

# **Polypharmacy in elderly people: A Simple Review**

## **ABSTRACT**

With increasing age, there is chance of developing different chronic condition which is often accompanied by use of multiple medicines that can lead to polypharmacy. Geriatric people particularly those with multiple co-morbid condition may result in polypharmacy with high risk of Adverse Drug Events (ADE) and Drug Interaction (DI). Presence of multiple co morbidities makes them highest consumer of drugs, so a high degree of caution is required while prescribing drug to elderly population. Concept of Deprescribing and several tools like Medication Appropriateness Index, ARMOR (Assess, Review, Minimize, Optimize, and Reassess), and START/STOPP (Screening tool for older persons potentially inappropriate prescription/ Screening tool to alert doctors to right treatment) etc have been emerged as a practical guide to solve problem relating polypharmacy and these tools should be considered by the prescriber while prescribing the drug to the elderly population.

*Keywords: Polypharmacy; co morbidity; Deprescribing; Geriatric.*

## **INTRODUCTION**

With advancing age, pharmacokinetic and pharmacodynamic changes occur. Pharmacodynamic changes involve altered sensitivity to different classes of drug whereas; pharmacokinetic changes include changes in absorption, distribution, metabolism and excretion of drugs [1]. Various physiological changes like losses in hearing, seeing and moving occurs as well as the risks for older people developing disease like dementia, heart disease, stroke, chronic respiratory disorder, diabetes and osteoarthritis increase [2]. With increasing age, there is chance of developing different chronic condition which is often accompanied by use of multiple medicines that can lead to polypharmacy. The term "Polypharmacy" is defined as use of five or more medicine which include the one that has been prescribed, over the counter (OTC) as well as complementary medicine [3]. Geriatric people particularly those with multiple co-morbid condition may result in polypharmacy with high risk of Adverse Drug Events (ADE) and Drug Interaction (DI) [4]. Due to altered pharmacology of ageing, presence of multiple medical conditions and exclusion of elderly patients from clinical trial often leads to under prescribing and over prescribing to elderly patients. Adverse drug

events can be seen which can cause morbidity and mortality in this subgroup of population as well as having economic impact [5].

Use of these different medicines such as Hypnotic and Sedative, NSAIDs (Non Steroidal Anti-inflammatory Drugs), etc increase the chance of side effect and adherence to the therapy can be compromised [6]. Presence of multiple co morbidities makes them highest consumer of drugs, so a high degree of caution is required while prescribing drug to elderly population [7].

One of the main challenges for General Practitioner (GP) has been medical care for elderly people. Due to natural ageing process elderly often experience multiple chronic disease as well as decrease in both organ function and physiological reserves. Therapeutic confusion can be seen among younger GP as choice of medicine became a complex process for each particular disease. Adverse side effect can be seen in elderly who can be 7 times more frequent in comparison with younger patients. Responsible clinicians must consider possible Drug-Drug interaction and pharmacokinetic dynamic of ageing body while providing therapy for elderly patients [8, 9]. Application of published guideline for a hypothetical 79 years old woman with Chronic Obstructive Pulmonary Disease (COPD), Type II Diabetes Mellitus (DM), Osteoporosis, Hypertension (HTN) and Osteoarthritis led to use of 12 medicines and a complicated non pharmacological regimen with high risk of adverse interaction between drugs and disease [10]. As, polypharmacy is common phenomenon it can be associated with use of Potentially Inappropriate Medication (PIM) in geriatric population [11]. A person on PIM is associated with potential Drug Related Problem (DRP) and increase in healthcare cost and utilization compared to those people who are not on PIM [12]. Elderly patients are at high risk of experiencing DRP because of their complex medical problem and use of multiple drugs. Number of DRP like incorrect drug choice, dose too low or too high, no clear indication, etc increased with number of medication used. An effective strategy should be developed to reduce the risk of mortality, morbidity, and hospital readmission associated with DRP [13]. The biggest problem faced by health care professional is lack of adequate evidence and knowledge about response of elderly patients to drug because of the elderly patients are excluded from the clinical trials [14].

It is essential for health care professionals to be aware of medication need of geriatric people and necessary to follow guidelines and tools to formulate hospital policies and protocol to improve such need. Promoting both quality of life as well as better and safer prescribing practice in elderly people can be achieved by providing education, reporting DRP and further increasing the doctor patient interaction [15]. Use of PIM was associated with increase in cost in case of elderly which can be alleviated by use of program like continuing medical education program as well as providing education and training to doctors on rational prescribing [16].

