Appropriate Prescribing and Important Drug Interactions in Older Adults

Jeffrey Wallace, MD, MPH[a,*], Douglas S. Paauw, MD, MACP[b]

KEYWORDS

• Elderly • Polypharmacy • Drug interactions • Adverse drug events
• Potentially inappropriate medications • Adherence

KEY POINTS

- Polypharmacy, the use of 5 or more medications, is common in older adults.
- Polypharmacy is associated with increased rates of adverse drug events, use of potentially inappropriate medications, and increased drug interactions.
- Clinicians need to be aware of drug-drug and drug-disease interactions that are common and important.
- Tools and approaches to reducing polypharmacy can enhance the care and health outcomes of older adults.

INTRODUCTION

Adults 65 years of age and older represent 14% of the US population, but take 30% of prescription medications and 50% of over-the-counter medications.[1] Most adverse drug events occur in older adults, a fact that is attributable to their greater use of medications, increased vulnerability from underlying medical conditions, and age-related physiologic changes (**Box 1**).[2] The elderly also often suffer from suboptimal medication prescribing that ranges from underuse to overuse to misuse of medications. This article provides clinicians with approaches to optimize medication management in older adults with a focus on reducing polypharmacy and complications related to polypharmacy, medication adherence, use of potentially inappropriate medications, adverse drug reactions, and clinically important drug interactions in older adults.

[a] Division of Geriatric Medicine, Department of Internal Medicine, University of Colorado School of Medicine, 12631 East 17th Avenue, B-179, Aurora, CO 80045, USA; [b] Division of General Internal Medicine, Department of Medicine, University of Washington, 4245 Roosevelt way NE, #MC354760, Seattle, WA 98105, USA
* Corresponding author.
E-mail address: jeff.wallace@ucdenver.edu

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Box 1
Age-related changes that increase susceptibility to adverse drug effects

Pharmacodynamic changes: altered sensitivity to medications (very few)

Increased sensitivity

- Warfarin, opiates

Decreased sensitivity

- β-agonists

Pharmacokinetic changes: alterations in factors that affect drug concentration

Absorption: minimal clinical relevance (ie, if med is swallowed it generally will be absorbed)

Distribution: significant clinical relevance but not readily predictable

- Increased fat mass increases volume distribution and half-life of lipophilic medications
- Decreased total body water results in decreased volume of distribution and increased concentration of water-soluble drugs
- Decreased fat-free mass/plasma protein leads to higher percentage of unbound (active) drug

Hepatic metabolism: some clinical relevance but not consistently predictable

- Decreased first-pass metabolism leads to increased concentration of drugs that typically have high levels of first-pass metabolism (ie, hepatic clearance before reaching systemic circulation)
- Diazepam, propranolol, lidocaine

Renal clearance: significant impact and readily predictable

- Increased concentration of renally cleared drugs
- Serum creatinine alone does *not* provide adequate information to guide dosing
- Use Cockcroft-Gault (CG)[a] to estimate glomerular filtration rate (eGFR)
  - More conservative that other calculations (eg, modification of diet in renal disease [MDRD]), less likely to overestimate eGFR, especially in frail older adults
  - Drug company renal dose recommendations are based on CG

[a] CG = [(140 − age) × wt (kg)] × 0.85 if female/(72 × serum creatinine).

POLYPHARMACY

Polypharmacy, defined as taking 5 or more medications a day, is common in older adults.[3,4] One national survey found that more than 50% of female Medicare beneficiaries took 5 or more medications daily, with 12% taking 10 or more medications a day.[5] Although use of 5 or more medications often appears to be mandated by evidence-based care guidelines, evidence is generally lacking for applying such guidelines to older patients with multiple medical conditions. Conversely, evidence indicates that the use of more medications is associated with increased medication side effects and adverse health events, and these risks increase in a nonlinear fashion as number of drugs increases to 5 or more (**Fig. 1**). One study found that when compared with persons taking 4 or fewer medications, the risk of an adverse drug reaction nearly doubled (odds ratio [OR] 1.9, 95% confidence interval [CI] 1.35–2.68) for persons taking 5 to 7 medications, and quadrupled (OR 4.07, 95% CI 2.93–5.65) for those taking 8 or more medications.[4] Although not always inappropriate, the use of 5 or more medications is associated with higher rates of unwanted health outcomes (**Box 2**).[4,6] These and other issues related to polypharmacy are outlined in this section.