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RESEARCH ARTICLE

Anticholinergic and sedative medications exposure in older patients: a cross-sectional study

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Abstract

Background The Drug Burden Index is a risk assessment tool used to quantify anticholinergic and sedative medications burden of older patients. There have been no previously published reports the exposure of anticholinergic and sedative medications in China. *Objective* We investigated the prevalence and correlates risk factors of anticholinergic and sedative medications in hospitalized older patients with polypharmacy in China. *Settings* The Department of Geriatrics in a tertiary care teaching hospital. *Methods* A retrospective analysis of patient medical records of hospitalized older patients with polypharmacy was undertaken at a large university teaching hospital in China. Polypharmacy was defined as the regular use of more than five medications. Prescribing of anticholinergic and sedative medications was identified using the medication list of the Drug Burden Index, and logistic regression analysis determined associations between drug exposure and independent variables. Main outcome measure Anticholinergic and sedative medications identified by the Drug Burden Index. *Results* A total of 383 patients were included in this study, with an average age of 82.6 ± 7.0 years and included 72.9% (279/383) male patients. Of the study participants, 23.8% (91/383) were prescribed anticholinergic and sedative medications. Of the 106 medicines identified by the Drug Burden Index, the most frequently prescribed medications were estazolam in 51.9% (55/106), terazosin in 14.1% (15/106), loratadine in 10.4% (11/106), and cetirizine in 5.7% (6/106); these four medications accounted for 82.1% of the anticholinergic and sedative medications. Drug exposure was associated with age ≥ 80 years (OR 2.246; 95% CI 1.100–4.586), the number of prescribed medications (OR 1.102; 95% CI 1.018–1.193), and symptoms of insomnia (OR 28.990; 95% CI 14.197–59.200). *Conclusions* The findings of this study showed that the prevalence of anticholinergic and sedative exposure in hospitalized older patients with polypharmacy in China. The prevalence of exposure of anticholinergic and sedative medications was 23.8%. According to the Drug Burden Index estazolam and terazosin were the most common medications in the sedative or anticholinergic drug class, respectively.

Keywords Anticholinergic effects · China · Drug Burden Index · Polypharmacy · Sedatives

Impact of findings on practice

- The Drug Burden Index could be a valuable tool for clinicians considering prescribing or deprescribing medications for older people in China.
- According to the Drug Burden Index, estazolam and terazosin are the most common medications in the sedative or anticholinergic drug class in a Chinese geriatric department. Clinicians should be cautious in prescribing.

Introduction

Older people are more susceptible to adverse drug reactions (ADR) due to a variety of physiological and environmental factors, while polypharmacy has also been recognized as an important risk factor for ADR in older patients [1]. The prevalence of polypharmacy, which is usually defined as the use of five or more regular medications, increases with age and multiple chronic diseases and has been estimated to occur in between 40–70% of people aged 65 years and above [2]. The consequence of ADR attributed to polypharmacy may be the

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cause of one or more of the 'geriatric syndromes' that impact the functional ability and quality of life of older people [1].

Some of the most widely used medications in older people are anticholinergic and sedative drugs, which are commonly prescribed to treat urinary incontinence, insomnia, anxiety, allergies, and chronic obstructive pulmonary disease (COPD) [3]. Anticholinergic medications may cause dry mouth, constipation, blurred vision, increased heart rate, and confusion. Sedative medications commonly produce adverse cognitive and psychomotor events, increased falls, delirium, increased risk of bone fractures, daytime fatigue, and impaired cognitive function [4]. Previous studies have supported that medications with either anticholinergic or sedative properties are associated with impaired motor and cognitive function [5, 6].

The Drug Burden Index (DBI) was developed and published in 2007 by Hilmer et al. [7] and provides a model for the measurement of the effects of cumulative exposure to both anticholinergic and sedative medications on physical and cognitive function in older adults. Previous reports from several countries, other than China, have shown that an increased DBI is associated with poor physical function, frailty, delirium, falls, reduced speed of gait and reduced grip strength in older patients [8, 9]. No previously papers report the exposure of anticholinergic and sedative medications and the correlates risk factors of DBI exposure in hospitalized older patients with polypharmacy in China.

Aim of the study

The aim of this study was to use the DBI to investigate the prevalence and correlated risk factors of anticholinergic and sedative medications in hospitalized older patients with polypharmacy in China.

