Title: Adopting STOPP/START Criteria Version 3 in Clinical Practice: A Q&A Guide for healthcare professionals

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Supplementary Table 1. Evidence supporting the introduction of new STOPP criteria in the third version of the STOPP/START criteria

Criteria		Evidence source
B4	Ventricular rate-limiting drugs i.e., beta blocker, verapamil, diltiazem, digoxin with bradycardia (< 50/min), type II heart block or complete heart block (risk of complete heart block, asystole).	British National Formulary, No. 81, March - September 2021. BMJ Group the Royal Pharmaceutical Society of Great Britain, pages 107-118.
B5	Beta-blocker as monotherapy for uncomplicated hypertension i.e., not associated with angina pectoris, aortic aneurysm or other condition where beta-blocker therapy is indicated (no firm evidence of efficacy).	(i): Wiysonge CS, Bradley HA, Volmink J, Mayosi BM, Opie LH. Beta-blockers for hypertension. Cochrane Database Syst Rev. 2017 Jan 20;1(1):CD002003. (ii): Thomopoulos C, Bazoukis G, Tsioufis C, Mancia G. Beta-blockers in hypertension: overview and meta-analysis of randomized outcome trials. J Hypertens. 2020 Sep;38(9):1669-1681.
B15	Drugs that predictably prolong the QTc interval (QTc = QT/RR) in patients with known with demonstrable QTc prolongation (to >450 msec in males and >470 msec in females), including quinolones, macrolides, ondansetron, citalopram (doses > 20 mg/day), escitalopram (doses > 10 mg/day), tricyclic antidepressants, lithium, haloperidol, digoxin, class 1A antiarrhythmics, class III antiarrhythmics, tizanidine, phenothiazines, astemizole, mirabegron (risk of life-threatening ventricular arrhythmias).	(i): Skullbacka S, Airaksinen M, Puustinen J, Toivo T. Risk assessment tools for QT prolonging pharmacotherapy in older adults: a systematic review. Eur J Clin Pharmacol. 2022 May;78(5):765-779. (ii): Fazio G, Vernuccio F, Grutta G, Re GL. Drugs to be avoided in patients with long QT syndrome: Focus on the anaesthesiological management. World J Cardiol. 2013 Apr 26;5(4):87-93.
B16	Statins for primary cardiovascular prevention in persons aged ≥ 85 and established frailty with expected life expectancy likely less than 3 years (lack of evidence of efficacy).	(i): Cholesterol Treatment Trialists' (CTT) Collaborators, Mihaylova B, Emberson J, Blackwell L, Keech A, Simes J, Barnes EH, Voysey M, Gray A, Collins R, Baigent C. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. Lancet. 2012 Aug 11;380(9841):581-90. (ii): Chou R, Dana T, Blazina I, Daeges M, Jeanne TL. Statins for Prevention of Cardiovascular Disease in Adults: Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2016 Nov 15; 316(19):2008-2024. (iii): Marcellaud E, Jost J, Tchalla A, Magne J, Aboyans V. Statins in Primary Prevention in People Over 80 Years. Am J Cardiol. 2023 Jan 15; 187:62-73.
B17	Long-term systemic i.e., non-topical NSAIDs with known history of coronary, cerebral or peripheral vascular disease (increased risk of thrombosis).	(i): McGettigan P, Henry D. Cardiovascular risk and inhibition of cyclooxygenase: a systematic review of the observational studies of selective and nonselective inhibitors of cyclooxygenase 2. JAMA. 2006 Oct 4;296(13):1633-44.

		(ii): McGettigan P, Henry D. Cardiovascular risk with non-steroidal anti-inflammatory drugs: systematic review of population-based controlled observational studies. PLoS Med. 2011 Sep;8(9):e1001098. (iii): Coxib and traditional NSAID Trialists' (CNT) Collaboration, Bhala N, Emberson J, Merhi A, Abramson S, Arber N, Baron JA, Bombardier C, Cannon C, Farkouh ME, FitzGerald GA, Goss P, Halls H, Hawk E, Hawkey C, Hennekens C, Hochberg M, Holland LE, Kearney PM, Laine L, Lanas A, Lance P, Laupacis A, Oates J, Patrono C, Schnitzer TJ, Solomon S, Tugwell P, Wilson K, Wittes J, Baigent C. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. Lancet. 2013 Aug 31;382(9894):769-79.
B18	Long-term antipsychotics with known history of coronary, cerebral or peripheral vascular disease (increased risk of thrombosis).	(i): Yu ZH, Jiang HY, Shao L, Zhou YY, Shi HY, Ruan B. Use of antipsychotics and risk of myocardial infarction: a systematic review and meta-analysis. Br J Clin Pharmacol. 2016 Sep;82(3):624-32. (ii): Foley DL, Morley KI. Systematic review of early cardiometabolic outcomes of the first treated episode of psychosis. Arch Gen Psychiatry. 2011 Jun;68(6):609-16.
B19	NSAIDs or systemic corticosteroids with heart failure requiring loop diuretic therapy (risk of exacerbation of heart failure).	(i): Coxib and traditional NSAID Trialists' (CNT) Collaboration, Bhala N, Emberson J, Merhi A, Abramson S, Arber N, Baron JA, Bombardier C, Cannon C, Farkouh ME, FitzGerald GA, Goss P, Halls H, Hawk E, Hawkey C, Hennekens C, Hochberg M, Holland LE, Kearney PM, Laine L, Lanas A, Lance P, Laupacis A, Oates J, Patrono C, Schnitzer TJ, Solomon S, Tugwell P, Wilson K, Wittes J, Baigent C. Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: meta-analyses of individual participant data from randomised trials. Lancet. 2013 Aug 31;382(9894):769-79. (ii): Arfè A, Scotti L, Varas-Lorenzo C, Nicotra F, Zambon A, Kollhorst B, Schink T, Garbe E, Herings R, Straatman H, Schade R, Villa M, Lucchi S, Valkhoff V, Romio S, Thiessard F, Schuemie M, Pariente A, Sturkenboom M, Corrao G; Safety of Non-steroidal Anti-inflammatory Drugs (SOS) Project Consortium. Non-steroidal anti-inflammatory drugs and risk of heart failure in four European countries: nested case-control study. BMJ. 2016 Sep 28;354:i4857. (iii): Souverein PC, Berard A, Van Staa TP, Cooper C, Egberts AC, Leufkens HG, Walker BR. Use of oral glucocorticoids and risk of cardiovascular and cerebrovascular disease in a population based case-control study. Heart. 2004 Aug;90(8):859-65.

