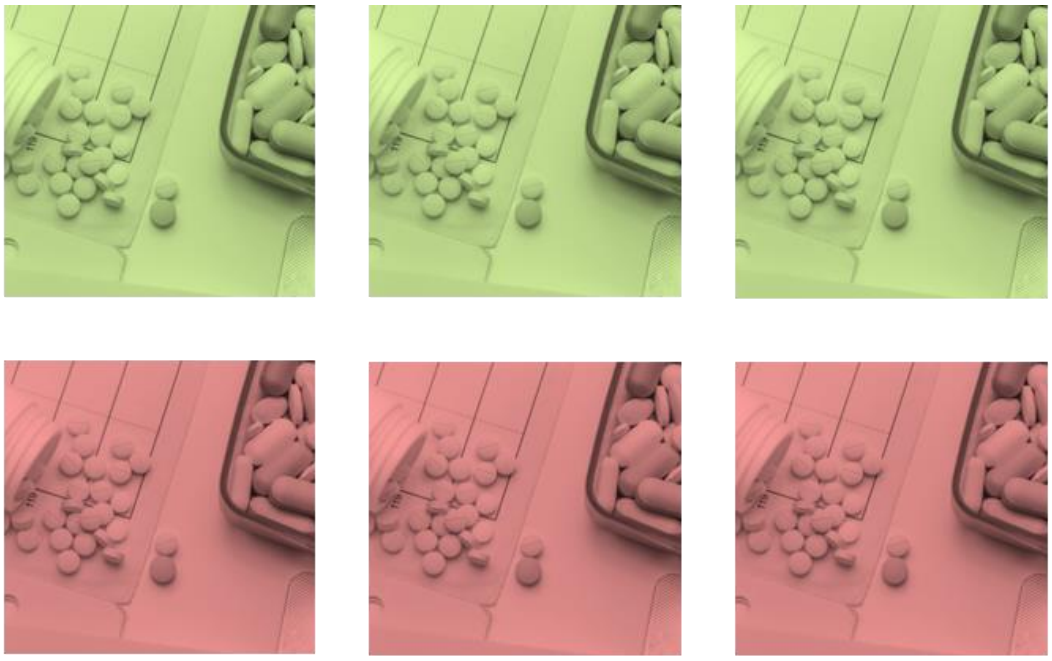
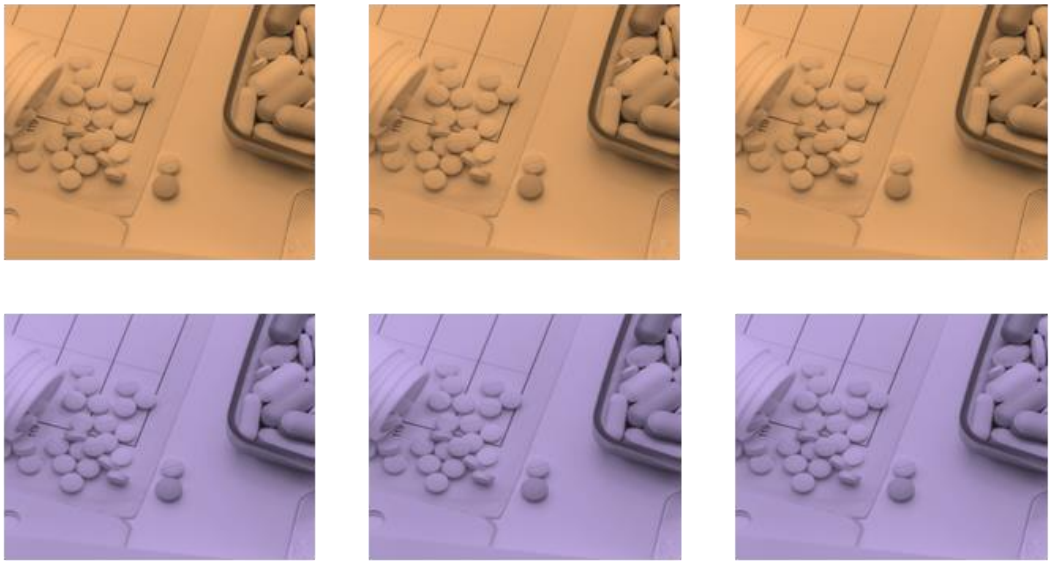


Polypharmacy Guidance
Realistic Prescribing

3rd Edition, 2018



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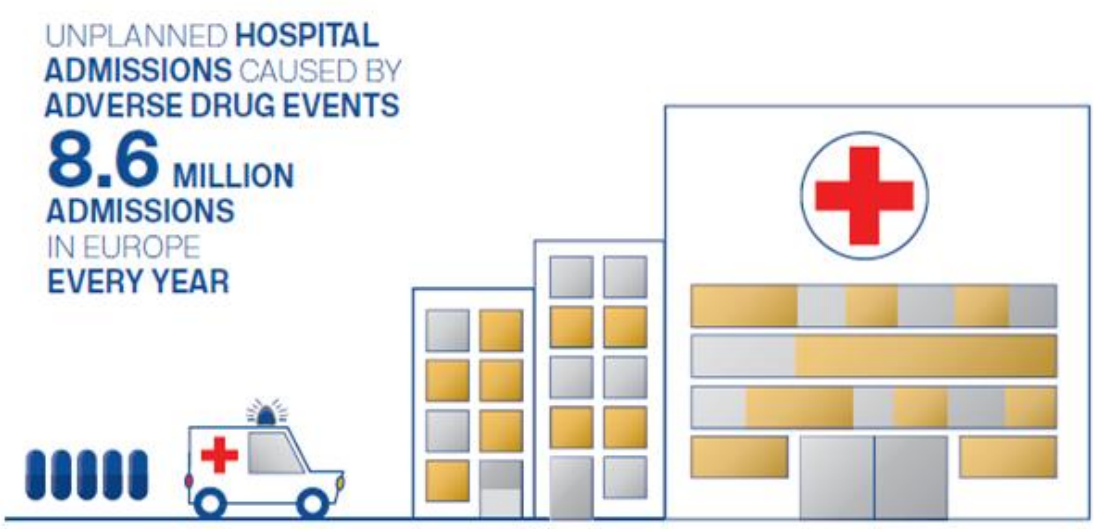
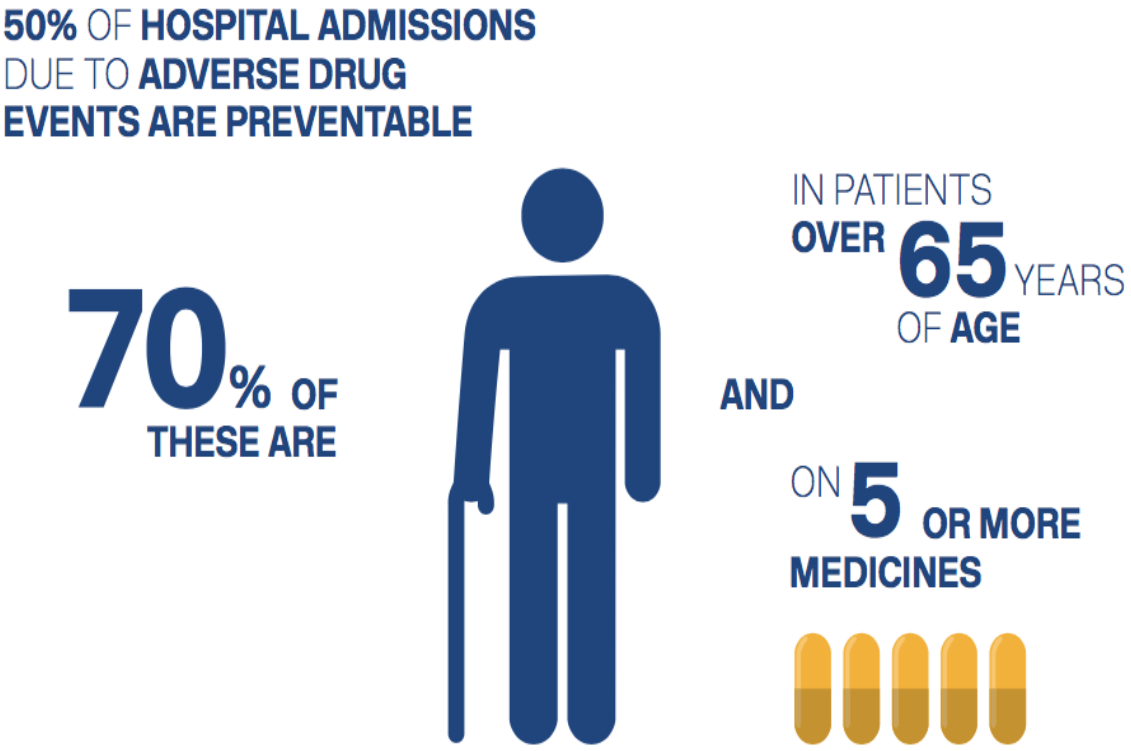

UNPLANNED HOSPITAL ADMISSIONS CAUSED BY ADVERSE DRUG EVENTS
8.6 MILLION ADMISSIONS IN EUROPE EVERY YEAR


50% OF HOSPITAL ADMISSIONS DUE TO ADVERSE DRUG EVENTS ARE PREVENTABLE
70% OF THESE ARE
IN PATIENTS OVER 65 YEARS OF AGE
AND
ON 5 OR MORE MEDICINES

Foreword

The care of patients with multi-morbidities (multiple medical conditions) is the greatest challenge now faced by the health service, as it can create overly complex health care for some of the most vulnerable in society. The vast majority of medical research, guidelines and contractual agreements have focussed on single targets for single disease states, whereas in reality most patients have multi-morbidities, requiring multiple treatments.[1] The resulting polypharmacy (use of multiple medicines) can be appropriate or inappropriate and the key healthcare aim for the individual patient is to ensure the safe and effective use of their multiple medicines. Despite research into this area being in relative infancy there exists a requirement to produce guidance for both patients and healthcare providers, based on the best evidence to date.

Polypharmacy becomes inappropriate when the medication risks begin to outweigh benefits for an individual patient. The aim of addressing this is to identify those patients at greatest risk of harm and to agree a medication regimen that is tailored to their changing needs and expectations.

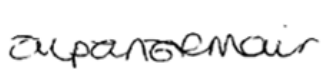
An important principle in improving the care of patients with multi-morbidities is to ensure minimised fragmentation of health and social services through improved integrated care, which can help address medication systems, processes and procedures that are flawed or dysfunctional. In addition, there is a need to address polypharmacy management as a public health issue, as multi-morbidities do not just affect the elderly. For example, 29% of people with multi-morbidities are under the age of 65 years of age, and come from the most deprived communities.[1]

Since the publication of *Choosing Wisely*, key policy documents, including *Realistic Medicine* and *Prudent Healthcare*, have raised awareness of using resources wisely and the importance of the patient's involvement in decision making about their healthcare.

We are delighted to present the third edition of *Polypharmacy Guidance, Realistic Prescribing 2018*, which aims to provide guidance on preventing inappropriate polypharmacy at every stage of the patient journey. The *7-Steps* is a clear structure for both the **initiation** of new and the **review** of existing treatments, which has been updated to place a greater emphasis on *'what matters to the patient'*? The *Drug Efficacy (NNT)* tables have been refined and provide the relative clinical efficacy of common interventions, for the patient. Harm reduction can be targeted through the use of the *Cumulative Toxicity* and *Anticholinergic Burden* tools. An extensive set of *Polypharmacy Indicators* have been developed and prioritised by a clinical consensus approach, in order to standardise *Case Finding*, understand prevalence, and provide *Clinical Outcomes* monitoring. We are also excited to launch a patient app which will support patients in shared decision making about their medicines.

Interest in the importance of polypharmacy management is now international, and the WHO Third Global Patient Safety Challenge, *Medication without Harm*, has included the appropriate management of polypharmacy as a key flagship area to address. The aim is to reduce severe avoidable medication related harm by 50% over 5 years, globally. This polypharmacy guidance also addresses the use of high risk medicines and ensures that information on appropriateness of medicines is shared across transitions of care.

With the publication of this *Polypharmacy Guidance, Realistic Prescribing 2018*, and supported by *Realistic Medicine*, the requirement now is that the NHS Boards will build on the foundational work of the last five years and focus resource on accelerating the capacity of polypharmacy reviews in order to further increase the benefit to patients.



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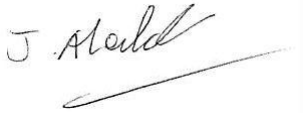

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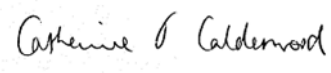

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Chief Medical Officer

Acknowledgements

It has been a pleasure to chair the development of third edition of *Polypharmacy Guidance, Realistic Prescribing 2018*, working with a team who are committed to improving outcomes for patients. This has been produced by the collaborative efforts of a multidisciplinary team of clinicians, academic and policy makers from across Scotland, who are already delivering polypharmacy reviews to improve the levels of appropriate prescribing and patient safety. The development of *Case Finding* and *clinical outcome* indicators was led by Tobias Dreischulte, in collaboration with Sean MacBride-Stewart. Data relating to numbers needed to treat and adverse drug reactions have been updated by medicines information pharmacists, represented by Craig Rore. The polypharmacy app has been updated to include a new patient facing facility, developed with colleagues from Scottish Government eHealth. Thanks also to those who contributed comments to the consultation. Finally, I would like to thank Jake Laurie for the support he has provided in terms of presentation of this document.

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Executive Summary

Caring for patients with multi-morbidities and polypharmacy is an increasing global challenge. With up to 11% of unplanned hospital admissions being attributable to harm from medicines and over 70% of these being due to elderly patients on multiple medicines, there are significant opportunities to reduce this burden by timely and effective interventions.[2]

The case for effective polypharmacy management is quite clear, but in a complex healthcare setting with many competing priorities it is useful to outline the quality and economic reasons why it should be prioritised. A holistic polypharmacy patient review has the potential to address all six dimensions of quality: efficacy, safety, efficiency, timely, equity and acceptability.[3] Including discussion of the relative clinical effectiveness of commonly used medicines (e.g. *Drug Efficacy (NNT)* table) or identifying safety issues (e.g. *Cumulative Toxicity* and *Anticholinergic Burden* tools) can help empower patients, families and their carers to become actively involved and engaged with their treatment and care decisions. A holistic polypharmacy review will often result in an element of deprescribing, but stopping medicines should not be the primary driver.

