

Appendix. A) STOPP.v3: appraisal of the 308 references supporting the 133 criteria

in **bold** characters: the reference with the best evidence level.

in *italic* characters: the 43 references considered as inappropriate (Evidence: -), and the reason.

underlined: the 10 criteria with no appropriate reference.

For full references, see file 2 (docx. 163 KB): [STOPP/START criteria for potentially inappropriate prescribing in older people: version 3 | European Geriatric Medicine](#)

Section A: Drug indication

A1. Any drug prescribed without a clinical indication.

No references (self-evident)

A2. Any drug prescribed beyond the recommended duration, where treatment duration is well defined.

No references (self-evident)

A3. Any duplicate drug class prescription for daily regular use (as distinct from PRN use)

A3 (i): **Quality of drug prescribing in elderly people in NHomes... Clin Drug Investig 2010**

Study: register

Age ≥ 65: yes

Citations: 39 (3/y)

Evidence: IV

A3 (ii): *Contrasting measures of adherence with ... therapeutic duplication. Ann Pharm. 2009*

Study: register

Age ≥ 65: no

Citations: 101 (7/y)

Evidence: -

Inappropriate: No message found on prevalence and on risk of drug duplication

A3 (iii): Health survey on potentially inappropriate geriatric drug use. Ann Pharm 2002

Study: survey

Age ≥ 65: yes

Citations: 9 (0.4/y)

Evidence: IV

Section B: Cardiovascular system

B1. Digoxin for HFpEF (heart failure with preserved systolic ventricular function)

B1 (i). *Diagnosis and management of heart failure in adults. Circulation 2009*

Study: guideline

Age ≥ 65: no

Citations: 486(32/y)

Evidence: -

Inappropriate: No message found on HFpEF and on digoxin

B1 (ii): *Heart failure management in the elderly population. Am J Geriatr Pharmacother 2009*

Study: systematic review

Age ≥ 65: yes

Citations: 24 (1.6/y)

Evidence: -

Inappropriate: No message found on HFpEF outcomes beside mortality

B2. Verapamil or diltiazem with severe heart failure (NYHA Class III or IV)

B2 (i): A review of potentially dangerous medications. Arch Intern Med 2004

Study: narrative review

Age ≥ 65: no

Citations: 12 (0.6 /y)

Evidence: V

B2 (ii): **Calcium channel blockers in cardiovascular diseases. Prog CV Dis 2000**

Study: narrative review

Age ≥ 65: no

Citations: 22 (0.9 /y)

Evidence: V

B3. Beta-blocker in combination with verapamil or diltiazem.

B3 (i): British National Formulary No. 81, 2021. page 1430.

Study: narrative review

Age ≥ 65: N/A

Citations: N/A

Evidence: N/A

B3 (ii): **...Combined beta-adrenergic and calcium entry-blocking agents. J CV Pharm 2000**

Study: 1 case serie

Age ≥ 65: yes

Citations: 8 (0.3/y)

Evidence: IV

B4. Ventricular rate-limiting drugs with bradycardia (< 50/min), type II heart block or complete heart block

B4 (i). British National Formulary, No. 81, pp 107-118, 2021

Study: narrative review

Age ≥ 65: no

Citations: N/A

Evidence: N/A

B5. Beta-blocker as monotherapy for uncomplicated hypertension

B5 (i): **Beta-blockers for hypertension. Cochrane Database Syst Rev. 2017**

Study: meta-analysis

Age ≥ 65: yes

Citations: 67 (10/y)

Evidence: I a

B5 (ii): Beta-blockers in hypertension. J Hypertens. 2020

Study: meta-analysis

Age ≥ 65: no

Citations: 14 (4/y)

Evidence: I a

- B6. Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias
- B6 (i): **Antiarrhythmics for maintaining sinus rhythm in AFibrillation. Arch Int Med 2006**
Study: meta-analysis **Age ≥ 65: no** **Citations: 63 (4/y)** **Evidence: I a**
- B6 (ii): *Amiodarone for the prevention of sudden cardiac death. Eur Heart J 2009*
Study: meta-analysis *Age ≥ 65: no* *Citations: 55 (4/y)* *Evidence: -*
Inappropriate: Mismatch in endpoint (prevention of sudden cardiac death)
- B7. Loop diuretic as first-line treatment for hypertension unless HFfailure requiring diuretic therapy
- B7 (i): **Thiazide and loop diuretics. J Clin Hypertens (Greenwich) 2011.** [same as B9 (i)]
Study: narrative review **Age ≥ 65: no** **Citations: 48 (4/y)** **Evidence: V**
- B7 (ii): *Guidelines for hypertension management 2004 (BHS-IV): summary. BMJ 2004*
Study: guideline *Age ≥ 65: no* *Citations: 204 (10/y)* *Evidence: -*
Inappropriate: No message found on loop diuretics
- B8. Loop diuretic for dependent ankle oedema
- B8 (i): **Epidemic overuse of a widely applied group of drugs. J Am Med Dir Assoc 2013**
Study: narrative review **Age ≥ 65: yes** **Citations: 15 (1.4/y)** **Evidence: V**
- B8 (ii): *Diuretics in clinical practice. Part I. Expert Opin Drug Saf 2010*
Study: narrative review *Age ≥ 65: no* *Citations: 11 (0.8/y)* *Evidence: -*
Inappropriate: No message found on loop diuretics and dependant ankle oedema
- B9. Thiazide diuretic with current K⁺ < 3.0, Na⁺ < 130, corrected Ca⁺⁺ > 2.65 or with history of gout
- B9 (i): *Thiazide and loop diuretics. J Clin Hypertens (Greenwich) 2011* [same as B7 (i)]
Study: narrative review *Age ≥ 65: no* *Citations: 48 (4 /y)* *Evidence: V*
- B9 (ii): **Thiazide diuretics and the initiation of anti-gout therapy. J Clin Epidemiol 1997**
Study: cohort **Age ≥ 65: yes** **Citations: 24 (0.9/y)** **Evidence: II b**
- B10. Loop diuretic for treatment of hypertension with concurrent urinary incontinence
- B10 (i): *Overactive bladder and diuretic use in the elderly. Curr Urol Rep 2009*
Study: narrative review *Age ≥ 65: yes* *Citations: 5 (0.3/y)* *Evidence: V*
- B10 (ii): **Diuretic use and overactive bladder syndrome. Arch Geronto Geria 2009**
Study: Survey **Age ≥ 65: yes** **Citations: 18 (1.2/y)** **Evidence: IV**
- B10 (iii): *Medical conditions, medications, and urinary incontinence. Can Fam Phys 2002.*
Study: Survey *Age ≥ 65: no* *Citations: 15 (0.7/y)* *Evidence: IV*
- B11. Centrally-acting antihypertensives unless intolerance/lack of efficacy with other antihypertensives
- B11 (i): **Hypertension. Brocklehurst's Textbook of Geriatric Medicine, p 403, 2003**
Study: narrative review **Age ≥ 65: no** **Citations: N/Av** **Evidence: I b**
- B11 (ii): *Hypertension. In: Prescribing for Elderly Patients, Wiley-Blackwell, UK, pp97-98, 2009*
Study: narrative review *Age ≥ 65: no* *Citations: N/Av* *Evidence: V*
- B12. Angiotensin-converting enzyme inh. (ACE-I) or angiotensin receptor blockers (ARBs) and K⁺ > 5.5
- B12 (i): *Angiotensin-converting enzyme inhibitors. J Clin Hypertens (Greenwich) 2011*
Study: narrative review *Age ≥ 65: no* *Citations: 35 (3/y)* *Evidence: V*
- B12 (ii): **Incidence and predictors of hyperkalemia in heart failure. J Am Coll Cardiol 2007**
Study: 1 RCT **Age ≥ 65: yes** **Citations: 48 (3/y)** **Evidence: I b**
- B12 (iii): *Hyperkalemia in outpatients using ACE-I. Arch Intern Med 1998*
Study: 1 case-control *Age ≥ 65: no* *Citations: 49 (1.9/y)* *Evidence: III b*
- B13. Aldosterone antagonists with concurrent potassium-conserving drugs without K⁺ monitoring
- B13 (i): *Aldosterone antagonism in addition to ACE-I in heart failure. Minerva Cardioangiol 2003*
Study: narrative review *Age ≥ 65: no* *Citations: 8 (0.4/y)* *Evidence: V*
- B13 (ii): **...hyperkalaemia in heart failure: aldosterone antagonism. Postgrad Med J 2010**
Study: narrative review **Age ≥ 65: no** **Citations: 10 (0.7/y)** **Evidence: I b**
- B13 (iii): *Aldosterone antagonists in the treatment of heart failure. Am J Health Syst Pharm 2006*
Study: narrative review *Age ≥ 65: no* *Citations: 5 (0.3/y)* *Evidence: V*
- B13 (iv): *Aldosterone receptor antagonists in chronic heart failure. Mayo Clin Proc 2005*
Study: narrative review *Age ≥ 65: no* *Citations: 13 (0.7/y)* *Evidence: V*
- B14. Phosphodiesterase type-5 inhibitors with severe heart failure and sBP < 90 mmHg, or with concurrent daily nitrate therapy for angina
- B14 (i): *British National Formulary, No. 81, pp 858-863., 2021*
Study: narrative review *Age ≥ 65: no* *Citations: N/A* *Evidence: N/A*

B14 (ii): Interaction between tadalafil and nitrates. J Am Coll Cardiol 2003				
Study: 1 RCT	Age ≥ 65: no	Citations: 26 (1.3/y)	Evidence: I b	
B15: Drugs that predictably prolong the QTc interval in patients with known QTc prolongation				
B15 (i): Risk assessment tools for QT prolonging in older adults. Eur J Clin Pharm. 2022				
Study: systematic review	Age ≥ 65: yes	Citations: 1 (0.5/y)	Evidence: II a	
B15 (ii): Drugs to be avoided in patients with long QT syndrome. World J Cardiol. 2013				
Study: narrative review	Age ≥ 65: no	Citations: 22 (2/y)	Evidence: IV	
B16: Statins for primary CV prevention in persons ≥ 85 years with frailty / expected LExpectancy < 3 years				
B16 (i): Lowering LDL cholesterol with statin in low risk of vascular disease. Lancet. 2012				
Study: meta-analysis	Age ≥ 65: no	Citations: 830 (69/y)	Evidence: I a	
B16 (ii): Statins for prevention of cardiovascular disease in adults. JAMA 2016				
Study: meta-analysis	Age ≥ 65: no	Citations: 197 (25/y)	Evidence: -	
Inappropriate: Mismatch in patients (adults 51-66 years and not ≥ 85 years with frailty)				
B16 (iii): Statins in primary prevention in people over 80 years. Am J Cardiol 2023				
Study: systematic review	Age ≥ 65: yes	Citations: 0 (recent)	Evidence: I a	
B17: Long-term systemic NSAIDs with known history of coronary, cerebral or peripheral vascular disease				
B17 (i): Cardiovascular risk and inhibition of cyclooxygenase. JAMA. 2006				
Study: meta-analysis	Age ≥ 65: no	Citations: 266 (15/y)	Evidence: II a	
B17 (ii): Cardiovascular risk with non-steroidal anti-inflammatory drugs: Med. 2011				
Study: meta-analysis	Age ≥ 65: no	Citations: 154 (12/y)	Evidence: II a	
B17 (iii): Vascular and upper GI effects of NSAIDs. Lancet. 2013				
Study: meta-analysis	Age ≥ 65: no	Citations: 419 (45/y)	Evidence: I a	
B18: Long-term antipsychotics with history of coronary, cerebral or peripheral vascular disease				
B18 (i): Use of antipsychotics and risk of myocardial infarction. Br J Clin Pharm 2016				
Study: meta-analysis	Age ≥ 65: no	Citations: 10 (1.3/y)	Evidence: II a	
B18 (ii): Cardiometabolic outcomes of the first treated episode of psychosis. Arch Gen Psych 2011				
Study: systematic review	Age ≥ 65: no	Citations: 76 (6/y)	Evidence: II b	
B19: NSAIDs or systemic corticosteroids with heart failure requiring loop diuretic therapy				
B19 (i): Vascular and upper GI effects of NSAIDs. Lancet. 2013				
Study: meta-analysis	Age ≥ 65: no	Citations: 491 (45/y)	Evidence: I a	
B19 (ii): NSAIDs and risk of heart failure in four European countries. BMJ. 2016				
Study: case-control	Age ≥ 65: yes	Citations: 57 (7/y)	Evidence: III b	
B19 (iii): Oral glucocorticoids and risk of cardiovascular and cerebral disease Heart. 2004				
Study: case-control	Age ≥ 65: yes	Citations: 119 (6/y)	Evidence: III b	
B20: Antihypertensive drugs in severe symptomatic aortic stenosis, except for RAS inhibitors				
B20 (i): Antihypertensive treatment in severe aortic stenosis. J Cardiovasc Imaging. 2018 Jun				
Study: narrative review	Age ≥ 65: no	Citations: 7 (1.2/y)	Evidence: -	
Inappropriate: Different message: "antihypertensive drugs may be safe and even beneficial"				
B20 (ii): Calcium channel blockers in moderate or severe aortic stenosis. Int J Card. 2020				
Study: case-series	Age ≥ 65: yes	Citations: 7 (1.8/y)	Evidence: IV	
B21: Digoxin as first line treatment for long-term (> 3 months) ventricular rate control in atrial fibrillation				
B21 (i): Digoxin and Mortality in Patients with Atrial Fibrillation. J Am Coll Cardiol. 2018				
Study: cohort	Age ≥ 65: yes	Citations: 38 (6/y)	Evidence: II b	
B21 (ii): Digoxin-associated mortality. Eur Heart J. 2015				
Study: meta-analysis	Age ≥ 65: no	Citations: 64 (7/y)	Evidence: I a	

Section C: Coagulation system

C1. Long-term aspirin at doses greater than 100 mg per day

C1 (i). Aspirin to prevent heart attack and stroke: the right dose? Am J Med 2006				
Study: narrative review	Age ≥ 65: no	Citations: 7 (9/1.1y)	Evidence: -	
Inappropriate: Different message: "most appropriate dosage is 160 mg par day"				
C1 (ii). The dose of aspirin for the prevention of CV events. Curr Med Res Opin 2006				
Study: narrative review	Age ≥ 65: no	Citations: 6 (0.3/y)	Evidence: -	
Inappropriate: Different message: "no difference in safety across the range 75-325 mg"				

