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Polypharmacy and falls in older people: balancing evidence-based medicine against falls risk

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Abstract

The term polypharmacy has negative connotations due to its association with adverse drug reactions and falls. This spectrum of adverse events widens when polypharmacy occurs among the already vulnerable geriatric population. To date, there is no consensus definition of polypharmacy, and diverse definitions have been used by various researchers, the most common being the consumption of multiple number of medications. Taking multiple medications is considered a risk factor for falls through the adverse effects of drug–drug or drug–disease interactions. Falls studies have determined that taking ≥ 4 drugs is associated with an increased incidence of falls, recurrent falls, and injurious falls. In light of existing evidence, careful and regular medication reviews are advised to reduce the effect of polypharmacy on falls. However, intervention studies on medication reviews and their effectiveness on falls reduction have been scarce. This article reviews and discusses the evidence behind polypharmacy and its association with falls among older individuals, and highlights important areas for future research.

Polypathy is prevalent in the geriatric population and is associated with adverse effects and hospital admissions. One Italian study using an outpatient pharmacy database, including 887 165 medication users aged ≥ 65 years, reported that 39.4% of this sample was exposed to ≥ 1 episode of polypharmacy during the 1-year study period. The prevalence of polypharmacy substantially increases with age and with a greater number of chronic conditions [8]. In a German study involving 466 older people aged ≥ 70 years, 26.7% of patients used ≥ 5 drugs chronically [9]. The prevalence was even higher in an Austrian study involving 543 community participants aged ≥ 75 years, in which 58% of participants fulfilled the criterion for polypharmacy, defined as ≥ 6 drugs [10]. The prevalence of polypharmacy is highest among frail hospitalized patients. In a study involving 109 hospital patients aged 75 years only, the prevalence of polypharmacy (use of ≥ 5 drugs) was 87.2% on admission and 91.8% on discharge [11]. However, with the increasing number of large multicenter trials demonstrating significant survival benefits in prophylactic treatment for common chronic conditions, many geriatricians consider polypharmacy to be unavoidable among the elderly. This article provides an overview of the changing evidence on polypharmacy among older patients and its role as a risk factor for falls among the elderly in order to provide up-to-date recommendations for the management of polypharmacy among older fallers as well as identify clear gaps in the evidence for future research.

Methods

We searched Medline, Web of Science, EMBASE, Science direct, and CINAHL for English-language articles published

History

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The use of multiple medications is considered essential as standard treatment between 2000 and 2014. We searched for subject headings, article keywords, titles, and abstracts using the search terms polypharmacy OR inappropriate prescribing OR multiple medications, and accidental falls OR falls, and aged OR elderly OR older people. Additional articles were obtained through the authors’ existing collections and by cross-referencing relevant articles. We included articles reporting a mean age of ≥ 65 years that evaluated the issue of polypharmacy, multiple medications, inappropriate prescribing, and falls. Articles were excluded if they were information based or related to specific classes of medicines. The titles and abstracts of 256 articles were examined, following which 60 full-text articles were selected and reviewed. Twenty articles were subsequently selected by two researchers independently based on the above inclusion and exclusion criteria. Seven articles were excluded as they were information based. Data extracted from the 13 selected articles on polypharmacy and falls is summarized in Table I.

### Definitions and trends of polypharmacy

There is currently no consensus definition for polypharmacy [12]. Definitions used in studies usually included the total number of medications consumed by the patient [13]. Existing definitions may or may not include over-the-counter and complementary treatments. Published papers have used varying cutoffs for polypharmacy, ranging from 2 to 9 medications [14]. Table II lists several published definitions used to define polypharmacy.

Polypharmacy in a patient can occur for the treatment of one disease or several diseases. In addition, the use of multiple medications is considered essential as standard treatment.
for conditions such as diabetes, tuberculosis, and acquired immune deficiency syndrome [15]. The term polypharmacy has also been used interchangeably with inappropriate prescribing [12]. Inappropriate prescribing or over-the-counter inappropriate medication use leads to an increased risk of polypharmacy, and vice versa: polypharmacy leads to an increased risk of inappropriate prescribing [16,17]. Therefore, some authors refer to appropriate or rational polypharmacy and inappropriate or irrational polypharmacy, with rational polypharmacy being justified among older people because of the existence of multiple morbidities [18].

