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Improving health and care in Bristol, North Somerset and South Gloucestershire

STOPP START Tool to Support Medication Review

Older people are known to be at greater risk of adverse effects from their medicines due to age related changes in pharmacokinetics and pharmacodynamics. Therefore, as a result of increasing age and frailty, some treatments may cause more harm than benefit.

Polypharmacy and inappropriate prescribing are well known risk factors for adverse drug reactions (ADRs) and side-effects, which commonly cause negative health outcomes in older people. [1]

There is a growing body of evidence showing that some drugs are associated with more adverse reactions and hospital admissions in the elderly[2,3]. Hence, reviewing these medications contributes to reducing problematic polypharmacy and address inappropriate prescribing in this group of patients.

NICE guidance on Medication Optimisation[4] recommends using a screening tool – for example the STOPP/START tool in older people – to identify potentially inappropriate medications (STOPP criteria) and potential prescribing omissions (START criteria) for those on multiple medicines or with long term conditions.

This document is an adaptation of the

STOPP START medication review screening tool
(STOPP-Screening Tool of Older Persons Prescriptions START -Screening Tool to Alert doctors to Right i.e. appropriate, indicated Treatments)

which consists of various criteria devised to identify potentially inappropriate medicines in older people. These criteria are based on an up-to-date literature review and consensus validation among a European panel of experts in geriatric pharmacotherapy[1,5].

Clinical guidelines and recommendations usually focus on starting treatments and/or managing single conditions without taking into consideration or addressing, for instance, how the benefit/risk ratio changes as the patient ages/becomes more frail, or when it may be appropriate to stop or reduce the dose of a medication (particularly those ones used for preventing conditions or where the indication is no longer valid).

The tool was validated in patients aged 65 and over but physicians must use their clinical judgement when deciding if a person is “elderly” in terms of using the toolkit and also consider other drug interactions or contra-indications not listed here. This approach is indicated in those who are recognized as frail. During the process of medicines optimization, the level of frailty should be taken into consideration rather than the patient’s age. Frailty can be assessed using the Rockwood Clinical Frailty Score (CFS)

The final decision to stop the drug should be weighed against the daily symptomatic benefit or prevention of rapid worsening of symptoms.
Where there is any doubt with the above information please check that it is in line with manufacturers recommendations, published literature or changes in national and local guidance. Bristol, North Somerset and South Gloucestershire guidance can be found at http://www.bnssgformulary.nhs.uk/

The Cockroft and Gault formula for Creatinine Clearance is the preferred method for estimating renal function in elderly patients aged 75 years and over (BNF, Estimating renal function).

Medstopper.com a useful tool to prioritise stopping or reducing medications and provides detailed information about the safe rates of reductions, potential withdrawal effects and references to STOPP/START and Beers criteria.

PrescQipp have produced an interactive Polypharmacy appropriateness clinical tool (IMPACT[6]), that identifies clinical and deprescribing priority with recommendations and considerations for appropriately continuing or stopping medicines.

South Gloucestershire version adapted by Raquel Iniesta, Care Homes Pharmacist South Gloucestershire Clinical Commissioning Group. Permission obtained to adapt from STOPP/START Tool V9 – Dr D O’Mahony (denis.omahony@ucc.ie). Acknowledgements to NHS Wirral CCG STOPP/START Toolkit March 2015 (adapted with permission), Midlands & Lancashire CSU, NHS Cumbria STOPP/START Toolkit June 2016
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STOP medications (age ≥ 65 years)	Circumstances to review	Reason to review
α-blockers (i.e. alfuzosin, doxazosin, tamsulosin) and 5-alfa reductase inhibitors (i.e. finasteride, dutasteride)	Long-term urinary catheter in situ >2 months Males with frequent incontinence Hypotension/ Symptomatic postural hypotension *Please note that some α- blockers e.g. doxazosin are also used to treat hypertension*	No longer indicated for the relief of benign prostatic hyperplasia (BPH) symptoms (i.e. urinary retention) Risk of urinary frequency and worsening of incontinence Risk of falls. Ensure that patient is hydrated before making medication changes as dehydration may lead to orthostatic hypotension which may resolve following fluid replacement.
Anti-anginal medication	Consider reducing, particularly if mobility has decreased with less need for medication Caution: Nitrates are potent coronary vasodilators Nicorandil and present ulceration	 Risk of unwanted effects such as flushing headache, hypotension, postural hypotension Nicorandil can cause serious skin, mucosal, and eye ulceration, including gastrointestinal ulcers which may progress to perforation, haemorrhage, fistula, or abscess. Stop nicorandil treatment if ulceration occurs—consider the need for alternative treatment or specialist advice if angina symptoms worsen https://www.gov.uk/drug-safety-update/nicorandil-ikorel-now-second-line-
Antibiotics Review	Long term prophylactic antibiotics for UTI are not routinely recommended (including catheterised patients). C. difficile infection (CDI)	Risk of adverse effects, including development of resistance. Antibiotic prescribing guidance including for recurrent UTIs available at: https://remedy.bnssgccg.nhs.uk/formulary-adult/local-guidelines/5-infections-guidelines/ Patients should be reviewed at regular intervals to assess the risk/benefits in relation to C. difficile infection. Where possible discontinue antibiotics other than those prescribed for Clostroides difficile in the Community. Guideline available at: https://remedy.bnssgccg.nhs.uk/formulary-adult/local-guidelines/5-infections-guidelines/ Review any proton pump inhibitor (PPI) that the patient is prescribed as taking a PPI can be linked to recurrent CDI.
Anticoagulants **DOACS/ Warfarin**	For 1st uncomplicated DVT or PE for longer than 3months Bleeding disorders, peptic ulcer, severe hypertension, severe renal impairment Hepatic impairment with impaired clotting ability and raised INR Review Warfarin patients with poor INR control or difficulties with monitoring consider switching to DOAC for suitable patients	At 3 months, assess the risks and benefits of continuing treatment, taking into account the patient's risk of VTE recurrence and whether they are at increased risk of bleeding see https://www.nice.org.uk/guidance/ng158 Increased risk of bleeding as a result of impaired ability to produce clotting factors BNSSG Anticoagulant guidelines Where life expectancy is limited, the benefits of anticoagulants is likely to be very small or negligable, though the risks of complications remains the same. In these cases, there may be no net clinical benefit they should be reviewed.

