The pharmacological deprescription in elderly patients

Chelsey Ali,[1] Daniel Huang,[1] Charlene Tugwete,[1] Stefano Del Canale,[2] Vittorio Maio[1,3]

[1]Jefferson College of Population Health, Thomas Jefferson University, Philadelphia, PA, USA; [2]Local Health Authority of Parma, Parma, Italy; [3]Asano-Gonnella Center for Research in Medical Education and Health Care, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA, USA

The demographic of individuals aged 65 and above represents one of the fastest-growing populations globally. As of 2020, there were 727 million individuals (9.3%) aged 65 years or older worldwide.[1] Projections indicate that the number of older adults will double to reach 1.5 billion (16%) by 2050.[1] At that point, 1 in 6 people globally will be over 65, and in Europe and North America, 1 in 4 individuals may fall into this age bracket.[2]

Italy, having one of the largest populations of older adults globally, had approximately 13.9 million individuals (23%) aged 65 and above in 2019. This figure is anticipated to rise to around 16.4 million (27.9%) by 2030.[3] In 2012, the public expenditure on pharmaceuticals in primary care exceeded 11 billion Euros (approximately 15.2 billion USD), with individuals aged 65 or older constituting over 60% of these costs.[4] This age group also accounts for 46% of inpatient admissions and 55% of associated costs.[5] Around half of Italy's older adult population had at least one severe chronic disease or had more than three chronic diseases in 2015.[6] Among those aged 80 years and above, an estimated 64% had more than three chronic diseases.[6]

Multi-morbid older adults, dealing with multiple health conditions, tend to possess a higher amount of prescribed medications. Polypharmacy, defined as the regular use of at least five medications, is notably prevalent among older adults.[7] This phenomenon arises from the necessity to address multiple morbidities associated with aging, including chronic conditions. Contributing factors to polypharmacy may extend to potential self-medication with nonprescription medications and a lack of coordination among various healthcare providers.[8]

While polypharmacy may be deemed necessary for managing multiple chronic conditions in the elderly, it concurrently introduces significant risks and challenges. The heightened incidence of adverse drug reactions and interactions associated with polypharmacy becomes particularly problematic in the elderly, given age-related alterations in drug metabolism and sensitivity. Moreover, the adoption of polypharmacy often results in intricate medication regimens, presenting a formidable challenge for elderly individuals to navigate effectively. This complexity raises the likelihood of medication errors and non-adherence.

Adding to the complexity, older adults are inherently predisposed to an increased risk of falls, cognitive impairment, frailty, and exhibit pharmacokinetic changes that amplify the potential for drug toxicity.[9] The repercussions of these complications are far-reaching, encompassing poor outcomes such as increased risk of morbidity, escalated healthcare spending due to increased hospitalizations, diminished quality of life, exacerbated mobility issues, and increased mortality rates.[7,10]

Regular, individualized care is a crucial component of managing polypharmacy to mitigate its inherent risks. This involves assessing the ongoing need for each medication, monitoring for side effects, adjusting the regimen as necessary, as well as discontinuing

Correspondence: Vittorio Maio, Jefferson College of Population Health, Thomas Jefferson University, 901 Walnut Street, 10th Floor, Philadelphia, PA 19107, USA.
Tel.: 2159551821.
Fax: 2159237583.
E-mail: vittorio.maio@jefferson.edu

Key words: polypharmacy management; deprescribing in elderly; medication optimization in older adults; care coordination; geriatric patient care.

Conflict of interest: the authors declare no potential conflict of interest.

Funding: none.

Received: 6 November 2023.
Accepted: 6 November 2023.

Italian Journal of Medicine 2023; 17:1676
doi:10.4081/itjm.2023.1676

those that may be causing harm or providing limited benefit. In this commentary, we will review the principles of the deprescribing process and define when deprescribing is deemed appropriate. We will also elaborate on the barriers that are currently impeding deprescribing and propose solutions for increasing the adoption of such processes.

The deprescribing process

Deprescribing is the process of identifying and discontinuing drugs for which the potential harms outweigh the existing benefits and is done under the supervision of a healthcare professional.[11,12] This entails a careful medication review by examining medication-related issues: unnecessary drug therapy, ineffective drug therapy, adverse drug reactions, and noncompliance.[13]

Deprescribing is a part of the prescribing process and should be considered at every patient encounter. A patient assessment should be done in which all drugs the patient is currently taking (including prescription, over-the-counter medications, supplements, herbals, and vitamins) and the reasons for taking each one are ascertained.[11] Additionally, the "prescribing cascade", often seen with older adults, occurs when an adverse drug event is misinterpreted as a new medical condition, leading to the addition of another, potentially avoidable, medication.[14] This could be avoided through consideration of patient-specific factors to determine the best course of therapy from all available options and examination of possible underlying causes of conditions.

