Inappropriate medications and physical function: a systematic review

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Abstract

Background and aims: Inappropriate medication prescription is highly prevalent in older adults and is associated with adverse health outcomes. The aim of this study was to examine the associations between potentially inappropriate medications (PIMS) and potential prescribing omissions with physical function in older adults situated in diverse environments.

Methods: A systematic search was completed using the following databases: MEDLINE, CINAHL, PsycINFO, EMBASE and COCHRANE. Results were extracted from the included studies.

Results: In total, 55 studies reported on 2,767,594 participants with a mean age of 77.1 years (63.5% women). Study designs comprised 26 retrospective cohort studies, 21 prospective cohort studies and 8 cross-sectional studies. Inappropriate medications in community and hospital settings were significantly associated with higher risk of falls (21 out of 30 studies), higher risk of fractures (7 out of 9 studies), impaired activities of daily living (ADL; 8 out of 10 studies) and impaired instrumental ADL (IADL) score (4 out of 6 studies). Five out of seven studies also showed that PIMs were associated with poorer physical performance comprising the Timed Up and Go test, walking speed, grip strength, time to functional recovery, functional independence and scale of functioning. Many medication classes were implicated as PIMs in falls, fractures and impairment in physical performance including antipsychotic, sedative, anti-anxiety, anticholinergic, antidiabetic, opioid and antihypertensive medications. For patients not receiving musculoskeletal medications, such as calcium, vitamin D and bisphosphonates, older adults were found to be at risk of a hospital admission for a fall or fracture.

Conclusion: Inappropriate medication prescriptions are associated with impaired physical function across longitudinal and cross-sectional studies in older adults situated in diverse settings. It is important to support older people to reduce their use of inappropriate medications and prevent prescribing omissions.

Plain language summary

Inappropriate medications and physical function

Background and aims: The use of inappropriate medications is very common in older adults and is associated with harmful health problems. The aim was to examine associations between potentially inappropriate medications and potential prescribing omissions with physical function in older adults situated in diverse environments. **Methods:** Library databases were examined for possible studies to include and a systematic search was completed. Relevant information was obtained from the included studies. **Results:** In total, 55 studies reported on 2,767,594 participants who were an average age of 77.1 years and about 6 out of 10 were women. A variety of different study designs were used. Inappropriate medication prescriptions in community and hospital settings were significantly associated with higher risk of falls (21 out of 30 studies), higher risk of fractures (7 out of 9 studies),

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problems with activities of daily living (ADL), such as eating, bathing, dressing, grooming, walking and toileting (8 out of 10 studies) and problems with instrumental ADL such as managing medications, house cleaning and shopping (4 out of 6 studies). Five out of seven studies also showed that inappropriate medications were associated with poorer physical performance involving the Timed Up and Go test, walking speed, grip strength, time to functional recovery, functional independence and scale of functioning. Many types of medication classes were shown to be associated with a risk of falls, fractures and problems with physical performance. Omitted medications were also associated with falls and fractures. **Conclusion:** Inappropriate medication prescriptions are associated with problems relating to physical function. It is important to support older people to reduce their use of inappropriate medications and prevent prescribing omissions.

Keywords: activities of daily living, aged, functional independence, independent living, medication therapy management, physical function

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Introduction

Prescription of a medication is defined as inappropriate if the potential harm from it outweighs the benefit. Inappropriate medications comprises two subtypes: potentially inappropriate medications (PIMs), which include the prescribing of medications with an increased risk of side effects or drug-interactions, or over-prescription of medications that lack a therapeutic benefit, and potential prescribing omissions (PPOs), which include the absence of medications being proven to be beneficial.[1]

The prevalence of inappropriate medication prescriptions provided to community dwelling older adults is around 20% and between 36% and 51% in institutionalised older adults.[2] The prevalence can be attributed to multi-morbidity, polypharmacy and age-related physiological changes that alter pharmacokinetics and increase sensitivity to pharmacodynamics.[3,4] Inappropriate prescriptions are related to poor health outcomes, such as increased hospitalisations, emergency department visits, and increased risk of mortality.[5] Physical function, which is defined as a person's ability to carry out activities requiring mobility, physical performance, balance, muscle strength or endurance, is critical for maintaining independence.[6] Inappropriate prescriptions have been shown to be associated with a significant decline in physical performance,[7] ADL during hospitalisation,[8] as well as falls and injuries in frail older adults.[9] Previous reviews have examined associations between polypharmacy and physical function in older adults,[10] and between inappropriate medication use and functional decline.[11]

The aim of this systematic review is to examine the associations between inappropriate medication prescriptions and physical function in older adults situated in diverse environments.

Methods

Search strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement was used for reporting this review. The search strategy was completed with a senior university librarian and included terms relating to PIMs and physical function (Supplemental file S1). The search timeframe was from inception up to 3 April 2021. Articles were included by searching MEDLINE, CINAHL, PsycINFO EMBASE and COCHRANE (within MEDLINE).

Article titles and abstracts as well as full-texts of all included articles were independently screened by two reviewers (EM, MZK), and any discrepancies were resolved by a third reviewer (ABM). The study selection was undertaken on the Rayyan QCRI Platform.[12]

Eligibility criteria

Articles that utilised a validated tool to assess medication appropriateness, along with reporting

physical function were included. Physical function was defined as falls, fractures, ADL, instrumental activities of daily living (IADL), physical performance balance, muscle strength and cardiovascular endurance. Articles focussing on a specific medication or a class of medication were included if a validated tool was used to assess its appropriateness of use. For this systematic review, older adults were situated in diverse settings, including hospitals, aged care facilities and the community. Conference abstracts, case reports with fewer than five cases, letters to the Editor, reviews and any non-English articles were excluded from the review.

Data extraction

The data extraction process for each study was conducted independently by two authors (EM, MZK) into a standardised electronic data extraction sheet. Any discrepancies were resolved by a third reviewer (ABM). The following information were extracted: first author/year, country, mean age, sex ratio, sample size, study setting, the PIMs and PPOs examined as predictors, the approach used to identify PIMs and PPOs and the method for measuring the outcome. Attempts were made to contact authors of studies if there appeared to be missing information.

Quality assessment

Two authors (EM, MZK) independently assessed the quality of included studies using a modified Newcastle–Ottawa Scale (Supplemental Files S2 and S3). Points were given to the eligible categories: (a) selection of the study population, (b) comparability and (c) description of the outcome.

Results

The article selection is outlined in Figure 1. A total of 14,303 studies were initially identified. After title and abstract screening, 193 full-text articles were retrieved and 55 studies met the inclusion criteria reporting on 2,767,594 participants (mean age 77.1 years, 63.5% were female). It was not possible to undertake a quantitative synthesis using meta-analysis due to the heterogeneity in physical function results that were obtained.