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STOP medications (age ≥ 65 years)	Circumstances to review	Reason to review
Anticholinergics **Minimise use wherever possible and review efficacy and tolerance regularly.** **(e.g. Hyoscine, Tolterodine Oxybutynin, Solifenacin, Trospium, Procyclidine, Trihexyphenidyl)**	To treat extra-pyramidal side-effects of antipsychotic medications Patients with dementia, chronic constipation, glaucoma or prostatic enlargement. To reduce muscarinic side effects of acetylcholinesterase inhibitors (AChEIs).	Elderly patients are more likely to experience adverse effects (including confusion, delirium, constipation, tachycardia, urinary retention, dry mouth/eyes, sedation, falls and cognitive impairment). Risk of worsening respective condition. Anticholinergic drugs which cross blood-brain barrier directly oppose the action of AChEIs and adversely affect the course of dementia[7]. **Refer to Appendix1 for Anticholinergic Cognitive Burden Scale.** BNSSG joint formulary – Bladder and Urinary disorders https://remedy.bnssgccg.nhs.uk/formulary-adult/chapters/7-obstetrics-gynaecology-and-urinary-tract-disorders/71-bladder-and-urinary-disorders/ NICE CG171 Urinary Incontinence in Women https://www.nice.org.uk/guidance/cg171
Antidiarrhoeal drugs (co-phenotrope, loperamide or codeine phosphate)	For treatment of diarrhoea of unknown cause **N.B. Please be aware of C. difficile in undiagnosed diarrhoea** For the treatment of severe infective gastroenteritis	Risk of delayed diagnosis, may exacerbate constipation with overflow diarrhoea, may precipitate toxic mega colon in inflammatory bowel disease, may delay recovery in unrecognised gastroenteritis Risk of colitis and toxic mega colon if Clostroides difficile Risk of exacerbation or protraction of infection
Antihistamines	First generation antihistamines (cyclizine, cholrphenamine, promethazine) If fallen in past 3 months Prolonged use or no clear/current indication (also for the newer generations)	Risk of sedation and anti-cholinergic side effects (may precipitate glaucoma, urinary retention, tachycardia, GI obstruction) Risk of falls Tablet burden, drowsiness (less than in first generation, but also reported, especially in the elderly)
Anti-hyperglycaemics eg Metformin, SGLT2I, glitazones,	Conditions leading to dehydration eg vomiting, diarrhoea, fever Renal impairment Heart Failure	Restart when well (after 24-48h of eating and drinking normally) https://www.thinkkidneys.nhs.uk/ BNSSG Sick day guidance Diabetes and frailty:guidance on the management of older adults with type 2 diabetes Guidance NG28, T2 diabetes in adults:management
Antiplatelets eg Clopidogrel, Prasugrel and Ticagrelor	With concurrent bleeding disorder Aspirin/ Antiplatelet combination	High risk of bleeding Ensure reviewed as per cardiology advice (usually indicated for a max of 12 months after ACS only) refer to BNSSG Antiplatelet guidelines

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STOP medications (age ≥ 65 years)	Circumstances to review	Reason to review
Antipsychotics **NB. Reduce slowly monitoring effect**	>1 month use as long-term hypnotic (check notes for duration- unlicensed for this indication) >1 month use in parkinsonism If fallen in last 3 months >6 weeks treatment of behavioural and psychological symptoms of dementia patients (BPSD) and stable symptoms (review ongoing need)	Confusion, postural hypotension, extrapyramidal side effects, falls Risk of worsening extrapyramidal symptoms May cause gait dyspraxia, parkinsonism Risk of gait disturbances, dehydration, prolonged sedation, cognitive decline, falls, stroke and death. Priority groups for review: care home patients (more frail and BPSD more common than in general population) vascular dementia patients and dementia patients with a history of cardiovascular disease, cerebrovascular disease or vascular risk factors. Benefits are limited over longer periods (>12 weeks) Guidance from Alzheimer's society is available online at https://www.alzheimers.org.uk/categories/treatments-and-therapies/antipsychotic-medications NICE guidelines: http://pathways.nice.org.uk/pathways/dementia Guidance on tapering doses available online: https://deprescribing.org/wp-content/uploads/2018/08/AP-deprescribing-algorithm-2018-English.pdf
Aspirin	Dose >150mg / day, restart at 75mg if still indicated With a concurrent bleeding disorder Risk of gastrointestinal bleeding (e.g. peptic ulcer disease) without histamine H2 receptor antagonist or PPI Primary prevention of CVD (aspirin is not licensed for primary prevention) If being used as monotherapy for stroke prevention in AF	Risk of bleeding; no evidence of increased efficacy High risk of bleeding Risk of bleeding Guidance for antiplatelet prescribing for primary and secondary prevention of CVD: http://cks.nice.org.uk/antiplatelet-treatment Refer to BNSSG antiplatelet guidelines Guidance at: https://www.nice.org.uk/guidance/cg180
Benzodiazepines ***Reduce slowly & monitor effect***	>1 month use of long-acting benzodiazepines, e.g. chlordiazepoxide, oxazepam, diazepam, flurazepam, nitrazepam Regular and prolonged use If fallen in last 3 months	Risk of prolonged sedation, confusion, impaired balance, falls Benzodiazepines and Z drug withdrawal and insomnia guidelines available at: http://cks.nice.org.uk/insomnia In older people in particular, the magnitude of the beneficial effect of hypnotics may not justify the increased risk of adverse effects (such as cognitive impairment and increased risk of falls). The severity of withdrawal symptoms will depend on the degree of dependence. Abrupt discontinuation should be avoided. Reduce slowly and monitor effect.

