Appendix A: Potentially Inappropriate Prescriptions (PIPs)

for older people (modified from 'STOPP/START 2' O'Mahony et al 2014)

Consider holding (or deprescribing - consult with patient):

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

2. **Any** drug prescribed beyond the recommended duration, where well-defined

3. **Any** duplicate drug class (optimise monotherapy)

Avoid **hazardous combinations** e.g.:

1. *The Triple Whammy*:

NSAID + ACE/ARB + diuretic in all ≥ 65 year olds (NHS Scotland 2015)

2. *Sick Day Rules* drugs:

Metformin or **ACEi/ARB** or a **diuretic** or **NSAID** in ≥ 65 year olds presenting with dehydration and/or acute kidney injury (AKI) (NHS Scotland 2015)

3. *Anticholinergic Burden* (ACB):

Any additional medicine with **anticholinergic** properties when already on an Anticholinergic/antimuscarinic (listed overleaf) in ≥ 65 year olds (risk of falls, increased anticholinergic toxicity: confusion, agitation, acute glaucoma, urinary retention, constipation). The following are known to contribute to the ACB:

Amantadine
Antidepressants, tricyclic: Amitriptyline, Clomipramine, Dosulepin, Doxepin, Imipramine, Nortriptyline, Trimipramine and SSRIs: Fluoxetine, Paroxetine
Antihistamines, first generation (sedating): Clemastine, Chlorphenamine, Cyproheptadine, Diphenhydramine/-hydrinate, Hydroxyzine, Promethazine; also Cetirizine, Loratidine
Antipsychotics: especially Clozapine, Fluphenazine, Haloperidol, Olanzepine, and phenothiazines e.g. Prochlorperazine, Trifluoperazine
Baclofen
Carbamazepine

Disopyramide
Loperamide
Oxcarbazepine
Pethidine
Pizotifen
Tizanidine

ACE inhibitors (e.g. Enalapril)

- in patients with persistent postural hypotension[1] (risk of syncope and falls)

- in patients with hyperkalaemia (risk of death)

- in combination with spironolactone without regular (6 monthly) monitoring (risk of fatal hyperkalaemia[2])

See also the *Triple Whammy* and *Sick Day Rules* (Hazardous Combinations) on page 1

Aldosterone antagonists (Spironolactone, Eplerenone) with concurrent potassium conserving drugs (e.g. ACEI's) without regular (6 monthly) monitoring of serum potassium

Alpha-1 blockers (**Alfuzosin, Doxazosin, Prazosin, Tamsulosin, Terazosin**) with symptomatic postural hypotension or micturition syncope

Amiodarone as first-line antiarrhythmic therapy in supraventricular tachyarrhythmias (higher risk of side-effects than beta-blockers, Digoxin, Verapamil or Diltiazem)

Angiotensin Receptor Blockers (ARBs, e.g. Candesartan) with persistent postural hypotension or hyperkalaemia as for ACE inhibitors.

Antacids (some proprietary over-the-counter liquid/tablet preparations containing aluminium e.g. Mucogel®) in patients with chronic constipation where non-constipating alternatives are available (aluminium salts are constipating)

Anticholinergics/antimuscarinics including:

antimuscarinics used in Parkinson's Disease: **Orphenadrine, Procyclidine, Trihexyphenidyl**

bladder antimuscarinics/ antispasmodics: e.g. **Flavoxate, Oxybutinin, Tolterodine**

bronchodilator antimuscarinics e.g. **Ipratropium, Tiotropium**

intestinal antimuscarinics: **Hyoscine, Dicycloverine, Propantheline**

mydriatics and cycloplegics: **Atropine, Homatropine**

- to treat extra-pyramidal side-effects of neuroleptic medications (risk of anticholinergic toxicity)

[1] recurrent drop in systolic blood pressure ≥ 20mmHg
[2] MHRA Drug Safety Update 17th Feb 2016 www.gov.uk/drug-safety-update

- in patients with delirium or dementia (risk of exacerbation of cognitive impairment, increased confusion, agitation)

- with narrow-angle glaucoma (risk of acute exacerbation), or chronic prostatism (risk of urinary retention)

- in patients with chronic constipation where non-constipating alternatives are available (risk of exacerbation of constipation)

See also 'hazardous combinations' (ACB) on page 1

Anticoagulants, oral (includes vitamin K antagonists, direct thrombin inhibitors and factor Xa inhibitors): caution with other drugs that may increase bleeding. See also Warfarin, Aspirin and other antiplatelets, bisphosphonates, NSAIDs, SSRIs.