Polypharmacy is an important issue in the elderly which involves Adverse Drug Reaction (ADR). Incidence of adverse drug reaction and interaction increases with polypharmacy in elderly due to altered metabolism and excretion of medications. Since ADR are a significant cause of morbidity and mortality as well as important cause for hospital admission, minimizing polypharmacy is an important consideration.

The general principle of “Start Low, Go slow but Use enough” should be considered to achieve desired therapeutic effect in elderly [17].

## **1. EPIDEMIOLOGY**

The prevalence of polypharmacy found in different literature varies greatly ranging from 4% to about 57% [18]. A study had shown the variation in prevalence of polypharmacy in between 10% to 90% in different population [19]. Likewise, another study found out the prevalence of polypharmacy ranging from 26.3% to 39.9%. Beside, the countries with the lowest prevalence of polypharmacy was found out to be Switzerland, Croatia and Slovenia while Portugal, Israel and Czech Republic being highest in terms of prevalence [20].

It has been shown that polypharmacy was seen in 58.6% and inappropriate medication use were seen in 70% resident in geriatric age group residing in selected nursing home in Singapore [21]. Similarly, a retrospective study conducted in Nepal on prescribing pattern to geriatric patient at Tribhuvan University Teaching Hospital (TUTH) medical ward showed that polypharmacy was prevalent indicating considerable scope for improving geriatric prescribing practice in TUTH medical ward [22]. A study done on intermediate care nursing home showed that, from admission to discharge the prevalence of PIM has been increased from 24% to 35% [23]. A study showed that 44% of elderly patient were taking PIM and 33% patient were taking drugs that contribute serious Drug-Drug interaction [24]. A Meta analysis showed that twice as much elderly people are hospitalized due to an ADR than non elderly patients [25]. According to IMS (Intercontinental Marketing Statistics) Institute for Health care informatics estimates, in year 2012 AD health care cost exceeded nearly \$200 billion due to improper and unnecessary use of medicine and avoidable health care cost from mismanaged polypharmacy among elderly resulted in \$1.3 billion in United States Health Care System [26].

## **2. FACTORS CONTRIBUTING POLYPHARMACY**

One of the common etiologies contributing to polypharmacy is lack of primary care physician and use of multiple prescriber as well as pharmacies. Depending on convenience, distance and cost, patients may go to more than one pharmacy to receive medication. The problem with this is that it often leads to incomplete medication histories, which can result in multitude of problems that can cause more medications to prescribe than necessary.

Another factor contributing to polypharmacy occur when patient expect the physician to prescribe a medication at every visit. Polypharmacy is mostly seen in older adults having different level of impairment ranging from cognitive to developmental. Further, elderly having co-morbid condition are also primary risk factor for polypharmacy. Likewise, keeping poor medical record of a patient can be another risk factor that can be seen from healthcare system level as those patients are more likely to get refilled by old medication that has been discontinued by the prescriber [27 – 33].

### **3. CONSEQUENCES OF POLYPHARMACY**

Polypharmacy has been linked to number of complication in case of elderly [34]. Concomitantly administered drug can lead to drug interaction resulting in decline therapeutic effect and increase in occurrence of ADR. Elderly patient also fail to adhere to the drug prescribed that contain multiple drug or regimen that can lead to decrease patient compliance and ultimately therapeutic failure. Likewise, sometime due to polypharmacy therapeutic duplication can occur that can be associated with overdosing [35]. Several studies in community dwelling elderly as well as nursing home resident have shown a link between polypharmacy and hospitalization [36-38]. Various studies done on Taiwan [39], Australia [40], and Korea [41] have shown association between polypharmacy and hospitalization. Likewise, the relationship of frailty with polypharmacy is still unclear but the association is highly prevalent in case of elderly and more research is required in this area to explore the relationship between frailty and polypharmacy [42, 43]. Numerous studies also have revealed that polypharmacy is associated with increased risk of falls in case of elderly [44-46]. Similarly, polypharmacy has also been associated with cognitive impairment and associate with development of dementia [47, 48]. A low score was seen in Mini Mental State Examination (MMSE) of those participants with polypharmacy [49]. Likewise, association between physical impairment and polypharmacy was also see in elderly [50, 51]. Further, some studies even concluded that polypharmacy can be one of the factors that can increase the risk of mortality [52, 53].