We all have a role to play in driving the change to manage polypharmacy, whether patient, clinician, academic or policy maker. The combined knowledge and experience of physician, pharmacist, nurse and the patient are required to ensure the patients treatment is optimised to achieve their preferred outcomes. Further research is required to help inform clinical practice, and policy needs to continue to be shaped to support effective polypharmacy management.

The EU funded project SIMPATHY [4] has spent the last two years studying polypharmacy management in Europe. This work has identified six key recommendations to improve medication safety of which polypharmacy is an essential element:

1. Use a systems approach that has multidisciplinary clinical and policy leadership
2. Nurture a culture that encourages and prioritises the safety and quality of prescribing
3. Ensure that patients are integral to the decisions made about their medicines and are empowered and supported to do so
4. Use data to drive change and measure outcomes
5. Adopt an evidence based approach with a bias towards action
6. Utilise, develop and share tools to support implementation

Lessons learnt from SIMPATHY and the continuous improvement of polypharmacy management in Scotland have helped to shape this *Polypharmacy Guidance, Realistic Prescribing 2018*.

Greater emphasis has been placed on shared decision making to actively engage the patient with the *7-Step* medication review. The *Drug Efficacy (NNT)* tables help discussion with the patient regarding the relative potential benefits of a range of common therapeutic interventions. *Polypharmacy Indicators* have been developed through consensus to identify patients at increased risk of drug related harm (*Case Finding),* understand prevalence and monitor *Clinical Outcomes.* The *Sick Day Rule* guidance has been modified to allow patients and clinicians to highlight additional medications that may cause acute kidney injury during episodes of illness with dehydration. Where possible, all of these resources have been made available electronically through integration with the GP clinical systems and revised *polypharmacy app* which supports patients in shared decision making about their medicines.

The challenge to safely use multiple medicines for patients with multi-morbidity is now gaining international attention. The WHO Third Global Patient Safety Challenge, *Medication without Harm*, has included the appropriate management of polypharmacy as a key flagship area to address. This polypharmacy guidance also addresses the use of high risk medicines and ensures that information on appropriateness of medicines is shared across transitions of care.

Contents

1. General Principles

1.1 What is polypharmacy and why is it important?

Medication is by far the most common form of medical intervention for many acute and chronic conditions. Drug therapy can be highly effective in preventing disease or slowing disease progression, with guidelines for single diseases recommending the use of a variety of evidence based drug treatments. However, there is often a mismatch between prescribing guidelines for specific medical conditions and the range of clinical complexity found in individuals. For complex patients with multiple conditions; frailty; a dominant condition (e.g. dementia) or approaching the end of their lives, the implementation of the sum of evidence based recommendations may not be rational, may increase the risk of adverse drug events and may not align with the patient's preferences.

> **Appropriate polypharmacy** is present, when: (a) all drugs are prescribed for the purpose of achieving specific therapeutic objectives that have been agreed with the patient; (b) therapeutic objectives are actually being achieved or there is a reasonable chance they will be achieved in the future; (c) drug therapy has been optimised to minimise the risk of adverse drug reactions (ADRs) and, (d) the patient is motivated and able to take all medicines as intended.

The term polypharmacy itself just means "many medications" and is defined to be present when a patient takes two or more medications. It is recognised that polypharmacy is often beneficial. For example, secondary prevention of myocardial infarction requires the use of at least four different classes of drugs (antiplatelets, statin, ACE inhibitor, beta blocker).

> **Inappropriate polypharmacy** is present, when one or more drugs are prescribed that are not or no longer needed, either because: (a) there is no evidence based indication, the indication has expired or the dose is unnecessarily high; (b) one or more medicines fail to achieve the therapeutic objectives they are intended to achieve; (c) one, or the combination of several drugs cause inacceptable adverse drug reactions (ADRs), or put the patient at an unacceptably high risk of such ADRs, or because (d) the patient is not willing or able to take one or more medicines as intended.

Appropriate polypharmacy requires consideration at any point of contact involving medication but there are five clear stages which should be used as a trigger to do this:

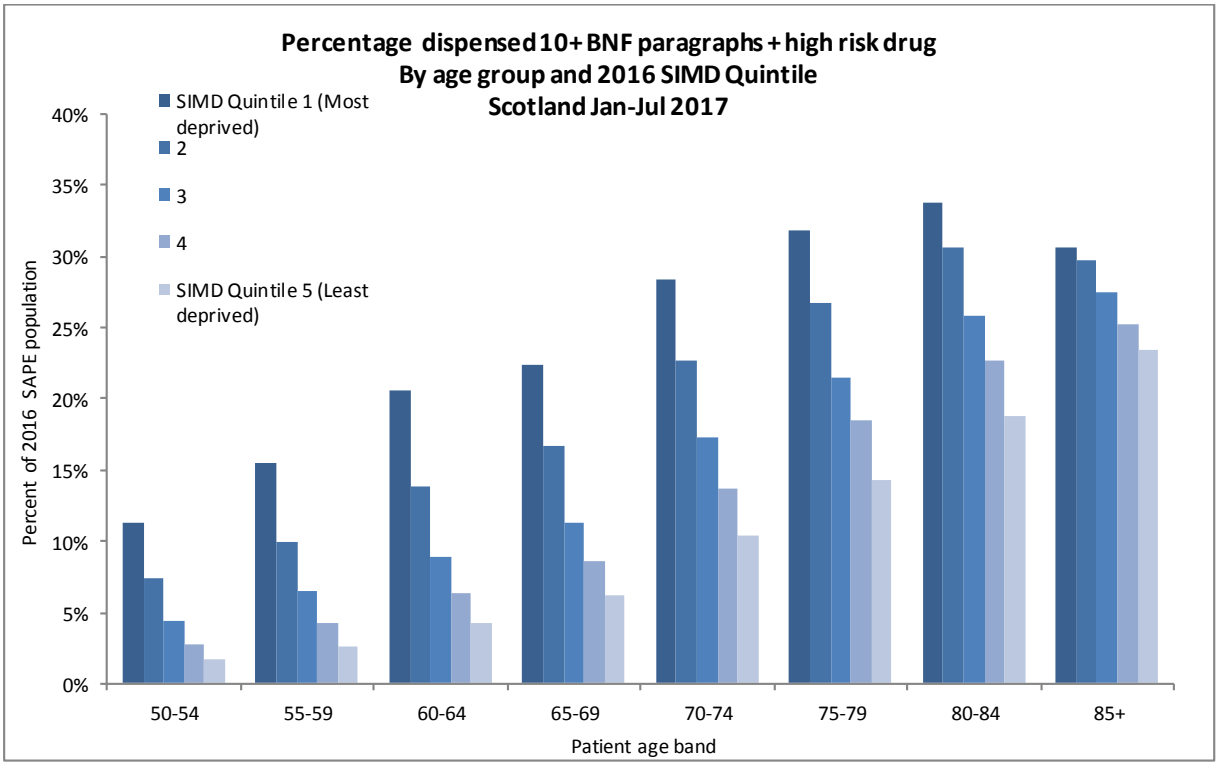
1. Prescribing (and risk assessment)
2. Medication review
3. Dispensing and administration
4. Communication and patient engagement
5. Medication reconciliation (at care transitions)

Although *Polypharmacy Guidance, Realistic Prescribing 2018* concentrates on the holistic patient-centred medication review, the principles, tools and recommendations can be used at any stage, especially at the point of prescribing.

1.2 Which patients should be targeted for review?

Patients at highest risk of inappropriate polypharmacy are those with the greatest frailty, on the most medicines and taking high risk medicines. There has been a comprehensive review of the case finding criteria by which patients, who may benefit the most from a polypharmacy review are identified. In the previous version of this guideline, these criteria were based on age, residency in a care home, number of repeat medicines prescribed and Scottish Patients at Risk of Readmission and Admission (SPARRA) score of 40-60% (Appendix G).

Emerging trial evidence demonstrates the importance and impact of targeting patients with high-risk prescribing.[5-13] Holistic face-to-face review of these patients reduced risk for the individuals and also demonstrated a reduction in hospital admissions for acute kidney injury. The success of this approach has been used by the guideline development group to consider a wider range of *Case Finding* indicators to target patients on high risk medications (Appendix E).



Another important area that the guideline development group considered was the effect of deprivation on rates of polypharmacy. The review of polypharmacy prescribing data (10+ BNF paragraphs plus a high risk medicine) by deprivation demonstrates that multi-morbidity, and its associated problems, presents 10 to 15 years earlier in more deprived communities.

The following revised case finding criteria are recommended as a way to prioritise patients for a polypharmacy medication review:

A. Aged 50 years and older and resident in a care home, regardless of the number of medicines prescribed
B. Approaching the end of their lives: adults of any age, approaching the end of their life due to any cause, are likely to have different medication needs, and risk versus benefit discussions will often differ from healthy adults with longer expected life spans. Consider frailty score (see section 1.6.1)
C. Prescribed 10 or more medicines (this will identify those from deprived communities where the average age is lower when taking 10 or more medications)
D. On high-risk medication (as defined by the *Case Finding* indicators (Appendix E), regardless of the number of medicines taken

1.2.1 High Risk Medicines

During a study in 2004 carried out by Pirmohamed[64] into the burden of Adverse Drug Reactions (ADRs) on hospital admissions, a number of high risk medicines were identified; they are:

BNF Section	Examples
2.1 Positive inotropic medicines	*Diclofenac, digoxin*
2.2 Diuretics	*Bendroflumethiazide, spironolactone, furosemide*
2.5 Hypertension / heart failure	*Ramipril, enalapril, losartan*
2.8 Anticoagulants and protamine	*Warfarin, rivaroxaban, edoxaban, apixaban, dabigatran*
2.9 Antiplatelets	*Clopidogrel, dipyridamole*
4.1 Hypnotics and anxiolytics	*Benzodiazepines, Z-drugs*
4.2 Antipsychotic / antimanic drugs	*Amisulpride, risperidone*
4.3 Antidepressants	*Amitriptyline, fluoxetine, paroxetine*
4.7.2 Opioid analgesics	*Tramadol, co-codamol, morphine, fentanyl*
10.1 Rheumatic diseases and gout	*NSAIDs, corticosteroids, methotrexate*

The study concluded that while these drugs have proven benefit for patients, they still present a potential harm to the patient and measures should be put in place to reduce the burden of ADRs and further improve the benefit:harm ratio.

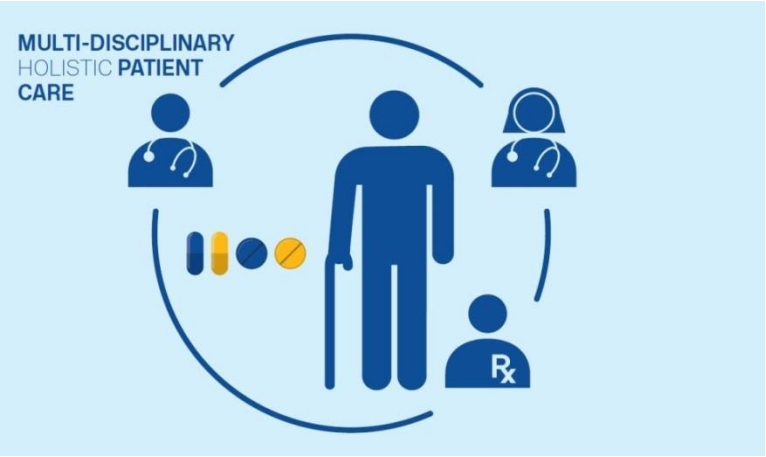
1.2.2 Coding for Review

When reviews are undertaken, in order to facilitate evaluation on the impact of polypharmacy reviews and patient outcomes, the reviews should be coded with the READ code **8B31B**. This will ensure that as patients move across transitions of care there is continuity in the management of their medicines.

A polypharmacy review is a medication review following the principles of the 7 steps, that considers all the clinical information and where outcomes from the review are discussed with the patient and/or carer; either face to face or by telephone.

1.3 Who is this guideline targeted at?

Everyone, including patients, policy makers and healthcare professionals, has a role to play in ensuring that when polypharmacy is used it is safe and appropriate. This guideline aims to provide resources, expertise and insight for all involved with polypharmacy management, despite the need for far more published research. It will take all members of the healthcare team to bring about significant improvement in this area, and utilising the multidisciplinary team for more complex interventions should be considered.



The core foundation of *Polypharmacy Guidance, Realistic Prescribing 2018* approach remains the holistic patient centred *7-Steps* medication review. However, once embedded, the principles should be considered at all critical stages of the medication use process: prescribing; reviewing; dispensing; communicating and reconciling. This is of particular importance at initiation of treatment in order to support shared decision making between the patient (and/or carers, and/or welfare proxies) and clinician.

Patients play a vital role if provided with the right information, tools and resources to make informed decisions about their medicines. Although many of the resources provided are aimed at clinicians, an App, patient leaflets and revised *Sick Day Rule* guidance will be available to aid patient understanding and involvement, in the review and supports shared decision making.

1.3.1 Recommended actions for Boards/IJBs

Boards and IJBs should consider this information alongside the data provided by the indicators (Appendix F) and identify a lead within the medicines management team and a local clinical lead, geriatrician or GP. These two leads should work together to drive delivery and implementation of the recommendations within this document, ensuring that the primary and secondary care interface is appropriately developed.

1.3.2 Recommended actions for clusters

Clusters should engage with local medicines management team to review data and consider utilising a quality improvement based approach to deliver change. They should also consider the adoption of Kotter's framework as set out in the SIMPATHY handbook[4] and shown below:

1 Establishing a sense of urgency
Communicating to stakeholders the need to change current ways of reviewing medication to benefit patient care- improvement in patient safety and outcomes from medicines. Examining other projects that are developing and whether they pose a threat to the development of the framework. Existing projects may focus on cost efficiencies rather than on patient safety due to budgetary pressures.

2 Forming a powerful guiding coalition
A project group is assembled including both primary and secondary care clinicians made up of doctors, pharmacists and geriatricians and Long-term Conditions collaborative leads locally and nationally. Have discussions about working together to inform work of Director of Pharmacy and public health both locally and nationally.