Characteristics of included studies

The characteristics of included studies are summarised in Table 1. A total of 37 studies used various versions of the Beers criteria,[8,13–48] 19 studies used the Screening Tool of Older Person's prescriptions (STOPP) criteria,[21,23,25,34,36,37,43,48–59] 9 studies used the Screening to Alert to Right Treatment (START) criteria,[36,47–50,52,55,56,59] 2 studies used the Meds 75+ Database,[60,61] 2 studies used the European Union (EU) (7)-PIM list,[28,62] 4 studies used the Drug Burden Index,[24,43,63,64] and 1 study used the Norwegian General Practice (NORGEP) criteria list to identify inappropriate medications.[8] In three studies, the Anticholinergic Cognitive Burden scale was used,[24,34,65] while in one study, the Quantitative Drug Index was used.[66] In some studies, more than one tool was used.[8,15,17,21,23–25,28,34,36,37,43,47–50,52,55,56,59] Table 2 shows the associations between inappropriate medication prescriptions and physical function. Table 3 provides an illustrative summary of the associations between inappropriate medication prescriptions and physical function.

Associations of PIMs and PPOs with falls and fractures

A total of 30 studies examined the association between inappropriate medications and falls (Table 2)[13–32,49–53,55–57,62,63]; 18 studies used the Beer's criteria, 5 used the STOPP/START criteria, 5 used the STOPP, 2 used the EU (7)-PIM list, 2 used the Drug Burden Index, 1 used the PRISCUS list, and 1 used the Anticholinergic Drug Burden. Out of 30 studies, 21 showed a significant positive association between PIMs and risk of falls.[14–18,22–24,26,28–32,49,51,53,56,57,62] One study showed a positive predictive value of 25% for the proportion of patients with PPO-related admissions for a fall with a fracture.[56] Benzodiazepine, opiate and sedative use were common PIMs associated with falls.[14,23,31,51,52]

Nine studies examined inappropriate medication use and its association with fractures.[27,29,31–33,56,57,60,61] Seven out of nine studies showed a significantly higher number of fractures when exposed to PIMs.[29,32,33,56,57,60,61] In the one study that examined the effect of PPOs on fractures, multivariate logistic regression analysis showed PPO-related admission was associated with increased odds of osteoporotic fracture [odds ratio (OR) = 5.0, 95% confidence interval (CI) 2.2–11.4, $p < 0.001$].[56] Antidiabetic, psychotropic, opioid and antihypertensive use impacted on older people's associated risk of experiencing fractures.[32,61]

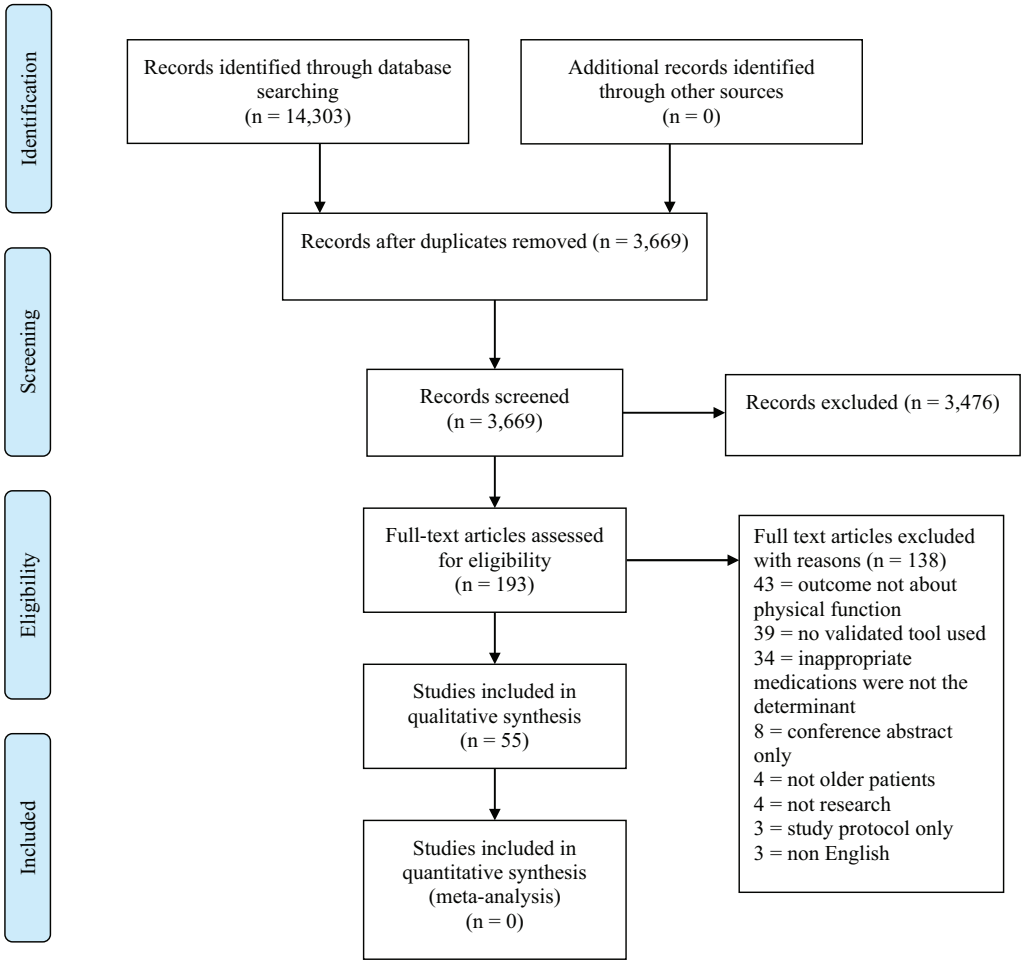

Figure 1. PRISMA flow diagram.
PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis.

Associations of PIMs and PPOs with ADL and IADL

A total of 10 studies examined associations between inappropriate medication use and ADL,[34–37,52,54,58,59,62,65] while 6 studies examined associations between inappropriate medication use and IADL (Table 2).[35,38,52,58,63,64] Of the 10 studies focusing on ADLs, 8 showed that inappropriate medication use was associated with ADL impairment,[34,36,37,52,54,59,62,65] while 4 studies involving IADLs showed that inappropriate medication use was associated with IADL impairment.[35,38,52,64] In the one study involving anticholinergic burden and ADLs, patients who were prescribed any anticholinergic medication had a mean Bartel Index of 83.5 (95% CI 81.9–85.0), while those who were not prescribed any anticholinergic medication had a mean Bartel Index of 86.3 (95% CI 84.4–88.1, $p = 0.03$).[65] In the study by Tosato *et al.*, there were variations in results depending on the type of tool used for inappropriate medication use.[37] They showed PIM use defined with the STOPP criteria was significantly associated with ADL impairment, while PIM use defined with the Beer's criteria showed no significant association with ADL impairment.

