La complessità terapeutica nelle comorbidità dell’anziano

Enrico Benvenuti - *Firenze*

The importance of regular medication review in older people

+

= ?

- **Increase in co-morbidities with age**
- **Physiological changes**
  - pharmacokinetics
  - pharmacodynamics

- **Increased susceptibility to:**
  - Polypharmacy
  - Drug interactions
  - Adverse drug reactions
  - Prescribing cascade
  - Poor compliance
  - Potentially inappropriate prescribing

Potentially inappropriate prescribing defined

- Risk > Benefit
- Over-prescribing
  - Excessive doses/duration of medicines
  - Polypharmacy
- Mis-prescribing
  - Unfavourable choice of medicine, dose, or duration
- Under-prescribing
  - Not prescribing a clinically indicated medicine, despite the patient not having any contra-indication to that medicine

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STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation

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CLINICAL INVESTIGATIONS

American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

By the American Geriatrics Society 2015 Beers Criteria Update Expert Panel

STOPP: Screening Tool of Older People's Potentially Inappropriate Prescriptions

The following drug prescriptions are potentially inappropriate in persons aged ≥ 65 years of age

Cardiovascular System

1. Digoxin at a long-term dose > 125µg/day with impaired renal function
2. Loop diuretic for dependent ankle oedema only i.e. no clinical signs of heart failure
3. Loop diuretic as first-line monotherapy for hypertension
4. Thiazide diuretic with a history of gout
5. Non cardioselective Beta-blocker with Chronic Obstructive Pulmonary Disease
6. Beta-blocker in combination with verapamil
7. Use of diltiazem or verapamil with NYHA Class III or IV heart failure
8. Calcium channel blockers with chronic constipation
9. Use of aspirin and warfarin in combination without histamine H_2 receptor antagonist
10. Dipyridamole as monotherapy for cardiovascular secondary prevention
11. Aspirin with a past history of peptic ulcer disease without histamine H_2 receptor antagonist or Proton Pump Inhibitor
12. Aspirin at dose > 150mg day
13. Aspirin with no history of coronary, cerebral or peripheral vascular symptoms or occlusive event
14. Aspirin to treat dizziness not clearly attributable to cerebrovascular disease
15. Warfarin for first, uncomplicated deep venous thrombosis for longer than 6 months duration
16. Warfarin for first uncomplicated pulmonary embolus for longer than 12 months duration
17. Aspirin, clopidogrel, dipyridamole or warfarin with concurrent bleeding disorder

STOPP: Screening Tool of Older People's Potentially Inappropriate Prescriptions

The following drug prescriptions are potentially inappropriate in persons aged ≥ 65 years of age

Central Nervous System and Psychotropic Drugs.

1. Tricyclic antidepressants (TCAs) with dementia
2. TCAs with glaucoma
3. TCAs with cardiac conductive abnormalities
4. TCAs with constipation
5. TCAs with an opiate or calcium channel blocker
6. TCAs with prostatism or prior history of urinary retention
7. Long-term (i.e. > 1 month), long-acting benzodiazepines and benzodiazepines with long-acting metabolites
8. Long-term (i.e. > 1 month) neuroleptics as long-term hypnotics
9. Long-term neuroleptics (> 1 month) in those with parkinsonism
10. Phenothiazines in patients with epilepsy
11. Anticholinergics to treat extra-pyramidal side-effects of neuroleptic medications
12. Selective serotonin re-uptake inhibitors (SSRIs) with a history of clinically significant hyponatraemia
13. Prolonged use (> 1 week) of first generation antihistamines i.e. diphenydramine, chlorpheniramine, cyclizine, promethazine

STOPP: Screening Tool of Older People's Potentially Inappropriate Prescriptions

Gastrointestinal System

1. Diphenoxylate, loperamide or codeine phosphate for treatment of diarrhoea of unknown cause
2. Diphenoxylate, loperamide or codeine phosphate for treatment of severe infective gastroenteritis
3. Prochlorperazine (Stemetil) or metoclopramide with Parkinsonism
4. PPI for peptic ulcer disease at full therapeutic dosage for > 8 weeks
5. Anticholinergic antispasmodic drugs with chronic constipation

Respiratory System

1. Theophylline as monotherapy for COPD
2. Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD
3. Nebulised ipratropium with glaucoma

Musculoskeletal System

1. NSAID with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent histamine H_2 receptor antagonist, PPI or misoprostol
2. NSAID with moderate-severe hypertension
3. NSAID with heart failure
4. Long-term use of NSAID (>3 months) for symptom relief of mild osteoarthtitis
5. Warfarin and NSAID together
6. NSAID with chronic renal failure
7. Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthrtitis or osterarthritis
8. Long-term NSAID or colchicine for chronic treatment of gout where there is no contraindication to allopurinol

STOPP: Screening Tool of Older People's Potentially Inappropriate Prescriptions

The following drug prescriptions are potentially inappropriate in persons aged ≥ 65 years of age

Urogenital System

1. Bladder antimuscarinic drugs with dementia
2. Antimuscarinic drugs with chronic glaucoma
3. Antimuscarinic drugs with chronic constipation
4. Antimuscarinic drugs with chronic prostatism
5. Alpha-blockers in males with frequent incontinence i.e. one or more episodes of incontinence daily
6. Alpha-blockers with long-term urinary catheter *in situ* i.e. more than 2 months

Endocrine System

1. Glibenclamide or chlorpropamide with type 2 diabetes mellitus
2. Oestrogens with a history of breast cancer or venous thromboembolism
3. Beta-blockers in those with diabetes mellitus and frequent hypoglycaemic episodes i.e. ≥ 1 episode per month
4. Oestrogens without progestogen in patients with intact uterus

STOPP: Screening Tool of Older People's Potentially Inappropriate Prescriptions

The following drug prescriptions are potentially inappropriate in persons aged ≥ 65 years of age

Drugs that adversely affect fallers.