Ethics approval

The study protocol was approved by the Ethics Committee of Peking University (2017 RESEARCH No. 39), First Hospital. Each participant provided written informed consent to be included in the study.

Methods

Study design and patient selection

This retrospective, cross-sectional study was conducted at Peking University First Hospital, a 1500-bed tertiary care teaching hospital in China. The Department of Geriatrics cares for aging patients and patients with age-related diseases that include cardio-cerebral vascular disease, respiratory disease, and digestive disease. Hospitalized patients in the geriatric department aged ≥ 65 years with polypharmacy were enrolled from May 2015 to December 2015. Polypharmacy was defined as the use of more than five regular medications. If a patient had more than one hospital admission within the study period, only the first occurrence was used in the analysis. The patients were excluded if no medication was used or the medication administration records were unavailable or incomplete. The participants taking anticholinergic or sedative medicines were included in exposure group, otherwise they were included in non-exposure group.

Data collection and measurements

Data including age, gender, primary diagnosis, comorbidities, prescribed drugs and precise dosages and length of stay were extracted from the patient medical records. Barthel index [10], an ordinal scale used to measure performance in activities of daily living was also recorded. The Charlson Comorbidity Index (CCI) [11] was used to assess health status, as this is a reliable and commonly utilized tool for calculating the risk of mortality with comorbid illness. Common comorbidity and geriatric syndrome, including heart failure, syncope, delirium, dementia or cognitive impairment, history of falls, insomnia, peptic ulcer, and prostatic hyperplasia, were recorded.

The Drug Burden Index

The DBI was used to measure total exposure to medicines with anticholinergic and sedative effects [7]. Anticholinergic and sedative medications are weighted equally and summed according to the equation below:

$$DB = B_{AC} + B_s,$$

B_{AC} and Bs indicated the burden from anticholinergic (AC) drugs or sedative (S) drugs respectively. The DBI for each drug was then calculated as follows:

$$DBI = D/(\delta + D)$$

D was the daily dose taken by the subject, and δ was the minimum efficacious daily dose approved by the China Food and Drug Administration. The minimum recommended daily dose was used as an estimate of the dose required to achieve 50% of the maximum anticholinergic effect. Topical dermatological medications, inhaled medications, and ophthalmologic medications or medications instructed to be taken as required (ad libitum) were excluded from the DBI calculations. For each medication, the DBI ranged from 0 to 1, with a DBI of 0.5 indicating that an individual was exposed to an anticholinergic or sedative medication at the minimum recommended daily dose. For each patient, we have calculated

the DBI for each medicine with anticholinergic and sedative effects and added them together. As previous study, a high exposure to DBI medicines was classified as ≥ 1, and a low DBI medicines exposure classified as < 1 [12]. To minimize interpretation bias, two raters were trained to use the DBI. Each rater evaluated the data set independently, and all disagreements were resolved through discussion and consensus.

Statistical analysis

Statistical analysis was performed using SPSS version 23.0. A two-tailed P value < 0.05 was considered to be statistically significant. Descriptive statistics for continuous data are reported as mean ± standard deviation (SD), such as age, number of prescribed medications. Nonparametric variables were expressed as the median and interquartile range (IQR), such as CCI points and length of stay. Categorical data were expressed as frequencies. A Chi-squared (χ^2) test was applied to compare dichotomous variables between groups, and Fisher's exact test was used when expected cell counts were below five. The Student's t test or a nonparametric test was applied to compare the mean or median of continuous variables. Multivariate logistic regression was used to examine factors related to DBI exposure. Logistic regression analysis was carried out to identify the independent factors associated with DBI exposure. Univariate analysis was carried out and the variables which were statistically significant were included in multivariate stepwise regression.

Results

Patient demographics of the study participants

A total of 611 participants aged 65 years or older were initially included in the study, with 140 participants being excluded for repeated admissions, 15 participants were excluded because no medication was prescribed, and 73 participants were excluded as the number of prescribed medications was less than five during hospitalization.

Among the remaining 383 patients, 33.7% (129/383) of patients were aged between 65–79 years and 66.3% (254/383) of patients were 80 years old and above. The average age was 82.6 ± 7.0 years (range 66–103 years), and 72.9% (279/383) were male patients. Table 1 shows the clinical characteristics of the study population.