### **4. ASSESSMENT TOOLS FOR POLYPHARMACY**

Several tools have been emerged as a practical guide to solve the problem relating polypharmacy but all those are based on Interventional trials [54]. Tools like MAI (Medication Appropriateness Index) may have value in providing a structure and process for clinical learners to conduct a comprehensive review of complex drug regimen taken by older adults [55]. Others tools like STOPP/START (Screening tool for older persons potentially inappropriate prescription/ Screening tool to alert doctors to right treatment) criteria has been considered while providing therapy to elderly patients. The list aid practice support to practioner daily work and reduces the chance of both medication error and inappropriate prescription in elderly population [56]. Beers criteria have been developed to assist healthcare practioner to improve medication safety and quality of care in older adults and is mainly concern with the reduction of exposure to PIM (Potential Inappropriate Medication) as polypharmacy can lead to use of inappropriate medication in elderly population [57, 58]. The criteria will guide clinicians in making decision about safe use of drug in elderly and will continue to encourage in making careful consideration about risk of particular drug in elderly. Further these criteria can be integrated in electronic health record where instant feedback on suggestion for alternative can be given for a particular inappropriate medication [59].

### **5. MANAGEMENT**

Polypharmacy can be associated with greater health care costs and an increased risk of ADE, drug-interactions, medication non-adherence, reduced functional capacity and multiple geriatric syndromes.

Health care professionals must try to make effort to identify a diagnosis for every medication on the list and asking a series of question like:

- Is the indication for which the medication was originally prescribed still present?
- Are there duplication in drug therapy from the same class, and does the list include medications prescribed for an adverse reaction?
- Are the medication dosages therapeutic and, is there any significant drug-drug or drug-disease interaction?
- Have non pharmacological treatment been considered whenever possible?

Tools like ARMOR (Assess, Review, Minimize, Optimize, and Reassess) are used to evaluate polypharmacy in older adults. This tool is a systematic and organized stepwise approach that assesses medications, minimizes non essential medication, optimizes by addressing duplication and adjusting dosages and reassesses the patient for functional, cognitive and clinical status along with medication adherence. This tool considers a patients functional ability and clinical status in an effort to balance best prescribing practice with the patient's physical profile so that a patient's quality of life is improved [60].

The key for treating elderly is to find the right drug at right dose and for shortest possible duration on an individualized basis. Non pharmacological treatment should be considered whenever possible. Further developing safe and evidence based medicine regimen and determining benefit to risk ratio helps to minimize polypharmacy and risk associated with it [61]. Two issues must be addressed in near future; first being introducing strategies and intervention to improve prescribing appropriateness and second the patient need to make clear about taking more medicine to prevent disease or disability often lead to potential harm from Potentially Inappropriate Prescription (PIP) drugs [62].

Introducing a specialty of geriatric medicine in developing countries is indispensable in order to safe guard geriatric population from poor health and a life of destitution, exploitation or neglect [63]. There is also need of separate geriatric nursing care unit as well as training for nursing staff in order to provide geriatric care for elderly patients [64].

The role of clinical pharmacist in optimizing prescription and rational use of drug in elderly involves different approaches like pharmaceutical care, medication reviews and educational interventions. Clinical pharmacist can play a proactive role in performing medication review and provide education to other health care professionals. In conclusion, optimizing prescription in elderly involve integrated approach that involves physician, clinical pharmacologist, clinical pharmacist and patient [65, 66].

## **5.1. APPROACHES TO DEPRESCRIBING**

A concept of Deprescribing has been introduced which is part of good prescribing that provide the concept of backing off if the dose seem too high or completely stopping the intake of medicine if they are

no longer needed [67]. Reduction in number of drug intake can be associated with decrease in adverse event and improvement in quality of life [68]. Physician should include the concept of deprescribing while planning the treatment plan; discuss potential deprescribing with patient [69]. Patients are interested if they are included in treatment plan and their frequency of medicine intake is reduced [70]. Certain things like patient's overall health, therapeutic goal, compliance and willingness to deprescribe should be considered while going through deprescribing process [71]. However, more research is needed regarding Benefit/Risk of continuation and discontinuation of certain medicine and one should also be knowledgeable regarding appropriate time to discontinue certain medicine for better result [72].