B20	Antihypertensive drugs in severe symptomatic aortic stenosis (risk of severe hypotension, syncope).	(i): Kang TS, Park S. Antihypertensive Treatment in Severe Aortic Stenosis. J Cardiovasc Imaging. 2018 Jun;26(2):45-53. (ii): Saeed S, Mancia G, Rajani R, Parkin D, Chambers JB. Antihypertensive treatment with calcium channel blockers in patients with moderate or severe aortic stenosis: Relationship with all-cause mortality. Int J Cardiol. 2020 Jan 1;298:122-125.
B21	Digoxin as first line treatment for long-term (> 3 months) ventricular rate control in atrial fibrillation (increased mortality from long-term digoxin use; cardio-selective beta-blockers are generally preferable).	(i): Lopes RD, Rordorf R, De Ferrari GM, Leonardi S, Thomas L, Wojdyla DM, Ridefelt P, Lawrence JH, De Caterina R, Vinereanu D, Hanna M, Flaker G, Al-Khatib SM, Hohnloser SH, Alexander JH, Granger CB, Wallentin L; ARISTOTLE Committees and Investigators. Digoxin and Mortality in Patients With Atrial Fibrillation. J Am Coll Cardiol. 2018 Mar 13;71(10):1063-1074. (ii): Vamos M, Erath JW, Hohnloser SH. Digoxin-associated mortality: a systematic review and meta-analysis of the literature. Eur Heart J. 2015 Jul 21;36(28):1831-8.
C7	Antiplatelet agents as alternatives to vitamin K antagonists, direct thrombin inhibitors or factor Xa inhibitors for stroke prevention in patients with chronic atrial fibrillation (no evidence of efficacy).	(i): Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have nonvalvular atrial fibrillation. Ann Intern Med. 2007 Jun 19;146(12):857-67. (ii): Aguilar MI, Hart R, Pearce LA. Oral anticoagulants versus antiplatelet therapy for preventing stroke in patients with non-valvular atrial fibrillation and no history of stroke or transient ischemic attacks. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD006186.
C11	Vitamin K antagonist as first-line anticoagulant for atrial fibrillation, unless there is concurrent metallic heart valve in-situ, moderate-to-severe mitral stenosis, or eGFR < 15 mls/min./1.73m2 (direct thrombin inhibitors or factor Xa inhibitors are equally efficacious and safer than vitamin K antagonists).	(i): Ruff CT, Giugliano RP, Braunwald E, Hoffman EB, Deenadayalu N, Ezekowitz MD, Camm AJ, Weitz JI, Lewis BS, Parkhomenko A, Yamashita T, Antman EM. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials. Lancet. 2014 Mar 15;383(9921):955-62. (ii): Bruins Slot KM, Berge E. Factor Xa inhibitors versus vitamin K antagonists for preventing cerebral or systemic embolism in patients with atrial fibrillation. Cochrane Database Syst Rev. 2018 Mar 6;3(3):CD008980 (iii): Salazar CA, del Aguila D, Cordova EG. Direct thrombin inhibitors versus vitamin K antagonists for preventing cerebral or systemic embolism in people with non-valvular atrial fibrillation. Cochrane Database Syst Rev. 2014 Mar 27;2014(3):CD009893.
C12	Selective serotonin reuptake inhibitors (SSRIs) in combination with Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitor with a previous history of major haemorrhage	(i): Nochaiwong S, Ruengorn C, Awiphan R, Chai-Adisaksopha C, Tantraworasin A, Phosuya C, Kanjanarat P, Chongruksut W, Sood MM, Thavorn K. Use of serotonin reuptake inhibitor antidepressants and the

	(increased risk of bleeding due to antiplatelet effects of SSRIs)	risk of bleeding complications in patients on anticoagulant or antiplatelet agents: a systematic review and meta-analysis. Ann Med. 2022 Dec;54(1):80-97. (ii): Laporte S, Chapelle C, Caillet P, Beyens MN, Bellet F, Delavenne X, Mismetti P, Bertoletti L. Bleeding risk under selective serotonin reuptake inhibitor (SSRI) antidepressants: A meta-analysis of observational studies. Pharmacol Res. 2017 Apr;118:19-32.
C13	Direct thrombin inhibitor (e.g., dabigatran) and diltiazem or verapamil (increased risk of bleeding).	(i): Pham P, Schmidt S, Lesko L, Lip GYH, Brown JD. Association of Oral Anticoagulants and Verapamil or Diltiazem With Adverse Bleeding Events in Patients With Nonvalvular Atrial Fibrillation and Normal Kidney Function. JAMA Netw Open. 2020 Apr 1;3(4):e203593. Observational study. (ii): Härtter S, Sennewald R, Nehmiz G, Reilly P. Oral bioavailability of dabigatran etexilate (Pradaxa(®)) after co-medication with verapamil in healthy subjects. Br J Clin Pharmacol. 2013 Apr;75(4):1053-62.
C14	Apixaban, dabigatran, edoxaban, rivaroxaban and P-glycoprotein (P-gp) drug efflux pump inhibitors e.g., amiodarone, azithromycin, carvedilol, cyclosporin, dronedarone, itraconazole, ketoconazole (systemic), macrolides, quinine, ranolazine, tamoxifen, ticagrelor, verapamil (increased risk of bleeding).	(i): Gronich N, Stein N, Muszkat M. Association Between Use of Pharmacokinetic-Interacting Drugs and Effectiveness and Safety of Direct Acting Oral Anticoagulants: Nested Case-Control Study. Clin Pharmacol Ther. 2021 Dec;110(6):1526-1536. (ii): British National Formulary, volume 81, March-September 2021. BMJ Group & The Royal Pharmaceutical Press of Great Britain 2021, pp 1513-4.
C15	Systemic oestrogens or androgens with pervious history of venous thromboembolism (increased risk of recurrent venous thromboembolism).	(i): Canonico M, Plu-Bureau G, Lowe GD, Scarabin PY. Hormone replacement therapy and risk of venous thromboembolism in postmenopausal women: systematic review and meta-analysis. BMJ. 2008 May 31;336(7655):1227-31 (ii): Walker RF, Zakai NA, MacLehose RF, Cowan LT, Adam TJ, Alonso A, Lutsey PL. Association of Testosterone Therapy With Risk of Venous Thromboembolism Among Men With and Without Hypogonadism. JAMA Intern Med. 2020 Feb 1;180(2):190-197.
C16	Aspirin for primary prevention in cardiovascular disease (no evidence of benefit).	(i): Zheng SL, Roddick AJ. Association of Aspirin Use for Primary Prevention With Cardiovascular Events and Bleeding Events: A Systematic Review and Meta-analysis. JAMA. 2019 Jan 22;321(3):277-287. (ii)Gelbenegger G, Postula M, Pecen L, Halvorsen S, Lesiak M, Schoergenhofer C, Jilma B, Hengstenberg C, Siller-Matula JM. Aspirin for primary prevention of cardiovascular disease: a meta-analysis with a particular focus on subgroups. BMC Med. 2019 Nov 4;17(1):198.