3 Creating a vision
A vision is created as to what the project might achieve for patient care and for the Healthcare Provider. Project plan outlines strategies for achieving the vision.

4 Communicating the vision
Share this in written communication and have face to face dialogue with people both locally and nationally.

5 Empowering others to act on the vision
Looking at the obstacles to change the biggest one will be ownership so provide feedback and adaptation of the protocol e.g. link with anticipatory care plans

6 Planning for and creating short-term wins
To gather data and provide feedback within a relatively short space of time after review framework is piloted; share data from pilots and used to build the business case. Break the project down into smaller tasks so that results can be seen and shared. E.g. design of guidance for review.

7 Consolidating improvements and producing still more change
Engage with individuals that might influence change in policy to adopt the vision. Transfer of project to other areas to reinvigorate the project e.g. running project in another locality and other health care providers.

8 Institutionalising new approaches
Sharing of benefits to the new process to the organisation e.g. reduced admissions and improved patient care. Adoption of project into nationally delivered service development, e.g. sharing outcomes with local and national leads on service development.

1.4 How does this guideline aim to help?

Polypharmacy Guidance, Realistic Prescribing 2018, provides expert knowledge, structure and tools to enable targeted polypharmacy management through:

- Structured *7-Steps* patient-centred medicines review
- Increased knowledge of medicines safety with the *Anticholinergic Burden* and *Cumulative Toxicity* tools
- Worked examples as case studies
- Hot topics and further advice on how to stop medication
- Validated *Polypharmacy Indicators* to target *Case Finding*, identify prevalence and monitor *Clinical Outcomes*

1.5 The *7-Steps* medication review

The following *7-Steps* are intended as a guide to structure the review process and are presented as:

table 2a an overview of key considerations at each step
table 2b an overview of therapeutic groups by each step
table 2c provides greater detail on table 2b by therapeutic area and is an amalgamation of existing collections of medication assessment tools (START/STOP, DQIP and others)

N.B. No list can be comprehensive and the reviewers clinical judgement and experience continues to be essential in tailoring the advice given to the needs of an individual patient and to identify other additional medication related problems.

Step 1: (Aim) What matters to the patient?

- Identify aims and objectives of drug therapy by asking the patient ***what matters to you*?**
- Explain any key information such as laboratory markers
- Establish treatment objectives with the patient through shared decision making

Step 2: (Need) Identify essential drug therapy.

- Separate the list of medicines which the patient is taking
- Ensure the patient understands the importance of essential drug therapy
- All medication whether herbal, prescribed or traditional remedies should be included

Step 3: (Need) Does the patient take unnecessary drug therapy?

- For the remaining drugs, it should be verified that each has a function in achieving the therapeutic goals or outcomes that matter most to the patient
- Review preventative treatment to ensure the patient is able to continue taking medicine for required time to gain benefit (*Drug Efficacy (NNT)* table).
- Can lifestyle changes replace any unnecessary drug therapy?

Step 4: (Effectiveness) Are therapeutic objectives being achieved?

- Check treatment choice is the most effective to achieve intended outcomes
- If this is not the case, the possibility of patient non-adherence should be investigated as a potential explanation. Otherwise, the need for dose titration may also be considered. 50% of patients taking four or more medicines don't take them as prescribed (Medication Adherence: WHO Cares?).

Step 5: (Safety) Is the patient at risk of ADRs or suffers actual ADRs?

- The presence of ADRs can sometimes be identified from laboratory data (e.g. hypokalaemia from diuretic use)
- The patient may report such symptoms (including drug-drug and drug-disease interactions, but also the patient's ability to self-medicate)
- Ask the patient specific questions (e.g. about the presence of anticholinergic symptoms, dizziness or drowsiness). If patient is experiencing ADRs, use Yellow Card Reporting

Step 6: (Efficiency) Is drug therapy cost-effective?

- Opportunities for cost minimisation should be explored, but changing drugs for cost reasons should only be considered if effectiveness, safety or adherence would not be comprised
- Ensure prescribing is in line with current formulary recommendations

Step 7: (Patient-centred) Is the patient willing and able to take drug therapy as intended?

- Does the patient understand the outcome of the review?
- Ensure drug therapy is tailored to patient preferences
- Agree and communicate plan with patient and/or welfare proxy
- Even if adult lacks capacity, adults with Incapacity Act still requires that the adult's views are sought. Ensure "Adults with Incapacity Documentation" in place

Table 2a: An overview of key considerations at each step

Domain	Steps		Process
Aims	1.	What matters to the patient?	**Review diagnoses and identify therapeutic objectives with respect to:** • What matters to me (the patient)? • Understanding of objectives of drug therapy • Management of existing health problems • Prevention of future health problems
Need	2.	Identify essential drug therapy	**Identify essential drugs (not to be stopped without specialist advice):** • Drugs that have essential replacement functions (e.g. levothyroxine) • Drugs to prevent rapid symptomatic decline (e.g. drugs for Parkinson's disease, heart failure)
	3.	Does the patient take unnecessary drug therapy?	**Identify and review the (continued) need for drugs:** • With temporary indications • With higher than usual maintenance doses • With limited benefit in general for the indication they are used for • With limited benefit in the patient under review (See: *Drug Efficacy (NNT)* table)
Effectiveness	4.	Are therapeutic objectives being achieved?	**Identify the need for adding/intensifying drug therapy in order to achieve therapeutic objectives:** • To achieve symptom control • To achieve biochemical/clinical targets • To prevent disease progression/exacerbation
Safety	5.	Does the patient have ADR/Side Effects or is at risk of ADRs/Side Effects? Does the patient know what to do if they're ill?	**Identify patient safety risks by checking for:** • Drug-disease interactions • Drug-drug interactions (see *Cumulative Toxicity* tool) • Robustness of monitoring mechanisms for high-risk drugs • Drug-drug and drug-disease interactions • Risk of accidental overdosing (Yellow Card Scheme) **Identify adverse drug effects by checking for** • Specific symptoms/laboratory markers (e.g. hypokalaemia) • Cumulative adverse drug effects (see *Cumulative Toxicity* tool) • Drugs that may be used to treat ADRs caused by other drugs (*Sick Day Rule* guidance can be used to help patients know what do with their medicines if they fall ill)
Cost-effectiveness	6.	Is drug therapy cost-effective?	**Identify unnecessarily costly drug therapy by:** • Consider more cost-effective alternatives (but balance against effectiveness, safety, convenience)
Patient centeredness	7.	Is the patient willing and able to take drug therapy as intended?	**Does the patient understand the outcomes of the review?** • Does the patient understand why they need to take their medication? • Consider Teach back **Ensure drug therapy changes are tailored to patient preferences** • Is the medication in a form the patient can take? • Is the dosing schedule convenient? • Consider what assistance the patient might have and when this is available • Is the patient able to take medicines as intended? **Agree and Communicate Plan** • Discuss with the patient/carer/welfare proxy therapeutic objectives and treatment priorities • Decide with the patient/carer/welfare proxies what medicines have an effect of sufficient magnitude to consider continuation or discontinuation • Inform relevant healthcare and social care carers change in treatments across the care interfaces Add the READ code **8B31B** to the patients record so that when they move across transitions of care it is clear their medication has been reviewed

1.5.1 The *7-Steps* to appropriate polypharmacy

The *7-Steps* to appropriate polypharmacy demonstrates that the patient review process is not in fact a linear one off event, but cyclical, requiring regular repeat and review. The circle is centred around *what matters to the patient*, as they play a vital part in making informed decisions about their medicines, as long as they provided with the right information, tools and resources.

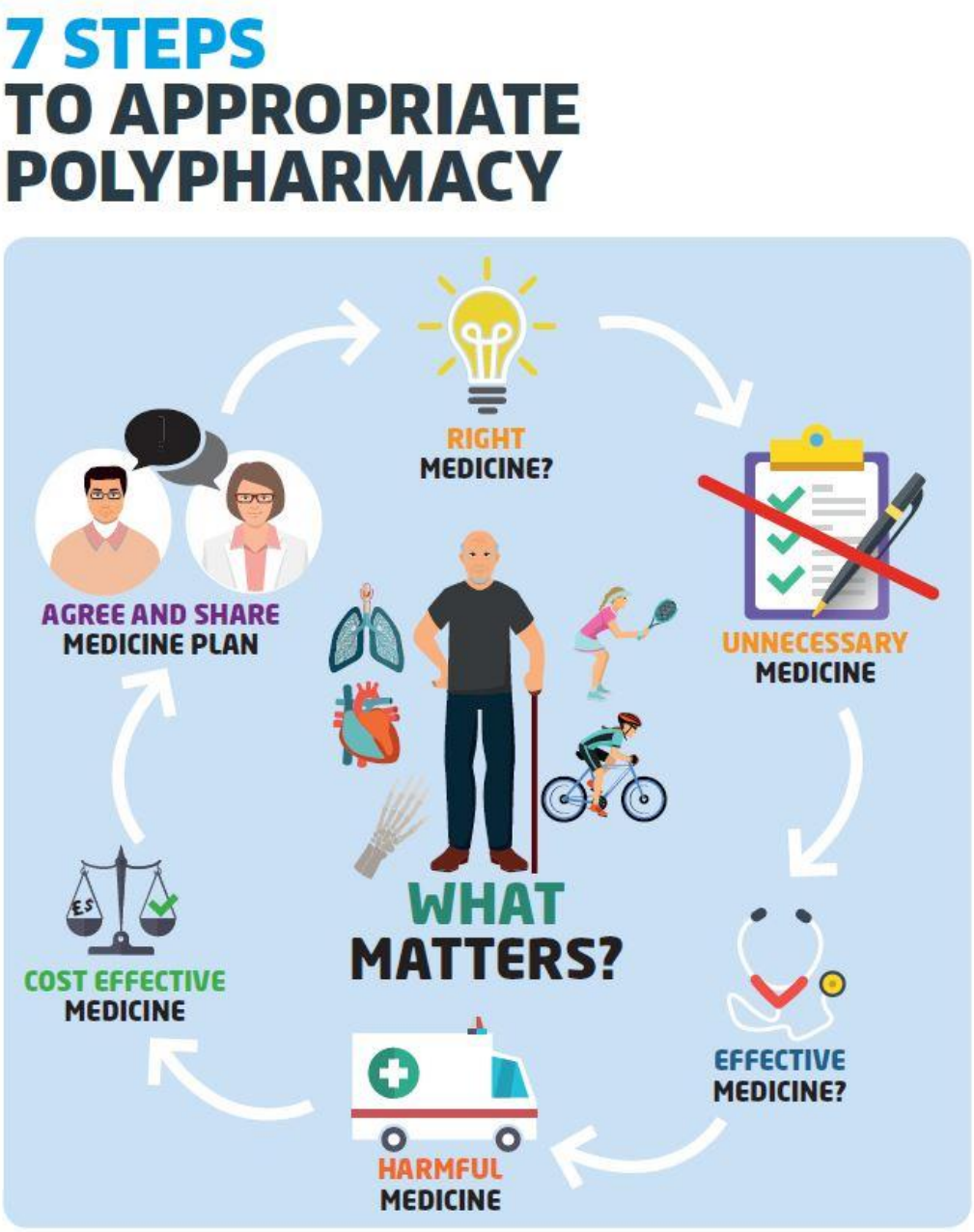


Table 2b: An overview of therapeutic groups under each step

Step 2: Essential drug therapy – Only consider stopping following specialist advice

Discuss with expert before stopping	Discuss with expert before altering	
○ Diuretics - in LVSD (7)	○ Anti-epileptics	○ Thyroid hormones
○ ACE inhibitors - in LVSD (17)	○ Antipsychotics	○ Amiodarone
○ Steroids	○ Mood stabilisers	○ Antidiabetics (34)
○ Heart rate controlling drugs	○ Antidepressants	○ Insulin
	○ DMARDs	

Step 3: Potentially unnecessary drug therapy

Check for expired indication	Check for valid indication	Benefit versus Risk
○ PPI (1) /H^2 blocker (2)	○ Anticoagulant (5)	○ Antianginals (12)
○ Laxatives (3)	○ Anticoagulant + antiplatelet (6)	○ BP control (15)
○ Antispasmodics (4)	○ Aspirin (6)	○ Statins (14)
○ Oral steroid (22, 36)	○ Dipyridamole (6)	○ Corticosteroids (20)
○ Hypnotics/anxiolytics (24)	○ Diuretics (7)	○ Dementia drugs (26)
○ H^1 blockers (29)	○ Digoxin (9)	○ Bisphosphonates (37)
○ Metoclopramide (28)	○ Peripheral vasodilators (10)	○ HbA_{1c} control (34)
○ Antibacterials (oral/topical) (32)	○ Quinine (11)	○ Female hormones (42)
○ Antifungals (oral/topical) (33)	○ Antiarrhythmics (13)	○ DMARDs (48)
○ Sodium/potassium supplements (44, 45)	○ Theophylline (21)	(see *Drug Efficacy (NNT)* table)
○ Iron supplements (44)	○ Antipsychotics (25)	
○ Vitamin supplements (44)	○ Tricyclic antidepressants (27)	
○ Calcium/Vitamin D (44)	○ Opioids (30)	
○ Sip feeds (44)	○ Levodopa	
○ NSAIDs (46)	○ Nitrofurantoin (32)	
○ Drops, ointments, sprays etc. (49)	○ Alpha-blockers (39)	
	○ Finasteride (40)	
	○ Antimuscarinics (urological) (41)	
	○ Cytotoxics/immunosuppressants (43)	
	○ Muscle relaxants (47)	

Step 4: Effectiveness

If therapeutic objectives are not achieved:	For patients with the following indications:
Consider intensifying existing drug therapy	**Consider if patient would benefit from specified drug therapy**
○ Laxative - Constipation (3)	○ see *Drug Efficacy (NNT)* table
○ Antihypertensives - BP control (15)	○ CHD - Antithrombotic, statins, ACEI/ARB, beta blocker
○ Antidiabetics - HbA_{1c} control (34)	○ Previous stroke/TIA - Antithrombotic, statin, ACEI/ARB
○ Warfarin - INR control	○ LVSD - Diuretic, ACEI/ARB, beta blocker
○ Rate limiting drugs - Heart rate?	○ AF - Antithrombotic, rate control
○ Respiratory drugs – Symptoms?	○ DMT2 - Metformin
○ Pain control	○ High fracture risk – Bone protection