Associations of PIMs and PPOs with physical performance

Seven studies involved examination of associations between inappropriate medication use and physical performance (Table 2).[8,39,40,49,59,64,66] Aside from two studies,[8,49] the included studies showed significant associations between PIM use and physical performance. In the study by Kersten *et al.*,[8] PIM use had no significant association with the Timed Up and Go test. In the

Table 1. Characteristics of included studies ($N = 55$).

Author	Country	Study design	Setting	Age, years		Sample size, *N*	Female, %
				Cut-off	Mean (SD)		
Longitudinal studies							
Ackroyd-Stolarz *et al.*[13]	Canada	RCS	Tertiary care hospital	⩾65	NG	8976	NG
Agashivala and Wu[14]	US	RCS	Nursing home	⩾65	84.1 (7.97)	11,940	74.7
Beer *et al.*[15]	Australia	RCS	Community dwelling	65–83	77.0 (3.6)	4260	0
Berdot *et al.*[16]	France	PCS	Community dwelling	⩾65	73.7 (5.3)	6343	59.0
Borenstein *et al.*[17]	USA	PCS	Medical and surgical units	⩾65	75.0 (13.4)	214	57.9
Cardwell *et al.*[63]	New Zealand, UK	PCS	Community dwelling	80	Maori: 82.3 (2.6)	671	59.9
					Non-Maori: 84.6 (0.5)		
Chan *et al.*[41]	US	PCS	Geriatric psychiatry unit	NG	81.5 (6.2)	118	78.0
Chin *et al.*[42]	US	PCS	Emergency department	⩾65	76.3 (7.9)	898	63.0
Chun *et al.*[20]	US	RCS	Assisted living facilities	⩾65	83.9 [65–99]	95	68.4
De Vincentis *et al.*[34]	Italy	PCS	Medical units	⩾65	Median 79 [IQR 12]	2631	51.4
Delgado *et al.*[57]	UK	RCS	Community dwelling linked to hospitals	⩾65	84.4 (7.3)	11,175 with dementia + 43,463 controls	64.8
Early *et al.*[21]	US	PCS	Community dwelling	65–99	77	1,678,037	63.4 case group
Fernández *et al.*[22]	Columbia	PCS	Community dwelling	⩾65	69.3 (2.96)	273	48.0
Fick *et al.*[31]	US	RCS	Community dwelling	⩾65	72.9 (10.6)	960	41.1
Fick *et al.*[32]	US	RCS	Community dwelling	⩾65	73.5 (6.5) PIM exposed group	17,971	71.0 PIM exposed group
Frankenthal *et al.*[49]	Israel	PCS	Chronic care geriatric facility	⩾65	NG	542	62.5
García-Gollarte *et al.*[50]	Spain	PCS	Nursing home	>65	84.4 (12.7)	716	73.0
Gosch *et al.*[59]	Austria	PCS	Geriatric evaluation and management unit	>65	80.6 (7.1)	457	82.5
Hamilton *et al.*[23]	US	PCS	Medical and surgical units	⩾65	Median 77.0 [IQR 72.0–83.0]	600	59.8
Hill-Taylor *et al.*[51]	Canada	RCS	Community and hospital	66	NG	1327	83.1
Hyttinen *et al.*[60]	Finland	RCS	Community dwelling	⩾65	80.6	47,850	63.8

(Continued)

Table 1. (continued)

Author	Country	Study design	Setting	Age, years		Sample size, *N*	Female, %
				Cut-off	Mean (SD)		
Hyttinen *et al.*[61]	Finland	RCS	Community dwelling	⩾65	74.6 (5.5)	20,666	62.3
Iaboni *et al.*[44]	US	PCS	Various hospitals	60	78.5 (8.4) PIM exposed group	477	68.7 PIM exposed group
					78.4 (9.1) Non PIM exposed group		82.0 Non PIM exposed group
Ie *et al.*[24]	US	RCS	Community dwelling	⩾65	78.3 (6.6)	343	89.4
Kersten *et al.*[8]	Norway	RCS	Emergency department	75	86.0 (5.7)	232	59.1
Kose *et al.*[45]	Japan	RCS	Rehabilitation ward	⩾65	79.0 (72–85)	272	62.5
Kose *et al.*[46]	Japan	RCS	Rehabilitation ward	⩾65	Median 79.0 [IQR 73.0–85.0]	569	66.4
Koyama *et al.*[38]	US	PCS	Community dwelling	>75	83.0 (3.1)	1429	100
Lu *et al.*[33]	Taiwan	RCS	Community and hospitals	⩾65	NG	59,042	48.8
Manias *et al.*[52]	Australia	RCS	Geriatric subacute wards	⩾65	88.0 [IQR 86.0–91.0]	249	61.4
McMahon *et al.*[25]	Ireland	RCS	Emergency department	>70	82.7 (6.1)	1016	69.7
Moriarty *et al.*[36]	Ireland	PCS	Community dwelling	⩾65	Median 76.0 [IQR 72.0–80.0]	1753	54.4
Nagai *et al.*[53]	Japan	RCS	Surgical units	⩾65	75.6 (8.6) PIM exposed group	253	86.6 PIM exposed group
					72.8 (7.7) non PIM exposed group	191 propensity matched group	85.3 non PIM exposed group
Nagai *et al.*[54]	Japan	RCS	Rehabilitation units	⩾65	81.3 (8.1)	170	66.5
Naples *et al.*[39]	US	PCS	Community dwelling	⩾65	74.6 (2.9)	2402	51.3
Narayan and Nishtala[26]	New Zealand	RCS	Community and hospitals	⩾65	74.7 (7.6)	537,387	54.9
Ota *et al.*[27]	US	RCS	Ambulatory setting	⩾65	71.9 (6.4)	2704	66.5
Pasina *et al.*[65]	Italy	PCS	Internal medicine and geriatric wards	⩾65	78.5 (7.2)	1380	48.8
Renom-Guiteras *et al.*[62]	England, Estonia, Finland, France, Germany, The Netherlands, Spain, Sweden	PCS	Long-term care or at risk of long-term care	⩾65	83.0 (6.6)	2004	67.5

(Continued)

Table 1. (continued)

