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START Criteria References

Section A: Cardiovascular System criteria.

A1. Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation.

A1 (i): Hughes M, Lip GY; Guideline Development Group, National Clinical Guideline forManagement of Atrial Fibrillation in Primary and Secondary Care, NationalInstitute for Health and Clinical Excellence. Stroke and thromboembolism inatrial fibrillation: a systematic review of stroke risk factors, riskstratification schema and cost effectiveness data. Thromb Haemost 2008; 99(2): 295-304Review. PubMed PMID: 18278178.

A1 (ii): Dentali F, Riva N, Crowther M, Turpie AG, Lip GY, Ageno W. Efficacy and safetyof the novel oral anticoagulants in atrial fibrillation: a systematic review and meta-analysis of the literature. Circulation 2012; 126(20): 2381-91. Review. PubMed PMID:23071159.

A1(iii): Hart RG, Pearce LA, Aguilar MI. Meta-analysis: antithrombotic therapy to prevent stroke in patients who have non-valvular atrial fibrillation. Ann Intern Med 2007; 146(12): 857-67. PubMed PMID: 17577005.

A1 (iv): Aguilar MI, Hart R. Oral anticoagulants for preventing stroke in patients with non-valvular atrial fibrillation and no previous history of stroke or transient ischemic attacks. Cochrane Database of Systematic Reviews 2005, Issue 3. Art. No.: CD001927. DOI: 10.1002/14651858.CD001927.pub2.

A2. Aspirin (75 mg – 160 mg once daily) in the presence of chronic atrial fibrillation, where Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors are contraindicated.

A2 (i): 1: Lip GY. The role of aspirin for stroke prevention in atrial fibrillation. Nat Rev Cardiol 2011; 8(10): 602-6. PubMedPMID: 21788962.

A2 (ii): Cairns JA, Connolly S, McMurtry S, Stephenson M, Talajic M; CCS AtrialFibrillation Guidelines Committee. Canadian Cardiovascular Society atrialfibrillation guidelines 2010: prevention of stroke and systemic thromboembolismin atrial fibrillation and flutter. Can J Cardiol 2011; 27(1): 74-90. PubMed PMID: 21329865.

A2 (iii): Gage BF, van Walraven C, Pearce L, Hart RG, Koudstaal PJ, Boode BS, PetersenP. Selecting patients with atrial fibrillation for anticoagulation: stroke risk stratification in patients taking aspirin. Circulation 2004; 110(16): 2287-92. PubMed PMID: 15477396.

A2 (iv): Ezekowitz MD, Levine JA. Preventing stroke in patients with atrial fibrillation. JAMA 1999; 281(19): 1830-5. PubMed PMID: 10340371.

A3. Antiplatelet therapy (aspirin or clopidogrel or prasugrel or ticagrelor) with a documented history of coronary, cerebral or peripheral vascular disease.

A3 (i): Zuckerman IH, Yin X, Rattinger GB, Gottlieb SS, Simoni-Wastila L, Pierce SA,Huang TY, Shenolikar R, Stuart B. Effect of exposure to evidence-based pharmacotherapy on outcomes after acute myocardial infarction in older adults. J Am Geriatr Soc 2012; 60(10): 1854-61. PubMed PMID: 23003000.

A3 (ii): Alonso-Coello P, Bellmunt S, McGorrian C, Anand SS, Guzman R, Criqui MH, AklEA, Olav Vandvik P, Lansberg MG, Guyatt GH, Spencer FA; American College of Chest Physicians. Antithrombotic therapy in peripheral artery disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141(2Suppl): e669S-90S. PubMed PMID: 22315275.

A3 (iii): Fleg JL, Aronow WS, Frishman WH. Cardiovascular drug therapy in the elderly: benefits and challenges. Nat Rev Cardiol 2011; 8(1): 13-28. Review. PubMed PMID: 20978470.

A3 (iv): Vandvik PO, Lincoff AM, Gore JM, Gutterman DD, Sonnenberg FA, Alonso-Coello P,Akl EA, Lansberg MG, Guyatt GH, Spencer FA; American College of Chest Physicians. Primary and secondary prevention of cardiovascular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of ChestPhysicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141(2Suppl): e637S-68S. Erratum in: Chest 2012; 141(4): 1129. Dosage error in article text. PubMed PMID: 22315274.

A4. Antihypertensive therapy where systolic blood pressure consistently > 160 mmHg and/or diastolic blood pressure consistently > 90 mmHg; if systolic blood pressure > 140 mmHg and /or diastolic blood pressure > 90 mmHg, if diabetic.

A4 (i): Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF, Sever PS,Thom SM; BHS guidelines working party, for the British Hypertension Society.British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): summary. BMJ 2004; 328(7440):634-40. Erratum in: BMJ 2004; 328(7445): 926. PubMed PMID: 15016698.

A4 (ii): Papademetriou V, Farsang C, Elmfeldt D, Hofman A, Lithell H, Olofsson B, Skoog I, Trenkwalder P, Zanchetti A; Study on Cognition and Prognosis in the Elderly study group. Stroke prevention with the angiotensin II type 1-receptor blocker candesartan in elderly patients with isolated systolic hypertension: the Study on Cognition and Prognosis in the Elderly (SCOPE). J Am Coll Cardiol 2004; 44(6): 1175-80. PubMed PMID: 15364316.

A4 (iii): Bejan-Angoulvant T, Saadatian-Elahi M, Wright JM, Schron EB, Lindholm LH, Fagard R, Staessen JA, Gueyffier F. Treatment of hypertension in patients 80years and older: the lower the better? A meta-analysis of randomized controlled trials. J Hypertens 2010; 28(7): 1366-72. PubMed PMID: 20574244.

A5. Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, unless the patient's status is end-of-life or age is > 85 years.

A5 (i): Mills EJ, Wu P, Chong G, Ghement I, Singh S, Akl EA, Eyawo O, Guyatt G,Berwanger O, Briel M. Efficacy and safety of statin treatment for cardiovascular disease: a network meta-analysis of 170,255 patients from 76 randomized trials. QJM 2011; 104(2): 109-24. Review. PubMed PMID: 20934984.