STOP medications (age ≥ 65 years)	Circumstances to review	Reason to review
Beta-blocker (Reduce gradually to avoid rebound effect)	In combination with verapamil In those with diabetes mellitus and frequent hypoglycaemic episodes In severe frailty/elderly Pulse persistently below 60bpm	Risk of symptomatic heart block Risk of masking hypoglycaemic symptoms Reduced reflex of tachycardia (increased risk of bradycardia and orthostatic hypotension) and falls
Beta-blocker (non-cardioselective)	In patients with asthma	Risk of bronchospasm
Bisphosphonates (oral)	Unable to sit upright / patient experiencing swallowing difficulties / compliance issues Low risk of fractures A fracture occurred while on treatment After 5 years of treatment with oral medications or 3 years after parenteral (zoledronic acid) Reduced renal function (as per SPCs)	Instruction for administration of medication, if not followed causes increased risk of serious upper GI disorder Refer to BNSSG Osteoporosis -oral treatment duration, denosumab and drug holiday guidance Bisphosphonates accumulate in bone during treatment, and when stopped there is some residual protection against fractures. The length of this varies according to duration of therapy and which agent is being administered. Review recommended after 5years with alendronate, risendronate or ibandronate and after 3 years for zoledronic acid.
BP lowering drugs **Reduce or stop one at a time, maintaining the dose of the others without change. Restart them if BP increases[11]:** - ***Diastolic >90mm Hg*** - ***Systolic > 150mm Hg (160mm Hg if no organ damage)***	Consider need for and intensity of treatment in light of CVD risk, life expectancy side effects/ADR and frailty risk If fallen in past 3 months and hypotension/postural hypotension present Symptomatic postural hypotension (abnormal decrease in blood pressure of at least 20 mm Hg systolic and 10 mm Hg diastolic within three minutes of standing upright). Ensure that patient is hydrated when assessing for postural hypotension. Withhold ACE inhibitors/ ARBs with severe risk of dehydration (e.g. vomiting/ diarrhoea)	Limited evidence supporting tight BP control in the older frail group. Aim for SBP<150mmHg (or <160mmHg if no organ damage) to reduce the risk of strokes and (further) organ damage *Seek specialist advice for patients with advanced heart failure as can decompensate rapidly off medication* Risk of syncope and falls Can be restarted when patient has improved (e.g. 24-48h of eating and drinking normally) https://www.thinkkidneys.nhs.uk/ BNSSG Sick day rules guidance

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STOP medications (age ≥ 65 years)	Circumstances to review	Reason to review
Calcium Channel Blocker	If ankle oedema present	This may be an adverse effect of the Calcium Channel Blocker UKMI QA322 3_ankle oedema with CCBs (www.sps.nhs.uk) link here. Diuretics should not be prescribed in this case as they reduce plasma volume and lead to electrolyte imbalance. Switching classes, dose reduction or prescribing ACEI+CCB or ARB+CCB are proven to be effective strategies if oedema occurs.
	Verapamil and diltiazem should usually be avoided in heart failure.	They may further depress cardiac function and cause clinically significant deterioration.
	Caution with Digoxin and Beta-blockers	Digoxin levels ↑↑ Enhanced hypotensive effect with Beta-blockers - Asystole, severe hypotension and heart failure with verapamil + beta-blockers – avoid - Possible severe hypotension and heart failure with nifedipine
	With chronic constipation	May exacerbate constipation
	Dihydropyridines- CAUTION: Avoid Nifedipine in CHD/CHF	Reflex tachycardia
Carbocisteine	If no benefit after 4 weeks	Unnecessary if no benefit shown https://remedy.bnssgccg.nhs.uk/formulary-adult/chapters/3-respiratory-system/33-conditions-affecting-sputum-viscosity/
	>1.5g/day	Over recommended maintenance dose
	Risk factors for peptic ulceration	May disrupt the gastric mucosa barrier (consider gastro-protection)
Corticosteroids **(Withdraw gradually if: use >3 weeks or >40mg prednisolone/day)**	Oral instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD	Unnecessary exposure to long-term side effects of systemic steroids. Risk of major systemic corticosteroids side effects Ensure use of steroids aligned with COPD GOLD guideline: BNSSG COPD guidelines and BNSSG COPD Step down guidelines
	Long term use (>3 weeks)	Guidance at http://cks.nice.org.uk/corticosteroids-oral Guidance on issuing the Steroid Emergency Card in adults – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice
Digoxin	At doses >125 microgram per day with impaired renal function (eGFR <50ml/minute) With hypokalemia, hypomagnesaemia and hypercalcaemia Pulse persistently below 60bpm	Risk of toxicity increased (e.g. nausea, diarrhoea, arrhythmias)