Anticoagulants, novel oral **(NOACs):** caution if reduced kidney function, avoid Dabigatran if eGFR <30, Rivaroxaban if eGFR <15ml/min/1.73m^2 (increased risk of bleeding)

Antidepressants (particularly SSRIs, Tricyclics) with current or recent significant hyponatraemia (Na+ < 130 mmol/l) see also anticholinergic burden, SSRIs

Antihistamines avoid first-generation (e.g. Chlorphenamine and see also anticholinergic burden) (safer, less toxic antihistamines now widely available)

Antiplatelet agents with oral anticoagulants in stable coronary, cerebrovascular or peripheral arterial disease (no added benefit from dual therapy) or with concurrent significant bleeding risk, i.e. uncontrolled severe hypertension, bleeding tendency, recent non-trivial spontaneous bleeding (high risk of bleeding). See also Aspirin

Antipsychotics/Neuroleptics particularly phenothiazines (e.g. Promazine)[3] and Butyrophenones (e.g.Haloperidol)

- concomitant with anticholinergic/antimuscarininc drugs

- with a history of prostatism or previous urinary retention (high risk of urinary retention)

- other than Quetiapine or Clozapine in Parkinsonism or Lewy Body Disease (risk of severe extra-pyramidal symptoms, gait dyspraxia)

- in patients with behavioural and psychological symptoms of dementia unless severe and other treatments have failed (increased risk of stroke)

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

Aspirin (See also antiplatelets):

- long term > 160mg per day (↑ risk of bleeding, no evidence for increased efficacy)

[3] phenothiazines are sedative, have significant anti-muscarinic toxicity – avoid in older people, with the exception of Prochlorperazine in severe nausea/vomiting/vertigo, Chlorpromazine for relief of persistent hiccoughs and Levomepromazine as an anti-emetic in palliative care

- with a past history of peptic ulcer disease without cover PPI (risk of recurrence)

- in combination with oral anticoagulants for chronic AF (no added benefit)

- with Clopidogrel as secondary stroke prevention, unless coronary stent(s) inserted in the previous 12 m or concurrent ACS or high grade symptomatic carotid arterial stenosis (no evidence of added benefit over Clopidogrel monotherapy)

Benzodiazepines (e.g. Diazepam)

- where sedation not appropriate (sedative, may cause reduced sensorium, impair balance)

- for ≥ 4 weeks (no indication for longer treatment; withdraw gradually)

- with acute or chronic respiratory failure i.e. $pO2 < 8.0$ kPa ± $pCO2 > 6.5$ kPa (risk of exacerbation of respiratory failure)

Beta-blocker (e.g. Atenolol and include/consider absorption from eye drops e.g. Timolol)

- in combination with Verapamil or Diltiazem (risk of heart block)

- in diabetics with frequent hypoglycaemic episodes (risk of masking hypoglycaemia)

- with bradycardia (< 50/min), type II[4] or complete heart block (risk of asystole)

Bisphosphonates, oral in patients with a current or recent history of upper GI disease or bleed i.e. dysphagia, oesophagitis, gastritis, duodenitis, or peptic ulcer disease

Calcium Channel Blockers (CCBs) (e.g. Amlodipine, Nifedipine) with persistent postural hypotension[5] (risk of syncope and falls). See also Verapamil, Diltiazem

Clonidine (all centrally-acting antihypertensives) unless clear intolerance of 1st line in hypertension (less well tolerated by older people than younger people) (can cause confusion, sedation dizziness withdraw slowly to avoid rebound hypertension)

Colchicine if eGFR <10ml/min/1.73m^2 or long term (>3 months) for chronic treatment of gout where there is no contraindication to a xanthine-oxidase inhibitor (e.g. Allopurinol, first choice prophylactic medicine in gout)

Digoxin for heart failure if normal systolic ventricular function (no clear evidence of benefit)

Diltiazem or Verapamil with NYHA Class III /IV[6] heart failure (may worsen heart failure); in combination with Beta-blocker (risk of heart block)

Diuretic, Loop (e.g. **Furosemide, Bumetanide)**

- as 1st line for hypertension (safer, more effective alternatives available)

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[4] Second-degree AV block, also known as Mobitz II: intermittent non-conducted P waves not preceded by PR prolongation and not followed by PR shortening. It may progress rapidly to complete heart block, in which no escape rhythm may emerge

[5] recurrent drop in systolic blood pressure ≥ 20mmHg

[6] Class III moderate HF: marked limitation in physical activity, comfortable only at rest. IV: end stage, symptoms even at rest

- with concurrent urinary incontinence (may exacerbate)

- for dependent ankle oedema without clinical, biochemical or radiological evidence of heart failure, liver failure, nephrotic syndrome or renal failure (leg elevation and/or TEDs appropriate). See also *Triple Whammy* and *Sick Day Rules* above **Diuretic, Thiazide (**e.g. **Bendroflumethiazide, Indapamide)** with current serum K^+ < 3.0 or Na^+ < 130 or hypercalcaemia (corrected > 2.6 mmol/L). See also *Triple Whammy* and *Sick Day Rules* above

Donepezil and other acetylcholinesterase inhibitors with a known history of persistent bradycardia (< 60 beats/min.), heart block or recurrent unexplained syncope

Doxazosin (see alpha blockers, vasodilators)