A5 (ii): Brugts JJ, Yetgin T, Hoeks SE, Gotto AM, Shepherd J, Westendorp RG, de CraenAJ, Knopp RH, Nakamura H, Ridker P, van Domburg R, Deckers JW. The benefits of statins in people without established cardiovascular disease but with cardiovascular risk factors: meta-analysis of randomised controlled trials. BMJ 2009; 338: b2376. Review. PubMed PMID: 19567909.

A5 (iii): Amarenco P, Labreuche J. Lipid management in the prevention of stroke: review and updated meta-analysis of statins for stroke prevention. Lancet Neurol 2009; 8(5): 453-63. Review. PubMed PMID:19375663.

A6. Angiotensin Converting Enzyme (ACE) inhibitor with systolic heart failure and/or documented coronary artery disease.

A6 (i): Fleg JL, Aronow WS, Frishman WH. Cardiovascular drug therapy in the elderly: benefits and challenges. Nat Rev Cardiol 2011; 8(1):13-28. Review. PubMed PMID: 20978470.

A6 (ii): Arif SA, Mergenhagen KA, Del Carpio RO, Ho C. Treatment of systolic heartfailure in the elderly: an evidence-based review. Ann Pharmacother 2010; 44(10): 1604-14. Review. PubMed PMID: 20841514.

A6 (iii): Lahoud R, Howe M, Krishnan SM, Zacharias S, Jackson EA. Effect of use of combination evidence-based medical therapy after acute coronary syndromes on long-term outcomes. Am J Cardiol 2012; 109(2): 159-64. PubMed PMID: 22011560.

A6 (iv): Dagenais GR, Pogue J, Fox K, Simoons ML, Yusuf S. Angiotensin-converting-enzyme inhibitors in stable vascular disease without left ventricular systolic dysfunction or heart failure: a combined analysis of three trials. Lancet 2006; 368(9535): 581-8. Review. PubMed PMID: 16905022.

A6 (v): Danchin N, Cucherat M, Thuillez C, Durand E, Kadri Z, Steg PG. Angiotensin-converting enzyme inhibitors in patients with coronary artery disease and absence of heart failure or left ventricular systolic dysfunction: an overview of long-term randomized controlled trials. Arch Intern Med 2006; 166(7): 787-96. PubMed PMID: 16606817.

A6 (vi): McAlister FA; Renin Angiotension System Modulator Meta-Analysis Investigators. Angiotensin-converting enzyme inhibitors or angiotensin receptor blockers are beneficial in normotensive atherosclerotic patients: a collaborative meta-analysis of randomized trials. Eur Heart J 2012; 33(4): 505-14. PubMed PMID: 22041554.

A7. Beta-blocker with ischaemic heart disease.

A7 (i): Gibbons RJ, Abrams J, Chatterjee K, Daley J, Deedwania PC, Douglas JS,Ferguson TB Jr, Fihn SD, Fraker TD Jr, Gardin JM, O'Rourke RA, Pasternak RC,Williams SV, Gibbons RJ, Alpert JS, Antman EM, Hiratzka LF, Fuster V, Faxon DP,Gregoratos G, Jacobs AK, Smith SC Jr; American College of Cardiology; American Heart Association Task Force on Practice Guidelines. Committee on the Management of Patients With Chronic Stable Angina. ACC/AHA 2002 guideline update for the

management of patients with chronic stable angina - summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Chronic Stable Angina). Circulation 2003 ; 107(1): 149-58. PubMed PMID: 12515758.

A7 (ii): Bangalore S, Messerli FH, Kostis JB, Pepine CJ. Cardiovascular protection using beta-blockers: a critical review of the evidence. J Am Coll Cardiol 2007; 50(7): 563-72. Review. PubMed PMID: 17692739.

A7 (iii): Rasmussen JN, Chong A, Alter DA. Relationship between adherence to evidence-based pharmacotherapy and long-term mortality after acute myocardial infarction. JAMA 2007 ; 297(2): 177-86. PubMed PMID: 17213401.

A7 (iv): Everly MJ, Heaton PC, Cluxton RJ Jr. Beta-blocker underuse in secondary prevention of myocardial infarction. Ann Pharmacother 2004; 38(2): 286-93.Review. PubMed PMID: 14742768.

A8. Appropriate beta-blocker (bisoprolol, nebivolol, metoprolol orcarvedilol) with stable systolic heart failure.

A8 (i): Ambrosio G, Flather MD, Böhm M, Cohen-Solal A, Murrone A, Mascagni F, Spinucci G, Conti MG, van Veldhuisen DJ, Tavazzi L, Coats AJ. β-blockade with nebivolol for prevention of acute ischaemic events in elderly patients with heart failure. Heart 2011; 97(3): 209-14. PubMed PMID: 21138861.

A8 (ii): Lipsic E, van Veldhuisen DJ. Nebivolol in chronic heart failure: current evidence and future perspectives. Expert Opin Pharmacother 2010; 11(6): 983-92. Review. PubMed PMID: 20307222.

A8 (iii): Tangeman HJ, Patterson JH. Extended-release metoprolol succinate in chronic heart failure. Ann Pharmacother 2003; 37(5): 701-10. Review. PubMed PMID:12708950.

Section B: Respiratory System criteria.

B1. Regular inhaled beta 2 agonist or antimuscarinic bronchodilator (e.g. ipratropium, tiotropium) for mild to moderate asthma or COPD.

B1(i): Pauwels RA, Buist AS, Ma P, Jenkins CR, Hurd SS; GOLD Scientific Committee. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: National Heart, Lung, and Blood Institute and World Health Organization Global Initiative for Chronic Obstructive Lung Disease (GOLD): executive summary. Respir Care 2001; 46(8): 798-825. Review. PubMed PMID: 11463370.

B1(ii): Keating GM. Tiotropium bromide inhalation powder: a review of its use in the management of chronic obstructive pulmonary disease. Drugs 2012; 72(2):273-300. Review. PubMed PMID: 22217233.

B1(iii): Yohannes AM, Hardy CC. Treatment of chronic obstructive pulmonary disease in older patients: a practical guide. Drugs Aging 2003; 20(3): 209-28. Review. PubMed PMID: 12578401.