- C2. Antiplatelet agent or anticoagulant agent with concurrent significant bleeding risk
- C2 (i): The CHA₂DS₂-VASc and HAS-BLED scores in atrial fibrillation. Am J Med. 2011
 Study: narrative review Age ≥ 65: no Citations: 45 (3.5/y) Evidence: II b
- C2 (ii): **HAS-BLED score to assess risk of major bleeding in atrial fibrillation. Chest 2010**
Study: cohort Age ≥ 65: yes Citations: 1390 (99/y) Evidence: II b
- C3. Aspirin plus clopidogrel as long-term (> 4 weeks) secondary stroke prevention, unless coronary stent(s) inserted < 12 months or concurrent acute coronary syndrome or high grade symptomatic carotid stenosis.
- C3 (i): Aspirin and/or clopidogrel after recent ischaemic stroke or TIA. Lancet 2004
 Study: 1 RCT Age ≥ 65: yes Citations: 473 (24/y) Evidence: I b
- C3 (ii): Clopidogrel and/or aspirin for the prevention of atherothrombotic events. N Engl J Med. 2006
 Study: 1 RCT Age ≥ 65: no Citations: 571 (32/y) Evidence: I b
- C3 (iii): **Combination antiplatelet therapy for secondary stroke prevention. Am J Cardiol 2009**
Study: narrative review Age ≥ 65: yes Citations: 14 (0.9/y) Evidence: I a
- C3 (iv): Clopidogrel and/or aspirin for preventing CV disease. Cochrane Database Syst Rev 2011
 Study: meta-analysis Age ≥ 65: no Citations: 11 (0.8/y) Evidence: I b
- C3 (v): Clopidogrel and aspirin in vascular diseases. Expert Opin Pharmacother 2008
 Study: narrative review Age ≥ 65: no Citation: 0 (0/y) Evidence: I b
- C4. Antiplatelet agents in combination with anticoagulant therapy in patients with chronic atrial fibrillation unless coronary artery stent(s) inserted or high grade (> 50%) coronary artery stenosis
- C4 (i): ... **combining aspirin with anticoagulant therapy in atrial fibrillation. Am Heart J 2006**
Study: cohort Age ≥ 65: yes Citations: 45 (3/y) Evidence: II b
- C4 (ii): *Should aspirin be continued in patients started on warfarin? J Gen Intern Med 2004*
 Study: meta-analysis Age ≥ 65: no Citations: 8 (0.4/y) Evidence: -
Inappropriate: Mismatch in condition (mechanical valve or MI/infarction, and not AFib)
- C5. Antiplatelet agents with anticoagulant therapy in patients with stable arterial disease
- C5 (i): **Antiplatelet and anticoagulant therapies. J Am Coll Cardiol 2009**
Study: narrative review Age ≥ 65: no Citations: 24 (1.6/y) Evidence: V
- C5 (ii): *Antithrombotic therapy for coronary stenting in patients on anticoagulation. Ann Med 2008*
 Study: systematic review Age ≥ 65: no Citation: 28 (1.8/y) Evidence: -
Inappropriate: Mismatch in intervention (triple therapy; not antiplatelet and anticoagulant)
- C6. Ticlopidine in any circumstances
- C6 (i): **Prevention of stroke in patients with stroke or TIA. Stroke 2011**
Study: guideline Age ≥ 65: no Citations: 487 (38/y) Evidence: V
- C6 (ii): *Platelet P2Y₁₂ receptor inhibition by thienopyridines. Expert Opin Investig Drugs 2009*
 Study: narrative review Age ≥ 65: no Citations: 6 (0.4/y) Evidence: -
Inappropriate: No message found on avoiding Ticlopidine
- C7. Antiplatelet instead of anticoagulant therapy for stroke prevention in patients with atrial fibrillation (AF).
- C7 (i): **Antithrombotic therapy to prevent stroke in patients with AF. Ann Int Med 2007**
Study: meta-analysis Age ≥ 65: yes Citations: 1386(82/y) Evidence: I a
- C7 (ii): Anticoagulant vs antiplatelet for first stroke prevention in AF. Cochrane 2007
 Study: meta-analysis Age ≥ 65: yes Citations: 78 (5/y) Evidence: I a
- C8. Oral anticoagulant therapy > 6 months for first DVThrombosis without continuing provoking risk factor(s)
- C8 (i): *3 vs 6 months of anticoagulant therapy after a first proximal DVP/PE. Circulation 2001*
 Study: 1 RCT Age ≥ 65: no Citations: 63 (3/y) Evidence: -
Inappropriate: Different message: "equivalence between 3 and 6 months"
- C8 (ii): *Antithrombotic therapy for VTE disease, guideline. Chest 2012*
 Study: guideline Age ≥ 65: no Citations: 976 (81/y) Evidence: -
Inappropriate: Different message: "we recommend 3 months of therapy"
- C9. Oral anticoagulant therapy > 12 months for first PEmbolus without continuing provoking risk factor(s)
- C9 (i): *Antithrombotic therapy for VTE disease, guideline. Chest 2012*
 Study: guideline Age ≥ 65: no Citations: 976 (81/y) Evidence: -
Inappropriate: Different message: "we recommend 3 months of therapy"
- C10. NSAID and anticoagulant therapy in combination
- C10 (i): **Cyclo-oxygenase specificity of NSAIDs and bleeding in coumarin users. QJM 2003**
Study: case-control Age ≥ 65: yes Citations: 4 (0.2/y) Evidence: III b

- C10 (ii): Gastrointestinal adverse effects of NSAIDs. Expert Opin Drug Saf 2005
Study: narrative review Age ≥ 65: yes Citations: 13 (0.7/y) Evidence: V
- C11: VKAntagonist as first-line anticoagulant for atrial fibrillation (AF), unless metallic heart valve, moderate-to-severe mitral stenosis, or creatinine clearance < 15ml/min
- C11 (i): **Comparison of NAOcs with warfarin in patients with AF. Lancet 2014**
Study: meta-analysis Age ≥ 65: yes Citat. 1482 (148/y) Evidence: I a
- C 11 (ii): Factor Xa inhibitors vs VKA for preventing embolism in AF. Cochrane Syst Rev. 2018
Study: meta-analysis Age ≥ 65: no Citations: 26 (4/y) Evidence: I a
- C11 (iii): Direct thrombin inhibitors vs VKA for preventing embolism in AF. Cochrane Syst Rev. 2014
Study: meta-analysis Age ≥ 65: no Citations: 28 (3/y) Evidence: I a
- C12: SSRI with anticoagulant therapy and history of major haemorrhage
- C12 (i): SSRIs and bleedings in patients on anticoagulant or antiplatelet agents. Ann Med 2022
Study: meta-analysis Age ≥ 65: yes Citations: 11 (6/y) Evidence: II a
- C12 (ii): **Bleeding risk under SSRIs: meta-analysis of observational studies. Phar Res 2017**
Study: meta-analysis Age ≥ 65: no Citations: 45 (6/y) Evidence: II a
- C13: Direct thrombin inhibitor (dabigatran) and diltiazem or verapamil.
- C13 (i): Oral anticoagulants with verapamil/diltiazem and bleeding events. JAMA Netw Open 2020
Study: cohort Age ≥ 65: yes Citations: 18 (5/y) Evidence: II b
- C13 (ii): **Bioavailability of dabigatran after co-medication with verapamil. Br J Clin Pharm 2013**
Study: cross-over trial Age ≥ 65: no Citations: 63 (6/y) Evidence: I b
- C14: DOACs and P-glycoprotein drug efflux pump inhibitors (listed in the SS.v3 article)
- C14 (i): **Pharmacokinetic-interacting drugs and DOACs. Clin Pharmacol Ther 2021**
Study: case-control Age ≥ 65: yes Citations: 26 (9/y) Evidence: III b
- C14 (ii): British National Formulary, vol 81, March-Sept 2021, pp 1513-1514, 2021
Study: narrative study Age ≥ 65: no Citations: N/Ap Evidence: N/A
- C15: Systemic oestrogens or androgens with previous history of venous thromboembolism (VTE)
- C15 (i) **Hormone replacement therapy and risk of VTE in postmenopausal women. BMJ 2008**
Study: meta-analysis Age ≥ 65: no Citations: 98 (6/y) Evidence: I a
- C15 (ii): Testosterone therapy and risk of VTE among men. JAMA Int Med 2020
Study: case-series Age ≥ 65: no Citations: 36 (9/y) Evidence: IV
- C16: Aspirin for primary prevention of cardiovascular disease.
- C16 (i): **Aspirin for primary prevention, cardiovascular and bleeding events. JAMA 2019**
Study: meta-analysis Age ≥ 65: no Citations: 177 (35/y) Evidence: I a
- C16 (ii): Aspirin for primary prevention of CV disease, focus on subgroups. BMC Med. 2019
Study: meta-analysis Age ≥ 65: no Citations: 30 (6/y) Evidence: I a

Section D: Central nervous system

- D1. Tricyclic antidepressants in patients with dementia, narrow angle glaucoma, cardiac conduction abnormalities, LUTSymptoms related to BPHyperplasia, urinary retention, chronic constipation, recent falls.
- D1 (i): Anticholinergic side effects of drugs in elderly people. J R Soc Med 2000
Study: narrative review Age ≥ 65: yes Citations: 96 (4/y) Evidence: V
- D1 (ii): Drug-induced urinary retention: management and prevention. Drug Saf 2008
Study: narrative review Age ≥ 65: no Citations: 52 (3/y) Evidence: II b
- D1 (iii): Proarrhythmic risk with antipsychotic and antidepressant drugs. Drugs Aging 2009
Study: narrative review Age ≥ 65: yes Citations: 31 (2/y) Evidence: IV
- D1 (iv): Drug-induced glaucomas: mechanism and management. Drug Saf 2003
Study: narrative review Age ≥ 65: no Citations: 35 (1.7/y) Evidence: V
- D1 (v): **Drug-induced orthostatic hypotension. PLoS Med. 2021**
Study: narrative review Age ≥ 65: no Citations: 17 (6/y) Evidence: I a
- D2. Initiation of tricyclic antidepressant (TCA) as first-line treatment for major depression
- D2 (i): TCA and SSRI: use during ... elderly. Acta Psych. Scand Suppl. 2000
Study: narrative review Age ≥ 65: yes Citations: 9 (0.4/y) Evidence: IV
- D2 (ii) **Antidepressants for depressed elderly. Cochrane Syst Rev 2006**
Study: meta-analysis Age ≥ 65: yes Citations: 64 (4/y) Evidence: I a

- D3. Serotonin/noradrenaline reuptake inhibitor (SNRI) and severe hypertension (sBP>180 ± dBP>105 mmHg)
- D3 (i): Effects of SSRIs and SNRIs on blood pressure. Neuropsych Dis Treat 2017
Study: meta-analysis Age ≥ 65: no Citations: 11 (1.6/y) Evidence: I a
- D3 (ii): Effects of venlafaxine on blood pressure. J Clin Psychiatry
Study: meta-analysis Age ≥ 65: no Citations: 62 (3/y) Evidence: I a
- D3 (iii): Supratherapeutic doses of duloxetine, blood pressure and pulse rate. J CV Pharm 2007
Study: RCT Age ≥ 65: no Citations: 12 (0.7/y) Evidence: I b
- D4. Antipsychotics with moderate-marked anticholinergic effects and LUTSymptoms or previous urinary retention
- D4 (i): **Drug-induced urinary retention: management and prevention. Drug Saf 2008**
Study: narrative review Age ≥ 65: no Citations: 52 (3/y) Evidence: IV
- D4 (ii): British National Formulary, volume 81, BMJ Group & Pharm Press, p 1431, 2021.
Study: narrative review Age ≥ 65: no Citations: N/A Evidence: N/A
- D5. Antipsychotics for BPSDementia at unchanged dose for > 3 months without medication review.
- D5 (i): Pharmacological treatment of neuropsychiatric symptoms of dementia. JAMA 2005.
Study: systematic review Age ≥ 65: no Citations: 234 (12/y) Evidence: I a
- D5 (ii): Atypical antipsychotic drugs in the treatment of BPSD. BMJ 2004.
Study: systematic review Age ≥ 65: yes Citations: 54 (3/y) Evidence: I a
- D5 (iii): Risk of death with conventional vs. atypical antipsychotics. N Engl J Med 2005.
Study: narrative review Age ≥ 65: yes Citations: 256 (14/y) Evidence: II b
- D5 (iv): **Risk of death with atypical antipsychotics for dementia. JAMA 2005.**
Study: narrative review Age ≥ 65: yes Citations: 467 (25/y) Evidence: I a
- D6. SSRIs with current or recent significant hyponatraemia (serum Na+ < 130 mmol/l)
- D6 (i): **Hyponatremia associated with SSRIs in older adults. Ann Pharmacother 2006**
Study: systematic review Age ≥ 65: yes Citations: 64 (4/y) Evidence: II b
- D6 (ii): Tolerability of SSRIs: issues relevant to the elderly. Drugs Aging 2008
Study: narrative review Age ≥ 65: yes Citations: 18 (1.1/y) Evidence: IV
- D7. SSRIs with current or recent significant bleeding
- D7 (i): **Bleeding risk under SSRIs: meta-analysis of observational studies. Pharm Res 2017**
Study: meta-analysis Age ≥ 65: no Citations: 45 (6/y) Evidence: II a
- D7 (ii): SSRIs and brain hemorrhage: a meta-analysis. Neurology 2012
Study: meta-analysis Age ≥ 65: no Citations: 63 (5/y) Evidence: II a
- D7 (iii): SSRIs and risk of upper gastrointestinal bleeding. Clin Gastroenterol Hepatol. 2015
Study: meta-analysis Age ≥ 65: no Citations: 46 (5/y) Evidence: II a
- D8. Benzodiazepines for ≥ 4 weeks
- D8 (i): Safety of benzodiazepines in the geriatric population. Expert Opin Drug Saf 2004
Study: narrative review Age ≥ 65: yes Citations: 58 (3/y) Evidence: V
- D8 (ii): Cognitive effects of long-term benzodiazepine use. CNS Drugs 2004.
Study: meta-analysis (C-C) Age ≥ 65: no Citations: 137 (7/y) Evidence: III a
- D8 (iii): **Sedative hypnotics in older people with insomnia. BMJ 2005**
Study: meta-analysis Age ≥ 65: yes Citations: 321 (17/y) Evidence: I a
- D9. Benzodiazepines for agitated behaviour or non-cognitive symptoms of dementia
- D9 (i): **Benzodiazepines for BPSDementia. Am J Alzh Dis Other Dement 2014**
Study: systematic review Age ≥ 65: no Citations: 25 (3/y) Evidence: I a
- D9 (ii): Benzodiazepines in Alzheimer's Disease. Int J Neuropsychopharmacol. 2015
Study: systematic review Age ≥ 65: yes Citations: 38 (4/y) Evidence: I b
- D10. Benzodiazepines for insomnia for ≥ 2 weeks
- D10 (i): **Benzodiazepine use among older adults. Harv Rev Psychiatry. 2018**
Study: systematic review Age ≥ 65: no Citations: 19 (3/y) Evidence: I a
- D10 (ii): Impact of 9 medication classes on falls in elderly. Arch Intern Med. 2009
Study: meta-analysis Age ≥ 65: yes Citations: 425 (28/y) Evidence: II a
- D10 (iii): Road-traffic accidents and benzodiazepine use. Lancet 1998
Study: cross-over Age ≥ 65: no Citations: 121 (5/y) Evidence: IV
- D11. Z-drugs (zolpidem, zopiclone, zaleplon) for insomnia for ≥ 2 weeks
- D11 (i): Z-substances in the management of insomnia in older adults. BMC Geriatr 2022
Study: meta-analysis Age ≥ 65: yes Citations: 3 (1.5/y) Evidence: I a