Iron oral doses greater than elemental iron 200 mg daily (no further amount absorbed); in patients with chronic constipation where non-constipating alternatives are available (risk of exacerbation)

Isosorbide Nitrates, (all long acting Nitrates) with persistent postural hypotension[7] (risk of syncope and falls)

Metformin if eGFR < 30 ml/min/1.73m2 (risk of lactic acidosis). See also *Sick Day Rules* above

Methyldopa (all centrally-acting antihypertensives) unless clear intolerance of 1st line drugs in hypertension (less well tolerated by older people than younger people) (can cause depression, sedation, dizziness, blood dyscrasias)

Non-Steroidal Anti Inflammatory Drugs (NSAIDs)

- if on anticoagulant (vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors) (risk of major gastrointestinal bleeding)

- with concurrent antiplatelet agent or corticosteroid without PPI cover (risk of peptic ulcer)

-with severe hypertension[8] (risk of exacerbation of hypertension) or severe heart failure (risk of exacerbation of heart failure) or if eGFR<50mL/min/1.73m^2 (risk of AKF)

- long term (>3 months) for symptom relief of osteoarthritis pain where paracetamol has not been tried (simple analgesics preferable and usually as effective for pain relief) or for chronic treatment of gout where there is no contraindication to a xanthine-oxidase inhibitor (e.g. Allopurinol, first choice prophylactic drug in gout)

- with concurrent cardiovascular disease (increased risk of MI and stroke)

See also *Triple Whammy* and *Sick Day Rules* on page 1

Opioid analgesics (e.g. Buprenorphine, Morphine, Tramadol) with confusion, postural hypotension, chronic constipation, cardiac arrhythmias (some), Methadone additionally associated with prolonged QT interval; Tramadol with syncope and blood disorders.

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[7] recurrent drop in systolic blood pressure ≥ 20mmHg
[8] systolic > 160 mmHg and/or diastolic > 90 mmHg

Phenothiazines (see antipsychotics and ACB) are sedative, have significant antimuscarinic toxicity. Safer and more efficacious alternatives exist[9]

Proton Pump Inhibitors (PPI) for uncomplicated peptic ulcer disease or erosive peptic oesophagitis at full therapeutic dosage for > 8 weeks (dose reduction or earlier discontinuation indicated) (Risk of *C.diff* especially in elderly on broad spectrum antibiotics)

Quinine for prevention/relief of night cramps unless very frequent and painful. Treatment should be interrupted at intervals of approximately 3 months to assess need and effectiveness (BNF 2014)

Selective Serotonin Reuptake Inhibitors (SSRIs) with current or recent significant hyponatraemia (Na+ < 130 mmol/l), caution if bleeding disorder especially with other medicines that might increase risk of bleed (e.g. NSAIDs), closed angle glaucoma, prolonged QT interval (Citalopram, Escitalopram) (risk of exacerbating/ precipitating). Paroxetine (see also anticholinergic burden) may additionally cause confusion, extra-pyramidal effects

Tricyclic Antidepressants (e.g. Amitriptyline and see anticholinergic burden) with hyponatraemia, dementia, narrow angle glaucoma, cardiac conduction abnormalities, prostatism, or history of urinary retention; for pain relief in elderly consider Pregabalin or Gabapentin

Vasodilator drugs (**Hydralazine, Minoxidil,** and see **Alpha blockers, ACE Inhibitors, ARBs, CCBs,** Isosorbide mono-/di-**Nitrates** with persistent postural hypotension[10] (risk of syncope and falls)

Verapamil or Diltiazem with NYHA Class III/IV[11] heart failure (may worsen), in combination with Beta-blocker (risk of heart block) or with chronic constipation

Warfarin (vitamin K antagonists) or other oral anticoagulant, for more than 6 months for first DVT or for more than 12 months for first PE without continuing, provoking risk factors (e.g. thrombophilia) (no added benefit). Consider interactions with Warfarin. See also Anticoagulants, (NOACs: caution if poor kidney function) Aspirin and other antiplatelet drugs, bisphosphonates, NSAIDs, SSRIs and other drugs that may increase bleeding

Z-drugs e.g. Zopiclone, Zolpidem, Zaleplon (may cause protracted daytime sedation, ataxia)

Ref: STOPP/START2 2014 (with additional information from BNF Sept 2014 and NHS Scotland 2015)

Adapted for use in CLAHRC NWL www.clahrc-northwestlondon.nihr.ac.uk

VM BJ MB IB Chelsea and Westminster Hospital NHS FT April 2015

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[9] with the exception of Prochlorperazine in severe nausea/vomiting/vertigo, Chlorpromazine for relief of persistent hiccoughs and Levomepromazine as an anti-emetic in palliative care

[10] recurrent drop in systolic blood pressure ≥ 20mmHg

[11] Class III moderate HF: marked limitation in physical activity, comfortable only at rest. IV: end stage, symptoms even at rest