B1(iv): McCrory DC, Brown CD. Anticholinergic bronchodilators versus beta2-sympathomimetic agents for acute exacerbations of chronic obstructive pulmonary disease Editorial Group: Cochrane Airways Group Published Online: 8 OCT 2008. Assessed as up-to-date: 3 OCT 2005 DOI: 10.1002/14651858.CD003900

B2. Regular inhaled corticosteroid for moderate-severe asthma or COPD, where FEV1 <50% of predicted value and repeated exacerbations requiring treatment with oral corticosteroids.

B2(i): Spencer S, Evans DJ, Karner C, Cates CJ.Inhaled corticosteroids versus long-acting beta 2-agonists for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2011 Oct 5;(10):CD007033. doi: 10.1002/14651858.CD007033.pub2. Review. Update in: Cochrane Database Syst Rev 2011; (12):CD007033. PubMed PMID: 21975759.

B2(ii): Gaebel K, McIvor RA, Xie F, Blackhouse G, Robertson D, Assasi N, Hernandez P, Goeree R. Triple therapy for the management of COPD: a review. COPD 2011; 8(3): 206-43. Review. PubMed PMID: 21513437.

B2(iii): Sutherland ER, Allmers H, Ayas NT, Venn AJ, Martin RJ. Inhaled corticosteroids reduce the progression of airflow limitation in chronic obstructive pulmonary disease: a meta-analysis. Thorax 2003; 58(11): 937-41. PubMed PMID: 14586043.

B3. Home continuous oxygen with documented chronic hypoxaemia (i.e. pO2 < 8.0 kPa or 60 mmHg or SaO2 < 89%).

B3(i): Cranston JM, Crockett AJ, Moss JR, Alpers JH. Domiciliary oxygen for chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2005 Oct 19; (4):CD001744. Review. PubMed PMID: 16235285.

B3(ii): Weitzenblum E, Chaouat A, Kessler R. [Long-term oxygen therapy for chronic respiratory failure. Rationale, indications, modalities]. Rev Pneumol Clin 2002; 58(4 Pt 1): 195-212. Review. French. PubMed PMID: 12407284.

Section C: Central Nervous System & Ophthalmic Criteria.

C1. L-DOPA or a dopamine agonist in idiopathic Parkinson's disease with functional impairment and resultant disability.

C1(i): Marjama-Lyons JM, Koller WC. Parkinson's disease. Update in diagnosis and symptom management. Geriatrics 2001; 56(8): 24-5, 29-30, 33-5. Review. PubMed PMID: 11505857.

C1(ii): Danisi F. Parkinson's disease. Therapeutic strategies to improve patient function and quality of life. Geriatrics 2002; 57(3): 46-50; quiz 52. Review. PubMed PMID: 11899548.

C2. Non-TCA antidepressant drug in the presence of persistent major depressive symptoms.

C2(i): Lebowitz BD, Pearson JL, Schneider LS, Reynolds CF 3rd, Alexopoulos GS, Bruce ML, Conwell Y, Katz IR, Meyers BS, Morrison MF, Mossey J, Niederehe G, ParmeleeP. Diagnosis and treatment of

depression in late life.Consensus statementupdate. JAMA 1997; 278(14): 1186-90. Review. PubMed PMID: 9326481.

C2(ii): Mottram P, Wilson K, Strobl J. Antidepressants for depressed elderly. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD003491. Review. PubMed PMID: 16437456.

C3. Acetylcholinesterase inhibitor (e.g. donepezil, rivastigmine, galantamine) for mild or moderate Alzheimer's dementia or Lewy Body dementia (rivastigmine).

C3(i): Raina P, Santaguida P, Ismaila A, Patterson C, Cowan D, Levine M, Booker L, Oremus M. Effectiveness of cholinesterase inhibitors and memantine for treating dementia: evidence review for a clinical practice guideline. Ann Intern Med 2008; 148(5): 379-97. Review. PubMed PMID: 18316756.

C3(ii): Birks J. Cholinesterase inhibitors for Alzheimer's disease. Cochrane Database Syst Rev 2006 Jan 25;(1):CD005593. Review. PubMed PMID: 16437532.

C3(iii): 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. doi: 10.1002/14651858.CD006504.pub2. Review. PubMed PMID: 22419314.

C4. Topical prostaglandin, prostamide or beta-blocker for primary open-angle glaucoma.

C4 (i): Cheng JW, Li Y, Wei RL. Systematic review of intraocular pressure-loweringeffects of adjunctive medications added to latanoprost. Ophthalmic Res 2009; 42(2): 99-105. Review. PubMed PMID:19546601.

C4 (ii): Aptel F, Cucherat M, Denis P. Efficacy and tolerability of prostaglandin analogs: a meta-analysis of randomized controlled clinical trials. J Glaucom 2008; 17(8): 667-73. PubMed PMID: 19092464.

C5 (iii): Cheng JW, Cheng SW, Gao LD, Lu GC, Wei RL. Intraocular pressure-lowering effects of commonly used fixed-combination drugs with timolol: a systematic review and meta-analysis. PLoS One 2012; 7(9): e45079. Review. PubMed PMID: 23028770.

C5. Selective serotonin reuptake inhibitor (or SNRI or pregabalin if SSRI contraindicated) for persistent severe anxiety that interferes with independent functioning.

C5 (i): Ballenger JC. Remission rates in patients with anxiety disorders treated with paroxetine. J Clin Psychiatry 2004; 65(12):1696-707. PubMed PMID: 15641876.

C5 (ii): Allgulander C, Hartford J, Russell J, Ball S, Erickson J, Raskin J, Rynn M.Pharmacotherapy of generalized anxiety disorder: results of duloxetine treatment from a pooled analysis of three clinical trials. Curr Med Res Opin 2007; 23(6): 1245-52. PubMed PMID: 17559726.

C5 (iii): Rickels K, Rynn M, Iyengar M, Duff D. Remission of generalized anxiety disorder: a review of the paroxetine clinical trials database. J Clin Psychiatry 2006; 67(1): 41-7. PubMed PMID: 16426087.