Polypharmacy, or the use of “too many” medications, may be necessary in the older population with multiple pathologies in view of clear substantiation on improved clinical end points for diseases affecting mainly older people, such as ischemic heart disease, stroke, osteoporosis, and hypertension [12]. However, the risk of cumulative side effects and drug interactions increases with the consumption of multiple medications, even if an individual is prescribed multiple medications for clinically justified reasons. Polypharmacy can be associated with several adverse outcomes, and the risk of falls increases with the use of 4 or 5 medications, as demonstrated by various studies [19–22]. Therefore, research studies on “falls” have generally defined polypharmacy as the use of 4 or 5 medications by a patient.

The trend towards polypharmacy is increasing with time. A Swedish study analyzed the number of drugs dispensed for the entire country from 2005 to 2008, and found that the prevalence of polypharmacy (defined as ≥ 5 drugs) had increased by 8.2% and the prevalence of excessive polypharmacy (defined as ≥ 10 drugs) increased by 15.7% during this time span. The prevalence of excessive polypharmacy displayed a clear age trend, with the largest increase being for patients aged ≥ 70 years [23]. A population-based study that included 339 participants aged ≥ 70 years reported that the use of common cardiovascular medications increased dramatically with age, and the use of ≥ 3 cardiovascular medications increased from 39% to 54% during a 5-year follow-up period [24]. Not only cardiovascular medications but also psychotropic medications contribute to increasing polypharmacy, with a 22.2% increase in the prescription of ≥ 3 psychotropic medications in the past 3 decades [25]. The increase in polypharmacy with increasing age is linked to an age-related increased prevalence of diseases such as hypertension, ischemic heart disease, and heart failure.

### Assessment of polypharmacy

The risk of falls increases linearly with the increase in the number of medications. However, this increase in the number of medications is also proportional to the increase in fall-risk increasing drugs which are independent predictors of falls [26]. Different tools have been developed by researchers to assess drug-induced adverse events among older people. The GastroNet score predicts an increased risk of adverse drug events; the score takes into account the number of comorbidities, number of drugs, heart failure, renal failure, liver disease, and previous adverse drug reactions [27]. Similarly, the Medication Regimen Complexity Index can assess the complexity of medication regimens based on the dosage of drugs [28]. However, the risk factors for falls as well as the medications that increase the risk of falling differ from those associated with increased risk of adverse effects among older people, with there being no published tool to assess the risk of falls by taking into account the presence of polypharmacy, the medications that increase the risk of falling, and concomitant illness.

A universal definition of polypharmacy that includes the number of medicines, the duration of use, and the use of nonprescription medications would aid research efforts, which in turn would improve clinical practice by the development of standard guidelines to address potential risks to the elderly population. Needless to say, there is an urgent need for large, well-designed, and adequately powered studies to provide answers to this pressing problem of polypharmacy in association with falls and other adverse events. Furthermore, the growing number of trials suggesting the long-term benefits of newer medications alongside the rapidly expanding older population with multiple comorbidities is likely to dictate that both the definition of polypharmacy and safe prescribing will be a fluid process that will need to be updated on a regular basis.

### Why is polypharmacy a problem?

Older patients are two to three times more likely to experience adverse effects of drugs than younger patients [29]. With the increasing trend toward multiple comorbidities and multiple medications with aging, the risk of adverse drug events including falls also increases [30]. Adverse drug events account for up to 25% of hospitalizations in elderly patients [30]. Gurwitz et al. [31] evaluated the records of 30,397 Medicare enrollees aged ≥ 65 years and reported the incidence of adverse drug events as 50.1 per 1000 person years. The authors, however, did not explore the cumulative effect of multiple prescribing in their setting. Viktil et al. [32] conducted a study of 827 older patients and found a linear increase in adverse drug events with the increase in number of drugs; 47% of the patients used ≥ 5 drugs, and the number of adverse events of “drug interactions” was significantly higher in this group.

As mentioned earlier, polypharmacy increases the likelihood of inappropriate medication intake. A Singaporean study involving 454 older nursing home residents found a significant association between polypharmacy and inappropriate medication use [33]. We have classified factors associated with polypharmacy into extrinsic and intrinsic factors, as described in the following subsections; inappropriate prescribing is an extrinsic factor that could be modified, while intrinsic factors occur within the patient’s body and usually cannot be modified but should be carefully considered for safe prescribing.

