POLYPHARMACY and OPTIMIZATION of TREATMENTS in OLDER ADULTS

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Octobre 27, 2018

Medication-related deaths

- If medication-related problems were ranked as a disease by cause of death, it would be the fifth leading cause of death in the United States !

Lazarou J, Pomeranz BH, Corey PN. *JAMA.* 1998;2791200- 1205

Polypharmacy

- More than 5 medications in the community
  - 10 to 15% of men
  - 15 to 25% of women

- Use of med. that are not clinically indicated

  - multiple, high risk (concurrent),
  - inappropriate medications (Beers),
  - inappropriate prescription (J Hanlon)

Etiology of polypharmacy in older adults

- Number of prescriptors over life-time and and currently prescribing (75% of visits end with a prescription)
- Multiple chronic medical conditions, and symptoms (prescription cascade)
- Self-medication (free available increase), complementary and alternative products

Etiology of medication-related problems in older adults

- Polymedication
- Frailty/Vulnerability
- Cognitive and behavor problems
- Co-morbidities
- Changes in pharmacocinetics (decline of hepatic and renal functions, reduction of total body water, malnutrition, dehydration
- Atypical manifestations of side effects
- Guidelines studies excluded the most frail old patients
- Insufficient hierarchization of the needs
- Insufficient deprescription

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

Medication-related problems
Some important numbers

- 30% of hospital admissions in elderly patients may be linked to drug-related problems or drug toxic effects (1)
- Adverse drug events (ADEs) have been linked to preventable problems in elderly patients such as depression, constipation, falls, immobility, confusion, and hip fractures (1,2)
- 35% of ambulatory older adults experienced an ADE
- 29% required health care services (physician, emergency department, or hospitalization) for the ADE(1)
- 65% of nursing facility residents have ADEs over a 4-year period (3)
- Of these ADEs, 1 out of 7 results in hospitalization (4)

(1) Hanlon JT et al. *J Am Geriatr Soc*. 1997;45:945- 948 (2) Bootman JL et al. *Arch Intern Med.* 1997;157:2089- 2096 (3) Cooper JW. *J Am Geriatr Soc.* 1996;44:194-197 (4) Cooper JW. South Med J. 1999;92: 485- 490

Clinical practice guidelines in the older adults. Indications for treatment for chronic diseases are often based on extrapolations from:

- Younger to older populations
- Robust subjects with single pathologies to frail subjects with several co-morbidities
- High selected patients in Clinical trials to « real » patients
- Short term to long term effects

…Some examples…

- HYVET and SPRINT studies: Examples of the exclusion of the frail older subjects

Main exclusion criteria in HYVET and SRINT

Main Exclusion criteria in HYVET

- Living in NHs,
- Limited autonomy,
- Clinical dementia,
- Heart failure needing treatment with ACEI, ARA, Diuretics
- SBP<140mmHg in upright position
- Renal failure
- Patients presenting a high probability of having a major health problem during the 5 year follow-up period

Main Exclusion criteria in SPRINT:

- Type 2 diabetes,
- History of stroke,
- Symptomatic heart failure within the past 6 months or reduced LVEF (<35%),
- Clinical diagnosis of or treatment for dementia,
- Expected survival of less than 3 years,
- Unintentional weight loss (>10% of body weight) during the preceding 6 months,
- SBP of less than 110 mm Hg following 1 minute of standing,
- Living in NHs.

PROSPER Study: the study that shows some interest of statins in older adults did not include patients after 82 years (70-82 yo, mean 75 yo)

- Pravastatin given for 3 years reduced the risk of coronary disease in elderly individuals.
- No effect on total mortality
- No effect on strokes
- Slight though statistically significant increase in cancers

Shepherd J et al Lancet. 2002;360(9346):1623-30.

Most hospitalized patients do not meet the enrollment criteria for clinical trials in heart failure

- 20,388 over 64 y.o.
- With diagnosis of HF
- discharged from acute care hospitals

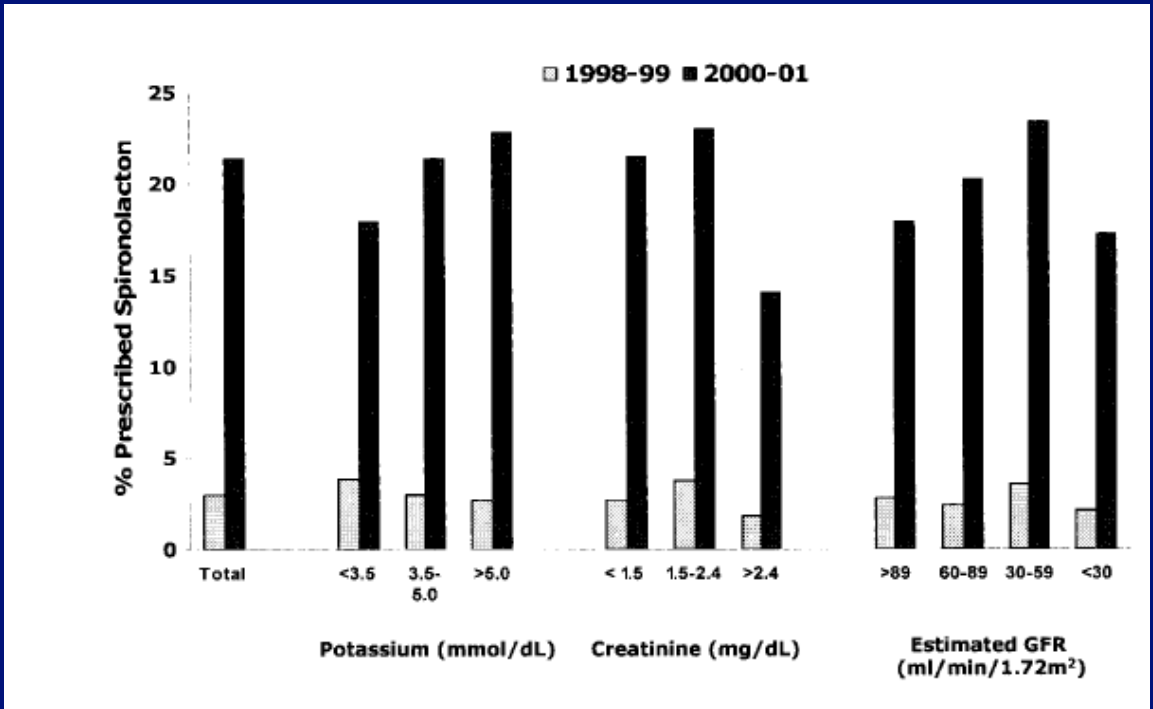
Masoudi et al, Am Heart J 2003; 146:250-257

Hospitalized patients for HF who meet the enrollment criteria for clinical trials

	MEN	WOMEN
SOLV	23%	13%
MERIT-HF	17%	11%
RALES	32%	21%

Masoudi et al, Am Heart J 2003; 146:250-257

Prescription of spironolactone increased 7-fold after publication of RALES.



Of the discharge prescriptions written after RALES, almost one third were provided to patients not fitting the study enrollment criteria, many of whom were at high risk for hyperkalemia

Masoudi et al, Am Heart J 2003; 146:250-257

Rates of hyperkalemia after publication of the RALES.

