pharmacoepidemiology

SUPPLEMENTAL MATERIAL

Table S1. Overview of the number of participants with at least one inappropriate prescription for each STOPP criteria.

Criteria	N (%)
Cardiovascular System	
B1	0 (0.00)
B2	0 (0.00)
B3	0 (0.00)
B4	1 (0.10)
B5	0 (0.00)
B6	1 (0.10)
B7	0 (0.00)
B8	21 (2.00)
B9	1 (0.10)
B10	0 (0.00)
B11	0 (0.00)
B12	0 (0.00)
B13	38 (3.63)
Coagulation System	
C1	0 (0.00)
C2	0 (0.00)
C3	1 (0.10)
C4	0 (0.00)
C5	0 (0.00)
C6	10 (0.76)
C7	0 (0.00)
C8	4 (0.38)
C9	9 (0.86)
C10	11 (1.05)
C11	63 (6.01)
Central Nervous System	
D1	9 (0.86)
D2	19 (1.81)
D3	0 (0.00)
D4	2 (0.19)
D5	16 (1.53)
D6	0 (0.00)
D7	12 (1.15)
D8	2 (0.19)
D9	0 (0.00)
D10	0 (0.00)
D11	1 (0.10)
D12	0 (0.00)
D13	0 (0.00)
D14	99 (9.45)
Renal System Criteria	
E1	0 (0.00)

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E2	0 (0.00)
E3	0 (0.00)
E4	0 (0.00)
E5	0 (0.00)
E6	0 (0.00)
Gastrointestinal System Criteria	
F1	0 (0.00)
F2	2 (0.19)
F3	4 (0.38)
F4	0 (0.00)
Respiratory System Criteria	
G1	0 (0.00)
G2	11 (1.05)
G3	0 (0.00)
G4	0 (0.00)
Musculoskeletal System Criteria	
H1	12 (1.15)
H2	21 (2.00)
H3	74 (7.06)
H4	5 (0.48)
H5	22 (2.10)
H6	7 (0.67)
H7	133 (12.69)
H8	151 (14.41)
H9	0 (0.00)
Urogenital System Criteria	
I1	3 (0.29)
I2	3 (0.29)
Endocrine System Criteria	
J1	0 (0.00)
J2	0 (0.00)
J3	3 (0.29)
J4	2 (0.19)
J5	20 (1.91)
J6	20 (1.91)
Fall Risk Drug Criteria	
K1	15 (1.43)
K2	0 (0.00)
K3	22 (2.10)
K4	0 (0.00)
Analgesic Drugs	
L1	0 (0.00)
L2	172 (16.41)
L3	0 (0.00)
Antimuscarinic/Anticholinergic	
M1	71 (6.77)

Table S2. Comparison of fit statistics for the Poisson, negative binomial, zero-inflated, and zero-inflated negative binomial models comparing the association between age and PIP.

Model	AIC	Log-Likelihood
Poisson	3282.58	-1021.76
Negative Binomial	2942.36	-850.65
Zero-inflated	2946.68	-851.81
Zero-inflated Negative Binomial	2924.28	-1457.14

Table S3. Detailed definitions of defining STOPP criteria in the study sample. Please see original list of STOPP criteria for full references [9].

Criteria Label	Criteria Definition	Study Definition
B1	Digoxin for heart failure with preserved systolic ventricular function (no clear evidence of benefit).	If Digoxin (DIGOXIN) has been prescribed at any point after heart failure (HEARTFAIL) then B1 = 1. If Digoxin (DIGOXIN) has been prescribed 90 days before or after supraventricular tachycardia (SUPRATACHY) then B1 = 0.
B2	Verapamil or diltiazem with NYHA Class III or IV heart failure (may worsen heart failure).	If Verapamil (VERAPAMIL) or Diltiazem (DILTIAZEM) was prescribed in the year prior to or the year after the occurrence of heart failure (HEARTFAIL) then B2 = 1.
B3	Beta-Blocker in combination with verapamil or diltiazem (risk of heart block).	If a Beta-Blocker (BETABLOCK) has been prescribed 90 days before or after Verapamil (VERAPAMIL) or Diltiazem (DILTIAZEM) has been prescribed, then B3 = 1.
B4	Beta-blocker with symptomatic bradycardia (< 50/min), type II heart block or complete heart block (risk of profound hypotension, asystole).	If a Beta-Blocker (BETABLOCK) has been prescribed in the year prior to or the year after the occurrence of a heart block (HEARTBLOCK) diagnosis or bradycardia diagnosis (BRADYCARDIA). *Note:* Can use the "FLAG_BRADYCARDIA" variable for a wider definition, there are also no heart rate measures stored in DRV_VS so that aspect of the definition was not included.
B5	Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias (higher risk of side-effects than beta-blockers, digoxin, verapamil, or diltiazem).	If an Amiodarone (AMIODARONE) has ever been prescribed in the 90 days before or after a supraventricular tachyarrhythmia diagnosis (SUPRATACHY) then B5 = 1.
B6	Loop diuretic as first-line treatment for hypertension (lack of outcome data for this indication, safer, more effective alternatives available).	If the first medication given for hypertension was a loop diuretic (LOOPDIURETIC) and it was prescribed in the 90 days before or

		after the first ever diagnosis of hypertension, then B6 = 1. If heart failure (HEARTFAIL) has ever been diagnosed prior to the start date of the loop diuretic (LOOPDIURETIC), then B6 = 0.
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).	If a loop diuretic (LOOPDIURETIC) was prescribed in the year prior or the year after an ankle edema (ANKLEEDEMA) diagnosis then B7 = 1. If a diagnosis of heart failure (HEARTFAIL), liver failure (LIVERFAIL), renal failure (RENALFAIL), or nephrotic syndrome (NEPHSYN) was diagnosed at any point prior to the loop diuretic (LOOPDIURETIC), then B7 = 0.
B8	Thiazide diuretic with current significant hypokalemia (i.e., serum K+ < 3.0 mmol/l), hyponatremia (i.e., serum Na+ < 130 mmol/l), hypercalcemia (i.e., corrected serum calcium > 2.65 mmol/l) or with a history of gout (hypokalemia, hyponatremia, hypercalcemia, and gout can be precipitated by thiazide diuretic).	If Thiazide (THIAZIDE) has been prescribed in the year prior to or year after a hypokalemia (HYPOKALEMIA) diagnosis then B8 = 1. If Thiazide (THIAZIDE) has been prescribed in the year prior to or year after a hyponatremia (HYPONATREMIA) diagnosis then B8 = 1. If Thiazide (THIAZIDE) has been prescribed in the year prior to or year after a hypercalcemia (HYPERCALCEMIA) diagnosis then B8 = 1. If Thiazide (THIAZIDE) has been prescribed at any point after the first diagnosis of gout (GOUT) then B8 = 1.
B9	Loop Diuretic for treatment of hypertension with concurrent urinary incontinence (may exacerbate incontinence).	If a loop diuretic (LOOPDIURETIC) has been prescribed at any point in the year prior to or the year after a urinary incontinence (UR_INCONTINENCE) diagnosis then B9 = 1. If a the first ever heart failure (HEARTFAIL) diagnosis occurred at any point prior to the loop diuretic (LOOPDIURETIC) start date, then B9 = 0.
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	If a centrally-acting antihypertensive has ever been prescribed. Note that we are only able to assess the presence of a centrally-acting antihypertensive and not whether there was a clear intolerance of other medications.

	generally less well tolerated by older people than younger people).	
B11	ACE Inhibitors or Angiotensin Receptor Blockers in patients with hyperkalemia.	If an ACE Inhibitor (ACEINHIBIT) has ever been prescribed at any point after the 30 days following the first Hyperkalemia (HYPERKALEMIA) diagnosis date, then B11 = 1.
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 hyperkalemia i.e., > 6.0 mmol/l – serum K should be monitored regularly, i.e., at least every 6 months).	If an Aldosterone antagonist (ALDOST_ANTAGONIST) has ever been prescribed in the 90 days before or after a potassium-conserving drug (POTASSIUM_CONSERVE) then B12 = 1. The index date of this concurrent prescription period is equivalent to either the ALDOST_ANTAGONIST start date or the POTASSIUM_CONSERVE start date (whichever one comes second). If an Aldosterone antagonist and potassium conserving drug were prescribed concurrently and any Potassium labs were taken in the year following the index date, then B12 = 0.
B13	Phosphodiesterase type-5 inhibitors (e.g., sildenafil, tadalafil, vardenafil) in severe heart failure characterized by hypotension i.e., systolic BP < 90 mmHg, or concurrent daily nitrate therapy for angina (risk of cardiovascular collapse).	If a Phosphodiesterase type-5 (PHOSPHO_TYPE5) inhibitor has ever been prescribed at any point after a hypotension diagnosis (HYPOTENSION), in someone who has previously had heart failure, then B13 = 1. If a Phosphodiesterase type-5 inhibitor (PHOSPHO_TYPE5) has ever been prescribed in the 90 days before or after a nitrate therapy (NITRATE) start date, in someone who has previously had heart failure, then B13 = 1.
C1	Long-term aspirin at doses greater than 160mg per day (increased risk of bleeding, no evidence for increased efficacy).	If aspirin (ASPIRIN) has been prescribed and the dosage is "300", "325"," 600", "200", or "500" and the frequency was daily, and the aspirin was given consistently at least every 2 months over a 6-month period then C1 = 1.
C2	Aspirin with a past history of peptic ulcer disease without concomitant PPI (risk of recurrent peptic ulcer).	If aspirin (ASPIRIN) has ever been prescribed after a peptic ulcer (PEPTIC_ULC) diagnosis then C2 = 1. If PPI (PPI) has been prescribed in the year prior to or the year after either the aspirin (ASPIRIN) or peptic ulcer