Author	Country	Study design	Setting	Age, years		Sample size, *N*	Female, %
				Cut-off	Mean (SD)		
Schiek *et al.*[28]	Germany	PCS	Military hospital	⩾65	Median 79 [IQR 69–86]	174	54
Sengul Aycicek *et al.*[40]	Turkey	PCS	Tertiary care hospital	⩾65	72 (65–86)	101	55.4
Shibasaki *et al.*[47]	Japan	RCS	Neurology and Rehabilitation Hospital	⩾65	82.9 (6.6)	217	80.6
Stockl *et al.*[29]	US	RCS	Community and hospitals	⩾65	75.2 (6.4)	27,084	69.0 PIM exposed group
Tosato *et al.*[37]	Italy	PCS	Internal medicine and geriatric wards	⩾65	80.2 (7.0)	871	53.2
Umit *et al.*[48]	Turkey	RCS	Tertiary hospital	⩾65	69.5 (65–86)	80	57.5
Walker *et al.*[30]	US	RCS	Trauma centre	⩾65	78.5 (range 65–104)	2181	52.0
Weeks *et al.*[55]	Spain	RCS	Nursing home	70–99	86.7 (6.5) Antipsychotic exposed group	1653	76.8
Cross-sectional studies							
Anson *et al.*[66]	US	CSS	Community dwelling	>65	79 (range 66–92)	57	72
Bonfiglio *et al.*[58]	Italy	CSS	Outpatient department	⩾64	78.3 (5.8)	160	54.4
Cameron *et al.*[18]	Canada	CSS	Long term care facility	⩾65	Median 85.0 [IQR 77–90]	395	68.1
Carter *et al.*[19]	US	CSS	Emergency department	⩾65	75.2 (6.4)	259,775	69.0 PIM exposed group
Dalleur *et al.*[56]	Belgium	CSS	Teaching hospital	75	Median 84.0 [IQR 81–88]	302	62.6
Gnjidic *et al.*[64]	Australia	CSS	Community dwelling	70	76.9 (5.5)	1705	0
Hasan *et al.*[43]	Malaysia	CSS	Tertiary care hospital	60	70.0 (6.77)	344	44.9
Mohamed *et al.*[35]	US	CSS	Cancer center	⩾65	76.9 (5.4)	439	45

Study by Anson *et al.*[66] involved a secondary analysis of patient results at baseline of an RCT.
CSS, cross-sectional study; IQR, interquartile range; NG, not given; PCS, prospective cohort study; PIM, potentially inappropriate medications; RCS, retrospective cohort study; SD, standard deviation; UK, United Kingdom; US, United States.

study by Naples *et al.*,[39] while variable results were found in terms of effects of inappropriate medication use on physical performance, the investigators showed that any drug–drug or drug–disease interaction was significantly associated with a meaningful decline in gait speed of ⩾0.1 m/s, for slow *versus* fast walkers based on a median split at 1.15 m/s (OR 1.27, 95% CI 1.02–1.57, $p < 0.05$).

Associations of PIMs and PPOs with functional independence scores

Of the 10 studies involved in the examination of inappropriate medication use and measures of functional independence, 9 demonstrated that inappropriate medication use was significantly associated with increased impediment with functional independence.[35,41–48] PIM use was associated significantly with a decrease in the

Table 2. Results of included studies (*N* = 55).

Author	Criteria used	Type of medications	Outcome measured	Adjustments	Statistical unit	Result (95% CI)	*p* value
Falls							
Ackroyd-Stolarz *et al.*[13]	Beers	Benzodiazepine	Fall	Unadjusted	Prevalence	4.5% (PIM use) 3.8% (no PIM use)	0.30
			Fall-related injuries			2.6% (PIM use) 1.8% (no PIM use)	0.08
Agashivala and Wu[14]	Beers	PIPM	Falls in past 30 days	Unadjusted	OR	1.349 (1.333–1.366)	<0.01
					OR of other Psychoactive medications with PIPM as reference	0.83 (0.702–0.980)	0.028
					OR of non-psychoactive medications with PIPM as reference	0.624 (0.517–0.754)	<0.01
Beer *et al.*[15]	Beers McLeod	PIM use	Falls history	Unadjusted	OR	1.66 (1.42–1.94)	<0.001
		Potential under utilisation		Unadjusted	OR	1.24 (1.06–1.45)	0.008
		Any marker for suboptimal medication use		Unadjusted	OR	1.63 (1.29–2.04)	<0.001
		PIM use		Adjusted	OR	1.23 (1.04–1.45)	0.018
		Potential under utilisation		Adjusted	OR	1.10 (0.93–1.31)	0.278
		Any marker for suboptimal medication use		Adjusted	OR	1.17 (0.91–1.49)	0.227
Berdot *et al.*[16]	Beers	PIM occasional user	Falls	Unadjusted	OR	1.48 (1.26–1.74)	<0.001
			Falls	Adjusted	OR	1.23 (1.04–1.5)	0.016
		PIM regular user	Falls	Unadjusted	OR	1.45 (1.26–1.66)	<0.001
			Falls	Adjusted	OR	1.08 (0.94–1.25)	0.29
Borenstein *et al.*[17]	McLeod Beers	PIM	Falls	Unadjusted	OR	2.93 (1.17–7.34)	<0.05
			Falls	Adjusted	OR	3.05 (1.19–7.83)	<0.05
Cameron *et al.*[18]	Beers	PIM	Falls	Adjusted – any PIM	Beta	0.34 (0.037–0.65)	0.028
		PIM	Falls	Adjusted – benzodiazepine	Beta	NG – reduced falls	0.009

(Continued)

Table 2. (continued)

Author	Criteria used	Type of medications	Outcome measured	Adjustments	Statistical unit	Result (95% CI)	*p* value
		PIM	Falls	Adjusted – Selective serotonin reuptake inhibitor/ serotonin noradrenaline reuptake inhibitor use	Beta	NG – increased falls	0.007
Cardwell *et al.*[63]	Drug burden index	PIM	Falls	Adjusted	Relative risk	Maori:	
						12 months: 1.49 (0.76–2.92)	0.25
						24 months: 1.32 (0.68–2.57)	0.41
						36 months: 1.08 (0.53–2.19)	0.83
						Non-Maori:	
						12 months: 1.09 (0.76–1.56)	0.65
						24 months:1.06 (0.75–1.51)	0.73
						36 months: 1.13 (0.80–1.62)	0.49
Carter *et al.*[19]	Beers	PIM	Fall related ED visit	Not adjusted	Observed counts	3442 falls comprising 47.8% of ED visits. 735 (11.7%) of ED visits had at least 1 PIM	NG
Chun *et al.*[20]	Beers	PIM	Falls	NG	Nagelkerke R2	0.017	0.079
Early *et al.*[21]	Beers, STOPP	Fall-risk drugs, PIM	Falls	Adjusted	OR	Single PIM: 1.021 (0.998–1.044)	>0.05
						Two classes of PIM: 1.128 (1.102–1.154)	<0.05
						Five or more classes of PIM: 1.579 (1.540–1.619)	<0.05
Fernández *et al.*[22]	Beers	PIM	Recurring falls	Adjusted	OR	2.43 (1.08–5.84)	0.028
Frankenthal *et al.*[49]	STOPP/START	PIM and PPO	Average number of falls	NG	Difference	–0.5 (–0.9245 to –0.0755)	0.006
			Physical component score	NG	Difference	1.1 (–0.59 to 2.80)	0.07

(Continued)

Table 2. (continued)