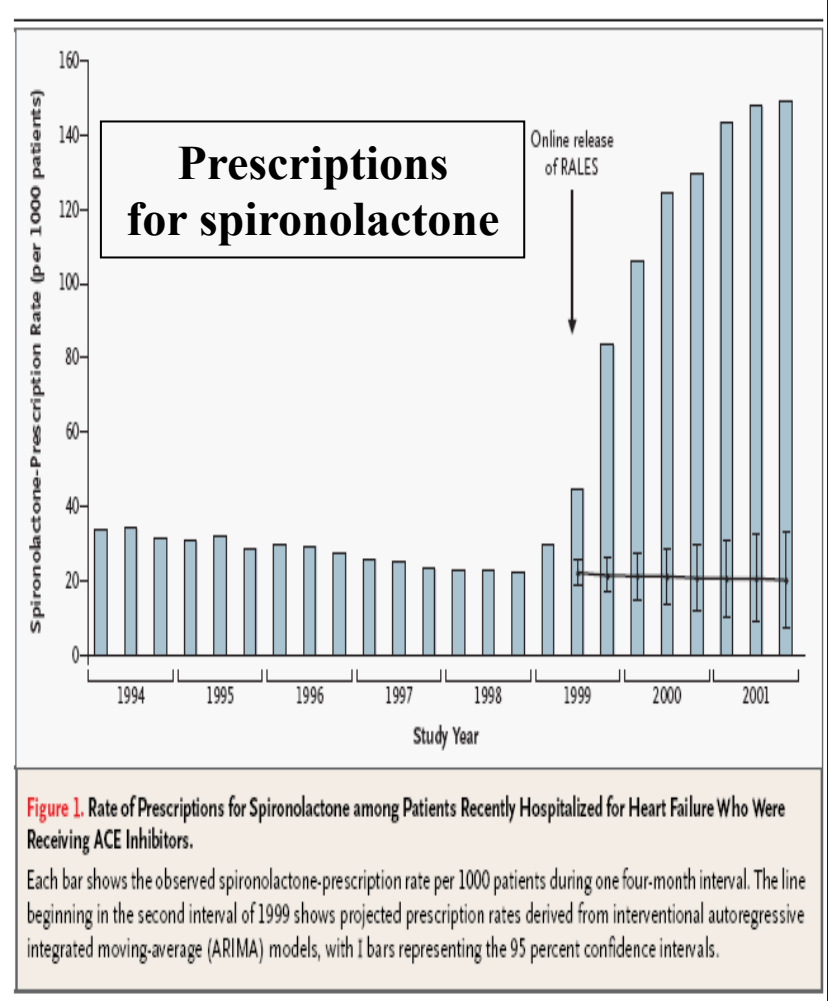


Figure 1. Rate of Prescriptions for Spironolactone among Patients Recently Hospitalized for Heart Failure Who Were Receiving ACE Inhibitors.

Each bar shows the observed spironolactone-prescription rate per 1000 patients during one four-month interval. The line beginning in the second interval of 1999 shows projected prescription rates derived from interventional autoregressive integrated moving-average (ARIMA) models, with I bars representing the 95 percent confidence intervals.

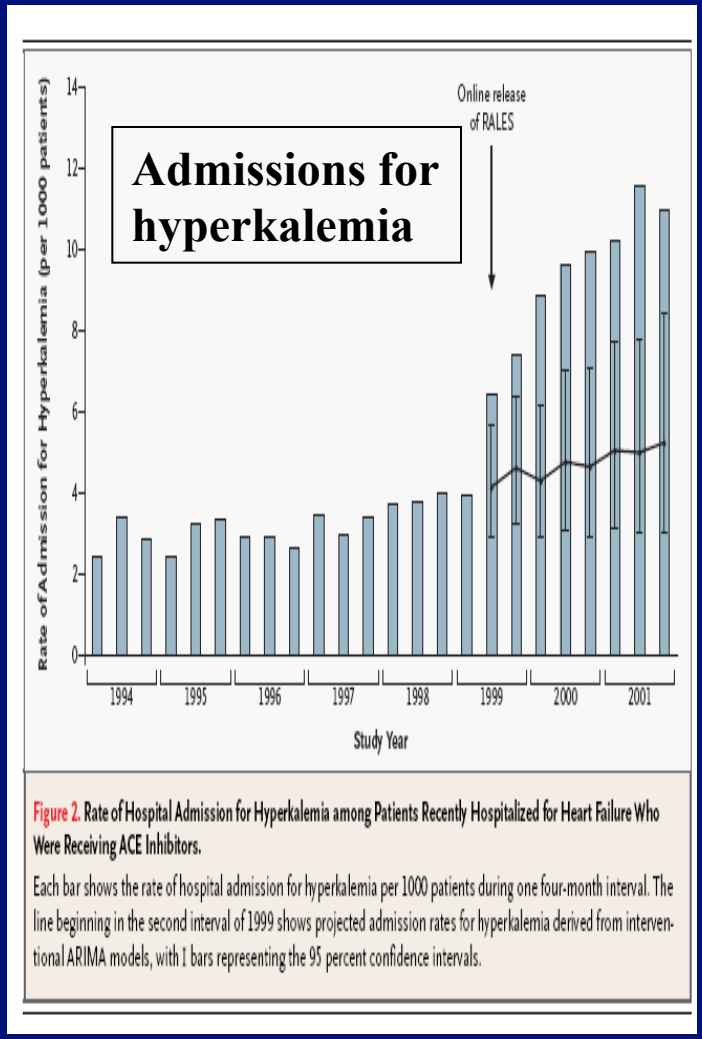


Figure 2. Rate of Hospital Admission for Hyperkalemia among Patients Recently Hospitalized for Heart Failure Who Were Receiving ACE Inhibitors.

Each bar shows the rate of hospital admission for hyperkalemia per 1000 patients during one four-month interval. The line beginning in the second interval of 1999 shows projected admission rates for hyperkalemia derived from interventional ARIMA models, with I bars representing the 95 percent confidence intervals.

Juurlink DN et al, N Engl J Med. 2004;351:543-51.

Prescription cascade

- Drug 1 gives an adverse effect which is misinterpreted as a new medical condition
- Drug 2 is prescribed to treat this « new medical condition…
- Drug 3 ….

  NH patients with anticholinesterase inhib recieving medication with anticholinergic effect
  Gill et al Arch Int Med 2005 165: 808

Screening tools to detect inappropriate prescriptions

Explicit screening tools

Screening Tool	Content	Method	Prevalence of PIP Globally	Prevalence of PIP in Ireland
McLeod (1997)	38 Indicators	Delphi Validation	3.0%-31.78%	-
IPET (2000)	14 Indicators	Based of McLeod criteria	18.3%	Primary Care: 10% Secondary Care: 22% Nursing Homes: -
Beers' Criteria ('03)	48 Indicators	Delphi Validation	Primary Care: 9.8-38.5% Secondary Care: 34% Nursing Home: 40.3%	Primary Care: 11-13% Secondary Care:34% Nursing Homes: 56.8%

Key: PIP: Potentially Inappropriate Prescribing

Update of the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Results of a US Consensus Panel of Experts

Donna M. Fick, et al Arch Intern Med. 2003;163(22):2716-2724.

Table 1. 2002 Criteria for Potentially Inappropriate Medication Use in Older Adults: Independent of Diagnoses or Conditions