C5 (iv): National Institute for Health and Clinical Excellence. Generalized anxiety disorder and panic disorder (with or without agoraphobia) in adults. Clinical Guideline 113. 2011. http://guidance.nice.org.uk/CG113 (accessed 22 September, 2012).

C6. Dopamine agonist (ropinirole or pramipexole or rotigotine) for Restless Legs Syndrome, once iron deficiency and severe renal failure have been excluded.

C6 (i): Zintzaras E, Kitsios GD, Papathanasiou AA, Konitsiotis S, Miligkos M, Rodopoulou P, Hadjigeorgiou GM. Randomized trials of dopamine agonists in restless legs syndrome: a systematic review, quality assessment, and meta-analysis. Clin Ther 2010; 32(2): 221-37. Review. PubMed PMID: 20206780.

C6 (ii): Hansen RA, Song L, Moore CG, Gilsenan AW, Kim MM, Calloway MO, Murray MD. Effect of ropinirole on sleep outcomes in patients with restless legs syndrome: meta-analysis of pooled individual patient data from randomized controlled trials. Pharmacotherapy 2009; 29(3): 255-62. PubMed PMID: 19249945.

C6 (iii): Scholz H, Trenkwalder C, Kohnen R, Riemann D, Kriston L, Hornyak M. Dopamine agonists for restless legs syndrome. Cochrane Database Syst Rev. 2011 Mar 16;(3):CD006009. doi: 10.1002/14651858.CD006009.pub2. Review. PubMed PMID: 21412893.

Section D: Gastrointestinal System criteria.

D1. Proton Pump Inhibitor with severe gastro-oesophageal reflux disease or peptic stricture requiring dilatation.

D1 (i): Hungin AP, Raghunath A. Managing gastro-oesophageal reflux disease in the older patient. Digestion 2004; 69 Suppl 1: 17-24. Review. PubMed PMID: 15001831.

D1 (ii): Pilotto A, Franceschi M, Paris F. Recent advances in the treatment of GERD in the elderly: focus on proton pump inhibitors. Int J Clin Pract 2005; 59(10): 1204-9. Review. PubMed PMID: 16178989.

D1 (iii): Metz DC. Managing gastroesophageal reflux disease for the lifetime of the patient: evaluating the long-term options. Am J Med 2004; 117, Suppl 5A :49S-55S. PubMed PMID: 15478853.

D2. Fibre supplement (e.g. bran, ispaghula, methylcellulose, sterculia) for diverticulosis with a history of constipation.

D2(i): Aldoori WH, Giovannucci EL, Rimm EB, Wing AL, Trichopoulos DV, Willett WC. A prospective study of diet and the risk of symptomatic diverticular disease in men. Am J Clin Nutr 1994; 60(5): 757-64. PubMed PMID: 7942584.

D2(ii): Ünlü C, Daniels L, Vrouenraets BC, Boermeester MA. A systematic review of high-fibre dietary therapy in diverticular disease. Int J Colorectal Dis 2012; 27(4): 419-27. Review. PubMed PMID: 21922199.

D2(iii): Rocco A, Compare D, Caruso F, Nardone G. Treatment options for uncomplicated diverticular disease of the colon. J Clin Gastroenterol 2009; 43(9): 803-8. Review. PubMed PMID: 19652620.

Section E: Musculoskeletal System criteria.

E1. Disease-modifying anti-rheumatic drug (DMARD) with active, disabling rheumatoid disease.

E1(i): Saag KG, Teng GG, Patkar NM, Anuntiyo J, Finney C, Curtis JR, Paulus HE,Mudano A, Pisu M, Elkins-Melton M, Outman R, Allison JJ, Suarez Almazor M,Bridges SL Jr, Chatham WW, Hochberg M, MacLean C, Mikuls T, Moreland LW, O'DellJ, Turkiewicz AM, Furst DE; American College of Rheumatology. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. Arthritis Rheum 2008; 59(6): 762-84. PubMed PMID: 18512708.

E1(ii): Köller MD, Aletaha D, Funovits J, Pangan A, Baker D, Smolen JS. Response of elderly patients with rheumatoid arthritis to methotrexate or TNF inhibitors compared with younger patients. Rheumatology (Oxford) 2009; 48(12): 1575-80.PubMed PMID: 19812228.

E1(iii): Fleischmann R, Baumgartner SW, Weisman MH, Liu T, White B, Peloso P. Long term safety of etanercept in elderly subjects with rheumatic diseases. Ann Rheum Dis 2006; 65(3): 379-84. PubMed PMID: 16150792.

E2. Bisphosphonates and vitamin D and calcium in patients taking long-term systemic corticosteroid therapy.

E2(i): Homik J, Suarez-Almazor ME, Shea B, Cranney A, Wells G, Tugwell P. Calcium and vitamin D for corticosteroid-induced osteoporosis. Cochrane Database Syst Rev 2000; (2): CD000952. Review. PubMed PMID: 10796394.

E2(ii): Homik J, Cranney A, Shea B, Tugwell P, Wells G, Adachi R, Suarez-Almazor M. Bisphosphonates for steroid induced osteoporosis. Cochrane Database Syst Rev 2000; (2):CD001347. Review. PubMed PMID: 10796432.

E2(iii): Iwamoto J, Takeda T, Sato Y. Effects of antifracture drugs in postmenopausal, male and glucocorticoid-induced osteoporosis--usefulness of alendronate and risedronate. Expert Opin Pharmacother 2007; 8(16): 2743-56. Review. PubMedPMID: 17956196.

E3. Vitamin D supplement in patients with known osteoporosis and previous fragility fracture(s) and/or (Bone Mineral Density T-scores more than -2.0 in multiple sites).

E3(i): Avenell A, Gillespie WJ, Gillespie LD, O'Connell D. Vitamin D and vitamin D analogues for preventing fractures associated with involutional and post-menopausal osteoporosis. Cochrane Database Syst Rev 2009 Apr15; (2):CD000227. doi: 10.1002/14651858.CD000227.pub3. Review. PubMed PMID:19370554.