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STOP medications (age ≥ 65 years)	Circumstances to review	Reason to review
Dipyridamole	With concurrent bleeding disorder As monotherapy for cardiovascular secondary prevention	High risk of bleeding No evidence for efficacy except in ischaemic stroke. https://www.nice.org.uk/guidance/TA210/chapter/1-guidance Antiplatelet prescribing guidelines: http://cks.nice.org.uk/antiplatelet-treatment#!management BNSSG Guidelines for prescribing antiplatelets: https://remedy.bnssgccg.nhs.uk/formulary-adult/local-guidelines/2-cardiovascular-system-guidelines/
Diuretics	Dependent ankle oedema and no signs of heart failure As first line monotherapy for hypertension Thiazides with history of gout Advise patient to stop during intercurrent illness	No benefit; compression hosiery more appropriate. Consider medication causes, e.g. CCBs. Safer, more effective alternatives available Risk of exacerbating gout Restart when well (after 24-48h of eating and drinking normally) https://www.thinkkidneys.nhs.uk/ BNSSG Sick day rules guidance
Domperidone	Indications except nausea/ vomiting Duration > 1 week Underlying cardiac conditions, impaired cardiac conduction, Co-prescribed other medications known to prolong QT interval or potent CYP3A4 inhibitors or with severe hepatic impairment	See MHRA warning issued https://www.gov.uk/drug-safety-update/domperidone-risks-of-cardiac-side- effects Duration of treatment: • The maximum treatment duration should not usually exceed one week Patients currently receiving long-term treatment with domperidone should be reassessed at a routine appointment to advise on treatment continuation, dose change, or cessation
Ipratropium (nebulised)	Prescribing as required (prn) in addition to regular prescribing With glaucoma	Can lead to exceeding licensed dosage and therefore exacerbate side effects May exacerbate glaucoma
Laxatives – stimulant (e.g. bisacodyl, senna)	For patients with intestinal obstruction If >1 laxative: Do not stop abruptly. Reduce stimulant first and monitor effect	Risk of bowel perforation BNSSG Constipation Guidelines
Metoclopramide	Long term use Parkinson's disease (domperidone more suitable as unlikely to cross blood-brain barrier but note contra-indications in cardiac disease and severe liver disease)	Licensed for a max of 5 days (does not apply to off label use in palliative care). https://www.gov.uk/drug-safety-update/metoclopramide-risk- of-neurological-adverse-effects The risks of neurological effects such as extrapyramidal disorders and tardive dyskinesia outweigh the benefits in long term or high dose treatment. Metoclopramide readily crosses the blood brain barrier, causing central effects such as sedation and dystonic reactions.

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STOP medications (age ≥ 65 years)	Circumstances to review	Reason to review
NSAID (oral)	Moderate severe hypertension (moderate 160/100mm Hg - 179/109mm Hg; severe: >180/110mm Hg	Risk of exacerbation of hypertension
	CVD risk>20%, previous CVD events, heart failure.	Risk of exacerbation and cardiovascular ADRs
	Age>65, on ACEI/ARBs and/or diuretics ("triple whammy"), CKD (GFR <60ml/min) or heart failure).	Risk of deterioration in renal function and renal ADRs
	GI ulcer, warfarin or new anticoagulants, steroids, SSRIs, high alcohol use	Gastro-intestinal ADRs (e.g. bleeding) If NSAIDs are essential: Consider gastro-protection with a PPI in those with GI risk factors
	On long-term NSAID and colchicine for chronic treatment of gout when there is no C/I to allopurinol	Allopurinol first choice prophylactic in gout
	Long-term NSAIDs as monotherapy (>3 month for arthritis)	Simple analgesics preferable (paracetamol and topical NSAIDs should be considered ahead of systemic NSAIDs or COX-2 inhibitors)
	Cox-2 inhibitors and diclofenac in cardiovascular disease Ibuprofen (at total daily dose above 1200mg per day) in cardiovascular disease	Increased risk of thrombotic events Increased risk of thrombotic events
	Advise patient to stop during intercurrent illness	Restart when well (after 24-48h of eating and drinking normally) https://www.thinkkidneys.nhs.uk/ BNSSG Sick day rules guidance
Oestrogen (systemic)	With history of breast cancer or venous thromboembolism Without progesterone in patients with intact uterus	Increased risk of reoccurrence Risk of endometrial cancer Risk/benefits should be discussed when undertaking a medication review as part of the shared decision making process https://www.gov.uk/drug-safety-update/hormone-replacement-therapy-hrt-further-information-on-the-known-increased-risk-of-breast-cancer-with-hrt-and-its-persistence-after-stopping
Omega-3 fatty acids	Prescribed for secondary prevention of MI Primary or Secondary prevention of CVD For CVD prevention in patients with CKD and/or Diabetes (type 1 and 2)	Omega-3 fatty acid compounds are essential fatty acids which can be obtained from the diet. NICE have advised that Omega 3 fatty acid supplements should not be prescribed Do Not Do recommendation for Omega 3 fatty acid NHSE also advise that prescribers in primary care should not initiate omega-3 Fatty Acids for any new patient and should support prescribers in deprescribing them: NHSE Items which should not routinely be prescribed in primary care -MI: cardiac rehabilitation and prevention of further CVD http://www.nice.org.uk/guidance/cg172/resources/guidance-mi-secondary- prevention-pdf -CVD:risk assessment and reduction, including lipid modification https://www.nice.org.uk/guidance/cg181 There is no evidence to support that omega-3 fatty acid compounds help to prevent CVD