Drug	Concern	Severity Rating (High or Low)
Propoxyphene (Darvon) and combination products (Darvon with ASA, Darvon-N, and Darvocet-N)	Offers few analgesic advantages over acetaminophen, yet has the adverse effects of other narcotic drugs.	Low
Indomethacin (Indocin and Indocin SR)	Of all available nonsteroidal anti-inflammatory drugs, this drug produces the most CNS adverse effects.	High
Pentazocine (Talwin)	Narcotic analgesic that causes more CNS adverse effects, including confusion and hallucinations, more commonly than other narcotic drugs. Additionally, it is a mixed agonist and antagonist.	High
Trimethobenzamide (Tigan)	One of the least effective antiemetic drugs, yet it can cause extrapyramidal adverse effects.	High
Muscle relaxants and antispasmodics: methocarbamol (Robaxin), carisoprodol (Soma), chlorzoxazone (Paraflex), metaxalone (Skelaxin), cyclobenzaprine (Flexeril), and oxybutynin (Ditropan). Do not consider the extended-release Ditropan XL.	Most muscle relaxants and antispasmodic drugs are poorly tolerated by elderly patients, since these cause anticholinergic adverse effects, sedation, and weakness. Additionally, their effectiveness at doses tolerated by elderly patients is questionable.	High
Flurazepam (Dalmane)	This benzodiazepine hypnotic has an extremely long half-life in elderly patients (often days), producing prolonged sedation and increasing the incidence of falls and fracture. Medium- or short-acting benzodiazepines are preferable.	High
Amitriptyline (Elavil), chlordiazepoxide-amitriptyline (Limbitrol), and perphenazine-amitriptyline (Triavil)	Because of its strong anticholinergic and sedation properties, amitriptyline is rarely the antidepressant of choice for elderly patients.	High
Doxepin (Sinequan)	Because of its strong anticholinergic and sedating properties, doxepin is rarely the antidepressant of choice for elderly patients.	High
Meprobamate (Miltown and Equanil)	This is a highly addictive and sedating anxiolytic. Those using meprobamate for prolonged periods may become addicted and may need to be withdrawn slowly.	High
Doses of short-acting benzodiazepines: doses greater than lorazepam (Ativan), 3 mg; oxazepam (Serax), 60 mg; alprazolam (Xanax), 2 mg; temazepam (Restoril), 15 mg; and triazolam (Halcion), 0.25 mg	Because of increased sensitivity to benzoadiazepines in elderly patients, smaller doses may be effective as well as safer. Total daily doses should rarely exceed the suggested maximums.	High
Long-acting benzodiazepines: chlordiazepoxide (Librium), chlordiazepoxide-amitriptyline (Limbitrol) clidinium-chlordiazepoxide (Librax), diazepam (Valium), quazepam (Doral), halazepam (Paxipam), and chlorazepate (Tranxene)	These drugs have a long half-life in elderly patients (often several days), producing prolonged sedation and increasing the risk of falls and fractures. Short- and intermediate-acting benzodiazepines are preferred if a benzodiazepine is required.	High
Disopyramide (Norpace and Norpace CR)	Of all antiarrhythmic drugs, this is the most potent negative inotrope and therefore may induce heart failure in elderly patients. It is also strongly anticholinergic. Other antiarrhythmic drugs should be used.	High
Digoxin (Lanoxin) (should not exceed >0.125 mg/d except when treating atrial arrhythmias)	Decreased renal clearance may lead to increased risk of toxic effects.	Low
Short-acting dipyridamole (Persantine). Do not consider the long-acting dipyridamole (which has better properties than the short-acting in older adults) except with patients with artificial heart valves	May cause orthostatic hypotension.	Low
Methyldopa (Aldomet) and methyldopa-hydrochlorothiazide (Aldoril)	May cause bradycardia and exacerbate depression in elderly patients.	High
Reserpine at doses >0.25 mg	May induce depression, impotence, sedation, and orthostatic hypotension.	Low
Chlorpropamide (Diabinese)	It has a prolonged half-life in elderly patients and could cause prolonged hypoglycemia. Additionally, it is the only oral hypoglycemic agent that causes SIADH.	High
Gastrointestinal antispasmodic drugs: dicyclomine (Bentyl), hyoscyamine (Levsin and Levsinex), propantheline (Pro-Banthine), belladonna alkaloids (Donnatal and others), and clidinium-chlordiazepoxide (Librax)	GI antispasmodic drugs are highly anticholinergic and have uncertain effectiveness. These drugs should be avoided (especially for long-term use).	High
Anticholinergics and antihistamines: chlorpheniramine (Chlor-Trimeton), diphenhydramine (Benadryl), hydroxyzine (Vistaril and Atarax), cyproheptadine (Periactin), promethazine (Phenergan), tripelennamine, dexchlorpheniramine (Polaramine)	All nonprescription and many prescription antihistamines may have potent anticholinergic properties. Nonanticholinergic antihistamines are preferred in elderly patients when treating allergic reactions.	High
Diphenhydramine (Benadryl)	May cause confusion and sedation. Should not be used as a hypnotic, and when used to treat emergency allergic reactions, it should be used in the smallest possible dose.	High
Ergot mesyloids (Hydergine) and cyclandelate (Cyclospasmol)	Have not been shown to be effective in the doses studied.	Low
Ferrous sulfate >325 mg/d	Doses >325 mg/d do not dramatically increase the amount absorbed but greatly increase the incidence of constipation.	Low
All barbiturates (except phenobarbital) except when used to control seizures	Are highly addictive and cause more adverse effects than most sedative or hypnotic drugs in elderly patients.	High
Meperidine (Demerol)	Not an effective oral analgesic in doses commonly used. May cause confusion and has many disadvantages to other narcotic drugs.	High
Ticlopidine (Ticlid)	Has been shown to be no better than aspirin in preventing clotting and may be considerably more toxic. Safer, more effective alternatives exist.	High

Update of the Beers Criteria

Fick D et al; Arch Intern Med. 2003;163:2716-24.

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Meperidine (Demerol)	Not an effective oral analgesic in doses commonly used. May cause confusion and has many disadvantages to other narcotic drugs.	High
Ticlopidine (Ticlid)	Has been shown to be no better than aspirin in preventing clotting and may be considerably more toxic. Safer, more effective alternatives exist.	High
Ketorolac (Toradol)	Immediate and long-term use should be avoided in older persons, since a significant number have asymptomatic GI pathologic conditions.	High
Amphetamines and anorexic agents	These drugs have potential for causing dependence, hypertension, angina, and myocardial infarction.	High
Long-term use of full-dosage, longer half-life, non–COX-selective NSAIDs: naproxen (Naprosyn, Avaprox, and Aleve), oxaprozin (Daypro), and piroxicam (Feldene)	Have the potential to produce GI bleeding, renal failure, high blood pressure, and heart failure.	High
Daily fluoxetine (Prozac)	Long half-life of drug and risk of producing excessive CNS stimulation, sleep disturbances, and increasing agitation. Safer alternatives exist.	High
Long-term use of stimulant laxatives: bisacodyl (Dulcolax), cascara sagrada, and Neoloid except in the presence of opiate analgesic use	May exacerbate bowel dysfunction.	High
Amiodarone (Cordarone)	Associated with QT interval problems and risk of provoking torsades de pointes. Lack of efficacy in older adults.	High
Orphenadrine (Norflex)	Causes more sedation and anticholinergic adverse effects than safer alternatives.	High
Guanethidine (Ismelin)	May cause orthostatic hypotension. Safer alternatives exist.	High
Guanadrel (Hylorel)	May cause orthostatic hypotension.	High
Cyclandelate (Cyclospasmol)	Lack of efficacy.	Low
Isoxsurpine (Vasodilan)	Lack of efficacy.	Low
Nitrofurantoin (Macrodantin)	Potential for renal impairment. Safer alternatives available.	High
Doxazosin (Cardura)	Potential for hypotension, dry mouth, and urinary problems.	Low
Methyltestosterone (Android, Virilon, and Testrad)	Potential for prostatic hypertrophy and cardiac problems.	High
Thioridazine (Mellaril)	Greater potential for CNS and extrapyramidal adverse effects.	High
Mesoridazine (Serentil)	CNS and extrapyramidal adverse effects.	High
Short acting nifedipine (Procardia and Adalat)	Potential for hypotension and constipation.	High
Clonidine (Catapres)	Potential for orthostatic hypotension and CNS adverse effects.	Low
Mineral oil	Potential for aspiration and adverse effects. Safer alternatives available.	High
Cimetidine (Tagamet)	CNS adverse effects including confusion.	Low
Ethacrynic acid (Edecrin)	Potential for hypertension and fluid imbalances. Safer alternatives available.	Low
Desiccated thyroid	Concerns about cardiac effects. Safer alternatives available.	High
Amphetamines (excluding methylphenidate hydrochloride and anorexics)	CNS stimulant adverse effects.	High
Estrogens only (oral)	Evidence of the carcinogenic (breast and endometrial cancer) potential of these agents and lack of cardioprotective effect in older women.	Low

Abbreviations: CNS, central nervous system; COX, cyclooxygenase; GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

Update of the Beers Criteria

Fick D et al; Arch Intern Med. 2003;163:2716-24.