E3(ii): Bischoff-Ferrari HA, Willett WC, Orav EJ, Lips P, Meunier PJ, Lyons RA,Flicker L, Wark J, Jackson RD, Cauley JA, Meyer HE, Pfeifer M, Sanders KM,Stähelin HB, Theiler R, Dawson-Hughes B. A pooled analysis of vitamin D dose requirements for fracture prevention. N Engl J Med 2012; 367(1):40-9. Erratum in: N Engl J Med. 2012 Aug 2;367(5):481. Oray, Endel J [corrected to Orav, Endel J]. PubMed PMID: 22762317.

E4. Bone anti-resorptive or anabolic therapy (e.g. bisphosphonate, strontium ranelate, teriparatide, denosumab) in patients with documented osteoporosis, where no pharmacological or clinical status contraindication exists (Bone Mineral Density T-scores -> 2.5 in multiple sites) and/or previous history of fragility fracture(s).

E4(i): Wells GA, Cranney A, Peterson J, Boucher M, Shea B, Robinson V, Coyle D,Tugwell P. Alendronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Cochrane Database Syst Rev 2008 Jan23; (1): CD001155. doi: 10.1002/14651858.CD001155.pub2. Review. PubMed PMID: 18253985.

E4(ii): O'Donnell S, Cranney A, Wells GA, Adachi JD, Reginster JY. Strontium ranelate for preventing and treating postmenopausal osteoporosis. Cochrane Database Syst Rev 2006 Oct 18;(4):CD005326. Review. PubMed PMID: 17054253.

E4 (iii): Nakamura T, Tsujimoto M, Hamaya E, Sowa H, Chen P. Consistency of fracture risk reduction in Japanese and Caucasian osteoporosis patients treated with teriparatide: a meta-analysis. J Bone Miner Metab 2012; 30(3): 321-5. PubMed PMID: 21938382.

E4(iv): von Keyserlingk C, Hopkins R, Anastasilakis A, Toulis K, Goeree R, Tarride JE,Xie F. Clinical efficacy and safety of denosumab in postmenopausal women with low bone mineral density and osteoporosis: a meta-analysis. Semin Arthritis Rheum 2011; 41(2):178-86. PubMed PMID: 21616520.

E5. Vitamin D supplement in older people who are housebound or experiencing falls or with osteopenia (Bone Mineral Density T-score is > -1.0 but < -2.5 in multiple sites).

E5(i): Cameron ID, Gillespie LD, Robertson MC, Murray GR, Hill KD, Cumming RG, Kerse N. Interventions for preventing falls in older people in care facilities and hospitals. Cochrane Database Syst Rev 2012 Dec 12;12:CD005465. doi:10.1002/14651858.CD005465.pub3. Review. PubMed PMID: 23235623.

E5(ii): Michael YL, Whitlock EP, Lin JS, Fu R, O'Connor EA, Gold R; US Preventive Services Task Force. Primary care-relevant interventions to prevent falling in older adults: a systematic evidence review for the U.S. Preventive Services Task Force. Ann Intern Med 2010; 153(12): 815-25. Review. PubMed PMID: 21173416.

E5(iii): Kalyani RR, Stein B, Valiyil R, Manno R, Maynard JW, Crews DC. Vitamin D treatment for the prevention of falls in older adults: systematic review and meta-analysis. J Am Geriatr Soc 2010; 58(7): 1299-310. Review. PubMed PMID:20579169.

E6. Xanthine-oxidase inhibitors (e.g. allopurinol, febuxostat) with a history of recurrent episodes of gout.

E6(i): Fravel MA, Ernst ME. Management of gout in the older adult. Am J Geriatr Pharmacother 2011; 9(5): 271-85. Review. PubMed PMID: 21849262.

E6(ii): Zhang W, Doherty M, Bardin T, Pascual E, Barskova V, Conaghan P, Gerster J,Jacobs J, Leeb B, Lioté F, McCarthy G, Netter P, Nuki G, Perez-Ruiz F, Pignone A,Pimentão J, Punzi L, Roddy E, Uhlig T, Zimmermann-Gòrska I; EULAR Standing Committee for International Clinical Studies Including Therapeutics. EULAR evidence based recommendations for gout. Part II: Management. Report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis. 2006; 65(10): 1312-24. Review. PubMed PMID: 16707532.

E6(iii): Tayar JH, Lopez-Olivo MA, Suarez-Almazor ME. Febuxostat for treating chronic gout. Cochrane Database Syst Rev. 2012 Nov 14;11:CD008653. doi:10.1002/14651858.CD008653.pub2. Review. PubMed PMID: 23152264.

E7. Folic acid supplement in patients taking methotexate.

E7(i): Visser K, Katchamart W, Loza E, Martinez-Lopez JA, Salliot C, Trudeau J,Bombardier C, Carmona L, van der Heijde D, Bijlsma JW, Boumpas DT, Canhao H,Edwards CJ, Hamuryudan V, Kvien TK, Leeb BF, Martín-Mola EM, Mielants H,Müller-Ladner U, Murphy G, Østergaard M, Pereira IA, Ramos-Remus C, Valentini G, Zochling J, Dougados M. Multinational evidence-based recommendations for the use of methotrexate in rheumatic disorders with a focus on rheumatoid arthritis: integrating systematic literature research and expert opinion of a broad international panel of rheumatologists in the 3E Initiative. Ann Rheum Dis 2009; 68(7): 1086-93. PubMed PMID: 19033291.

E7(ii): Ortiz Z, Shea B, Suarez Almazor M, Moher D, Wells G, Tugwell P. Folic acid and folinic acid for reducing side effects in patients receiving methotrexate for rheumatoid arthritis. Cochrane Database Syst Rev 2000; (2):CD000951. Review. PubMed PMID: 10796393.

Section F: Endocrine System criteria.

F1. ACE inhibitor or Angiotensin Receptor Blocker (if intolerant of ACE inhibitor) in diabetes with evidence of renal disease i.e. overt dipstick proteinuria or microalbuminuria (>30mg/24 hours) with or without serum biochemical renal impairment.