1. Benzodiazepines
2. Neuroleptic drugs
3. First generation antihistamines
4. Vasodilator drugs with persistent postural hypotension i.e. recurrent > 20mmHg drop in systolic blood pressure
5. Long-term opiates in those with recurrent falls

Analgesic Drugs

1. Use of long-term powerful opiates e.g. morphine or fentanyl as first line therapy for mild-moderate pain
2. Regular opiates for more than 2 weeks in those with chronic constipation without concurrent use of laxatives
3. Long-term opiates in those with dementia unless indicted for palliative care or management of moderate/severe chronic pain syndrome

Duplicate Drug Classes

Any duplicate drug class prescription e.g. two concurrent opiates, NSAID's, SSRI's, loop diuretics, ACE inhibitors

Table 1. 2105 Selected American Geriatric Society Beers Criteria Highlights[11]

Medication	Recommendation	Reason
Anticholinergics, first-generation antihistamines, such as diphenhydramine, doxylamine, hydroxyzine	Avoid (Strong)	↓ Clearance, ↑ dry mouth, confused, sleepy, tolerant of sedative effects, highly anticholinergic
Anticholinergics, antiparkinson agents, such as benztropine, trihexyphenidyl	Avoid (strong)	Better Parkinson's disease treatments; not recommended for use in preventing extrapyramidal symptoms with antipsychotic use
Anti-infective, nitrofurantoin	Avoid for long-term suppression and when creatinine clearance < 30 mL/min (strong)	Pulmonary toxicity, hepatotoxicity, peripheral neuropathy
Dronedarone	Avoid in patients with permanent atrial fibrillation or recent or severely decompensated heart failure (strong)	Worse outcomes reported, better to control rate than rhythm in atrial fibrillation
Digoxin doses > 125 µg/day in heart failure or atrial fibrillation	Avoid (strong)	In heart failure and atrial fibrillation no more benefit, but ↑ toxicity at high doses
Tricyclic antidepressants, such as amitriptyline	Avoid (strong)	Highly anticholinergic, confused, sleepy, orthostatic effects
Antipsychotics first and second generation (halperidol, fluphenazine, aripiprazole, olanzapine)	Avoid (strong)	Avoid for behavioral problems in dementia unless nondrug solutions fail and patient is a threat to self/others; ↑ risk of stroke and mortality in elderly with dementia; olanzapine syncope
Benzodiazepines, such as diazepam, clonazepam, lorazepam, alprazolam, flurazepam	Avoid (strong)	Avoid any of these for insomnia, agitation, or delirium (may cause falls); elderly have sensitivity to longer acting agents (eg, clonazepam)
Megestrol acetate	Avoid (strong)	Minimal effect on weight gain; ↑ risk for clots and possibly death
Amiodarone	Avoid (strong)	Greater toxicities than others in atrial fibrillation, unless heart failure or left ventricular hypertrophy
Skeletal muscle relaxants, such as cyclobenzaprine, carisoprodol	Avoid (strong)	Poorly tolerated by elderly due to anticholinergic effects, confused, sleepy side effects; ↑ risk of fracture
Non-benzodiazepine, sedative-hypnotics, such as zolpidem, eszopiclone, zaleplon	Avoid (strong)	Similar effects as benzodiazepines (falls, fractures, delirium, high rate of physical dependence) and minimal improvement on sleep latency and duration
Sliding scale insulin (sole use of rapid or short-acting insulins without basal or long-acting insulins to manage or prevent hyperglycemia	Avoid (strong)	↑ Risk of hypoglycemia and falls without overall better control of blood sugar

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PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

Potentially inappropriate prescribing and adverse drug reactions in the elderly: a population-based study

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Table 3 Most common potentially inappropriate prescriptions

Criterion	*n* (%)	*n* (%) causing ADRs
Aspirin with no history of coronary, cerebral or peripheral arterial symptoms or occlusive arterial event	154 (18.9)	7 (6.5)
Benzodiazepines in those prone to fall	43 (5.4)	10 (23.3)
NSAID with moderate-severe hypertension	41 (5.0)	1 (2.4)
Long-term long-acting benzodiazepines	37 (4.6)	3 (8.1)
Prolonged use (>1 week) of first generation antihistamines	28 (3.4)	7 (25.0)
Use of long-term powerful opiates as first-line therapy for mild-moderate pain	27 (3.3)	0 (0)
Long-term opiates in those with recurrent falls	26 (3.2)	6 (23.1)
Long-term (i.e. >1 month) neuroleptics as long-term hypnotics	26 (3.2)	12 (46.2)
Oestrogens without progestogen in patients with intact uterus	23 (2.8)	0 (0)
Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthritis or osteoarthritis	19 (2.3)	2 (10.5)
Aspirin at dose >150 mg/day	17 (2.1)	0
Long-term use of NSAID (>3 months) for relief of mild joint pain in osteoarthritis	14 (1.7)	0
Vasodilator drugs known to cause hypotension in those with persistent postural hypotension	13 (1.6)	12 (92.3)
Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate–severe COPD	12 (1.5)	0
First-generation antihistamines in those prone to fall	11 (1.4)	1 (9.1)
Neuroleptic drugs in those prone to fall	10 (1.2)	0
Total	607 PIPs (374 persons)	64 (10.5)

ADR adverse drug reaction, *NSAID* non-steroidal anti-inflammatory drugs, *COPD* chronic obstructive pulmonary disease

Detection of potentially inappropriate prescribing in the very old: cross-sectional analysis of the data from the BELFRAIL observational cohort study

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Abstract

Background: Little is known about the prevalence and clinical importance of potentially inappropriate prescribing instances (PIPs) in the very old (>80 years). The main objective was to describe the prevalence of PIPs according to START (Screening Tool to Alert doctors to Right Treatment; omissions) and,STOPP (Screening Tool of Older Person's Prescriptions; over/misuse) and the Beers list (over/misuse). Secondary objectives were to identify determinants if PIPs and to assess the clinical importance to modify the treatment in case of PIPs.

Methods: Cross-sectional analysis of baseline data of the BELFRAIL cohort, which included 567 Belgian patients aged 80 and older in primary care. Two independent researchers applied the screening tools to the study population to detect PIPs. Next, a multidisciplinary panel of experts rated the clinical importance of the PIPs on a subsample of 50 patients.