D5	Antipsychotics prescribed for behavioural and psychological symptoms of dementia (BPSD) an unchanged dose for > 3 months without medication review (increased risk of extrapyramidal side-effects and chronic worsening of cognition, increased risk of major cardiovascular morbidity and mortality)	(i): Sink KM, Holden KF, Yaffe K. Pharmacological treatment of neuropsychiatric symptoms of dementia: a review of the evidence. JAMA 2005; 293:596. (ii): Lee PE, Gill SS, Freedman M, et al. Atypical antipsychotic drugs in the treatment of behavioural and psychological symptoms of dementia: systematic review. BMJ 2004; 329:75. (iii): Wang PS, Schneeweiss S, Avorn J, et al. Risk of death in elderly users of conventional vs. atypical antipsychotic medications. N Engl J Med 2005; 353:2335. (iv): Schneider LS, Dagerman KS, Insel P. Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. JAMA 2005; 294:1934.
D7	Selective serotonin re-uptake inhibitors (SSRI's) with current or recent significant bleeding (risk of exacerbation or recurrence of bleeding due to antiplatelet effects of SSRI's).	(i): Laporte S, Chapelle C, Caillet P, Beyens MN, Bellet F, Delavenne X, Mismetti P, Bertoletti L. Bleeding risk under selective serotonin reuptake inhibitor (SSRI) antidepressants: A meta-analysis of observational studies. Pharmacol Res. 2017 Apr; 118:19-32. (ii): Hackam DG, Mrkobrada M. Selective serotonin reuptake inhibitors and brain hemorrhage: a meta-analysis. Neurology. 2012 Oct 30;79(18):1862-5. (iii): Jiang HY, Chen HZ, Hu XJ, Yu ZH, Yang W, Deng M, Zhang YH, Ruan B. Use of selective serotonin reuptake inhibitors and risk of upper gastrointestinal bleeding: a systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2015 Jan;13(1):42-50.e3.
D9	Benzodiazepines for agitated behaviour or psychotic symptoms of dementia (no evidence of efficacy).	(i): Tampi RR, Tampi DJ. Efficacy and tolerability of benzodiazepines for the treatment of behavioral and psychological symptoms of dementia: a systematic review of randomized controlled trials. Am J Alzheimers Dis Other Demen. 2014 Nov;29(7):565-74. (ii): Defrancesco M, Marksteiner J, Fleischhacker WW, Blasko I. Use of Benzodiazepines in Alzheimer's Disease: A Systematic Review of Literature. Int J Neuropsychopharmacol. 2015 May 19;18(10):pyv055.
D10	Benzodiazepines for insomnia for ≥ 2 weeks (high risk of dependency, increased risk of falls, fractures and road traffic accidents).	(i): Gerlach LB, Wiechers IR, Maust DT. Prescription Benzodiazepine Use Among Older Adults: A Critical Review. Harv Rev Psychiatry. 2018 Sep/Oct;26(5):264-273. (ii): Woolcott JC, Richardson KJ, Wiens MO, et al. Meta-analysis of the impact of 9 medication classes on falls in elderly persons. Arch Intern Med. 2009;169:1952–60. (iii) Barbone F, McMahon AD, Davey PG, et al. Association of road-traffic accidents with benzodiazepine use. Lancet 1998; 352:1331–6.

D11	Z-drugs (zolpidem, zopiclone, zaleplon) for insomnia for ≥ 2 weeks (increased risk of falls, fractures).	(i): Scharner V, Hasieber L, Sönnichsen A, Mann E. Efficacy and safety of Z-substances in the management of insomnia in older adults: a systematic review for the development of recommendations to reduce potentially inappropriate prescribing. BMC Geriatr. 2022 Feb 1;22(1):87. (ii): Machado FV, Louzada LL, Cross NE, Camargos EF, Dang-Vu TT, Nóbrega OT. More than a quarter century of the most prescribed sleeping pill: Systematic review of zolpidem use by older adults. Exp Gerontol. 2020 Jul 15;136:110962.
D19	Memantine with known current or previous seizure disorder (increased risk of seizures).	(i): British National Formulary, No. 81, March - September 2021, BMJ Group & Pharmaceutical Press, p320.
D20	Nootropics in dementia including Gingko Biloba, piracetam, pramiracetam, phenylpiracetam, aniracetam, phosphatidylserine, modafinil, L-theanine, omega-3 fatty acids, panax ginseng, rhodiola, creatine (no evidence of efficacy).	(i): Solomon PR, Adams F, Silver A, Zimmer J, DeVeaux R. Ginkgo for memory enhancement: a randomized controlled trial. JAMA. 2002 Aug 21;288(7):835-40. (ii): Flicker L, Grimley Evans J. Piracetam for dementia or cognitive impairment. Cochrane Database Syst Rev. 2000;(2):CD001011.
D23	Levodopa or dopamine agonists for treatment of extrapyramidal side-effects of antipsychotics or other forms of drug-induced Parkinsonism (inappropriate prescribing cascade to be avoided).	(i): Hardie RJ, Lees AJ. Neuroleptic-induced Parkinson's syndrome: clinical features and results of treatment with levodopa. J Neurol Neurosurg Psychiatry. 1988;51:850–854. (ii): Hassin-Baer S, Sirota P, Korczyn AD, Treves TA, Epstein B, Shabtai H, et al. Clinical characteristics of neuroleptic-induced parkinsonism. J Neural Transm. 2001;108:1299–1308. (iii): Shin HW, Chung SJ. Drug-induced parkinsonism. J Clin Neurol. 2012 Mar;8(1):15-21.
E7	Mineralocorticoid receptor antagonists (e.g. spironolactone, eplerenone) if eGFR < 30 ml/min/1.73m2 (risk of dangerous hyperkalaemia).	(i): Currie, G., Taylor, A.H.M., Fujita, T. *et al.* Effect of mineralocorticoid receptor antagonists on proteinuria and progression of chronic kidney disease: a systematic review and meta-analysis. *BMC Nephrol* 17, 127 (2016). (ii): Juurlink DN, Mamdani MM, Lee DS, Kopp A, Austin PC, Laupacis A, Redelmeier DA. Rates of hyperkalemia after publication of the Randomized Aldactone Evaluation Study. N Engl J Med. 2004 Aug 5;351(6):543-51. (iii): Lainscak M, Pelliccia F, Rosano G, Vitale C, Schiariti M, Greco C, Speziale G, Gaudio C. Safety profile of mineralocorticoid receptor antagonists: Spironolactone and eplerenone. Int J Cardiol. 2015 Dec 1;200:25-9. (iv): Khan MS, Khan MS, Moustafa A, Anderson AS, Mehta R, Khan SS. Efficacy and Safety of Mineralocorticoid Receptor Antagonists in