		(PEPTIC_ULC) diagnosis (whichever comes second) then C2 = 0.
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).	If Aspirin (ASPIRIN), clopidogrel (CLOPIDOGREL), dipyridamole (DIPYRIDAMOLE), a direct thrombin inhibit (THROMBIN_INHIBIT), coumadin (COUMADIN), or a factor Xa inhibitor (XA_INHIBIT) has been prescribed in the year prior to or the year after a bleeding risk disorder diagnosis (BLEEDRISK) then C3 = 1. If Aspirin (ASPIRIN), clopidogrel (CLOPIDOGREL), dipyridamole (DIPYRIDAMOLE), a direct thrombin inhibit (THROMBIN_INHIBIT), coumadin (COUMADIN), or a factor Xa inhibitor (XA_INHIBIT) has been prescribed in the year prior to or the year after an uncontrolled hypertension (UNC_HYPERTENSION) diagnosis then C3 = 1.
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)	If aspirin (ASPIRIN) has ever been prescribed in the year prior to or the year after clopidogrel (CLOPIDOGREL) was prescribed in people who have previously been diagnosed with stroke (STROKE) then C4 = 1. If someone has had a stent inserted prior to the aspirin (ASPIRIN) or clopidogrel (CLOPIDOGREL) prescription then C4 = 0. This second step was conducted by reviewing anyone who C4 = 1.
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)	If aspirin (ASPIRIN) has been prescribed in the 90 days before or after a direct thrombin inhibitor (THROMBIN_INHIBIT) or factor Xa inhibitor (XA_INHIBIT) start date in a participant where a chronic atrial fibrillation (CHRONIC_AFIB) diagnosis occurred before the aspirin (ASPIRIN) start date then C5 = 1.
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	If an Antiplatelet (ANTIPLATELET) and direct thrombin inhibitor (THROMBIN_INHIBIT) were prescribed within one year of each other and the second prescription started after a diagnosis with coronary artery disease

	therapy (no added benefit from dual therapy).	(CORONARY_ARTDISEASE), cerebrovascular disease (CEREBROVASCULAR), or peripheral artery disease (PERIPHERAL_ARTDISEASE), then C6 = 1. If an Antiplatelet (ANTIPLATELET) and factor Xa inhibitor (XA_INHIBIT_ were prescribed within one year of each other and the second prescription started after a diagnosis with coronary artery disease (CORONARY_ARTDISEASE), cerebrovascular disease (CEREBROVASCULAR), or peripheral artery disease (PERIPHERAL_ARTDISEASE), then C6 = 1.
C7	Ticlopidine in any circumstances (clopidogrel and prasugrel have similar efficacy, stronger evidence and fewer side-effects).	If ticlopidine (TICLOPIDINE) has ever been prescribed, then C7 = 1.
C8	Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first deep venous thrombosis without continuing provoking risk factors for > 6 months, (no proven added benefit).	If a direct thrombin inhibitor (THROMBIN_INHIBITOR) or factor Xa inhibitor (XA_INHIBITOR) was prescribed in the 90 days before or after the first diagnosis of deep venous thrombosis (DVT) then C8 = 1.
C9	Vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors for first pulmonary embolus without continuing provoking risk factors for > 12 months (no proven added benefit).	If a direct thrombin inhibitor (THROMBIN_INHIBITOR) or factor Xa inhibitor (XA_INHIBITOR) was prescribed in the year prior to or the year after the first diagnosis of pulmonary embolism then C9 = 1.
C10	NSAID and vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors in combination (risk of gastrointestinal bleeding).	If an NSAID (NSAID) has ever been prescribed in the 90 days before or after a Direct Thrombin Inhibitor (THROMBIN_INHIBIT), coumadin (COUMADIN) or factor Xa Inhibitor was prescribed (XA_INHIBITOR) then C10 = 1.
C11	NSAID with concurrent antiplatelet agent(s) without PPI prophylaxis (increased risk of peptic ulcer disease)	If an NSAID (NSAID) has ever been prescribed in the 90 days before or after an antiplatelet (ANTIPLATELET) was prescribed then C11 = 1. If the above criteria was met, but a PPI (PPI) was prescribed in the 90 days before or after the NSAID (NSAID) or antiplatelet (ANTIPLATELET) prescription (whichever comes second), then C11 = 0.

D1	Tricyclic antidepressants with dementia, narrow angle glaucoma, cardiac conduction abnormalities, prostatism, or prior history of urinary retention (risk of worsening these conditions).	If a tricyclic antidepressant (TRICYCLIC) has ever been prescribed after a diagnosis of dementia (DEMENTIA), narrow angle glaucoma (NARROW_GLAUC), cardiac conduction abnormality (CARDIAC_COND), prostatism (PROSTATISM), or prior history of urinary retention (UR_RETENTION) then D1 = 1.
D2	Initiation of tricyclic antidepressants as first-line antidepressant treatment (higher risk of adverse drug reactions with TCAs than with SSRIs or SNRIs).	If a tricyclic antidepressant has ever been prescribed then D2 = 1. If a tricyclic antidepressant has been prescribed at any point after an antidepressant that is non-tricyclic, then D2 = 0.
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)	If a neuroleptic (NEUROLEPTIC) has ever been prescribed after a diagnosis of prostatism (PROSTATISM) or urinary retention (UR_RETENTION) then D3 = 1.
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)	If a selective serotonin re-uptake inhibitor (SSRI) has been prescribed in the year prior to or the year after a hyponatremia diagnosis (HYPONATREMIA) then D4 = 1.
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)	If a benzodiazepine (BENZODIAZEPINE) has ever been prescribed within 6 months of another benzodiazepine (BENZODIAZEPINE) prescription then D5 = 1.
D6	Antipsychotics (i.e., other than quetiapine or clozapine) in those with parkinsonism or Lewy Body Disease (risk of severe extra-pyramidal symptoms)	If an antipsychotic (ANTIPSYCHOTIC) has ever been prescribed at any point after a Parkinson's diagnosis (PARKINSONS) or after a Lewy Body Disease Diagnosis (LEWY_BODY) then D6 = 1. If the drug label contains the phrase "QUETIAPINE" or "CLOZAPINE" then D6 = 0.
D7	Anticholinergics/antimuscarinics to treat extra-pyramidal side-effects of	If an anticholinergic (ANTICHOLINERGIC) or antimuscarinic (ANTIMUSCARINIC) has ever been prescribed in

	neuroleptic medications (risk of anticholinergic toxicity)	the 90 days prior to or the 90 days after an antipsychotic (ANTIPSYCHOTIC) then D7 = 1.
D8	Anticholinergics/antimuscarinics in patients with delirium or dementia (risk of exacerbation of cognitive impairment)	If an anticholinergic (ANTICHOLINERGIC) or antimuscarinic (ANTIMUSCARINIC) has ever been prescribed at any point after a delirium (DELIRIUM) or dementia (DEMENTIA) diagnosis then D8 = 1.
D9	Neuroleptic antipsychotic in patients with behavioural and psychological symptoms of dementia (BPSD) unless symptoms are severe and other treatments have failed (increased risk of stroke)	If a neuroleptic (NEUROLEPTIC) has ever been prescribed after a dementia (DEMENTIA) diagnosis then D9 = 1. Note we are unable to account for prior treatment failures.
D10	Neuroleptics as hypnotics, unless sleep disorder is due to psychosis or dementia (risk of confusion, hypotension, extra-pyramidal side effects, falls)	If a neuroleptic (NEUROLEPTIC) has been prescribed in the year prior to or the year after a sleep disorder (SLEEP_DISORDER) diagnosis then D10 = 1.
D11	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)	If an acetylcholinesterase inhibitor (ACETYLCHOLINESTERASE) has ever been prescribed after a diagnosis of bradycardia (BRADYCARDIA), syncope (SYNCOPE) or heart block (HEARTBLOCK) then D11 = 1. If an acetylcholinesterase inhibitor (ACETYLCHOLINESTERASE) has ever been prescribed in the year prior to or year after a prescription for beat-blocker (BETABLOCK), digoxin (DIGOXIN), diltiazem (DILTIAZEM), or verapamil (VERAPAMIL) then D11 = 1.
D12	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)	If a Phenothiazine (PHENOTHIAZINE) has ever been prescribed in the 3 months before or after a Hiccough (HICCUP) diagnosis then D12 = 1. Note we cannot determine whether this was the first-line treatment given.
D13	Levodopa or dopamine agonists for benign essential tremor (no evidence of efficacy)	If a dopamine agonist (DOPAMINE) has ever been prescribed in the year prior to or the year after a benign essential tremor (TREMOR) then D13 = 1.