### Extrinsic factors

Extrinsic factors are those that do not occur within the patient and can be associated with the choice of drugs, drug dosing, duration, contraindications, potential interactions,
and duplications. Medications are considered inappropriate if they are prescribed despite being contraindicated, if the risk of treatment potentially outweighs the benefits or if the medication can potentially interact with the existing pathology or with another medication [13]. In addition, medications are sometimes prescribed at inappropriately high doses or for longer periods than recommended [34]. In the study by Steinman et al. [17], involving 196 community-dwelling seniors aged ≥ 65 years who were prescribed ≥ 5 medications daily, 65% were using ≥ 1 inappropriate medications; 57% were taking medications that were ineffective, not indicated, or therapeutically duplicative; and 37% were taking medications considered to be inappropriate according to the Beers criteria. A meta-analysis of 19 studies, 14 of which used the Beers criteria to assess appropriateness, found that majority of prescriptions given to older persons could be considered inappropriate [35]. Inappropriate polypharmacy is in turn responsible for many potentially avoidable emergency department visits by older patients [30].

In a 7-year study involving 909 patients aged ≥ 66 years, it was found that hospital admissions due to drug interactions can often be avoided because they are due to known drug-drug interactions [36]. The most convincing evidence for this exists in the case of psychotropic medications that have been commonly and inappropriately prescribed to the elderly over the past 50 years [37]. An analysis of 2.5 million Medicare beneficiaries living in nursing homes found that 27.6% of residents were receiving ≥ 1 psychotropic drug with only 41.8% compliance with available prescribing guidelines, whereas the remaining 58.2% were being prescribed these medications without proper indications, as duplicative drugs with different trade names, or in inappropriate doses [38].

Although drug–drug interactions are usually mentioned in the drug formulary, the cumulative effect of the use of multiple drugs is not necessarily well documented. For example, more than one antihypertensive agent may be required to control blood pressure, while recent evidence has suggested that the high-intensity dosage of antihypertensives is associated with an increased risk of falls due to their cumulative hypotensive effects [39]. It remains to be established, however, whether the risk of adverse events from polypharmacy outweighs the potential benefits gained from strict adherence to blood pressure targets.

**Intrinsic factors**

Aging is associated with changes in physiological mechanisms that alter the pharmacodynamics and pharmacokinetics of drugs [40]. The pharmacokinetic changes associated with aging occur as a result of a reduction in renal or hepatic clearance, leading to increased serum drug levels and consequent drug toxicity even with the prescription of normal recommended adult doses [40]. Nutritional status and body composition also affect drug metabolism. As lean body mass may decrease by 12% to 19%, body water content may decrease by 10% to 15%, and total body fat may increase by 14% to 35% in an older person, the plasma levels of drugs primarily absorbed by muscle increase, resulting in increased plasma concentration of hydrophilic drugs [41]. The pharmacodynamic changes associated with increasing age include decreased responsiveness to β-adrenergic receptor agonists (β-agonists) and decreased α-adrenergic receptor activity. In addition, the brain may be exposed to higher drug levels due to the reduced effectiveness of the blood–brain barrier in the elderly [29]. The alteration in drug handling associated with aging, however, is unpredictable due to the highly varied number of deficits found in each individual. Additionally, the presence of dementia may lead to patient errors, especially among those with complex medication regimens [30].

**Polypharmacy and falls**

Polypharmacy has been considered as a significant risk factor for falls among the older population [42]. The risk of falls differs with the type of medication ingested, with central nervous system drugs, including antipsychotics, antiparkinsonian drugs, and narcotic analgesics, considered to be most strongly associated with falls [43], whereas cardiovascular drugs, especially antihypertensives, have an inconsistent relationship [39,44]. These drugs are therefore termed “fall-risk-increasing drugs”, listed in Table III, based on findings from systematic reviews. The Swedish National Board of Health and Welfare classified opioids, antipsychotics (lithium excluded), anxiolytics, hypnotics and sedatives, and antidepressants as fall-risk-increasing drugs, whereas cardiovascular drugs, including vasodilators, antihypertensives, diuretics, beta-blocker agents, calcium channel blockers, renin-angiotensin system inhibitors, and adrenergic receptor antagonists, and dopaminergic agents are drugs that cause or worsen orthostatic hypotension and are indirectly related to falls [45]. Along with specific drugs, the number of drugs is a crucial factor for falls among the elderly population.