Step 5: Safety

Drugs poorly tolerated in frail adults	High –risk clinical scenarios	
See Gold National Framework on frailty	○ *Cumulative Toxicity* tool	○ NSAID + age >75 (without PPI)
○ Antipsychotics (incl. phenothiazines)	○ *Sick day rule* guidance	○ NSAID + history of peptic ulcer
○ NSAIDs (46)	○ Metformin + dehydration	○ NSAID + antithrombotic
○ Digoxin (doses ≥ 250 micrograms) (9)	○ ACEI/ARBs + dehydration	○ NSAID + CHF
○ Benzodiazepines (24)	○ Diuretics + dehydration	○ Glitazone + CHF
○ Anticholinergics (incl. TCAs) (27)	○ NSAIDs + dehydration	○ TCA + CHF
○ Combination analgesics	○ NSAID + ACEI/ARB + diuretic	○ Warfarin + macrolide/quinolone
	○ NSAID + CKD	○ ≥2 anticholinergics (*Anticholinergic Burden* Tool)

Step 6: Cost-effectiveness

Check for		
○ Costly formulations (e.g. dispersible)	○ Branded products	○ Unsynchronised dispensing intervals (28 or 56 day supplies)
○ Costly unlicensed 'specials'	○ >1 strength or formulation of same drug	

Step 7: Adherence/patient centredness

Check Self-Administration (Cognitive)	Check Self-Administration (Technical)	
○ Warfarin/DOACs	○ Inhalers	○ Any other devices
○ Anticipatory care meds e.g. COPD	○ Eye drops	○ Bisphosphonates/calcium
○ Analgesics		
○ Methotrexate		
○ Tablet burden		

Table 2c: Detail by therapeutic area based on amalgamated medication assessment tools

Gastrointestinal system			
1	PPIs		○ If long term treatment is necessary, ensure dose does not exceed usual maintenance doses. Use the minimum dose required to treat symptoms ○ CAUTION: Clostridium difficile, osteoporosis, hypomagnesaemia
2	H2 blockers		○ CAUTION: Anticholinergic ADRs. *Anticholinergic Burden* tool
3	Laxatives		○ CAUTION: Vicious cycle of fluid loss > hypokalaemia > constipation ○ If >1 laxative, Do not stop abruptly. Reduce stimulant first and monitor effect ○ See advice from NICE on non-pharmacological options
4	Antispasmodics		○ Rarely effective, rarely indicated long term ○ CAUTION: Anticholinergic side effects
Cardiovascular System			
5	Anticoagulants		○ Check for expired indications (e.g. temporary loss of mobility that has now resolved) ○ Much more effective for stroke prevention in AF than anti-platelets ○ CAUTION: Bleeding events. Avoid combination of anticoagulants, antiplatelets and NSAIDs ○ Ensure patient adherence to dosing and monitoring regimen ○ Is patient is unfit for anticoagulation (warfarin and DOACs) for cognitive reasons
6	Antiplatelets		○ NOTE: Antiplatelets are no longer indicated for primary prevention of CHD ○ Aspirin plus clopidogrel indicated for maximum 12 months after ACS only ○ CAUTION: Bleeding events. Avoid combination of anticoagulants, antiplatelets and NSAIDs ○ Consider PPI in those with additional GI risk factors (consider lansoprazole or pantoprazole in preference to (es)omeprazole in patients taking clopidogrel) ○ Consider antiplatelets as part of secondary prevention strategy after CVD events ○ First line antiplatelet for secondary stroke prevention is clopidogrel
7	Diuretics		○ Usually essential for symptom control in heart failure ○ Note: Not indicated for dependent ankle oedema (consider medication causes, e.g. CCBs) ○ CAUTION: AKI and electrolyte disturbances ○ Advise patient to stop during intercurrent illness (*Sick Day Rule* guidance); is U&E monitoring robust?
8	Spironolactone		○ CAUTION: Hyperkalaemia. Risk factors include CKD (CI if eGFR<30ml/min), dose >25 mg daily , co-treatment with ACEI/ARBs, amiloride, triamterene, potassium supplements
9	Digoxin		○ CAUTION: Toxicity. Risk factors are: CKD, dose>125 micrograms daily, poor adherence, hypokalaemia, drug-drug interactions
10	Peripheral vasodilators		○ Rarely effective; rarely indicated long term
11	Quinine		○ Use short term only when nocturnal leg cramps cause regular disruption of sleep ○ Review effectiveness regularly ○ CAUTION: Thrombocytopenia, blindness, deafness
12	Antianginals		○ Consider reducing antianginal treatment if mobility has decreased ○ CAUTION: Hypotension (consider use of other BP lowering drugs; avoid the combination of nitrates with PDE-5 inhibitors)
13	Antiarrhythmic *Amiodarone*		○ In AF: Rate control usually has better benefit/risk balance than rhythm control ○ CAUTION: Overdosing. Maintenance should be max 200mg/day ○ CAUTION: Thyroid complications. Ensure monitoring tests are being done
14	Statins		○ Recommended for primary and secondary prevention in patients at high risk of CVD ○ CAUTION: Rhabomyolysis: Interactions (e.g. fibrates, dihydropyridines, antiinfectives) ○ Consider need for and intensity of treatment in light of life expectancy and ADR risk
15	BP Lowering Drugs		○ Limited evidence supporting tight BP control in older frail group ○ Individualise BP targets for primary and secondary prevention of CVD guidelines ○ Consider intensity of treatment in light of CVD risk life expectancy and ADR risk
16	Beta-blockers		○ Usually essential for rate and angina control in CHD and CHF (and often in AF) ○ BNF recommends up-titration of beta-blockers dose in CHF to evidence based target doses ○ CAUTION: Bradycardia in combination with diltiazem/verapamil, digoxin and amiodarone
17	ACEI/ARBs		○ Usually essential for symptom control in CHF. For other potential benefits, see *Drug Efficacy (NNT)* table ○ BNF recommends up-titration of ACEI/ARB doses in CHF to evidence based target doses ○ CAUTION: AKI. Avoid combination with NSAIDs and advise patient to stop when at risk of dehydration (*Sick Day Rule* guidance)
18	CCBs		○ CAUTION: Constipation, ankle oedema

			○ Dihydropyridines – CAUTION: Reflex tachycardia/cardiodepression: Avoid nifedipine in CHD/CHF ○ Diltiazem/verapamil – CAUTION: Bradycardia in combination with beta-blockers or digoxin
19	Spironolactone		○ Recommended in moderate to severe CHF: *Drug Efficacy (NNT)* table ○ CAUTION: Hyperkalaemia. Risk factors CKD, combination with ACEI/ARB, triamterene, amiloride ○ CAUTION: AKI. Avoid combination with NSAIDs and advise patient to stop when at risk of dehydration (*Sick Day Rule* guidance)
Respiratory System			
20	Inhalers		○ Assess symptom control (SIGN 153 ; ask about frequency of inhaler use/adherence) ○ Assess inhaler technique and adherence to dosing schedule ○ Also see *Quality Prescribing in Respiratory*
21	Theophylline		○ Monotherapy in COPD is not appropriate – safer, more effective alternatives are available ○ CAUTION: Toxicity (tachycardia, CNS excitation) ○ Avoid combination with macrolides or quinolones
22	Steroids		○ Long term oral use for respiratory disease is rarely indicated ○ Withdraw gradually if: use >3 weeks, >40 mg prednisolone/day ○ Stepping down steroid inhalers: Reduce slowly (by 50% every 3 months) ○ CAUTION: Osteoporotic fractures: Bone protection if long term treatment necessary ○ Ensure use of steroids aligned with COPD GOLD guideline
23	Antihistamines (1st generation)		○ Rarely indicated long term ○ CAUTION: Anticholinergic ADRs. *Anticholinergic Burden* tool
Central Nervous System			
24	Hypnotics and anxiolytics		○ CAUTION: Risk of falls/fractures, confusion, memory impairment. See Section 3.4 and NICE guidance on Insomnia ○ CAUTION: Risk of dependency
25	Antipsychotics		○ CAUTION: Risk of stroke and death in elderly patients with dementia. See antipsychotics ○ CAUTION: Anticholinergic ADRs for phenothiazines (e.g. chlorpromazine). See *Anticholinergic Burden* tool. ○ CAUTION: Worsening of Parkinson's disease (specialist advice is recommended)
26	Antidementia Drugs		○ Formally assess benefit: Continue if functional or behavioural symptoms improve Cognitive scores e.g. MMSE can help as a guide but should not rely only on cognition scores if these are inappropriate in the individual patient e.g. communication, language difficulty. See NICE Guidance.
27	Antidepressant Tricyclics		○ Confirm need (First episode: Treat for 6-9 months; Second + episode: Treat for ≥2 years) ○ CAUTION: Anticholinergic ADRs. *Anticholinergic Burden* tool. SSRIs are better tolerated ○ CAUTION: Risk of GI bleeding may be increased ○ Avoid combination with MAOIs because of the risk of serotonin syndrome
28	Metoclopramide		○ Now only licensed for a maximum of 5 days (does not apply to use in palliative care) ○ CAUTION: Worsening of Parkinson's disease (domperidone is more suitable but note contra-indications in cardiac disease and severe liver disease)
29	Antihistamines		○ Rarely indicated for long term treatment of vertigo ○ Anticholinergic ADRs. See *Anticholinergic Burden* tool
30	Opioids		○ Assess effectiveness/choice (is pain neuropathic or otherwise not responsive to opiates? e.g. chronic back pain, widespread pain, fibromyalgia, medically unexplained symptoms) ○ Refer to *Quality Prescribing in Chronic Pain* ○ SIGN 136 Management of Chronic Pain ○ SIGN 106 Control of Pain in Adults with Cancer ○ CAUTION: Constipation. Use laxatives ○ CAUTION: Cognitive impairment and respiratory depression, dependency, immunosuppression and suppression of sex hormones
31	Paracetamol		○ CAUTION: Overdosing ○ Ensure patient is aware of minimum interval between doses and maximum daily dose ○ Avoid more than 1 paracetamol containing product ○ Dose reduction where low body weight [<50kg] or renal or hepatic impairment
32	Antiepileptics		○ Assess effectiveness/dose if used for pain management: Is pain neuropathic, use DN4 or LANSS to aid diagnosis. Titrate dose up to assess effectiveness. Limited evidence for musculoskeletal pain/fibromyalgia) See SIGN 136, *Quality Prescribing in Chronic Pain* ○ CAUTION: Dizziness, blurred vision and sedation. Check renal function. Reduce dose in CKD.

Anti-Infective			
32	Antibacterials (Oral) *Nitrofurantoin*		○ No benefit for treating asymptomatic bacteriuria (ASB) in diabetes or older adults ○ Review use of long term antibiotics for recurrent UTI (every 6 months) ○ Lack of evidence for antibiotic use in preventing catheter-associated ASB ○ CAUTION: Pulmonary/renal ADRs; avoid in renal impairment; contraindicated if eGFR<30ml/min
33	Antifungals		○ CAUTION: Risk of exacerbation of heart failure with azole antifungals. ○ CAUTION: Many serious drug interactions with azole antifungals.
Endocrine System			
34	Antidiabetics		○ Indicated to control symptoms of hyperglycaemia (metformin is first line in DMT2) ○ NOTE: It takes years for the benefit (microvascular) of tight HbA_{1C}. Establish individual HbA_{1C} targets balancing any benefits vs hypoglycaemia risk. See *Drug Efficacy (NNT)* table
35	Metformin Sulfonylureas Glitazones		○ CAUTION: Risk of lactic acidosis. Avoid if eGFR < 30 ml/min. Stop with dehydration ○ CAUTION: Hypoglycaemia: Active metabolites accumulate with impaired renal function ○ Avoid in patients with heart failure ○ Refer to Quality Prescribing in Diabetes
36	Steroids		○ Rarely indicated for long term use. Consider dose reduction/withdrawal where possible

37	Bisphosphonates		○ Consider need for treatment in light of risk factors for osteoporotic fractures: previous osteoporotic fragility fracture, parental history of hip fracture, alcohol intake ≥ 4 units/d, rheumatoid arthritis, oral steroids, BMI<22kg/m^2), ankylosing spondylitis, Crohn's disease, prolonged immobility, untreated menopause. See *Drug Efficacy (NNT)* table
			○ Check patient's ability and willingness to take bisphosphonates (and calcium) as instructed
			○ If the patient has been taking a bisphosphonate for osteoporosis for at least 3 years, discuss the option of discontinuing. There is no consistent evidence of benefit or harm of continued use after at least 3 years therapy. NICE NG56. Continue calcium and vitamin D.
			  ○ There are no current guidelines for bisphosphonate holidays/discontinuation in the UK. See NICE NG56
			  ○ There is no evidence to guide monitoring after discontinuation
			  ○ Women who stop alendronate after 5 years rather than continuing for 10 years show moderate decline in bone mineral density and a gradual rise in biochemical markers but no high fracture risk except clinically asymptomatic fractures.
			  ○ Women at high fracture risk may benefit from continuing alendronate beyond 5 years but this should be a considered, rather than automatic decision

Genito-urinary system			
39	Alpha-blockers		○ Generally not indicated if patient has a long term catheter
40	Finasteride		○ Generally not indicated if a patient has a long term catheter – discuss with urology
41	Antimuscarinics		○ Review continued need/effectiveness after 3 to 6 months ○ CAUTION: Anticholinergic ADRs (oxybutynin may decrease MMSE score in dementia)
42	Female Hormones		○ NOTE: There is no cardio-protective effect or cognitive protection in older women ○ CAUTION: Carcinogenic potential in breast and endometrium ○ Discuss with patient individual balance of benefits and risk
Malignant Disease			
43	Cytotoxics etc.		○ Is treatment still consistent with treatment objectives? Refer to initiating prescriber
Nutrition & Metabolic Disorders			
44	Supplements		○ Confirm continued need/effectiveness after 3 to 6 months – monitor weight
45	Potassium		○ CAUTION: Hyperkalaemia. Risk factors: Use without stop/review date, CKD, co-treatment with ACEI/ARBs, spironolactone, amiloride, triamterene, trimethoprim)
Musculoskeletal System			
46	NSAIDs		○ CAUTION: Gastro-intestinal ADRs (Risk factors: age>75, GI ulcer, antithrombotics, steroids, SSRIs, high alcohol use). If NSAIDs are essential: Consider gastro-protection with a PPI ○ CAUTION: Cardiovascular ADRs (Risk factors: CVD risk>20%, previous CVD events, HF) ○ CAUTION: Renal ADRs (Risk factors: age>65, on ACEI, ARBs and/or diuretics, CKD or HF). If NSAIDs are essential: Monitor eGFR; stop during intercurrent illness
47	Skeletal Muscle Relaxants		○ Rarely indicated long term (except for spasticity) ○ CAUTION: Anticholinergic ADRs
48	DMARDs		○ Assess effectiveness and discuss any need for changes with secondary care specialist ○ Ensure patient adherence to dosing/monitoring regimen ○ CAUTION: Methotrexate overdosing. Avoid preparations with different strengths
Eye, skin, nose & oropharynx			
49	Drops, sprays, ointments		○ Set a review/stop date for topical antibacterials/antifungals and sympathomimetics ○ Review need for preservative free eye drops (e.g. previous preservative toxicity)

1.6 Reviewing medication need and effectiveness

1.6.1 Assessing the need for preventative treatment in patients with shortened life expectancy or frailty

Identifying patients with shortened life expectancy

Good palliative care is not just about supporting someone in their last months, days or hours of their life, but about enhancing the quality of life for both patients and families at every stage of the disease process.