D14	First-generation antihistamines (safer, less toxic antihistamines now widely available)	If a first-generation antihistamine (FIRSTGEN_ANTIHIST) has ever been prescribed then D14 = 1.
E1	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).	If Digoxin (DIGOXIN) was prescribed for more than 6 months lin the year prior to or the year after an eGFR (EGFR) result < 30 and the dosage was 250 MCG, 0.25 MG or 187.5 MCG then E1 = 1.
E2	Direct thrombin inhibitors (e.g., dabigatran) if eGFR < 30 ml/min/1.73m2 (risk of bleeding).	If a direct thrombin inhibitor (THROMBIN_INHIBIT) was prescribed at all in the year prior to or the year after an eGFR (EGFR) result < 30 then E2 = 1.
E3	Factor Xa inhibitors (e.g., rivaroxaban, apixaban) if eGFR < 15 ml/min/1.73m2 (risk of bleeding).	If a Factor Xa Inhibitor (XA_INHIBIT) was prescribed at all in the year prior to or the year after an eGFR (EGFR) result < 15 then E3 = 1.
E4	NSAID's if eGFR < 50 ml/min/1.73m2 (risk of deterioration in renal function).	If an NSAID (NSAID) was prescribed at all in the year prior to or the year after an eGFR (EGFR) result < 50 then E4 = 1.
E5	Colchicine if eGFR < 10 ml/min/1.73m2 (risk of colchicine toxicity).	If colchicine (COLCHICINE) was prescribed at all in the year prior to or the year after an eGFR (EGFR) result < 10 then E5 = 1.
E6	Metformin if eGFR < 30 ml/min/1.73m2 (risk of lactic acidosis).	If metformin (METFORMIN) was prescribed at all in the year prior to or the year after an eGFR (EGFR) result < 30 then E6 = 1.
F1	Prochlorperazine or metoclopramide with Parkinsonism (risk of exacerbating Parkinsonian symptoms).	If Prochlorperazine (PROCHLORPERAZINE) or Metoclopramide (METOCLOPRAMIDE) has ever been prescribed at any point after a Parkinsonism (PARKINSONISM) or Parkinson's diagnosis (PARKINSONS), then F1 =1.
F2	PPI for uncomplicated peptic ulcer disease or erosive peptic oesophagitis at full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated).	If a PPI (PPI) has been prescribed in the year prior to or the year after a peptic ulcer (PEPTIC_ULC) diagnosis then F2 =1.
F3	Drugs likely to cause constipation (e.g., antimuscarinic/anticholinergic drugs, oral iron, opioids, verapamil, aluminium antacids) in patients with chronic constipation where non-consipating alternatives are appropriate (risk of exacerbation of constipation).	If an antimuscarinic (ANTIMUSCARINIC), anticholinergic (ANTICHOLINERGIC), oral iron (IRON), opioids (OPIOID), verapamil (VERAPAMIL), or aluminium antacid (ANTACID) is prescribed at any point after a chronic constipation

		(CHRONIC_CONST) diagnosis then F3 = 1.
F4	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).	If someone had an iron prescription with any of the following doses: 220 MG/5 ML ELIX, 300 MG/5 ML LIQ, 300 MG/6.8ML SOLN, 324 MG TABLET, 325 MG TABLET, 325 (65 FE) MG, 325 MG TABLET, 325 MG TABLET
G1	Theophylline as monotherapy for COPD (safer, more effective alternative; risk of adverse effects due to narrow therapeutic index).	If theophylline (THEOPHYLLINE) was prescribed at all in the year prior to or the year after a COPD diagnosis then G1 = 1. If the theophylline (THEOPHYLLINE) prescription was given in the 90 days prior to or 90 days after a COPD medication (COPD_MED), then G1 = 0.
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).	If systemic corticosteroids (SYS_CORTICOSTEROID) have been prescribed over a period of more than 183 days at any point after a COPD (COPD) diagnosis then G2 = 1.
G3	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).	If an Anti-muscarinic bronchodilator (ANTIMUSCARINIC_BRONCH) was prescribed at any point after a diagnosis of narrow angle glaucoma (NARROW_GLAUC) or bladder outflow obstruction (BLADDER_OBS) then G3 = 1.
G4	Benzodiazepines with acute or chronic respiratory failure i.e., pO2 < 8.0 kPa ± pCO2 > 6.5 kPa (risk of exacerbation of respiratory failure).	If a Benzodiazepine (BENZODIAZEPINE) was prescribed at any point in the year prior to or the year after an acute or chronic or unspecified respiratory failure (RESPFAIL) diagnosis then G4 = 1.
H1	Non-COX-2 selective non-steroidal anti-inflammatory drug (NSAID) with history of peptic ulcer disease or gastrointestinal bleeding, unless with concurrent PPI or H2 antagonist (risk of peptic ulcer relapse).	If a Non-COX-2 selective NSAID (NONCOX2_NSAID) has ever been prescribed after a diagnosis of peptic ulcer (PEPTIC_ULC) or gastrointestinal bleeding (GASTRO_BLEED) then H1 = 1. If PPI (PPI) or an H2 antagonist (H2_ANTAG) has been prescribed in the year prior to or the year after the Non-COX-2 selective NSAID (NONCOX2_NSAID) then H1 = 0.
H2	NSAID with established hypertension (risk of exacerbation of hypertension)	If an NSAID (NSAID) has been prescribed in the year prior to or the year after a hypertension

	or heart failure (risk of exacerbation of heart failure).	(HYPERTENSION) or heart failure (HEARTFAIL) diagnosis then H2 = 1.
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)	If an NSAID (NSAID) has been prescribed in the year prior to or the year after an osteoarthritis (OSTEOARTHRITIS) diagnosis then H3 = 1. If paracetamol (PARACETAMOL) has been prescribed prior to the osteoarthritis (OSTEOARTHRITIS) diagnosis, then H3 = 0.
H4	Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthritis (risk of systemic corticosteroid side-effects).	If a corticosteroid (CORTICOSTEROID) has been prescribed in the year prior to or the year after a rheumatoid arthritis diagnosis (ARTHRITIS) then H4 = 1. If corticosteroids (CORTICOSTEROID) have been prescribed more than 90 days apart at any point after a rheumatoid arthritis (ARTHRITIS) diagnosis then H4 = 1. If an NSAID (NSAID) or drug with the class "ANTI-ARTHRITIC" or "DISEASE-MODIFYING ANTIRHEUMATIC AGENTS" was prescribed within 30 days of one of the corticosteroids, then H4 = 0.
H5	Corticosteroids (other than periodic intra-articular injections for mono-articular pain) for osteoarthritis (risk of systemic corticosteroid side-effects).	If a corticosteroid (CORTICOSTEROID) has been prescribed in the year prior to or the year after an osteoarthritis (OSTEOARTHRITIS) diagnosis then H5 = 1. If the corticosteroid drug label contains one of the following phrases: "INJ", "MG/" then H5 =0.
H6	Long-term NSAID or colchicine for prevention of relapses 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).	If an NSAID (NSAID) or colchicine (COLCHICINE) has ever been prescribed after a gout (GOUT) diagnosis then H6 = 1. If xanthine-oxidase inhibitor (XANTHINE_OXIDASE) has been prescribed prior to any of the NSAID (NSAID) or colchicine (COLCICHINE) prescriptions then H6 = 0.
H7	COX-2 selective NSAIDs with concurrent cardiovascular disease (increased risk of myocardial infarction and stroke)	If a COX-2 selective NSAID (COX2_NSAID) has ever been prescribed in the year prior to or the year after a cardiovascular disease (CVD) diagnosis then H7 = 1.