		Patients With Heart Failure and Chronic Kidney Disease. Am J Cardiol. 2020 Feb 15;125(4):643-650.
E8	Nitrofurantoin if eGFR < 45 ml/min/1.73m2 (increased risk of nitrofurantoin toxicity).	(i): Sachs J, Geer T, Noell P, et al. Effect of renal function on urinary recovery of orally administered nitrofurantoin. N Engl J Med 1968; 278:1032–5. (ii): British National Formulary, No. 81, March – September, BMJ Group & Pharmaceutical Press, 2021, p629.
E9	Bisphosphonates if eGFR<30 ml/min/1.73m2 (increased risk of acute renal failure).	(i): Miller PD, Jamal SA, Evenepoel P, Eastell R, Boonen S. Renal safety in patients treated with bisphosphonates for osteoporosis: a review. J Bone Miner Res. 2013 Oct;28(10):2049-59. (ii): British National Formulary, No. 81, March – September, BMJ Group & Pharmaceutical Press 2021, p768.
E10	Methotrexate if eGFR <30 ml/min/1.73m2 (increased risk of methotrexate toxicity).	(i): Saag K.G., Teng G.G., Patkar N.M., Anuntiyo J., Finney C., Curtis J.R., Paulus H.E., Mudano A., Pisu M., Elkins-Melton M., et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59:762–784. (ii): British National Formulary, No. 81, March – September, BMJ Group & Pharmaceutical Press, 2021, p958 .
F5	Corticosteroids with a history of peptic ulcer disease or erosive oesophagitis (risk of relapse unless proton pump inhibitor is co-prescribed).	(i): Ellershaw JE, Kelly MJ. Corticosteroids and peptic ulceration. Palliat Med. 1994 Oct;8(4):313-9. (ii): Conn HO, Poynard T. Corticosteroids and peptic ulcer: meta-analysis of adverse events during steroid therapy. J Intern Med. 1994 Dec;236(6):619-32.
F6	Antiplatelet or anticoagulant drugs with a history of Gastric Antral Vascular Ectasia (GAVE, “watermelon stomach”) (risk of major gastrointestinal bleeding).	(i): Eccles J, Falk V, Montano-Loza AJ, Zepeda-Gómez S. Long-term follow-up in patients with gastric antral vascular ectasia (GAVE) after treatment with endoscopic band ligation (EBL). Endosc Int Open. 2019 Dec;7(12):E1624-E1629. (ii): Boltin D, Gingold-Belfer R, Lichtenstein L et al. Long-term treatment outcome of patients with gastric antral vascular ectasia treated with argon plasma coagulation. *Eur J Gastroenterol Hepatol.* 2014;26:588–593.
F7	Antipsychotics with dysphagia (increased risk of aspiration pneumonia).	(i): van der Maarel-Wierink CD, Vanobbergen JN, Bronkhorst EM, Schols JM, de Baat C. Risk factors for aspiration pneumonia in frail older people: a systematic literature review. J Am Med Dir Assoc. 2011 Jun;12(5):344-54. (ii): Trifirò G. Antipsychotic drug use and community-acquired pneumonia. Curr Infect Dis Rep. 2011 Jun;13(3):262-8.

		(iii): Nosè M, Recla E, Trifirò G, Barbui C. Antipsychotic drug exposure and risk of pneumonia: a systematic review and meta-analysis of observational studies. Pharmacoepidemiol Drug Saf. 2015 Aug;24(8):812-20. (iv): Miarons Font M, Rofes Salsench L. Antipsychotic medication and oropharyngeal dysphagia: systematic review. Eur J Gastroenterol Hepatol. 2017 Dec;29(12):1332-1339.
F8	Megestrol acetate to increase appetite (increased risk of thrombosis and death with unproven efficacy)	(i): Bolen JC, Andersen RE, Bennett RG. Deep vein thrombosis as a complication of megestrol acetate therapy among nursing home residents. J Am Med Dir Assoc. 2000 Nov-Dec;1(6):248-52. (ii): Wen FK, Millar J, Oberst-Walsh L, Nashelsky J. Clinical Inquiry: Is megestrol acetate safe and effective for malnourished nursing home residents? J Fam Pract. 2018 Feb;67(2):112-113.
H9	Long-term opioids for osteoarthritis (lack of evidence of efficacy, increased risk of serious side-effects).	(i): Welsch P, Petzke F, Klose P, Häuser W. Opioids for chronic osteoarthritis pain: An updated systematic review and meta-analysis of efficacy, tolerability and safety in randomized placebo-controlled studies of at least 4 weeks double-blind duration. Eur J Pain. 2020 Apr;24(4):685-703. (ii): Bialas P, Maier C, Klose P, Häuser W. Efficacy and harms of long-term opioid therapy in chronic non-cancer pain: Systematic review and meta-analysis of open-label extension trials with a study duration ≥26 weeks. Eur J Pain. 2020 Feb;24(2):265-278. (iii): da Costa BR, Nüesch E, Kasteler R, Husni E, Welch V, Rutjes AW, Jüni P. Oral or transdermal opioids for osteoarthritis of the knee or hip. Cochrane Database Syst Rev. 2014 Sep 17;(9):CD003115.
I3	Systemic antimuscarinic (e.g., oxybutynin, tolterodine, trospium) drugs for lower urinary tract symptoms with benign prostatic hyperplasia (BPH) and high post-void residual volume i.e. > 200 ml (uncertain efficacy and increased risk of urinary retention in older men).	(i): Wolff DT, Adler KA, Weinstein CS, Weiss JP. Managing Nocturia in Frail Older Adults. Drugs Aging. 2021 Feb;38(2):95-109. Review. (ii): Wang X, Wang X, Li S, Meng Z, Liu T, Zhang X. Comparative effectiveness of oral drug therapies for lower urinary tract symptoms due to benign prostatic hyperplasia: a systematic review and network meta-analysis. PLoS One. 2014 Sep 12;9(9):e107593. (iii): Chapple C. Antimuscarinics in men with lower urinary tract symptoms suggestive of bladder outlet obstruction due to benign prostatic hyperplasia. Curr Opin Urol. 2010 Jan;20(1):43-8.
I4	Systemic antimuscarinic drugs (e.g., oxybutynin, tolterodine, trospium) with constipation (risk of exacerbation of constipation).	(i): Usmani SA, Reckenberg K, Johnson O, Stranges PM, Teshome BF, Kebodeaux CD, Vouri SM. Relative Risk of Adverse Events and Treatment Discontinuations Between Older and Non-Older Adults Treated with

		Antimuscarinics for Overactive Bladder: A Systematic Review and Meta-Analysis. Drugs Aging. 2019 Jul;36(7):639-645.
I6	Mirabegron in labile or severe hypertension (risk of exacerbation of hypertension).	(i): Sacco E, Bientinesi R. Mirabegron: a review of recent data and its prospects in the management of overactive bladder. Ther Adv Urol. 2012 Dec;4(6):315-24. (ii): Nitti VW, Khullar V, van Kerrebroeck P, Herschorn S, Cambronero J, Angulo JC, Blauwet MB, Dorrepaal C, Siddiqui E, Martin NE. Mirabegron for the treatment of overactive bladder: a prespecified pooled efficacy analysis and pooled safety analysis of three randomised, double-blind, placebo-controlled, phase III studies. Int J Clin Pract. 2013 Jul;67(7):619-32.
I7	Duloxetine with urinary urgency or urge incontinence (duloxetine is indicated in stress incontinence but not in urinary urgency or urge incontinence).	(i): van Kerrebroeck P, Abrams P, Lange R, Slack M, Wyndaele JJ, Yalcin I, Bump RC; Duloxetine Urinary Incontinence Study Group. Duloxetine versus placebo in the treatment of European and Canadian women with stress urinary incontinence. BJOG. 2004 Mar;111(3):249-57. (ii): Norton PA, Zinner NR, Yalcin I, Bump RC; Duloxetine Urinary Incontinence Study Group. Duloxetine versus placebo in the treatment of stress urinary incontinence. Am J Obstet Gynecol. 2002 Jul;187(1):40-8.
I8	Antibiotic use in asymptomatic bacteriuria (no indication for treatment).	(i): Cortes-Penfield NW, Trautner BW, Jump RLP. Urinary Tract Infection and Asymptomatic Bacteriuria in Older Adults. Infect Dis Clin North Am. 2017 Dec;31(4):673-688. (ii): Nicolle LE, Bradley S, Colgan R, et al. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis.* 2005;40(5):643–54.
J4	Sodium glucose co-transporter (SGLT2) inhibitors (e.g., canagliflozin, dapagliflozin, empagliflozin, ertugliflozin) with symptomatic hypotension (risk of exacerbation of hypotension).	(i): Baker WL, Smyth LR, Riche DM, Bourret EM, Chamberlin KW, White WB. Effects of sodium-glucose co-transporter 2 inhibitors on blood pressure: a systematic review and meta-analysis. J Am Soc Hypertens. 2014 Apr;8(4):262-75.e9. (ii): Oliva RV, Bakris GL. Blood pressure effects of sodium-glucose co-transport 2 (SGLT2) inhibitors. J Am Soc Hypertens. 2014 May;8(5):330-9.
J7	Menopausal hormone therapy (oestrogen plus progestin) with a history of stenotic coronary, cerebral or peripheral arterial disease (increased risk of acute arterial thrombosis).	(i): Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, Jackson RD, Beresford SA, Howard BV, Johnson KC, Kotchen JM, Ockene J; Writing Group for the Women's Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. JAMA. 2002 Jul 17;288(3):321-33.