A conceptual framework made by Bain *et al*. proposes that after the assessment, the prescriber will either initiate a new medication, change the current regimen, continue therapy, and/or discontinue a medication.[15] The four proposed steps of deprescribing include: i) recognizing an indication for discontinuing a medication; ii) identifying and prioritizing the medication(s) to be targeted for discontinuation; iii) discontinuing the medication along with proper planning, communicating, and coordinating with the patient and in concert with the care of other clinicians; iv) monitoring the patient closely for improvement or harmful effects.

Some indications for discontinuing a medication are increased risk of drug-induced harm including high-risk drugs in older adults, drug-drug interactions (DDIs) after a new medication or supplement is started, a new medication being initiated to substitute an old one, or that no clinically meaningful benefit was observed from the medication.[15] Thus, drugs for discontinuation should be prioritized by the highest benefit-harm ratio and lowest likelihood of adverse withdrawal reactions.[11] If multiple medications are considered, it is recommended that they be discontinued one by one so a withdrawal event can be easily traced to a single medication.[15]

When is deprescribing appropriate?

Several deprescribing algorithms offer valuable guidance for streamlining the process of reducing medication burden.[11,16] Notably, the Canadian Medication Appropriateness and Deprescribing Network provides detailed guidelines for the deprescribing of specific medication classes, emphasizing a strong and patient-centric approach.[17] In the case of antihyperglycemic agents, there is a significant emphasis on either reducing dosages or discontinuing medications most likely to induce hypoglycemia, such as sulfonylureas and insulin, or switching to agents with a lower risk of hypoglycemia and other side effects. For proton pump inhibitors (PPIs), the network advocates for a dose reduction or for a complete cessation and shift to an on-demand use of PPIs, with careful monitoring of the patient at 4 and 12-week intervals. Similarly, there is a strong recommendation made for gradual tapering and cessation of antipsychotics, proposing a 25-50% dose reduction every 1-2 weeks, in close collaboration with the patient and/or their caregiver. For Alzheimer's treatments like cholinesterase inhibitors and memantine, the network recommends a structured deprescribing trial, involving step-by-step dose reduction and careful monitoring of cognitive and neuropsychiatric symptoms. Additionally, the network recommends a careful tapering of benzodiazepine receptor agonists (BZRAs) for adults, especially those over 65 and those using BZRAs for insomnia. These recommendations underscore the importance of tailoring deprescribing strategies to individual patient needs, ensuring both safety and effectiveness in medication management.[a] Additionally, the Primary Health Tasmania also provides specific guides for various medication classes, such as statins, contributing to a more nuanced approach.[16]

The application of deprescribing warrants consideration in elderly patients exhibiting specific conditions, such as the onset of new symptoms, terminal illness, extreme frailty, dependence on others for care and use of high-risk drugs or combinations. For individuals with a limited life expectancy, drugs that are aimed at reducing the risk of acute events or those with a delayed onset of effects may not provide substantial benefits and may be considered for discontinuation.[10]

[a] Authorized by their respective authors, the Italian translation of the guidelines for deprescribing of proton pump inhibitors, antihyperglycemics, antipsychotics, benzodiazepines, and statins can be found at the following webpage of the Local Health Authority of Parma, Italy: https://www.ausl.pr.it/azienda/deprescrizione/deprescrizione.aspx

Thus, deprescribing results in many advantages. This includes enhanced patient adherence, improved quality of life and functional capacity, reduced healthcare system costs, better provider-patient relationship, and avoidance of contribution to issues like antibiotic resistance and the opioid epidemic.[12,18] Additional benefits include decreased risk of adverse drug events, drug-drug and drug-disease interactions, and multiple geriatric syndromes.[9]

Barriers to deprescribing

While reducing or stopping the use of medications can clearly minimize harm and improve outcomes, hesitancies persist regarding the practice of deprescribing. A major challenge is the prevalent lack of care coordination, which leaves gaps in information and patient care goals.[11] Patients with polypharmacy often have multiple morbidities that require clinical management by multiple specialists. However, the fragmented care they receive across different specialists and settings can lead to a range of harmful effects as a result of duplication of therapy, medical errors, or DDIs. Another challenge with lack of integrated care involves the intricate process of trying to get a prescriber to discontinue a drug that was prescribed by another physician.