Patients aged 80 years or older had more prescribed medications than those aged between 65 and 79 years (10.3 ± 3.9 vs. 8.8 ± 3.3) (P < 0.001). The group of patients aged 80 years or more had a significantly increased length of stay in hospital (17 days; IQR 11–23 days vs. 13 days; IQR 9–20 days) (P < 0.001) compared with patients aged between 65–79 years. A total of 64 patients (16.7%) had a Barthel index ≤ 60, which indicated a physical disability, and patients aged 80 years or above suffered more physical disability (P < 0.001).

Anticholinergic and sedative drug exposure and Drug Burden Index

According to the DBI, this study identified 91 of the 383 patients using anticholinergic and sedative medications. Table 2 shows that 106 medications were identified and the most frequently prescribed medications were estazolam in 51.9% (55/106), terazosin in 14.1% (15/106), loratadine in 10.4% (11/106), and cetirizine in 5.7% (6/106), which meant that these four medications accounted for 82.1% of the anticholinergic and sedative drugs identified by the DBI model.

The DBIs were calculated based on the equation. In the exposure group, the median DBI was 0.75 (IQR 0.65–0.75). There were 11 (12.1%) patients of the exposure group with a DBI ≥ 1 classified as high exposure to DBI medicines. A

Table 1 Baseline and clinical characteristics of 383 older patients with polypharmacy

Characteristics	Total	Age (years)		P value
	n = 383	65–79 (n = 129)	≥80 (n = 254)	
Gender				
Men	279 (72.9%)	95 (73.6%)	184 (72.4%)	0.903
Women	104 (27.1%)	34 (26.4%)	70 (27.6%)	
Prescribed medications (mean ± SD)	9.8 ± 3.8	8.8 ± 3.3	10.3 ± 3.9	< 0.001
CCI (points): median and IQR	2 (IQR 1–4)	2 (IQR 1–3)	2 (IQR 1–4)	0.001
Length of stay in hospital in days: median and IQR	15 (IQR 10–22)	13 (IQR 9–20)	17 (IQR 11–23)	< 0.001
Barthel index				
≤ 60	64 (16.7%)	8 (6.2%)	56 (22.0%)	< 0.001
> 60	319 (83.3%)	121 (93.8%)	198 (78.0%)	

IQR interquartile range

Table 2 The most commonly used anticholinergic and sedative medications

Medication	N = 106	%
Estazolam	55	51.9
Terazosin	15	14.1
Loratadine	11	10.4
Cetirizine	6	5.7
Tramadol	4	3.8
Oxycodone	4	3.8
Chlorpheniramine	3	2.8
Tolterodine	2	1.9
Levetiracetam	1	0.9
Paroxetine	1	0.9
Fluoxetine	1	0.9
Belladonna	1	0.9
Diazepam	1	0.9
Citalopram	1	0.9

total of 80 (87.9%) patients had a DBI < 1 classified as low exposure to DBI medicines.

Factors associated with exposure of anticholinergic and sedative medications

Exposure of anticholinergic and sedative medications was detected using the DBI. Table 3 summarizes the clinical and comorbidity characteristics between exposure group and non-exposure group. According to the DBI, the exposure group exhibited differences regarding age ≥ 80 years ($P < 0.001$), the number of prescribed medications ($P < 0.001$), length of hospital stay ($P = 0.021$) and symptoms of insomnia ($P < 0.001$) when compared with the non-exposure group. These factors were included in multivariate logistic regression analysis.

In the multivariate logistic regression analysis, based on the DBI, exposure of anticholinergic and sedative medications was associated with age ≥ 80 years (OR 2.246; 95% CI 1.100–4.586), number of prescribed drugs (OR 1.102; 95% CI 1.018–1.193), and symptoms of insomnia (OR 28.990; 95% CI 14.197–59.200), as shown in Table 4.