Table 2. 2002 Criteria for Potentially Inappropriate Medication Use in Older Adults: Considering Diagnoses or Conditions

Disease or Condition	Drug	Concern	Severity Rating (High or Low)
Heart failure	Disopyramide (Norpace), and high sodium content drugs (sodium and sodium salts [alginate bicarbonate, biphosphate, citrate, phosphate, salicylate, and sulfate])	Negative inotropic effect. Potential to promote fluid retention and exacerbation of heart failure.	High
Hypertension	Phenylpropanolamine hydrochloride (removed from the market in 2001), pseudoephedrine; diet pills, and amphetamines	May produce elevation of blood pressure secondary to sympathomimetic activity.	High
Gastric or duodenal ulcers	NSAIDs and aspirin (>325 mg) (coxibs excluded)	May exacerbate existing ulcers or produce new/additional ulcers.	High
Seizures or epilepsy	Clozapine (Clozaril), chlorpromazine (Thorazine), thioridazine (Mellaril), and thiothixene (Navane)	May lower seizure thresholds.	High
Blood clotting disorders or receiving anticoagulant therapy	Aspirin, NSAIDs, dipyridamole (Persantin), ticlopidine (Ticlid), and clopidogrel (Plavix)	May prolong clotting time and elevate INR values or inhibit platelet aggregation, resulting in an increased potential for bleeding.	High
Bladder outflow obstruction	Anticholinergics and antihistamines, gastrointestinal antispasmodics, muscle relaxants, oxybutynin (Ditropan), flavoxate (Urispas), anticholinergics, antidepressants, decongestants, and tolterodine (Detrol)	May decrease urinary flow, leading to urinary retention.	High
Stress incontinence	α-Blockers (Doxazosin, Prazosin, and Terazosin), anticholinergics, tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride), and long-acting benzodiazepines	May produce polyuria and worsening of incontinence.	High
Arrhythmias	Tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride)	Concern due to proarrhythmic effects and ability to produce QT interval changes.	High
Insomnia	Decongestants, theophylline (Theodur), methylphenidate (Ritalin), MAOIs, and amphetamines	Concern due to CNS stimulant effects.	High
Parkinson disease	Metoclopramide (Reglan), conventional antipsychotics, and tacrine (Cognex)	Concern due to their antidopaminergic/ cholinergic effects.	High
Cognitive impairment	Barbiturates, anticholinergics, antispasmodics, and muscle relaxants. CNS stimulants: dextroAmphetamine (Adderall), methylphenidate (Ritalin), methamphetamine (Desoxyn), and pemolin	Concern due to CNS-altering effects.	High
Depression	Long-term benzodiazepine use. Sympatholytic agents: methyldopa (Aldomet), reserpine, and guanethidine (Ismelin)	May produce or exacerbate depression.	High
Anorexia and malnutrition	CNS stimulants: DextroAmphetamine (Adderall), methylphenidate (Ritalin), methamphetamine (Desoxyn), pemolin, and fluoxetine (Prozac)	Concern due to appetite-suppressing effects.	High
Syncope or falls	Short- to intermediate-acting benzodiazepine and tricyclic antidepressants (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride)	May produce ataxia, impaired psychomotor function, syncope, and additional falls.	High
SIADH/hyponatremia	SSRIs: fluoxetine (Prozac), citalopram (Celexa), fluvoxamine (Luvox), paroxetine (Paxil), and sertraline (Zoloft)	May exacerbate or cause SIADH.	Low
Seizure disorder	Bupropion (Wellbutrin)	May lower seizure threshold.	High
Obesity	Olanzapine (Zyprexa)	May stimulate appetite and increase weight gain.	Low
COPD	Long-acting benzodiazepines: chlordiazepoxide (Librium), chlordiazepoxide-amitriptyline (Limbitrol), clidinium-chlordiazepoxide (Librax), diazepam (Valium), quazepam (Doral), halazepam (Paxipam), and chlorazepate (Tranxene). β-blockers: propranolol	CNS adverse effects. May induce respiratory depression. May exacerbate or cause respiratory depression.	High
Chronic constipation	Calcium channel blockers, anticholinergics, and tricyclic antidepressant (imipramine hydrochloride, doxepin hydrochloride, and amitriptyline hydrochloride)	May exacerbate constipation.	Low

Abbreviations: CNS, central nervous systems; COPD, chronic obstructive pulmonary disease; INR, international normalized ratio; MAOIs, monoamine oxidase inhibitors; NSAIDs, nonsteroidal anti-inflammatory drugs; SIADH, syndrome of inappropriate antidiuretic hormone secretion; SSRIs, selective serotonin reuptake inhibitors.

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Table 3. Summary of Changes From 1997 Beers Criteria to New 2002 Criteria

Medicines Modified Since 1997 Beers Criteria

1. Reserpine (Serpasil and Hydropres)*
2. Extended-release oxybutynin (Ditropan XL)†
3. Iron supplements >325 mg†
4. Short-acting dipyridamole (Persantine)‡

Medicines Dropped Since 1997 Beers Criteria

Independent of Diagnoses

1. Phenylbutazone (Butazolidin)

Considering Diagnoses

2. Recently started corticosteroid therapy with diabetes
3. β-Blockers with diabetes, COPD or asthma, peripheral vascular disease, and syncope or falls
4. Sedative hypnotics with COPD
5. Potassium supplements with gastric or duodenal ulcers
6. Metoclopramide (Reglan) with seizures or epilepsy
7. Narcotics with bladder outflow obstruction and narcotics with constipation
8. Desipramine (Norpramin) with insomnia
9. All SSRIs with insomnia
10. β-Agonists with insomnia
11. Bethanechol chloride with bladder outflow obstruction

Medicines Added Since 1997 Beers Criteria

Independent of Diagnoses

1. Ketorolac tromethamine (Toradol)
2. Orphenadrine (Norflex)
3. Guanethidine (Ismelin)
4. Guanadrel (Hylorel)
5. Cyclandelate (Cyclospasmol)
6. Isoxsuprine (Vasodilan)
7. Nitrofurantoin (Macrodantin)
8. Doxazosin (Cardura)
9. Methyltestosterone (Android, Virilon, and Testrad)
10. Mesoridazine (Serentil)
11. Clonidine (Catapres)
12. Mineral oil
13. Cimetidine (Tagamet)
14. Ethacrynic acid (Edecrin)
15. Desiccated thyroid
16. Ferrous sulfate >325 mg
17. Amphetamines (excluding methylpenidate and anorexics)
18. Thioridazine (Mellaril)
19. Short-acting nifedipine (Procardia and Adalat)
20. Daily fluoxetine (Prozac)
21. Stimulant laxatives may exacerbate bowel dysfunction (except in presence of chronic pain requiring opiate analgesics)
22. Amiodarone (Cordarone)
23. Non–COX-selective NSAIDs (naproxen [Naprosyn], oxaprozin, and piroxicam)
24. Reserpine doses >0.25 mg/d
25. Estrogens in older women

Considering Diagnoses

26. Long-acting benzodiazepines: chlordiazepoxide (Librium), chlordiazepoxide-amitriptyline (Limbitrol), clidinium-chlordiazepoxide (Librax), diazepam (Valium), quazepam (Doral), halazepam (Paxipam), and chlorazepate (Tranxene) with COPD, stress incontinence, depression, and falls
27. Propanolol with COPD/asthma
28. Anticholinergics with stress incontinence
29. Tricyclic antidepressants (imipramine hydrochloride, doxepine hydrochloride, and amitriptyline hydrochloride) with syncope or falls and stress incontinence
30. Short to intermediate and long-acting benzodiazepines with syncope or falls
31. Clopidogrel (Plavix) with blood-clotting disorders receiving anticoagulant therapy
32. Tolterodine (Detrol) with bladder outflow obstruction
33. Decongestants with bladder outflow obstruction
34. Calcium channel blockers with constipation
35. Phenylpropanolamine with hypertension
36. Bupropion (Wellbutrin) with seizure disorder
37. Olanzapine (Zyprexa) with obesity
38. Metoclopramide (Reglan) with Parkinson disease
39. Conventional antipsychotics with Parkinson disease
40. Tacrine (Cognex) with Parkinson disease
41. Barbiturates with cognitive impairment
42. Antispasmodics with cognitive impairment
43. Muscle relaxants with cognitive impairment
44. CNS stimulants with anorexia, malnutrition, and cognitive impairment

Abbreviations: CNS, central nervous system; COPD, chronic obstructive pulmonary disease; COX, cyclooxygenase; NSAIDs, nonsteroidal anti-inflammatory drugs; SSRIs, selective serotonin reuptake inhibitors.