Results: In this very old population (median age 84 years, 63 % female), the screening detected START-PIPs in 59 % of patients, STOPP-PIPs in 41 % and Beers-PIPs in 32 %. Assessment of the clinical importance revealed that the most frequent PIPs were of moderate or major importance. In 28 % of the subsample, the relevance of the PIP was challenged by the global medical, functional and social background of the patient hence the validity of some criteria was questioned.

Conclusion: Potentially inappropriate prescribing is highly prevalent in the very old. A good understanding of the patients' medical, functional and social context is crucial to assess the actual appropriateness of drug treatment.

Keywords: Inappropriate Prescribing, Aged 80 and older, Primary care, General practice, STOPP&START, Beers

Table 3 Determinants of potentially inappropriate prescribing in the study population (multivariate analysis)

	Covariates	OR [95 % CI]	*p* value
START-PIP			
	ADL lowest quintile[a]	0.8 [0.4–1.5]	0,523
	Age, per year	1.0 [0.9–1.1]	0,227
	CIRS >4	1.0	
	CIRS <4	0.2 [0.1–0.3]	<0,001
	CIRS=4	0.6 [0.3–1.1]	0,090
	GDS-15 >4[b]	1.2 [0.7–2.0]	0,442
	Gender, women	0.9 [0.6–1.4]	0,727
	Tinetti ≤ 18[c]	1.0	
	Tinetti 25–28	0.5 [0.2–1.2]	0,130
	Tinetti 19–24	0.9 [0.3–2.2]	0,840
STOPP-PIP			
	ADL lowest quintile	1.5 [1.0–2.4]	0.050
	Age, per year	1.0 [0.9–1.0]	0.957
	Gender, women	1.2 [0.9–1.8]	0.211
	Resident in a nursing home	1.8 [0.9–3.2]	0.056
BEERS-PIP			
	ADL lowest quintile	1.1 [0.7–1.9]	0.558
	Age, per year	0.9 [0.9–1.0]	0.515
	CIRS >4	1.0	
	CIRS < 4	0.4 [0.3–0.7]	<0.001
	CIRS = 4	0.6 [0.4–0.9]	0.041
	GDS-15 >4	1.5 [0.9–2.3]	0.094
	Gender, women	1.2 [0.8–1.8]	0.364
	Resident in a nursing home	1.8 [1.0–3.4]	0.045

Hosmer-Lemeshow goodness-of-fit *P*-value for START = 0.42; STOPP = 0.15; Beers = 0.89 indicating that the models are a good fit for the data
Abbreviations: ADL activities of daily living, *CI* confidence interval, *CIRS* cumulative illness rating scale, *GDS* geriatric depression scale, *OR* odds ratio, *PIPs* potentially inappropriate prescribing
[a]ADL lowest quintile: lower ADL score is related to functional dependency
[b]GDS-15 score >4 was considered as "possible depression"
[c]Tinetti score >24 was considered as "low fall risk"; ≤ 18 was "high fall risk"

Determinanti nella scelta farmacologica

Dallauer, 2015

Detection of potentially inappropriate prescribing in the very old: cross-sectional analysis of the data from the BELFRAIL observational cohort study

Dalleur *et al. BMC Geriatrics* (2015) 15:156
DOI 10.1186/s12877-015-0149-2

Table 2 Most frequent potentially inappropriate prescribing events according

	Therapeutic class/medication ± disease
Under prescribing according to START	
	Aspirin or clopidogrel with a documented histor peripheral vascular disease in patients with sinus
	Calcium and vitamin D supplement in patients ir
	ACE inhibitor in the presence of chronic heart fa
	Statin therapy with a documented history of cor disease, where the patient's functional status ren living and life expectancy is greater than 5 years
	Antiplatelet therapy in diabetes mellitus with co (hypertension, hypercholesterolemia, smoking hi
Over/misprescribing according to STOPP or/and Beers	
STOPP and Beers	Aspirin for primary cardiovascular prevention[a]

Table 5 How a holistic approach of the patient challenges the PIPs detected by explicit screening tools

Elements of the patient's record that influence the applicability of the criteria[a]
• Level of severity of a disease • Certainty of the diagnoses • Timing of the medical history (recent event vs. long ago) • Actual intake of the drug that differs from the prescription • Patient's preferences and objectives • Mental status of the patient and associated psychiatric conditions • Absence of alternative treatment • Patient's pain status • Drug-drug interactions • Risk factors for bleeding or for stroke • Contra-indication • Allergies
Situations that question the content validity of the criteria:
• START-PIP in patients already treated by suitable alternative medications e.g., "Proton pump inhibitor with severe gastroesophageal acid reflux disease" in a patient already on histamine H2-receptor antagonist.

Table 6 Recommendations to improve the validity and applicability of explicit tools

Recommendations to improve the validity of the criteria	Recommendations to improve the applicability of the criteria
• mention of contra-indications of the criteria • no contradictions between criteria • no overlap between criteria • precise range of application of the criteria (inclusion criteria) • mention of time to benefit [45, 46]	• clear definitions (conditions, diseases, drug categories) • monitoring tips • suggestions of alternatives (pharmacological and non-pharmacological) • mention of adaptation to functional and cognitive status, life expectancy, and multimorbidity.

cerebral, or peripheral vascular symptoms or occlusive events in STOPP

Pharmacoepidemiol Drug Saf. 2016 Sep;25(9):1070-8. doi: 10.1002/pds.4026. Epub 2016 May 17.

Polytherapy and the risk of potentially inappropriate prescriptions (PIPs) among elderly and very elderly patients in three different settings (hospital, community, long-term care facilities) of the Friuli Venezia Giulia region, Italy: are the very elderly at higher risk of PIPs?

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Author information

Abstract

PURPOSE: The aim of this point-prevalence study was to assess the occurrence of polypharmacy and hyperpolypharmacy and the risk of potentially inappropriate prescriptions (PIPs) among elderly and very elderly patients in different health-care settings of the Friuli-Venezia Giulia region in the North-East of Italy.

METHODS: Prescription pattern of elderly (65-79 years) and very elderly (>79 years) patients in three different health-care settings [hospitals, general practitioners, and long-term care facilities (LTCFs)] was assessed in March 2014, and PIPs were assessed according to the Beers criteria. Other situations at potentially high risk were checked.