## **5.2. GOOD PRESCRIBING PRACTICE [73, 74]**

Before starting a new drug accurate medical and medication history must be obtained in order to avoid drug-disease and drug-drug interaction. If possible non pharmacological treatment should be considered and must treat underlying cause rather than symptoms. The drug that are not indicated or having non beneficial should be stopped. Only clear indication drug should be prescribed and such indication should be documented in order to avoid use of unnecessary drug. Furthermore each physician or medical prescriber must be cautious while adding new medicine and must be chosen safest medicine as possible in an alternative way. The drug regimen should be simple with appropriate administration system. The therapeutic goal should be discussed with patient explaining about drug its uses, ADR, how to take medicine, duration of treatment etc. Further pharmacokinetic or pharmacodynamic changes that are likely to occur in elderly and their effect on dosing requirement can also be taken in consideration.

After starting a drug the therapeutic response must be documented and if necessary the dose must be increased in order to achieve desired effect. The developed symptom must be assumed to be dose related until proved in order to prevent prescribing cascade. Further monitoring patient for possible adverse effect and re-evaluating the need to continue drug therapy or to stop medicine that have no beneficial effect can also be done.

Medication reconciliation should occur at time of admission, transfer and discharge which ensure transfer of information about drug regimen at any transition point in health care system. The process include verification of all drugs that patient are taking and comparing with physician's order. Programs like computerized physician ordering program can be used that can alert clinician to problem like allergy, dose reduction, drug interaction, impaired function and allows clinicians to monitor patient for possible adverse effect. Electronic prescribing can be used which minimizes prescribing and administration error. It helps to anticipate confusion due to sound alike and look alike drug name e.g. Chlorpropamide and Chlorpromazine in which Chlorpropamide is oral hypoglycaemic drugs whereas, Chlorpromazine is a Neuroleptics.

## **6. CONCLUSION**

Geriatric people particularly those with multiple co-morbid condition makes them highest consumer of drugs which can lead to polypharmacy so a high degree of caution is required while prescribing drug to elderly population in order to prevent the consequences of polypharmacy. Concept of Deprescribing and several tools like MAI, ARMOR, and START/STOPP etc have been emerged as a practical guide to solve problem relating polypharmacy and these tools should be considered by the prescriber while prescribing the drug to the elderly population. These tools can act as guideline to the prescriber while prescribing the drug to geriatric patients. Further, these tools can be useful to pharmacist and other health care professionals in assessing the appropriateness of prescription before dispensing medication to geriatric patients and suggesting a safer alternative by consulting with physician so that proper decision is made regarding the appropriate choice of drug in elderly population.

Sufficient study on medicine used in Geriatric should be carried out in order to know the exact percentage of inappropriate prescription used in geriatric patients. The elderly patients who are on medication need to be knowledgeable regarding the drug so that:-

- Appropriate decision is made regarding the right choice of drug.
- Quality and efficacy of medical care given to elderly can be increased.
- Use of safer alternative and avoidance of complication can be achieved.
- Reduction in financial burden can be achieved.

## CONSENT

It is not applicable

## ETHICAL APPROVAL

It is not applicable

## REFERENCE

1. AA Mangoni; SHD Jackson. Age related changes in pharmacokinetic and pharmacodynamic: basic principles and practical applications, Br J Clin pharmacol, 2004, 57(1), 6-14. doi: 10.1046/j.1365-2125.2003.02007.x
2. Integrated care for older people: guideline on community-level interventions to manage declines in intrinsic capacity. Geneva: World Health Organization, 2017. <http://apps.who.int/iris/handle/10665/258981> Accessed on 5 Jan 2023.
3. Hilmer SN. The dilemma of polypharmacy. Aust Prescr 2008;31:2-3. <https://doi.org/10.18773/austprescr.2008.001>