Most studies have used the definition “multiple number of drugs used by an older person” and ≥ 4 medications had been used as a determinant of an increased fall risk. Published studies uniformly demonstrate a significantly increased risk of falls with polypharmacy despite variable sample populations, and the 2010 American Geriatrics Society/British Geriatric Society Joint Falls Prevention Guidelines advocate medication reduction and withdrawal for all older fallers [46]. Table I summarises the findings of available studies relating polypharmacy to falls. In a longitudinal survey of patients with diabetes, the elderly users of ≥ 4 prescription medications were twice as likely to fall as those who used one or two prescription medications [47]. The longitudinal Concord Health and Ageing in Men Project study aimed to determine the number of medications associated with geriatric syndromes and found that taking 4.5 medications was associated with frailty, disability, falls, and mortality. The authors, therefore, suggest that the use of ≥ 5 medications is associated with an increased risk of falls [48].

A recent Australian hospital–based study including 204 patients ≥ 60 years found that drug–drug interactions along with the number of fall-risk-increasing drugs and the total number of drugs were significantly associated with falls among the frail elderly. Polypharmacy and increased number of fall-risk-increasing drugs on discharge prescriptions was
It is only possible to attribute falls to a single medication should that particular drug be inappropriately prescribed or when the falls occur as a result of physical illness or frailty; in fact, the multifactorial nature of falls dictates that it is likely to be a combination of both, along with additional factors [50].