RESULTS: A total of 1582 patients (hospital, n = 528; outpatients, n = 527; nursing homes, n = 527) were included. Very elderly were more represented in hospitals (60.4%) and LTCFs (77.1%) than among general practitioners (37.6%). Polypharmacy and hyperpolypharmacy rates ranged 57.7-73.7% and 9.7-15.6%, respectively. The most frequently prescribed drugs were the proton pump inhibitors, whereas the most common PIPs resulted the benzodiazepines. Multinomial regression analysis showed that female sex, age > 79 years, hyperpolypharmacy, and chronic kidney disease were associated with the risk of having ≥2 PIPs. Two situations at high risk of PIPs not contemplated by the Beers criteria were recurrent in the study population and concerned the statins and metformin.

CONCLUSIONS: Polypharmacy and hyperpolypharmacy among elderly and very elderly are strictly associated with the risk of multiple PIPs. The findings offer the opportunity to remark that improvement of the knowledge of safe drug use is generally needed in aging societies and may become of utmost relevance among health-care workers operating in LTCFs.

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Potentially inappropriate prescribing in community-dwelling older people across Europe: a systematic literature review.

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Author information

Abstract

BACKGROUND: Potentially inappropriate prescribing (PIP) is one of the main risk factors for adverse drug events (ADEs) in older people.

PURPOSE: This systematic literature review aims to determine prevalence and type of PIP in community-dwelling older people across Europe, as well as identifying risk factors for PIP.

METHODS: The PubMed and Web of Science database were searched systematically for relevant manuscripts (January 1, 2000-December 31, 2014). Manuscripts were included if the study design was observational, the study participants were community-dwelling older patients in Europe, and if a published screening method for PIP was used. Studies that focused on specific pathologies or that focused on merely one inappropriate prescribing issue were excluded. Data analysis was performed using R statistics.

RESULTS: Fifty-two manuscripts were included, describing 82 different sample screenings with an estimated overall PIP prevalence of 22.6 % (CI 19.2-26.7 %; range 0.0-98.0 %). Ten of the sample screenings were based on the Beers 1997 criteria, 19 on the Beers 2003 criteria, 14 on STOPP criteria (2008 version), 8 on START-criteria (2008 version), and 7 on the PRISCUS list. The 24 remaining sample screenings were carried out using compilations of screening methods or used country-specific lists such as the Laroche criteria. It appears that only PIP prevalence calculated from insurance data significantly differs from the other data collection method categories. Furthermore, risk factors most often positively associated with PIP prevalence were polypharmacy, poor functional status, and depression. Drug groups most often involved in PIP were anxiolytics (ATC-code: N05B), antidepressants (N06A), and nonsteroidal anti-inflammatory and anti-rheumatic products (M01A).

CONCLUSION: PIP prevalence in European community-dwelling older adults is high and depends partially on the data collection method used. Polypharmacy, poor functional status, and depression were identified as the most common risk factors for PIP.

Functional Decline Associated With Polypharmacy and Potentially Inappropriate Medications in Community-Dwelling Older Adults With Dementia

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Abstract

This study provides empirical evidence on whether polypharmacy and potentially inappropriate prescription medications (PIRx, as defined by the 2003 Beers criteria) increase the likelihood of functional decline among community-dwelling older adults with dementia. Data were from the National Alzheimer's Coordinating Center, Uniform Data Set (9/2005–9/2009). Study sample included 1994 community-dwelling participants aged ≥65 with dementia at baseline. Results showed that participants having ≥5 medications were more likely to have functional decline than participants having <5 medications. However, the increased likelihood was only apparent in participants who did not have PIRx. Instead of magnifying the associated risk as hypothesized, PIRx appeared to have a protective effect albeit marginally statistically significant. Therefore, increased medication burden may be associated with functional decline in community-dwelling older adults with dementia who are not prescribed with PIRx. More research is needed to understand which classes of medications have the most deleterious effect on this population.

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Medication Use and Functional Status Decline in Older Adults: A Narrative Review

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RESULTS—Nineteenstudies met the inclusion criteria. Five studies addressed the impact of suboptimal prescribing on function, three of which found an increased risk of worse function in community-dwelling subjects receiving polypharmacy. Three of the four studies that assessed benzodiazepine use and functional status decline found a statistically significant association. One cohort study identified no relationship between antidepressant use and functional status while a randomized trial found that amitriptyline, but not desipramine or paroxetine, impaired certain measures of gait. Two studies found that increasing anticholinergic burden was associated with worse functional status. In a study of hospitalized rehabilitation patients, users of hypnotics/ anxiolytics (e.g., phenobarbital, zolpidem) had lower relative Functional Independence Measure motor gains than nonusers. Use of multiple central nervous system (CNS) drugs (using different definitions) was linked to greater declines in self-reported mobility and Short Physical Performance Battery (SPPB) scores in two community-based studies. Another study of nursing home patients did not report a significant decline in SPPB scores in those taking multiple CNS drugs. Finally, two studies found mixed effects between antihypertensive use and functional status in the elderly.

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PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

Potentially inappropriate prescribing and adverse drug reactions in the elderly: a population-based study

Khedidja Hedna[1,2] · Katja M. Hakkarainen[2,3] · Hanna Gyllensten[2,4] · Anna K. Jönsson[5] · Max Petzold[6] · Staffan Hägg[1,7]

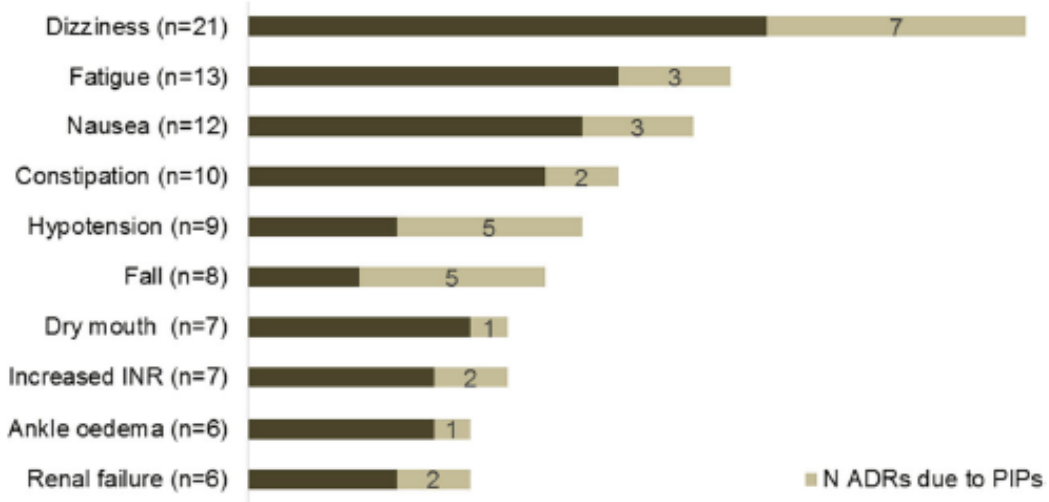

Fig. 2 The most common symptoms of adverse drug reactions and the proportion caused by potentially inappropriate prescriptions