4. Hilmer SN, Gnjjidic D. The effects of polypharmacy in older adults. *Clin Pharmacol Ther.* 2009;85(1):86-88. doi:10.1038/clpt.2008.224
5. Ananthhanam S, Powis RA, Cracknell AL, Robson J. Impact of prescribed medications on patient safety in older people. *Ther Adv Drug Saf.* 2012;3(4):165-174. doi:10.1177/2042098612443848
6. Dijk C, Verheij R, Schellevis F. Polyfarmacie bij ouderen, *Huisarts En wetenschap.* 2009; 52(7):315-315.
7. Momin TG, Pandya RN, Rana DA, Patel VJ. Use of potentially inappropriate medications in hospitalized elderly at a teaching hospital: A comparison between Beers 2003 and 2012 criteria, *Indian J Pharmacol.* 2013; 45(6): 603-607.
8. Masand PS. Side effects of antipsychotics in the elderly. *J Clin Psychiatry.* 2000;61 Suppl 8:43-51.
9. Brooks JO, Hoblyn JC. Neurocognitive costs and benefits of psychotropic medications in older adults. *J Geriatr Psychiatry Neurol.* 2007;20(4):199-214. doi:10.1177/0891988707308803
10. Boyd CM, Darer J, Boulton C, Fried LP, Boulton L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. *JAMA.* 2005;294(6):716-724. doi:10.1001/jama.294.6.716
11. Zeenny R; Wakim S; Kuyumjian YM. "Potentially inappropriate medication use in community based aged patients: a cross sectional study using 2012 Beer's criteria", clinical intervention in aging. Accessed 5 Jan 2023. Available: <https://www.dovepress.com/by 150.107.204.225>.
12. Fick DM, Mion LC, Beers MH, Waller JL. Health outcome associated with potentially inappropriate medication use in older adults. *Res Nurs Health.* 2008; 31(1): 42-51. doi:10.1002/nur.20232.
13. Ahmad A, Mast MR, Nijpels G, Elders PJM, Dekker JM, Hugtenburg JG. Identification of drug-related problems of elderly patients discharged from hospital. *Patient Preference and Adherence.* 2014;8:155-165. <https://doi.org/10.2147/PPA.S48357>
14. Shenoy P, Harugeri A. Elderly patients' participation in clinical trials. *Perspect clin Res.* 2015; 6(4): 184-189. doi:10.4103/2229-3485.167099.
15. Narvekar RS, Bhandare NN, Gouveia JJ, Bhandare PN. Utilization Pattern of Potentially Inappropriate Medications in Geriatric Patients in a Tertiary Care Hospital: A Retrospective Observational Study. *J Clin Diagn Res.* 2017;11(4):FC04-FC08. doi:10.7860/JCDR/2017/21080.9731
16. Shah KN, Joshi HM, Christian RP, Patel KP, Malhotra SD. Prevalence of potentially inappropriate medications and prescription cost analysis among older cardiac patients in an outpatient department of a tertiary care hospital in India. *J Basic Clin Pharm.* 2016;7(4):110-115. doi:10.4103/0976-0105.189434
17. Masoodi NA. Polypharmacy: To err is human, to correct divine, *British Journal of Medical Practitioners.* 2008; 1: 6-9.