Identifying shortened life expectancy

- Where *'no'* is the answer to the question, *'would you be surprised if this person were to die in the next 6 to 12 months*?'
- Where a patient with advanced disease is making a choice for *comfort care* rather than *curative* treatment
- Where help is required for multiple activities of daily living, either at home or in care home due to:
  - advanced organ failure
  - multiple co-morbidity giving significant impairment in day to day function
  - advanced dementia

The Gold Standards Framework from Living Well/Dying Well provides prognostic indicators to identify those requiring supportive palliative care. The Supportive and Palliative Care Indicators Tool (SPICT) is an alternative means to identify these patients.

Identifying patients with frailty

The Gold Standards Framework also gives specific information as to what tends to indicate poor prognosis in a number of conditions, including frailty.

Identifying frailty

Frailty is well defined as a 'reduced ability to withstand illness without loss of function'. The Gold Standards Framework defines this further as:

- Multiple co-morbidities with signs of impairment in day to day functioning
- Combination of at least three of:
  - Weakness
  - Slow walking speed
  - Low physical activity
  - Weight loss
  - Self-reported exhaustion

NICE guidance on identifying frailty can be found here.

There are a number of recognised frailty identification tools (e.g. electronic frailty index(eFI)). Those carrying out medication reviews should use the recommended tool, as chosen by their Board.

The NHS Scotland Palliative Care Guidelines sets out the consensus opinion on good practice for the management of adults with life limiting illnesses.

1.7 Understanding Drug Efficacy and numbers needed to treat (NNT)

To understand the probable clinical efficacy of a drug for the individual patient the numbers needed to treat (NNT) have been calculated to see the likely impact over a 12 month period. E.g., if the NNT to prevent one death in 5 years is 25 people, then the *annualised NNT* will be 125.

The *annualised NNT*s for common primary care drug interventions are summarised in the *Drug Efficacy (NNT)* table, which was first put together in 2012 has been updated for this guidance and can be found in Appendix C, along with the methodology for developing and maintaining NNTs.

> The **number needed to treat (NNT)** is a measure used in assessing the effectiveness of a particular intervention. The NNT is the *average* number of patients who require to be treated for one to benefit compared with a control in a clinical trial. It can be expressed as the reciprocal of the absolute risk reduction.

Although the *annualised NNT* provides a numerical comparison between therapeutic interventions this information should **not** be viewed in isolation as there is always a need to consider:

- **What is the outcome being avoided?** Death is more significant than a vertebral fracture, but different outcomes will be more or less significant to the individual patient
- **Over what period does the benefit accrue?** Two drugs may have the same NNT to avoid one death, but the drug that achieves that over 6 months is more effective than that which takes 10 years. NNTs can be put on the same timescale by multiplying or dividing the NNT appropriately, but there is then the untested assumption that benefit accrues consistently over time
- **What are the TRUE costs of the drug?** If a medicine saves the life of one patient in 25, but causes debilitating side effects for the rest, its costs may outweigh its benefits

> The ideal NNT is 1, where everyone improves with treatment: the higher the NNT, the less effective is the treatment in terms of the trial outcome and timescale.
>
> So if treatment with a medicine reduces the death rate over 5 years from 5% to 1% (very effective), the absolute risk reduction is 4% (5 minus 1), and the NNT is 100/4, (25).

NNTs are only estimates of average benefit, and it is rarely possible to know precisely what the likely benefit will be in a particular patient. Clinicians and patients should be aware of a degree of uncertainty since it is usually not possible to calculate valid confidence intervals around NNTs.

> The **number needed to harm (NNH)** is the *average* number of people taking a medication for one to suffer an adverse event. Specify the specific end point and note that risk of ADR is higher in frail elderly.
>
> The overall benefit to risk ratio (NNT/ NNH) should be weighed in the individual patient and may vary considerably in people with polypharmacy.

Applicability of Trial Data to Individual Adults

The *Drug Efficacy (NNT)* table provides trial population and duration information. The closer an individual is in terms of characteristics and duration of treatment to the trial the more likely they will achieve the expected benefits.

Adults approaching end of life have an increased risk of many events, so each individual event has a higher absolute risk. This means that interventions may have a much lower NNT for that adult. This should be balanced against the shorter time they have in life to obtain a benefit and the increased risk that any harm may also have a higher impact.

1.8 *Cumulative Toxicity* tool and adverse drug reactions (ADR)

The chart below cross-tabulates medication and ADR risks associated with them. It can help identify actual ADRs and the risk of developing them. It identifies where an ADR may be due to a cumulative effect. Generally, the shaded areas represent side effects which are listed in SPCs as having an incidence greater than 1 in 10,000 (where the incidence is listed), or from knowledge of the mode of action of a medicine. **Please, note that the list focuses on commonly used drugs and commonly preventable ADRs, and is not meant to replace more detailed medicines information sources.**

BNF Chapter	Medication	Falls and fractures	Constipation	Urinary retention	CNS depression	Bleeding	Heart failure	Bradycardia	CV events	Respiratory	Hypoglycaemia	Renal injury	Hypokalaemia	Hyperkalaemia	Serotonin syndrome	Angle closure glaucoma
1	H2 Blocker	■	■													
	Laxatives												■			
	Loperamide	■	■	■	■											
	Prochlorperazine etc [A]	■			■			■	■				■			■
	Metoclopramide	■			■			■	■							
2	ACE/ARB	■	■						■	■		■		■		
	Thiazide diuretics	■	■		■							■	■			
	Loop diuretics	■	■						■			■	■			
	Amiloride[F]/triamterene	■	■		■	■				■		■		■		■
	Spironolactone	■			■							■		■		
	Beta-blocker	■	■				■	■		■						
	CCB (dihydropyridine)	■	■		■				■	■						
	CCB (verapamil/diltiazem)	■	■				■	■	■							
	Nitrates and nicorandil	■														
	Digoxin	■						■	■							
3	Theophylline								■				■			
	Oral steroids	■			■	■	■						■			■
4	Opiates	■	■	■	■					■					■	
	Benzodiazepines	■		■	■					■						
	Sedative antihistamines[D]	■	■	■	■											
	H1 Blockers	■	■	■	■											
	Antipsychotics [E]	■	■	■	■				■							
	SSRI and related			■	■	■			■						■	
	TCAs[C]	■	■	■	■		■		■		■				■	■
	MAO inhibitors		■	■	■			■	■						■	■
5	Antibiotics/antifungals						■					■		■		
6	Sulfonylureas, gliptins, glinides	■	■								■					
	Pioglitazone	■					■			■	■					
7	Urinary antispasmodics	■	■	■	■				■		■					■
	Dosulepin[B]	■	■	■	■				■		■					■
	Alpha blocker	■			■				■	■						
10	NSAIDs					■			■	■		■				

[A] - STRONG anticholinergics are: dimenhydrinate, scopolamine, dicyclomine, hyoscyamine, propantheline; [B] - STRONG anticholinergics are: tolterodine, oxybutynin, flavoxate; [C] - STRONG anticholinergics are: amitriptyline, desipramine, doxepine, imipramine, nortriptyline, trimipramine, protriptyline; [D] - STRONG anticholinergics are: promethazine; [E] - STRONG anticholinergics are: diphenhydramine, clemastine, chlorphenamine, hydroxyzine. Full list of anticholinergics. Full list of medicines linked to falls. [F] - Amiloride side effect frequency unknown

2. Case Studies: The *7-Steps* in action

Case 1: Frailty without overt multimorbidity

Case summary

Patient Details	
69 year old man	
Current medical history	
• Fracture neck of femur 2 years ago • Dementia – mixed Alzheimer's disease / alcohol abuse	• Ex-smoker • Frequent falls
Results	
• BP 120/84 mmHg • eGFR >60 ml/min	• FBC and U+E normal • MMSE score 14
Current Medication [stable since admission]	
• Trazodone 150 mg at night • Thiamine 50 mg three times daily • Bendroflumethiazide 2.5 mg once daily • Tramadol 50 mg four times daily	• Cetirizine 10 mg once daily • Amisulpride 100 mg twice daily • Diprobase cream (as required) • Fucibet cream topically twice daily
Current Function	
69 year old man who has been a care home resident for 2 years. Long term heavy alcohol use in the past. Developed dementia exacerbated by alcohol related brain damage. Fell at home leading to fractured hip. Very confused and distressed post-surgery. When settled, unable to manage at home post-fracture and transferred to care home. Lacked capacity at time of admission, however with additional support this has improved. Assistance of two carers required for transfer to chair. Patient falls frequently as he attempts to mobilise unaided. Conversation is confused with occasional verbal aggression. Patient also has poor short term memory. Prompting is required to ensure that he eats and drinks. Spends most of the day sleeping in his chair. Sleeps well at night. Over the last 12 months has developed ankle swelling and shortness of breath.	
Most Recent Consultations	
Communication is sometimes difficult due to cognitive impairment. He has had three consultations in the last 6 months. One was for a chest infection for which he was prescribed an antibiotic. A second consultation for review following a fall, only minor bruising was noted on examination. The most recent consultation was regarding concern over leg oedema. There is minimal contact with the family.	

Applying the *7-steps*

Checks	Medication related risks/problems identified
1. What matters to the patient? ➢ Review diagnoses and identify therapeutic objectives	• **Patient reports**: feeling tired and short of breath • **Therapeutic objectives**: Improve ability to self-manage and interact socially; reduce ankle swelling; reduce sedation; reduce falls risk
2. Need ➢ Review need for *essential* drugs (stop only on expert advice)	• None

3. Need • Review the need for *unnecessary* drugs – **consider stopping or reducing dose (deprescribe)**	• **Thiamine**: may be redundant if well-nourished in care home • **Bendroflumethiazide**: No longer hypertensive. Potential for withdrawal • **Tramadol**: Indication unclear (may have been started after surgery) • **CNS medication**: Indication is not clear for trazodone or amisulpride. Consider withdrawal if not agitated (See 3.3) • **Antihistamine and emollient**: Required for itch? Clarify cause (i.e. dermatological versus CNS problem or drug side effect). If dermatological problem, non-pharmacological measures e.g. attention to washing powder, natural fabrics, reducing use of perfumed products etc., as well as regular use of emollients in sufficient quantity • **Antimicrobial cream**: Should only be used short term so this can be stopped
4. Therapeutic objectives achieved? ➢ Identify if therapeutic objectives are being met and whether therapy should be added or intensified	• **Thyroid function**: Check TFT and correct hypothyroidism if present • **Ankle swelling and shortness of breath**: Consider presence of LVSD. Potentially highly effective treatment available (ACEI/ARB, Beta-blocker) if present. Consider ECG, ECHO, BNP • **Reduce falls and fracture risk**: Falls risk mainly associated with sedative load; fracture risk modification with osteoporosis prevention (e.g. bisphosphonates) could be considered. Decision to treat needs to be balanced against expected efficacy (See NNT) and ability to comply with treatment. Dental health needs to be considered if moving to active treatment. Unlikely to have time to benefit if life expectancy felt to be < 1 year
5. Safety ➢ Identify patient safety risks ➢ Identify adverse drug effects	• **Actual ADR**: Over sedation • **Risk of CVD events**: Antipsychotics carry a markedly elevated risk of cardiovascular events in dementia (See Section 3.3) • **Risk of cognitive deterioration**: Antipsychotics, antihistamines, tramadol • **Risk of falls and fractures**: Antipsychotics, antidepressant (sedative), antihistamines • **Risk of serotonin syndrome**: Tramadol and antidepressant • **Risk of steroid adverse effects** (topical and systemic): High dose topical steroid • **Risk of acute kidney injury**: Stop bendroflumethiazide if dehydrated • ***Sick Day Rules*** guidance: Ensure staff have clear information on prescription to withhold if dehydrated.
6. Cost-effectiveness	Opportunities for cost minimisation (e.g. generic substitution) should be explored Ensure prescribing in keeping with current formulary recommendations
7. Patient centeredness ➢ Are the outcomes of the review clear? ➢ Are changes the patients preferences? ➢ Agree and communicate plan	• **Preferences and understanding**: Involve patient where possible. If deemed to lack capacity, discuss with relevant others, e.g. welfare guardian, power of attorney, nearest relative if one exists. Even if adult lacks capacity, adults with Incapacity Act still requires that the adult's views are sought. Ensure "Adults with Incapacity Documentation" in place • **Reduce risk of falls and fractures**: Reduce trazodone and amisulpride to reduce sedation and falls risk: decision to start bisphosphonate should balance ability to take versus expected benefit.