ADR adverse drug reaction
PIP potentially inappropriate prescribing
INR international normalised ratio

Research article

Open Access

Inappropriate medication use and risk of falls – A prospective study in a large community-dwelling elderly cohort

Sarah Berdot[1,2], Marion Bertrand[1,2], Jean-François Dartigues[3], Annie Fourrier[4], Béatrice Tavernier[5], Karen Ritchie[6] and Annick Alpérovitch*[1,2]

Table 3: Association between Inappropriate Medication Use and Risk of Fall

Medication n (%)	≤ 1 fall (N = 4961)	≥ 2 falls (N = 1382)	RR (95% CI)	crude P-value	RR (95% CI)*	P-value*
Inappropriate medication, full list	1500 (30.2)	504 (36.5)				
Inappropriate medication, excluding cerebral vasodilators	924 (18.6)	315 (22.8)	1.27 (1.12–1.43)	<.001	1.05 (0.92–1.20)	.47
Long-acting benzodiazepines	351 (7.1)	144 (10.4)	1.46 (1.23–1.74)	<.001	1.20 (1.00–1.43)	.048
Inappropriate psychotropic drugs	108 (2.2)	47 (3.4)	1.60 (1.20–2.14)	.002	1.31 (0.97–1.76)	.08
Inappropriate medication with anticholinergic properties	223 (4.5)	92 (6.7)	1.50 (1.21–1.85)	<.001	1.18 (0.96–1.47)	.13
Short- or intermediate-half-life benzodiazepines	568 (11.5)	206 (14.9)	1.31 (1.13–1.51)	<.001	0.99 (0.85–1.16)	.89

* Adjusted for age, sex, study centre, body mass index, diurnal drowsiness, number of drugs (excluding inappropriate medication), cognitive functioning, depressive symptoms and impaired mobility.

Anesthesiology 2009; 110:1176–81

Perioperative Drug Therapy in Elderly Patients

Richard Rivera, M.D., Joseph F. Antognini, M.D.†*

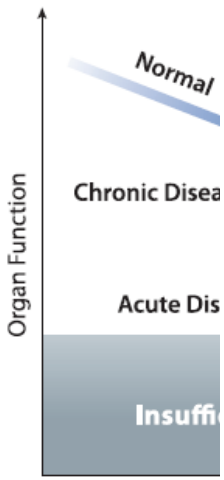

Fig. 1. Organ function c humans, as indicated by this decline, as noted by rary rapid but reversible less of cause, reserve f declines into the *shaded* with permission.

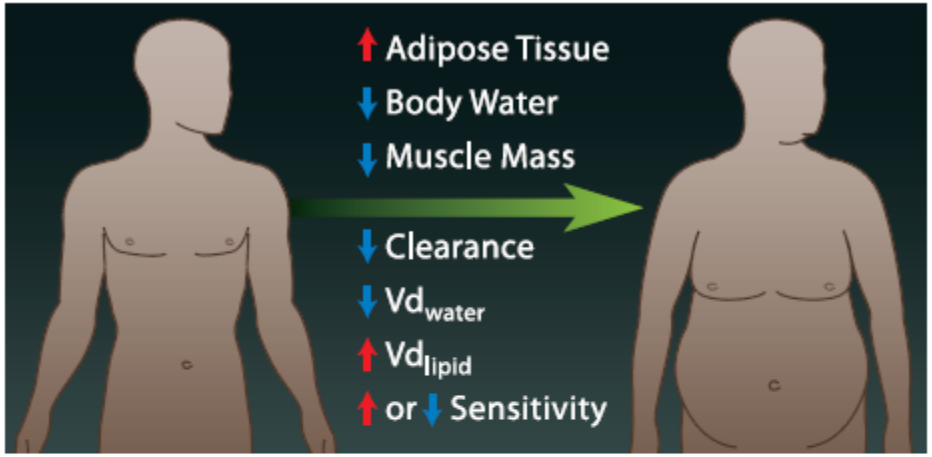

Fig. 2. Compared with young patients, elderly patients tend to have more adipose tissue, decreased body water, and less muscle mass. These changes will cause water-soluble drugs to have decreased volume of distribution (Vd_{water}), whereas lipid-soluble drugs may have increased volume of distribution (Vd_{lipid}). Clearance for most drugs is decreased in the elderly. Drug sensitivity (especially to anesthetics) is usually increased in elderly patients but may be decreased for other drugs, such as β blockers.

Table 1. Age-related Changes in Physiological Parameters

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acology (chapter 61). In
10th edition; 2007. Available
2512888.

Optimal Perioperative Management of the Geriatric Patient: A Best Practices Guideline from the American College of Surgeons NSQIP and the American Geriatrics Society

Sanjay Mohanty, MD, MS, Ronnie A Rosenthal, MD, MS, FACS, Marcia M Russell, MD, FACS, Mark D Neuman, MD, MSc, Clifford Y Ko, MD, MS, MSHS, FACS, Nestor F Esnaola, MD, MPH, MBA, FACS

Table 1. Immediate Preoperative and Intraoperative Management Consensus Recommendations

Immediate preoperative management
Confirm and document patient goals and treatment preferences, including advance directives.
Confirm and document patient's health care proxy or surrogate decision-maker.
In patients with existing advance directives, discuss new risks associated with the surgical procedure and an approach for potentially life-threatening problems consistent with the patient's values and preferences ("required reconsideration").
Consider shortened fluid fast (clear liquids up to 2 hours before anesthesia).
Adhere to existing best practices regarding antibiotic and venous thromboembolism prophylaxis.
Ensure nonessential medications have been stopped and essential medications have been taken.
Intraoperative management
Consideration of regional techniques to avoid postoperative complications and improve pain control.
Directed pain history.
Multi-modal or opioid-sparing techniques.
Postoperative nausea risk stratification and prevention strategies.
Strategies to avoid pressure ulcers and nerve damage.
Prevention of postoperative pulmonary complications and hypothermia.
Judicious use of intravenous fluids.
Appropriate hemodynamic management.
Continuation of indicated cardiac medications.