		(ii): Oliver-Williams C, Glisic M, Shahzad S, Brown E, Pellegrino Baena C, Chadni M, Chowdhury R, Franco OH, Muka T. The route of administration, timing, duration and dose of postmenopausal hormone therapy and cardiovascular outcomes in women: a systematic review. Hum Reprod Update. 2019 Mar 1;25(2):257-271.
J8	Systemic oestrogens without progestogens in patients with intact uterus (risk of endometrial cancer).	(i): Dick SE, DeWitt DE, Anawalt BD. Postmenopausal hormone replacement therapy and major clinical outcomes: a focus on cardiovascular disease, osteoporosis, dementia, and breast and endometrial neoplasia. Am J Manag Care 2002; 8(1): 95-104. Review. (ii): Furness S, Roberts H, Marjoribanks J, Lethaby A. Hormone therapy in postmenopausal women and risk of endometrial hyperplasia. Cochrane Database Syst Rev 2012 Aug 15;8:CD000402. (iii): Marjoribanks J, Farquhar C, Roberts H, Lethaby A. Long term hormone therapy for perimenopausal and postmenopausal women. Cochrane Database Syst Rev 2012 Jul 11;7:CD004143.
J9	Levothyroxine in subclinical hypothyroidism i.e., normal free T4, elevated TSH but < 10 mU/L (no evidence of benefit, risk of iatrogenic thyrotoxicosis).	(i): Stott DJ, Rodondi N, Kearney PM, Ford I, Westendorp RGJ, Mooijaart SP, Sattar N, Aubert CE, Aujesky D, Bauer DC, Baumgartner C, Blum MR, Browne JP, Byrne S, Collet TH, Dekkers OM, den Elzen WPJ, Du Puy RS, Ellis G, Feller M, Floriani C, Hendry K, Hurley C, Jukema JW, Kean S, Kelly M, Krebs D, Langhorne P, McCarthy G, McCarthy V, McConnachie A, McDade M, Messow M, O'Flynn A, O'Riordan D, Poortvliet RKE, Quinn TJ, Russell A, Sinnott C, Smit JWA, Van Dorland HA, Walsh KA, Walsh EK, Watt T, Wilson R, Gussekloo J; TRUST Study Group. Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism. N Engl J Med. 2017 Jun 29;376(26):2534-2544. (ii): Zhao C, Wang Y, Xiao L, Li L. Effect of Levothyroxine on Older Patients With Subclinical Hypothyroidism: A Systematic Review and Meta-Analysis. Front Endocrinol (Lausanne). 2022 Jul 14;13:913749.
J10	Vasopressin analogues (e.g., desmopressin, vasopressin) for urinary incontinence or urinary frequency (risk of symptomatic hyponatraemia).	(i): Choi EY, Park JS, Kim YT, Park SY, Kim GH. The risk of hyponatremia with desmopressin use for nocturnal polyuria. Am J Nephrol. 2015;41(3):183-90. (ii): Wang CJ, Lin YN, Huang SW, Chang CH. Low dose oral desmopressin for nocturnal polyuria in patients with benign prostatic hyperplasia: a double-blind, placebo controlled, randomized study. J Urol. 2011 Jan;185(1):219-23.
K5	Anti-epileptic drugs in patients with recurrent falls (may impair sensorium, may adversely affect cerebellar function).	(i): Haasum Y, Johnell K. Use of antiepileptic drugs and risk of falls in old age: A systematic review. Epilepsy Res. 2017 Dec;138:98-104.

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K6	First generation antihistamines in patients with recurrent falls (may impair sensorium).	(i): Cho H, Myung J, Suh HS, Kang HY. Antihistamine use and the risk of injurious falls or fracture in elderly patients: a systematic review and meta-analysis. Osteoporos Int. 2018 Oct;29(10):2163-2170. (ii): Seppala LJ, Petrovic M, Ryg J, Bahat G, Topinkova E, Szczerbińska K, van der Cammen TJM, Hartikainen S, Ilhan B, Landi F, Morrissey Y, Mair A, Gutiérrez-Valencia M, Emmelot-Vonk MH, Mora MÁC, Denkinger M, Crome P, Jackson SHD, Correa-Pérez A, Knol W, Soulis G, Gudmundsson A, Ziere G, Wehling M, O'Mahony D, Cherubini A, van der Velde N. STOPPFall (Screening Tool of Older Persons Prescriptions in older adults with high fall risk): a Delphi study by the EuGMS Task and Finish Group on Fall-Risk-Increasing Drugs. Age Ageing. 2021 Jun 28;50(4):1189-1199.
K7	Opioids in patients with recurrent falls (may impair sensorium).	(i): Yoshikawa A, Ramirez G, Smith ML, Foster M, Nabil AK, Jani SN, Ory MG. Opioid Use and the Risk of Falls, Fall Injuries and Fractures among Older Adults: A Systematic Review and Meta-Analysis. J Gerontol A Biol Sci Med Sci. 2020 Sep 25;75(10):1989-1995. (ii): Seppala LJ, van de Glind EMM, Daams JG, Ploegmakers KJ, de Vries M, Wermelink AMAT, van der Velde N; EUGMS Task and Finish Group on Fall-Risk-Increasing Drugs. Fall-Risk-Increasing Drugs: A Systematic Review and Meta-analysis: III. Others. J Am Med Dir Assoc. 2018 Apr;19(4):372.e1-372.e8.
K8	Antidepressants in patients with recurrent falls (may impair sensorium).	(i): Hart LA, Phelan EA, Yi JY, Marcum ZA, Gray SL. Use of Fall Risk-Increasing Drugs Around a Fall-Related Injury in Older Adults: A Systematic Review. J Am Geriatr Soc. 2020 Jun;68(6):1334-1343. (ii): Hartikainen S, Lönnroos E, Louhivuori K. Medication as a risk factor for falls: critical systematic review. J Gerontol A Biol Sci Med Sci. 2007 Oct;62(10):1172-81. (iii): Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: a systematic review and meta-analysis: I. Psychotropic drugs. J Am Geriatr Soc. 1999 Jan;47(1):30-9.