SUMMARY: KEY CONCEPTS IN THIS CASE

1. Low number of conditions and medications but still high potential for drug related illness- consider stopping as detailed above
2. On-going review of medication commenced for symptomatic relief
3. Apparent low level of multimorbidity but potential for undiagnosed treatable conditions
4. Over sedation a major risk to quality of life, morbidity (falls) and mortality

Case 2: Multimorbidity without frailty

Case summary

Patient Details	
58 year old woman	
Current medical history	
• Diabetes type 2 (diagnosed 5 years ago) • Coronary heart disease (non-STEMI 1 year ago) • Hypertension • Atrial fibrillation	• COPD • Chronic back pain • Depression (2 episodes) • Hypothyroidism
Results	
• HbA_{1c} 86 mmol/mol (10%) • BP 150/85 mmHg • BMI 35 kg/m^2	• Spirometry shows mild obstruction • No urinary protein detected • eGFR 55 ml/min
Lifestyle	
• Smoking: 10–15 cigarettes a day	• Alcohol: 20 units/week
Current Medication	

• Aspirin 75 mg once daily
• Metformin 1 g three times daily
• Gliclazide 80 mg twice daily
• Pioglitazone 30 mg once daily
• Salbutamol inhaler as required
• Becotide inhaler 100 twice daily
• Levothyroxine liquid once daily
  ○ 50 micrograms/5 ml
  ○ 25 micrograms/5 ml
• Citalopram 20 mg once daily
	• Lisinopril 30 mg once daily
	• Amlodipine 10 mg once daily
	• Atenolol 50 mg once daily
	• Furosemide 40 mg once daily
	• Gabapentin 400 mg three times daily
	• Co-codamol 8/500 mg 2 tablets up to four times daily
	• Diclofenac 50 mg up to three times daily
	• Omeprazole 40 mg once daily
	• Bendroflumethiazide 2.5 mg once daily

Current Function	
Receptionist in local garage. Works 6 half days per week. Provides support for elderly mother who lives alone and has early dementia. Lives with husband who is out of work long term. Two previous acute admissions to hospital. Flu-like illness leading to exacerbation of COPD two years ago. Chest pain 12 months ago - found to be in atrial fibrillation on admission and troponin positive. Angiogram showed widespread coronary artery disease but not severe enough to warrant revascularisation. Echocardiography showed normal left ventricular systolic function. On dual aspirin and clopidogrel for 1 year. Recently moved to aspirin monotherapy.	
Most Recent Consultations	
Ongoing ankle swelling. Back pain difficult to manage and resistant to several strategies. Occasional palpitations, and persistent indigestion with heartburn. Long-term financial worries. Increasing carer strain. Concerns dominated by the heart attack last year and fear of recurrence, "I don't know what my mother and husband would do if I got too ill to work or look after her."	

Applying the *7-steps*

Checks	Medication related risks/problems identified
1. What matters to the patient? ➢ Review diagnoses and identify therapeutic objectives	• **Patient reports**: "I feel breathless whenever I have to rush or climbing the stairs; Do I really need to take so many pills; my ankles are getting really swollen" • **Therapeutic objectives**: Secondary prevention of cardiovascular events (incl. Stroke Prevention in AF); Rate control in atrial fibrillation; Management of CKD, COPD, diabetes and depression; Pain control

2. Need ➢ Review need for *essential* drugs (stop only on expert advice)	• **Levothyroxine**: to treat hypothyroidism • **Atenolol**: for rate control in Atrial Fibrillation • **Antidiabetic medication**: diabetes symptom control
3. Need ➢ Review need for *unnecessary* drugs – **consider stopping or reducing dose (deprescribe)**	• **Pain control**: Is the gabapentin for neuropathic pain or mechanical back pain; co-codamol v paracetamol; NSAID required? • **Antidepressant**: is duration acceptable? • **High dose omeprazole**: Active peptic ulcer or oesophagitis? Are symptoms of gastric origin; may require endoscopy or trial without NSAID?
4. Effectiveness ➢ Identify if therapeutic objectives are being met and whether therapy should be added or intensified	• **Secondary prevention of coronary events**: likely to derive macrovascular benefit from tight glycaemic control; consider statin and BP control • **Stroke prevention in atrial fibrillation**: CHA2DS2-VASc score 4, so consider replacing aspirin with anticoagulant; check rate control • **COPD management**: symptom control (MRC Breathlessness Score); inhaler technique; formulary compliance • **Pain control**: discuss symptom control and review expectations; if gabapentin prescribed for back pain then consider withdrawal; review NSAID • **Depression management**: discuss symptom control • **Hypothyroidism management**: check TFT result • **CKD management**: check and monitor for proteinuria • **Diabetic control**: HbA_{1c} high despite three antidiabetics; check adherence
5. Safety ➢ Identify patient safety risks ➢ Identify adverse effects	• **Actual ADR**: Ankle swelling – due to amlodipine or pioglitazone? • **Risk of GI bleeding**: NSAID + citalopram + aspirin (or anticoagulant added) • **Risk of acute kidney injury**: NSAID + CKD (eGFR 55ml/min), consider stopping; co-prescribed diuretic + ACEI/ARB + NSAID ('triple whammy'); co-prescribed thiazide and loop diuretic, stop one; increase U+E monitoring • ***Sick Day Rules*** **Guidance**: check awareness • **Risk of cardiac events**: NSAID + CHD – diclofenac (ibuprofen and naproxen preferred); pioglitazone (ankle swelling and ischaemic heart disease) • **Risk of arrhythmia**: QTc prolongation: omeprazole, citalopram and gabapentin
6. Cost-effectiveness	Opportunities for cost minimisation: generic substitution; formulary compliance; change liquid levothyroxine to tablet

7. Patient centeredness
➢ Are the outcomes of the review clear?
➢ Are changes the patients preferences?
➢ Agree and communicate plan
	• **Preferences and understanding:**
	  • **Secondary CVD prevention**: prioritise discussion that most effective intervention would be stopping smoking followed by anticoagulant for AF; BP control; addition of statin; weight reduction; $HbA1_c$ control
	  • **COPD management**: check patient understands how to monitor breathlessness score, check inhaler technique and suitability
	  ○ Non-medication interventions: Support and check willingness for lifestyle changes; signpost to social support, e.g. Alzheimer's Scotland helpline

SUMMARY: KEY CONCEPTS IN THIS CASE

1. Large number of medications are likely to be needed and effective, however more support may be required as adherence an issue
2. Potential to usefully detect and treat conditions (in this case atrial fibrillation)
3. Potential for high risk drug combinations particularly in patients on multiple medications which may need to be stopped
4. Need for direct advice to patient on medication, e.g. regarding dehydration
5. Link with non-pharmacological management
6. A longer than standard consultation will be required to ensure that there is time to cover the patient's concerns and issues, and focus on medication and deprescribe where appropriate.
7. The need for a multi-disciplinary approach

Case 3: Frailty with multimorbidity

Case summary

Patient Details	
87 year old woman	
Current medical history	

• Cerebrovascular disease
  ○ Partial anterior circulation stroke 5 yrs ago
  ○ Vascular dementia 3 yrs
• Hypertension
• Ischaemic heart disease
  ○ Atrial fibrillation 2 yrs
  ○ Myocardial infarction 15 yrs ago
	• Type 2 diabetes
	• Osteoporosis: Fracture vertebrae L2 1 year ago; T score -3.2 at hip on DEXA scan
	• Recurrent UTIs
	• MMSE 22/30 ACE-R 66/100
	• COPD with moderate airflow obstruction
	• Hypothyroidism

Results	
• HbA_{1c} 40 mmol/mol (6.6%) • BP 106/56 mmHg • Urine Alb/Creat ratio: trace micro-albuminuria	• Creatinine 124 umol/L; eGFR 38 ml/min and stable at this level • Weight 43 kg
Current Medication	
• Levothyroxine 150 micrograms once daily • Alendronate 70 mg once weekly • Calcichew D3 Forte twice daily • Metformin 1 g three times daily • Gliclazide 160 mg twice daily • Perindopril 4 mg once daily • Indapamide 2.5 mg once daily • Rivaroxaban 20 mg once daily • Clopidogrel 75 mg once daily • Atorvastatin 80 mg once daily	• Mirtazapine 30 mg at night • Zopiclone 7.5 mg at night • Paracetamol 1 g four times daily • Omeprazole 20 mg once daily • Seretide 250 1 puff twice/day • Salbutamol, as required • Ipratropium inhaler 4 times daily • Oxybutynin 5 mg twice daily • Trimethoprim 200 mg once daily prophylaxis
Current Function	
Lives at home with husband who is cognitively intact but mobility limited due to heart failure. Steadily worsening memory. Needs regular reorientation by husband. Marked increase in confusion with infection. Continence a particular issue with nocturia. Needs a lot of encouragement to eat and drink enough. Main trips out the house are to speciality hospital clinics and GP.	
Most Recent Consultations	
Recent Admissions: Osteoporotic fracture lead to sudden loss in mobility one year ago. Delirium whilst in hospital. Flu-like illness 3 months ago. Admitted with confusion, hypoglycaemia and AKI.	

Applying the *7-Steps*

Checks	Medication related risks/problems identified
1. What matters to the patient? ➢ Review diagnoses and therapeutic objectives	• Reduce potential for harms from drugs • Ameliorate effects of dementia • Minimise potential for future episodes of delirium • Maintain physical function and minimise unpleasant symptoms
2. Need ➢ Review need for *essential* drugs (only stop with expert advice)	• **Levothyroxine**: to treat hypothyroidism, but check for overtreatment

3. Need ➢ Review the need for *unnecessary* drugs – **consider stopping or reducing dose (deprescribe)**	• Huge medication burden • **Review need**: bisphosphonate, sedation, antidepressant, PPI and oxybutynin • **Clopidogrel** plus rivaroxaban is rarely indicated • **Trimethoprim** prophylaxis – no evidence beyond 6 months
4. Effectiveness ➢ Identify if therapeutic objectives are being met	• **Target control:** Pursuing surrogate targets (BP, HbA_{1C}, cholesterol) may not be appropriate in this case, and causing harm • Symptoms and daily function likely to assume greater importance • **COPD:** Check FEV1 and review treatment – ensure correct inhaler technique
5. Safety ➢ Identify patient safety risks ➢ Identify adverse drug effects	• **Risk of lactic acidosis**: On high dose metformin and tight $HbA1_c$ control. Reduce dose (deprescribe) as eGFR 38, and consider stopping • **Risk of hypoglycaemia:** Gliclazide should be stopped • **Risk of acute kidney injury**: Review ACE + diuretic + metformin • **Risk of paracetamol intoxication**: weight <50 kg reduce dose • **Risk of falls:** sedation (mirtazapine, zopiclone); anticholinergic (oxybutynin); hypoglycaemia (antidiabetics); hypotension (antihypertensives) • **Risk of Fractures**: reduced by bisphosphonate and calcium plus vitamin D supplementation, but decision to continue should be in context of NNT • **Risk of bleeding**: either stop DOAC or clopidogrel. Dose reduction of rivaroxaban required (creatinine clearance 19 ml/min) • **Risk of myalgia**: review statin dose • ***Sick Day Rules*** guidance
6. Cost-effectiveness	Opportunities for cost minimisation (e.g. generic substitution) should be explored Ensure prescribing in keeping with current formulary recommendations
7. Patient centeredness ➢ Does the patient understand the outcomes of the review? ➢ Ensure drug therapy changes are tailored to patient preferences ➢ Agree and Communicate Plan	• **Patient Preferences and understanding:** ○ **COPD management**: Check symptom control and inhaler acceptance ○ Consider whether patient has capacity to engage with review process ○ Ensure that carer views and expectations are heard and balanced, especially if carer has power of attorney ○ Discuss the effort required for the existing regimen ○ Consider narrowing medication to most effective agents and check understanding of risk versus benefit ○ Incorporate review into wider anticipatory care planning discussions ○ Consider adherence. If tablets are being missed and blood sugar control is tight, there is a severe risk of hypoglycaemia if compliance suddenly improves

SUMMARY: KEY CONCEPTS IN THIS CASE

1. Although most of the medications in this case have a clear indication, the cumulative effect is an enormous drug burden with pernicious ADR potential. Careful consideration is required to balance the potential for benefit for this patient versus a reasonable estimation of life expectancy
2. Consideration of potential adverse impact of high drug burden on other vital areas, such as nutrition
3. Strong potential for inadvertent high risk co-prescription for patients on such a long list of medications
4. Difference in risk between trial populations and frail elderly
5. Likely to have intercurrent illnesses and stressors requiring acute therapeutic review
6. Review management of COPD
7. Opportunity costs and potential savings are significant
8. This complex medication regimen is likely to put strain on the carer as well as patient, affecting the health of the household

Case 4: Care home resident with multiple morbidity

Case summary

Patient Details	
79 year old man	
Current medical history	
• Mild cognitive impairment • Coronary heart disease	• Moderately impaired left ventricular systolic function on ECHO
Results	
• BP 160/80 mmHg • Continues to smoke 5 cigarettes daily • Respiratory Rate 26 per minute (rest)	• U&Es all within normal range • Pulse 86 bpm regular • MMSE 18
Current Medication	
• Omeprazole 20 mg once daily • Simvastatin 40 mg at night • Clopidogrel 75 mg once daily • Bisoprolol 2.5 mg once daily • Amlodipine 10 mg once daily	• Furosemide 40 mg once daily • Trazodone 100 mg at night • Tolterodine MR 4 mg at night • Salbutamol MDI 2 puffs as required
Current Function	
Has been in care home for 12 months. Intermittent behavioural upset . Diet and general personal hygiene improved since been in care home. Generally inactive during the day, apart from when goes to have a cigarette. Becomes short of breath whilst walking to have a cigarette. Shows signs of early dementia and can be difficult to engage depending on mood. Sleeps deeply at night and is difficult to rouse in the mornings.	
Most Recent Consultations	
Nursing staff tell you that they have recently requested salbutamol as they think he has asthma as he's a little breathless. He is unable to co-ordinate using the salbutamol and it has had no effect on his symptoms of breathlessness. He is breathless at rest, and this becomes worse with a short walk. He has to be propped up in bed at night. Persistent issues with peripheral oedema, and lower limbs leak serous fluid at times.	

