Appendix 1: STOPP/START criteria version 2 applied to the TRUST dataset

Physiological system	Criteria (The relevant (✓) criteria for each participant were applied to the dataset and recorded in Microsoft Office Excel ® (2013))	Criteria included	Number (%) of criteria included out of total criteria
STOPP criteria			
Indication of medication	A1. Any drug prescribed without an evidence-based clinical indication.	X	1/3 (33.3)
	A2. Any drug prescribed beyond the recommended duration, where treatment duration is well defined.	X	
	A3. 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).	✓	
Cardiovascular system	B1. Digoxin for heart failure with preserved systolic ventricular function (no clear evidence of benefit).	X	7/13 (53.8)
	B2. Verapamil or diltiazem with NYHA Class III or IV heart failure (may worsen heart failure).	✓	

	B3. Beta-blocker in combination with verapamil or diltiazem (risk of heart block).	✓	
	B4. Beta blocker with symptomatic bradycardia (< 50/min), type II heart block or complete heart block (risk of profound hypotension, asystole).	✓	
	B5. Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias (higher risk of side-effects than beta-blockers, digoxin, verapamil or diltiazem).	X	
	B6. Loop diuretic as first-line treatment for hypertension (safer, more effective alternatives available).	✓	
	B7. 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).	✓	
	B8. 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).	X	

	B9. Loop diuretic for treatment of hypertension with concurrent urinary incontinence (may exacerbate incontinence).	✓	
	B10. 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).	X	
	B11. ACE inhibitors or Angiotensin Receptor Blockers in patients with hyperkalaemia.	X	
	B12. 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).	X	
	B13. Phosphodiesterase type-5 inhibitors (e.g. sildenafil, tadalafil, vardenafil) in severe heart failure characterised by hypotension i.e. systolic BP < 90 mmHg, or concurrent daily nitrate therapy for angina (risk of cardiovascular collapse).	✓	

Antiplatelet/Anticoagulant drugs	C1. Long-term aspirin at doses greater than 160mg per day (increased risk of bleeding, no evidence for increased efficacy).	X	7/11 (63.6)
	C2. Aspirin with a past history of peptic ulcer disease without concomitant PPI (risk of recurrent peptic ulcer).	✓	
	C3. 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).	✓	
	C4. 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).	X	

	C5. Aspirin in combination with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with chronic atrial fibrillation without a clear indication for aspirin (no added benefit from aspirin).	✓	
	C6. Antiplatelet agents with vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in patients with stable coronary, cerebrovascular or peripheral arterial disease without a clear indication for anticoagulant therapy (no added benefit from dual therapy).	✓	
	C7. Ticlopidine in any circumstances (clopidogrel and prasugrel have similar efficacy, stronger evidence and fewer side-effects).	✓	
	C8. 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).	X	
	C9. 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).	X	

	C10. NSAID and vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in combination (risk of gastrointestinal bleeding). C11. NSAID with concurrent antiplatelet agent(s) without PPI prophylaxis (increased risk of peptic ulcer disease).	✓ ✓	
CNS & Psychotropic drugs	D1. Tricyclic antidepressants with dementia, narrow angle glaucoma, cardiac conduction abnormalities, prostatism, or prior history of urinary retention (risk of worsening these conditions). D2. Initiation of tricyclic antidepressants as first-line antidepressant treatment (higher risk of adverse drug reactions with TCAs than with SSRIs or SNRIs). D3. 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). D4. 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).	✓ X ✓ X	10/18 (55.6)

	D5. 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 > 2 weeks as there is a risk of causing a benzodiazepine withdrawal syndrome if stopped abruptly).	X	
	D6. Antipsychotics (i.e. other than quetiapine or clozapine) in those with parkinsonism or Lewy Body Disease (risk of severe extra-pyramidal symptoms).	✓	
	D7. Anticholinergics/antimuscarinics to treat extra-pyramidal side-effects of neuroleptic medications (risk of anticholinergic toxicity).	✓	
	D8. Anticholinergics/antimuscarinics in patients with delirium or dementia (risk of exacerbation of cognitive impairment).	✓	
	D9. 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).	X	
	D10. Neuroleptics as hypnotics, unless sleep disorder is due to psychosis or dementia (risk of confusion, hypotension, extra-pyramidal side effects, falls).	X	

	D11. Peripheral vasodilators (e.g. cilostazol, inositol nicotinate, naftidrofuryl oxalate, pentoxifylline) for the treatment or prevention of dementia or cognitive impairment (no clear evidence of efficacy).	X	
	D12. Non-AChEI cholinergic ('nootropic') drugs (e.g. piracetam, oxitacitam, pramiractem, dihydroergotamine, nicergoline) in dementia (no clear evidence of efficacy).	✓	
	D13. 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).	✓	
	D14. 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).	X	
	D15. Levodopa or dopamine agonists for benign essential tremor (no evidence of efficacy).	✓	