K9	Alpha blockers as antihypertensives in patients with recurrent falls (may cause orthostatic hypotension).	(i): Verhaeverbeke I, Mets T. Drug-induced orthostatic hypotension in the elderly: avoiding its onset. Drug Saf. 1997 Aug;17(2):105-18. (ii): Mansbart F, Kienberger G, Sönnichsen A, Mann E. Efficacy and safety of adrenergic alpha-1 receptor antagonists in older adults: a systematic review and meta-analysis supporting the development of recommendations to reduce potentially inappropriate prescribing. BMC Geriatr. 2022 Sep 28;22(1):771.
K10	Alpha blockers for prostatic bladder outflow symptoms, other than silodosin in patients with recurrent falls (may cause orthostatic hypotension).	(i): Lepor H. Alpha blockers for the treatment of benign prostatic hyperplasia. Rev Urol. 2007 Fall;9(4):181-90. (ii): Seo JH, Han JS, Lee Y, Myong JP, Ha US. Fall risk related to subtype-specific alpha-antagonists for benign prostatic hyperplasia: a nationwide Korean population-based cohort study. World J Urol. 2022 Dec;40(12):3043-3048.
K11	Centrally acting antihypertensives (may impair sensorium and may cause orthostatic hypotension).	(i). Potter JF. Hypertension. In: Brocklehurst's Textbook of Geriatric Medicine & Gerontology, 6th edition, Churchill Livingstone, 2003, p403. (ii). Khindri S, Jackson S. Hypertension. In: Prescribing for Elderly Patients, S. Jackson, P. Jansen, A. Mangoni, eds., Wiley-Blackwell, Chichester, UK, 2009, pp97-98.
K12	Antimuscarinics for treatment of overactive bladder or urge incontinence (may impair sensorium).	(i): Kay GG, Granville LJ. Antimuscarinic agents: implications and concerns in the management of overactive bladder in the elderly. Clin Ther. 2005 Jan;27(1):127-38; quiz 139-40. (ii): Feinberg M. The problems of anticholinergic adverse effects in older patients. Drugs Aging. 1993 Jul-Aug;3(4):335-48.
L4	Topical lidocaine (lignocaine) patch for treatment of chronic osteoarthritis pain (lack of evidence of efficacy).	(i): Voute M, Morel V, Pickering G. Topical Lidocaine for Chronic Pain Treatment. Drug Des Devel Ther. 2021 Sep 29;15:4091-4103. (ii): Bruyère O, Cooper C, Pelletier J-P, Maheu E, Rannou F, Branco J et al. A consensus statement on the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) algorithm for the management of knee osteoarthritis— from evidence-based medicine to the real-life setting. Semin Arthritis Rheum 2016; 45:S3–S11
L5	Gabapentinoids (e.g., gabapentin, pregabalin) for non-neuropathic pain (lack of evidence of efficacy).	(i): Mathieson S, Lin CC, Underwood M, Eldabe S. Pregabalin and gabapentin for pain. BMJ. 2020 Apr 28;369:m1315. (ii): Goodman CW, Brett AS. Gabapentin and Pregabalin for Pain - Is Increased Prescribing a Cause for Concern? N Engl J Med. 2017 Aug 3;377(5):411-414.
L6	Paracetamol at doses ≥ 3 g/24 hours in patients with poor nutritional status i.e., BMI < 18 or chronic liver disease (risk of hepatotoxicity).	(i): Reid O, Ngo J, Lalic S, Su E, Elliott RA. Paracetamol dosing in hospital and on discharge for older people who are frail or have low body weight. Br J Clin Pharmacol. 2022 May 10.

		(ii): O'Neil CK, Hanlon JT, Marcum ZA. Adverse effects of analgesics commonly used by older adults with osteoarthritis: focus on non-opioid and opioid analgesics. Am J Geriatr Pharmacother. 2012 Dec;10(6):331-42.

Supplementary Table 2. Evidence supporting the introduction of new START criteria in the third version of the STOPP/START criteria

Criteria		Evidence source
B7	Mineralocorticoid receptor antagonist (spironolactone, eplerenone) in heart failure without severe renal function impairment i.e., eGFR > 30 ml/min/m2.	(i): Zannad F, McMurray JJ, Krum H, et al. Eplerenone in patients with systolic heart failure and mild symptoms. N Engl J Med 2011; 364:11. (ii): Pitt B, Zannad F, Remme WJ, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. N Engl J Med 1999; 341:709.
B8	SGLT-2 inhibitors (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin) in symptomatic heart failure with or without reduced ejection fraction regardless of diabetes being present or not.	(i): McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. N Engl J Med 2019; 381:1995. (ii): Packer M, Anker SD, Butler J, et al. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. N Engl J Med 2020; 383:1413. (iii): Zannad F, Ferreira JP, Pocock SJ, et al. SGLT2 inhibitors in patients with heart failure with reduced ejection fraction: a meta-analysis of the EMPEROR-Reduced and DAPA-HF trials. Lancet 2020; 396:819. (iv): Key Takeaways from the 2022 ACC/AHA/HFSA Guideline for the Management of Heart Failure.
B9	Sacubitril/valsartan in heart failure with reduced ejection fraction causing persistent heart failure symptoms despite optimal dose of ACE inhibitor or Angiotensin Receptor Blocker (Sacubitril/valsartan to replace ACE inhibitor or Angiotensin Receptor Blocker).	(i): McMurray JJ, Packer M, Desai AS, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med 2014; 371:993. (ii): Desai AS, McMurray JJ, Packer M, et al. Effect of the angiotensin-receptor-neprilysin inhibitor LCZ696 compared with enalapril on mode of death in heart failure patients. Eur Heart J 2015; 36:1990. (iii): Desai AS, Claggett BL, Packer M, et al. Influence of Sacubitril/Valsartan (LCZ696) on 30-Day Readmission After Heart Failure Hospitalization. J Am Coll Cardiol 2016; 68:241.
B10	Beta-blocker for chronic atrial fibrillation with uncontrolled heart rate.	(i): Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, Boriani G, Castella M, Dan GA, Dilaveris PE, Fauchier L, Filippatos G, Kalman JM, La Meir M, Lane DA, Lebeau JP, Lettino M, Lip GYH, Pinto FJ, Thomas GN, Valgimigli M, Van Gelder IC, Van Putte BP, Watkins CL; ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021 Feb 1;42(5):373-498. (ii): Xu T, Huang Y, Zhou H, Bai Y, Huang X, Hu Y, Xu D, Zhang Y, Zhang J. β-blockers and risk of all-cause mortality in patients with chronic heart failure and atrial fibrillation-a meta-analysis. BMC Cardiovasc Disord. 2019 Jun 3;19(1):135.
B11	Intravenous iron for symptomatic heart failure with reduced ejection fraction and iron deficiency.	(i): Anker SD, Comin Colet J, Filippatos G, Willenheimer R, Dickstein K, Drexler H, Lüscher TF, Bart B, Banasiak W, Niegowska J, Kirwan BA, Mori C, von Eisenhart Rothe B,