H8	NSAID with concurrent corticosteroids without PPI prophylaxis (increased risk of peptic ulcer disease)	If an NSAID (NSAID) has ever been prescribed in the 90 days before or after a corticosteroid (CORTICOSTEROID) prescription then H8 = 1. If PPI (PPI) has been prescribed in the 90 days before or after either of the NSAID (NSAID) or corticosteroid (CORTICOSTEROID) prescription, then H8 = 0.
H9	Oral bisphosphonates in patients with a 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)	If an oral bisphosphonate (BISPHOSPHONATE) has ever been prescribed after an upper gastrointestinal disease (UPPER_GASTRO) diagnosis then H9 = 1.
I1	Antimuscarinic drugs for overactive bladder syndrome with concurrent 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).	If an antimuscarinic (ANTIMUSCARINIC) was prescribed in the year prior or year after a dementia (DEMENTIA), chronic cognitive impairment (CHRONIC_COG_IMPAIR), or chronic prostatism (CHRONIC_PROST) diagnosis then I1 = 1.
I2	Selective alpha-1 selective alpha blockers in those with symptomatic orthostatic hypotension or micturition syncope (risk of precipitating recurrent syncope)	If a selective alpha-1 selective alpha blocker (SELECT_ALPHA_BLOCK) was prescribed in the year prior to or the year after a symptomatic orthostatic hypotension (ORTHO_HYPO) diagnosis or a micturition syncope (MICTUR_SYNCOPE) diagnosis then I1 = 1.
J1	Sulphonylureas with a long duration of action (e.g., glibenclamide, chlorpropamide, glimepiride) with type 2 diabetes mellitus (risk of prolonged hypoglycaemia).	If a Sulfonylureas (SULFONYLUREAS) was prescribed at any point after the earliest diabetes diagnosis date (the minimum of first diabetes medication, lab, or diagnosis date) then J1 = 1.
J2	Thiazolidenediones (e.g., rosiglitazone, pioglitazone) in patients with documented heart failure (risk of exacerbation of heart failure)	If a Thiazolidinedione (THIAZOLIDINEDIONE) has been prescribed at any point after a heart failure (HEARTFAIL) diagnosis then J2 = 1.
J3	Beta-blockers in diabetes mellitus with frequent hypoglycaemic episodes (risk of suppressing hypoglycaemic symptoms).	If a Beta-Blocker was prescribed at any point after the earliest diabetes diagnosis date (the minimum of first diabetes medication, lab, or diagnosis date) and the person has ever had more than 2 diagnoses of

		hypoglycemia within 90 days of each other then J3 = 1.
J4	Oestrogens with a history of breast cancer or venous thromboembolism (increased risk of recurrence).	If an estrogen (ESTROGEN) has ever been prescribed after the diagnosis date of breast cancer (BREAST-CANCER) or venous thromboembolism (VENOUSTHROMB) then J4 = 1.
J5	Oestrogens without progestogen in patients with intact uterus (risk of endometrial cancer).	If an estrogen (ESTROGEN) has ever been prescribed in a person assigned female sex at birth then J5 = 1. If a progesterone (PROGESTERON) has been prescribed in combination with estrogen (ESTROGEN) or in the year prior to or after the estrogen (ESTROGEN) prescription then J5 = 0. If the person has had a hysterectomy (HYSTERECTOMY) before the estrogen (ESTROGEN) start date, then J5 = 0.
J6	Androgens in the absence of primary or secondary hypogonadism (risk of androgen toxicity; no proven benefit outside of hypogonadism indication).	If an androgen (ANDROGEN) has been prescribed at any point then J6 = 1. If there has been a diagnosis of hypogonadism (HYPOGONADISM) at any point before the androgen prescription, then J6 = 0.
K1	Benzodiazepines (sedative, may cause reduced sensorium, impair balance)	If an individual has ever been age 65 or older on the start date of a benzodiazepine (BENZODIAZEPINE) prescription, then K1 = 1.
K2	Neuroleptic drugs (may cause gait dyspraxia, Parkinsonism)	If an individual has ever been age 65 or older on the start date of a neuroleptic (NEUROLEPTIC) drug prescription, then K2 = 1.
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)	If an individual has ever been age 65 or older on the start date of a vasodilator (VASODILATOR) drug prescription and the prescription was given at any point after a hypotension (HYPOTENSION) diagnosis, then K3 = 1.
K4	Hypnotic Z-drugs (e.g., zopiclone, zolpidem, zaleplon) (may cause protracted daytime sedation, ataxia)	If an individual has ever been age 65 or older on the start date of a hypnotic Z-drug (HYPNOTIC_Z) drug prescription, then K4 = 1.
L1	Use of oral or transdermal strong opioids (morphine, oxycodone, fentanyl, buprenorphine, diamorphine, methadone, tramadol, pethidine,	If a strong opioid (STRONG_OPIOID) has ever been prescribed then L1 = 1. If an NSAID (NSAID) or drug with one of the following labels: Acetaminophen, Tylenol, lyrica, duloxetine, or

	pentazocine) as first line therapy for mild pain (WHO analgesic ladder not observed)	gabapentin; has ever been prescribed prior to the opioid prescription, then L1 = 0 as this suggests the strong opioid was not a first-line treatment.
L2	Use of regular (as distinct from PRN) opioids without concomitant laxative (risk of severe constipation)	If someone has ever been prescribed a regular opioid then L2 = 1. If a laxative has been prescribed in the 90 days before or after an opioid, then L2 = 0.
L3	Long-acting opioids without short-acting opioids for break-through pain (risk of non-control of severe pain)	If someone has ever been prescribing a long-acting opioid (LONG_OPIOID) then L3 = 1. If a short-acting opioid (SHORT_OPIOID) was prescribed in the 30 days prior or 30 days after the long-acting opioid (LONG_OPIOID) then L3 = 0. *Note:* SHORT_OPIOID and LONG_OPIOID were defined on a separate spreadsheet found here: "C:\Users\laurenoconnor\Box\PolyPharm Project (DCHIV62)\Long vs Short Acting Opioids.xlsx"
M1	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)	If an antimuscarinic or anticholinergic has been prescribed in the 90 days before or after another antimuscarinic or anticholinergic prescription then M1 = 1. If the drug names are equivalent and the prescription dates were the same day, then M1 = 0.

Table S4. Detailed definitions of drug classifications in the study sample.

Drug Class Name	Variable Name	Criteria	Exclusions
Loop Diuretics	**LOOPDIURETIC**	If any of the drug classes contain the phrase "LOOP DIURETIC"	None
Thiazide	**THIAZIDE**	If any of the drug classes contain the phrase "THIAZIDE"	None
Ace Inhibitor	**ACEINHIBIT**	If any of the drug classes contain the following phrases: "ANTIHYPERTENSIVES, ACE INHIBITORS", "ANTIHYPERTENSIVES,ACE INHIBITOR/DIETARY SUPP.COMB.", "ACE INHIBITOR-THIAZIDE OR THIAZIDE-LIKE DIURETIC","ACE INHIBITOR-CALCIUM CHANNEL BLOCKER COMBINATION" or "ANGIOTENSIN"	If any of the drug classes contain the phrase "RENIN-ANGIOTENSIN-ALDOSTERONE SYST(RAAS)"

Diltiazem	**DILTIAZEM**	If the drug label contains any of the following phrases: “DILT”, “CARDIZEM”, “CARTIA”, “MATZIM”, “TAZTIA”, “TIADYLT” or “TIAZAC”	None
Verapamil	**VERAPAMIL**	If the drug label contains any of the following phrases: “VERAPAMIL”, “CALAN” or “VERELAN”	None
Beta Blockers	**BETABLOCK**	If any of the drug classes contain the phrase “BETA”	If any of the drug classes contain any of the following phrases: "AGONIST", "BETA-ADRENERGIC AGENTS", "BETA-ADRENERGIC AGENTS, INHALED, SHORT ACTING", "BETA-ADRENERGIC AGENTS, INHALED, ULTRA-LONG ACTING", "BETA-ADRENERGIC AGENTS, ORALLY INHALED,LONG ACTING", "BETA-ADRENERGIC AND ANTICHOLINERGIC COMBO, INHALED", "BETA-ADRENERGIC AND GLUCOCORTICOID COMBO, INHALED", "BETA-ADRENERGIC-ANTICHOLINERGIC-GLUCOCORT, INHALED", "BETALACTAMS", "NICOTINIC RECEPT.PARTIAL AGONIST, ALPHA4BETA2 SPEC", "OVERACTIVE BLADDER AGENTS, BETA-3 ADRENERGIC RECEP", or "NON-SELECT.BETA-ADRENERGIC AGONT(RESPIR)"
Amiodarone	**AMIODARONE**	If the drug label contains the phrase “AMIODARONE”	None
Centrally-Acting Antihypertensive	**CENTRAL_ANTIHYPER**	If the drug label contains any of the following phrases: “METHYLDOPA”, “CLONIDINE”, “MOXONIDINE”, “RILMENIDINE”, “GUANFACINE”, “GUANABENZ”, “TIZANID” or “MEDETOMID”	None
Aldosterone Antagonist	**ALDOST_ANTAGONIST**	If any of the drug classes contain any of the following phrases: “MINERALOCORTICOID (ALDOSTERONE) ANTAGNTS”, “MINERALOCORTICOID(ALDOSTER.)ANTAG(HYPOT)”	