### Table III. Risk of falls and drugs usage in older people: results from meta-analysis.

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Examples</th>
<th>Odds ratio (95% confidence interval)</th>
<th>Bloch et al., 2013 [71]</th>
<th>Woolcott et al., 2009 [72]</th>
<th>Leipzig et al., 1999 [73,74]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taking drugs (yes/no)</td>
<td>Consuming any medication</td>
<td>4.24 (3.06–5.88)*</td>
<td>–</td>
<td></td>
<td>1.37 (1.25–1.64)*</td>
</tr>
<tr>
<td>Polypharmacy</td>
<td></td>
<td>1.71 (1.50–1.96)*</td>
<td>–</td>
<td>1.20 (0.92, 1.58)</td>
<td>1.59 (1.52–1.94)*</td>
</tr>
<tr>
<td>Cardiovascular drugs</td>
<td></td>
<td>0.78 (0.67–0.90)</td>
<td>–</td>
<td>1.08 (1.02, 1.16)*</td>
<td>1.22 (1.05, 1.42)*</td>
</tr>
<tr>
<td>Any antihypertensives</td>
<td></td>
<td>1.10 (1.05–1.16)*</td>
<td>1.24 (1.01–1.50)*</td>
<td></td>
<td>1.71 (1.50–1.96)*</td>
</tr>
<tr>
<td>β-blockers</td>
<td></td>
<td>1.12 (1.04–1.21)*</td>
<td>1.14 (0.97–1.33)</td>
<td>0.93 (0.94, 1.14)</td>
<td></td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td></td>
<td>1.21 (1.15–1.28)*</td>
<td>–</td>
<td>0.94 (0.77, 1.11)</td>
<td></td>
</tr>
<tr>
<td>Diuretics</td>
<td></td>
<td>–</td>
<td>–</td>
<td>1.08 (1.02, 1.16)*</td>
<td>1.22 (1.05, 1.42)*</td>
</tr>
<tr>
<td>Digoxin</td>
<td></td>
<td>1.48 (1.11–1.99)*</td>
<td>–</td>
<td>1.08 (1.02, 1.16)*</td>
<td>1.22 (1.05, 1.42)*</td>
</tr>
<tr>
<td>Type 1a antiarrhythmics</td>
<td></td>
<td>1.12 (0.94–1.36)</td>
<td>1.13 (0.95, 1.36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasodilators</td>
<td>α-blockers (prazosin, doxazosin, alfuzosin, tamsulosin)</td>
<td>1.12 (0.94–1.36)</td>
<td>1.13 (0.95, 1.36)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>nitrites (glyceryl trinitrate, isosorbide mononitrate, isosorbide dinitrate)</td>
<td>–</td>
<td>–</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychotropic</td>
<td></td>
<td></td>
<td>–</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Typical (chlorpromazine, haloperidol)</td>
<td>1.74 (1.55–1.95)*</td>
<td>1.73 (1.52–1.97)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Atypical (clozapine, olanzapine)</td>
<td>1.37 (1.36–1.61)*</td>
<td>1.59 (1.37–1.83)</td>
<td>1.50 (1.25–1.79)*</td>
<td></td>
</tr>
<tr>
<td>Sedative hypnotics</td>
<td>Barbiturate, methaqualone, thalidomide</td>
<td>1.53 (1.39–1.68)*</td>
<td>1.47 (1.35–1.62)*</td>
<td>1.54 (1.40, 1.70)*</td>
<td></td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td></td>
<td>1.61 (1.43–1.73)*</td>
<td>1.57 (1.43–1.72)*</td>
<td>1.48 (1.23, 1.77)*</td>
<td></td>
</tr>
<tr>
<td>Short acting</td>
<td>Lorazepam, alprazolam</td>
<td>–</td>
<td>–</td>
<td>1.44 (1.09, 1.90)*</td>
<td></td>
</tr>
<tr>
<td>Long acting</td>
<td>Diazepam, clonazepam</td>
<td>–</td>
<td>–</td>
<td>1.32 (1.09, 1.90)</td>
<td></td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Selective serotonin reuptake inhibitors (fluoxetine, citalopram, Paroxetine), selective norepinephrine reuptake inhibitors (venlafaxine, duloxetine), tricyclic antidepressants (imipramine, desipramine), nontricyclic (tetracyclic and anticyclic) antidepressants</td>
<td>1.59 (1.43–1.75)*</td>
<td>1.68 (1.47–1.91)*</td>
<td>1.66 (1.41, 1.95)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(mirtazapine, trazodone, bupropion)</td>
<td>–</td>
<td>–</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiepileptics</td>
<td>Acetazolamide, carbamazepine, gabapentin, lamotrigine</td>
<td>1.56 (1.28–1.90)*</td>
<td>–</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antiparkinsonians</td>
<td>Dopamine and dopamine receptor agonists (levodopa, levodopa and carboxylase-inhibitor), dopamine receptor antagonists (bromocriptine, pergolide, cabergoline, ropinirole, pramipexole)</td>
<td>1.55 (1.21–1.97)*</td>
<td>–</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Analgesics</td>
<td>Fentanyl, oxycodone, hydrocodone, morphine, hydromorphone</td>
<td>1.33 (1.07–1.65)*</td>
<td>–</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>1.43 (1.27–1.61)*</td>
<td>0.96 (0.78–1.18)</td>
<td>0.97 (0.78, 1.12)</td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Diclofenac sodium, ibuprofen, indomethacin, naproxen</td>
<td>1.25 (1.11–1.42)*</td>
<td>1.21 (1.01–1.44)*</td>
<td>1.16 (0.97, 1.38)</td>
<td></td>
</tr>
<tr>
<td>Metabolic and endocrine drugs</td>
<td>Sugars, insulin, amino acids, lipids, insulin, hormones</td>
<td>1.39 (1.20–1.62)*</td>
<td>–</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>2.03 (1.52–2.72)*</td>
<td>–</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significant OR.

Abbreviations: ACE = angiotensin-converting enzyme; NSAID = nonsteroidal anti-inflammatory drug.
The recent studies by Callisaya et al. [39] and Tinetti et al. [55] added a newer dimension to the question of medication burden. They evaluated the use of antihypertensives by calculating the dose burden, and found that individuals on higher doses were more likely to experience serious falls. Therefore, it may be unlikely that the risk of falls can be assessed by simply counting the number of medications. Instead, the attending physician needs to be armed with prior knowledge from validated studies about the potential adverse effects of individual medications and the risk of cumulative effects of multiple medications, as well as the underlying risk factors for falls that preexisted in the patient prior to embarking on the prescription of a new drug to an older individual.

