

# 1 EDITORIAL: Evidence for Assessing Drug Safety 2 and Drug Use in Older People

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20 Prescribing for older patients presents several challenges. Older people often suffer from two or more  
21 chronic diseases (multimorbidity) and therefore use a greater number of medications compared to other  
22 age groups. As a result, they are more susceptible polypharmacy, and associated drug-related problems,  
23 including potentially inappropriate medication (PIM), drug ineffectiveness, drug interactions, and  
24 adverse drug events (Nobili et al., 2011; Aggarwal et al., 2020). Consequently, optimizing drug therapy  
25 is a crucial part of caring for an elderly individual. This is increasingly important given the rising  
26 number of elderlies across countries in the coming years, with one in 6 of the world's population over  
27 60 by 2050 and the associated resource implications (World Health Organization, 2021).

28 Many studies (Oliveira et al., 2012; Shah and Hajjar, 2012; Khatter et al., 2021; Xu et al., 2021) point  
29 out that polypharmacy is a risk factor for PIM, particularly for older patients. The more medications a  
30 patient are taking, the more likely they are to have an adverse drug event (ADE), potentially experience  
31 a drug-drug interaction, take a PIM, or be non-compliant to one or more of the medications prescribed  
32 (Shah and Hajjar, 2012).

33 This Research Topic included 23 articles and nine of them (Ambrož et al., 2021; Candeias et al., 2021;  
34 Chen et al., 2021; Kardas et al., 2021; Kurczewska-Michalak et al., 2021; Machado-Duque et al., 2021;  
35 Perpétuo et al., 2021; Schneider et al., 2021; Bobrova et al., 2022) studied PIM and polypharmacy in  
36 elderly. Four of them (Kardas et al., 2021; Khatter et al., 2021; Machado-Duque et al., 2021; Schneider  
37 et al., 2021) estimate the prevalence of PIM or polypharmacy in elderly.

38 In recent years, several strategies and tools have been developed to identify the inappropriate  
39 prescribing of medications. Typically, adaptations and selections have to be made depending on the  
40 setting and the medications available in a country (Motter et al., 2018; Motter et al., 2019). STOPP  
41 (elderly prescription screening tool) and START (elderly prescribing screening tool) are criteria  
42 typically used as a tool for clinicians to review PIMs in older adults and have been endorsed as best  
43 practice by some organizations. The study of Bobrova et al. (Bobrova et al., 2022) developed an  
44 integrated PIM clinical decision support tool for identification of drug-related problems among  
45 geriatric patients in geriatric multi-morbid polypharmacy patients, using the EU-PIM and EURO-  
46 FORTA lists, with a focus on high-risk medications. The articles from Candeias et al. and Perpetuo et  
47 al. (Candeias et al., 2021; Perpétuo et al., 2021) analyzed the concordance and prevalence of PIM  
48 different tools.

49 In particular, polypharmacy is known to cause a higher risk of ADEs as well as drug-drug interactions,  
50 which often leads to poor compliance with prescribed medicines. All these negatively impact on the  
51 health of patients as well as increase the risk of geriatric syndromes, e.g., cognitive impairment or falls.  
52 An important disparity is the difference of sex and gender in the proportion of types of medication used  
53 among older patients (Lu et al., 2021), which needs to be factored into future prescribing.

54 Avoidable ADEs are the consequences of inappropriate drug prescribing including inappropriate  
55 polypharmacy. This, in turn, leads to increased costs and health care expenditures (Maher et al., 2014).  
56 The studies of Alnijadi et al. and Katsuno et al. (Alnijadi et al., 2021; Katsuno et al., 2021) analyzed  
57 the direct cost of managing adverse drug events and that of avoidable ADEs as well as cost-related  
58 medication non-compliance with medicines on healthcare utilization and patient-reported outcomes.  
59 Consequently, we are seeing health authorities across countries instigate activities to improve  
60 prescribing in the elderly and reduce ADEs and their associated costs, with these activities likely to  
61 grow with an increasing elderly population (MacBride-Stewart, 2021).