*Reserpine in doses >0.25 mg was added to the list.

†Ditropan was modified to refer to the immediate-release formulation only and not Ditropan XL and iron supplements was modified to include only ferrous sulfate.

‡Do not consider the long-acting dipyridamole, which has better properties than the short-acting dipyridamole in older adults (except with patients with artificial heart valves).

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Conclusions

This study is an important update of previously established criteria that have been widely used and cited. The application of the Beers criteria and other tools for identifying potentially inappropriate medication use will continue to enable providers to plan interventions for decreasing both drug-related costs and overall costs and thus minimize drug-related problems.

Fick D et al; Arch Intern Med. 2003;163(22):2716-2724.

Aims of STOPP/START

- Provide explicit, evidence based rules of avoidance of commonly encountered instances of potentially inappropriate prescribing and potential prescribing omissions
  - Improve medication appropriateness
  - Prevent adverse drug events
  - Reduce drug costs

65 STOPP and 22 START Criteria (2008)

International Journal of Clinical Pharmacology and Therapeutics, Vol. 46 – No. 2/2008 (72-83)

Original

ISSN 0946-1965

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

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- Consensus panel of 18 experts
- Delphi process (2 rounds)
- Final agreed list of STOPP criteria (n=65) and START (n=22)
- Good inter-rater reliability (STOPP k=0.75; START k= 0.68)

65 STOPP Criteria (2008)

Physiological System	Number of criteria
Cardiovascular system	17
Central nervous system	13
Gastro-intestinal system	5
Musculoskeletal system	8
Respiratory system	3
Urogenital system	6
Endocrine system	4
Drugs that adversely affect fallers	5
Analgesics	3
Duplicate drug classes	1

22 START Criteria (2008)

Physiological System	Number of criteria
Cardiovascular system	8
Respiratory system	3
Central nervous system	2
Gastro-intestinal system	2
Musculoskeletal system	3
Endocrine system	4

Prevalence of Potentially Inappropriate Prescribing using STOPP/START

- Primary Care
  - Potentially inappropriate prescribing (STOPP): 21.4%
  - Potential prescribing omissions (START): 22.7%

Ryan C *et al.* Br J Clin Pharmacol 2009

- Secondary Care
  - Potentially inappropriate prescribing (STOPP): 34.5%
  - Potential prescribing omissions (START): 57.9%

Gallagher *et al.* Age Ageing 2008
Barry PJ *et al.* Age Ageing 2007

- Nursing Home
  - Potentially inappropriate prescribing (STOPP): 55-49.8%

Ryan C *et al.* Ir J Med Sci 2009
O'Sullivan D *et al.* Eur Ger Med 2010

STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions): application to acutely ill elderly patients and comparison with Beers' criteria

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Age and Ageing 2008; 37: 673–679

Study in 715 consecutive acute admissions to a university teaching hospital. STOPP and Beers' criteria were applied.

	Inappropriate medicines (PIMs)	Adverse drug events (ADE)
Beer's	226	43 (6% of admissions)
STOPP	336	82 (11.5% of admissions)

STOPP criteria identified a significantly higher proportion of patients requiring hospitalisation as a result of PIM-related adverse events than Beers' criteria

Gallagher P. Age and Ageing 2008; 37: 673–679

Need for revising regularly the criteria in order to adapt them to the latest scientific and medical data

The 2015 version of the Beers criteria

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

The 2015 American Geriatrics Society (AGS) Beers Criteria are presented. Like the 2012 AGS Beers Criteria, they include lists of potentially inappropriate medications to be avoided in older adults. New to the criteria are lists of select drugs that should be avoided or have their dose adjusted based on the individual's kidney function and select drug–drug interactions documented to be associated with harms in older adults. The specific aim was to have a 13-member interdisciplinary panel of experts in geriatric care and pharmacotherapy update the 2012 AGS Beers Criteria using a modified Delphi method to systematically review and grade the evidence and reach a consensus on each existing and new criterion. The process followed an evidence-based approach using Institute of Medicine standards. The 2015 AGS Beers Criteria are applicable to all older adults with the exclusion of those in palliative and hospice care. Careful application of the criteria by health professionals, consumers, payors, and health systems should lead to closer monitoring of drug use in older adults. J Am Geriatr Soc 63:2227–2246, 2015.

older adults is one strategy to decrease the risk of adverse events. Interventions using explicit criteria have been found to be an important component of strategies for reducing inappropriate medication usage.[3–5]

The AGS Beers Criteria for PIM Use in Older Adults are one of the most frequently consulted sources about the safety of prescribing medications for older adults. The AGS Beers Criteria are used widely in geriatric clinical care, education, and research and in development of quality indicators. In 2011, the AGS assumed the responsibility of updating and maintaining the Beers Criteria and, in 2012, released the first update of the criteria since 2003. The AGS has made a commitment to update the criteria regularly. The changes in the 2015 update are not as extensive as those of the previous update, but in addition to updating existing criteria, two major components have been added: 1) drugs for which dose adjustment is required based on kidney function and 2) drug–drug interactions. Neither of these new additions is intended to be comprehensive, because such lists would be too extensive. An interdisciplinary expert panel focused on those drugs

Need for revising regularly the criteria in order to adapt them to the latest scientific and medical data

In 2015 STOPP/START Version 2
80 STOPP and 34 START criteria
TOTAL 114

Age and Ageing 2015; **44:** 213–218
doi: 10.1093/ageing/afu145
Published electronically 16 October 2014

STOPP/START criteria for potentially inappropriate prescribing in older people: version 2

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STOPP version 1 criteria removed from the proposed version 2 because of weak or equivocal supporting evidence

STOPP criteria

- Aspirin with no history of coronary, cerebral or peripheral arterial occlusive symptoms
- Calcium channel blockers with chronic constipation
- Non-cardioselective beta-blocker with chronic obstructive pulmonary disease
- Use of aspirin and warfarin in combination without histamine H2 receptor antagonist (except cimetidine because of interaction with warfarin) or proton pump inhibitor
- Dipyridamole as monotherapy for cardiovascular secondary prevention
- Aspirin to treat dizziness not clearly attributable to cerebrovascular disease
- Phenothiazines in patients with epilepsy
- Diphenoxylate, loperamide or codeine phosphate for treatment of severe gastroenteritis
- Selective alpha-blockers in males with frequent urinary incontinence, i.e. one or more episodes of incontinence daily
- First-generation antihistamines in patients with falls
- Long-term opioids in patients with falls
- Long-term opioids in those with dementia unless indicated for palliative care or management of moderate/severe chronic pain syndrome

START version 1 criteria removed from the proposed version 2 because of weak or equivocal supporting evidence

START criteria

Metformin with type 2 diabetes mellitus +/− metabolic syndrome (in the absence of renal impairment, i.e. serum creatinine > 150 μmol/l, or estimated GFR < 50 ml/min/1.73 m^2)

Aspirin for primary prevention of cardiovascular disease in diabetes mellitus

Statin therapy for primary prevention of cardiovascular disease in diabetes mellitus

Version 2:
80 STOPP criteria

Screening Tool of Older Persons' Prescriptions (STOPP) version 2. The following prescriptions are potentially inappropriate to use in patients aged 65 years and older.

Age and Aging 2015; 44: 213-218

Version 2:
80 STOPP criteria

3 General
13 Cardiovascular System
11 Antiplatelet/Anticoagulant
14 Central Nervous System and Psychotropic
6 Renal System
4 Gastrointestinal System
5 Respiratory System
9 Musculoskeletal System
2 Urogenital System
6 Endocrine System
4 Drugs that predictably increase the risk of falls
3 Analgesic Drugs

3 STOPP criteria indication of medication

1. Any drug prescribed without an evidence-based clinical indication.

2. Any drug prescribed beyond the recommended duration, where treatment duration is well defined.

3. Any duplicate drug class prescription e.g. two concurrent NSAIDs, SSRIs, loop diuretics, ACE inhibitors, anticoagulants (optimisation of monotherapy within a single drug class should be observed prior to considering a new agent).