- D11 (ii): ... a quarter century of the most prescribed sleeping pill. *Exp Gerontol*. 2020
Study: systematic review Age ≥ 65: yes Citations: 7 (1.8/y) Evidence: I a
- D12. Antipsychotics (other than clozapine or quetiapine) in parkinsonism or Lewy Bodies Dementia
D12 (i): Drug-induced parkinsonism. *Expert Opin Drug Saf* 2006
Study: narrative review Age ≥ 65: no Citations: 16 (0.9/y) Evidence: V
D12 (ii): **Management of hallucinations and psychosis in Parkinson. *Am J Geriatr Pharm* 2010**
Study: systematic review Age ≥ 65: yes Citations: 15 (1.1/y) Evidence: I a
- D13. Anticholinergics drugs to treat extra-pyramidal side-effects of antipsychotic medications
D13 (i): Trihexyphenidyl and cognition in “elderly” with schizophrenia. *Int Psychogeriatr*. 1998
Study: case-control Age ≥ 65: no Citations: 3 (0.1/y) Evidence: III b
D13 (ii): Discontinuation of anticholinergic in elderly with schizophrenia. *Int Clin Psychopharmacol* 2004
Study: case-series Age ≥ 65: no Citations: 11 (0.6/y) Evidence: IV
- D14. Drugs with potent anticholinergic effects (listed in SS.v3 article) in patients with delirium or dementia.
D14 (i): Antimuscarinic drugs and cognitive in elderly with overactive bladder. *Curr Urol Rep* 2011
Study: narrative review Age ≥ 65: yes Citations: 25 (1.9/y) Evidence: V
D14 (ii): **Drugs with anticholinergic properties. *Expert Opin Drug Saf* 2011**
Study: narrative review Age ≥ 65: no Citations: 53 (4.1/y) Evidence: V
- D15. Antipsychotics in patients for non-cognitive symptoms of dementia, > 12 weeks, unless severe and failures
D15 (i): Cerebrovascular accidents in elderly people on antipsychotic drugs. *Drug Saf* 2010
Study: systematic review Age ≥ 65: yes Citations: 29 (2/y) Evidence: I a
D15 (ii): **Risk in elderly demented treated with antipsychotics. *Am J Alz Dis Other Dem* 2011**
Study: systematic review Age ≥ 65: yes Citations: 42 (3/y) Evidence: I a
D15 (iii): The elderly safety imperative and antipsychotic usage. *Harvard Rev Psychiatr* 2010
Study: systematic review Age ≥ 65: yes Citations: 5 (0.4/y) Evidence: I a
- D16. Antipsychotics as hypnotics, unless sleep disorder due to psychosis or BPSDementia
D16 (i): Sleep disorders in the elderly. In: *Prescribing for Elderly Patients*, pp 45-52, 2009
Study: narrative review Age ≥ 65: yes Citations: 1 (0.1/y) Evidence: V
D16 (ii): **Using antipsychotic agents in older patients. *J Clin Psychiatry* 2004**
Study: survey Age ≥ 65: yes Citations: 93 (5/y) Evidence: V
- D17. Acetylcholinesterase inh. with history of bradycardia (< 60/min), heart block, unexplained syncope
D17 (i): [Cardiac effects of cholinesterase inhibitors]. *Tijdschr Geront Geriatr* 2009 [in Dutch]
Study: case-series Age ≥ 65: yes Citations: 0 (0/y) Evidence: IV
D17 (ii): **Prolonged QT interval, syncope, and delirium with galantamine *Ann Pharm* 2008**
Study: case-series Age ≥ 65: yes Citations: 12 (0.8/y) Evidence: IV
D17 (iii): Complete atrioventricular block associated with donepezil. *Emerg Med J* 2006
Study: case-series Age ≥ 65: yes Citations: 12 (0.7/y) Evidence: IV
D17 (iv): Syncope in patients with Alzheimer's disease on donepezil. *Drugs Aging* 2005
Study: case-series Age ≥ 65: yes Citations: 11 (0.6/y) Evidence: IV
- D18. Acetylcholinesterase inhibitors with concurrent treatment with drugs that reduce heart rate
D18 (i): [Cardiac effects of cholinesterase inhibitors]. *Tijdschr Geront Geriatr* 2009 [in Dutch]
Study: case-series Age ≥ 65: yes Citations: 0 (0/y) Evidence: IV
D18 (ii): **Prolonged QT interval, syncope, and delirium with galantamine *Ann Pharm* 2008**
Study: case-series Age ≥ 65: yes Citations: 12 (0.8/y) Evidence: IV
D18 (iii): Complete atrioventricular block associated with donepezil. *Emerg Med J* 2006
Study: case-series Age ≥ 65: yes Citations: 12 (0.7/y) Evidence: IV
D18 (iv): Syncope in patients with Alzheimer's disease on donepezil. *Drugs Aging* 2005
Study: case-series Age ≥ 65: yes Citations: 11 (0.6/y) Evidence: IV
- D19. Memantine with known current or previous seizure disorder
D19 (i): *British National Formulary*, No. 81, BMJ Group & Pharm Press, p320, 2021
Study: narrative review Age ≥ 65: no Citations: N/A Evidence: N/A
- D20. Nootropics (listed in SS.v3 article) in dementia
D20 (i): *Ginkgo for memory enhancement: a randomized controlled trial. JAMA* 2002
Study: RCT Age ≥ 65: no Citations: 53 (3/y) Evidence: -
Inappropriate: Mismatch in patients (with no cognitive impairment, not with dementia)
D20 (ii): **Piracetam for dementia or cognitive impairment. *Cochrane Syst Rev* 2000**

	Study: systematic review	Age ≥ 65: yes	Citations: 17 (0.7/y)	Evidence: I a
D20 (iii): Docosahexaenoic acid and cognitive decline in Alzheimer disease. JAMA 2010				
	Study: RCT	Age ≥ 65: yes	Citations: 270 (19/y)	Evidence: I b
D21. Phenothiazines as first-line treatment for psychosis or BPSDementia				
D21 (i): The elderly safety imperative and antipsychotic usage. Harvard Rev Psych 2010				
	Study: narrative review	Age ≥ 65: yes	Citations: 5 (0.4/y)	Evidence V
D21 (ii): <i>The differential pharmacology of atypical antipsychotics. Consult Pharm 2006.</i>				
	Study: narrative review	Age ≥ 65: no	Citations: 0 (0/y)	Evidence: -
	<i>Inappropriate: Mismatch in medication (atypical and not typical antipsychotics)</i>			
D22. Levodopa or dopamine agonists for benign essential tremor				
D22 (i): Guideline update- treatment of essential tremor-report. Neurology 2011				
	Study: guideline	Age ≥ 65: no	Citations: 94 (7/y)	Evidence: V
D22 (ii): Treatment of patients with essential tremor. Lancet Neurol 2011				
	Study: narrative review	Age ≥ 65: no	Citations: 115 (9/y)	Evidence: V
D23. Levodopa or dopamine agonists for treatment of extrapyramidal side effects of antipsychotics				
D23 (i): Neuroleptic-induced Parkinson's syndrome. J Neurol Neurosurg Psych 1988.				
	Study: case-series	Age ≥ 65: no	Citations: 36 (0.1/y)	Evidence: IV
D23 (ii): <i>Clinical characteristics of neuroleptic-induced parkinsonism. J Neural Transm 2001</i>				
	Study: case-series	Age ≥ 65: no	Citations: 25 (1.1/y)	Evidence: -
	<i>Inappropriate: No message found on Levodopa or dopamine agonists</i>			
D23 (iii): <i>Shin HW, Chung SJ. Drug-induced parkinsonism. J Clin Neurol. 2012</i>				
	Study: narrative review	Age ≥ 65: no	Citations: 107 (9/y)	Evidence: -
	<i>Inappropriate: No message found on Levodopa or dopamine agonists</i>			
D24. First-generation antihistamines as first line treatment for allergy or pruritis				
D24 (i): Pharmacological management of allergic rhinitis in the elderly. Drugs Aging 2005				
	Study: survey	Age ≥ 65: yes	Citations: 14 (0.7/y)	Evidence: V
D24 (ii): ... treatment of allergic rhinitis in the elderly. Allergy Asthma Proc 2010				
	Study: narrative review	Age ≥ 65: yes	Citations: 11 (0.8/y)	Evidence: V
D24 (iii): Risk of first-generation H1-antihistamines. Allergy 2010				
	Study: narrative review	Age ≥ 65: no	Citations: 93 (7/y)	Evidence: IV
D25. First-generation antihistamines for insomnia				
D25 (i): Manifestations and magement of chronic insomnia in adults. Sleep 2005				
	Study: narrative review	Age ≥ 65: no	Citations: 302 (16/y)	Evidence: V

Section E. Renal system

E1. Digoxin at a long-term (> 90 days) at maintenance dose ≥ 125µg/day if eGFR < 30 ml/min				
E1 (i) <i>Safety and efficacy of digoxin. BMJ 2015</i>				
	Study: meta-analysis	Age ≥ 65: no	Citations: 83 (1.2/y)	Evidence: -
	<i>Inappropriate: No message found on severe renal failure (eGFR < 30 ml/min)</i>			
E1 (ii): Digoxin in geriatric heart failure. J Gerontol A Biol Sci Med 2007				
	Study: RCT	Age ≥ 65: yes	Citations: 7 (0.3/y)	Evidence: I b
E1 (iii): Cardiovascular pharmacology of aging. Cardiol Clin 1999				
	Study: narrative review	Age ≥ 65: yes	Citations: 7 (0.5/y)	Evidence: V
E2. Direct thrombin inhibitor (dabigatran) if eGFR < 30 ml/min				
E2 (i): Clinical pharmacology of dabigatran in severe renal impairment. J Clin Pharm 2012				
	Study: case series	Age ≥ 65: no	Citations: 23 (1.5/y)	Evidence: IV
E2 (ii): ... New anticoagulants in elderly patients with renal impairment. Drugs Aging 2011				
	Study: narrative review	Age ≥ 65: yes	Citations: 7 (0.5/y)	Evidence: V
E3. Factor Xa inhibitors (e.g. rivaroxaban, apixaban) if eGFR < 15 ml/min				
E3 (i): Renal impairment and rivaroxaban, a direct Factor Xa inhibitor. Br J Clin Pharm 2010				
	Study: case series	Age ≥ 65: no	Citations: 7 (0.5/y)	Evidence: IV
E3 (ii): Rivaroxaban vs warfarin in AFibrillation and moderate renal impairment. Eur Heart J 2011				
	Study: RCT	Age ≥ 65: yes	Citations: 160 (13/y)	Evidence: V

E4. NSAIDs if eGFR < 50 ml/min

E4 (i): Renal adverse effects of NSAIDs. Expert Opin Drug Saf 2009

Study: narrative review	Age ≥ 65: no	Citations: 60 (4/y)	Evidence: V
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E4 (ii): Renal effects of NSAIDs and selective cyclooxygenase-2 inhibitors. Curr Pharm Des 2005

Study: narrative review	Age ≥ 65: no	Citations: 27 (1.4/y)	Evidence: V
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E5. Colchicine if eGFR < 10 ml/min

E5 (i): Management of gout in older adults: barriers to optimal control. Drugs Aging 2007

Study: narrative review	Age ≥ 65: yes	Citations: 13 (0.8/y)	Evidence: -
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Inappropriate: No message found on very severe renal failure (eGFR < 15 ml/min)

E5 (ii): Oral dosing of primarily renally cleared medications in older adults. JAGS 2009

Study: guidelines	Age ≥ 65: yes	Citations: 36 (3/y)	Evidence: V
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E6. Metformin if eGFR < 30 ml/min.

E6 (i): Non-insulin treatment of type 2 diabetes mellitus in geriatric patients. Clin Ther 2011

Study: narrative review	Age ≥ 65: yes	Citations: 12 (0.9/y)	Evidence: V
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E6 (ii): Lactic acidosis induced by metformin. Drug Safety 2010

Study: narrative review	Age ≥ 65: no	Citations: 69 (5/y)	Evidence: -
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Inappropriate: No message found on severe renal failure (eGFR < 30 ml/min)

E7. Mineralocorticoid receptor antagonists if eGFR < 30 ml/min.

E7 (i): Mineralocorticoid receptor antagonists and progression of CKD. BMC Nephrol 2016.

Study: meta-analysis	Age ≥ 65: no	Citations: 59 (8/y)	Evidence: V
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E7 (ii): Rates of hyperkalemia after publication of RALEStudy. N Engl J Med 2004

Study: case series	Age ≥ 65: yes	Citations: 424 (21/y)	Evidence: V
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E7 (iii): Safety profile of mineralocorticoid receptor antagonists. Int J Cardiol 2015

Study: narrative review	Age ≥ 65: no	Citations: 52 (5/6y)	Evidence: V
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E7 (iv): Mineralocorticoid receptor antagonists in HF failure and CKD disease. Am J Cardiol 2020

Study: systematic review	Age ≥ 65: no	Citations: 6 (1.5/y)	Evidence: V
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E8. Nitrofurantoin if eGFR < 45 ml/min

E8 (i): Effect of renal function on orally administered nitrofurantoin. N Engl J Med 1968

Study: case series	Age ≥ 65: no	Citations: 13 (0.2/y)	Evidence: IV
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E8 (ii): British National Formulary, No. 81, BMJ Group & Pharm Press, p629, 2021.

Study: narrative review	Age ≥ 65: no	Citations: N/A	Evidence: N/A
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E9. Bisphosphonates if eGFR < 30 ml/min

E9 (i): Renal safety of bisphosphonates for osteoporosis. J Bone Miner Res. 2013

Study: narrative review	Age ≥ 65: no	Citations: 32 (3/y)	Evidence: -
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Inappropriate: Different message: "no effects on renal function"

E9 (ii): British National Formulary, No. 81, BMJ Group & Pharm Press, p768, 2021.

Study: narrative review	Age ≥ 65: no	Citations: N/A	Evidence: N/A
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E10. Methotrexate if eGFR < 30 ml/min/1.73m².

E10 (i): Disease-modifying antirheumatic drugs in rheumatoid arthritis. Arthritis Rheum. 2008;

Study: guidelines	Age ≥ 65: no	Citations: 443 (28/y)	Evidence: IV
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E10 (ii): British National Formulary, No. 81, BMJ Group & Pharm. Press, p958, 2021.