62 Numerous factors contribute to the appropriateness and comprehensive quality of drug prescribing.  
63 The process of prescribing a medication is multifaceted and includes: verifying that a drug is indicated  
64 and avoiding overuse of medicines for prevention, selecting the best drug, determining a dose and  
65 duration appropriate for the patient's physiologic status, monitoring for effectiveness and toxicity,  
66 educating the patient about expected side effects, and indications for seeking a consultation.

67  
68 Zazzara et al. (Zazzara et al., 2022) verified the medication use and costs among older adults aged  
69 90 years and conclude that the persistent use of preventive medications highlights the potential lack of  
70 awareness regarding medication rationalization among clinicians and provided guidance for optimizing  
71 prescriptions. Chen et al. (Chen et al., 2021) identified factors that have an impact on the management  
72 of potentially inappropriate prescribing and concluded that gerontology practitioners should be prudent  
73 in applying clinical guidelines to provide personalized, comprehensive assessment of decision making  
74 of prescriptions, especially in socioeconomically deprived areas. Qu et al. (Qu et al., 2021) explored  
75 the relationship between drug literacy and frailty and conclude that the first was an important  
76 consideration in the development, implementation, and evaluation of frailty.

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78 Approaches to decrease inappropriate prescribing in older adults include educational interventions,  
79 peer comparison feedback, computerized order entry and decision support, multidisciplinary team care  
80 led by physicians, clinical pharmacists, and combinations of these approaches (Rochon, 2022). The  
81 scoping review of (Kurczewska-Michalak et al., 2021) published in this Research Topic mapped  
82 available interventions and more complex strategies to prevent and manage polypharmacy in the older

83 adults and discussed their potential implementation. The authors concluded that the development of  
84 strategies for the detection and prevention of drug-related problems is important to guide and support  
85 clinical decision-making and strengthen research into drug safety. This is an essential condition for  
86 achieving wide-ranging improvements in the management of elderly patients. Whilst different  
87 approaches have been identified to avoid drug-related problems in older patients, there is still  
88 insufficient information about their clinical importance or their public health impact. The authors also  
89 suggested that guidance on polypharmacy management in older adults is still limited. Initiatives to  
90 understand and conceptualize healthcare professional's barriers and enablers can be used to increase  
91 knowledge translation and strengthen capacity for appropriate interventions in routine clinical practice  
92 (Motter et al., 2021)

93  
94 This Research Topic also included studies comparing the efficacy and safety of anticoagulants or  
95 antiplatelets in cardiovascular disease (Wawruch et al., 2021; Zhao et al., 2021; Li et al., 2022). This  
96 is important as there were concerns with excessive bleeding in the elderly when dabigatran, the first  
97 non-vitamin K antagonist oral anticoagulants (NOAC) was first launched (Malmström et al., 2013).  
98 Physician knowledge has now grown, with more recent studies comparing key issues such as  
99 effectiveness and safety among the NOACs (Mueller et al., 2019; Komen et al., 2021).

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101 Studies that analyzed the safety and efficacy of medications in other common problems in older  
102 patients were also included in this research topic. Two studies (Huang et al., 2021; Yang et al., 2022)  
103 estimated the efficacy of propofol in adult or elderly patients with different conditions. Two  
104 systematic reviews (Huang et al., 2021; Zhang et al., 2021) studied the efficacy and safety of drug use  
105 in secondary care. Gao et al. (Gao et al., 2021) conducted a network meta-analysis to summarize all  
106 available evidence about relative effectiveness of different pharmacotherapy of macular edema  
107 secondary to retinal vein occlusion. Yu et al. (Yu et al., 2021) conducted a cross-sectional study,  
108 analyzing the trends in the topical prescription's treatment of old patients with dry eye disease.

109 Optimizing the use of medications is increasingly recognized as an important pillar in the health care  
110 of older people. Collectively, this research topic highlights pertinent concerns related to the safe use of  
111 medications in this age group and promotes awareness of optimizing older adults' medication regimens.  
112 The results demonstrate that improving the quality of medication use and medication safety are still  
113 important challenges for healthcare professionals who care for older patients. Other initiatives are  
114 required for this field to reach its full potential of optimizing drug use in older patient to improve their  
115 health care outcomes within available resources.

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