The hesitation among physicians to embark on deprescribing for older patients is heightened by the risk of legal repercussions, should adverse effects arise or the patient's condition deteriorates after halting a guideline-recommended medication. However, Barnett and Kelly assert that prescribers are just as vulnerable to claims of clinical negligence in deprescribing situations as in prescribing situations.[19] In a legal context, the act of deprescribing is considered parallel to prescribing because the failure to deprescribe can also lead to harm and/or a breach of duty of care.[19] Therefore, practitioners who do not consider deprescribing and omit advising patients on potential benefits and risks could expose themselves up to claims of clinical negligence.[20]

A critical way to avoid negligence cases is to ensure that informed consent is acquired. Informed consent entails obtaining explicit agreement from patients before initiating deprescribing efforts. This necessitates comprehensive discussions with patients about the inherent risks associated with both deprescribing and maintaining current medication regimens. In essence, prescribers must navigate the complexities of deprescribing with the same level of diligence and consideration as they do when initiating medications, ensuring that patients are well-informed and actively involved in the decision-making process related to their treatment plans.

Providers should also be aware of which specialists the patient is seeing and ask patients for their updated medication list at each encounter. Some physicians have upgraded electronic health record systems to improve interoperability and facilitate care coordination. Additionally, during a transition of care of referral, providers should come to an agreement on each of their responsibilities for the patient by communicating with one another, establishing clear goals of care, and exchanging updated and comprehensive medical records with each other.

Additional challenges providers may face include balancing complex care needs with time constraints, which is a multifactorial hurdle in itself. Patients often perceive physicians' lack of follow-up or limited appointment times as the physician not caring, but the reality is that they simply lack time. Studies show that on average, physicians may be spending more time typing data in electronic health record systems than with patients.[21,22] Some proposed strategies to mitigate this include the implementation of team-based care which would not only reduce clinician burnout but also help with the provision of coordinated services to patients.[23] Another proposal is the potential use of artificial intelligence to improve workflow models, automate exchange of information across previously siloed electronic health record systems, using population analysis to help deliver services more efficiently, appropriately reduce cognitive burden for physicians, and reduce administrative burden so physicians can have more time to spend with patients.[24,25]

Part of physicians' hesitancy about deprescribing also stems from uncertainty about benefits and harms for patients.[11] One safety concern is adverse drug withdrawal events (ADWEs). ADWEs may be prevented by slowly tapering medications over the course of days to weeks, especially if they were used long-term.[15] However, the overall chance of serious harm from ADWEs is rare, especially with tapering.[12] ADWEs may also be prevented by considering the pharmacokinetics, pharmacodynamics, dose, and duration of use when discontinuing a medication.[15] It is helpful for providers to be aware of which medications are at the highest risk for ADWEs. For example, the most common cardiovascular medications associated with withdrawal reactions are beta-blockers, and the most common central nervous system medications associated with physiological withdrawal reactions are benzodiazepines.[15]

Physicians may also have safety concerns that involve the risks associated with the return of medical conditions if a medication is discontinued. However, this can be mitigated by closely monitoring surrogate markers that were followed during treatment when possible and understanding the effects of the medication class and patient-specific factors.[12] For example, depending on the bisphosphonate taken, a drug holi-

day may be considered after treatment for 3-5 years.[12] Another safety concern is the risk of reversal of DDIs when removing a medication. For example, smoking cessation can cause the reversal of DDIs due to changes in CYP450 enzyme levels. Medication half-lives and duration of action can also affect pharmacokinetic and pharmacodynamic drug interactions. Consulting with other health professionals such as pharmacists when considering a change in the medication list can be helpful to know if there will be any clinically significant interactions.[12]

Increasing deprescribing

In the domain of care for older adults, the optimization of medication regimens is a critical undertaking, particularly when it comes to deprescribing. Enhancing the process of deprescribing is not only a clinical imperative but also a nuanced task that necessitates active collaboration between healthcare providers, patients, and caregivers. As the aging population continues to grow, so does the importance of refining deprescribing practices to align with the unique needs and circumstances of older adults. This calls for a dual approach: involving patients in the decision-making process and augmenting physician awareness and proficiency in deprescribing. In this context, fostering a comprehensive understanding of deprescribing principles among patients and caregivers, and concurrently bolstering the knowledge base of physicians, emerges as a crucial avenue for advancing the quality of care provided to the elderly.