		Pocock SJ, Poole-Wilson PA, Ponikowski P; FAIR-HF Trial Investigators. Ferric carboxymaltose in patients with heart failure and iron deficiency. N Engl J Med. 2009 Dec 17;361(25):2436-48. (ii): Ponikowski P, Kirwan BA, Anker SD, McDonagh T, Dorobantu M, Drozdz J, Fabien V, Filippatos G, Göhring UM, Keren A, Khintibidze I, Kragten H, Martinez FA, Metra M, Milicic D, Nicolau JC, Ohlsson M, Parkhomenko A, Pascual-Figal DA, Ruschitzka F, Sim D, Skouri H, van der Meer P, Lewis BS, Comin-Colet J, von Haehling S, Cohen-Solal A, Danchin N, Doehner W, Dargie HJ, Motro M, Butler J, Friede T, Jensen KH, Pocock S, Jankowska EA; AFFIRM-AHF investigators. Ferric carboxymaltose for iron deficiency at discharge after acute heart failure: a multicentre, double-blind, randomised, controlled trial. Lancet. 2020 Dec 12;396(10266):1895-1904.
D4	Rivastigmine for Dementia with Lewy Bodies or Parkinson's disease dementia.	(i): Rolinski M, Fox C, Maidment I, McShane R. Cholinesterase inhibitors for dementia with Lewy bodies, Parkinson's disease dementia and cognitive impairment in Parkinson's disease. Cochrane Database Syst Rev 2012 Mar 14;3:CD006504. (ii): Noufi P, Khoury R, Jeyakumar S, Grossberg GT. Use of Cholinesterase Inhibitors in Non-Alzheimer's Dementias. Drugs Aging. 2019 Aug;36(8):719-731.
D7	Propranolol for essential tremor with functional impairment and resultant disability.	(i): Zappia M, Albanese A, Bruno E, Colosimo C, Filippini G, Martinelli P, Nicoletti A, Quattrocchi G, Abbruzzese G, Berardelli A, Allegra R, Aniello MS, Elia AE, Martino D, Murgia D, Picillo M, Squintani G. Treatment of essential tremor: a systematic review of evidence and recommendations from the Italian Movement Disorders Association. J Neurol. 2013 Mar;260(3):714-40. (ii): Ferreira JJ, Mestre TA, Lyons KE, Benito-León J, Tan EK, Abbruzzese G, Hallett M, Haubenberger D, Elble R, Deuschl G; MDS Task Force on Tremor and the MDS Evidence Based Medicine Committee. MDS evidence-based review of treatments for essential tremor. Mov Disord. 2019 Jul;34(7):950-958.
E1	One-alpha hydroxycholecalciferol or calcitriol supplementation in severe chronic kidney (i.e., eGFR < 30 ml/min/m2) disease with hypocalcaemia (corrected serum calcium < 2.10 mmol/l) and associated secondary hyperparathyroidism.	(i): Moe SM, Drüeke TB. Management of secondary hyperparathyroidism: the importance and the challenge of controlling parathyroid hormone levels without elevating calcium, phosphorus, and calcium-phosphorus product. Am J Nephrol. 2003 Nov-Dec;23(6):369-79. (ii): Yuen NK, Ananthakrishnan S, Campbell MJ. Hyperparathyroidism of Renal Disease. Perm J. 2016 Summer;20(3):15-127.
E2	Phosphate binder in severe chronic kidney disease (i.e., eGFR < 30 ml/min/m2) if serum phosphate concentration persistently >1.76 mmol/l (5.5 mg/dl) despite adherence to renal diet.	(i): Floege J. Phosphate binders in chronic kidney disease: a systematic review of recent data. J Nephrol. 2016 Jun;29(3):329-340. (ii): Barreto FC, Barreto DV, Massy ZA, Drüeke TB. Strategies for Phosphate Control in Patients With CKD. Kidney Int Rep. 2019 Jun 20;4(8):1043-1056.
E3	Erythopoietin analogue in severe chronic kidney disease (i.e., eGFR < 30 ml/min/m2) with symptomatic	(i): Mikhail A, Brown C, Williams JA, Mathrani V, Shrivastava R, Evans J, Isaac H, Bhandari S. Renal association clinical practice guideline on Anaemia of Chronic Kidney Disease. BMC Nephrol. 2017 Nov 30;18(1):345.

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E4	Angiotensin receptor blocker (ARB) or Angiotensin Converting Enzyme Inhibitor (ACE-I) in chronic kidney disease with proteinuria i.e., urine albumin excretion >300 mg/24 hours.	(i): Cheung AK, Chang TI, Cushman WC, Furth SL, Hou FF, Ix JH, Knoll GA, Muntner P, Pecoits-Filho R, Sarnak MJ, Tobe SW, Tomson CRV, Lytvyn L, Craig JC, Tunnicliffe DJ, Howell M, Tonelli M, Cheung M, Earley A, Mann JFE. Executive summary of the KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. Kidney Int. 2021 Mar;99(3):559-569. (ii): Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int. 2021 Oct;100(4S):S1-S276.
F2	Proton pump inhibitor with initiation of low-dose aspirin and previous history of peptic ulcer or reflux oesophagitis.	(i): Mo C, Sun G, Lu ML, Zhang L, Wang YZ, Sun X, Yang YS. Proton pump inhibitors in prevention of low-dose aspirin-associated upper gastrointestinal injuries. World J Gastroenterol. 2015 May 7;21(17):5382-92. (ii): Szabó IL, Mátics R, Hegyi P, Garami A, Illés A, Sarlós P, Bajor J, Szűcs A, Mosztbacher D, Márta K, Szemes K, Csekő K, Kővári B, Rumbus Z, Vincze Á. PPIs Prevent Aspirin-Induced Gastrointestinal Bleeding Better than H2RAs. A Systematic Review and Meta-analysis. J Gastrointestin Liver Dis. 2017 Dec;26(4):395-402. (iii): Valkhoff VE, Sturkenboom MC, Kuipers EJ. Risk factors for gastrointestinal bleeding associated with low-dose aspirin. Best Pract Res Clin Gastroenterol. 2012 Apr;26(2):125-40.
F3	Proton pump inhibitor with short-term (< 2 weeks) or longer-term (> 2 weeks) NSAID.	(i): Medlock S, Eslami S, Askari M, Taherzadeh Z, Opondo D, de Rooij SE, Abu-Hanna A. Co-prescription of gastroprotective agents and their efficacy in elderly patients taking nonsteroidal anti-inflammatory drugs: a systematic review of observational studies. Clin Gastroenterol Hepatol. 2013 Oct;11(10):1259-1269.e10. (ii): Rostom A, Dube C, Wells G, Tugwell P, Welch V, Jolicoeur E, McGowan J. Prevention of NSAID-induced gastroduodenal ulcers. Cochrane Database Syst Rev. 2002;(4):CD002296.
F5	Osmotic laxative (e.g., lactulose, macrogol, sorbitol) for chronic persistent idiopathic or secondary benign constipation.	(i): Klaschik E, Nauck F, Ostgathe C. Constipation--modern laxative therapy. Support Care Cancer. 2003 Nov;11(11):679-85. (ii): Emmanuel A, Mattace-Raso F, Neri MC, Petersen KU, Rey E, Rogers J. Constipation in older people: A consensus statement. Int J Clin Pract. 2017 Jan;71(1). (iii): Mounsey A, Raleigh M, Wilson A. Management of Constipation in Older Adults. Am Fam Physician. 2015 Sep 15;92(6):500-4.