Recommendations for the Peri-operative Management of Medications in the Elderly

Medication	Potential Risks in Elderly	Peri-operative Recommendations
ACE inhibitors, Angiotensin receptor blockers (ARBs)[104,105]	Hypotensive episodes due to blunting of renin-angiotensin system compensatory action with general anesthesia	Consider stopping these agents 12–24 hours prior to surgery and using beta blockers for BP and HR control on day of surgery
Alpha 2 agonists	↓ stress response to general anesthesia/surgery vs rebound Htn if stopped.	Continue on day of surgery due to potential benefits and consequences of acute withdrawal.
Alzheimers drugs[106]	Cholinesterase inhibitors have cholinergic side effects, mildest with donepezilMemantine has fewer side effects and is disease-modifying.	No clear recommendation peri-operatively. Stopping the cholinesterase inhibitors for 6 weeks appears to erase cognitive benefits suggesting that this class of medications do not alter the disease process.
Anti-coagulants[77,104,107]	lower dose in elderly to achieve equivalent effect, ↑bleeding risk (baseline 1.6% but RR 3.0 with INR 2.5)	If low risk for thrombosis, stop 2–5 days prior to surgery. If high risk of bleeding, keep INR < 1.5. If high risk for thrombosis, change over to heparin.
Anti-depressants-SSRIs[69,70,104]	May ↑bleeding due to effect on platelet aggregation (OR 3.71 for risk of transfusion), idiosyncratic ↑ hyponatremia risk	Recommendation for SSRI is that consequences of bleeding vs severity of psychologic disorder must be balanced. SSRI wash-out period is up to 3 weeks, which could exacerbate mood disorders.
AntiParkinson agents[104,106]	Hemodynamic and arrhythmogenic effects with use vs acute withdrawal and neuroleptic malignant syndrome	No clear recommendations – slow taper to lowest effective dose several weeks before surgery
Anti-psychotics[6,104,108]	Sedative properties	Consider haloperidol and atypical neuroleptics (ie.risperidone) if at risk for psychosis. Safer due to fewer active metabolites, lower extrapyramidal and anticholinergic effects.
Benzodiazepines[31,78]	Impaired cognition and memory, sedation, confusion, unsteadiness	Use short-acting agents at 50% of dose if medical necessity outweighs risks (including discontinuation syndrome)
Beta blockers[79,104]	↓myocardial oxygen demands, ↓peri-operative ischemic events	Continue on day of surgery due to benefits of ↓postoperative CV events and consequences of acute withdrawal.
Digoxin[31]	↑Toxicity with renal disease,verapamil, amiodarone, quinidine, ↓K, ↓Mg, ↑Ca.	Toxicity occurs more frequently in elderly and is more difficult to recognize. Digoxin levels alone do not reliably reflect level of drug activity in the elderly but EKG is a better test.
Dipyridamole[104]	↑bleeding complications due anti-platelet and vasodilatory effects.	Stop at least 2 days prior, if warranted- weigh consequences of peri-operative hemorrhage vs thrombotic events.

Diuretics[31,44]	Hypovolemia and systemic vasodilation can predispose to hypotension with general anesthesia, hypokalemia risk	No consensus
Estrogen (systemic)[80,81]	Dose-dependent risk of VTE of 2.1–6.9	Insufficient evidence to initiate or stop systemic ERT peri-operatively. British national formulary and International Consensus recommend stopping 4–6 weeks prior to surgery.
Herbal therapy[82,104]	↓ability to metabolize active components, proper dosing unclear, many potential drug-interactions	All herbal agents should be stopped at least 1 wk prior to surgery and probably permanently. No evidence that herbal medications improve surgical outcomes and some that suggest they may increase perioperative morbidity.
Hypoglycemics[83]	Cognitive deficits due to neuroglucopenia with hypoglycemia vs hyperglycemic risks	Avoid hypoglycemia and severe hyperglycemia but optimal peri-operative glucose range unknown. Hold oral hypoglycemic agents on AM of surgery.
Hypolipidemics[28,29,104]	Small risk of myopathy and rhabdomyolysis but statins may ↓risk of peri-operative vascular events	Discontinuation of all hypolipidemic agents at least 24 hours prior to surgery except statins.
Proton pump inhibitors and H2 antogonists[104]	Decrease gastric pH and volume-avoid cimetidine due drug interactions	Continuation of proton pump inhibitors due to increase risk of gastric mucosal injury during the perioperative period

Medication	**Potential Risks in Elderly**	**Peri-operative Recommendations**
Thiazide diuretics[31]	Hypokalemia, hyponatremia can cause delirium in the elderly. Hyperuricemia.	Best used in low doses 12.5 mg/d. Loses diuretic effect if CrCl < 20mL/min.
Traditional NSAIDs, ASA[104]	↑bleeding (surgical, gastric), Chronic renal insufficiency + NSAID + hypovolumia = ↑ risk of acute renal failure	Optimal management uncertain-weigh consequences of peri-operative hemorrhage vs thrombotic events. Stop 3–5 days prior, if warranted.