Potassium-Conserving Drugs	**POTASSIUM_CONSERVE**	If ACEINHIBIT = 1 or the drug label contains any of the following phrases: "AMILORIDE", "TRIAMTERENE", "SPIRONOLACTONE", "EPLERENONE", "FINERENONE", "BENAZEPRIL", "CAPTOPRIL", "ENALAP", "AMILORIDE", "EPLERENONE", "INSPRA", "ALDACTONE", "CAROSPIR", "TRIAMTERENE", or "DYRENIUM"	None
Phosphodiesterase type-5 Inhibitors	**PHOSPHO_TYPE5**	If the drug label contains any of the following phrases: "SILDENAFIL", "TADALAFIL", or "VARDENAFIL" OR if any of the drug classes contain the following phrase: "PHOSPHODIESTERASE TYPE 5 INHIBITORS"	None
Digoxin	**DIGOXIN**	If the drug label contains any of the following phrases: "DIGITEK", "DIGOX", or "LANOXIN"	
Nitrate Therapy	**NITRATE**	If the drug label contains the phrase: "NITROGLYCERIN" or "ISOSORBIDE" or "NITRO-DUR" or "NITRO-TIME"	None
Direct Thrombin Inhibitor	**THROMBIN_INHIBIT**	If any of the drug classes contain one of the following phrases: "THROMBIN INHIBIT" or "HEPARIN" OR if the drug label contains the phrase: "FONDAPARINUX"	None
Direct Factor Xa Inhibitor	**XA_INHIBIT**	If any of the drug classes contain the following phrase: "FACTOR XA INHIBITOR"	None
Non-Steroidal Anti-Inflammatory Drug (NSAID)	**NSAID**	If any of the drug classes contain one of the following phrases: "NSAID", "NONSTEROIDAL ANTI-INFLAM", "ANALGESICS, NON-OPIOID", "NON-OPIOID ANTITUS-1ST ANTIHIST-DECON-ANALG-EXPECT", "NON-OPIOID ANTITUS-1ST GEN ANTIHIST-ANALGESIC COMB", "NON-OPIOID ANTITUS-1STGEN	If any of the drug classes contain the phrase "SKIN" or "EYE"

		ANTIHIST-DECON-ANALGESIC", "NON-OPIOID ANTITUSS-DECONGESTANT-ANALGESIC-EXPECT", "NON-OPIOID ANTITUSSIVE-ANALGESIC COMBINATIONS", "NON-OPIOID ANTITUSSIVE-ANALGESIC-EXPECTORANT COMB.", or "NON-OPIOID ANTITUSSIVE-DECONGESTANT-ANALGESIC COMB" OR If the drug class contains both of the following phrases "COX-2" and "INHIBITOR"	
Colchicine	**COLCHICINE**	If any of the drug classes contain the following phrase: "COLCHICINE" Or if the drug label contains one of the following phrases: "COLCRYS" or "MITIGARE"	None
Metformin	**METFORMIN**	If the drug label contains one of the following phrases: "METFORMIN" or "ANTIHYPERGLYCEMIC"	None
Theophylline	**THEOPHYLLINE**	If the drug label contains one of the following phrases: "THEOPHYLLINE", "THEO-24", or "ELIXOPHYLLIN"	None
Systemic Corticosteroids	**SYS_CORTICOSTEROID**	If any of the drug classes contain one of the following phrases: "CORTICOSTER" or "GLUCOCORTICOID"	If any of the drug classes or drug label contain one of the following phrases: "SKIN", "TOPICAL", "EYE", "INHALE", "NASAL", "OINTMENT", "CREAM", "SHAMPOO", "POWDER", "PWD"
Anti-muscarinic	**ANTIMUSCARINIC**	If any of the drug classes contain the following phrase: "ANTIMUSCARINIC"	
Anti-muscarinic Bronchodilator	**ANTIMUSCARINIC_BRONCH**	If any of the drug classes contain the following phrase: "ANTIMUSCARINIC"	To Be Determined
Benzodiazepines	**BENZODIAZEPINE**	If any of the drug classes contain the following phrase: "BENZODIAZEPINE"	
Prochlorperazine	**PROCHLORPERAZINE**	If the drug label contains the following phrase: "PROCHLORPERAZINE"	None

Metoclopramide	**METOCLOPRAMIDE**	If the drug label contains the following phrase: "METOCLOPRAMIDE"	None
Proton-Pump Inhibitor	**PPI**	If any of the drug classes contain the phrase: "PROTON-PUMP INHIBITOR"	If the drug label contains the phrase "DAPIPRAZOLE" or "ARIPIPRAZOLE"
Anticholinergic	**ANTICHOLINERGIC**	If any of the drug classes contain the following phrase: "ANTICHOLINERGIC" or if ANTIMUSCARINIC = 1	None
Opioids	**OPIOID**	If any of the drug classes contain one of the following phrases: "OPIOID ANALGESIC"; "OPIOID ANTITISSIV", "OPIATE AGONISTS", "OPIATE PARTIAL AGONISTS"	
Aluminium Antacids	**ANTACID**	If any of the drug classes contain the following phrase: "ANTACID"	
Aluminium Antacids Confirmed Brand Names	**ANTACID_BRANDS**	If ANTACID = 1 and the drug label contains one of the following brand names: ""	
Oral Iron	**IRON**	If any of the drug classes contain one of the following phrases: "FERROUS FUMARATE", "FERROUS GLUCONATE", "FERROUS SULF", "FERROUSUL", "FERRIC SULF", "FERROUS BISGLYCINATE CHELATE"	
Selective alpha-1 selective alpha blockers	**SELECT_ALPHA_BLOCK**	If any of the drug classes contain the following phrase: "SELECTIVE ALPHA-1-ADRENERGIC BLOCK.AGENT" OR if the drug label contains one of the following phrases: "ALFUZOSIN", "PRAZOSIN", "DOXAZOSIN", "TAMSULOSIN", "TERAZOSIN", "SILODOSIN", "PHENOXYBENZAMINE" or "ERGOTAMINE"	
Sulfonylureas with long duration of action	**SULFONYLUREAS**	If a drug label contains one of the following phrases: "CHLORPROPAMIDE", "GLIMEPIRIDE" OR "GLYBURIDE" OR if the drug label contains the phrase "GLIPIZIDE" and either "ER" or "EXTEND"	

Thiazolidinediones	**THIAZOLIDINEDIONE**	If any of the drug classes contain the following phrase: "THIAZOLIDINEDIONE"	
Estrogens	**ESTROGEN**	If any of the drug classes contain the following phrase: "ESTROGEN"	If any of the drug classes contain one of the following phrases: "ESTROGEN AGONIST-ANTAGONISTS" OR if the drug label contains any of the following phrases "POWDER", "CREAM", "PWD", "GEL"
Progesterone	**PROGESTIN**	If the any of the drug classes contain the phrase "PROGESTIN"	If the drug label contains any of the following phrases "POWDER", "CREAM", "PWD", "GEL"
Androgens	**ANDROGEN**	If any of the drug classes contain the phrase: "ANDROGEN"	If any of the drug classes contain the phrase: "ANTIANDRO" OR if the drug label contains any of the following phrases "POWDER", "CREAM", "PWD", "GEL"
Antipsychotics	**ANTIPSYCHOTIC**	If any of the drug classes contain the following phrase: "ANTIPSYCH"	
Hypnotic Z-Drugs	**HYPNOTIC_Z**	If the drug label contains any of the following phrases: "ZOPICLONE", "ZOLPIDEM", "ZALEPLON"	
Alpha-1 Receptor Blockers	**ALPHA1_BLOCK**	If any of the drug classes contain the phrase "ALPHA" AND any of the drug classes contain the phrase "BLOCK" or "ANTAG"	
Calcium Channel Blockers	**CALCIUM_BLOCK**	If any of the drug classes contain the phrase "CALCIUM" AND any of the drug classes contain the phrase "BLOCK"	
Vasodilators	**VASODILATOR**	If the drug was marked previously as "ALPHA1_BLOCK", "CALCIUM_BLOCK" or "ACEINHIBIT" OR if any of the drug classes contain the phrase "VASODILAT" OR if the drug label contains one of the following phrases: "ISOSORBIDE MONONIT ER"	