F6	Probiotics used with antibiotics in patients who are not immunocompromised or severely debilitated for the prevention of Clostridioides difficile-associated diarrhoea.	(i): Ma Y, Yang JY, Peng X, Xiao KY, Xu Q, Wang C. Which probiotic has the best effect on preventing Clostridium difficile-associated diarrhea? A systematic review and network meta-analysis. J Dig Dis. 2020 Feb;21(2):69-80. (ii): Goldenberg JZ, Yap C, Lytvyn L, Lo CK, Beardsley J, Mertz D, Johnston BC. Probiotics for the prevention of Clostridium difficile-associated diarrhea in adults and children. Cochrane Database Syst Rev. 2017 Dec 19;12(12):CD006095. (iii): Pattani R, Palda VA, Hwang SW, Shah PS. Probiotics for the prevention of antibiotic-associated diarrhea and Clostridium difficile infection among hospitalized patients: systematic review and meta-analysis. Open Med. 2013 May 28;7(2):e56-67.
F7	Helicobacter pylori eradication therapy in HP-associated active peptic ulcer disease.	F7 (i): Rokkas T, Rokka A, Portincasa P. A systematic review and meta-analysis of the role of Helicobacter pylori eradication in preventing gastric cancer. Ann Gastroenterol. 2017;30(4):414-423. (ii): Wong CS, Chia CF, Lee HC, Wei PL, Ma HP, Tsai SH, Wu CH, Tam KW. Eradication of Helicobacter pylori for prevention of ulcer recurrence after simple closure of perforated peptic ulcer: a meta-analysis of randomized controlled trials. J Surg Res. 2013 Jun 15;182(2):219-26. (iii): Kuipers EJ. Helicobacter pylori and the risk and management of associated diseases: gastritis, ulcer disease, atrophic gastritis and gastric cancer. Aliment Pharmacol Ther. 1997 Apr;11 Suppl 1:71-88. (iv): Dooley CP, Cohen H, Fitzgibbons PL, Bauer M, Appleman MD, Perez-Perez GI, Blaser MJ. Prevalence of Helicobacter pylori infection and histologic gastritis in asymptomatic persons. N Engl J Med. 1989 Dec 7;321(23):1562-6.
H6	Anti-resorptive treatment after discontinuation of at least two doses of denosumab (rebound increased bone turnover markers, BMD loss, and increased risk of vertebral fracture following denosumab discontinuation).	(i): Bone HG, Bolognese MA, Yuen CK, Kendler DL, Miller PD, Yang YC, Grazette L, San Martin J, Gallagher JC. Effects of denosumab treatment and discontinuation on bone mineral density and bone turnover markers in postmenopausal women with low bone mass. J Clin Endocrinol Metab. 2011 Apr;96(4):972-80. (ii): Tsourdi E, Zillikens MC, Meier C, Body JJ, Gonzalez Rodriguez E, Anastasilakis AD, Abrahamsen B, McCloskey E, Hofbauer LC, Guañabens N, Obermayer-Pietsch B, Ralston SH, Eastell R, Pepe J, Palermo A, Langdahl B. Fracture risk and management of discontinuation of denosumab therapy: a systematic review and position statement by ECTS. J Clin Endocrinol Metab. 2020 Oct 26:dgaa756.
H7	Anti-resorptive treatment after discontinuation of teriparatide/abaloparatide treatment for osteoporosis.	(i): Ebina K, Hashimoto J, Kashii M, Hirao M, Kaneshiro S, Noguchi T, Tsukamoto Y, Yoshikawa H. The effects of switching daily teriparatide to oral bisphosphonates or denosumab in patients with primary osteoporosis. J Bone Miner Metab. 2017 Jan;35(1):91-98. (ii): Cosman F, Miller PD, Williams GC, Hattersley G, Hu MY, Valter I, Fitzpatrick LA, Riis BJ, Christiansen C, Bilezikian JP, Black D. Eighteen Months of Treatment With Subcutaneous Abaloparatide Followed by 6 Months of Treatment With Alendronate in

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I4	Topical vaginal oestrogen or vaginal oestrogen pessary in women for recurrent urinary tract infections.	(i): Dueñas-Garcia OF, Sullivan G, Hall CD, Flynn MK, O'Dell K. Pharmacological Agents to Decrease New Episodes of Recurrent Lower Urinary Tract Infections in Postmenopausal Women. A Systematic Review. Female Pelvic Med Reconstr Surg. 2016 Mar-Apr;22(2):63-9. (ii): Perrotta C, Aznar M, Mejia R, Albert X, Ng CW. Oestrogens for preventing recurrent urinary tract infection in postmenopausal women. Cochrane Database Syst Rev. 2008 Apr 16;(2):CD005131. (iii): Raz R, Stamm WE. A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. N Engl J Med. 1993 Sep 9;329(11):753-6.
I5	Phosphodiesterase type-5 inhibitors (e.g., avanafil, sildenafil, tadalafil, vardenafil) for persistent erectile dysfunction that causes distress.	(i): Fink HA, Mac Donald R, Rutks IR, Nelson DB, Wilt TJ. Sildenafil for male erectile dysfunction: a systematic review and meta-analysis. Arch Intern Med. 2002 Jun 24;162(12):1349-60. (ii): Corbin JD, Francis SH. Pharmacology of phosphodiesterase-5 inhibitors. Int J Clin Pract. 2002 Jul-Aug;56(6):453-9. (iii): Huang SA, Lie JD. Phosphodiesterase-5 (PDE5) Inhibitors In the Management of Erectile Dysfunction. P T. 2013 Jul;38(7):407-19.
K3	Topical 5% lidocaine (lignocaine) patch for localized neuropathic pain, e.g. post-herpetic neuralgia.	(i): Finnerup NB, Attal N, Haroutounian S, McNicol E, Baron R, Dworkin RH, Gilron I, Haanpää M, Hansson P, Jensen TS, Kamerman PR, Lund K, Moore A, Raja SN, Rice ASC, Rowbotham M, Sena E, Wallace M. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurol. 2015;14(2):162–73. (ii): Dworkin RH, O'Connor AB, Backonja M, Farrar JT, Finnerup NB, Jensen TS, Kalso EA, Loeser JD, Miaskowski C, Nurmikko TJ, Portenoy RK, Rice ASC, Stacey BR, Treede RD, Turk DC, Wallace MS. Pharmacologic management of neuropathic pain: Evidence-based recommendations. Pain. 2007;132(3):237–51.
L3	Varicella-zoster vaccine according to national guidelines.	(i): Gagliardi AM, Andriolo BN, Torloni MR, Soares BG, de Oliveira Gomes J, Andriolo RB, Canteiro Cruz E. Vaccines for preventing herpes zoster in older adults. Cochrane Database Syst Rev. 2019 Nov 7;2019(11):CD008858. (ii): Tseng HF, Smith N, Harpaz R, Bialek SR, Sy LS, Jacobsen SJ. Herpes zoster vaccine in older adults and the risk of subsequent herpes zoster disease. JAMA. 2011 Jan 12;305(2):160-6.

L4	SARS-CoV2 vaccine according to national guidelines.	(i): Creech CB, Walker SC, Samuels RJ. SARS-CoV-2 Vaccines. JAMA. 2021 Apr 6;325(13):1318-1320. (ii): Ghazy RM, Ashmawy R, Hamdy NA, Elhadi YAM, Reyad OA, Elmalawany D, Almaghraby A, Shaaban R, Taha SHN. Efficacy and Effectiveness of SARS-CoV-2 Vaccines: A Systematic Review and Meta-Analysis. Vaccines (Basel). 2022 Feb 23;10(3):350.