18. Guillot J, Maumus-Robert S, Bezin J. Polypharmacy: A general review of definitions, descriptions and determinants. *Therapie*. 2020;75(5):407-416. doi:10.1016/j.therap.2019.10.001
19. Khezrian M, McNeil CJ, Murray AD, Myint PK. An overview of prevalence, determinants and health outcomes of polypharmacy. *Ther Adv Drug Saf*. 2020;11:2042098620933741. Published 2020 Jun 12. doi:10.1177/2042098620933741
20. Midão L, Giardini A, Menditto E, Kardas P, Costa E. Polypharmacy prevalence among older adults based on the survey of health, ageing and retirement in Europe. *Arch Gerontol Geriatr*. 2018;78:213-220. doi:10.1016/j.archger.2018.06.018
21. Mamun K, Lien CT, Goh-Tan CY, Ang WS. Polypharmacy and inappropriate medication use in Singapore nursing home. *Ann Acad Med Singapore*. 2004; 33(1): 49-52.
22. Joshi MP, Sugimoto T, Santoso B. Geriatric prescribing in the medical wards of a teaching hospital in Nepal. *Pharmacoepidemiol Drug saf*. 1997; 6(6): 417-21.
23. Bakken MS, Ranhoff AH, Engeland A, Ruths S. Inappropriate prescribing for older adults admitted to an intermediate care nursing home unit and hospital wards. *Scand J prim Health care*. 2012; 30(3): 169-175. doi: 10.3109/02813432.2012.704813.
24. Metanovic SM, Vlahovic Palcevski V. Potentially inappropriate prescribing to the elderly: comparison of new protocol to Beer's criteria with relation to hospitalization for ADRs. *Eur J Clin Pharmacol*. 2014; 70(4): 483-90. doi: 10.1007/s00228-014-1648-3.
25. Beijer HJ, de Blaey CJ. Hospitalisations caused by adverse drug reactions (ADR): a meta-analysis of observational studies. *Pharm World Sci*. 2002;24(2):46-54. doi:10.1023/a:1015570104121
26. Aitkan M, Valkova S. Avoidable cost in US healthcare: The \$200 Billion opportunity from using medicines more responsibly. Report by IMS institute for healthcare information. 2013. Accessed 7 January 2023. Available: [Avoidable Costs in U.S. Healthcare the \\$200 Billion Opportunity from Using Medicines More Responsibly Introduction - DocsLib](#)
27. Pesante-Pinto JL. Clinical Pharmacology and the Risks of Polypharmacy in the Geriatric Patient. *Phys Med Rehabil Clin N Am*. 2017;28(4):739-746. doi:10.1016/j.pmr.2017.06.007
28. Yazici E, S Cilli A, Yazici AB, et al. Antipsychotic Use Pattern in Schizophrenia Outpatients: Correlates of Polypharmacy. *Clinical Practice and Epidemiology in Mental Health : CP & EMH*. 2017 ;13:92-103. DOI: 10.2174/1745017901713010092.
29. Haider SI, Ansari Z, Vaughan L, Matters H, Emerson E. Prevalence and factors associated with polypharmacy in Victorian adults with intellectual disability. *Res Dev Disabil*. 2014;35(11):3071-3080. doi:10.1016/j.ridd.2014.07.060
30. Rijal S, Adhikari K, Sigdel D, Mallik SK. Prescribing Pattern of Drugs in Geriatrics Patients Using Beers Criteria. *J Nepal Health Res Counc*. 2019;17(2):153-157. Published 2019 Aug 4. doi:10.33314/jnhrc.v0i0.1774

31. Jokanovic N, Tan EC, Dooley MJ, Kirkpatrick CM, Bell JS. Prevalence and factors associated with polypharmacy in long-term care facilities: a systematic review. *J Am Med Dir Assoc.* 2015;16(6):. doi:10.1016/j.jamda.2015.03.003
32. Lunskey Y, Modi M. Predictors of Psychotropic Polypharmacy Among Outpatients With Psychiatric Disorders and Intellectual Disability. *Psychiatr Serv.* 2018;69(2):242-246. doi:10.1176/appi.ps.201700032
33. Hovstadius B, Petersson G. Factors leading to excessive polypharmacy. *Clin Geriatr Med.* 2012;28(2):159-172. doi:10.1016/j.cger.2012.01.001
34. Salazar JA, Poon I, Nair M. Clinical consequences of polypharmacy in elderly: expect the unexpected, think the unthinkable. *Expert Opin Drug Saf.* 2007;6(6):695-704. doi:10.1517/14740338.6.6.695
35. Chitra B, Senthilvel N, Sowmya R, Sathyan S, Srisha R. A Study on Prescribing Pattern of drugs in Geriatric using Beers Criteria at a private Corporate hospital. *Int J Pharm Sci Res.* 2015; 6(11): 4810-4825. doi: 10.13040/IJPSR.0975-8232.6(11).4810-25.
36. Beer C, Hyde Z, Almeida OP, et al. Quality use of medicines and health outcomes among a cohort of community dwelling older men: an observational study. *Br J Clin Pharmacol.* 2011;71(4):592-599. doi:10.1111/j.1365-2125.2010.03875.x
37. Lalic S, Jansen KM, Wimmer BC, et al. Polypharmacy and medication regimen complexity as factors associated with staff informant rated quality of life in residents of aged care facilities: a cross-sectional study. *Eur J Clin Pharmacol.* 2016;72(9):1117-1124. doi:10.1007/s00228-016-2075-4
38. Wastesson JW, Morin L, Tan ECK, Johnell K. An update on the clinical consequences of polypharmacy in older adults: a narrative review. *Expert Opin Drug Saf.* 2018;17(12):1185-1196. doi:10.1080/14740338.2018.1546841
39. Lu WH, Wen YW, Chen LK, Hsiao FY. Effect of polypharmacy, potentially inappropriate medications and anticholinergic burden on clinical outcomes: A retrospective cohort study. *CMAJ.* 2015 Mar 3;187(4):E130-E137. doi: 10.1503/cmaj.141219
40. Lalic S, Sluggett JK, Ilomäki J, et al. Polypharmacy and Medication Regimen Complexity as Risk Factors for Hospitalization Among Residents of Long-Term Care Facilities: A Prospective Cohort Study. *J Am Med Dir Assoc.* 2016;17(11):1067.e1-1067.e6. doi:10.1016/j.jamda.2016.08.019
41. Chang TI, Park H, Kim DW, et al. Polypharmacy, hospitalization, and mortality risk: a nationwide cohort study. *Sci Rep.* 2020;10(1):18964. Published 2020 Nov 3. doi:10.1038/s41598-020-75888-8
42. Palmer K, Villani ER, Vetrano DL, et al. Association of polypharmacy and hyperpolypharmacy with frailty states: a systematic review and meta-analysis. *Eur Geriatr Med.* 2019;10(1):9-36. doi:10.1007/s41999-018-0124-5