13 STOPP criteria Cardiovascular System

1. Digoxin for heart failure with normal systolic ventricular function (no clear evidence of benefit)
2. Verapamil or diltiazem with NYHA Class III or IV heart failure (may worsen heart failure).
3. Beta-blocker in combination with verapamil or diltiazem (risk of heart block).
4. Beta-blocker with bradycardia (< 50/min), type II heart block or complete heart block (risk of complete heart block, asystole).
5. Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias (higher risk of side-effects than beta-blockers, digoxin, verapamil or diltiazem).
6. Loop diuretic as first-line treatment for hypertension (safer, more effective alternatives available).

13 STOPP criteria Cardiovascular System (2)

7. Loop diuretic for dependent ankle oedema without clinical, biochemical evidence or radiological evidence of heart failure, liver failure, nephrotic syndrome or renal failure (leg elevation and /or compression usually more appropriate).

8. Thiazide diuretic with current significant hypokalaemia (i.e. serum K+ < 3.0 mmol/l), hyponatraemia (i.e. serum Na+ < 130 mmol/l) hypercalcaemia (i.e. corrected serum calcium > 2.65 mmol/l) or with a history of gout (hypokalaemia, hyponatraemia, hypercalcaemia and gout can be precipitated by thiazide diuretic)

9. Loop diuretic for treatment of hypertension with concurrent urinary incontinence (may exacerbate incontinence).

13 STOPP criteria Cardiovascular System (3)

10. Centrally-acting antihypertensives (e.g. methyldopa, clonidine, moxonidine, rilmenidine, guanfacine), unless clear intolerance of, or lack of efficacy with, other classes of anti hypertensives (centrally-active antihypertensives are generally less well tolerated by older people than younger people)

11. ACE inhibitors or Angiotensin Receptor Blockers in patients with hyperkalaemia.

12. Aldosterone antagonists (e.g. spironolactone, eplerenone) with concurrent potassium-conserving drugs (e.g. ACEI's, ARB's, amiloride, triamterene) without monitoring of serum potassium (risk of dangerous hyperkalaemia i.e. > 6.0 mmol/l – serum K should be monitored regularly, i.e. at least every 6 months).

13. Phosphodiesterase type-5 inhibitors (e.g. sildenafil, tadalafil, vardenafil) in severe heart failure characterised by hypotension i.e. systolic BP < 90 mmHg, or concurrent nitrate therapy for angina (risk of cardiovascular collapse)

11 STOPP criteria Antiplatelet/ Anticoagulant Drugs

1. Long-term aspirin at doses greater than 160mg per day (increased risk of bleeding, no evidence for increased efficacy).
2. Aspirin with a past history of peptic ulcer disease without concomitant PPI (risk of recurrent peptic ulcer).
3. Aspirin, clopidogrel, dipyridamole, vitamin K antag, direct thrombin inhibitor or factor Xa inhibitor with concurrent significant bleeding risk, i.e. uncontrolled severe Htn, bleeding diathesis, recent non-trivial spontaneous bleeding) (high risk of bleeding).
4. Aspirin plus clopidogrel as secondary stroke prevention, unless the patient has a coronary stent(s) inserted in the previous 12 months or concurrent acute coronary syndrome or has a high grade symptomatic carotid arterial stenosis (no evidence of added benefit over clopidogrel monotherapy)

11 STOPP criteria Antiplatelet/ Anticoagulant Drugs (2)

5. Aspirin in combination with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with chronic atrial fibrillation (no added benefit from aspirin)

6. Antiplatelet agents with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with stable coronary, cerebrovascular or peripheral arterial disease (No added benefit from dual therapy).

7. Ticlopidine in any circumstances (clopidogrel and prasugrel have similar efficacy, stronger evidence and fewer side-effects).

11 STOPP criteria Antiplatelet/ Anticoagulant Drugs(3)

8. Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first deep venous thrombosis without continuing provoking risk factors (e.g. thrombophilia) for > 6 months, (no proven added benefit).

9. Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first pulmonary embolus without continuing provoking risk factors (e.g. thrombophilia) for > 12 months (no proven added benefit).

10. NSAID and vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in combination (risk of major gastrointestinal bleeding).

11. NSAID with concurrent antiplatelet agent(s) without PPI prophylaxis (increased risk of peptic ulcer disease)

14 STOPP criteria Central Nervous System and Psychotropic Drugs

1. TriCyclic Antidepressants (TCAs) with dementia, narrow angle glaucoma, cardiac conduction abnormalities, prostatism, or prior history of urinary retention (risk of worsening these conditions).
2. Initiation of TriCyclic Antidepressants (TCAs) as first-line antidepressant treatment (higher risk of adverse drug reactions with TCAs than with SSRIs or SNRIs).
3. Neuroleptics with moderate-marked antimuscarinic/ anticholinergic effects (chlorpromazine, clozapine, flupenthixol, fluphenzine, pipothiazine, promazine, zuclopenthixol) with a history of prostatism or previous urinary retention (high risk of urinary retention).
4. Selective serotonin re-uptake inhibitors (SSRI's) with current or recent significant hyponatraemia i.e. serum Na+ < 130 mmol/l (risk of exacerbating or precipitating hyponatraemia).

14 STOPP criteria Central Nervous System and Psychotropic Drugs (2)

5. Benzodiazepines for ≥ 4 weeks (no indication for longer treatment; risk of prolonged sedation, confusion, impaired balance, falls, road traffic accidents; all benzodiazepines should be withdrawn gradually if taken for more than 4 weeks as there is a risk of causing a benzodiazepine withdrawal syndrome if stopped abruptly).

6. Antipsychotics (i.e. other than quetiapine or clozapine) in those with parkinsonism or Lewy Body Disease (risk of severe extra-pyramidal symptoms)

7. Anticholinergics/antimuscarinics to treat extra-pyramidal side-effects of neuroleptic medications (risk of anticholinergic toxicity),

8. Anticholinergics/antimuscarinics in patients with delirium or dementia (risk of exacerbation of cognitive impairment).

9. Neuroleptic antipsychotic in patients with behavioural and psychological symptoms of dementia (BPSD) unless symptoms are severe and other non-pharmacological treatments have failed (increased risk of stroke).

14 STOPP criteria Central Nervous System and Psychotropic Drugs (3)

10. Neuroleptics as hypnotics, unless sleep disorder is due to psychosis or dementia (risk of confusion, hypotension, extra-pyramidal side effects, falls).

11. Acetylcholinesterase inhibitors with a known history of persistent bradycardia (< 60 beats/min.), heart block or recurrent unexplained syncope or concurrent treatment with drugs that reduce heart rate such as beta-blockers, digoxin, diltiazem, verapamil (risk of cardiac conduction failure, syncope and injury).

12. Phenothiazines as first-line treatment, since safer and more efficacious alternatives exist (phenothiazines are sedative, have significant anti-muscarinic toxicity in older people, with the exception of prochlorperazine for nausea/vomiting/vertigo, chlorpromazine for relief of persistent hiccoughs and levomepromazine as an anti-emetic in palliative care).

13. Levodopa or dopamine agonists for benign essential tremor (no evidence of efficacy)

14. First-generation antihistamines (safer, less toxic antihistamines now widely available).

6 STOPP criteria Renal System

The following drugs are potentially inappropriate in older people with acute or chronic kidney disease with renal function below particular levels of eGFR (refer to summary of product characteristics datasheets and local formulary guidelines)

1. Digoxin at a long-term dose greater than 125µg/day if eGFR < 30 ml/min/1.73m2 (risk of digoxin toxicity if plasma levels not measured).
2. Direct thrombin inhibitors (e.g. dabigatran) if eGFR < 30 ml/min/1.73m2 (risk of bleeding)
3. Factor Xa inhibitors (e.g. rivaroxaban, apixaban) if eGFR < 15 ml/min/1.73m2 (risk of bleeding)
4. NSAID's if eGFR < 50 ml/min/1.73m2 (risk of deterioration in renal function).
5. Colchicine if eGFR < 10 ml/min/1.73m2 (risk of colchicine toxicity)
6. Metformin if eGFR < 30 ml/min/1.73m2 (risk of lactic acidosis).