Strong Opioids	**STRONG_OPIOID**	If the drug label contains any of the following phrases: "MORPHINE", "OXYCODONE", "FENTANYL", "BUPRENORPHINE", "DIAMORPHINE", "METHADONE", "TRAMADOL", "PETHIDINE", "PENTAZOCINE"	
Laxatives	**LAXATIVE**	If the drug class contains the following phrase: "LAXATIVE"	
Aspirin	**ASPIRIN**	If the drug label contains the phrase "ASPIRIN"	If the drug label contains the phrase "NON"
Clopidogrel	**CLOPIDOGREL**	If the drug label contains the following phrase "CLOPIDOGREL"	
Dipyridamole	**DIPYRIDAMOLE**	If the drug label contains the following phrase "DIPYRIDAMOLE"	
Ticlopidine	**TICLOPIDINE**	If the drug label contains the following phrase: "TICLOPIDINE"	
Antiplatelet	**ANTIPLATELET**	If any of the drug classes contain one of the following phrases: "PLATELET AGGREGATION INHIBITORS", "PLATELET REDUCING AGENTS", "PLATELET-AGGREGATION INHIBITORS", "PLATELET-REDUCING AGENTS"	
Tricyclic Antidepressants	**TRICYCLIC**	If any of the drug classes contain one of the following phrases: "TRICYCLICS, OTHER NOREPI-RU INHIBITORS", "TRICYCLIC ANTIDEPRESSANT"	
Neuroleptics with Antimuscarinic/Anticholinergic Effects	**NEURO_ANTIMUSC_ANTICHOL**	If the drug label contains one of the following phrases: "CHLORPROMAZINE", "CLOZAPINE", "FLUPENTHIXOL", "FLUPHENZINE", "PIPOTHIAZINE", "PROMAZINE", "ZUCLOPENTHIXOL"	
Selective Serotonin Re-uptake Inhibitor (SSRI)	**SSRI**	If any of the drug classes contain one of the following phrases: "FIBROMYALGIA AGENTS,SEROTONIN-NOREPINEPH RU INHIB", "SELECTIVE SEROTONIN REUPTAKE INHIBITOR	

		(SSRIS)", "SEROTONIN-2 ANTAGONIST/REUPTAKE INHIBITORS (SARIS)", "SEROTONIN-NOREPINEPHRINE REUPTAKE-INHIB (SNRIS)", "SSRI-ANTIPSYCH, ATYPICAL,DOPAMINE,SEROTONIN ANTAG", "SEL.SEROTONIN,NOREPI REUPTAKE INHIBITOR", "SELECTIVE-SEROTONIN REUPTAKE INHIBITORS", "SEL.SEROTONIN,NOREPI REUPTAKE INHIBITOR"
Acetylcholinesterase inhibitor	**ACETYLCHOLINESTERASE**	If any of the drug classes contain any of the following phrases: "CHOLINESTERASE INHIBITOR", "PARASYMPATHOMIMETIC (CHOLINERGIC AGENTS)"
Phenothiazines	**PHENOTHIAZINE**	If any of the drug classes contain the phrase: "PHENOTHIAZINE"
Dopamine Agonist	**DOPAMINE**	If any of the drug labels contain one of the following phrases: "BROMOCRIPTINE", "CYCLOSET", "PARLODEL", "CABERGOLINE", "DOSTINEX". "AMANTADINE", "GOCOVRI", "OSMOLEX", "APOMORPHINE", "APOKYN", "KYNMOBI", "FENOLDOPAM", "CORLOPAM", "PRAMIPEXOLE", "MIRAPEX", "ROPINIROLE", "REQUIP", "ROTIGOTINE", "NEUPRO"
First-Generation Antihistamines	**FIRSTGEN_ANTIHIST**	If any of the drug classes contain one of the following phrases: "1ST GEN ANTIHIST", "1ST GENERATION ANTIHIST", "1ST GEN ANTIHIST", "1ST GEN.ANTIHISTAMINE", "1ST GEN. ANTIHISTAMINE", "ANTIHISTAMINES - 1ST GENERATION", "1ST ANTIHIST", "1STGEN ANTIHIST", "FIRST GEN. ANTIHIST.", "FIRST GENERATION ANTIHIST"

Non-COX-2 selective NSAID	**NONCOX2_NSAID**	If NSAID = 1	If COX2_NSAID = 1
Paracetamol	**PARACETAMOL**	If the drug label contains the phrase "ACETAMINOPHEN" or "TYLENOL"	
Corticosteroid	**CORTICOSTEROID**	If any of the drug classes contain one of the following phrases: "CORTICOSTER" or "GLUCOCORTICOID"	
COX-2 selective NSAID	**COX2_NSAID**	If the any of the drug classes contain the phrase: "COX" or "CYCLOOXYGENASE" OR If the drug class contains both of the following phrases "COX-2" and "INHIBITOR"	
Xanthine-Oxidase Inhibitor	**XANTHINE_OXIDASE**	If any of the drug classes contain the phrase "XANTHINE OXIDASE INHIBITOR"	
Oral Bisphosphonates		If the drug label contains the phrase "ALENDRONATE", "RISEDRONATE", "IBANDRONATE", "ZOLEDRONIC ACID"	If the drug label contains the phrase "SYRINGE" or "VIAL"
H2 Antagonist	**H2_ANTAG**	If any of the drug classes contain one of the following phrases: "HISTAMINE H2-ANTAGONISTS", "HISTAMINE H2-RECEPTOR INHIBITORS"	
Coumadin	**COUDMADIN**	If the drug label contains the phrase "COUMADIN"	
Antidepressant	**ANTIDEPRESSANT**	If the drug class contains the phrase "ANTIDEPRESSANT"	
Neuroleptic (first-line antipsychotic)	**NEUROLEPTIC**	If the drug label contains one of the following phrases: "CHLORPROMAZINE", "CLOZAPINE", "FLUPENTHIXOL", "FLUPHENZINE", "PIPOTHIAZINE", "PROMAZINE", "ZUCLOPENTHIXOL"	
COPD Medication	**COPD_MED**	If the drug label contains one of the following phrases: "AFORMOTEROL", "BROVANA", "FORMOTEROL", "PERFOROMIST", "FORADIL", "OXEZE TURBUHALER", "INDACATEROL", "ARCAPTA	

NEOHALER", "ONBREZ BREEZHALER", "OLODATEROL", "STRIVERDI RESPIMAT", "SALMETEROL", "SEREVENT DISKUS", "ACLIDINIUM", "TUDORZA PRESSAIR", "TUDORZA GENUAIR", "GLYCOPYRROLATE", "GLYCOPYRRONIUM", "SEEBRI BREEZHALER", "LONHALA MAGNAIR", "TIOTROPIUM", "SPIRIVA", "UMECLIDINIUM", "INCRUSE ELLIPTA", "REVEFENACIN", "YUPELRI", "DUAKLIR PRESSAIR", "ULTIBRO BREEZHALER", "BEVESPI AEROSPHERE", "STIOLTO RESPIMAT", "INSPIOLTO RESPIMAT", "ANORO ELLIPTA", "FLUTICASONE", "TRELEGY ELLIPTA", "BUDESONIDE", "BREZTRI AEROSPHERE", "MOMETASONE", "BECLOMETASONE", "BUDESONIDE"

Table S5. Detailed overview of diagnosis and other comorbidity definitions.