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STOP medications (age ≥ 65 years)	Circumstances to review	Reason to review
Opioids (all type)	Long-term use of powerful opiates (e.g. morphine, fentanyl) as first line therapy for mild-moderate pain	WHO analgesic ladder not observed Cognitive impairment, respiratory depression, dependency, arrhythmias, hallucinations, constipation, urinary retention
	Equivalent to Morphine >120mg/day and not at end of life	BNSSG Chronic Pain Guidelines (currently under review) Opioids aware highlight that the risk of harm increases substantially at doses above an oral morphine equivalent of 120mg/day, but there is no increased benefit: tapering or stopping high dose opioids needs careful planning and collaboration. Opioids Aware | Faculty of Pain Medicine (fpm.ac.uk)
	Regular prescription >2 weeks in chronic constipation without concurrent use of laxatives	Risk of severe side effects, including constipation
	Long-term in dementia unless for palliative care or management of chronic pain	Exacerbation of cognitive impairment
	Recurrent Falls	Risk of drowsiness, postural hypotension, vertigo
	Slow-release opioids in severe pain without short-acting opioids for break-through pain	Risk of persistence of severe pain
	Combination opiates with pregabalin / gabapentin/ benzodiazepines	CNS depressant effect may be additive(of drowsiness, sedation, respiratory depression and, at the extreme, death). https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385791/PHE-NHS_England_pregabalin_and_gabapentin_advice_Dec_2014.pdf
	Frequency of repeats / scripts quantity exceeding expected amounts	Risk patients pain may be uncontrolled and requires review
	Patients discharged from secondary care on opioids for acute pain	Risk of tolerance/dependence and adverse effects where opioids intended for short term use are continued long term
Phenothiazines (e.g. Prochlorperazine)	With Parkinsonism	Risk of exacerbating Parkinsonism
	In CNS depression	Risk of increased confusion and cognitive decline
	With other anticholinergic medications	Risk of cumulative anticholinergic side effects
Quinine	Long term use (review every 3 moths)	https://www.gov.uk/drug-safety-update/quinine-not-to-be-used-routinely-for-nocturnal-leg-cramps
	Contraindicated in tinnitus, optic neuritis and haemoglobinuria	Risk of toxicity, QT interval prolongation (arrhythmias, heart block), abdominal pain, confusion,
SSRIs	If sodium <130mEq/L in past 2 months	SSRIs can cause/worsen hyponatraemia
	Citalopram & escitalopram – risk of QT prolongation	Don't use in patients with congenital long QT syndrome or known pre-existing QT interval prolongation
	Citalopram >20mg/day Escitalopram >10mg/day	In combination with other drugs known to prolong the QT intervals BNSSG guidance: http://www.bnssgformulary.nhs.uk/includes/documents/Citalopram%20dose%20reduction%20flow%20chart%20based%20on%20advice%20from%20the%20 MHRA%20version5.pdf
	High risk of gastrointestinal bleeding	Can increase risk of bleeding consider gastroprotection https://remedy.bnssgccg.nhs.uk/formulary-adult/local-guidelines/1-gastro-intestinal-system-guidelines/

STOP medications (age ≥ 65 years)	Circumstances to review	Reason to review
Statins (Primary Prevention)	Indications of shortened life expectancy[10], unless there is an acute vascular syndrome	In the absence of a recent acute coronary syndrome or cerebrovascular event, the discontinuation of a statin toward the end of life is reasonable www.medicinesresources.nhs.uk/GetDocument.aspx?pageId=797557
	In patients displaying symptoms of muscle weakness and pain	Risk of myopathy and rhabdomyolysis. Check creatinine kinase if patient presents with muscular symptoms. Refer to AAC Statin intolerance Pathway
		Risks may outweigh potential benefits
	Consider review in light of comorbidities, polypharmacy, general frailty, life expectancy, patient preference and ADR risk	NICE CG181: Cardiovascular disease https://www.nice.org.uk/guidance/CG181
Sulfonylureas (particularly Glibenclamide or Chlorpropamide)	With Type 2 diabetes	Risk of prolonged hypoglycaemia
Theophylline	Monotherapy for COPD	Safer, more effective alternatives, risk of adverse effects due to narrow therapeutic index http://www.bnssgformulary.nhs.uk/includes/documents/ COPD%20guidelines%20-April%2016%20v6.pdf
Tricyclic antidepressants ***NB. Withdraw gradually over at least 4 weeks – monitor effect***	With other anticholinergic medications	Risk of cumulative anticholinergic side effects
	Dementia	Risk of worsening cognitive impairment
	Glaucoma	May exacerbate glaucoma if untreated
	Cardiac conductive abnormalities	Pro-arrhythmic effects
	Constipation	May worsen constipation
	Combination with opiate or calcium channel blocker	Risk of severe constipation
	Prostatism or history of urinary retention	Risk of urinary retention
	Patients taking dosulepin	Increased cardiac risk & toxicity in overdose

STOP medications (age ≥ 65 years)	Circumstances to review	Reason to review
Ulcer healing drugs	PPI and H2RAs: dose for PUD > 8 weeks (withdraw gradually to prevent rebound hypersecretion of gastric acid) clopidogrel+ [es]omeprazole	Earlier discontinuation or dose reduction for maintenance/prophylactic treatment of PUD, oesophagitis or GORD indicated. Increased risk of C. *difficile* infection, pneumonia, osteoporosis and bone fractures,hyponatremia and hypomagnesemia www.sps.nhs.uk/articles/clostridium-difficile-infection-is-use-of-proton-pump- inhibitors-a-risk-factor-2/ GORD and dyspepsia in adults: investigation & management: www.nice.org.uk/guidance/CG184/ MHRA Drug Safety Update 2010 advises that concurrent use should be discouraged due to reduced antiplatelet effect, see www.gov.uk/drug-safety-update/clopidogrel-and-proton-pump-inhibitors-interaction-updated- advice https://remedy.bnssgccg.nhs.uk/formulary-adult/local-guidelines/1-gastro-intestinal-system-guidelines/
Vasodilator drugs (e.g. hydralazine, minoxidil)	With persistent postural hypotension i.e. recurrent > 20 mmHg drop in Sys BP In persistent oedema/fluid retention or tachycardia	Risk of syncope and falls Risk of exacerbation
Vitamins	Does not have a disorder that requires vitamin and mineral supplements.	Dietary supplements or 'pick-me-up' should be purchased as self -care.
Any regular duplicate drug class prescription	E.g. Two concurrent opiates, multiple NSAIDs, multiple diuretics. Two or more anticholinergics (antimuscarinics)	Optimisation of monotherapy within a single drug class prior to considering a new drug class Increased risk of side-effects including confusion falls and death