F1(i): Lv J, Perkovic V, Foote CV, Craig ME, Craig JC, Strippoli GF. Antihypertensive agents for preventing diabetic kidney disease. Cochrane Database Syst Rev 2012 Dec 12;12:CD004136. doi: 10.1002/14651858.CD004136.pub3. Review. PubMed PMID:23235603.

F1(ii): Strippoli GF, Bonifati C, Craig M, Navaneethan SD, Craig JC. Angiotensin converting enzyme inhibitors and angiotensin II receptor antagonists for preventing the progression of diabetic kidney disease.Cochrane Database Syst Rev 2006 Oct 18;(4):CD006257. Review. PubMed PMID: 17054288.

F1(iii): Blacklock CL, Hirst JA, Taylor KS, Stevens RJ, Roberts NW, Farmer AJ. Evidence for a dose effect of renin-angiotensin system inhibition on progression of microalbuminuria in Type 2 diabetes: a meta-analysis. Diabet Med 2011; 28(10): 1182-7. PubMed PMID: 21627686.

Section G: Urogenital System criteria.

G1. Alpha-1 receptor blocker with symptomatic prostatism, where prostatectomy is not considered necessary.

G1(i): Lowe FC. Role of the newer alpha, -adrenergic-receptor antagonists in the treatment of benign prostatic hyperplasia-related lower urinary tract symptoms. Clin Ther 2004; 26(11): 1701-13. Review. PubMed PMID: 15639685.

G1(ii): Schwinn DA, Roehrborn CG. Alpha1-adrenoceptor subtypes and lower urinary tracsymptoms. Int J Urol 2008; 15(3):193-9. Review. PubMed PMID: 18304211

G1(iii): Dunn CJ, Matheson A, Faulds DM. Tamsulosin: a review of its pharmacology and therapeutic efficacy in the management of lower urinary tract symptoms. Drugs Aging 2002; 19(2):135-61. Review. PubMed PMID: 11950378.

G2. 5-alpha reductase inhibitor with symptomatic prostatism, where prostatectomy is not considered necessary.

G2(i): Tacklind J, Fink HA, Macdonald R, Rutks I, Wilt TJ. Finasteride for benign prostatic hyperplasia. Cochrane Database Syst Rev. 2010 Oct 6;(10): CD006015. doi: 10.1002/14651858.CD006015.pub3. Review. PubMed PMID: 20927745.

G2(ii): O'Leary MP, Roehrborn CG, Black L. Dutasteride significantly improves quality of life measures in patients with enlarged prostate. Prostate Cancer Prostatic Dis 2008; 11(2):129-33. PubMed PMID: 17592479.

G2(iii): Roehrborn CG. BPH progression: concept and key learning from MTOPS, ALTESS, COMBAT, and ALF-ONE. BJU Int 2008; 101 Suppl 3: 17-21. Review. PubMed PMID: 18307681.

G3. Topical vaginal oestrogen or vaginal oestrogen pessary for symptomatic atrophic vaginitis.

G3 (i): Lynch C. Vaginal estrogen therapy for the treatment of atrophic vaginitis. J Womens Health (Larchmt) 2009; 18(10): 1595-606. Review. PubMed PMID: 19788364.

G3 (ii): Bachmann G, Bouchard C, Hoppe D, Ranganath R, Altomare C, Vieweg A, Graepel J, Helzner E. Efficacy and safety of low-dose regimens of conjugated estrogens cream administered vaginally. Menopause 2009; 16(4): 719-27.PubMed PMID: 19436223.

G3 (iii): Mainini G, Scaffa C, Rotondi M, Messalli EM, Quirino L, Ragucci A. Local estrogen replacement therapy in postmenopausal atrophic vaginitis: efficacy and safety of low dose 17beta-estradiol vaginal tablets. Clin Exp Obstet Gynecol 2005; 32(2): 111-3. PubMed PMID: 16108394.

Section H: Analgesics criteria.

H1. High-potency opioids in moderate-severe pain, where paracetamol, NSAIDs or low-potency opioids are not appropriate to the pain severity or have been ineffective.

H1(i): Papaleontiou M, Henderson CR Jr, Turner BJ, Moore AA, Olkhovskaya Y, Amanfo L,Reid MC. Outcomes associated with opioid use in the treatment of chronic non-cancer pain in older adults: a systematic review and meta-analysis. J Am Geriatr Soc 2010; 58(7): 1353-69. Review. PubMed PMID: 20533971.

H1(ii): van Ojik AL, Jansen PA, Brouwers JR, van Roon EN. Treatment of chronic pain in older people: evidence-based choice of strong-acting opioids. Drugs Aging 2012; 29(8): 615-25. Review. PubMed PMID: 22765848.

H2. Laxatives in patients receiving opioids regularly.

H2(i): Cook SF, Lanza L, Zhou X, Sweeney CT, Goss D, Hollis K, Mangel AW, Fehnel SE. Gastrointestinal side effects in chronic opioid users: results from a population-based survey. Aliment Pharmacol Ther 2008; 27(12): 1224-32. PubMed PMID: 18363893.

H2(ii): Chodosh J, Ferrell BA, Shekelle PG, Wenger NS. Quality indicators for pain management in vulnerable elders. Ann Intern Med 2001; 135(8 Pt 2): 731-5. PubMed PMID: 11601956.

Section I: Vaccines criteria.

I1: Seasonal trivalent influenza vaccine annually.

I1 (i): Lam S, Jodlowski TZ. Vaccines for older adults. Consult Pharm 2009; 24(5): 380-91. Review. PubMed PMID: 19555147.

I1 (ii): Nichol KL, Nordin JD, Nelson DB, Mullooly JP, Hak E. Effectiveness of influenza vaccine in the community-dwelling elderly. N Engl J Med 2007; 357(14): 1373-81. PubMed PMID: 17914038.

I1 (iii): Michel JP, Chidiac C, Grubeck-Loebenstein B, Johnson RW, Lambert PH, Maggi S, Moulias R, Nicholson K, Werner H. Advocating vaccination of adults aged 60 years and older in Western Europe: statement by the Joint Vaccine Working Group of the European Union Geriatric Medicine Society and the International Association of Gerontology and Geriatrics-European Region. Rejuvenation Res 2009; 12(2): 127-35. PubMed PMID: 19415978.