Study: narrative review	Age ≥ 65: no	Citations: N/A	Evidence: N/A
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Section F: Gastrointestinal system

F1. Prochlorperazine or metoclopramide with Parkinsonism

F1 (i): Drug-induced parkinsonism in the elderly. Lancet 1984

Study: case-series	Age ≥ 65: yes	Citations: 38 (1/y)	Evidence: IV
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F1 (ii): Metoclopramide-induced tardive dyskinesia. Arch Intern Med 1993

Study: case-control	Age ≥ 65: yes	Citations: 55 (1.8/y)	Evidence: III b
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F1 (iii): Benefits and risks of metoclopramide. Nat Clin Pract Gastr Hepatol 2006

Study: narrative review	Age ≥ 65: no	Citations: 39 (2/y)	Evidence: V
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F2. PPI full dosage > 8 weeks for uncomplicated peptic ulcer disease or erosive peptic oesophagitis

F2 (i): British National Formulary No. 81, BMJ Group & Pharm. Press, pp 83-88, 2021.

Study: narrative review	Age ≥ 65: no	Citations: N/A	Evidence: N/A
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F2 (ii): NICE guideline (actual reference: CG184, 09/2014, updated 10/2019)			
Study: guidelines	Age ≥ 65: no	Citations: N/A	Evidence: I a
F3. Drugs likely to cause constipation (listed in SS.v3 article) in patients with chronic constipation.			
F3 (i): Overactive bladder drugs and constipation. Dig Dis Sci 2011; 56(1): 7-18.			
Study: meta-analysis	Age ≥ 65: no	Citations: 26 (2/y)	Evidence: I a
F3 (ii): Constipation and faecal incontinence. Best Pract Res Clin Gastroenterol 2002			
Study: narrative review	Age ≥ 65: yes	Citations: 9 (0.4/y)	Evidence: V
F3 (iii): Correlates of regular laxative use by frail elderly persons. Am J Med 1995			
Study: case-control	Age ≥ 65: yes	Citations: 14 (0.5/y)	Evidence III b
F3 (iv): Choosing the correct drug for the individual hypertensive patient. Drugs 1992			
Study: narrative review	Age ≥ 65: no	Citations: 1 (0.03/y)	Evidence: V
F4. Oral elemental iron doses greater than 200 mg daily			
F4 (i): Low-dose iron therapy is effective in octogenarians. Am J Med 2005			
Study: RCT	Age ≥ 65: yes	Citations: 63 (3/y)	Evidence: I b
F4 (ii): British National Formulary No. 81, BMJ Group & Pharm. Press, pp 1065-71, 2021.			
Study: narrative review	Age ≥ 65: no	Citations: N/A	Evidence: N/A
F5. Corticosteroids with a history of peptic ulcer disease or erosive oesophagitis			
F5 (i): Corticosteroids and peptic ulceration. Palliat Med. 1994			
Study: narrative review	Age ≥ 65: no	Citations: 9 (0.3/y)	Evidence: IV
F5 (ii): <i>Corticosteroids and peptic ulcer. J Int Med. 1994</i>			
Study: meta-analysis	Age ≥ 65: no	Citations: 61 (2/y)	Evidence: -
<i>Inappropriate: Mismatch in patients (no history of peptic ulcer disease)</i>			
F6. Antiplatelet or anticoagulant agents with gastric antral vascular ectasia (GAVE)			
F6 (i): <i>Long-term follow-up in patients with GAVE. Endosc Int Open. 2019</i>			
Study: case-series	Age ≥ 65: no	Citations: 9 (1.8/y)	Evidence: -
<i>Inappropriate: No message found on antiplatelet or anticoagulant agents</i>			
F6 (ii): Long-term treatment outcome of patients with GAVE. Eur J Gastr Hepatol 2014			
Study: case-series	Age ≥ 65: yes	Citations: 13 (1.3/y)	Evidence: IV
F7. Antipsychotics with dysphagia			
F7 (i): Factors for aspiration pneumonia in frail older people. J Am Med Dir Assoc. 2011			
Study: systematic review	Age ≥ 65: yes	Citations: 76 (6/y)	Evidence: III b
F7 (ii): Antipsychotic drug use and community-acquired pneumonia. Curr Infect Dis Rep. 2011			
Study: narrative review	Age ≥ 65: no	Citations: 18 (1.4/y)	Evidence: III b
F7 (iii): Antipsychotic drug exposure and risk of pneumonia. Pharmacoepidemiol Drug Saf. 2015			
Study: meta-analysis	Age ≥ 65: no	Citations: 13 (1.6/y)	Evidence: III a
F7 (iv): Antipsychotic medication and oropharyngeal dysphagia. Eur J Gastr Hepatol 2017			
Study: systematic review	Age ≥ 65: no	Citations: 10 (1.4/y)	Evidence: I a
F8. Megestrol acetate to increase appetite			
F8 (i): Deep vein thrombosis as a complication of megestrol therapy. J Am Med Dir Assoc. 2000			
Study: case-series	Age ≥ 65: yes	Citations: 7 (0.9/y)	Evidence: IV
F8 (ii): Is megestrol safe and effective for malnourished NHome residents? J Fam Pract. 2018			
Study: narrative review	Age ≥ 65: yes	Citations: 0 (0.0/y)	Evidence: I b

Section G. Respiratory system

G1. Theophylline as monotherapy for COPD			
G1 (i): Global strategy for COPD: GOLD executive summary. Am J Respir Crit Care Med 2007			
Study: Guidelines	Age ≥ 65: no	Citations: 2855 (168/y)	Evidence: I a
G1 (ii): Use of theophylline in the treatment of COPD. Chest 1995			
Study: narrative review	Age ≥ 65: no	Citations: 5 (0.2/y)	Evidence: V
G2. Systemic corticosteroids instead of inhaled corticosteroids for maintenance in moderate-severe COPD			
G2 (i): Global strategy for COPD: GOLD executive summary. Am J Respir Crit Care Med 2007			
Study: Guidelines	Age ≥ 65: no	Citations: 2855 (168/y)	Evidence: III b
G2 (ii): Systemic corticosteroids in COPD. Respir Med 2007			
Study: systematic review	Age ≥ 65: no	Citations: 4 (0.2/y)	Evidence: I a

- G3. LAMAntagonists with a history of narrow angle glaucoma or bladder outflow obstruction
 G3 (i): *Adverse effects of bronchodilators in older people. Drugs Aging 2008*
 Study: narrative review Age ≥ 65: no Citations: 28 (1.8/y) Evidence: -
Inappropriate: Different message: "no problem for urinary outflow nor intraocular pressure"
 G3 (ii): **Risk benefit analysis of tiotropium in COPD. Int J Chron Obstruct Pulmon Dis 2008**
 Study: narrative review Age ≥ 65: no Citations: 11 (0.7/y) Evidence: IV
- G4. Benzodiazepines with acute or chronic respiratory failure (i.e. $pO_2 < 8.0 \text{ kPa} \pm pCO_2 > 6.5 \text{ kPa}$)
 G4 (i): *Effects of chlorthalidone in respiratory failure due to chronic bronchitis. Lancet 1974*
 Study: case-series Age ≥ 65: no Citations: 9 (0.2/y) Evidence: IV
 G4 (ii): **Prognostic factors of lower respiratory tract infections in the elderly. Fam Pract 2005**
 Study: case-series Age ≥ 65: no Citations: 17 (0.9/y) Evidence: IV

Section H: Musculoskeletal system

- H1. Non-selective NSAIDs in patients with history of peptic ulcer or GI bleeding and no PPI or H2 antagonist
 H1 (i): *Esomeprazole in the prevention of GI toxicity associated with NSAIDs. Drugs Aging 2008*
 Study: narrative review Age ≥ 65: no Citations: 4 (0.3/y) Evidence: IV
 H1 (ii): *Inappropriate prevention of NSAID-induced GI events. Drugs Aging 2007*
 Study: narrative review Age ≥ 65: yes Citations: 23 (1.4/y) Evidence: IV
 H1(iii): **Prevention of NSAID-induced gastroduodenal ulcers. Cochrane 2010**
 Study: meta-analysis Age ≥ 65: no Citations: 113 (8/y) Evidence: I a
- H2. NSAIDs with severe persistent hypertension (sBP > 170 mmHg and/or dBP > 100 mmHg).
 H2 (i): **... Treating the patient with hypertension and arthritis pain.**
 Study: narrative review Age ≥ 65: no Citations: 10 (0.7/y) Evidence: I a
 H2 (ii): *NSAIDs and their effects in the elderly. Aging Health 2012*
 Study: narrative review Age ≥ 65: yes Citations: 0 (0.0/y) Evidence: -
Inappropriate: No message found on hypertension
- H3. NSAIDs >3 months for osteoarthritis pain where paracetamol has not been tried
 H3 (i): **The role of paracetamol in chronic pain. Am J Ther 2005**
 Study: narrative review Age ≥ 65: no Citations: 13 (0.7/y) Evidence: I a
 H3 (ii): *Osteoarthritis: a review of treatment options. Geriatrics 2009*
 Study: narrative review Age ≥ 65: no Citations: 22 (1.5/y) Evidence: V
 H3 (iii): *Analgesics and osteoarthritis: clinical practice. Am J Ther 2005*
 Study: narrative review Age ≥ 65: no Citations: 13 (0.7/y) Evidence: V
- H4. Corticosteroids >3 months as monotherapy for rheumatoid arthritis
 H4 (i): *Management of elderly-onset rheumatoid arthritis. J Clin Immunol 2010*
 Study: narrative review Age ≥ 65: yes Citations: 1 (0.1/y) Evidence: V
 H4 (ii): **Guidelines for the management of rheumatoid arthritis. Arthritis Rheum 2002**
 Study: guidelines Age ≥ 65: no Citations: 302 (14/y) Evidence: I a
 H4 (iii): *Elderly-onset rheumatoid arthritis. Joint Bone Spine 2010*
 Study: narrative review Age ≥ 65: yes Citations: 20 (1.4/y) Evidence: I a
- H5. Corticosteroids for osteoarthritis (other than periodic intra-articular injections for mono-articular pain).
 H5 (i): *British National Formulary No. 81, BMJ Group & Pharm Press, p1140, 2021*
 Study: narrative review Age ≥ 65: no Citations: N/A Evidence: N/A
 H5 (ii): *Medical management of osteoarthritis of the hip and knee. Arthritis Rheum 2000*
 Study: guidelines Age ≥ 65: no Citations: 526 (22/y) Evidence: -
Inappropriate: No message found on systemic steroid therapy
- H6. NSAID or colchicine >3 months for gout relapses where no contraindication to xanthine-oxidase inhibitor
 H6 (i): **Elderly-onset gout. Rheumatol Int 2007**
 Study: narrative review Age ≥ 65: yes Citations: 14 (0.8/y) Evidence: I a
 H6 (ii): *Management of gout in older adults. Drugs Aging 2007*
 Study: narrative review Age ≥ 65: yes Citations: 13 (0.8/y) Evidence: V
- H7. NSAID with concurrent corticosteroids for treatment of arthritis/rheumatism of any kind
 H7 (i): *Gastrointestinal adverse effects of NSAIDs. Expert Opin Drug Saf 2005*
 Study: narrative review Age ≥ 65: no Citations: 13 (0.7/y) Evidence: V

- H7 (ii): **Bleeding peptic ulcer in the elderly. Drugs Aging 2007**
Study: narrative review **Age ≥ 65: yes** **Citations: 32 (2/y)** **Evidence: IV**
- H7 (iii): NSAID-induced peptic ulcer disease. Dig Dis 1994; 12(4): 210-22.
Study: narrative review Age ≥ 65: no Citations: 4 (0.1/y) Evidence: V
- H8. Oral bisphosphonates with upper GI disease (dysphagia, oesophagitis, gastritis, peptic ulcer, GI bleeding)
H8 (i): **Safety of bisphosphonates. Bone 2011**
Study: narrative review **Age ≥ 65: no** **Citations: 46 (4/y)** **Evidence: II b**
- H8 (ii): *Use of intravenous bisphosphonates in osteoporosis. Curr Osteoporos Rep 2007*
Study: narrative review Age ≥ 65: no Citations: 6 (0.4/y) Evidence:-
Inappropriate: mismatch in drug route (intravenous, and not oral)
- H8 (iii): Management of severe postmenopausal osteoporosis. Drugs Aging 2005
Study: narrative review Age ≥ 65: yes Citations: 1 (0.1/y) Evidence: V
- H9. Long-term opioids for osteoarthritis
H9 (i): Opioids for chronic osteoarthritis pain. Eur J Pain. 2020
Study: systematic review Age ≥ 65: no Citations: 16 (4/y) Evidence: I a
- H9 (ii): *Long-term opioid therapy in chronic non-cancer pain. Eur J Pain. 2020*
Study: meta-analysis Age ≥ 65: no Citations: 28 (7/y) Evidence: X
Inappropriate: different message ("can be considered in selected patients")
- H9 (iii): **Opioids for osteoarthritis of the knee or hip. Cochrane Database Syst Rev. 2014**
Study: meta-analysis **Age ≥ 65: no** **Citations: 77 (8/y)** **Evidence: I a**

Section I: Urogenital system

11. Systemic antimuscarinic drugs in patients with dementia or chronic cognitive impairment
11 (i): Antimuscarinic drugs: cognitive impact in elderly with overactive bladder. Curr Urol Rep 2011
Study: narrative review Age ≥ 65: yes Citations: 25 (2/y) Evidence: V
- 11 (ii): **Antimuscarinic drugs for overactive bladder: cognitive effects. JAGS 2005**
Study: narrative review **Age ≥ 65: yes** **Citations: 58 (3.1/y)** **Evidence: IV**
12. Systemic antimuscarinic drugs in patients with narrow-angle glaucoma
12 (i): *Anticholinergic Medication in Open-Angle Glaucoma. Arch Ophthalmol. 1970*
Study: cohort Age ≥ 65: no Citations: 2 (0.04/y) Evidence: -
Inappropriate: Mismatch in condition (open- and not narrow-angle glaucoma)
- 12 (ii): British National Formulary, No. 81, BMJ Group & Pharm Press, p1223-24, 2021.
Study: narrative review Age ≥ 65: N/A Citations: N/A Evidence: N/A
13. Systemic antimuscarinic drugs with LUTSymptoms due to BPH and post-void residual volume > 200 ml
13 (i): Managing Nocturia in Frail Older Adults. Drugs Aging 2021
Study: narrative review Age ≥ 65: yes Citations: 4 (1.3/y) Evidence: V
- 13 (ii): **Oral drug therapies for LUTS due to BPHyperplasia. PLoS One 2014**
Study: meta-analysis **Age ≥ 65: yes** **Citations: 21 (2/y)** **Evidence: V**
- 13 (iii): Antimuscarinics in men with LUTSymptoms. Curr Opin Urol. 2010
Study: narrative review Age ≥ 65: yes Citations: 9 (0.6/y) Evidence: V
14. Systemic antimuscarinic drugs with constipation
14 (i): **Antimuscarinics for overactive bladder: adverse events. Drugs Aging 2019**
Study: meta-analysis **Age ≥ 65: yes** **Citations: 4 (0.8/y)** **Evidence: I a**
15. Alpha-1 receptor antagonists (other than silodosin) with orthostatic hypotension or history of syncope
15 (i): Newer alpha, -adrenergic-receptor antagonists for BPH-related LUTSymptoms. Clin Ther 2004
Study: narrative review Age ≥ 65: yes Citations: 22 (1/y) Evidence: V
- 15 (ii): **Silodosin for the treatment of benign prostatic hyperplasia. Clin Interv Aging. 2011**
Study: narrative review **Age ≥ 65: no** **Citations: 10 (0.8/y)** **Evidence: I b**
16. Mirabegron in labile or severe hypertension
16 (i): *Mirabegron: a review of recent data. Ther Adv Urol 2012*
Study: narrative review Age ≥ 65: yes Citations: 42 (4/y) Evidence: -
Inappropriate: Different message: "side effects similar to antimuscarinics"
- 16 (ii): *Mirabegron for the treatment of overactive bladder. Int J Clin Pract. 2013*