START medications (age ≥ 65 years)	Circumstances
ACE Inhibitor	Chronic heart failure – titrate up to maximum tolerated doses Following acute myocardial infarction Diabetes with nephropathy (e.g. overt urinalysis proteinuria or microalbuminuria (>30mg / 24 hours) ± serum biochemical renal impairment) Caution in CKD 4-5 – decision to start should be made by a renal physician
Anticoagulation (DOAC or warfarin)	Atrial fibrillation as per http://www.nice.org.uk/guidance/cg180 Following diagnosis of DVT and PE if benefit outweighs the risk of treatment For BNSSG guidelines https://remedy.bnssgccg.nhs.uk/formulary-adult/local-guidelines/2-cardiovascular-system-guidelines/
Antidepressants	In presence of moderate to severe depressive symptoms lasting at least 4 weeks SSRIs are in general better tolerated in patients with dementia and depression, however try to avoid Fluoxetine (long half-life) Paroxetine (anticholinergic activity) and Citalopram at doses >20mg. Paroxetine and fluoxetine also have a higher propensity for interactions than the other SSRIs as they are CYP inhibitors.
Antihypertensive	Systolic blood pressure consistently >160mm Hg
Antiplatelets	For ischaemic stroke or PVD as per http://www.nice.org.uk/guidance/ta210
Antipsychotic medication	Patients with a co-morbid mental illness (e.g. schizophrenia, persistent delusional disorder, psychotic depression or bipolar affective disorder) should not have this medication reduced without specialist advice[11]
Aspirin	Documented history of atherosclerotic coronary, cerebral or peripheral vascular disease in patients with sinus rhythm Following an acute MI Please note that if patient is already on another antiplatelet or anticoagulant the risks of starting Aspirin might outweigh the benefits
Beta-blocker (oral)	Chronic heart failure – titrate up to maximum tolerated doses With chronic stable angina, unless heart rate persistently <60bpm
Beta-agonist (inhaled)	BNSSG COPD guidance Review patients with mild, moderate or severe COPD at least once a year, and very severe COPD at least twice a year as per NICE guidance - Overview | Chronic obstructive pulmonary disease in over 16s: diagnosis and management | Guidance | NICE
Bisphosphonates	In patients taking maintenance oral corticosteroid therapy with previous fragility fractures or incident fractures during glucocorticoid therapy. Ensure there are no absorption interactions e.g. Calcium. Counsel patient on the correct way to take a bisphosphonate.
Calcium and vitamin D	In patients with known osteoporosis (radiological evidence or previous fragility fracture) or acquired dorsal kyphosis BNSSG guidelines for treatment of vitamin D deficiency in adults in Primary Care: BNSSG Vitamin D Prescribing guidelines
DMARD	With active moderate-severe rheumatoid disease lasting >12 weeks, unless chronic infections, anaemia or liver disease present
Fibre supplement	For chronic symptomatic diverticular disease with constipation
Laxatives	In patients taking opioids - to prevent constipation Refer to BNSSG guidelines for opioid induced constipation. https://remedy.bnssgccg.nhs.uk/media/3896/management-of-constipation-in-adults-guideline-2020.pdf

Ulcer healing drugs (PPI, H2RA) **(clopidogrel+[es]omeprazole should be avoided due to reduced antiplatelet effect)**	For severe reflux or peptic stricture requiring dilatation The risk of bleeding is increased when low-dose aspirin is combined with other drugs that can increase the risk of bleeding. If these drugs are used concurrently with low-dose aspirin, consider the need for gastro-protection with a proton pump inhibitor (such as omeprazole) More information available at http://cks.nice.org.uk/antiplatelettreatment#!prescribinginfosub Drugs that can increase the risk of bleeding include: - **Antiplatelet drugs** (such as clopidogrel, prasugrel, or ticagrelor). - Nonsteroidal anti-inflammatory drugs (**NSAIDs**) (for example ibuprofen). - **Oral and parenteral anticoagulants** (for example warfarin or heparin). Low dose aspirin and oral anticoagulants are usually co-prescribed on the advice of a specialist. Close monitoring is required. - **SSRIs** (such as fluoxetine), venlafaxine, or duloxetine. Consider alternatives that may be safer, such as trazodone, mianserin, mirtazapine, or reboxetine. - Other drugs known to increase gastrointestinal bleeding (for example **corticosteroids**).
Statins	NICE CG181 (https://www.nice.org.uk/guidance/CG181) BNSSG Management of Blood Lipid Levels For older people with mild to moderate frailty statins (mainly Atorvastatin) may be of benefit in reducing the risk of non-fatal myocardial infarction. Be aware of factors that may make treatment inappropriate (comorbidities, polypharmacy, general frailty, life expectancy (evidence shows that benefits of statins for primary prevention are seen at the earliest after 2 years of therapy), patient preference and ADR risk). Whenever possible avoid using Simvastatin due to higher side effects risk Primary prevention of CVD when 10% or greater 10-year risk of developing CVD. (Estimate the level of risk using the QRISK2 assessment tool) Adults with T1 diabetes who are older than 40 years **or** have had diabetes for more than 10 years **or** have established nephropathy **or** have other CVD risk factors CKD and Secondary prevention of CVD (documented history of coronary, cerebral or peripheral vascular disease)