Table 3 Clinical and comorbidity characteristics between the exposure group and the non-exposure group using the Drug Burden Index (DBI)

Patient clinical characteristics	DBI exposure (n = 91)	Non-DBI exposure (n = 292)	*P* value
Age (years)			
65–79	19 (20.9%)	182 (62.3%)	< 0.001
≥ 80	72 (79.1%)	110 (37.7%)	
Gender			
Men	59 (64.8%)	220 (75.3%)	0.059
Women	32 (35.2%)	72 (24.7%)	
Number of prescribed medications (mean ± SD)	11.1 ± 4.6	9.3 ± 3.4	< 0.001
CCI (points); median (IQR)	2 (IQR 1–4)	2 (IQR 1–3)	0.689
Length of stay in hospital in days; median (IQR)	16 (IQR 12–25)	14 (IQR 10–21)	0.021
Barthel Index			
≤ 60	21 (23.1%)	43 (14.7%)	0.076
> 60	70 (76.9%)	249 (85.3%)	
Common comorbidity or geriatric syndrome			
Heart failure	5 (5.5%)	17 (5.8%)	1.000
Syncope	1 (1.1%)	2 (0.7%)	0.558
Delirium	1 (1.1%)	3 (1.0%)	1.000
Dementia or cognitive impairment	3 (3.3%)	8 (2.7%)	0.727
History of falls	7 (7.7%)	16 (5.5%)	0.451
Insomnia	53 (58.2%)	14 (4.8%)	< 0.001
Peptic ulcer	7 (7.7%)	18 (6.2%)	0.628
Prostatic hyperplasia	29 (31.9%)	112 (38.3%)	0.319

Table 4 Multivariate analysis of variables independently associated with exposure of anticholinergic and sedative medications according to the Drug Burden Index (DBI)

Variables	OR	95% CI	*P* value
Age ≥ 80 years	2.246	(1.100–4.586)	0.026
Number of medications	1.102	(1.018–1.193)	0.016
Insomnia	28.990	(14.197–59.200)	0.000

Discussion

The present study reported the use of anticholinergic and sedative medications included in the DBI and prescribed to older patients with polypharmacy in China for the first time. The findings showed that the prevalence of exposure of anticholinergic and sedative medications identified by the DBI was 23.8%, the most frequently used drugs were estazolam, terazosin, loratadine and cetirizine, and exposure to anticholinergic and sedative medicines was associated with age ≥ 80 years, the number of prescribed medications, and symptoms of insomnia. These findings have important significant for reducing potentially inappropriate medications (PIMs), reducing ADR and improving prognosis.

The prevalence of DBI exposure in this study was slightly lower than that found in studies conducted in other countries. Previous studies from Australia and Finland showed that between 27.8 and 37.5% of the community-dwelling older people [13] and between 34 and 49.5% of hospitalized elderly patients [12] were being treated with medications on the DBI. A cross-sectional study conducted in 17 residential aged care facilities in Australia showed that 83.1% of the participants received at least one anticholinergic or sedative medication included in DBI, and exposure to DBI-associated medications was associated with reduced Dementia Quality of Life (DEMQOL) self-reported questionnaire scores [14].

As the DBI has not previously been used in China, this single-center study may not reflect the exposure of anticholinergic and sedative medications comprehensively. Moreover, older people with dementia or physical frailty, who have been prescribed more anticholinergic or sedative drugs, usually have a history of residing in long-term care facilities or secondary hospitals in China, and not in tertiary care teaching hospitals. Multicenter studies from different level medical settings are needed to show the actual prevalence in further studies.

Previous studies have reported that the most common drug classes for DBI exposure were antidepressants and opioid receptor agonists [12]. In the present study, the most common medication identified by the DBI was estazolam, which was the most frequently prescribed medications of benzodiazepines. With aging, people are more troubled with insomnia and depression, and benzodiazepines are commonly used in hospitalized elderly patients by physicians to treat these conditions. A previously published study from our research group showed that benzodiazepines were the second most widely prescribed potentially inappropriate medication (PIMs) identified by Beers 2015 criteria [15]. A potential reason for the high prevalence of benzodiazepines use in hospitalized elderly in China are often solely for the convenience of the staff. Furthermore, few doctors are willing to prescribe no drug therapy for elderly patients to help them with problems such as insomnia or delirium before prescribing medication [16]. A recently published study reported that insomnia was highly prevalent in the elderly, but the average Insomnia Severity Index score was only 12.3, which indicated that the level of insomnia was mild [17]. This finding suggests that non-pharmacological options may be recommended to treat mild insomnia, including sleep hygiene combined with behavioral interventions [18]. Some physicians have begun to focus on reducing the number of benzodiazepine prescriptions, as direct patient education by physicians or pharmacists has been shown to effective in reducing the overuse of benzodiazepines [19]. Recently, a multidisciplinary program comprising medication audit and feedback, staff education, and interdisciplinary case review has achieved significant reductions in the overuse of benzodiazepines [20].