Applying the *7-steps*

Checks	Medication related risks/problems identified
1. What matters to the patient? ➢ Review diagnoses and identify therapeutic objectives	• Manage the breathlessness • Manage heart failure • Manage the use of preventative treatments • Minimise medication related harm • Help patient quit smoking
2. Need ➢ Review need for essential drugs (stop only on expert advice)	• None • The drugs for symptomatic deterioration of moderate heart failure need to be titrated for optimal benefit
3. Need ➢ Identify non-essential drugs and review continued need – **consider stopping or reducing dose (deprescribe)**	• **Proton pump inhibitor:** review need and identify indication for use if possible. If symptomatic then use lowest dose to manage symptoms (maintenance dose is 15 mg/day) • **Heart failure:** examination indicates that shortness of breath is more likely to be due to heart failure than airways disease. Consider stopping salbutamol inhaler

	• **Trazodone:** Good candidate for dose reduction (desprescribing) as is drowsy in the mornings (See 3.3)
4. Effectiveness ➢ Identify if therapeutic objectives are being met and whether therapy should be added or intensified	• **Heart failure**: In order to manage symptoms consider titrating all relevant medicines whilst balancing benefit with increased risk of ADRs. Monitor pulse and U+Es ○ Consider adding ACE inhibitor (*Drug Efficacy (NNT)* Table) ○ Titrate (up) bisoprolol
5. Safety ➢ Identify patient safety risks ➢ Identify adverse drug effects	• **Actual ADR:** over sedation • **Actual ADR:** amlodipine contribution to ankle swelling • **Actual ADR:** anticholinergic effect of tolterodine may contribute to confusion. Are there other anticholinergic symptoms? Review whether tolterodine is providing benefit and consider stopping (deprescribe) • **Drug-drug interaction:** simvastatin and amlodipine. Reduce dose of amlodipine as ACEI is added and dose titrated • **Drug-drug interaction:** clopidogrel and omeprazole. Review need for clopidogrel. Consider switching to lansoprazole 15mg or H2 receptor antagonist • **Risk of falls and fractures:** over sedation • ***Sick Day Rules* guidance:** Ensure staff have clear information on drugs to withhold if dehydrated, especially if ACEI added
6. Cost-effectiveness	Opportunities for cost minimisation (e.g. generic substitution) should be explored Ensure prescribing in keeping with current formulary recommendations
7. Patient centeredness ➢ Are the outcomes of the review understood? ➢ Are changes tailored to patient preferences ➢ Agree and communicate plan	• **Preferences and understanding:** ○ May need support with inhaler and inhaler technique if continuing treatment ○ Ensure patient understands breathlessness is due to heart failure rather than asthma ○ Ensure patient and care home staff understand the reason for medication changes, i.e. increase in bisoprolol and addition of ACE Inhibitor ○ Consider options for smoking cessation

SUMMARY: KEY CONCEPTS IN THIS CASE

1. Low number of conditions and medications but still high potential for drug related illness and need to reduce dose of some medicines
2. Identify the main condition causing the main symptom (shortness of breath)
3. Significant number of probable actual adverse drug reactions
4. Number of drug to drug interactions
5. Review of medicines needed for those for symptomatic relief for heart failure will need regular follow up for side effects and monitoring (respiratory rate, BP, pulse, U+E), especially with dose (up) titration
6. Additional medication (ACEI) will increase risk of acute kidney injury with dehydrating illness
7. Over sedation at night is a major risk to quality of life, morbidity (falls) and mortality

Case 5: Chronic Pain with multimorbidity

Case Summary

Patient Details

- 70 year old woman

Current Medical History

- Total knee replacement
- GI reflux
- Hypothyroidism
- Hypertension

Results

- All blood results are normal
- Normal X ray
- Normal MRI
- BMI 23.5 kg/m2
- BP 123/74 mmHg (sitting)
- Cholesterol 4.5 mmol/l

Lifestyle

- Retired cleaner
- Ex-smoker 20 years
- Little exercise
- Alcohol units 20 /week

Current Medication

- Co-codamol 30/500 8 tablets daily
- Ibuprofen 400 mg 1 three times daily as required (max 1.2 g in 24 hrs)
- Omeprazole 20 mg once daily
- Levothyroxine 25 micrograms once daily
- Bendroflumethiazide 2.5 mg once daily
- Simvastatin 40 mg every night

Previous medication

- Buprenorphine patch 20 micrograms/hour , post knee replacement 18 months ago

Current Function

- A brief Pain Inventory questionnaire was completed showing an average pain score of 6 and an average interference score of 4 (*Quality Prescribing in Chronic Pain*)
- No inflammation or swelling of joints, some stiffness on remaining in the same position for a long time
- Good range of movement
- No neuropathic symptoms
- Some symptoms of postural hypotension on standing

Most Recent Consultations

- At her most recent consultation her pain management was stable and she was feeling a bit constipated and tired
- Feels tiredness is impacting on looking after her granddaughter
- Dizzy on standing

Applying the *7-Steps*

Checks	Medication related risks/problems identified
1. What matters to the patient? ➢ Review diagnoses and identify therapeutic objectives	• **Patient reports:** pain control is her main priority while minimising side effects. Patient wonders whether she can begin using buprenorphine patches again as these worked really well ○ Constipation and Drowsiness • **Therapeutic objectives:** include minimising GI Symptom and managing hypertension

2. Need ➢ Review need for essential drugs (stop only on expert advice)	• **Levothyroxine:** to treat hypothyroidism
3. Need ➢ Review need for non-essential drugs – **consider stopping or reducing dose (deprescribe)**	• **Pain control:** is the NSAID really required. Consider stopping with follow up and review • **Hypertension management:** is hypertension still an issue? Normotensive whilst sitting, and is dizzy on standing. Consider stopping bendroflumethiazide (deprescribe) • **Lipid management:** does patient need a statin? No indication is recorded so consider stopping (deprescribe)
4. Effectiveness ➢ Identify if therapeutic objectives are being met and whether therapy should be added or intensified	• **Pain control:** is relatively good and not interfering with function too much and she felt that she was coping well. Realistic expectation of pain control discussed as well as self-management. Is ibuprofen required? • **Tiredness:** review hypothyroidism control. Is on a low dose with fatigue, so check TFTs
5. Safety ➢ Identify patient safety risks ➢ Identify adverse drug effects	• **Actual ADR:** sedation and constipation due to co-codamol. Consider for dose reduction (deprescribe) • **Actual ADR:** dyspepsia due to ibuprofen. Consider stopping or dose reduction (deprescribe) • **Actual ADR:** Postural hypotension due to bendroflumethiazide. Normotensive so consider stopping (deprescribe). • ***Sick Day Rules*** **Guidance:** Check that patient is aware of what medication to stop with dehydration, however no longer an issue if stops diuretic
6. Cost-effectiveness	Opportunities for cost minimisation (e.g. generic substitution) should be explored Ensure prescribing in keeping with current formulary recommendations

7. Patient centeredness
➢ Does the patient understand the outcomes of the review?
➢ Ensure drug therapy changes are tailored to patient preferences
➢ Agree and Communicate Plan
	• **Preferences and understanding** to form action plan:
	  • **Pill burden:** keen to reduce tablet burden and try alternatives, including non-pharmacological interventions
	  • **Pain management:** pain is under control so side effects can be minimised by reducing current medication rather than adding any additional medication. Explore non-medication interventions to maintain function
	  • **ADR reduction:** keen to reduce or stop co-codamol 30/500 because of side effects, risks and limited effectiveness
	  • **ADR reduction:** keen to reduce or stop ibuprofen as she felt it was making her indigestion worse
	  • **Discussion:** benefits and risks of medication reduction
	  ○ Co-codamol 30/500 reduced from 2 four times a day to 1 four times a day with paracetamol added 1 four times a day with plan to review and further reduce if possible
	  ○ Flexibility of increased dose of co-codamol during flare-up of pain
	  ○ Antihypertensive stopped and reviewed 1/12
	  ○ Statin stopped
	  ○ NSAID stopped
	  ○ Plan to review GI side effect and stop omeprazole at next consultation

SUMMARY: KEY CONCEPTS IN THIS CASE

1. Need for on-going review of need, efficacy and stopping or reducing medication (deprescribe)
2. Minimising side effects of medication
3. Self-management options – pacing, increasing activity
4. A "What matters to me?" approach – person-centred goals and a plan for what to do in flare ups e.g. patient's wish was to reduce medication burden and attend the local walking group and the local patient education classes

Case 6: Acute pain and depression with asthma

Case Summary

Patient Details	
59 year old woman	
Current medical history	
• Back pain • Asthma since childhood • Depression last two years since losing job after marriage break up	
Results	
• BP 150/80 mmHg • Continues to smoke 5-10 cigarettes per day • Respiratory rate 22 per minute	• U&E's all within normal range • Peak Flow Rate 300 (Predicted 390) • SaO2 97% on air
Current Medication	
• Lansoprazole 30 mg once daily • Gabapentin 600 mg three times daily • Tramadol 50 mg - 100 mg 4-6 hours • Salbutamol MDI 2 puffs as required	• Beclomethasone 100 micrograms 2 puffs twice daily • Mirtazapine 30 mg every night • Zopiclone 7.5 mg 1 every night
Current Function	
Has been suffering from pain and complaining of drowsiness and weight gain. Has suffered from low mood for the last two years and has tried multiple antidepressants. Can be difficult to engage depending on mood, but has sought advice today as says pain unbearable and received letter to review medication.	
Most Recent Consultations	
Most recent consultations have been for pain and management. Prior to that consultations were regarding low mood after break up of marriage and poor sleep. Also complaining about increased breathlessness. Ordering at least one salbutamol inhaler each month.	

Applying the *7-Steps*

Checks	Medication related risks/problems identified
1. What matters to the patient ➢ Review diagnoses and identify therapeutic objectives	• **Patient reports:** In pain constantly, but especially when getting up from chair. Feel like I cannot catch my breath and needing to use salbutamol inhaler frequently. Manage the pain • **Therapeutic objectives:** Pain and asthma management. Smoking cessation
2. Need ➢ Review need for essential drugs (stop only on expert advice)	• **Inhalers** to manage asthma. Patient complains of breathlessness and examination confirms that asthma treatment is suboptimal. Inhaler technique and suitability should be checked
3. Need ➢ Review need for unnecessary drugs – **consider stopping or reducing dose (deprescribe)**	• **Treatment dose PPI:** check indication and aim for lowest dose to manage symptoms (deprescribe) • **Pain management:** Pain is constant and in the low back with no referred pain or neurological effects. Gabapentin is not indicated so consider alternatives and dose reduction and withdrawal (deprescribe) • **Insomnia management:** has taken long term zopiclone, which will no longer be effective and is causing symptoms. Dose reduction and withdrawal should be considered (Section 3.4) • **Depression management:** discuss depression and review current treatment. Explore other support that may be available locally

4. Effectiveness ➢ Identify the need for adding/intensifying drug therapy in order to achieve therapeutic objectives	• **Pain control:** Review expectations and current regimen in order to manage pain more appropriately. Existing treatments should be reduced and withdrawn before considering additional analgesia. Lack of success may be due to unrealistic expectations and lack of physical activity • **Insomnia control:** review expectations and need for ongoing hypnotic • **Smoking cessation:** Consider options for smoking cessation and referral for support • **Asthma control:** ensure adequate treatment plan for asthma. There is over use of salbutamol suggesting under treatment. Review inhaler technique and use of preventative treatment. If these are appropriate then consider stepping up treatment
5. Safety ➢ Identify patient safety risks ➢ Identify adverse drug effects	• **Actual ADR:** drowsiness with zopiclone and drug to drug interaction with tramadol and gabapentin. Resulting cognitive impairment may effect activities such as driving • **Risk of dependence:** zopiclone, gabapentin and tramadol • **Risk of overdose:** high doses of analgesics and adjuvants increase potential for accidental overdose
6. Cost-effectiveness	Opportunities for cost minimisation (e.g. generic substitution) should be explored Ensure prescribing in keeping with current formulary recommendations

7. Patient centeredness
➢ Does the patient understand the outcomes of the review?
➢ Ensure drug therapy changes are tailored to patient preferences
➢ Agree and Communicate Plan
	• **Preferences and understanding:**
	  • **Asthma management:** struggles to remember to use preventer inhaler and relies of frequent use of reliever when feels short of breath. Management plan, education and support may help
	  ○ Smoking cessation: patient doesn't feel ready to stop and so 'park' this for now and review at some stage
	  ○ Non-medication pain management: Signpost to other strategies patients can engage with for pain management. She is not yet convinced of the benefits so will require further encouragement
	  ○ Medication reduction: patient agrees to a go slow approach to medication reduction and thinks that she will benefit from regular support and review

SUMMARY: KEY CONCEPTS IN THIS CASE

1. Low number of conditions and medications but still high potential for drug dependence, consider dose reduction and the need to prescribe
2. Unrealistic expectations regarding pain management and insomnia
3. Non medication interventions will be key to long term management of symptoms, e.g. counselling, increased activity and exercise
4. Education regarding the importance of preventative treatment for asthma. Short term stepping up of therapy may provide a window of opportunity to address life style issues
5. All medication changes will require regular review and follow up, but especially changes to analgesics, hypnotics and antidepressants

3. Hot Topics: Further reading and deprescribing

Deprescribing is a term that is used to refer to *the stopping or reduction in dose of prescribed medications.* It should be undertaken in the context of reviews for appropriate polypharmacy and should not be the main purpose for the review. Any decision about stopping or reducing medication should be done in partnership with the patient as part of joint decision making following the *7- Steps* process

The following hot topics provide further detail regarding common areas that are considered to be potentially problematic.

3.1 Anticholinergics

Why are anticholinergics problematic?

Anticholinergics have long been recognised as causing symptoms such as dry mouth, constipation and urinary retention. Exposure to anticholinergic agents has also been linked to impaired cognition and physical decline. There may also be an association with falls, and increased mortality and cardiovascular events. The table below shows that anticholinergic effects are dose dependent.[14] Of note is, however, that there is significant inter-individual variability regarding anticholinergic dose and manifestations of signs and symptoms of toxicity, which is why it is essential to understand the patient's perspective.

Table 3a: Anticholinergic effects

Atropine dose equivalent	Digestive tract	Urinary tract	Skin	Eyes	Cardiovascular	CNS
10 mg			Red, hot, dry	+++Mydriasis +++Blurred vision	+++ Tachycardia Fast and weak pulse	Ataxia Agitation Delirium Hallucinations Delusions Coma
5 mg	Decreased gut motility	Urinary retention	Hot and dry	++Mydriasis	++ Tachycardia	Restlessness Fatigue Headache
2 mg	++ Mouth dryness			+Mydriasis Blurred vision	+ Tachycardia Palpitations	
1 mg	+ Mouth dryness Thirst			Mydriasis	Tachycardia	
0.5 mg	Mouth dryness		Anhidrosis			

Drugs with anticholinergic properties continue to be commonly prescribed to older people and those with mental illness, who are particularly susceptible to adverse effects, even at therapeutic doses.