- Study: meta-analysis* *Age ≥ 65: no* *Citations: 66 (6/y)* *Evidence:-*
Inappropriate: Different message: "efficacy and safety", based on 3 RCTs
17. Duloxetine with urinary urgency or urge incontinence
 17 (i): *Duloxetine versus placebo in women with stress urinary incontinence. BJOG 2004*
Study: RCT *Age ≥ 65: no* *Citations: 55 (3/y)* *Evidence: -*
Inappropriate: Mismatch in medical condition (stress and not urge incontinence)
 17 (ii): *Duloxetine vs placebo in stress urinary incontinence. Am J Obs Gynecol 2002*
Study: RCT *Age ≥ 65: no* *Citations: 73 (3/y)* *Evidence: -*
Inappropriate: Mismatch in medical condition (stress and not urge incontinence)
18. Antibiotic use in asymptomatic bacteriuria
 18 (i): *Urinary tract infection and asymptomatic bacteriuria in older adults. Inf Dis Clin North Am. 2017*
Study: narrative review *Age ≥ 65: yes* *Citations: 59 (8/y)* *Evidence: V*
 18 (ii): **Diagnosis and treatment of asymptomatic bacteriuria in adults. Clin Inf. Dis. 2005**
Study: guidelines **Age ≥ 65: yes** **Citations: 408 (21/y)** **Evidence: I a**

Section J: Endocrine system

- J1. Sulphonylureas with a long half-life for type 2 diabetes
 J1(i): **Hypoglycemic safety of gliclazide. Diabetes Res Clin Pract. 2015**
Study: meta-analysis **Age ≥ 65: no** **Citations: 24 (3/y)** **Evidence: I a**
 J1 (ii): *The use of sulphonylureas in the elderly. Drugs Aging 1999*
Study: narrative review *Age ≥ 65: yes* *Citations: 61 (2/y)* *Evidence: V*
 J1 (iii): *Glimepiride in the management of type 2 diabetes mellitus. Drugs 1998*
Study: narrative review *Age ≥ 65: no* *Citations: 23 (0.9/y)* *Evidence: V*
- J2. Thiazolidinediones in patients with heart failure
 J2 (i) *Noninsulin treatment of type 2 diabetes in geriatric patients. Clin Ther 2011*
Study: cohort *Age ≥ 65: yes* *Citations: 12 (0.9/y)* *Evidence: I a*
 J2 (ii): **Congestive heart failure and CV death with thiazolidinediones. Lancet 2007**
Study: RCT **Age ≥ 65: yes** **Citations: 235 (14/y)** **Evidence: I a**
- J3. Non-selective beta-blockers in diabetes mellitus with frequent hypoglycaemic episodes
 J3 (i): **Hypoglycaemia in elderly patients with diabetes mellitus. Drugs Aging 2004**
Study: narrative review **Age ≥ 65: yes** **Citations: 40 (2/y)** **Evidence: V**
 J3 (ii): *Hypoglycaemia from a cardiologist's perspective. Clin Cardiol. 2014*
Study: narrative review *Age ≥ 65: no* *Citations: 17 (1.7/y)* *Evidence: V*
- J4. SGLT2 inhibitors with symptomatic hypotension
 J4 (i): **Effects of SGLT2 inhibitors on blood pressure. J Am Soc Hypertens. 2014**
Study: meta-analysis **Age ≥ 65: yes** **Citations: 167 (17/y)** **Evidence: I a**
 J4 (ii): *Blood pressure effects of SGLT2 inhibitors. J Am Soc Hypertens. 2014*
Study: narrative review *Age ≥ 65: no* *Citations: 85 (9/y)* *Evidence: I a*
- J5. Systemic oestrogens with a history of breast cancer
 J5 (i): **Postmenopausal hormone use and breast cancer. Cancer 2009**
Study: cohort **Age ≥ 65: no** **Citations: 25 (1.7/y)** **Evidence: II b**
 J5 (ii): *... estrogen plus progestin and risk of breast cancer. Cancer Epid. Bio. Prev 2008*
Study: case-control *Age ≥ 65: no* *Citations: 26 (1.6/y)* *Evidence: III b*
- J6. Systemic oestrogens with a history of venous thromboembolism (VTE)
 J6 (i): *Estradiol and risk of VTE. Thromb Haemost. 1999*
Study: case-control *Age ≥ 65: no* *Citations: 12 (0.5/y)* *Evidence: III b*
 J6 (ii): *Hormone therapy and VTE among postmenopausal women. Circulation. 2007*
Study: case-control *Age ≥ 65: yes* *Citations: 130 (8/y)* *Evidence: III b*
 J6 (iii): **Increased risk of recurrent VTE during HRT therapy. Thromb Haem. 2000**
Study: RCT **Age ≥ 65: no** **Citations 30 (1.3/y)** **Evidence I b**
- J7: Oestrogen plus progestin with a history of stenotic coronary, cerebral or peripheral arterial disease
 J7 (i): *... estrogen plus progestin in postmenopausal women. JAMA 2002*
Study: RCT *Age ≥ 65: no* *Citations 3510 (159/y)* *Evidence I b*
 J7 (ii): **... postmenopausal hormone therapy and CV outcomes. Hum Reprod Update 2019**

	Study: systematic review	Age ≥ 65: no	Citations: 28 (6/y)	Evidence: I a
J8. Systemic oestrogens without progestogens in women with intact uterus				
J8 (i): Postmenopausal hormone replacement therapy... Am J Manag Care 2002				
Study: narrative review	Age ≥ 65: no	Citations: 2 (0.1/y)	Evidence: II a	
J8 (ii): Hormone therapy in postmenopause and endometrial hyperplasia. Cochrane Syst Rev 2012				
Study: systematic review	Age ≥ 65: no	Citations: 42 (4/y)	Evidence: I a	
J8 (iii): Hormone therapy for peri- and postmenopausal women. Cochrane Syst Rev 2012				
Study: meta-analysis	Age ≥ 65: yes	Citations: 82 (7/y)	Evidence: I a	
J9. Levothyroxine in subclinical hypothyroidism (normal free T4, elevated TSH but < 10 mU/L)				
J9 (i): Thyroid hormone therapy for older adults with subclinical hypothyroidism. N Engl J Med 2017				
Study: RCT	Age ≥ 65: no	Citations: 137 (20/y)	Evidence: I b	
J9 (ii): Levothyroxine in older patients with subclinical hypothyroidism. Front Endocrinol 2022				
Study: meta-analysis	Age ≥ 65: yes	Citations: 7 (4/y)	Evidence: II a	
J10. Vasopressin analogues for urinary incontinence or urinary frequency				
J10 (i): The risk of hyponatremia with desmopressin for nocturnal polyuria. Am J Nephrol. 2015				
Study: narrative review	Age ≥ 65: yes	Citations: 8 (0.9/y)	Evidence: II b	
J10 (ii): Low dose oral desmopressin for nocturnal polyuria in BPHyperplasia. J Urol. 2011.				
Study: RCT	Age ≥ 65: no	Citations: 14 (1/y)	Evidence: I b	

Section K: Drugs that predictably increase the risk of falls in older people

K1. Benzodiazepines in patients with recurrent falls				
K1 (i): Medication-related falls in the elderly. Drugs Aging 2012				
Study: narrative review	Age ≥ 65: yes	Citations: 128 (4/y)	Evidence: V	
K1 (ii): Impact of 9 medication classes on falls in elderly persons. Arch Int Med 2009				
Study: cohort	Age ≥ 65: yes	Citations: 439 (31/y)	Evidence: II a	
K2. Antipsychotic drugs in patients with recurrent falls				
K2 (i): Psychotropic drug-induced falls in older people. Drugs Aging 2012				
Study: narrative review	Age ≥ 65: no	Citations: 51 (4/y)	Evidence: I a	
K2 (ii): Impact of 9 medication classes on falls in elderly persons. Arch Int Med 2009				
Study: narrative review	Age ≥ 65: yes	Citations: 439 (31/y)	Evidence: II a	
K3. Vasodilator drugs with recurrent falls and persistent postural hypotension				
K3 (i): Treating hypertension in older adults: safety considerations. Drug Saf 2009				
Study: narrative review	Age ≥ 65: yes	Citations: 13 (0.9/y)	Evidence: V	
K3 (ii): <i>Drug-induced orthostatic hypotension in the elderly. Drug Saf 1997</i>				
Study: narrative review	Age ≥ 65: yes	Citations: 21 (0.8/y)	Evidence: -	
<i>Inappropriate: different message: "not with amlodipine nor IEC inhibitors" (p. 111)</i>				
K4. Hypnotic Z-drugs (i.e., zopiclone, zolpidem, zaleplon) with recurrent falls				
K4 (i): Effect of hypnotic drugs on body balance and standing steadiness. Sleep Med Rev 2010				
Study: narrative review	Age ≥ 65: yes	Citations: 28 (2/y)	Evidence: I a	
K4 (ii): Medication use as a risk factor for inpatient falls. Br J Clin Pharm 2010				
Study: case-control	Age ≥ 65: yes	Citations: 26 (1.9/y)	Evidence: III b	
K5. Anti-epileptic drugs in patients with recurrent falls				
K5 (i): Use of antiepileptic drugs and risk of falls in old age. Epilepsy Res. 2017				
Study: narrative review	Age ≥ 65: yes	Citations: 7 (1.0/y)	Evidence: II b	
K5 (ii): Delphi study on fall-risk-increasing drugs. Age Ageing 2021				
Study: narrative review	Age ≥ 65: yes	Citations: 49 (16/y)	Evidence: II b	
K6. First generation antihistamines in patients with recurrent falls				
K6 (i): Antihistamine use and injurious falls or fracture in elderly patients. Osteoporos Int. 2018				
Study: narrative review	Age ≥ 65: yes	Citations: 9 (1.5/y)	Evidence: II b	
K6 (ii): Delphi study on fall-risk-increasing drugs. Age Ageing. 2021				
Study: cohorts	Age ≥ 65: yes	Citations: 49 (16/y)	Evidence: II b	
K7. Opioids in patients with recurrent falls				
K7 (i): Opioid use and the risk of falls and fractures in older adults. J Ger A Biol Sci Med Sci. 2020				
Study: systematic review	Age ≥ 65: no	Citations: 41 (10/y)	Evidence: II a	

- K7 (ii): **Fall-Risk-Increasing Drugs: a systematic review and meta-analysis. JAMDA 2018**
Study: survey **Age ≥ 65: yes** **Citations: 94 (16/y)** **Evidence: I a**
- K8. Antidepressants in patients with recurrent falls
- K8 (i): **Fall Risk-Increasing Drugs around a fall-related injury in older adults. JAGS 2020**
Study: meta-analysis **Age ≥ 65: yes** **Citations: 26 (7/y)** **Evidence: II a**
- K8 (ii): **Medication as a risk factor for falls. J Ger A Biol Sci Med Sci. 2007**
Study: systematic review **Age ≥ 65: yes** **Citations: 175 (10/y)** **Evidence: II a**
- K8 (iii): **Drugs and falls in older people: psychotropic drugs. JAGS 1999**
Study: meta-analysis **Age ≥ 65: yes** **Citations: 295 (12/y)** **Evidence: II a**
- K9. Alpha blockers as antihypertensives in patients with recurrent falls
- K9 (i): **Drug-induced orthostatic hypotension in the elderly: avoiding its onset. Drug Saf. 1997**
Study: meta-analysis **Age ≥ 65: yes** **Citations: 21 (0.8/y)** **Evidence: IV**
- K9 (ii): **Adrenergic alpha-1 receptor antagonists in older adults. BMC Geria. 2022**
Study: systematic review **Age ≥ 65: yes** **Citations: 7 (3.5/y)** **Evidence: I a**
- K10. Alpha blockers (other than silodosin) for prostatic bladder outflow symptoms, with recurrent falls
- K10 (i): *Alpha blockers for the treatment of benign prostatic hyperplasia. Rev Urol. 2007*
Study: systematic review **Age ≥ 65: yes** **Citations: 58 (3/y)** **Evidence: -**
Inappropriate: No message found on risk of falls
- K10 (ii): **Fall risk related to subtype-specific alpha-antagonists for BPHyperplasia. World J Urol. 2022**
Study: meta-analysis **Age ≥ 65: yes** **Citations: 0 (0/y)** **Evidence: II b**
- K11. Centrally acting antihypertensives
- K11 (i). **Hypertension. In: Brocklehurst's Textbook of Geriatric Medicine & Gerontology, p403, 2003**
Study: narrative review **Age ≥ 65: yes** **Citations: N/A** **Evidence: V**
- K11 (ii). **Hypertension. In: Prescribing for Elderly Patients, pp97-98, 2009**
Study: meta-analysis **Age ≥ 65: yes** **Citations: N/A** **Evidence: V**
- K12. Antimuscarinics for treatment of overactive bladder or urge incontinence
- K12 (i): **Antimuscarinic agents in the management of overactive bladder in the elderly. Clin Ther 2005**
Study: narrative review **Age ≥ 65: yes** **Citations: 23 (1.2/y)** **Evidence: V**
- K12 (ii): **The problems of anticholinergic adverse effects in older patients. Drugs Aging 1993**
Study: narrative review **Age ≥ 65: yes** **Citations: 86 (3/y)** **Evidence: V**