As a part of including the patient in the care process, all older patients and caregivers should be well informed on deprescribing, including low health literacy populations. Providers may consider distributing patient educational materials to inform them on the benefits and risks in an easy-to-digest manner.[26] For example, the Deprescribing Network provides infographics and handouts for patients on what deprescribing is and on the risks of certain types of medications.[27]

Discontinuing a drug can be unsettling, particularly for those who have been on the same medication for many years.[15] Resources like the guidance from Farrell and Mangin offer specific examples on how to discuss deprescribing with patients.[28] Their approach includes communicating about the availability of choices, discussing the benefits and risks, and exploring options and decision-making processes.[28] This kind of sensitive and compassionate communication is especially important in end-of-life care contexts. There are many tools that can help guide communication such as the SPIKES 6-step protocol,[29] the ABCDE plan,[30] and the PREPARED model from Australian clinical practice guidelines.[31] In some cases, when medications are discontinued, a patient may feel abandoned, that their diagnosis is terminal or that death is near, even if that is not the case.[15] If a patient is experiencing clinical improvement or no longer deriving benefit from the drug, language should also be clear as to why the medication is being discontinued. For example, a physician practicing effective communication may say to the patient depending on the context, "this medication can be discontinued because your condition is improving" or "as we get older, medications that worked well may no longer have the same benefit; in particular, I'm thinking that this medication may no longer be needed. If we discontinue it, the risks are (y) but the benefits are (z). Is this something you would consider discontinuing?"[15,28]

Recognizing the hesitancy among physicians to engage in the deprescribing process for their patients, it becomes imperative to highlight the significance of comprehensive physician training in this area. Effective implementation of deprescribing in both new encounters and routine follow-ups requires a well-informed plan. Education is a key facilitator, encompassing tools like the Beers Criteria, the screening tool for older people's prescriptions (STOPP), the screening tool to alert to right treatment (START) criteria, and the Medication Appropriateness Index.[7] To better align with physicians' perspectives and the evolving landscape of available medications, an Italy-specific tool, recognized in literature as the Maio Criteria and developed by the Local Health Authority of Parma and Thomas Jefferson University, is accessible online.[32,33] Regularly assessing patients for adverse events and medication adherence, coupled with proactive follow-ups through various communication channels, enhances the deprescribing process. Collaborating with pharmacists, trained in comprehensive medication reviews (CMRs), further streamlines the identification and prevention of inappropriate therapy. CMRs are a type of medication therapy management that comprises a medication reconciliation, clinical assessment of patient-specific factors like medical conditions, allergies, socioeconomic and cultural assessments, prioritization of drug-related problems and therapeutic recommendations.[34] This holistic approach ensures a smoother integration of deprescribing into the continuum of patient care.

Conclusions

In conclusion, the rising challenges associated with an aging population, coupled with the complexities of polypharmacy highlight the critical need for effective deprescribing strategies. Polypharmacy, with its potential to contribute to morbidity and mortality, remains a complex issue in older adults. Despite the effectiveness of deprescribing in mitigating these risks, raising awareness and implementing deprescribing practices

may pose challenges. The success of deprescribing relies on healthcare professionals' ability to evaluate risks versus benefits on an individualized basis, emphasizing the need for a tailored approach. Active engagement of providers and pharmacists, fostering collaborative efforts, is essential to address the multifaceted nature of polypharmacy and enhance patient care. Future directions involve promoting deprescribing culture through continuous medical education, incorporating deprescribing guidelines into routine clinical practice, and educating patients on the benefits and risks. By incorporating these next steps, the healthcare community can contribute significantly to enhancing the well-being and quality of life for the elderly population while mitigating the associated risks of polypharmacy.