Diagnosis	Variable Name	Criteria	Exclusions
Class I Heart Failure	**CLASSIHEARTFAIL**	If the ICD diagnosis description contains the phrase "NYHA class I"	None
Heart Failure	**HEARTFAIL**	If the ICD9 code contains the code "428." or if the ICD10 code contains the code "I50."	None
Bradycardia	**BRADYCARDIA**	If the ICD diagnosis description contains the phrase "Symptomatic bradycardia"	None
Flagged Bradycardia	**FLAG_BRADYCARDIA**	If the ICD diagnosis description contains the phrase "radycardia"	None
Supraventricular Tachyarrhythmia	**SUPRATACHY**	If the ICD diagnosis description contains either of the following phrases: "SUPRAVENTRICULAR TACHYCARDIA" or "Supraventricular tachycardia"	None
Heart Block	**HEARTBLOCK**	If the ICD diagnosis description contains any of the following phrases: "I45.9; Heart block", "426.6; Other heart block", "426.9; Heart block NOS", "I44.1; Second degree heart block", "I45.5; Other specified heart block", "AV block" or "trioventricular block"	None
Ankle Oedema/Edema	**ANKLEEDEMA**	If the ICD diagnosis description contains any of the following phrases: "EDEMA" or "edema" AND contains one of the following phrases: "ANKLE" or "nkle"	None
Liver Failure	**LIVERFAIL**	If the ICD diagnosis description contains any of the following phrases: "LIVER", "Liver" or "liver" AND contains at least one of the following phrases: "FAIL", "Fail", "fail", "TRANS", "Trans", or "trans" Also, if the ICD diagnosis description contains any of the following phrases: "HEPATIC", "Hepatic" or "hepatic" AND at least one of the following phrases "FAIL", "Fail" or "fail" Also, if the ICD diagnosis description is: "572.2; HEPATIC ENCEPHALOPATHY","572.2; Hepatic encephalopathy", or "572.2; HEPATIC COMA"	If the ICD code description is equal to one of the following: "642.31; TRANSIENT HYPERTENSION OF PREGNANCY W/DELIVERY", "O34.211; Maternal care for low transverse scar from previous cesarean delivery", "R74.01; ELEVATION LEVELS LIVER TRANSAMINASE LEVELS", "R74.01; Elevated liver transaminase level", "R74.01; Elevation of levels of liver transaminase levels"
Nephrotic Syndrome	**NEPHSYN**	If the ICD diagnosis description contains any of the following phrases:	If the ICD diagnosis description is equivalent to

		“NEPHROTIC”, “Nephrotic”, or “nephrotic” AND contains at least one of the following phrases: “SYN”, “Syn”, or “syn”	"Z87.441; Personal history of nephrotic syndrome" OR if the ICD diagnosis code contains the phrase “N04”
Renal Failure	**RENALFAIL**	If the ICD diagnosis description contains any of the following phrases: “RENAL”, “Renal”, or “renal” AND it contains at least one of the following phrases: “FAIL”, “fail”, or “Fail” Also, if the ICD diagnosis description contains any of the following phrases: “KIDNEY”, “Kidney”, or “kidney” AND it contains at least one of the following phrases: “FAIL”, “fail”, or “Fail” Also, if the ICD diagnosis contains one of the following phrases: “ESRD” or “esrd” OR If the ICD diagnosis contains the phrase “Z99.2”	If the ICD diagnosis description is equivalent to one of the following: "Z87.448; History of acute renal failure", "Z87.448; History of renal failure", "I13.2; Hypertensive heart and chronic kidney disease with heart failure and with s", "I13.10; Hypertensive heart and chronic kidney disease without heart failure, with s", "I13.0; Hypertensive heart and chronic kidney disease with heart failure and stage 1 through stage 4 chronic kidney disease, or unspecified chronic kidney disease", "I13.0; Hypertensive heart and chronic kidney disease with heart failure and stage", "404.03; Hypertensive Heart and Chronic Kidney Disease, Malignant, with Heart Failur", "404.10; Hypertensive Heart and Chronic Kidney Disease, Benign, without Heart Failur"
Cirrhosis	**CIRRHOSIS**	If the ICD diagnosis description contains any of the following phrases: “irrhosis” or “CIRRHOSIS”	If the ICD diagnosis description is equivalent to the following: "Z87.19; History of cirrhosis of liver"
Urinary Incontinence	**UR_INCONTINENCE**	If the ICD9 code is “788.3”, “788.39”, “788.30” or “788.91” OR the ICD10 code is “R32”, “N39.49”, “N39.498”, “N39.4”, or “R39.81”	If the ICD diagnosis description is equivalent to the following: "788.3; INCONTINENCE, STOOL", "788.30; Incontinence", "788.3; INCONTINENCE", "788.3; Incontinence”, "R32; Incontinence", or "R32; Incontinence in female"

Hyperkalemia	**HYPERKALEMIA_DX & HYPERKALEMIA _LX**	If the ICD9 code is "276.8" or if the ICD10 code is "E87.6" OR There is a lab that contains one of the following phrases: "otassium" or "POTASSIUM" and the result is above 6 OR There is a lab that is labeled "K" and the result is above 6 The diagnosis date is whichever date comes first.	The lab units are missing.
Hypokalemia	**HYPOKALEMIA_DX & HYPOKALEMIA _LX**	If the ICD9 code is "276.8" or if the ICD10 code is "E87.6" OR There is a lab that contains one of the following phrases: "otassium" or "POTASSIUM" and the result is below 3 OR There is a lab that is labeled "K" and the result is below 3 The diagnosis date is whichever date comes first.	The lab units are missing.
Hyponatremia	**HYPONATREMIA_DX & HYPONATREMIA_LX**	If the ICD9 code is "276.1" OR There is a lab that contains one of the following phrases: "odium" or "SODIUM" and the result is below 130 OR There is a lab that is labeled "Na" and the result is below 130 The diagnosis date is whichever date comes first.	The lab units are missing.

Hypercalcemia	**HYPERCALCEMIA_DX & HYPERCALCEMIA_LX**	If the ICD9 code is "275.42" or if the ICD10 code is "E83.52" OR There is a lab that contains one of the following phrases: "alcium" or "CALCIUM" and the result is above 25 OR There is a lab that is labeled "Ca" and the result is above 2.65 The diagnosis date is whichever date comes first.	The lab units are missing
Gout	**GOUT**	If the ICD diagnosis description contains any of the following phrases: "GOUT", "Gout", "gout", "PODAGRA" or "odagra"	None
Hypotension/Severe Heart Failure	**HYPOTENSION**	If there has ever been a systolic blood pressure < 50 mm/Hg	None
Estimates Glomerular Filtration Rate	**EGFR**	Any labs are considered an EGFR lab if they have LXC code "LXC635" or "LXC636"	None
Chronic Obstructive Pulmonary Disease (COPD)	**COPD**	If the ICD code diagnosis description contains any of the following phrases: "COPD", "Chronic Obstructive Pulmonary", "chronic obstructive pulmonary", "CHRONIC OBSTRUCTIVE PULMONARY", "Chronic obstructive pulmonary", "Chronic Lung Pulmonary", "chronic lung pulmonary", "CHRONIC LUNG PULMONARY", "Chronic lung pulmonary"	None
Narrow Angle Glaucoma	**NARROW_GLAUC**	If the ICD code contains either "H40" or "365" AND the ICD diagnosis code description contains either the phrase "NARROW" or "arrow"	
Bladder Outflow Obstruction	**BLADDER_OBSTRUCT**	If the ICD code contains "N32.0"	
Chronic Respiratory Failure	**CHRONIC_RESPFAIL**	If the diagnosis code description contains the phrase "J96" and at least one of the following phrases: "CHRONIC", "hronic"	
Acute Respiratory Failure	**ACUTE_RESPFAIL**	If the diagnosis code description contains the phrase "J96" and at least one of the following phrases: "ACUTE", "acute", "Acute"	

Acute/Chronic/Unspecified Respiratory Failure	**RESPFAIL**	If the ICD diagnosis code contains the phrase "J96"	
Parkinson's Disease	**PARKINSONS**	If the ICD code contains either "G20" or "332".	If the ICD Code contains the phrase ".332" (refers to a lot of injury diagnoses)
Peptic Ulcer Disease	**PEPTIC_ULC**	If the ICD code contains either "533.", "K27", "531.", "530.2", "K22.1", "K25", "K26", "532." – *Note:* Must contain the period after some of these criteria it or else other diagnoses get included	
Chronic Constipation	**CHRONIC_CONST**	If the ICD code contains one of the following: "564" or "K59" AND the ICD code description contains one of the following phrases: "Chronic"; "CHRONIC"; "chronic"	
Dementia	**DEMENTIA**	If the ICD Code description contains one of the following phrases: "DEMENTIA" or "ementia"	Z81.8; Family history of dementia
Chronic Cognitive Impairment	**CHRONIC_COG_IMPAIR**	If the ICD code description contains the phrase" "R41.8"	
Chronic Prostatism	**CHRONIC_PROST**	If the ICD code is equivalent to "601.1" or "N41.1"	
Orthostatic Hypotension	**ORTHO_HYPO**	If the ICD code is "195.1" or "458.0" OR if the ICD code is "458" and the diagnosis description contains the phrase "ORTHO" or "rtho"	
Micturition Syncope	**MICTUR_SYNCOPE**	If the ICD code description contains one of the following phrases: "VASOVAGAL" or "asovagal"	If the ICD Code description contains the following phrase: "Barriers and spermicide, NFP, FAM, LAM; treatment for vasovagal episode or complication due to treatment for secondary related reproductive health condition"
Breast Cancer	**BREASTCANCER**	If the ICD Code contains one of the following: "174", "233", "C50", "D05", "Z85", or "Z86" AND the ICD Code description contains one of the following phrases: "BREAST" or "reast"	
Venous Thromboembolism	**VENOUSTHROMB**	If the ICD Code contains one of the following: "I82", "Z86", "453" AND the ICD Code description contains one of the following phrases: "EMB", "emb", or "Emb"	