Author	Criteria used	Type of medications	Outcome measured	Adjustments	Statistical unit	Result (95% CI)	*p* value
García-Gollarte *et al.*[50]	STOPP/START	PIM and PPO	Falls	NG	Mean Difference	−0.08	0.251
Hamilton *et al.*[23]	STOPP Beers	PIM	Benzodiazepines users (STOPP) + Falls		Proportion (%)	100	
			Benzodiazepines users (Beers) + Falls			91.7	
			Opiate users (STOPP) + Falls			100	
			Opiate users (Beers) + Falls			0	
			Sedative-Hypnotics users (STOPP) + Falls			0	
			Sedative-Hypnotics users (Beers) + Falls			0	
			Neuroleptics-users (STOPP) + Fall			100	
			Neuroleptics-users (Beers) + Falls			20	
Hill-Taylor *et al.*[51]	STOPP	Benzodiazepine and zoplicone	Proportion of fallers taking these PIMs		Proportion	21.60%	
Ie *et al.*[24]	Fall risk-increasing drugs	PIM	Fall-months	Adjusted	Rate ratio	⩾2: 1.67 (1.04–2.68)	<0.05
	Beers	PIM				⩾1: 1.15 (0.72–1.84)	>0.05
	Anticholinergic Cognitive Burden	PIM				>0.655 score: (1.24 (0.80–1.92)	>0.05
	Drug Burden Index	PIM				>0.15 score: 1.51 (0.88–2.58)	>0.05
Manias *et al.*[52]	STOPP/START	PIM	Falls	Adjusted	Exp(B) incident count	1.071 (0.883–1.299)	0.484
		PPO	Falls	Adjusted		1.096 (1.000–1.202)	0.051
McMahon *et al.*[25]	STOPP	PIM	% prescribing in fallers (pre-fall)	NG	Prevalence	42.2%	0.70
	Beers	PIM	% prescribing in fallers (pre-fall)		Prevalence	44.0%	0.10

(Continued)

Table 2. (continued)

Author	Criteria used	Type of medications	Outcome measured	Adjustments	Statistical unit	Result (95% CI)	*p* value
Nagai *et al.*[53]	STOPP-J	PIM	Subsequent falls in patients with distal radius fractures	Adjusted	OR	1.713 (1.246–2.357)	<0.001
Narayan and Nishtala[26]	Beers	PIM	Fall-related hospitalisation	Adjusted	IRR	1.45 (1.37–1.52)	<0.05
Ota *et al.*[27]	Beers	PIM	Fall, or fracture or injury	Adjusted	OR	0.77 (0.51–1.13)	>0.05
Renom-Guiteras *et al.*[62]	EU(7) - PIM List	PIM	Falls	Adjusted	OR	1.54 (1.04–2.30)	<0.05
Schiek *et al.*[28]	PRISCUS	PIM	FRIARs (fall-risk-increasing adverse reactions)	Unadjusted	OR	1.966 (1.164–3.320)	<0.05
	EU(7)-PIM	PIM				1.668 (0.900–3.091)	>0.05
	Beers	PIM				1.345 (1.065–1.698)	<0.05
Stockl *et al.*[29]	Beers	PIM	Fall or Fracture	Adjusted	HR	1.22 (1.10–1.35)	<0.001
Walker *et al.*[30]	Beers	PIM	Risk of falling	Adjusted	OR	1.14 (1.00–1.29)	0.0492
Weeks *et al.*[55]	STOPP/START	PIM and PPO	Fall and physical restraints	NG	NG	No difference between exposure and controls	>0.05
Falls and Fractures							
Dalleur *et al.*[56]	STOPP/START	PIM	Fall	Adjusted	OR	5.2 (2.2–12.3)	<0.001
		PPO	Osteoporotic fractures	Adjusted	OR	5.0 (2.2–11.4)	<0.001
		PIM	PIM related fall admission in patients with fall-risk-PIM	NG	PPV	0.68	
		PPO	PPO related fall admission in patients with fall-risk-PPO		PPV	0.25	
Delgado *et al.*[57]	STOPP	PIM	Fall	Adjusted	HR	1.37 (1.15–1.63)	<0.01
		PIM	Fracture	Adjusted	HR	0.92 (0.70–1.19)	0.51
Fick *et al.*[31]	Beers	PIM	Fall	Adjusted	OR	4.00 (1.76–9.76)	<0.0001
	Beers	PIM	Fracture	Adjusted	OR	1.14 (0.50–2.65)	0.72
Fick *et al.*[32]	Beers	PIM	Fall	Adjusted	OR	4.05 (1.89–8.69)	<0.01

(Continued)

Table 2. (continued)

Author	Criteria used	Type of medications	Outcome measured	Adjustments	Statistical unit	Result (95% CI)	*p* value
	Beers	PIM	Hip fracture	Adjusted	OR	3.10 (1.71–5.62)	<0.01
	Beers	PIM	Femur fracture	Adjusted	OR	6.80 (1.95–23.67)	<0.01
Fractures							
Hyttinen *et al.*[60]	Meds75+ Database	PIM	Hip fracture rates	Unadjusted but time-varying model	HR	1.15 (0.94–1.40)	>0.05
				Unadjusted but time-varying model for the incident PIM use period	HR	1.26 (1.02–1.56)	<0.05
				Adjusted time varying model	HR	1.21 (1.00–1.48)	0.056
				Adjusted time varying model for the incident PIM use period	HR	1.31 (1.06–1.63)	0.014
Hyttinen *et al.*[61]	Meds75+ Database	PIM	Fracture related hospitalisations (1 month after exposure)	Adjusted	HR	1.61 (1.11–2.33)	0.013
			Fracture related hospitalisations (3 months after exposure)	Adjusted	HR	1.50 (1.22–1.84)	<0.01
			Fracture related hospitalisations (6 months after exposure)	Adjusted	HR	1.38 (1.21–1.57)	<0.01
Lu *et al.*[33]	Beers	PIM	Fracture related hospitalisations	Adjusted	OR	1.55 (1.48–1.62)	<0.001
ADL							
Bonfiglio *et al.*[58]	STOPP-J	PIM	Bartel Index	Not adjusted	Independent *t*-test	With PIM: mean = 97.8 (SD = 5.5)	0.541
						Without PIM: mean = 98.7 (SD = 3.1)	
De Vincentis *et al.*[34]	Beers	PIM	Barthel Index at 3-month follow up	Adjusted	HR	−2 (−7.03 to 3.31)	0.454
	STOPP	PIM	Barthel Index at 3-month follow up	Adjusted	HR	−1 (−6.59 to 4.92)	0.734
	Anticholinergic Cognitive Burden	PIM	Barthel Index at 3-month follow up	Adjusted	HR	−7.55 (−12.37 to −2.47)	0.004

(Continued)

Table 2. (continued)