Section L: Analgesic drugs

- L1. Use of oral or transdermal strong opioids (listed in SS.v3 article) as first line therapy for mild pain
- L1 (i): **Cancer pain relief. Guide to opioid availability, Geneva 1996: WHO. ISBN 92-4-154482-1.**
Study: narrative review **Age ≥ 65: no** **Citations: N/A** **Evidence: V**
- L1 (ii): *Pharmacological treatment of persisting pain in adults, Geneva 2012, GRC-08-04-0052A.*
Study: systematic review **Age ≥ 65: no** **Citations: N/A** **Evidence: -**
Inappropriate: Mismatch in patients (children, not older adults)
- L2. Use of regular (as distinct from PRN) opioids without concomitant laxative.
- L2 (i): **Opioid analgesic drugs in the elderly. Clin Ger Med 1996.**
Study: narrative review **Age ≥ 65: yes** **Citations: 12 (0.4/y)** **Evidence: V**
- L2 (ii): **Opioids in chronic non-cancer pain: efficacy and safety. Pain 2004**
Study: narrative review **Age ≥ 65: no** **Citations: 357 (18/y)** **Evidence: II a**
- L3. Long-acting opioids without short-acting opioids for break-through moderate or severe pain
- L3 (i): *Adverse drug interactions with NSAIDs. Drug Saf 1993*
Study: narrative review **Age ≥ 65: no** **Citations: 9 (0.3/y)** **Evidence: -**
Inappropriate: Mismatch in medication (NSAIDs and not opioids)
- L3 (ii): *Bleeding peptic ulcer in the elderly. Drugs Aging 2007*
Study: narrative review **Age ≥ 65: yes** **Citations: 32 (2/y)** **Evidence: -**
Inappropriate: Mismatch in medication (NSAIDs and not opioids)
- L3 (iii): *Gastrointestinal adverse effects of NSAIDs. Expert Opin Drug Saf 2005*
Study: systematic review **Age ≥ 65: no** **Citations: 13 (0.7/y)** **Evidence: -**
Inappropriate: Mismatch in medication (NSAIDs and not opioids)
- L3 (iv): *Prevention of NSAID-associated gastrointestinal complications. Am J Med 2004*

- Study: narrative review* *Age ≥ 65: no* *Citations: 11 (0.6/y)* *Evidence: -*
Inappropriate: Mismatch in medication (NSAIDs and not opioids)
- L4. Topical lidocaine (lignocaine) patch for treatment of chronic osteoarthritis pain
L4 (i): **Topical lidocaine for chronic pain treatment. Drug Des Devel Ther 2021.**
Study: narrative review **Age ≥ 65: no** **Citations: 3 (14.0/y)** **Evidence: V**
L4 (ii): *Algorithm for the management of knee osteoarthritis. Sem Arthritis Rheum 2016*
Study: narrative review *Age ≥ 65: no* *Citations: 79 (10/y)* *Evidence: -*
Inappropriate: No message found on topical lignocaine
- L5. Gabapentinoids (e.g., gabapentin, pregabalin) for non-neuropathic pain.
L5 (i): **Pregabalin and gabapentin for pain. BMJ. 2020**
Study: narrative review **Age ≥ 65: no** **Citations: 30 (8/y)** **Evidence: I a**
L5 (ii): *Gabapentin and pregabalin for pain - increased prescribing. N Engl J Med 2017*
Study: narrative review *Age ≥ 65: no* *Citations: 109 (16/y)* *Evidence: V*
- L6. Paracetamol ≥ 3 g/24 h in patients with poor nutritional status (BMI < 18) or chronic liver disease.
L6 (i): *Paracetamol dosing in older people with frailty or low body weight. Br J Clin Pharm 2022*
Study: narrative review *Age ≥ 65: yes* *Citations: 3 (1.5/y)* *Evidence: V*
L6 (ii): **Adverse effects of analgesics in older adults with osteoarthritis. Am J Ger. Pharma. 2012**
Study: narrative review **Age ≥ 65: yes** **Citations: 95 (8/y)** **Evidence: IV**

Section M: Antimuscarinic/anticholinergic drug burden

- M1: Concomitant use of two or more drugs with antimuscarinic/anticholinergic properties
M1 (i): *The problems of anticholinergic adverse effects in older patients. Drugs Aging 1993*
Study: narrative review *Age ≥ 65: yes* *Citations: 88 (3/y)* *Evidence: V*
M1 (ii): **Drugs with anticholinergic properties. Expert Opin Drug Saf 2011**
Study: narrative review **Age ≥ 65: yes** **Citations: 58 (5/y)** **Evidence: V**
M1 (iii): *Anticholinergic burden: clinical implications. Consult Pharm 2012*
Study: narrative review *Age ≥ 65: yes* *Citations: 8 (0.7/y)* *Evidence: V*

Appendix. B) START.v3: appraisal of the 160 references supporting the 57 criteria

in **bold** characters: the reference with the best evidence level.

in *italic*: the 13 references considered as inappropriate (Evidence: -), and the reason.

For full references, see file 2 (docx. 163 KB): [STOPP/START criteria for potentially inappropriate prescribing in older people: version 3 | European Geriatric Medicine](#)

Section A: Indicated drugs

A1. Where a drug is clearly indicated and considered appropriate in the particular clinical context and there is no clear contraindication, that drug should be initiated as per formulary guidelines for dose and duration.

A1: No reference. Self-evident.

Section B: Cardiovascular system

B1. Antihypertensive therapy where systolic BP > 140 mmHg and/or diastolic BP > 90 mmHg, unless moderate or severe physical frailty in whom the threshold is 150 mmHg sBP and/or 90 mmHg dBP

B1 (i): Management of hypertension in the elderly and frail elderly. High Blood Press CV Prev. 2017

Study: narrative review	Age ≥ 65: yes	Citations: 13 (1.9/yr)	Evidence: V
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B1 (ii): Management of hypertension in very old, frail subjects. Hypertension 2016

Study: narrative review	Age ≥ 65: yes	Citations: 51 (6/yr)	Evidence: V
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B1 (iii): **Blood pressure control and CV outcomes in adults ≥ 75 years (SPRINT). JAMA 2016**

Study: 1 RCT	Age ≥ 65: yes	Citations 419 (52/yr)	Evidence I b
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B1 (iv): Pharmacological treatment of hypertension in frail older patients. Dtsch Arztebl Int. 2019

Study: Systematic review	Age ≥ 65: yes	Citations: 14 (3/yr)	Evidence: V
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~~B1 (v): duplication of B1 (iv)~~

B2. Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, unless the patient's status is end-of-life or established moderate or severe frailty.

B2 (i): Statin for cardiovascular disease. QJM 2011

Study: meta-analysis	Age ≥ 65: no	Citations: 88 (67/yr)	Evidence: I a
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B2 (ii): *Statins in people without CVDisease but with CV risk factors. BMJ 2009*

<i>Study: meta-analysis</i>	<i>Age ≥ 65: yes</i>	<i>Citations: 254 (17/yr)</i>	<i>Evidence: -</i>
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Inappropriate: Mismatch in the patients (primary and not secondary CV prevention)

B2 (iii): **Lipid management in the prevention of stroke: statins. Lancet Neurol 2009**

Study: meta-analysis	Age ≥ 65: no	Citations: 187 (13/yr)	Evidence: I a
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B2 (iv): *Statins for prevention of cardiovascular disease in adults. JAMA 2016*

<i>Study: meta-analysis</i>	<i>Age ≥ 65: no</i>	<i>Citations: 219 (27/yr)</i>	<i>Evidence: -</i>
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Inappropriate: Mismatch in the patients (primary and not secondary CV prevention)

B3. Angiotensin Converting Enzyme Inhibitor (ACE-I) with coronary artery disease (CAD).

B3 (i): **ACE- I in stable vascular disease without LV systolic dysfunction. Lancet 2006**

Study: meta-analysis	Age ≥ 65: no	Citations: 85 (5/yr)	Evidence: I a
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B3 (ii): ACE-I in CAD in patients without heart failure or LV systolic dysfunction. Arch Int Med 2006

Study: meta-analysis	Age ≥ 65: no	Citations: 29 (1.9/yr)	Evidence: I a
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B3 (iii): ACE-inhibitors or ARB in normotensive atherosclerotic patients. Eur Heart J 2012

Study: meta-analysis	Age ≥ 65: yes	Citations: 20 (1.7 /yr)	Evidence: I a
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B4. Beta-blocker with symptomatic coronary artery disease (CAD)

B4 (i): *β-Blocker use in stable outpatients with and without CAD. JAMA. 2012*

<i>Study: cohort</i>	<i>Age ≥ 65: yes</i>	<i>Citations: 118 (9.8/yr)</i>	<i>Evidence: -</i>
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Inappropriate: No message found on symptoms of CAD

B4 (ii): Current use of beta-blockers in patients with CAD. Trends CV. Med. 2018

Study: narrative review	Age ≥ 65: yes	Citations: 5 (0.8/yr)	Evidence: I a
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B4 (iii): Beta-blockade after myocardial infarction. BMJ. 1999

Study: meta-analysis	Age ≥ 65: yes	Citations: 286 (11.4/yr)	Evidence: I a
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B5: Angiotensin Converting Enzyme (ACE) inhibitor for heart failure with reduced ejection fraction (HFrEF)

B5 (i): Enalapril and mortality in asymptomatic reduced ejection fractions. N Engl J Med 1992.

Study: 1 RCT	Age ≥ 65: no	Citations: 659 (5.6/yr)	Evidence: I b
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B5 (ii): A comparison of enalapril with hydralazine in chronic CHF failure. N Engl J Med 1991	Study: 1 RCT	Age ≥ 65: no	Citations: 435 (13.2/yr)	Evidence: I b
B5 (iii): Effects of enalapril on mortality in severe congestive heart failure. N Engl J Med 1987	Study: 1 RCT	Age ≥ 65: no	Citations: 1024 (27.7/yr)	Evidence: I b
B5 (iv): Enalapril and survival in reduced left LV ejection fraction and CHF. N Engl J Med 1991	Study: 1 RCT	Age ≥ 65: no	Citations: 1305 (39.5/yr)	Evidence: I b
B5 (v): ACE-inhibitor therapy in heart failure or left-ventricular dysfunction. Lancet 2000	Study: systematic review	Age ≥ 65: no	Citations: 34 (3.9/yr)	Evidence: I a
B6. Cardioselective beta-blocker for stable heart failure with reduced ejection fraction (HFrEF)				
B6 (i): Carvedilol and morbidity-mortality in chronic heart failure. N Engl J Med 1996.	Study: 1 RCT	Age ≥ 65: no	Citations: 853 (30/yr)	Evidence: Ib
B6 (ii): Bisoprolol for the treatment of chronic heart failure. Am Heart J 2002.	Study: meta-analysis (2RCTs)	Age ≥ 65: no	Citations: 17 (0.8/yr)	Evidence: I b
B6 (iii): Beta-blockers in congestive heart failure. Ann Intern Med 2001.	Study: meta-analysis	Age ≥ 65: no	Citations: 90 (4/yr)	Evidence: Ia
B7. Mineralocorticoid receptor antagonist in heart failure without severe renal failure (eGFR > 30)				
B7 (i): Eplerenone in patients with systolic heart failure and mild symptoms. N Engl J Med 2011.	Study: 1 RCT	Age ≥ 65: no	Citations: 806 (62/yr)	Evidence: I b
B7 (ii): Spironolactone and morbidity/mortality in severe heart failure. N Engl J Med 1999	Study: 1 RCT	Age ≥ 65: no	Citations: 2016 (81/yr)	Evidence I b
B8. SGLT-2 inhibitor in symptomatic heart failure with or without reduced ejection fraction.				
B8 (i): Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. N Engl J Med 2019.	Study: 1 RCT	Age ≥ 65: yes	Citations: 1954 (391/yr)	Evidence: I b
B8 (ii): Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. N Engl J Med 2020.	Study: 1 RCT	Age ≥ 65: yes	Citations: 1421 (355/yr)	Evidence: I b
B8 (iii): SGLT2 inhibitors in patients with heart failure with reduced ejection fraction. Lancet 2020.	Study: M-A (2 RCTs)	Age ≥ 65: yes	Citations: 385 (96/yr)	Evidence: I b
B8 (iv): ACC/AHA/HFSA guideline for the management of heart failure. AJMC 2022	Study: Guideline	Age ≥ 65: no	Citations: 352 (176/yr)	Evidence I a
B9. Sacubitril/valsartan in heart failure with reduced ejection fraction causing persistent heart failure ...				
B9 (i): Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med 2014	Study: 1 RCT	Age ≥ 65: yes	Citations: 2011 (201/yr)	Evidence I b
B9 (ii): Angiotensin-neprilysin inh. compared with enalapril on death in heart failure. Eur Heart J 2015.	Study: 1 RCT	Age ≥ 65: no	Citations: 135 (15/yr)	Evidence: I b
B9 (iii): Sacubitril/Valsartan and readmission after heart failure hospitalization. J Am Coll Card 2016.	Study: 1 RCT	Age ≥ 65: no	Citations: 41 (5/yr)	Evidence: I b
B10. Beta-blocker for chronic atrial fibrillation (AF) with uncontrolled heart rate.				
B10 (i): 2020 ESC Guidelines for diagnosis and management of AF. Eur Heart J 2021	Study: guidelines	Age ≥ 65: no	Citations: 3190 (798/yr)	Evidence I a
B10 (ii): <i>β-blockers and risk of all-cause mortality in heart failure and AF. BMC CV Dis 2019</i>	<i>Study: meta-analysis</i>	<i>Age ≥ 65: yes</i>	<i>Citations: 4 (0.8/yr)</i>	<i>Evidence: -</i>
	<i>Inappropriate: No message found on uncontrolled heart rate</i>			
B11. Intravenous iron for symptomatic heart failure (HF) with reduced ejection fraction and iron deficiency.				
B11 (i): Ferric carboxymaltose in HF and iron deficiency. N Engl J Med 2009	Study: 1 RCT	Age ≥ 65: yes	Citations: 612 (41/yr)	Evidence I b
B11 (ii): Ferric carboxymaltose for iron deficiency at discharge after acute HF. Lancet. 2020	Study: 1 RCT	Age ≥ 65: yes	Citations: 212 (53/yr)	Evidence I b

Section C: Coagulation system

C1. Anticoagulant (Vitamin K antagonists or DOACs) in the presence of atrial fibrillation (AF).				
C1 (i): <i>Stroke and thromboembolism in AF: risk and cost-effectiveness. Thromb Haem 2008</i>	<i>Study: systematic review</i>	<i>Age ≥ 65: yes</i>	<i>Citations: 78 (5/yr)</i>	<i>Evidence: -</i>
	<i>Inappropriate: No message found on anticoagulant therapy</i>			
C1 (ii): Efficacy and safety of the novel oral anticoagulants in AF. Circulation 2012				

	Study: meta-analysis	Age ≥ 65: yes	Citations: 121 (10/yr)	Evidence: I a
C1 (iii):	Antithrombotic therapy to prevent stroke in AF. Ann Int Med 2007			
	Study: meta-analysis	Age ≥ 65: yes	Citations 1383(81/yr)	Evidence: I a
C1 (iv):	Oral anticoagulants for preventing first stroke in AF. Cochrane D S Rev 2005			
	Study: meta-analysis	Age ≥ 65: yes	Citations: 63 (4/yr)	Evidence: I a
C2.	Antiplatelet therapy with a documented history of coronary, cerebral or peripheral vascular disease			
C2 (i):	... outcomes after acute myocardial infarction in older adults. J Am Ger Soc 2012			
	Study: register	Age ≥ 65: yes	Citations: 9 (0.8/yr)	Evidence: IV
C2 (ii):	Antithrombotic therapy in peripheral artery disease. Chest 2012			
	Study: guidelines	Age ≥ 65: no	Citations: 62 (5/yr)	Evidence: I a
C2 (iii):	Cardiovascular drug therapy in the elderly. Nat Rev Cardiol 2011			
	Study: narrative review	Age ≥ 65: yes	Citations: 58 (5/yr)	Evidence: V
C2 (iv):	Primary and secondary prevention of cardiovascular disease. Chest 2012			
	Study: guidelines	Age ≥ 65: yes	Citations: 143 (12/yr)	Evidence: Ia