43. Gutiérrez-Valencia M, Izquierdo M, Cesari M, Casas-Herrero Á, Inzitari M, Martínez-Velilla N. The relationship between frailty and polypharmacy in older people: A systematic review. *Br J Clin Pharmacol*. 2018;84(7):1432-1444. doi:10.1111/bcp.13590
44. Fried TR, O'Leary J, Towle V, Goldstein MK, Trentalange M, Martin DK. Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. *J Am Geriatr Soc*. 2014;62(12):2261-2272. doi:10.1111/jgs.13153
45. Laflamme L, Monárrez-Espino J, Johnell K, Elling B, Möller J. Type, number or both? A population-based matched case-control study on the risk of fall injuries among older people and number of medications beyond fall-inducing drugs. *PLoS One*. 2015;10(3):e0123390. Published 2015 Mar 27. doi:10.1371/journal.pone.0123390
46. Dhalwani NN, Fahami R, Sathanapally H, Seidu S, Davies MJ, Khunti K. Association between polypharmacy and falls in older adults: a longitudinal study from England. *BMJ Open*. 2017;7(10):e016358. Published 2017 Oct 16. doi:10.1136/bmjopen-2017-016358.
47. Niikawa H, Okamura T, Ito K, et al. Association between polypharmacy and cognitive impairment in an elderly Japanese population residing in an urban community. *Geriatr Gerontol Int*. 2017;17(9):1286-1293. doi:10.1111/ggi.12862
48. Park HY, Park JW, Song HJ, Sohn HS, Kwon JW. The Association between Polypharmacy and Dementia: A Nested Case-Control Study Based on a 12-Year Longitudinal Cohort Database in South Korea. *PLoS One*. 2017;12(1):e0169463. Published 2017 Jan 5. doi:10.1371/journal.pone.0169463
49. Ishii N, Mochizuki H, Sakai K, Ogawa G, Shiomi K, Nakazato M. Polypharmacy Associated with Cognitive Decline in Newly Diagnosed Parkinson's Disease: A Cross-Sectional Study. *Dement Geriatr Cogn Dis Extra*. 2019;9(3):338-343. Published 2019 Sep 10. doi:10.1159/000502351
50. Rawle MJ, Cooper R, Kuh D, Richards M. Associations Between Polypharmacy and Cognitive and Physical Capability: A British Birth Cohort Study. *J Am Geriatr Soc*. 2018;66(5):916-923. doi:10.1111/jgs.15317
51. George C, Verghese J. Polypharmacy and Gait Performance in Community-dwelling Older Adults. *J Am Geriatr Soc*. 2017;65(9):2082-2087. doi:10.1111/jgs.14957
52. Leelakanok N, Holcombe AL, Lund BC, Gu X, Schweizer ML. Association between polypharmacy and death: A systematic review and meta-analysis. *J Am Pharm Assoc (2003)*. 2017;57(6):729-738.e10. doi:10.1016/j.japh.2017.06.002
53. Brockhattingen KK, Anru PL, Masud T, Petrovic M, Ryg J. Association between number of medications and mortality in geriatric inpatients: a Danish nationwide register-based cohort study. *Eur Geriatr Med*. 2020;11(6):1063-1071. doi:10.1007/s41999-020-00390-3
54. Dovjak P. Tools in polypharmacy. Current evidence from observational and controlled studies. *Zeitschrift für Gerontologie und Geriatrie*. 2012; 45(6): 468–472. <https://doi.org/10.1007/s00391-012-0362-y>