Author	Criteria used	Type of medications	Outcome measured	Adjustments	Statistical unit	Result (95% CI)	*p* value
Gosch *et al.*[59]	STOPP/START	PIM and PPO	ADLs	NG	NG	Low Functional Status	<0.001
Manias *et al.*[52]	STOPP/START	PIM	Independence in personal activities of daily living	Adjusted	OR	1.07 (0.95–1.19)	0.261
			Independence in domestic ADL	Adjusted	OR	1.17 (1.01–1.34)	0.036
			Independence in community ADL	Adjusted	OR	1.25 (1.06–1.48)	0.010
Mohamed *et al.*[35]	Beers	PIM	Katz ADLs	Adjusted	OR	1.42 (0.87–2.32)	>0.05
Moriarty *et al.*[36]	STOPP	PIM	ADL	Adjusted	OR	⩾2 PIM 1.22 (0.74– 2.01)	0.439
	Beers	PIM				⩾2 PIM 2.11 (1.36–3.28)	0.001
	ACOVE PIMs	PIM				⩾2 PIM 1.10 (0.54–2.24)	0.792
	START	PPO				⩾2 PPO 1.98 (1.20–3.26)	0.008
	ACOVE PPOs	PPO				⩾2 PPO 1.82 (1.16–2.86)	0.009
Nagai *et al.*[54]	STOPP-J	PIM	Bartel Index gain	Adjusted	Beta	−0.313 (−13.188 to −4.430)	<0.001
Pasina *et al.*[65]	Anticholinergic Cognitive Burden	With anticholinergic medications	Barthel Index ADL	Adjusted	ANOVA	83.5 (81.9–85.0)	0.03
		No anticholinergic medications				86.3 (84.4–88.1)	
Renom-Guiteras *et al.*[62]	EU(7) - PIM List	PIM	Katz-index of 0–2 *versus* 6	Adjusted	OR	2.93 (1.85–4.65)	<0.001
			Katz-index of 3–5 *versus* 6	Adjusted	OR	1.848 (1.19–2.86)	0.006
Tosato *et al.*[37]	STOPP Beers	STOPP (PIM *versus* no PIM)	Decline in physical ADL	Adjusted	OR	2.00 (1.10–3.64)	<0.05
		Beers (PIM *versus* no PIM)	Decline in physical ADL	Adjusted	OR	1.57 (0.85–2.89)	>0.05
		STOPP (⩾2 PIMs)	Decline in physical ADL	Adjusted	OR	3.50 (1.77–6.91)	<0.05
		Beers (⩾2 PIMs)	Decline in physical ADL	Adjusted	OR	1.90 (0.95–3.81)	>0.05

(Continued)

Table 2. (continued)

Author	Criteria used	Type of medications	Outcome measured	Adjustments	Statistical unit	Result (95% CI)	*p* value
IADL							
Bonfiglio *et al.*[58]	STOPP-J	PIM	IADL	Not adjusted	Independent *t*-test	With PIM: mean = 0.8 (SD = 0.1)	0.203
						Without PIM: mean = 0.9 (SD = 0.1)	
Cardwell *et al.*[63]	Drug burden index	PIM	Functional status, change in Nottingham Extended ADL	Adjusted	Difference in mean score	Māori:	
						12 months: 0.49 (0.82–1.11)	0.77
						24 months: 0.55 (–1.36 to 0.81)	0.62
						36 months: 1.01 (–1.99 to 1.98)	1.00
						Non-Māori:	
						12 months: 0.36 (–1.22 to 0.20)	0.16
						24 months: 0.41 (–1.20 to 0.39)	0.31
						36 months: 0.49 (–1.01 to 0.89)	0.90
Koyama *et al.*[38]	Beers	PIM	IADL impairments	Adjusted	OR	1.36 (1.05–1.75)	<0.05
Mohamed *et al.*[35]	Beers	PIM	IADL impairment	Adjusted	OR	1.72 (1.09–2.73)	<0.05
Physical performance							
Anson *et al.*[66]	Quantitative drug index	Falls-risk medications	Berg Balance Scale	Adjusted	Multiple regression	Standardised beta: –0.26	0.02
			TUG Test	Adjusted	Multiple regression	Standardised beta: 0.32	0.007
			TUG Test with cognitive dual task	Adjusted	Multiple regression	Standardised beta: 0.27	0.02
			Activities-specific Balance Confidence	Adjusted	Multiple regression	Standardised beta: –0.32	0.009
Gosch *et al.*[59]	STOPP/START	PIM and PPO	TUG Test	Adjusted	NG	Low mobility patients have more STOPP items	0.036
				Unadjusted	NG	Low mobility patients have more STOPP items	0.006

(Continued)

Table 2. (continued)

Author	Criteria used	Type of medications	Outcome measured	Adjustments	Statistical unit	Result (95% CI)	*p* value
Gnjidic *et al.*[64]	Drug burden index	Anticholinergic and sedative medications	Chair Stand Test (CST)	NG	Difference in time	CST: 0.58 (−0.11 to 1.27)	>0.05
			6 m Walking Speed (6WS)		Difference in speed	6WS: −0.03 (−0.05 to 0.00)	<0.05
			20 cm NWS		Difference in speed	NWS: −0.03 (−0.05 to −0.01)	<0.05
			Grip Strength (GS)		Difference in kg (GS)	GS: −1.09 (−1.90 to −0.28)	<0.01
			Balance		Difference in performance score (Balance)	Balance: −0.11 (−0.18 to −0.03)	<0.01
			IADL		Difference in IADL Score	IADL: 0.18 (0.04–0.32)	<0.01
Kersten *et al.*[8]	NORGEP Beers	PIM	TUG Test	Adjusted	ANOVA F	0.20	0.80
			HGS (Left Hand)		ANOVA F	2.20	0.10
			HGS (Right Hand)		ANOVA F	1.10	0.30
Naples *et al.*[39]	Beers	PIM	GSD	Unadjusted	OR	1.06 (0.92–1.24)	>0.05
			GSD	Adjusted (with time- varying age)	OR	1.08 (0.93–1.26)	>0.05
			GSD	Adjusted (without time-varying age)	OR	1.06 (0.90–1.24)	>0.05
			GSD (slow walkers)	Unadjusted	OR	1.28 (1.03–1.58)	<0.05
			GSD (slow walkers)	Adjusted (with time- varying age)	OR	1.27 (1.02–1.57)	<0.05
			GSD (slow walkers)	Adjusted (without time-varying age)	OR	1.23 (0.97–1.55)	>0.05
			GSD (fast walkers)	Unadjusted		1.15 (0.92–1.44)	>0.05
			GSD (fast walkers)	Adjusted (with time- varying age)		1.13 (0.90–1.42)	>0.05
			GSD (fast walkers)	Adjusted (without time-varying age)		1.03 (0.81–1.31)	>0.05
Sengul Aycicek *et al.*[40]	Beers	PIM	BPBS – balance	Adjusted	OR	11.05 (2.39–51.10)	0.002

(Continued)

Table 2. (continued)