The present study showed that terazosin was the most commonly prescribed medication of the anticholinergic drug class in this study population. Terazosin was usually prescribed for older male patients with prostatic hyperplasia [21]. It is known that alpha-1 adrenoceptor antagonists are not recommended to elderly as the first-line treatment for hypertension because of the adverse events of postural hypotension [22]. Mild anticholinergic effects of terazosin were usually disregarded, as more than 600 drugs have been shown to have some degree of anticholinergic activity [23], and the physicians may be less aware that some of the medications they prescribed have anticholinergic effects peripherally and centrally. Considering the side effects of anticholinergic drugs, all anticholinergic properties of combined medicines should be identified, especially for older patients with polypharmacy.

The focus of the present study was on the anticholinergic and sedative drugs burden in older hospitalized patients with polypharmacy. A significant factor associated with DBI exposure was the number of medications, even after adjusting for confounding variables. 'Deprescribing' is a complex process that is required for the safe and effective cessation of inappropriate medications [24]. Systematic reviews of medications withdrawal trials show that reducing specific classes of medications, especially psychotropic and anticholinergic drugs, may decrease adverse events and improve the quality of life [25]. Considering

the advantages of evaluating the burden of anticholinergic and sedative drugs, the DBI may apply as a deprescribing tool of polypharmacy management.

Patients aged 80 years or older were more likely to be treated with anticholinergic and sedative medications. Consistent with other studies, these older patients had more prescribed medications, more physical disability, more complication and increased the duration of stay in hospital. It should also be noted that frailty is common in later life and increases with age [26]. Common comprehensive tools for guiding patient prescriptions, such as Beers criteria [22] and STOPP/START criteria [27], were designed for the general older people. Either potentially inappropriate medications or the burden of anticholinergic and sedative drugs should be re-evaluated in frail older people with limited life expectancy.

This study had several limitations. (1) First, as this was a retrospective observational study, the study analysis was dependent on the quality of the medical records and the amount of detail they contained. (2) Second, this was a single-center study, and only included hospitalized patients. A larger sample size of hospitalized and community-based patients should be included in future studies. (3) Third, the exclusion of Over-The-Counter medicines may underestimate anticholinergic and sedative exposure. (4) Finally, the consequences of DBI exposure were not analyzed. The associations between potential adverse effects, physical function outcomes and DBI scores should be assessed in the future studies.

Conclusions

For hospitalized older patients with polypharmacy in China, according to the Drug Burden Index (DBI) model, the prevalence of anticholinergic and sedative medications used was 23.8%. The most frequent medications found were estazolam, terazosin, loratadine, and cetirizine. Prescription of anticholinergic and sedative medications was shown to be associated with patient age $\geq$ 80 years, the number of other prescribed medications, and with the symptoms of insomnia.

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Conflicts of interest The authors declare that they have no conflicts of interest.