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SUMMARY OF MEDICATIONS COMMONLY USED FOR PONV PROPHYLAXIS AND TREATMENT IN ADULTS[58,68]

Drug	Beers criteria recommendation	Caution
5-HT_3 receptor antagonists (for example, ondansetron)	Use as alternative	Serotonin syndrome QT prolongation
Corticosteroids (for prophylaxis)	Avoid in older adults with or at high risk for delirium	May induce or worsen delirium
Transdermal scopolamine (for prophylaxis)	Avoid unless no other alternatives	Strong anticholinergic properties (increased risk for delirium/cognitive impairment) Can worsen constipation
Metoclopramide	Avoid, unless for gastroparesis	Risk of extrapyramidal effects may be increased in frail older adults
Low-dose promethazine	Avoid	Anticholinergic (increased risk for delirium/cognitive impairment) Increased risk of constipation
Prochlorperazine	Avoid	Anticholinergic (increased risk for delirium/cognitive impairment)

PONV, postoperative nausea and vomiting

Anesthesiology 2009; 110:1176–81

Perioperative Drug Therapy in Elderly Patients

Richard Rivera, M.D., Joseph F. Antognini, M.D.†*

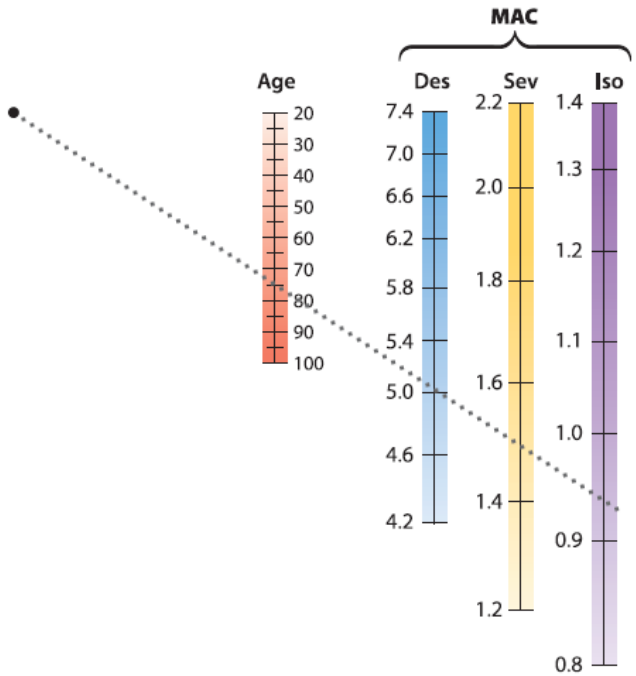

Fig. 3. Normogram for minimum alveolar concentration (MAC) as a function of age. The MACs for desflurane (Des), sevoflurane (Sev), and Isoflurane (Iso) can be determined by placing a ruler on the *dot* at left and drawing a line through the age of the patient. Where the line crosses the respective MAC normogram line yields the MAC value for that age. The *dotted line* shows an example for MAC in a 75-yr-old patient. As an approximation, MAC_{awake} (the concentration that produces unconsciousness in 50% of patients) can be determined by dividing the MAC by 3. The normograms are based on the formula: MAC fraction = $1.32 \cdot 10^{-0.00303 \cdot age}$, where MAC is the MAC fraction based on 1 MAC = MAC at age 40 yr. We assumed MAC at age 40 yr for desflurane, sevoflurane, and isoflurane to be 6.45, 1.9, and 1.2 vol%, respectively. Data and formula are from Eger.[11]

	Drugs	Young Patient	Elderly Patient
Sedative/Hypnotics	Midazolam	0.05 mg/kg	0.02 mg/kg
	Propofol	2-2.5 mg/ kg	1-2 mg/kg
	Maintenance:	**100-200 µg/kg/min**	**50-100 µg/kg/min**
	Ketamine	0.5-2mg/kg	0.3-1.5mg/kg
	Etomidate	0.2-0.3 mg/kg	0.1-0.2mg/kg
	Thiopental	3-5 mg/kg	1.5-3 mg/kg
Opiates	Fentanyl	1-2 µg/kg	0.5-1 µg/kg
	Morphine	0.03-0.06 mg/kg	0.02-0.03 mg/kg
	Sufentanil	0.5-10 µg/kg	0.25-5 µg/kg
	Remifentanil	Bolus: 0.1 µg/kg	0.05 µg/kg
	Maintenance:	**0.5-2 µg/kg/min**	**0.3-1.5 µg/kg/min**
Neuromuscular Blocking Drugs	Succinylcholine	0.5-1.0 mg/kg	0.5-1.0 mg/kg
	Rocuronium	0.1-0.6 mg/kg	0.05-0.4 mg/kg
	Vecuronium	0.02-0.06 mg/kg	0.01-0.04 mg/kg
	Pancuronium	0.02-0.1 mg/kg	0.01-0.05 mg/kg
	Cisatracurium	0.05-0.2 mg/kg	0.05-0.2 mg/kg
	Atracurium	0.2-0.5 mg/kg	0.2-0.5 mg/kg
	Doxacurium	0.01-0.03 mg/kg	0.005-0.03 mg/kg

J Gen Intern Med. 2015 Nov;30(11):1688-95. doi: 10.1007/s11606-015-3350-2. Epub 2015 May 9.

Functional Status Outperforms Comorbidities in Predicting Acute Care Readmissions in Medically Complex Patients.

Shih SL[1,2], Gerrard P[3], Goldstein R[1], Mix J[4], Ryan CM[5,6], Niewczyk P[4,7], Kazis L[8], Hefner J[9], Ackerly DC[10,11], Zafonte R[1,2], Schneider JC[12,13].

Author information

Abstract

OBJECTIVE: To examine functional status versus medical comorbidities as predictors of acute care readmissions in medically complex patients.

DESIGN: Retrospective database study.

SETTING: U.S. inpatient rehabilitation facilities.

PARTICIPANTS: Subjects included 120,957 patients in the Uniform Data System for Medical Rehabilitation admitted to inpatient rehabilitation facilities under the medically complex impairment group code between 2002 and 2011.

INTERVENTIONS: A Basic Model based on gender and functional status was developed using logistic regression to predict the odds of 3-, 7-, and 30-day readmission from inpatient rehabilitation facilities to acute care hospitals. Functional status was measured by the FIM(®) motor score. The Basic Model was compared to six other predictive models-three Basic Plus Models that added a comorbidity measure to the Basic Model and three Gender-Comorbidity Models that included only gender and a comorbidity measure. The three comorbidity measures used were the Elixhauser index, Deyo-Charlson index, and Medicare comorbidity tier system. The c-statistic was the primary measure of model performance.