References

1. United Nations. Department Of Economic And Social Affairs. Population Division. World Population Ageing 2020 Highlights: Living Arrangements of Older Persons. United Nations, 2020.
2. Nations U. Ageing. United Nations. Available from: https://www.un.org/en/global-issues/ageing#:~:text=Trends%20in%20Population%20Ageing
3. United Nations. Department Of Economic And Social Affairs. Population Division. World Population Ageing, 2019 Highlights. New York: United Nations, 2019. Available from: https://www.un.org/en/development/desa/population/publications/pdf/ageing/WorldPopulationAgeing2019-Highlights.pdf
4. Onder G, Vetrano DL, Cherubini A, et al. Prescription drug use among older adults in Italy: a country-wide perspective. J Am Med Dir Assoc 2014;15:531.e11-531.e15.
5. Ricciardi W, Tarricone R. The evolution of the Italian National Health Service. The Lancet. Published online October 22, 2021.
6. The Elderly: health conditions in Italy and in the European Union. 2017. Available from: https://www.istat.it/en/archive/203827 (accessed November 15, 2023)
7. Halli-Tierney AD, Scarbrough C, Carroll D. Polypharmacy: Evaluating Risks and Deprescribing. American Family Physician 2019;100:32-8.
8. Sinha A, Mukherjee S, Tripathi S, Dutta S. Issues and challenges of polypharmacy in the elderly: A review of contemporary Indian literature. J Family Med Prim Care 2021;10:3544.
9. Thomas RB, Jang SR, Lombardi M, Maio V. The prescription paradox: a guide to appropriate prescribing in the elderly. Geriatr Care 2019;5.
10. Sultana J, Elisabetta Poluzzi, Lunghi C, et al. Deprescribing as a strategy for improving safety of medicines in older people: Clinical and regulatory perspective. Frontiers 2022;2.
11. Scott IA, Hilmer SN, Reeve E, et al. Reducing inappropriate polypharmacy: the process of deprescribing. JAMA Intern Med.2015;175:827-34.
12. Reeve E, Moriarty F, Nahas R, et al. A narrative review of the safety concerns of deprescribing in older adults and strategies to mitigate potential harms. Expert Opin Drug Saf 2018;17:39-49.
13. Niriayo YL, Kumela K, Kassa TD, Angamo MT. Drug therapy problems and contributing factors in the management of heart failure patients in Jimma University Specialized Hospital, Southwest Ethiopia. PLoS One 2018; 13:e0206120.
14. Sternberg SA, Guy-Alfandary S, Rochon PA. Prescribing cascades in older adults. CMAJ 2021;193:E215.
15. Bain KT, Holmes HM, Beers MH, et al. Discontinuing medications: a novel approach for revising the prescribing stage of the medication-use process. J Am Geriatr Soc 2008;56:1946-52.
16. Deprescribing resources. Primary Health Tasmania. Available from: https://www.primaryhealthtas.com.au/resources/deprescribing-resources/
17. Deprescribing algorithms. Do I still need this medication? Is deprescribing for you? Available from: https://www.deprescribingnetwork.ca/algorithms
18. Zarowitz B, Brandt N. Deprescribing In Assisted Living. Innov Aging 2022;6:250.
19. Barnett N, Kelly O. Deprescribing: is the law on your side? Eur J Hosp Pharma 2016;24:21-5.
20. Barnett N, Kelly Ó. Legal implications of deprescribing: a case scenario. Prescriber 2017;28:49-52.
21. Budd J. Burnout Related to Electronic Health Record Use in Primary Care. J Prim Care Community Health. 2023;14:21501319231166921.
22. EHR Poll Results. EHR National Symposium. Available from: https://www.med.stanford.edu/ehr/electronic-health-records-poll-results.html
23. Smith CD, Balatbat C, Corbridge S, et al. Implementing Optimal Team-Based Care to Reduce Clinician Burnout. NAM Perspectives. 2018;8.
24. Lawry T. AI in Health: A Leader's Guide to Winning in the New Age of Intelligent Health Systems. CRC Press, Taylor & Francis Group, 2020.
25. Lawry T. The future of AI in medicine and what it means for physicians and practices with Tom Lawry. American Medical Association, 2023. Available from: https://www.ama-assn.org/practice-management/digital/future-ai-medicine-and-what-it-means-physicians-and-practices-tom-lawry
26. Fajardo MA, Weir KR, Bonner C, et al. Availability and readability of patient education materials for deprescribing: An environmental scan. Br J Clin Pharmacol 2019;85:1396-406.
27. Patient handouts. Do I still need this medication? Is deprescribing for you? Available from: https://www.deprescribingnetwork.ca/patient-handouts
28. Farrell B, Mangin D. Deprescribing Is an Essential Part of Good Prescribing. Am Fam Physician 2019;99:7-9.
29. Baile WF, Buckman R, Lenzi R, et al. SPIKES-A six-step protocol for delivering bad news: application to the patient with cancer. Oncologist 2000;5:302-11.
30. Rabow MW, McPhee SJ. Beyond breaking bad news: how to help patients who suffer. West J Med 1999;171: 260-3.
31. Clayton JM, Hancock KM, Butow PN, et al. Clinical practice guidelines for communicating prognosis and end-of-life issues with adults in the advanced stages of a life-limiting illness, and their caregivers. Med J Aust 2007;186:S77-S105.

32. Kaufmann CP, Tremp R, Hersberger KE, et al. Inappropriate prescribing: a systematic overview of published assessment tools. Eur J Clin Pharmacol 2014; 70:1-11.
33. AUSL, Azienda. Available from: https://www.ausl.pr.it/azienda/appropriatezza_prescrittiva/default.aspx (accessed November 15, 2023)
34. Vaffis S, Dhatt H, Anderson EJ, et al. A checklist for a consistent, comprehensive medication review. J Am Pharma Associ 2023;63:1504-7.e1.