		AND the ICD Code description contains one of the following phrases: "THROMB", or "hromb" OR if deep vein thrombosis or pulmonary embolism were diagnosed (see definitions below)	
History of a Hysterectomy	**HYSTERECTOMY**	If the ICD Code description contains one of the following phrases: "ysterectomy" or "HYSTERECTOMY"	
Hypogonadism	**HYPOGONADISM**	If the ICD Code description contains one of the following phrases: "HYPOGON", "ypogon", "E29.1"	
Bleeding Risk	**BLEEDRISK**	If the code is ICD10 and equivalent to one of the following: - D66, D68, Q79.60, Q78.0 D68.1, Q96.9, Q90.9, Q87.19, D82.1, Q87.19, D68.8, D68.2, I78.0, D69.1, D69.9, K76.9, N19, E07.9, E24.9, E85.9, E56.9, D65, E54 OR If the code is ICD9 and equivalent to one of the following: - V83.02, 286.4, 756.83, 756.51, 286.2, 758.0, 279.11, 448.0, 571.8, 571.9, 584.5, 584.6, 584.7, 584.8, 584.9, 246.9, 246.8, 255.0, 277.30, 277.39, 269.0, 776.2, 964.2, 964.5	
Peripheral Artery Disease	**PERIPHERAL_ARTDISEASE**	If the ICD code descriCon contains the following phrase: "443.9" Or if the ICD code description contains the following phrase: "I73.9" as well as at least one of the following: "PERI", "peri", or "Peri" If the ICD code description contains one of the following phrases: "443.89; OTHER PERIPHERAL VASCULAR DISEASE", "443; Other peripheral vascular disease", or "I73.9; Microangiopathy"	
Coronary Artery Disease	**CORONARY_ARTDISEASE**	If an ICD9 code is used and the ICD code description contains the following: "414" Or	If the ICD Code description contains one of the following phrases: "414.9", "I25.10; Aneurysm of Heart Wall", "I25.10; CVD (cardiovascular disease)", "I25.10; Cardiovascular disease",

		If an ICD10 code is used and the ICD code description contains one of the following phrases: "I25.111; Cor", "I25.118; Cor", "I25.119; Cor", "I25.70", "I25.718", "I25.72", "I25.759", "I25.81", "I25.83", "I25.84"	"I25.10; Coronary heart disease", "I25.10; Pulmonary embolism"
Cerebrovascular Disease	**CEREBROVASCULAR**	If an ICD10 code is used and the ICD code description contains one of the following phrases: "I67.9" or "I67.89", "I69" OR If an ICD9 code is used and the ICD code description contains one of the following phrases: "436", "437.9", "433.10", "434.91", "438."	If the ICD Code description is equivalent to the following: "434.91; Cerebrovascular accident involving anterior circulation of left side"
Deep Vein Thrombosis	**DVT**	If the ICD 9 code contains the phrase "434.4" or the ICD10 code contains the phrase "I82.4"	If the ICD9 code contains the phrase: "434.4; Disease" or the ICD10 code contains the phrase "I82.403; Irreg"
Pulmonary Embolism	**PE**	If the ICD Code description contains the phrases "EMBOL" and "PULMON" OR If the ICD Code description contains the phrases "mbol" and "ulmon"	
Cardiac Conduction Abnormality	**CARDIAC_COND**	If the ICD code description contains one of the following phrases: "I44" or "I49"	
Prostatism	**PROSTATISM**	If the ICD 10 code contains the phrase "N40" or if the ICD 9 code contains the phrase "600"	
Urinary Retention	**UR_RETENTION**	If the ICD 10 code contains the phrase "R33" or the ICD 9 code contains the phrase "788.2"	If the ICD Code description contains the phrase "DRUG"
Lewy Body Disease	**LEWY_BODY**	If the ICD code description contains the phrase "G31.83"	
Delirium	**DELIRIUM**	If the ICD Code description contains at least one of the following phrases: "DELIRIUM" or "elirium" AND contains the phrase "293", "F05, "R41"	
Sleep Disorders	**SLEEP_DISORDER**	If the ICD code description contains any of the following phrases: "SLEEP", "leep", "INSOMNIA", "nsomnia", "HYPERSOMNOLENCE",	If the ICD code contains any of the following phrases: "327.52" "G47.62"(leg cramps while sleeping), "327.53", "G47.63"(sleep

		"ypersomnolence", "CIRCADIAN", "ircadian", "PARASOMNIA", "arasomnia", "G37.34", "G37.36", "HYPERSOMNIA", "ypersomnia", "NARCOLEPSY", "arcolepsy"	related bruxism), "F32.9; Majordepressivedisorder,singleepisode,unspecified", "F51.3" (sleep walking) , "R40" (sleepiness) , "Z72.82", "V69.4" (sleep deprivation), "Z86", "Z87" (history of sleep apnea), "Z91", "V49.89" (at risk for sleep apnea)
Benign Essential Tremor	**TREMOR**	If the ICD code description contains the phrase: "Benign essential tremor"	
Gastrointestinal Bleeding	**GASTRO_BLEED**	If the ICD 9 code contains the phrase "578.9" or "578.1" or if the ICD 10 code contains the phrase "K92.2" or "K92.1"	
Rheumatoid Arthritis	**ARTHRITIS**	If the ICD 9 code contains the phrase "714", "716.5" or if the ICD 10 code contains the phrase "M06", "M05", "M13.0" AND The ICD code description contains one of the following phrases: "RHEUMATOID" or "heumatoid" OR The ICD code description contains the phrase "M19.90; Inflammatory arthritis" OR If the ICD 9 code contains the phrase "716.5" or if the ICD 10 code contains the phrase "M13.0" OR If the ICD code description contains the phrase "714.9; Inflammatory polyarthritis NOS"	
Osteoarthritis	**OSTEOARTHRITIS**	If the ICD code description contains one of the following phrases: "OSTEOARTHRITIS", "steoarthritis"	
Cardiovascular Disease	**CVD**	Used the CVD Codes from Steven Towers Feasibility Analysis	

Dysphagia	**DYSPHAGIA**	If the ICD code description contains one of the following phrases: "DYSPHAGIA", "ysphagia", "SWALLOW", or "wallow"	If the ICD code description contains the phrase "V15.53; H/O swallowed foreign body"
Esophagitis	**ESOPHAGITIS**	If the ICD code descriptions contains one of the following phrases: "ESOPHAGITIS" or "sophagitis"	
Gastritis	**GASTRITIS**	If the ICD code description contains one of the following phrases: "GASTRITIS", "astritis", "yspepsia", or "DYSPEPSIA"	
Duodenitis	**DUODENITIS**	If the ICD code description contains one of the following phrases: "DUODENITIS" or "uodenitis"	
Upper Gastrointestinal Disease	**UPPER_GASTRO**	If DYSPHAGIA = 1 or ESOPHAGITIS = 1 or GASTRITIS = 1 or DUODENITIS = 1 or PEPTIC_ULC = 1 or GASTRO_BLEED = 1	
Chronic Atrial Fibrillation	**CHRONIC_AFIB**	If the ICD code description contains the phrase "I48.2"	
Uncontrolled Hypertension	**UNC_HYPERTENSION**	If the ICD code description contains one of the following phrases "HYPERTENSION" and "UNCONTROLLED" or "ypertension" and "ncontrolled"	None
Unexplained Syncope	**UNEXP_SYNCOPE**	If the ICD code description contains one of the following phrases "yncope" or "SYNCOPE"	
Hiccough/Hiccup	**HICCUP**	If the ICD Code description contains the phrase "R06.6"	
Parkinsonism	**PARKINSONISM**	If the ICD Code description contains the phrase "PARKINSONISM" or "arkinsonism"	
Hypoglycemia	**HYPOGLYCEMIA**	If the ICD Code description contains one of the following phrases: "251.2", "E13.649", "E16.1", "E16.2", "E10.649", "E11.649" OR the ICD code description is equivalent to: "E13.9; Hypoglycemia"	If the ICD code description is equivalent to one of the following: "E16.2; Disorder of pancreatic internal secretion" or "E16.2; Low blood sugar"
Stroke	**STROKE**	If the ICD Code description contains the phrase: "STROKE" or "troke"	If the ICD Code description is equivalent to one of the following phrases: "V17.1; FAMILY HISTORY OF STROKE (CEREBROVASCULAR)" or "Z82.3; FAMILY HISTORY OF STROKE" or "Z82.3; Family history of stroke" or

	"Z91.89; 10 year risk of MI or stroke 7.5% or greater"