**Effect of medication reviews on falls**

Although the above body of evidence suggests polypharmacy to be a risk factor for falls, and there is evidence suggesting the potential role of medication reviews, there is limited evidence demonstrating the actual benefit of medication reviews and drug withdrawal. A study from the Netherlands analyzing pharmacotherapy in 102 community-dwelling older patients on polypharmacy (aged ≥ 75 years, using ≥ 4 medicines regularly) reported that 98% of prescriptions could be modified with the use of regular medication reviews [56]. A systematic review including 31 trials concluded that some medications can be safely withdrawn without any harm. However, the evidence about whether the withdrawal has any benefits was demonstrated by only a few studies evaluating the withdrawal of psychotropic medications [57].

Based on currently available literature, we can deduce that a regular review of medications is advisable in older patients who are receiving regular-prescribed medications. Decisions about discontinuation of inappropriate or fall risk-increasing medications should be supported by available evidence. Unnecessary or duplicative medications should be withdrawn after review, and medications necessary for disease management should be replaced with safer alternatives or dose titrated as appropriate. The withdrawal of fall-risk-increasing drugs should help achieve the dual benefits of both decreasing the number of drugs consumed and decreasing the risk from specific culprit medications.

However, although medication reviews have been advocated by international guidelines in the management of falls [6], few trials have positively demonstrated a reduction in the risk of falls with the withdrawal of fall-risk-increasing medications or a reduction in dose burden. In a prospective study involving 139 older participants, psychotropic drugs (sedatives, antidepressants, neuroleptics), cardiovascular drugs (antihypertensives, nitrates, antiarrhythmics), analgesics, and hypoglycemics were withdrawn from 67 patients’ prescription, with a reduction in falls and with the greatest benefit observed with the withdrawal of cardiovascular medications [58].

Psychotropic medication withdrawal has been more fruitful as an intervention for falls reduction, as adverse events attributed to these medications are more common and easily preventable than those attributed to non-psychotropic medications [59]. In the study by Salonoja et al. [60] involving 591 participants (aged ≥ 65 years), the individuals who had psychotropic medications withdrawn were significantly less likely to sustain serious falls compared with those who had opiates and anticholinergic medications withdrawn. A systematic review on drug withdrawal stated that psychotropic withdrawal can be effective in fall prevention, whereas the reduction of polypharmacy was shown to improve cognitive function. The authors, however, were unable to demonstrate any significant association between a reduction in the number of medications in individuals with polypharmacy and fall prevention [61]. The randomized controlled trial by Campbell et al. [62] found that withdrawal of psychotropics led to a 66% reduction in the fall rate, but they concluded that it was difficult to achieve permanent withdrawal. The authors, therefore, emphasize that withdrawal of medications must be individually tailored depending on the patient’s condition and after weighing the benefit-versus-risk ratio, with the withdrawal intervention targeting mainly individuals at high risk of falls. Further research is needed to determine the effects of medication review and drug withdrawal on falls as well as on comorbidities for which these drugs are prescribed and the long-term effects of withdrawal on end-organ damage and survival rates.

**Conclusion**

The art of prescribing among older patients has become more complicated than ever before with the explosion of evidence-based medicine advocating the use of combinations of medications for primary prophylaxis and secondary prevention. Furthermore, the absence of a universal definition of polypharmacy has resulted in the use of diverse definitions by researchers, which makes it difficult to interpret and generalize the results of different studies. Studies of falls have mainly defined polypharmacy as prescribing ≥ 4 drugs. However, it is no longer reasonable to define polypharmacy just by the number of medications, as other factors such as the benefit-to-risk ratio of fall risk drugs versus efficient management of diseases and the existence of comorbidities must be also taken into account for safe prescribing. We have found that while inappropriate polypharmacy is associated with adverse drug reactions in older people, when it comes to the risk of falls, polypharmacy remains a significant factor regardless of whether the definition of ≥ 4 or ≥ 5 medications is used, with or without the use of fall-risk-increasing drugs. However, the use of fall-risk-increasing drugs and inappropriate medication intake tends to increase with the increase of polypharmacy. Prescriptions for older patients, therefore, should be individualized and subject to frequent periodic reviews, while consistently striving to minimize the total number and amount of medications consumed by the patient. In addition, ad hoc reviews should be precipitated by any
Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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