Section D: Central nervous system

D1.	L-DOPA or dopamine agonist in idiopathic Parkinson's disease with impairment and resultant disability.			
D1 (i):	Parkinson's disease. Update in management. Geriatrics 2001			
	Study: narrative review	Age ≥ 65: yes	Citations: 2 (0.1/yr)	Evidence: V
D1 (ii):	Parkinson's disease. Strategies to improve patient function and quality of life. Geriatrics 2002			
	Study: narrative review	Age ≥ 65: yes	Citations: 0 (0/yr)	Evidence: V
D2.	Non-TCA antidepressant drug for major depression.			
D2(i):	Diagnosis and treatment of depression in late life. Consensus statement update. JAMA 1997			
	Study: narrative review	Age ≥ 65: yes	Citations: 147 (5/yr)	Evidence V
D2(ii):	Antidepressants for depressed elderly. Cochrane Syst Rev 2006			
	Study: meta-analysis	Age ≥ 65: yes	Citations: 64 (4/yr)	Evidence: I a
D3.	Acetylcholinesterase inhibitor (donepezil, rivastigmine, galantamine) for mild-moderate Alzheimer's dementia.			
D3(i):	Cholinesterase inhibitors and memantine for treating dementia. Ann Intern Med 2008			
	Study: guideline	Age ≥ 65: no	Citations 242 (15/yr)	Evidence: I a
D3(ii):	Cholinesterase inhibitors for Alzheimer's disease. Cochrane Syst Rev 2006			
	Study: meta-analysis	Age ≥ 65: yes	Citations 619 (77/yr)	Evidence: I a
D4.	Rivastigmine for dementia with Lewy bodies or Parkinson's disease dementia.			
D4 (i):	Cholinesterase inhibitors for Lewy bodies, Parkinson's dementia... Cochrane Syst Rev 2012			
	Study: meta-analysis	Age ≥ 65: yes	Citations 120 (12/yr)	Evidence: I a
D4 (ii):	Use of Cholinesterase Inhibitors in Non-Alzheimer's Dementias. Drugs Aging. 2019			
	Study: narrative review	Age ≥ 65: no	Citations: 14 (3/yr)	Evidence: V
D5.	SSRI for persistent severe anxiety that affects independent functioning and quality of life.			
D5 (i):	Remission in patients with anxiety disorders treated with paroxetine. J Clin Psychiatry 2004			
	Study: narrative review	Age ≥ 65: no	Citations: 17 (0.9/yr)	Evidence: I a
D5 (ii):	Pharmacotherapy of generalized anxiety disorder: duloxetine. Curr Med Res Opin 2007			
	Study: narrative review	Age ≥ 65: no	Citations: 11 (0.6/yr)	Evidence: I a
D5 (iii):	Remission of generalized anxiety disorder: paroxetine clinical trials. J Clin Psychiatry 2006			
	Study: narrative review	Age ≥ 65: no	Citations: 10 (0.6/yr)	Evidence: I a
D5 (iv):	Generalized anxiety disorder and panic disorder in adults. NICE Clinical Guideline 2011			
	Study: guideline	Age ≥ 65: yes	Citations: N/Av	Evidence: I a
D6.	Dopamine agonist for restless legs syndrome, once iron deficiency and severe CKD excluded.			
D6 (i):	Randomized trials of dopamine agonists in restless legs syndrome. Clin Ther 2010			
	Study: meta-analysis	Age ≥ 65: no	Citations: 17 (0.9/yr)	Evidence: I a
D6 (ii):	Ropinirole on sleep outcomes in patients with restless legs syndrome. Pharmacotherapy 2009			
	Study: meta-analysis	Age ≥ 65: no	Citations: 9 (0.6/yr)	Evidence: I a
D6 (iii):	Dopamine agonists for restless legs syndrome. Cochrane Syst Rev 2011			
	Study: meta-analysis	Age ≥ 65: no	Citations: 39 (3/yr)	Evidence: I a
D7.	Propranolol for essential tremor with functional impairment and resultant disability.			
D7 (i):	Treatment of essential tremor: a systematic review of evidence. J Neurol. 2013			

Study: systematic review	Age ≥ 65: no	Citations: 33 (3/yr)	Evidence: I a
D7 (ii): Evidence-based review of treatments for essential tremor. Mov Disord 2019			
Study: systematic review	Age ≥ 65: no	Citations: 47 (9/yr)	Evidence: I a

Section E: Renal System

E1. 1-α hydroxycholecalciferol or calcitriol supplementation in severe chronic kidney disease (eGFR < 30) with hypocalcaemia (corrected serum calcium < 2.10 mmol/l) and secondary hyperparathyroidism.

E1 (i): Management of secondary hyperparathyroidism. Am J Nephrol 2003

Study: narrative review	Age ≥ 65: no	Citations: 28 (1.3/yr)	Evidence: V
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E1 (ii): **Hyperparathyroidism of renal disease. Perm J 2016**

Study: narrative review	Age ≥ 65: no	Citations: 36 (4.5/yr)	Evidence: II b
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E2. Phosphate binder in severe chronic kidney disease (eGFR < 30) if serum phosphate concentration persistently >1.76 mmol/l (5.5 mg/dl) despite adherence to renal diet.

E2 (i): Phosphate binders in chronic kidney disease: a systematic review. J Nephrol. 2016

Study: narrative review	Age ≥ 65: no	Citations: 24 (3/yr)	Evidence: V
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E2 (ii): **Strategies for phosphate control in patients with CKD. Kidney Int Rep 2019**

Study: narrative review	Age ≥ 65: no	Citations: 35 (7/yr)	Evidence: I a
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E3. Erythropoietin analogue in severe chronic kidney disease (eGFR < 30) with symptomatic anaemia not attributable to haematinic or iron deficiency, to achieve a haemoglobin of 10.0 to 12.0 g/dl.

E3 (i): Clinical practice guideline on Anaemia of Chronic Kidney Disease. BMC Nephrol. 2017

Study: guideline	Age ≥ 65: no	Citations: 85 (12/yr)	Evidence: I b
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E3 (ii): **Anaemia management in chronic kidney disease. Nephrol Dial Transpl 2013**

Study: guideline	Age ≥ 65: no	Citations: 149 (14/yr)	Evidence: I b
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E4. ARB or ACE-I in chronic kidney disease with proteinuria i.e., urine albumin excretion >300 mg/24 hours.

E4 (i): Management of Blood Pressure in Chronic Kidney Disease. Kidney Int 2021

Study: guideline	Age ≥ 65: no	Citations: 68 (23 /yr)	Evidence: I a
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E4 (ii): **Guideline for the management of glomerular diseases. Kidney Int. 2021**

Study: guideline	Age ≥ 65: no	Citations: 380 (126/yr)	Evidence: I a
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Section F: Gastrointestinal system

F1. Proton pump inhibitor with severe gastro-oesophageal reflux disease (GERD) or oesophageal stricture...

F1 (i): Managing GERD in the older patient. Digestion 2004

Study: narrative review	Age ≥ 65: no	Citations: 1 (0.1/yr)	Evidence: V
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F1 (ii): **Recent advances in the treatment of GERD in the elderly. Int J Clin Pract 2005**

Study: narrative review	Age ≥ 65: yes	Citations: 7 (0.4/yr)	Evidence: I b
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F1 (iii): Managing GERD for the lifetime of the patient. Am J Med 2004

Study: narrative review	Age ≥ 65: no	Citations: 11 (0.6/yr)	Evidence: IV
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F2. Proton pump inhibitor (PPI) with low-dose aspirin and history of peptic ulcer or reflux oesophagitis.

F2 (i): **PPIs in prevention of low-dose aspirin-associated upper GI injuries. W J Gastrol 2015**

Study: meta-analysis	Age ≥ 65: no	Citations: 36 (4/yr)	Evidence: I a
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F2 (ii): PPIs prevent aspirin-induced GI bleeding better than H2RAs. J G Liver Dis. 2017

Study: meta-analysis	Age ≥ 65: no	Citations: 5 (0.7/yr)	Evidence: I a
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F 2 (iii): GI bleeding associated with low-dose aspirin. Best Pract Res Clin Gastroenterol. 2012

Study: narrative review	Age ≥ 65: no	Citations: 26 (2/yr)	Evidence: II b
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F3. Proton pump inhibitor (PPI) with short-term (< 2 weeks) or longer-term (> 2 weeks) NSAID.

F3 (i): Gastroprotective agents in elderly patients taking NSAID. Clin Gastroenterol Hepatol. 2013

Study: systematic review	Age ≥ 65: yes	Citations: 15 (1.4/yr)	Evidence: II b
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F3 (ii): **Prevention of NSAID-induced gastroduodenal ulcers. Cochrane Syst Rev 2002**

Study: meta-analysis	Age ≥ 65: no	Citations 112(15/yr)	Evidence: I a
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F4. Fibre supplements for diverticulosis with a history of constipation.

F4 (i): *Diet and the risk of symptomatic diverticular disease. Am J Clin Nutr 1994*

Study: survey	Age ≥ 65: no	Citations: 74 (3/yr)	Evidence: -
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Inappropriate: Mismatch in intervention (diet and not fiber supplement)

- F4 (ii): High-fibre dietary therapy in diverticular disease. *Int J Colorectal Dis* 2012
Study: systematic review Age ≥ 65: no Citations: 24 (2/yr) Evidence: II b
- F4 (iii): **Treatments for uncomplicated diverticular disease of the colon. J Clin Gastro. 2009**
Study: systematic review Age ≥ 65: no Citations: 2 (0.1/yr) Evidence: I b
- F5. Osmotic laxative for chronic persistent idiopathic or benign constipation.
- F5 (i): Constipation--modern laxative therapy. *Support Care Cancer*. 2003
Study: narrative review Age ≥ 65: no Citations: 28 (13/yr) Evidence: V
- F5 (ii): Constipation in older people: A consensus statement. *Int J Clin Pract*. 2017
Study: narrative review Age ≥ 65: no Citations: 15 (2/yr) Evidence: V
- F5 (iii): **Management of constipation in older adults. Am Fam Physician** 2015
Study: narrative review Age ≥ 65: yes Citations: 18 (2/yr) Evidence: I a
- F6. Probiotics use with antibiotics in patients who are not immunocompromised or severely debilitated
- F6 (i): Which probiotic for preventing *Clostridium difficile*-associated diarrhea? *J Dig Dis*. 2020
Study: meta-analysis Age ≥ 65: no Citations: 10 (2.5/yr) Evidence: I a
- F6 (ii): **Probiotics for the prevention of *Clostridium difficile* diarrhea. Cochrane Syst Rev** 2017
Study: meta-analysis Age ≥ 65: no Citations 168 (24/yr) Evidence: I a
- F6 (iii): Probiotics for prevention of *Clostridium difficile* infection. *Open Med* 2013
Study: meta-analysis Age ≥ 65: no Citations: 32 (3/yr) Evidence: I a
- F7. *Helicobacter pylori* eradication therapy in HP-associated active peptic ulcer disease.
- F7 (i): **Role of HPylori eradication in preventing gastric cancer. Ann Gastroenterol** 2017
Study: meta-analysis Age ≥ 65: no Citations: 50 (7/yr) Evidence: I a
- F7 (ii): Eradication of HPylori for prevention of ulcer recurrence. *J Surg Res*. 2013
Study: meta-analysis Age ≥ 65: no Citations: 8 (0.7/yr) Evidence: I b
- F7 (iii): HPylori and the risk and management of associated diseases. *Aliment Pharmacol Ther* 1997
Study: narrative review Age ≥ 65: no Citations: 60 (2/yr) Evidence: V
- F7 (iv): *Prevalence of HPylori and histologic gastritis in asymptomatic persons. N Engl J Med*. 1989
Study: cases series Age ≥ 65: no Citations: 214 (6/yr) Evidence: -
Inappropriate: No message found on HPylori eradication

Section G: Respiratory system

- G1. LAMA or LABA for symptomatic COPD of GOLD 1 or 2 severity, or (mild) chronic asthma.
- G1 (i): **Global Strategy for Chronic Obstructive Lung Disease. Eur Respir J**. 2019
Study: guideline Age ≥ 65: no Citations 665(133/yr) Evidence: I a
- G1 (ii): Long-acting inhaled therapy for COPD. *Cochrane Syst Rev* 2014
Study: meta-analysis Age ≥ 65: no Citations: 83 (8/yr) Evidence: I a
- G1 (iii): Global Initiative for Asthma (GINA) strategy 2021. *Eur Respir J*. 2021
Study: guideline Age ≥ 65: no Citations: 96 (32/yr) Evidence: I a
- G2. Daily inhaled corticosteroid (ICS) for COPD of GOLD 3 or 4 severity, or moderate-severe asthma
- G2 (i): *Inhaled corticosteroids vs long-acting beta 2-agonists for COPD. Cochrane Syst Rev*. 2011
Study: meta-analysis Age ≥ 65: no Citations: 10 (0.8/yr) Evidence: -
Inappropriate: Different message: "ICS in patients with frequent exacerbations"
- G2 (ii): **Triple therapy for the management of COPD. COPD** 2011
Study: systematic review Age ≥ 65: no Citations: 7 (0.5/yr) Evidence: I a
- G2 (iii): Diagnosis, management and prevention of COPD. *Eur Respir J* 2019
Study: guideline Age ≥ 65: no Citations 666(133/yr) Evidence: I b
- G3. Home continuous oxygen with chronic hypoxaemia (i.e., pO₂ < 8.0 kPa or 60 mmHg or SaO₂ < 89%).
- G3 (i): **Domiciliary oxygen for COPD. Cochrane Syst Rev** 2005
Study: meta-analysis Age ≥ 65: no Citations: 61 (3/yr) Evidence: I a
- G3 (ii): Long-term oxygen therapy for chronic respiratory failure. *Rev Pneumol Clin* 2002 [French]
Study: narrative review Age ≥ 65: no Citations: 2 (0.1/yr) Evidence: V

Section H: Musculoskeletal system

- H1. Disease-modifying anti-rheumatic drug (DMARD) with chronic, active and disabling rheumatoid arthritis.