	D16. First-generation antihistamines (safer, less toxic antihistamines now widely available).	✓	
	D17. Fluoxetine as a de novo antidepressant (risk of worsening agitation and sleep disturbance; safer alternative SSRI's available as initiation drugs).	X	
	D18. Use of psychostimulants (e.g. methylphenidate) for the treatment of lethargy (no clear evidence of efficacy, increased risk of worsening hypertension and agitation).	✓	
Renal system	E1. Digoxin at a long-term dose greater than 125µg/day if eGFR < 30 ml/min/1.73m^2 (risk of digoxin toxicity if plasma levels not measured).	X	0/7 (0)
	E2. Direct thrombin inhibitors (e.g. dabigatran) if eGFR < 30 ml/min/1.73m^2 (risk of bleeding).	X	
	E3. Factor Xa inhibitors (e.g. rivaroxaban, apixaban) if eGFR < 15 ml/min/1.73m^2 (risk of bleeding).	X	
	E4. NSAID's if eGFR < 50 ml/min/1.73m^2 (risk of deterioration in renal function).	X	
	E5. Colchicine if eGFR < 10 ml/min/1.73m^2 (risk of colchicine toxicity).	X	
	E6. Metformin if eGFR < 30 ml/min/1.73m^2 (risk of lactic acidosis).	X	

	E7. Bisphosphonates if eGFR < 30 ml/min/1.73m^2 (risk of Bisphosphonate toxicity).	X	
Gastrointestinal system	F1. Diphenoxylate, loperamide or codeine phosphate for treatment of diarrhoea of unknown cause or gastroenteritis (risk of delayed diagnosis, may exacerbate constipation with overflow diarrhoea, may precipitate toxic megacolon in inflammatory bowel disease, may delay recovery in unrecognised gastroenteritis). F2. Prochlorperazine or metoclopramide with Parkinsonism (risk of exacerbating Parkinsonian symptoms). F3. PPI for uncomplicated peptic ulcer disease or erosive peptic oesophagitis at full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated). F4. 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). F5. 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).	✓ ✓ X ✓ X	3/5 (60)

Respiratory system	G1. Theophylline as monotherapy for COPD (safer, more effective alternative; risk of adverse effects due to narrow therapeutic index). G2. 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). G3. Antimuscarinic bronchodilators (e.g. ipratropium, tiotropium) with a history of narrow angle glaucoma (may exacerbate glaucoma) or bladder outflow obstruction (may cause urinary retention). G4. Non-selective beta-blocker (whether oral or topical for glaucoma) with a history of asthma requiring treatment (risk of increased bronchospasm). G5. Benzodiazepines with acute or chronic respiratory failure i.e. pO2 < 8.0 kPa ± pCO2 > 6.5 kPa (risk of exacerbation of respiratory failure).	✓ ✓ ✓ ✓ X	4/5 (80)
Musculoskeletal system	H1. 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).	✓	6/9 (66.7)

	H2. NSAID with severe hypertension (risk of exacerbation of hypertension) or severe heart failure (risk of exacerbation of heart failure).	✓	
	H3. 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).	X	
	H4. Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthrtitis (risk of systemic corticosteroid side-effects).	X	
	H5. Corticosteroids (other than periodic intra-articular injections for mono-articular pain) for osteoarthritis (risk of systemic corticosteroid side-effects).	✓	
	H6. 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).	X	
	H7. COX-2 selective NSAIDs with concurrent cardiovascular disease (increased risk of myocardial infarction and stroke).	✓	

	H8. NSAID with concurrent corticosteroids without PPI prophylaxis (increased risk of peptic ulcer disease). H9. 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).	✓ ✓	
Urogenital system	I1. 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). I2. Selective alpha-1 selective alpha blockers in those with symptomatic orthostatic hypotension or micturition syncope (risk of precipitating recurrent syncope).	✓ ✓	2/2 (100)
Endocrine system	J1. Sulphonylureas with a long duration of action (e.g. glibenclamide, chlorpropamide, glimepiride) with type 2 diabetes mellitus (risk of prolonged hypoglycaemia). J2. Thiazolidenediones (e.g. rosiglitazone, pioglitazone) in patients with heart failure (risk of exacerbation of heart failure). J3. Beta-blockers in diabetes mellitus with frequent hypoglycaemic episodes (risk of suppressing hypoglycaemic symptoms).	✓ ✓ X	5/6 (83.3)