4 STOPP criteria Gastrointestinal System

1. Prochlorperazine or metoclopramide with Parkinsonism (risk of exacerbating Parkinsonian symptoms).
2. PPI for uncomplicated peptic ulcer disease or erosive peptic oesophagitis at full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated).
3. Drugs likely to cause constipation (e.g. antimuscarinic/ anticholinergic drugs, oral iron, opioids, verapamil, aluminium antacids) in patients with chronic constipation where non-constipating alternatives are available (risk of exacerbation of constipation).
4. Oral elemental iron doses greater than 200 mg daily (e.g. ferrous fumarate> 600 mg/day, ferrous sulphate > 600 mg/day, ferrous gluconate> 1800 mg/day; no evidence of enhanced iron absorption above these doses).

5 STOPP criteria Respiratory System

1. Theophylline as monotherapy for COPD (safer, more effective alternative; risk of adverse effects due to narrow therapeutic index).
2. Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD (unnecessary exposure to long-term side-effects of systemic corticosteroids and effective inhaled therapies are available).
3. Anti-muscarinic bronchodilators (e.g. ipratropium, tiotropium) with a history of narrow angle glaucoma (may exacerbate glaucoma) or bladder outflow obstruction (may cause urinary retention).
4. Non-selective beta-blocker (whether oral or topical for glaucoma) with a history of asthma requiring treatment (risk of increased bronchospasm).
5. Benzodiazepines with acute or chronic respiratory failure i.e. pO_2 < 8.0 kPa ± pCO_2 > 6.5 kPa (risk of exacerbation of respiratory failure).

9 STOPP criteria Musculoskeletal System

1. Non-steroidal anti-inflammatory drug (NSAID) other than COX-2 selective agents with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent PPI or H2 antagonist (risk of peptic ulcer relapse).
2. NSAID with severe hypertension (risk of exacerbation of hypertension) or severe heart failure (risk of exacerbation of heart failure).
3. Long-term use of NSAID (>3 months) for symptom relief of osteoarthritis pain where paracetamol has not been tried (simple analgesics preferable and usually as effective for pain relief)
4. Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthrtitis (risk of systemic corticosteroid side-effects).
5. Corticosteroids (other than periodic intra-articular injections for mono-articular pain) for osteoarthritis (risk of systemic corticosteroid side-effects).

9 STOPP criteria Musculoskeletal System (2)

6. Long-term NSAID or colchicine (>3 months) for chronic treatment of gout where there is no contraindication to a xanthine-oxidase inhibitor (e.g. allopurinol, febuxostat) (xanthine-oxidase inhibitors are first choice prophylactic drugs in gout).

7. COX-2 selective NSAIDs with concurrent cardiovascular disease (increased risk of myocardial infarction and stroke)

8. NSAID with concurrent corticosteroids without PPI prophylaxis (increased risk of peptic ulcer disease)

9. Oral bisphosphonates in patients with a current or recent history of upper gastrointestinal disease i.e. dysphagia, oesophagitis, gastritis, duodenitis, or peptic ulcer disease, or upper gastrointestinal bleeding (risk of relapse/exacerbation of oesophagitis, oesophageal ulcer, oesophageal stricture)

2 STOPP criteria Urogenital System

1. Antimuscarinic drugs with dementia, or chronic cognitive impairment (risk of increased confusion, agitation) or narrow-angle glaucoma (risk of acute exacerbation of glaucoma), or chronic prostatism (risk of urinary retention).
2. Selective alpha-1 selective alpha blockers in those with symptomatic orthostatic hypotension or micturition syncope (risk of precipitating recurrent syncope)

6 STOPP criteria Endocrine System

1. Sulphonylureas with a long duration of action (e.g. glibenclamide, chlorpropamide, glimepiride) with type 2 diabetes mellitus (risk of prolonged hypoglycaemia).
2. Thiazolidenediones (e.g. rosiglitazone, pioglitazone) in patients with heart failure (risk of exacerbation of heart failure)
3. Beta-blockers in diabetes mellitus with frequent hypoglycaemic episodes (risk of suppressing hypoglycaemic symptoms).
4. Oestrogens with a history of breast cancer or venous thromboembolism (increased risk of recurrence).
5. Oral oestrogens without progestogen in patients with intact uterus (risk of endometrial cancer).
6. Androgens (male sex hormones) in the absence of primary or secondary hypogonadism (risk of androgen toxicity; no proven benefit outside of the hypogonadism indication).

4 STOPP criteria Drugs that predictably increase the risk of falls in older people

1. Benzodiazepines (sedative, may cause reduced sensorium, impair balance).
2. Neuroleptic drugs (may cause gait dyspraxia,Parkinsonism).
3. Vasodilator drugs (e.g. alpha-1 receptor blockers, calcium channel blockers, long-acting nitrates, ACE inhibitors, angiotensin I receptor blockers,) with persistent postural hypotension i.e. recurrent drop in systolic blood pressure ≥ 20mmHg (risk of syncope, falls).
4. Hypnotic Z-drugs e.g. zopiclone, zolpidem, zaleplon (may cause protracted daytime sedation, ataxia).

3 STOPP criteria Analgesic Drugs

1. Use of oral or transdermal strong opioids (morphine, oxycodone, fentanyl, buprenorphine, diamorphine, methadone, tramadol, pethidine, pentazocine) as first line therapy for mild pain (WHO analgesic ladder not observed).
2. Use of regular opioids without concomitant laxative (risk of severe constipation).
3. Long-acting opioids without short-acting opioids for break-through pain (risk of persistence of severe pain)

Antimuscarinic/Anticholinergic Drug Burden

- Concomitant use of two or more drugs with antimuscarinic/ anticholinergic properties (e.g. bladder antispasmodics, intestinal antispasmodics, tricyclic antidepressants, first generation antihistamines) (risk of increased antimuscarinic/ anticholinergic toxicity)

Version 2:
34 START criteria

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Version 2:
34 START criteria

8 Cardiovascular System
3 Respiratory System
6 Central Nervous System& Eyes
2 Gastrointestinal System
7 Musculoskeletal System
1 Endocrine System
3 Urogenital System
2 Analgesics
2 Vaccines

Screening Tool to Alert to Right Treatment (START), version 2

Unless an elderly patient's clinical status is end-of-life and therefore requiring a more palliative focus of pharmacotherapy, the following drug therapies should be considered where omitted for no valid clinical reason(s). It is assumed that the prescriber observes all the specific contraindications to these drug therapies prior to recommending them to older patients.

8 START criteria Cardiovascular System

1. Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation.
2. Aspirin (75 mg – 160 mg once daily) in the presence of chronic atrial fibrillation, where Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors are contraindicated.
3. Antiplatelet therapy (aspirin or clopidogrel or prasugrel or ticagrelor) with a documented history of coronary, cerebral or peripheral vascular disease.
4. Antihypertensive therapy where systolic blood pressure consistently > 160 mmHg and/or diastolic blood pressure consistently >90 mmHg; if systolic blood pressure > 140 mmHg and /or diastolic blood pressure > 90 mmHg, if diabetic.

8 START criteria Cardiovascular System (2)

5. Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, unless the patient's status is end-of-life or age is > 85 years.

6. Angiotensin Converting Enzyme (ACE) inhibitor with systolic heart failure and/or documented coronary artery disease.

7. Beta-blocker with ischaemic heart disease.

8. Appropriate beta-blocker (bisoprolol, nebivolol, metoprolol or carvedilol) with stable systolic heart failure.

3 START criteria Respiratory System

1. Regular inhaled b2 agonist or antimuscarinic bronchodilator (e.g. ipratropium, tiotropium) for mild to moderate asthma or COPD.