Author	Criteria used	Type of medications	Outcome measured	Adjustments	Statistical unit	Result (95% CI)	*p* value
Functional independence score							
Bonfiglio *et al.*[58]	STOPP-J	PIM	Quality of Life VAS	Adjusted	OR	0.973 (0.939–1.008)	0.131
	STOPP-J	PIM	Fried Criteria for Frailty	Adjusted	OR	1.171 (0.676–2.028)	0.573
Chan *et al.*[41]	Beers	PIM	SOF Score	NG	Correlation between change in # of PIMs and change in SOF score from admission to discharge	$r = -0.44$	<0.001
Chin *et al.*[42]	Beers	PIM	Health Related Quality of Life	NG	Score change if prescribed prior to admission	−3.5 (−6.9 to −0.1)	<0.05
					Score change if prescribed in the emergency department	−10.7 (−17.1 to −4.4)	<0.05
					Score change if prescribed upon discharge from emergency department	−12.7 (−20.5 to −4.8)	<0.05
Hasan *et al.*[43]	Beers	PIM	Groningen Frailty Indicator	NG	Spearman's correlation *r*	0.025 (outpatient)	0.745 (outpatient)
						0.097 (inpatient)	0.206 (inpatient)
	STOPP	Potential inappropriate prescribing				0.041 (outpatient)	0.595 (outpatient)
						−0.065 (inpatient)	0.399 (inpatient)
	Drug burden index	Sedatives and anticholinergics				−0.096 (outpatient)	0.210 (outpatient)
						−0.158 (inpatient)	0.038 (inpatient)
	Beers	PIM	Older People's Quality of Life	NG	Spearman's correlation *r*	−0.157 (outpatient)	0.040 (outpatient)
						−0.085 (inpatient)	0.267 (inpatient)
	STOPP	Potential inappropriate prescribing				−0.052 (outpatient)	0.501 (outpatient)
						0.022 (inpatient)	0.774 (inpatient)

(Continued)

Table 2. (continued)

Author	Criteria used	Type of medications	Outcome measured	Adjustments	Statistical unit	Result (95% CI)	*p* value
	Drug burden index	Sedatives and anticholinergics				−0.069 (outpatient)	0.369 (outpatient)
						0.034 (inpatient)	0.656 (inpatient)
Iaboni *et al.*[44]	Beers	PIM	Time to full functional recovery following hip fracture	Adjusted	HR	0.69 (0.52–0.92)	0.012
Kose *et al.*[45]	Beers	PIM	FIM	Adjusted	FIM gain	−1.393 × change in number of PIM + 5.7	<0.0001
Kose *et al.*[46]	Beers	PIM	FIM–motor	Adjusted	Linear regression, changes in number of PIMs	Beta = −0.988 (−1.919 to −0.056)	0.0377
Mohamed *et al.*[35]	Beers	PIM	OARS PH survey	Adjusted	OR	1.97 (1.15–3.37)	<0.05
Shibasaki *et al.*[47]	Beers	PIM	FIM gain: FIM at discharge –	Adjusted	Standardised β	0.084	0.260
	START	PPO	FIM at admission			0.180	0.016
Umit *et al.*[48]	Beers START/STOPP	Prolonged use of benzodiazepines	ECOG Performance status (men)	NG	OR	2.46 (1.91–3.27)	0.007

ACOVE, assessing care of vulnerable elders indicators; ADL, activities of daily living; BPBS, Biosway Portable Balance System; ECOG, Eastern Cooperative Oncology Group; FIM, functional independence measure; GSD, gait speed decline; HGS, hand grip strength; HR, hazard ratio; IADL, instrumental activities of daily living; IRR, incidence rate ratio; NG, not given; NORGEP, Norwegian General Practice; NWS, narrow walking speed; OARS PH, Older Americans Resources and Services Physical Health; OR, odds ratio; PIM, potentially inappropriate medications; PIPM, potential inappropriate psychoactive medications; PPO, potential prescribing omissions; PPV, positive predictive value; SOF, scale of functioning; START, screening tool to alert to right treatment; STOPP, screening tool of older people's prescriptions; TUG, timed up and go test.

Table 3. Effect of inappropriate medication prescriptions on physical function.

Type of physical function	Outcome		
Falls	21[a]	9[b]	0[c]
Fractures	7[a]	2[b]	0[c]
Activities of daily living	8[a]	2[b]	0[c]
Instrumental activities of daily living	4[a]	2[b]	0[c]
Physical performance	5[a]	2[b]	0[c]
Functional independence score	9[a]	1[b]	

[a]Significantly associated with impediment of physical function.
[b]No significant association with physical function.
[c]Significantly associated with improvement of physical function.

Health-Related Quality-of-Life Score.[42] In one study, a lowering in the number of PIMs was associated with a significant increase in the Functional Independence Measure.[45] In one study, PIM use was associated with a longer time to full functional recovery in older patients who had surgery for a hip fracture, especially those patients who were using two or more PIMs at 2–14 days after surgical hip fracture repair.[44]

Quality of included studies

Table 4 shows the results of the modified Newcastle-Ottawa Scale (Supplemental Files S2 and S3), which assesses the quality of included studies. The median total NOS score was 6.0 (IQR 5–7).

Table 4. Quality of included studies ($N = 55$).

Author	Selection				Comparability	Outcome			Total
	S1	S2	S3	S4	C1	O1	O2	O3	
Longitudinal studies									
Ackroyd-Stolarz *et al.*[13]	1	1	1	0	0	1	0	0	4
Agashivala and Wu[14]	1	1	1	1	1	1	0	0	6
Beer *et al.*[15]	1	1	1	0	1	1	1	1	7
Berdot *et al.*[16]	1	1	1	0	1	0	1	1	6
Borenstein *et al.*[17]	1	1	1	0	0	1	1	1	6
Cardwell *et al.*[63]	1	1	1	0	2	1	1	1	8
Chan *et al.*[41]	1	1	1	1	0	1	1	0	6
Chin *et al.*[42]	1	1	1	0	0	1	1	1	6
Chun *et al.*[20]	1	1	1	0	0	1	1	1	6
De Vincentis *et al.*[34]	1	1	1	0	1	1	1	1	7
Delgado *et al.*[57]	1	1	1	0	1	1	1	1	7
Early *et al.*[21]	1	1	1	1	1	1	1	1	8
Fernández *et al.*[22]	1	1	1	1	0	1	1	1	7
Fick *et al.*[31]	1	1	1	0	0	1	0	0	4
Fick *et al.*[32]	1	1	1	0	1	1	0	0	5
Frankenthal *et al.*[49]	1	1	1	0	0	1	1	1	6
García-Gollarte *et al.*[50]	1	1	1	0	0	1	1	1	6
Gosch *et al.*[59]	1	1	1	0	1	1	1	0	6
Hamilton *et al.*[23]	1	1	1	0	0	1	1	0	5
Hill-Taylor *et al.*[51]	1	1	1	0	0	1	1	0	5
Hyttinen *et al.*[60]	1	1	1	0	1	1	0	0	5
Hyttinen *et al.*[61]	1	1	1	1	1	1	1	1	8
Iaboni *et al.*[44]	1	1	1	0	1	0	1	0	5
Ie *et al.*[24]	1	1	1	0	1	1	1	1	7
Kersten *et al.*[8]	1	1	1	0	1	1	1	1	7
Kose *et al.*[45]	1	1	1	0	0	1	1	0	5
Kose *et al.*[46]	1	1	1	1	1	1	1	0	7
Koyama *et al.*[38]	1	1	1	0	1	1	1	0	6
Lu *et al.*[33]	1	1	1	0	1	1	0	0	5

