on refining this process, considering the increasing prevalence of multimorbidity and an ageing population.

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