- H1(i): **Use of DMARDs in rheumatoid arthritis. Arthritis Rheum 2008**
Study: guideline **Age ≥ 65: no** **Citations: 446 (28/yr)** **Evidence: I a**
- H1 (ii): Response of elderly patients with rheumatoid arthritis... Rheumatology (Oxford) 2009
Study: narrative review **Age ≥ 65: yes** **Citations: 22 (1.5/yr)** **Evidence: I b**
- H1 (iii): Safety of etanercept in elderly subjects with rheumatic diseases. Ann Rheum Dis 2006
Study: narrative review **Age ≥ 65: yes** **Citations: 34 (1.9/yr)** **Evidence: I a**
- H2. Bisphosphonates and vitamin D and calcium in patients taking long-term systemic corticosteroid therapy
- H2 (i): **Calcium and vitamin D for corticosteroid-induced osteoporosis. Cochrane Syst Rev 2000**
Study: meta-analysis **Age ≥ 65: no** **Citations: 47 (2/y)** **Evidence: I a**
- H2 (ii): Bisphosphonates for steroid induced osteoporosis. Cochrane Syst Rev 200
Study: meta-analysis **Age ≥ 65: no** **Citations: 33 (1.4/yr)** **Evidence: I a**
- H2(iii): ... ~~antifracture drugs in postmenopausal male and glucocorticoid-induced osteoporosis.~~
~~Expert Opin Pharmacother 2007; 8(16): 2743-56.~~ **Evidence: -**
Inappropriateness: retracted article
- H3. Vitamin D in patients with known osteoporosis and/or fragility fracture(s) and/or T-scores below -2.5
- H3 (i): **Vitamin D for preventing fracture in osteoporotic women. Cochrane Syst Rev 2009**
Study: meta-analysis **Age ≥ 65: yes** **Citations: 128 (9/yr)** **Evidence: -**
Inappropriate: Different message: "Vitamin D is unlikely to be effective"
- H3 (ii): **Pooled analysis of vitamin D dose requirements for fracture prevention. N Engl J Med 2012**
Study: meta-analysis **Age ≥ 65: yes** **Citations: 276 (23/yr)** **Evidence: Ia**
- H3 (iii): **World guidelines for falls prevention and management for older adults. Age Ageing 2022**
Study: guideline **Age ≥ 65: yes** **Citations: 125 (63/yr)** **Evidence: -**
Inappropriate: Mismatch in endpoints (falls and not fracture)
- H4. Bone anti-resorptive or anabolic therapy in patients with osteoporosis and/or history of fragility fracture
- H4 (i): **Alendronate for prevention of osteoporotic fractures. Cochrane Syst Rev 2008**
Study: meta-analysis **Age ≥ 65: yes** **Citations 189 (69/yr)** **Evidence: I a**
- H4 (ii): Strontium ranelate for postmenopausal osteoporosis. Cochrane Syst Rev 2006
Study: meta-analysis **Age ≥ 65: yes** **Citations: 21 (1.2/yr)** **Evidence: I a**
- H4 (iii): Fracture risk reduction in osteoporosis with teriparatide. J Bone Min Metab 2012
Study: meta-analysis **Age ≥ 65: yes** **Citations: 6 (0.5/yr)** **Evidence: I a**
- H4 (iv): Denosumab in postmenopausal women with osteoporosis. Sem Arthritis Rheum 2011
Study: meta-analysis **Age ≥ 65: yes** **Citations: 14 (1.1/yr)** **Evidence: I a**
- H5. Vitamin D when confirmed 25-hydroxycolecalciferol deficiency and housebound or falls or osteopenia.
- H5 (i): **Preventing falls in older people in care facilities and hospitals. Cochrane Syst Rev 2012**
Study: meta-analysis **Age ≥ 65: yes** **Citations 185 (15/yr)** **Evidence: I a**
- H5 (ii): Primary care-relevant interventions to prevent falling in older adults. Ann Intern Med 2010
Study: meta-analysis **Age ≥ 65: yes** **Citations: 93 (7/yr)** **Evidence: I a**
- H5 (iii): Vitamin D treatment for the prevention of falls in older adults. J Am Geriatr Soc 2010
Study: meta-analysis **Age ≥ 65: yes** **Citations: 71 (5/yr)** **Evidence: I a**
- H5 (iv): Role of vitamin D supplementation in musculoskeletal diseases. Aging Clin Exp Res. 2022
Study: meta-analysis **Age ≥ 65: yes** **Citations: 15 (8/yr)** **Evidence: I a**
- H6. Anti-resorptive treatment after discontinuation of at least two doses of denosumab.
- H6 (i): Denosumab discontinuation on BMD in postmenopausal women. J Clin Endo Metab 2011
Study: 1 RCT **Age ≥ 65: no** **Citations: 191 (15/yr)** **Evidence: II b**
- H6 (ii): **Management of discontinuation of denosumab. J Clin Endocr Metab. 2020**
Study: systematic review **Age ≥ 65: no** **Citations: 71 (35/yr)** **Evidence: I a**
- H7. Anti-resorptive treatment after discontinuation of teriparatide/abaloparatide for osteoporosis.
- H7 (i): Switching teriparatide to oral bisphosphonates or denosumab. J Bone Min Metab. 2017
Study: 1 cohort **Age ≥ 65: yes** **Citations: 18 (3/yr)** **Evidence: II b**
- H7 (ii): **Abaloparatide followed by alendronate in osteoporotic women. Mayo Clin Proc. 2017**
Study: 1 cohort **Age ≥ 65: yes** **Citations: 39 (6/yr)** **Evidence: II b**
- H7 (iii): Bisphosphonate therapy in men after therapy with teriparatide. Osteoporos Int. 2004
Study: 1 cohort **Age ≥ 65: no** **Citations: 49 (3/yr)** **Evidence: II b**
- H8. Xanthine-oxidase inhibitors with a history of recurrent episodes of gout.
- H8 (i): Management of gout in the older adult. Am J Geriatr Pharmacother 2011

	Study: systematic review	Age ≥ 65: no	Citations: 7 (0.85/yr)	Evidence: I a
H8 (ii):	<i>Evidence-based recommendations for gout. Diagnosis. Ann Rheum Dis. 2006</i>			
	Study: narrative review	Age ≥ 65: no	Citations: 155 (9/yr)	Evidence: -
	<i>Inappropriate: Mismatch in endpoint (diagnosis and not treatment)</i>			
H8 (iii):	Febuxostat for treating chronic gout. Cochrane Syst Rev. 2012			
	Study: meta-analysis	Age ≥ 65: no	Citations: 15 (1.3/yr)	Evidence: I a
H9.	Folic acid supplement in patients taking methotrexate			
H9 (i):	Methotrexate in rheumatic disorders: rheumatoid arthritis. Ann Rheum Dis 2009			
	Study: guideline	Age ≥ 65: yes	Citations: 130 (9/yr)	Evidence: I a
H9 (ii):	Folic/folinic acid when methotrexate for rheumatoid arthritis. Cochrane Syst Rev 2000			
	Study: meta-analysis	Age ≥ 65: yes	Citations: 29 (2/yr)	Evidence: I a

Section I: Urogenital system

- I1. Selective alpha-1 receptor blocker for LUTS (lower urinary tract symptoms) related to benign prostatic hyperplasia (HBP) where prostatectomy is not considered necessary or appropriate or safe.
- I1 (i): Newer alpha-adrenergic-receptor antagonists in HBP-related LUTS. Clin Ther 2004
Study: narrative review Age ≥ 65: no Citations: 22 (1.1/yr) Evidence: V
- I1 (ii): **Alpha1-adrenoceptor subtypes and lower urinary tract symptoms. Int J Urol 2008**
Study: narrative review Age ≥ 65: yes Citations: 67 (4.2/yr) Evidence: I a
- I1(iii): Tamsulosin: pharmacology and therapeutic efficacy in LUTS. Drugs Aging 2002
Study: narrative review Age ≥ 65: yes Citations: 37 (1.7/yr) Evidence: V
- I2. 5-alpha reductase inhibitor for LUTS (lower urinary tract symptoms) related to benign prostatic hyperplasia (HBP) where prostatectomy is not considered necessary or appropriate or safe.
- I2 (i): **Finasteride for benign prostatic hyperplasia. Cochrane Syst Rev. 2010**
Study: meta-analysis Age ≥ 65: yes Citations: 31 (3/yr) Evidence: I a
- I2 (ii): Dutasteride and quality of life in patients with enlarged prostate. Prost Canc Prost Dis 2008
Study: systematic review Age ≥ 65: no Citations: 11 (0.7/yr) Evidence: I a
- I2 (iii): BPH progression: concept and key learning from four studies. BJU Int 2008
Study: narrative review Age ≥ 65: yes Citations: 58 (4/yr) Evidence: V
- I3. Topical vaginal oestrogen or vaginal oestrogen pessary for symptomatic atrophic vaginitis.
- I3 (i): **Vaginal estrogen therapy for atrophic vaginitis. J Womens' Health 2009**
Study: narrative review Age ≥ 65: no Citations: 12 (0.8/yr) Evidence: I a
- I3 (ii): Low-dose conjugated estrogens cream administered vaginally. Menopause 2009
Study: 1 RCT Age ≥ 65: no Citations: 38 (2.5/yr) Evidence: I b
- I3 (iii): Local estrogen in postmenopausal atrophic vaginitis. Clin Exp Obstet Gynecol 2005
Study: 1 cohort Age ≥ 65: no Citations: 3 (0.2/yr) Evidence: 2 b
- I4. Vaginal oestrogen in women for recurrent urinary tract infections (UTIs).
- I4 (i): **Recurrent UTIs in postmenopausal women. Female Pelv Med Rec Surg 2016**
Study: systematic review Age ≥ 65: yes Citations: 6 (0.8/yr) Evidence: I a
- I4 (ii): Oestrogens for preventing UTIs in postmenopausal women. Cochrane Syst Rev 2008
Study: systematic review Age ≥ 65: no Citations: 71 (4/yr) Evidence: I b
- I4 (iii): Intravaginal estriol in postmenopausal women with recurrent UTIs. N Engl J Med 1993.
Study: 1 RCT Age ≥ 65: yes Citations: 144 (5/yr) Evidence: I b
- I5. Phosphodiesterase type-5 inhibitors for persistent erectile dysfunction that causes distress.
- I5 (i): **Sildenafil for male erectile dysfunction. Arch Intern Med. 2002**
Study: meta-analysis Age ≥ 65: no Citations: 37 (1.7/yr) Evidence: I a
- I5 (ii): Pharmacology of phosphodiesterase-5 inhibitors. Int J Clin Pract. 2002
Study: narrative review Age ≥ 65: no Citations: 62 (3/yr) Evidence: V
- I5 (iii): Phosphodiesterase-5 (PDE5) inhibitors in erectile dysfunction. P T. 2013
Study: narrative review Age ≥ 65: no Citations: 61 (6/yr) Evidence: V

Section J: Endocrine system

J1. ACE inhibitor in diabetes with renal disease (dipstick proteinuria or microalbuminuria) unless eGFR < 30 ml/min.

J1 (i): *Antihypertensive agents for preventing diabetic kidney disease. Cochrane Syst Rev 2012*

Study: meta-analysis Age ≥ 65: no Citations: 26 (2.2/yr) Evidence: -
Inappropriate: Mismatch in the patients (primary and not secondary prevention of CKD)

J1 (ii): **ACE-inhibitors and ARB and progression of diabetic kidney disease. Cochrane Syst Rev 2006**

Study: meta-analysis Age ≥ 65: no Citations: 78 (6/yr) Evidence: I a

J1 (iii): Renin-angiotensin system and progression of microalbuminuria in T2DM. Diabet Med 2011

Study: meta-analysis Age ≥ 65: no Citations: 10 (0.8/yr) Evidence: I a

Section K: Analgesics criteria

K1. High-potency opioids in moderate-severe non-arthritis pain, where paracetamol, NSAIDs or low-potency opioids are not appropriate to the pain severity or have been ineffective.

K1 (i): **Opioid use in chronic non-cancer pain in older adults. J Am Geriatr Soc 2010**

Study: meta-analysis Age ≥ 65: yes Citations: 92 (7/yr) Evidence: I a

K1 (ii): Treatment of chronic pain in older people. Drugs Aging 2012

Study: narrative review Age ≥ 65: yes Citations: 22 (2/yr) Evidence: V

K2. Laxatives in patients receiving opioids regularly i.e., other than PRN use.

K2 (i): **Gastrointestinal side effects in chronic opioid users. Aliment Pharmacol Ther 2008**

Study: population survey Age ≥ 65: yes Citations: 58 (4/yr) Evidence: IV

K2 (ii): Quality indicators for pain management in vulnerable elders. Ann Intern Med 2001

Study: narrative review Age ≥ 65: yes Citations: 8 (0.3/yr) Evidence: V

K3. Topical 5% lidocaine (lignocaine) patch for localized neuropathic pain, e.g. post-herpetic neuralgia.

K3 (i): **Pharmacotherapy for neuropathic pain in adults. Lancet Neurol 2015**

Study: meta-analysis Age ≥ 65: no Citations 1186(132/yr) Evidence: I b

K3 (ii): Pharmacologic management of neuropathic pain: recommendations. Pain. 2007

Study: narrative review Age ≥ 65: no Citations: 535 (32/yr) Evidence: I b

Section L: Vaccine criteria

L1: Seasonal influenza vaccine annually

L1 (i): Vaccines for older adults. Consult Pharm 2009

Study: narrative review Age ≥ 65: yes Citations: 262 (18/yr) Evidence: V

L1 (ii): **Effectiveness of influenza vaccine in community-dwelling elderly. N Engl J Med 2007**

Study: registry Age ≥ 65: yes Citation 239 (14/yr) Evidence: II a

L1 (iii): Advocating vaccination of adults aged ≥ 60 years in Western Europe. Rejuvenation Res 2009

Study: narrative review Age ≥ 65: yes Citations: 9 (0.6/yr) Evidence: V

L1 (iv): High dose trivalent influenza vaccine in adults and immunosuppressed... J Infect. 2021

Study: meta-analysis Age ≥ 65: yes Citations: 6 (2/yr) Evidence: V

L2: Pneumococcal vaccine at least once according to national guidelines.

L2 (i): Precise answers to the wrong question: pneumococcal vaccine in elderly... Vaccine 2004.

Study: narrative review Age ≥ 65: yes Citations: 26 (1.2/yr) Evidence: V

L2 (ii): **The 23-valent pneumococcal vaccine in the elderly. Clin Infect Dis 2006**

Study: 1 cohort Age ≥ 65: yes Citations: 66 (4/yr) Evidence: II b

L2 (iii): Preventing pneumococcal disease in the elderly. Drugs Aging 2013

Study: narrative review Age ≥ 65: yes Citations: 24 (2/yr) Evidence: V

L3. Varicella-zoster vaccine according to national guidelines.

L3 (i): **Vaccines for preventing herpes zoster in older adults. Cochrane Syst Rev. 2019**

Study: meta-analysis Age ≥ 65: yes Citations: 27 (5/yr) Evidence: I a

L3 (ii): Herpes zoster vaccine in older adults and the risk of herpes zoster disease. JAMA. 2011

Study: 1 cohort Age ≥ 65: yes Citations: 89 (7/yr) Evidence: II b

L4. SARS-CoV2 vaccine according to national guidelines.

L4 (i): SARS-CoV-2 Vaccines. JAMA. 2021

Study: narrative review Age ≥ 65: no Citations: 226 (75/yr) Evidence: V

L4 (ii): **SARS-CoV-2 Vaccines. Vaccines (Basel). 2022**

Study: meta-analysis Age ≥ 65: yes Citations: 333 (17/yr) Evidence: I a