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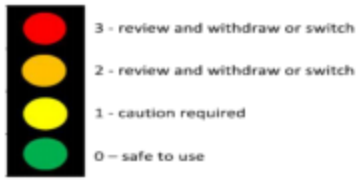
Appendix 1

South London and Maudsley NHS
NHS Foundation Trust

Mental Health of Older Adults and Dementia Clinical Academic Group



Anticholinergic Effect on Cognition (AEC) Scale

Limited data so unable to score		Drugs with AEC score of 0		Drugs with AEC score of 1	Drugs with AEC score of 2	Drugs with AEC score of 3
Alendronic Acid	Phenytoin	Alprazolam	Lorazepam	Amiodarone	Amantadine	Alimemazine (trimeprazine)
Allopurinol	Pregabalin	Amlodipine	Losartan	Aripiprazole	Chlorphenamine	Amitriptyline
Anastrozole	Ramipril	Amoxycillin	Lovastatin	Bromocriptine	Desipramine	Atropine
Apixaban	Rivaroxaban	Aspirin	Lurasidone	Carbamazepine	Dicycloverine (dicyclomine)	Benztropine
Baclofen	Rosuvastatin	Atenolol	Meloxicam	Citalopram	Dimenhydrinate	Chlorpromazine
Bisoprolol	Spironolactone	Atorvastatin	Metoclopramide	Diazepam	Diphenhydramine	Clemastine
Bumetanide	Tamoxifen	Buproprion	Metoprolol	Domperidone	Disopyramide	Clomipramine
Captopril	Topiramate	Cepahlexin	Moclobemide	Fentanyl	Levomepromazine (methotrimeprazine)	Clozapine
Carbimazole	Tizanidine	Cetirizine	Morphine	Fluoxetine		Cyproheptadine
Carvedilol	Verapamil	Chlordiazepoxide	Naproxen	Fluphenazine	Olanzapine	Dothiepin
Chlortalidone	Zopiclone	Cimetidine	Omeprazole	Hydroxyzine	Paroxetine	Doxepin
Clarithromycin	Zotepine*	Ciprofloxacin	Paracetamol	Iloperidone	Pethidine	Hyoscine hydrobromide
Clonazepam		Clopidogrel	Pantoprazole	Lithium	Pimozide	Imipramine
Codeine		Darifenacin	Pravastatin	Mirtazapine	Prochlorperazine	Lofepramine
Colchicine		Diclofenac	Propranolol	Perphenazine	Promazine	Nortriptyline
Dabigatran		Diltiazem	Rabeprazole	Prednisolone	Propantheline	Orphenadrine
Dexamethasone		Enalapril	Ranitidine	Quinidine	Quetiapine	Oxybutynin
Dextropropoxyphene		Entacapone	Risperidone	Sertindole	Tolterodine	Procyclidine
Digoxin		Fexofenadine	Rosiglitazone	Sertraline	Trifluoperazine	Promethazine
Erythromycin		Fluvoxamine	Simvastatin	Solifenacin		Trihexyphenidryl (benzhexol)
Flavoxate*		Furosemide	Theophylline	Temazepam		Trimipramine
Hydrocodone		Gabapentin	Thyroxine			
Irbesartan		Gliclazide	Tramadol			
Lansoprazole		Haloperidol	Trazodone			
Levetiracetam		Ibuprofen	Trimethoprim			
Metformin		Ketorolac	Trospium			
Methocarbamol		Lamotrigine	Venlafaxine			
Methotrexate		Levadopa	Valproate			
Nitrofurantoin		Lisinopril	Warfarin			
Oxcarbazepine		Loperamide	Ziprasidone			
Oxycodone		Loratadine	Zolpidem			

Bishara et al. Int J Geriatr Psychiatry 2016 June 9 doi: 10.1002/gps.4507

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Appendix 2

Rockwood frailty scale

Clinical Frailty Scale*

1 **Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 **Well** – People who have **no active disease syptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 **Managing Well** – People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 **Vulnerable** – While **not dependant** on others for daily help, often **syptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 **Mildly Frail** – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 **Moderately Frail** – People need help with **all outside activities** and with **keeping house.** Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **Severely Frail – Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 **Very Severely Frail** – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9 **Terminally Ill** – Approaching the end of life. This category applies to people with a **life expectancy <6 months**, who are **not otherwise evidently frail.**

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia.

Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia** recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

*1. Canadian Study on Health and Aging, Revised 2008.