(Continued)

Table 4. (continued)

Author	Selection				Comparability	Outcome			Total
	S1	S2	S3	S4	C1	O1	O2	O3	
Manias *et al.*[52]	1	1	1	0	0	1	0	0	4
McMahon *et al.*[25]	1	1	1	1	1	1	0	0	6
Moriarty *et al.*[36]	1	1	1	0	1	1	1	1	7
Nagai *et al.*[53]	1	0	1	0	1	1	1	1	6
Nagai *et al.*[54]	1	1	1	1	1	1	1	1	8
Naples *et al.*[39]	1	1	1	1	1	1	1	1	8
Narayan and Narayan[26]	1	1	1	0	1	1	1	0	6
Ota *et al.*[27]	1	1	1	1	1	1	1	1	8
Pasina *et al.*[65]	1	1	1	0	1	1	1	0	6
Renom-Guiteras *et al.*[62]	1	1	1	0	1	0	1	1	6
Schiek *et al.*[28]	1	1	1	1	0	1	1	1	7
Sengul Aycicek *et al.*[40]	1	1	1	1	1	1	1	0	7
Shibasaki *et al.*[47]	1	1	1	1	1	1	1	0	7
Stockl *et al.*[29]	1	1	1	1	1	1	0	0	6
Tosato *et al.*[37]	1	1	1	0	2	1	1	0	7
Umit *et al.*[48]	1	1	1	0	0	1	1	0	5
Walker *et al.*[30]	1	1	1	1	1	1	1	1	8
Weeks *et al.*[55]	1	1	1	0	1	1	1	0	6
Cross-sectional studies									
Anson *et al.*[66]	1	1	1	0	0	1	NA	NA	4
Bonfiglio *et al.*[58]	1	1	1	0	1	1	NA	NA	5
Cameron *et al.*[18]	1	1	1	0	1	1	NA	NA	5
Carter *et al.*[19]	1	1	0	0	0	0	NA	NA	2
Dalleur *et al.*[56]	1	1	1	0	1	1	NA	NA	5
Gnjidic *et al.*[64]	1	1	1	0	1	1	NA	NA	5
Hasan *et al.*[43]	0	1	1	0	1	1	NA	NA	4
Mohamed *et al.*[35]	1	1	1	1	1	1	NA	NA	6

Discussion

The systematic review showed that PIMs were associated with a higher rate of falls and fractures. There was one study examining the association of PPOs on falls and fractures. PIMs and PPOs were also associated with impairment in ADLs and

IADL impairment. PIMs and PPOs were also associated with poor physical performance comprising the Timed Up and Go test, walking speed, grip strength, time to functional recovery, functional independence and scale of functioning. In contrast to extensive work conducted with PIMs, there was a small amount of research related to associations of PPOs and physical function.

A number of medication classes were implicated as PIMs in falls, fractures and impairment in physical performance including antipsychotic, sedative, anti-anxiety, anticholinergic, antidiabetic, opioid and antihypertensive medications.[14,23,32,51,52,61,65] Aside from the use of PIMs, the combination of different medications can lead to drug interactions that could have exacerbated the adverse effects experienced by older adults, thereby leading to higher propensity for impaired physical function.[10] Furthermore, adverse drug reactions can occur independently of PIMs, which can contribute to accentuating the impact on physical function.[67] Anticholinergic cognitive burden is also associated with increased susceptibility of delirium, longer hospital stays and increased prescription of more medications. This combination of events may also further impede physical performance experienced by older patients.[68]

There has been limited research examining the association of PPOs on physical function. Of studies examining PPOs, their impact has been considered as a large group entity rather than determining which PPO criteria or medication groups may be associated with physical function.[49,50,55] Conversely, a study by Dalleur *et al.* study provided valuable insight into the association of prescribing omissions with physical function.[56] In that study, prescribing omissions were associated with a significant number of hospital admissions in relation to osteoporotic fractures and fall admissions in patients with fall-risk PPOs. For their study, a pharmacist and a geriatrician independently used the STOPP and START criteria to detect PIMs and PPOs and their association with outcomes, which could contribute to reporting bias. Furthermore, for patients not receiving musculoskeletal medications, such as calcium, vitamin D and bisphosphonates, patients were found to be at risk of a hospital admission for a fall with a fracture. Further work is needed on other PPOs, and their associations with physical function. Examples include the lack of use of angiotensin converting enzyme inhibitors for cardiac failure, or the lack of use of regular inhaled beta-2 agonist or anticholinergic medication for chronic obstructive pulmonary disease, or the lack of use of platelet aggregation inhibitors, statins or antithrombotic agents for ischaemic heart disease. Omissions of these medications may lead to symptoms affecting patients' physical function and mobility.

Methodological limitations of past studies related to their focus on PIMs rather than PPOs. Most studies focussed on older people living in the community and hospitals. The results may therefore not be extended to different clinical situations. There has been an increased focus in recent years on comparing results between screening tools for inappropriate medication prescribing. Further work is needed to determine the sensitivity in the use of various tools in terms of the associations between inappropriate prescribing and physical function. While many studies comprised large sizes, some studies had small samples, which could have impacted results related to physical function. In most studies, the dose effect of how the number of inappropriate medications was associated with physical function related adverse outcomes was not examined. Fewer than half of the studies involved a prospective cohort design. Further research is also needed on how changes in inappropriate prescribing across transitions of care are associated with physical function.

Strengths and limitations

A strength of the systematic review is that studies were included only if they used a validated tool to assess the appropriateness of medications. This approach was undertaken to eliminate sources of bias that could arise from a geriatrician or a pharmacist labelling a medication as inappropriate. All settings were included in the systematic review, which facilitated a comprehensive examination of the topic. A limitation of the systematic review was that only studies published in English were included. Conference papers were excluded from the systematic review because of the limited information contained in these sources. It is possible that additional insights may have been obtained from such sources.

Conclusion

Inappropriate medication prescribing is associated with poor physical function. Health professionals should focus on supporting older people to reduce the use of PIMs and PPOs. More research is required to investigate the associations of PPOs and physical function.

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