I2: Pneumococcal vaccine at least once after age 65, according to national guidelines.

I2 (i): Fedson DS, Liss C. Precise answers to the wrong question: prospective clinical trials and the meta-analyses of pneumococcal vaccine in elderly and high-risk adults. Vaccine 2004; 22(8): 927-46. PubMed PMID: 15161070.

I2 (ii): Vila-Córcoles A, Ochoa-Gondar O, Hospital I, Ansa X, Vilanova A, Rodríguez T, Llor C; EVAN Study Group. Protective effects of the 23-valent pneumococcal polysaccharide vaccine in the elderly population: the EVAN-65 study. Clin Infect Dis 2006; 43(7): 860-8. PubMed PMID: 16941367.

I2 (iii): Vila-Corcoles A, Ochoa-Gondar O. Preventing pneumococcal disease in the elderly: recent advances in vaccines and implications for clinical practice. Drugs Aging 2013; 30(5): 263-76. Review. PubMed PMID: 23420119.

Appendix 3: Screening Tool of Older Persons' Prescriptions (STOPP) version 2.

The following prescriptions are potentially inappropriate to use in patients aged 65 years and older.

Section A: Indication of medication

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

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

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

Section B: Cardiovascular System

1. Digoxin for heart failure with normal systolic ventricular function (no clear evidence of benefit)

2. Verapamil or diltiazem with NYHA Class III or IV heart failure (may worsen heart failure).

3. Beta-blocker in combination with verapamil or diltiazem (risk of heart block).

4. Beta blocker with bradycardia (< 50/min), type II heart block or complete heart block (risk of complete heart block, asystole).

5. Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias (higher risk of side-effects than beta-blockers, digoxin, verapamil or diltiazem)

6. Loop diuretic as first-line treatment for hypertension (safer, more effective alternatives available).

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

8. Thiazide diuretic with current significant hypokalaemia (i.e. serum K+ < 3.0 mmol/l), hyponatraemia (i.e. serum Na+ < 130 mmol/l) hypercalcaemia (i.e. corrected serum calcium

> 2.65 mmol/l) or with a history of gout (hypokalaemia, hyponatraemia, hypercalcaemia and gout can be precipitated by thiazide diuretic)

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

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

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

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

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

Section C: Antiplatelet/Anticoagulant Drugs

1. Long-term aspirin at doses greater than 160mg per day (increased risk of bleeding, no evidence for increased efficacy).

2. Aspirin with a past history of peptic ulcer disease without concomitant PPI (risk of recurrent peptic ulcer).

3. Aspirin, clopidogrel, dipyridamole, vitamin K antagonists, direct thrombin inhibitors or factor Xa inhibitors with concurrent significant bleeding risk, i.e. uncontrolled severe hypertension, bleeding diathesis, recent non-trivial spontaneous bleeding) (high risk of bleeding).

4. Aspirin plus clopidogrel as secondary stroke prevention, unless the patient has a coronary stent(s) inserted in the previous 12 months or concurrent acute coronary syndrome or has a high grade symptomatic carotid arterial stenosis (no evidence of added benefit over clopidogrel monotherapy)

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

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

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

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

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

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

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

Section D: Central Nervous System and Psychotropic Drugs

1. TriCyclic Antidepressants (TCAs) with dementia, narrow angle glaucoma, cardiac conduction abnormalities, prostatism, or prior history of urinary retention (risk of worsening these conditions).

2. Initiation of TriCyclic Antidepressants (TCAs) as first-line antidepressant treatment (higher risk of adverse drug reactions with TCAs than with SSRIs or SNRIs).

3. Neuroleptics with moderate-marked antimuscarinic/anticholinergic effects (chlorpromazine, clozapine, flupenthixol, fluphenzine, pipothiazine, promazine, zuclopenthixol) with a history of prostatism or previous urinary retention (high risk of urinary retention).

4. Selective serotonin re-uptake inhibitors (SSRI's) with current or recent significant hyponatraemia i.e. serum Na+ < 130 mmol/l (risk of exacerbating or precipitating hyponatraemia).

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

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

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

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

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

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

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

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

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

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

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

1. Digoxin at a long-term dose greater than 125µg/day if eGFR < 30 ml/min/1.73m2 (risk of digoxin toxicity if plasma levels not measured).

2. Direct thrombin inhibitors (e.g. dabigatran) if eGFR < 30 ml/min/1.73m2 (risk of bleeding)

3. Factor Xa inhibitors (e.g. rivaroxaban, apixaban) if eGFR < 15 ml/min/1.73m2 (risk of bleeding)

4. NSAID's if eGFR < 50 ml/min/1.73m2 (risk of deterioration in renal function).

5. Colchicine if eGFR < 10 ml/min/1.73m2 (risk of colchicine toxicity)

6. Metformin if eGFR < 30 ml/min/1.73m2 (risk of lactic acidosis).

Section F: Gastrointestinal System

1. Prochlorperazine or metoclopramide with Parkinsonism (risk of exacerbating Parkinsonian symptoms).

2. PPI for uncomplicated peptic ulcer disease or erosive peptic oesophagitis at full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated).

3. Drugs likely to cause constipation (e.g. antimuscarinic/anticholinergic drugs, oral iron, opioids, verapamil, aluminium antacids) in patients with chronic constipation where non-constipating alternatives are available (risk of exacerbation of constipation).

4. Oral elemental iron doses greater than 200 mg daily (e.g. ferrous fumarate> 600 mg/day, ferrous sulphate > 600 mg/day, ferrous gluconate> 1800 mg/day; no evidence of enhanced iron absorption above these doses).

Section G: Respiratory System

1. Theophylline as monotherapy for COPD (safer, more effective alternative; risk of adverse effects due to narrow therapeutic index).

2. Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD (unnecessary exposure to long-term side-effects of systemic corticosteroids and effective inhaled therapies are available).

3. Anti-muscarinic bronchodilators (e.g. ipratropium, tiotropium) with a history of narrow angle glaucoma (may exacerbate glaucoma) or bladder outflow obstruction (may cause urinary retention).