2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005; 173: 489-495

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Appendix 3

Anticholinergic side effects

Mild or moderate anticholinergic effects	Severe anticholinergic effects
Somatic symptoms	**Somatic symptoms**
Anhidrosis	Congestive heart failure
Blurry vision	Fecal impaction/paralytic ileus
Constipation	Malnutrition
Dry mouth	Respiratory infections
Fatigue	Tachyarrhythmia
Mydriasis	Urinary retention/urinary tract infection
Tachycardia/palpitations	Cardiac attack
Urinary hesitancy	
Neuropsychiatric symptoms	**Neuropsychiatric symptoms**
Drowsiness	Agitation
Nervousness, excitement	Ataxia
Mild amnesia and cognitive dysfunction	Complex visual hallucinations
Poor attention	Delirium
Restlessness	Epileptic seizures
	Hallucinations
	Hyperreflexia
	Nocturnal rhythm disturbance

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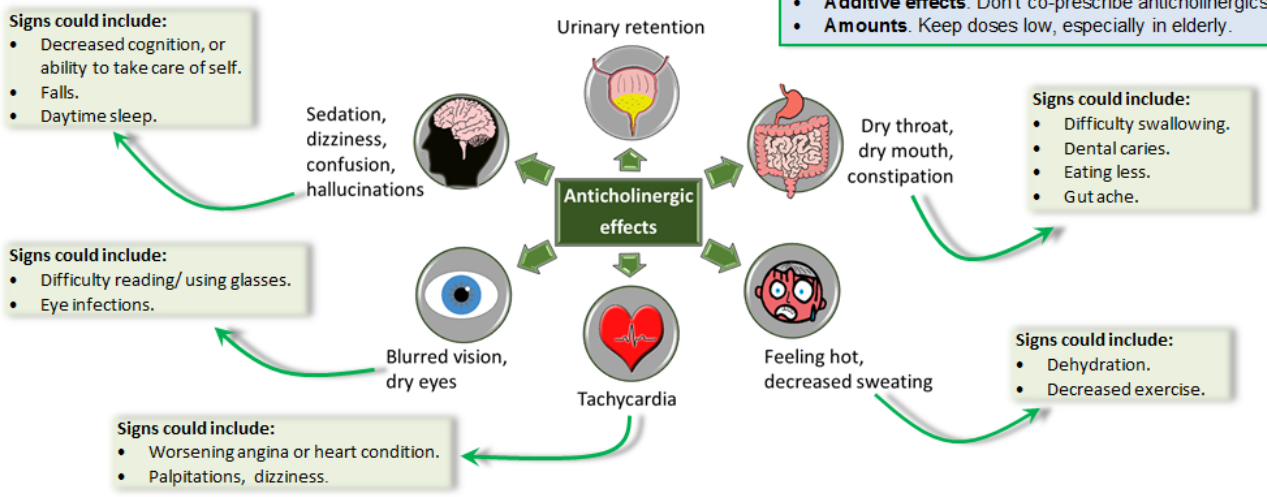
Managing Anticholinergic Side Effects

from **www.medicinesafety.co.uk**

General approach is to review patients regularly and:

- **Awareness**. Know your anticholinergic effects.
- **Alternatives**. Use lower risk medicines or non-drugs.
- **Additive effects**. Don't co-prescribe anticholinergics.
- **Amounts**. Keep doses low, especially in elderly.



Indication	Higher anticholinergic potential	Example LOWER anticholinergic choices
Analgesia for neuropathic pain	Amitriptyline, imipramine, nortriptyline carbamazepine	Gabapentin, pregabalin, capsaicin cream, non-pharmacological options
Antidepressant	Amitriptyline, imipramine, nortriptyline paroxetine, sertraline	Venlafaxine, trazodone, duloxetine, mirtazapine, citalopram, sertraline, psychotherapy
Antiemetics and vertigo	Prochlorperazine, cyclizine, promethazine, hyoscine	Ondansetron, domperidone, treat the cause of these symptoms (*e.g.* betahistine for Ménière's)
Antihistamine	Chlorphenamine, hydroxyzine, promethazine, diphenyhdramine	Cetirizine, desloratadine, fexofenadine, topical options (for e.g. hay fever, skin)
Antipsychotic	Chlorpromazine, clozapine, olanzapine	Aripiprazole, ziprasidone, quetiapine, risperidone
Gastrointestinal spasm	Dicycloverine, hyoscine, propantheline	Mebeverine, peppermint oil, diet changes
Urology: incontinence, overactive bladder	Oxybutynin, solifenacin, tolterodine, trospium, propiverine	Mirabegron, alpha blockers (for selected men), non-pharmacological options

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Appendix 4

Toxidromes Compared: Anticholinergic, Cholinergic, Opioid, Sympathomimetic, Sedative-Hypnotic https://www.grepmed.com/images/2593/sympathomimetics-anticholinergics-toxidromes-toxicology-comparison

	HR & BP	Resp.	Temperature	Pupils	Bowel Sounds	Diaphoresis
Anticholinergic **Anticholinergics** –Atropine, scopolamine, glycopyrrolate benztropine, trihexyphenidyl **Antihistamines** – Chlorpheniramine, Cyproheptadine, Doxylamine, Hydroxyzine, Dimenhydrinate, Diphenhydramine, Meclizine Promethazine	↑	No change	↑	Dilated	↓	↓
Cholinergic Organic Phosphorous Compounds: Carbamates • Arecholine, Pilocarpine, Urecholine (Betanechol), Carbachol, Choline, Metacholine, Mushrooms	No change	No change	No change	Pinpoint	↑	↑
Opioid Morphine • Codeine • Tramadol • Heroin • Meperidine • Diphenoxylate • Hydromorphone • Fentanyl • Methadone • Propoxyphene • Pentazocine • DXM • Oxycodone • Hydrocodone	↓	↓	↓	Pinpoint	↓	↓
Sympathomimetic Caffeine, cocaine, amphetamines, methamphetamines, Ritalin, LSD, Theophylline, MDMA	↑	↑	↑	Dilated	↑	↑
Sedative-Hypnotic anti-anxiety agents, muscle relaxants, antiepileptics and preanesthetic medications –Barbituates –Benzodiazepines	↓	↓	↓	No change	↓	↓