References

1. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. Expert Opin Drug Saf. 2014;13(1):57–65.
2. Alwhaibi M, Balkhi B, Alhawassi TM, Alkofide H, Alduhaim N, Alabdulali R, et al. Polypharmacy among patients with diabetes: a cross-sectional retrospective study in a tertiary hospital in Saudi Arabia. BMJ Open. 2018;8(5):e020852.
3. Nishtala PS, Hilmer SN, McLachlan AJ, Hannan PJ, Chen TF. Impact of residential medication management reviews on Drug Burden Index in aged-care homes: a retrospective analysis. Drugs Aging. 2009;26(8):677–86.
4. Glass J, Lanctot KL, Herrmann N, Sproule BA, Busto UE. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. BMJ. 2005;331(7526):1169.
5. Rothberg MB, Herzig SJ, Pekow PS, Avrunin J, Lagu T, Lindenauer PK. Association between sedating medications and delirium in older inpatients. J Am Geriatr Soc. 2013;61(6):923–30.
6. Rolita L, Spegman A, Tang X, Cronstein BN. Greater number of narcotic analgesic prescriptions for osteoarthritis is associated with falls and fractures in elderly adults. J Am Geriatr Soc. 2013;61(3):335–40.
7. Hilmer SN, Mager DE, Simonsick EM, Cao Y, Ling SM, Windham BG, et al. A Drug Burden Index to define the functional burden of medications in older people. Arch Intern Med. 2007;167(8):781–7.
8. Wouters H, van der Meer H, Taxis K. Quantification of anticholinergic and sedative drug load with the Drug Burden Index: a review of outcomes and methodological quality of studies. Eur J Clin Pharmacol. 2017;73(3):257–66.
9. Jamieson HA, Nishtala PS, Scrase R, Deely JM, Abey-Nesbit R, Connolly MJ, et al. Drug burden and its association with falls among older adults in New Zealand: a national population cross-sectional study. Drugs Aging. 2018;35(1):73–81.
10. Collin C, Wade DT, Davies S, Horne V. The Barthel ADL Index: a reliability study. Int Disabil Stud. 1988;10(2):61–3.
11. Charlson M, Pompei P, Ales K, MacKenzie C. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373–83.
12. Best O, Gnjidic D, Hilmer SN, Naganathan V, McLachlan AJ. Investigating polypharmacy and Drug Burden Index in hospitalised older people. Intern Med J. 2013;43(8):912–8.
13. Kouladjian L, Gnjidic D, Chen TF, Mangoni AA, Hilmer SN. Drug Burden Index in older adults: theoretical and practical issues. Clin Interv Aging. 2014;9:1503–15.
14. Harrison SL, Kouladjian O'Donnell L, Bradley CE, Milte R, Dyer SM, Gnanamanickam ES, et al. Associations between the Drug Burden Index, potentially inappropriate medications and quality of life in residential aged care. Drugs Aging. 2018;35(1):83–91.
15. Zhang X, Zhou S, Pan K, Li X, Zhao X, Zhou Y, et al. Potentially inappropriate medications in hospitalized older patients: a cross-sectional study using the Beers 2015 criteria versus the 2012 criteria. Clin Interv Aging. 2017;12:1697–703.
16. Mo L, Ding D, Pu SY, Liu QH, Li H, Dong BR, et al. Patients aged 80 years or older are encountered more potentially inappropriate medication use. Chin Med J. 2016;129(1):22–7.
17. Miner B, Gill TM, Yaggi HK, Redeker NS, Van Ness PH, Han L, et al. Insomnia in community-living persons with advanced age. J Am Geriatr Soc. 2018;66:1592–7.
18. Hanlon JT, Semla TP, Schmader KE. Alternative medications for medications in the use of high-risk medications in the elderly and potentially harmful drug–disease interactions in the elderly quality measures. J Am Geriatr Soc. 2015;63(12):e8–18.
19. Tannenbaum C, Martin P, Tamblyn R, Benedetti A, Ahmed S. Reduction of inappropriate benzodiazepine prescriptions among

older adults through direct patient education: the EMPOWER cluster randomized trial. JAMA Intern Med. 2014;174(6):890–8.
20. Westbury JL, Gee P, Ling T, Brown DT, Franks KH, Bindoff I, et al. RedUSe: reducing antipsychotic and benzodiazepine prescribing in residential aged care facilities. Med J Aust. 2018;208(9):398–403.
21. Oelke M, Gericke A, Michel MC. Cardiovascular and ocular safety of alpha1-adrenoceptor antagonists in the treatment of male lower urinary tract symptoms. Expert Opin Drug Saf. 2014;13(9):1187–97.
22. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2015;63(11):2227–46.
23. Cancelli I, Beltrame M, Gigli GL, Valente M. Drugs with anticholinergic properties: cognitive and neuropsychiatric side-effects in elderly patients. Neurol Sci. 2009;30(2):87–92.
24. Hasler S, Senn O, Rosemann T, Neuner-Jehle S. Effect of a patient-centered drug review on polypharmacy in primary care patients: study protocol for a cluster-randomized controlled trial. Trials. 2015;16:380.
25. van der Cammen TJ, Rajkumar C, Onder G, Sterke CS, Petrovic M. Drug cessation in complex older adults: time for action. Age Ageing. 2014;43(1):20–5.
26. Song X, Mitnitski A, Rockwood K. Prevalence and 10-year outcomes of frailty in older adults in relation to deficit accumulation. J Am Geriatr Soc. 2010;58(4):681–7.
27. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing. 2015;44(2):213–8.