55. Hanlon JT, Schmader KE. The Medication Appropriateness Index at 20: where it started, where it has been and where it may be going. *Drugs Aging*. 2013; 30(11): 1-12.
56. Vrdoljak D, Borovac JA. Medication in the elderly- consideration and therapy guidelines. *Acta Medica Academica*. 2015; 44(2): 159-168. DOI: 10.5644/ama2006-124.142.
57. American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc*. 2015; 63: 2227-2246.
58. Campanelli CM. The American Geriatric Society updated Beers criteria for potentially inappropriate medication use in older adults: The American Geriatric society 2012 Beers criteria updated expert panel. *J Am Geriatr Soc*. 2012; 60(4): 616–631. doi:10.1111/j.1532-5415.2012.03923.x.
59. Fick DM, Semla TP. 2012 American Geriatrics Society Beers Criteria: new year, new criteria, new perspective. *J Am Geriatr Soc*. 2012;60(4):614-615. doi:10.1111/j.1532-5415.2012.03922.x
60. Planton J, Edlund BJ. Strategies for Reducing Polypharmacy in older adults. *Journal of Gerontological Nursing*. 2010; 36: 8-12.
61. Rankin A, Cadogan CA, Patterson SM, et al. Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database Syst Rev*. 2018; (9): CD008165.
62. Moriarty F, Hardy C, Bennett K, Smith SM, Fahey T. Trends and interaction of polypharmacy and potentially inappropriate prescribing in primary care over 15 years in Ireland: a repeated cross-sectional study. *BMJ Open*. 2015;5(9):e008656. Published 2015 Sep 18. doi:10.1136/bmjopen-2015-008656
63. Gautam PC. Introducing geriatric medicine to Nepal: an outline of a training programme and a model for the delivery of service. *Kathmandu Univ Med J (KUMJ)*. 2008;6(1):135-140.
64. Pokharel T, Pandey N, Chitrakar G, . Awareness for the need of specialized geriatric health care unit in Tribhuvan University Teaching Hospital. *J Soc Surg Nep*. 2015; 16(3). ISSN 2392-4772.
65. Spinewine A, Fialová D, Byrne S. The role of the pharmacist in optimizing pharmacotherapy in older people. *Drugs Aging*. 2012;29(6):495-510. doi:10.2165/11631720-000000000-00000
66. Gupta M, Agarwal M. Understanding medication errors in the elderly. *NZmedj*. 2013; 126: 62-70.
67. Scott IA, Hilmer SN, Reeve E, et al. Reducing inappropriate polypharmacy: the process of deprescribing. *JAMA Intern Med*. 2015;175(5):827-834. doi:10.1001/jamainternmed.2015.0324
68. Jansen J, Naganathan V, Carter SM, et al. Too much medicine in older people? Deprescribing through shared decision making. *BMJ*. 2016;353:i2893. Published 2016 Jun 3. doi:10.1136/bmj.i2893
69. Endsley S. Deprescribing Unnecessary Medications: A Four-Part Process. *Fam Pract Manag*. 2018;25(3):28-32.
70. Holmes HM, Todd A. The Role of Patient Preferences in Deprescribing. *Clin Geriatr Med*. 2017;33(2):165-175. doi:10.1016/j.cger.2017.01.004

71. Salahudeen MS. Deprescribing medications in older people: a narrative review. *Drugs Today (Barc)*. 2018;54(8):489-498. doi:10.1358/dot.2018.54.8.2856495
72. Reeve E, Moriarty F, Nahas R, Turner JP, Kouladjian O'Donnell L, Hilmer SN. A narrative review of the safety concerns of deprescribing in older adults and strategies to mitigate potential harms. *Expert Opin Drug Saf*. 2018;17(1):39-49. doi:10.1080/14740338.2018.1397625
73. Ruscin JM; Linnebur SA. Drug-Related Problems in the Elderly, Merck Manual, 2014. <https://www.msdmanuals.com/professional/geriatrics/drug-therapy-in-the-elderly/drug-related-problems-in-the-elderly> Accessed on 15 January 2023.
74. Milton JC, Hill-Smith I, Jackson SH. Prescribing for older people. *BMJ*. 2008;336(7644):606-609. doi:10.1136/bmj.39503.424653.80

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