	J4. Oestrogens with a history of breast cancer or venous thromboembolism (increased risk of recurrence).	✓	
	J5. Oral oestrogens without progestogen in patients with intact uterus (risk of endometrial cancer).	✓	
	J6. Androgens (male sex hormones) in the absence of primary or secondary hypogonadism (risk of androgen toxicity; no proven benefit outside of hypogonadismindication).	✓	
Drugs that predictably increase the risk of falls in older people	K1. Benzodiazepines (sedative, may cause reduced sensorium, impair balance).	✓	3/4 (75)
	K2. Neuroleptic drugs (may cause gait dyspraxia, Parkinsonism).	✓	
	K3. Vasodilator drugs (e.g. alpha-1 receptor blockers, calcium channel blockers, long-acting nitrates, ACE inhibitors, angiotensin I receptor blockers, diazoxide, minoxidil, hydralazine) with persistent postural hypotension i.e. recurrent drop in systolic blood pressure ≥ 20mmHg (risk of syncope, falls).	X	
	K4. Hypnotic Z-drugs e.g. zopiclone, zolpidem, zaleplon (may cause protracted daytime sedation, ataxia).	✓	

Analgesic drugs	L1. 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). L2. Use of regular (as distinct from PRN) opioids without concomitant laxative (risk of severe constipation). L3. Long-acting opioids without short-acting opioids for break-through pain (risk of persistence of severe pain).	X ✓ ✓	2/3 (66.7)
Antimuscarinic/Anticholinergic drug burden	N. 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).	✓	1/1 (100)
Total STOPP criteria n=80			51/80 (63.75)

	START criteria		
Cardiovascular system	A1. Vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation.	✓	7/8 (87.5)
	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.	✓	
	A3. Antiplatelet therapy (aspirin or clopidogrel or prasugrel or ticagrelor) with a documented history of coronary, cerebral or peripheral vascular disease.	✓	
	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.	X	
	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.	✓	
	A6. Angiotensin Converting Enzyme (ACE) inhibitor with systolic heart failure and/or documented coronary artery disease.	✓	

	A7. Beta-blocker with ischaemic heart disease. A8. Appropriate beta-blocker (bisoprolol, nebivolol, metoprololorcarvedilol) with stable systolic heart failure.	✓ ✓	
Respiratory system	B1. Regular inhaled beta 2 agonist or antimuscarinic bronchodilator (e.g. ipratropium, tiotropium) for mild to moderate asthma or COPD. B2. Regular inhaled corticosteroid for moderate-severe asthma or COPD, where FEV1 <50% of predicted value and repeated exacerbations requiring treatment with oral corticosteroids. B3. Home continuous oxygen with documented chronic hypoxaemia (i.e. pO2 < 8.0 kPa or 60 mmHg or SaO2 < 89%).	✓ X X	1/3 (33.3)
Central nervous system & Eyes	C1. L-DOPA or a dopamine agonist in idiopathic Parkinson's disease with functional impairment and resultant disability. C2. Non-TCA antidepressant drug in the presence of persistent major depressive symptoms.	✓ X	3/6 (50)

	C3. Acetylcholinesterase inhibitor (e.g. donepezil, rivastigmine, galantamine) for mild-moderate Alzheimer's dementia or Lewy Body dementia (rivastigmine).	✓	
	C4. Topical prostaglandin, prostamide or beta-blocker for primary open-angle glaucoma.	✓	
	C5. Selective serotonin reuptake inhibitor (or SNRI or pregabalin if SSRI contraindicated) for persistent severe anxiety that interferes with independent functioning.	X	
	C6. Dopamine agonist (ropinirole or pramipexole or rotigotine) for Restless Legs Syndrome, once iron deficiency and severe renal failure have been excluded.	X	
Gastrointestinal system	D1. Proton Pump Inhibitor with severe gastro-oesophageal reflux disease or peptic stricture requiring dilatation.	✓	2/2 (100)
	D2. Fibre supplements (e.g. bran, ispaghula, methylcellulose, sterculia) for diverticulosis with a history of constipation.	✓	
Musculoskeletal system	E1. Disease-modifying anti-rheumatic drug (DMARD) with active, disabling rheumatoid disease.	✓	7/7 (100)
	E2. Bisphosphonates and vitamin D and calcium in patients taking long-term systemic corticosteroid therapy.	✓	

	E3. 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). 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). 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). E6. Xanthine-oxidase inhibitors (e.g. allopurinol, febuxostat) with a history of recurrent episodes of gout. E7. Folic acid supplement in patients taking methotexate.	✓ ✓ ✓ ✓ ✓	
Endocrine system	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.	X	0/1 (0)

Urogenital system	G1. Alpha-1 receptor blocker with symptomatic prostatism, where prostatectomy is not considered necessary. G2. 5-alpha reductase inhibitor with symptomatic prostatism, where prostatectomy is not considered necessary. G3. Topical vaginal oestrogen or vaginal oestrogen pessary for symptomatic atrophic vaginitis.	X X ✓	1/3 (33.3)
Analgesics	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**.** H2. Laxatives in patients receiving opioids regularly.	X ✓	1/2 (50)
Vaccines	I1: Seasonal trivalent influenza vaccine annually. I2: Pneumococcal vaccine every 5 years, according to national guidelines.	X X	0/2 (0)
Total START criteria n=34			22/34 (64.7)