4. Non-selective beta-blocker (whether oral or topical for glaucoma) with a history of asthma requiring treatment (risk of increased bronchospasm).

5. Benzodiazepines with acute or chronic respiratory failure i.e. $pO_2 < 8.0$ kPa ± $pCO_2 > 6.5$ kPa (risk of exacerbation of respiratory failure).

Section H: Musculoskeletal System

1. Non-steroidal anti-inflammatory drug (NSAID) other than COX-2 selective agents with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent PPI or H2 antagonist (risk of peptic ulcer relapse).

2. NSAID with severe hypertension (risk of exacerbation of hypertension) or severe heart failure (risk of exacerbation of heart failure).

3. Long-term use of NSAID (>3 months) for symptom relief of osteoarthritis pain where paracetamol has not been tried (simple analgesics preferable and usually as effective for pain relief)

4. Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthrtitis (risk of systemic corticosteroid side-effects).

5. Corticosteroids (other than periodic intra-articular injections for mono-articular pain) for osteoarthritis (risk of systemic corticosteroid side-effects).

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

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

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

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

Section I: Urogenital System

1. Antimuscarinic drugs with dementia, or chronic cognitive impairment (risk of increased confusion, agitation) or narrow-angle glaucoma (risk of acute exacerbation of glaucoma), or chronic prostatism (risk of urinary retention).

2. Selective alpha-1 selective alpha blockers in those with symptomatic orthostatic hypotension or micturition syncope (risk of precipitating recurrent syncope)

Section J. Endocrine System

1. Sulphonylureas with a long duration of action (e.g. glibenclamide, chlorpropamide, glimepiride) with type 2 diabetes mellitus (risk of prolonged hypoglycaemia).

2. Thiazolidenediones (e.g. rosiglitazone, pioglitazone) in patients with heart failure (risk of exacerbation of heart failure)

3. Beta-blockers in diabetes mellitus with frequent hypoglycaemic episodes (risk of suppressing hypoglycaemic symptoms).

4. Oestrogens with a history of breast cancer or venous thromboembolism (increased risk of recurrence).

5. Oral oestrogens without progestogen in patients with intact uterus (risk of endometrial cancer).

6. Androgens (male sex hormones) in the absence of primary or secondary hypogonadism (risk of androgen toxicity; no proven benefit outside of the hypogonadism indication).

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

1. Benzodiazepines (sedative, may cause reduced sensorium, impair balance).

2. Neuroleptic drugs (may cause gait dyspraxia, Parkinsonism).

3. Vasodilator drugs (e.g. alpha-1 receptor blockers, calcium channel blockers, long-acting nitrates, ACE inhibitors, angiotensin I receptor blockers,) with persistent postural hypotension i.e. recurrent drop in systolic blood pressure ≥ 20mmHg (risk of syncope, falls).

4. Hypnotic Z-drugs e.g. zopiclone, zolpidem, zaleplon (may cause protracted daytime sedation, ataxia).

Section L: Analgesic Drugs

1. Use of oral or transdermal strong opioids (morphine, oxycodone, fentanyl, buprenorphine, diamorphine, methadone, tramadol, pethidine, pentazocine) as first line therapy for mild pain (WHO analgesic ladder not observed).

2. Use of regular (as distinct from PRN) opioids without concomitant laxative (risk of severe constipation).

3. Long-acting opioids without short-acting opioids for break-through pain (risk of persistence of severe pain)

Section N: Antimuscarinic/Anticholinergic Drug Burden

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

Appendix: 4: Screening Tool to Alert to Right Treatment (START), version 2.

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

Section A: Cardiovascular System

1. Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation.

2. Aspirin (75 mg – 160 mg once daily) in the presence of chronic atrial fibrillation, where Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors are contraindicated.

3. Antiplatelet therapy (aspirin or clopidogrel or prasugrel or ticagrelor) with a documented history of coronary, cerebral or peripheral vascular disease.

4. Antihypertensive therapy where systolic blood pressure consistently > 160 mmHg and/or diastolic blood pressure consistently >90 mmHg; if systolic blood pressure > 140 mmHg and /or diastolic blood pressure > 90 mmHg, if diabetic.

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

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

7. Beta-blocker with ischaemic heart disease.

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

Section B: Respiratory System

1. Regular inhaled β2 agonist or antimuscarinic bronchodilator (e.g. ipratropium, tiotropium) for mild to moderate asthma or COPD.

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

3. Home continuous oxygen with documented chronic hypoxaemia (i.e. pO2 < 8.0 kPa or 60 mmHg or SaO2 < 89%)

Section C: Central Nervous System& Eyes

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

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

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

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

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

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

Section D: Gastrointestinal System

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

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

Section E: Musculoskeletal System

1. Disease-modifying anti-rheumatic drug (DMARD) with active, disabling rheumatoid disease.

2. Bisphosphonates and vitamin D and calcium in patients taking long-term systemic corticosteroid therapy.

3. Vitamin D and calcium supplement in patients with known osteoporosis and/or previous fragility fracture(s) and/or (Bone Mineral Density T-scores more than -2.5 in multiple sites).

4. Bone anti-resorptive or anabolic therapy (e.g. bisphosphonate, strontium ranelate, teriparatide, denosumab) in patients with documented osteoporosis, where no pharmacological or clinical status contraindication exists (Bone Mineral Density T-scores -> 2.5 in multiple sites) and/or previous history of fragility fracture(s).

5. Vitamin D supplement in older people who are housebound or experiencing falls or with osteopenia (Bone Mineral Density T-score is > -1.0 but < -2.5 in multiple sites).

6. Xanthine-oxidase inhibitors (e.g. allopurinol, febuxostat) with a history of recurrent episodes of gout.

7. Folic acid supplement in patients taking methotexate.

Section F: Endocrine System

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

Section G: Urogenital System

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

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

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

Section H: Analgesics

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

2. Laxatives in patients receiving opioids regularly.

Section I: Vaccines

1. Seasonal trivalent influenza vaccine annually

2. Pneumococcal vaccine at least once after age 65 according to national guidelines