2. Regular inhaled corticosteroid for moderate-severe asthma or COPD, where FEV1 <50% of predicted value and repeated exacerbations requiring treatment with oral corticosteroids.

3. Home continuous oxygen with documented chronic hypoxaemia (i.e. pO_2 < 8.0 kPa or 60 mmHg or SaO_2 < 89%)

6 START criteria Central Nervous System& Eyes

1. L-DOPA or a dopamine agonist in idiopathic Parkinson's disease with functional impairment and resultant disability.

2. Non-TCA antidepressant drug in the presence of persistent major depressive symptoms.

3. Acetylcholinesterase inhibitor (e.g. donepezil, rivastigmine, galantamine) for mild-moderate Alzheimer's dementia or Lewy Body dementia (rivastigmine).

4. Topical prostaglandin, prostamide or beta-blocker for primary open-angle glaucoma.

5. Selective serotonin reuptake inhibitor (or SNRI or pregabalin if SSRI contraindicated) for persistent severe anxiety that interferes with independent functioning.

6. Dopamine agonist (ropinirole or pramipexole or rotigotine) for Restless Legs Syndrome, once iron deficiency and severe renal failure have been excluded.

2 START criteria Gastrointestinal System

1. Proton Pump Inhibitor with severe gastro-oesophageal reflux disease or peptic stricture requiring dilatation.

2. Fibre supplements (e.g. bran, ispaghula, methylcellulose, sterculia) for diverticulosis with a history of constipation

7 START criteria Musculoskeletal System

1. Disease-modifying anti-rheumatic drug (DMARD) with active, disabling rheumatoid disease.
2. Bisphosphonates and vitamin D and calcium in patients taking long-term systemic corticosteroid therapy.
3. Vitamin D and calcium supplement in patients with known osteoporosis and/or previous fragility fracture(s) and/or (Bone Mineral Density T-scores more than -2.5 in multiple sites).
4. Bone anti-resorptive or anabolic therapy (e.g. bisphosphonate, strontium ranelate, teriparatide, denosumab) in patients with documented osteoporosis, where no pharmacological or clinical status contraindication exists (Bone Mineral Density T-scores -> 2.5 in multiple sites) and/or previous history of fragility fracture(s).

7 START criteria Musculoskeletal System (2)

5. Vitamin D supplement in older people who are housebound or experiencing falls or with osteopenia (Bone Mineral Density T-score is > -1.0 but < -2.5 in multiple sites).
6. Xanthine-oxidase inhibitors (e.g. allopurinol, febuxostat) with a history of recurrent episodes of gout.
7. Folic acid supplement in patients taking methotexate.

1 START criterion Endocrine System

1. ACE inhibitor or Angiotensin Receptor Blocker (if intolerant of ACE inhibitor) in diabetes with evidence of renal disease i.e. dipstick proteinuria or microalbuminuria (>30mg/24 hours) with or without serum biochemical renal impairment.

3 START criteria Urogenital System

1. Alpha-1 receptor blocker with symptomatic prostatism, where prostatectomy is not considered necessary.

2. 5-alpha reductase inhibitor with symptomatic prostatism, where prostatectomy is not considered necessary.

3. Topical vaginal oestrogen or vaginal oestrogen pessary for symptomatic atrophic vaginitis.

2 START criteria Analgesics

1. High-potency opioids in moderate-severe pain, where paracetamol, NSAIDs or low-potency opioids are not appropriate to the pain severity or have been ineffective.

2. Laxatives in patients receiving opioids regularly.

2 START criteria Vaccines

1. Seasonal trivalent influenza vaccine annually
2. Pneumococcal vaccine at least once after age 65 according to national guidelines

- Importance of taking into account the specific criteria for older people (ex: STOPP/START)
- Importance of considering also the different frailty and function profiles among the very old…

Improve prescription in older adults THoM (1)

- Evaluation of the prescription
  - Verify the indications
  - PComputer assisted prescription
  - Clinical pharmacist
- Patient-centered care
  - Education and involvement in drug management
  - Respect patients' preferences
- Prescriptor's education
  - Learn to deprescibe also
  - Fight against « prescription pressure »

Improve prescription in older adults THoM (1)

- Do not extrapolate treatment indications for chronic diseases from young, robust and highly selected patients to very old frail and poly-morbid patients.
- Use frailty level and functional capacities rather than age in order to adapt therapeutic strategies
- In very frail patients priorize according to the symptoms and quality of life criteria
- Use screening tools to optimize prescription and avoid over-use under-use and misuse.

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- merci

Mrs MB, aged 85 yo.
Hospitalized in the Geriatric Dpt following a fall at home staying on the floor for 4 hours.

14 different medications (21 pills + drops)

Previscan (fluindione) :	0-0-¾,
Daonil 5 mg (gibenclamide) :	1-1-1
Glucophage 850 (metformine) :	1-0-1
Lasilix 40mg (furosémide) :	1-0-0
Renitec 5mg (enalapril):	1-0-0
Hyperium 1mg (rilmenidine)	1-0-0
Tahor10 mg (atorvastatine)	0-0-1
Cordarone 200mg (amidarone)	1-0-0
Théralène (alimémazine) :	10 drops
Primpéran (métoclopramide) :	1-1-1
Topalgic LP 100 mg (tramadol) :	1-0-1
Solupsan 160 mg :	0-1-0
Inexium 20 mg (ésomeprazole) :	0-1-0
Kaleorid 1000 (K+)	1-0-1

Mrs MB, aged 85 yo.
Hospitalized in the Geriatric Dpt following a fall at home staying on the floor for 4 hours.

Previscan (fluindione) :	AC/FA
Daonil 5 mg (gibenclamide) :	Dtype2
Glucophage 850 (metformine) :	Dtype2
Lasilix 40mg (furosémide) :	HTn
Renitec 5mg (enalapril):	HTn
Hyperium 1mg (rilmenidine)	HTn
Tahor 10 mg (atorvastatine)	CV Risk
Cordarone 200mg (amidarone)	AF
Théralène (alimémazine) :	SLEEP pb
Primpéran (métoclopramide) :	Nauseas
Topalgic LP 100 mg (tramadol) :	Pain
Solupsan 160 mg (aspirine) :	CV Risk
Inexium 20 mg (ésomeprazole) :	« Solupsan »
Kaleorid 1000 (K+)	« Lasilix »

Mrs BW…., 81 yà with steo-muscular resistant pain

12 different medications (15 pills + drops)

SITAGLIPTINE 50 mg	1-0-0
METFORMINE 1000 mg	1-0-0
LORMETAZEPAM 2 mg	0-0-1
BROMAZEPAM 3 mg	0-0-1
LEVODOPA 50mg - BENSERAZIDE 12.5mg	1-1-1
RASAGILIN 1 mg	1-0-0
ALIMEMAZIN 4%	30 drops.
PARACETAMOL 300mg-CODEINE 25mg	1-1-1
SERTALIN 25 mg	0-1-0
MIANSERINE 30 mg	0-0-1
CELECOXIB 100 mg	1-0-0
LANZOPRAZOLE 20 mg	0-1-0

Mrs BW…., 81 yo with steo-muscular resistant pain

12 different medications (15 pills + drops)

SITAGLIPTINE 50 mg	1-0-0	Dtype2
METFORMINE 1000 mg	1-0-0	Dtype2
ZOLPIDEMEM 2 mg	0-0-1	Sleep disord.
BROMAZEPAM 3 mg	0-0-1	Anxiety
LEVODOPA 50mg - BENSERAZIDE 12.5mg	1-1-1	Parkinson D
RASAGILIN 1 mg	1-0-0	Parkinson D
ALIMEMAZIN 4%	30 drops.	Sleep disord
PARACETAMOL 300mg-CODEINE 25mg	1-1-1	Pain
SERTALIN 25 mg	0-1-0	Depression
MIANSERINE 30 mg	0-0-1	Depression
IBUPROFENE 200 mg	1-0-0	Pain
LANZOPRAZOLE 20 mg	0-1-0	«NSAID»