MAIN OUTCOME MEASURES: We investigated 3-, 7-, and 30-day readmission to acute care hospitals from inpatient rehabilitation facilities.

RESULTS: Basic Model c-statistics predicting 3-, 7-, and 30-day readmissions were 0.69, 0.64, and 0.65, respectively. The best-performing Basic Plus Model (Basic+Elixhauser) c-statistics were only 0.02 better than the Basic Model, and the best-performing Gender-Comorbidity Model (Gender+Elixhauser) c-statistics were more than 0.07 worse than the Basic Model.

CONCLUSIONS: Readmission models based on functional status consistently outperform models based on medical comorbidities. There is opportunity to improve current national readmission risk models to more accurately predict readmissions by incorporating functional data.

J Am Med Dir Assoc. 2016 Oct 1;17(10):921-6. doi: 10.1016/j.jamda.2016.06.003. Epub 2016 Jul 14.

Functional Status Outperforms Comorbidities as a Predictor of 30-Day Acute Care Readmissions in the Inpatient Rehabilitation Population.

Shih SL[1], Zafonte R[1], Bates DW[2], Gerrard P[3], Goldstein R[4], Mix J[5], Niewczyk P[6], Greysen SR[7], Kazis L[8], Ryan CM[9], Schneider JC[10].

Author information

Abstract

OBJECTIVES: Functional status is associated with patient outcomes, but is rarely included in hospital readmission risk models. The objective of this study was to determine whether functional status is a better predictor of 30-day acute care readmission than traditionally investigated variables including demographics and comorbidities.

DESIGN: Retrospective database analysis between 2002 and 2011.

SETTING: 1158 US inpatient rehabilitation facilities.

PARTICIPANTS: 4,199,002 inpatient rehabilitation facility admissions comprising patients from 16 impairment groups within the Uniform Data System for Medical Rehabilitation database.

MEASUREMENTS: Logistic regression models predicting 30-day readmission were developed based on age, gender, comorbidities (Elixhauser comorbidity index, Deyo-Charlson comorbidity index, and Medicare comorbidity tier system), and functional status [Functional Independence Measure (FIM)]. We hypothesized that (1) function-based models would outperform demographic- and comorbidity-based models and (2) the addition of demographic and comorbidity data would not significantly enhance function-based models. For each impairment group, Function Only Models were compared against Demographic-Comorbidity Models and Function Plus Models (Function-Demographic-Comorbidity Models). The primary outcome was 30-day readmission, and the primary measure of model performance was the c-statistic.

RESULTS: All-cause 30-day readmission rate from inpatient rehabilitation facilities to acute care hospitals was 9.87%. C-statistics for the Function Only Models were 0.64 to 0.70. For all 16 impairment groups, the Function Only Model demonstrated better c-statistics than the Demographic-Comorbidity Models (c-statistic difference: 0.03-0.12). The best-performing Function Plus Models exhibited negligible improvements in model performance compared to Function Only Models, with c-statistic improvements of only 0.01 to 0.05.

CONCLUSION: Readmissions are currently used as a marker of hospital performance, with recent financial penalties to hospitals for excessive readmissions. Function-based readmission models outperform models based only on demographics and comorbidities. Readmission risk models would benefit from the inclusion of functional status as a primary predictor.

PLoS One. 2015 Nov 23;10(11):e0142180. doi: 10.1371/journal.pone.0142180. eCollection 2015.

Functional Status Predicts Acute Care Readmissions from Inpatient Rehabilitation in the Stroke Population.

Slocum C[1,2], Gerrard P[1,2], Black-Schaffer R[1,2], Goldstein R[1], Singhal A[3], DiVita MA[4], Ryan CM[5,6], Mix J[4], Purohit M[7], Niewczyk P[4,8], Kazis L[9], Zafonte R[1,2], Schneider JC[1,2].

Author information

Abstract

OBJECTIVE: Acute care readmission risk is an increasingly recognized problem that has garnered significant attention, yet the reasons for acute care readmission in the inpatient rehabilitation population are complex and likely multifactorial. Information on both medical comorbidities and functional status is routinely collected for stroke patients participating in inpatient rehabilitation. We sought to determine whether functional status is a more robust predictor of acute care readmissions in the inpatient rehabilitation stroke population compared with medical comorbidities using a large, administrative data set.

METHODS: A retrospective analysis of data from the Uniform Data System for Medical Rehabilitation from the years 2002 to 2011 was performed examining stroke patients admitted to inpatient rehabilitation facilities. A Basic Model for predicting acute care readmission risk based on age and functional status was compared with models incorporating functional status and medical comorbidities (Basic-Plus) or models including age and medical comorbidities alone (Age-Comorbidity). C-statistics were compared to evaluate model performance.

FINDINGS: There were a total of 803,124 patients: 88,187 (11%) patients were transferred back to an acute hospital: 22,247 (2.8%) within 3 days, 43,481 (5.4%) within 7 days, and 85,431 (10.6%) within 30 days. The C-statistics for the Basic Model were 0.701, 0.672, and 0.682 at days 3, 7, and 30 respectively. As compared to the Basic Model, the best-performing Basic-Plus model was the Basic+Elixhauser model with C-statistics differences of +0.011, +0.011, and + 0.012, and the best-performing Age-Comorbidity model was the Age+Elixhauser model with C-statistic differences of -0.124, -0.098, and -0.098 at days 3, 7, and 30 respectively.

CONCLUSIONS: Readmission models for the inpatient rehabilitation stroke population based on functional status and age showed better predictive ability than models based on medical comorbidities.

Conclusioni

- La farmacocinetica e farmacodinamica dei farmaci è diversa negli anziani ed è condizionata dalla presenza di malattie
- Grande attenzione deve essere posta nella prescrizione di alcuni tipi di farmaci a prescindere dalla tipologia di paziente anziano
- Il livello funzionale motorio/cognitivo/sociale dovrebbero guidare nelle scelte terapeutiche
- Le scelte terapeutiche condizionano a loro volta il livello funzionale e cognitivo
- La valutazione geriatrica multidimensionale dovrebbe guidare nelle scelte terapeutiche