Anticholinergic burden principles:

- Anticholinergic effect of individual drugs vary greatly between individual patients
- Anticholinergic effect of multiple drugs are accumulative
- The comparative degree of anticholinergic drugs are based partly on clinical evidence and partly on pharmacological theory

How to assess and reduce the anticholinergic burden

Not all drugs with anticholinergic properties may individually put patients at risk of severe adverse effects, however when used in combination, effects may accumulate. Reducing the anticholinergic burden may result in improvements in short term memory, confusion, behaviours and delirium.

A scale or table that assigns a cumulative anticholinergic score to a patient's prescribed medication can be used to assess *Anticholinergic Burden*. A number of these scoring systems are available. While this approach is valid, the overall aim is to reduce overall anticholinergic exposure as much as possible. The table below is intended to be a guide as to which areas anticholinergic burden is likely to be the highest.

Table 3B Reducing *Anticholinergic Burden*

AVOID IF POSSIBLE Highly anticholinergic drugs	**CAUTION** Drugs with some anticholinergic activity	**Alternatives and general notes**
Antidepressants		
Tricyclic antidepressants	**SSRIs*** **Mirtazapine**	**Venlafaxine**, **trazodone** and **duloxetine** have low anticholinergic activity *SSRIs, **Sertraline** best choice. Avoid **paroxetine**
Antipsychotics		
Fluphenazine **Chlorpromazine** **Clozapine** **Doxepin** **Levomepromazine**	**Olanzapine** **Quetiapine** **Risperidone** **Haloperidol**	**Aripiprazole** is an acceptable choice **Trifluoperazine** and **perphenazine** have unknown activity (conflicting data)
Nausea and vertigo		
	Prochlorperazine	**Metoclopramide** has unknown activity (conflicting data). However, carries specific MHRA caution regarding parkinsonian and cognitive side effects **Domperidone** does not usually penetrate the CNS, but caution is required for QT prolongation Nausea treatments all cause potential problems. Keep courses as short as possible
Urinary antispasmodics		
Oxybutynin **Tolterodine** **Fesoterodine** **Flavoxate** **Darifenacin** **Solifenacin** **Propiverine**	**Dosulepin**	**Mirabegron** has no recorded anticholinergic activity and may be an option It is essential to ensure that medication is effective and stop if not
Sedatives		
		Zolpidem and **zopiclone** no anticholinergic activity but falls risk Avoid sedative antihistamines Non-drug measures are preferred

AVOID IF POSSIBLE Highly anticholinergic drugs	**CAUTION** Drugs with some anticholinergic activity	**Alternatives and general notes**
Antihistamines		
Chlorphenamine **Promethazine** **Hydroxyzine** **Clemastine** **Cyproheptadine**	**Cetirizine** **Loratadine** **Fexofenadine**	Consider locally acting products for hayfever symptoms If taken for seasonal conditions check this is happening
H2-receptor antagonists		
	Ranitidine **Cimetidine**	PPIs have no anticholinergic burden. Prescribe at the lowest dose to control symptoms **Omeprazole** or **pantoprazole** may be preferred over **lansoprazole**. Caution with increased risk of *Clostridium difficile* infection
Drugs used in Parkinson's Disease		
Procyclidine **Trixehiphenidyl (benzhexol)** **Orphenadrine**	**Amantadine** **Bromocriptine**	**Entacapone** has small potential for anticholinergic activity **Co-careldopa**, **pramipexole**, **ropinirole** and **selegiline** have no significant anticholinergic activity
Spasticity		
Tizanidine	**Baclofen** **Diazepam** **Methocarbamol**	
Analgesia		
	Opiates	**Paracetamol** and NSAIDs are not thought to have anticholinergic activity G**abapentin** has minimal anticholinergic activity
Others		
Atropine **Hyoscine** **Propantheline** **Dicycloverine** **Ipratropium**	**Loperamide** **Carbamazepine** **Theophylline** **Lithium**	**Furosemide** and **digoxin** have unknown anticholinergic activity. The following have no or negligible anticholinergic activity: **Corticosteroids**, **statins**, **beta-blockers**, **ACE inhibitors**, **calcium channel blockers**, **triptans**, **valproate**, **phenytoin**, **phenobarbitone**, **topiramate**.

Notes: This is a developing area with disagreements between different sources. Some of this table is based on incomplete or poor evidence, or on expert opinion. The anticholinergic effects of drugs may become better understood with time. Some of these therapeutic areas are highly specialised (for example Parkinson's disease) and would require expert advice before considering a change. As noted here less anticholinergic alternatives often have other concerns. If an anticholinergic agent must be used, consider reducing the dose. [15-21]

3.2 Medication and falls risk in the Older Person

This classification has been based upon a review of the clinical evidence of medicines most commonly implicated in falls.[22] The list is not meant to be fully comprehensive but intended to raise awareness. Advice is provided on how medicines should be stopped (deprescribed).

Highest risk	Guidance
Antidepressants	Avoid tricyclics with high anti-muscarinic activity, e.g. amitriptyline. SSRIs are associated with a reduced incidence of side effects. Trial of gradual antidepressant withdrawal should be attempted after 6 –12 months
Antipsychotics including atypicals	Risk of hypotension is dose related reduced by the 'start low go slow approach.' Atypical antipsychotics have similar falls risk to traditional ones. Attempted withdrawal **MUST** always be gradual. Prochlorperazine is often inappropriately prescribed for dizziness and causes drug induced Parkinson's disease
Anti-muscarinic drugs	Oxybutynin may cause acute confusional states in the elderly especially those with pre-existing cognitive impairment
Benzodiazepines & Hypnotics	Dose reduction is beneficial if withdrawal is not possible . Avoid long acting benzodiazepines. Newer hypnotics are associated with reduced hangover effects but all licensed for short-term use only
Dopaminergics in Parkinson's disease	Sudden excessive daytime sleepiness can occur with levodopa and other dopamine receptor agonists. Dose titration is important in initiation due risk of inducing confusion. Maintenance doses may need to be reduced with aging
Moderate risk	
Anti-arrhythmics	Dizziness and drowsiness are possible signs of digoxin toxicity. Risks of toxicity are greater in renal impairment or in the presence of hypokalaemia. Flecainide has a high risk for drug interactions and can also cause dizziness
Anti-epileptics	High risk for potential drug interactions. Important side effects include: Dizziness, drowsiness and blurred vision (dose related)
Opiate analgesics	Drowsiness is common with initiation, but tolerance to this is usually seen within 2 weeks of continuous treatment. Drowsiness is rare with codeine unless used in combination with other CNS drugs. Confusion reported with tramadol
Antihistamines	Somnolence may affect up-to 40% of patients with older antihistamines. The newer antihistamines cause less sedation and psychomotor impairment. Risk of hypotension with cinnarizine is a dose related side effect
Alpha-blockers	Doses used for treatment of BPH less likely to cause hypotension than those required to treat hypertension
ACEI/ARB	Risk of hypotension is potentiated by concomitant diuretic use. Incidence of dizziness affects twice as many patients with heart failure than hypertension
Diuretics	Postural hypotension, dizziness and nocturia are problems seen in the elderly. Diuretics should **not** be used in the long-term treatment of gravitational oedema
Beta-blockers	Postural hypotension and can affect up to 10% of patients. Can accumulate in renal impairment and therefore dose reduction is often necessary
Lower risk	
CCBs	Incidence of dizziness low especially for once daily dihydropyridine CCBs
Nitrates	Advise patient to sit when using GTN spray or tablets
Oral anti-diabetic drugs	Dizziness due to hypoglycaemia, but usually avoidable. Avoid long acting sulfonylureas e.g. chlorpropamide.
PPIs & H2 Antagonists	Avoid cimetidine in polypharmacy patients as high risk of drug interactions, and causes confusion.

3.3 Stopping (deprescribing) antipsychotics in patients with dementia

Reproduced from Mental Welfare Commission for Scotland, 2014.

Medication and management of stressed and distressed behaviours:

- Medication should be used as last, not first resort, to manage distress
- People with dementia on psychotropic medicines should be prioritised for multidisciplinary review
- People with dementia on psychotropic medicines should be reviewed every three months
- Psychotropic medicines should be withdrawn gradually

Antipsychotic drugs are frequently prescribed with the aim of reducing symptoms of stress and distress in people with dementia. In Scotland in 2007, 17.7% of people with a diagnosis of dementia were prescribed an antipsychotic, compared to approximately 12% in 2005–2007 in one US study. Despite this high rate of use, antipsychotics have only limited benefit in treating symptoms of stress and distress in older people with dementia and carry significant risk of harm (delirium, cerebrovascular events, falls and all-cause mortality). In 2009, antipsychotics were estimated to cause approximately 1800 deaths and 1620 cerebrovascular events in people with dementia in the UK annually. However, clinical trial evidence in nursing home patients with dementia indicates that chronically prescribed antipsychotic drugs can be safely discontinued in most patients, with longer term follow-up suggesting a significant reduction in mortality.

Which patients should be prioritised for review?

Patients who have dementia and who have been on antipsychotics for more than 3 months and have stable symptoms should be reviewed with a view to reducing or stopping antipsychotic medication. Priority groups for reducing antipsychotic medication include:

- People in care homes
- People with vascular dementia
- People with dementia plus history of cardiovascular disease

When should antipsychotic medication NOT be stopped?

Patients who have a co-morbid mental illness that is treated with antipsychotic medication, such as schizophrenia, persistent delusional disorder, psychotic depression or bipolar affective disorder should not have antipsychotic medication reduced without specialist advice.

How to reduce antipsychotic medication?

- Slow reduction (25% daily dose) with close monitoring
- Review the effect after one week to assess for: the re-emergence of the initial 'target' symptoms of stress and distress
- Discontinuation symptoms include nausea, vomiting, anorexia, diarrhoea, rhinorrhoea, sweating, myalgia, paraesthesia, insomnia, restlessness, anxiety and agitation. Generally begin within 1 to 4 days of withdrawal and abate within 7 to 14 days
- If either of the above occurs the clinician should make an assessment of the risks and benefits of re-instating the previous dose of antipsychotic. Further attempts to reduce the antipsychotic should be made one month later with smaller decrements (10% daily dose)
- If there are no particular problems after week 1 then the dose should remain the same with further review after week 2 to 4 weeks.
- If the reduction has been tolerated without any of the effects described above then reduce by a further 25% and repeat the process
- There may be practical issues when reducing the dose, for example the availability and form of small doses of medication. It is recommended that this is discussed with a pharmacist
- It is suggested that once the total daily dose is reduced to the recommended starting dose for the individual antipsychotic, it may be stopped

A best practice guide for optimising treatment and care for behavioural and psychological symptoms of dementia is also available from Alzheimer's Society.

3.4 Stopping (deprescribing) benzodiazepines and z-drugs

Reproduced from NICE

Hypnotics and anxiolytics are associated with considerable increase in risk of morbidity: addiction, falls and cognitive impairment. These risks are likely to be increased for patients on multiple medicines, which is why they should be prioritised for review

Assessing the persons readiness to stop

Does stopping the drug matter to the patient, and are their physical and psychological health and personal circumstances stable? Enquire about:

- **Symptoms of depression.** Withdrawal can worsen symptoms of clinical depression. The priority is to manage depression first, before attempting withdrawal
- **Symptoms of anxiety** Withdrawal in the presence of significant anxiety is unlikely to succeed. However, when symptoms are reasonably well controlled and stable it may be possible to attempt careful drug withdrawal
- **Symptoms of long-term insomnia.** If insomnia is severe, consider treating this with non-drug treatments prior to starting withdrawal
- **Medical problems are well controlled and stable.** If other problems are causing significant distress, consider managing these first, prior to starting withdrawal
- **Withdrawal in primary care**. Is there adequate social support with no previous history of complicated drug withdrawal and ability to attend regular reviews?
- **Specialist advice or referral**. Consider where there is a history of alcohol or other drug use or dependence. Also where there is severe medical or psychiatric disorder or personality disorder. A history of drug withdrawal seizures where low tapering is recommended

Managing someone who wants to stop

Decide if the person can stop their current benzodiazepine or z-drug without changing to diazepam.

- **Switching to diazepam** is recommended for:
    - People using short-acting potent benzodiazepines (alprazolam, lorazepam)
    - Preparations that do not allow small dose reductions (alprazolam, flurazepam, loprazolam, lormetazepam)
    - People likely to experience difficulty withdrawing directly from temazepam, nitrazepam, or z-drugs, due to a high degree of dependency (associated with long duration of treatment, high doses, and a history of anxiety problems)
- **Seek specialist advice before switching to diazepam in people with hepatic dysfunction .** Diazepam may accumulate to a toxic level in these individuals. An alternative benzodiazepine without active metabolites (oxazepam) may be preferred
- **Negotiate a gradual drug withdrawal schedule (dose tapering) that is flexible. Be guided by the person in making adjustments so that they remain comfortable with the withdrawal**
- Titrate the drug withdrawal according to the severity of withdrawal symptoms
- Withdrawal may take 3-12 months or longer. Some people take less time
- **Review frequently, to detect and manage problems early and to provide advice and encouragement during and after the drug withdrawal**
- **If they did not succeed on their first attempt, encourage the person to try again**
- Remind the person that reducing benzodiazepine dosage, even if this falls short of complete drug withdrawal, can still be beneficial
- If another attempt is considered, reassess the person first, and treat any underlying problems (such as depression) before trying again

How should benzodiazepines, or z-drugs be withdrawn?

- **Withdrawal should be gradual** (e.g. 5–10% reduction every 1–2 weeks, or an eighth of the original dose fortnightly, with a slower reduction at lower doses), and titrated according to the severity of withdrawal symptoms
- Withdrawal may take 3–12 months or longer. Some people take less time
- **Withdrawal may be undertaken with or without** switching to diazepam.
- **Additional information:** withdrawal should be tailored to the individual's needs. See NICE CKS - Benzodiazepine and Z-Drug Withdrawal and the Ashton Manual.

Managing withdrawal symptoms

- **Review frequently** to detect and manage problems early, and to provide encouragement and reassurance during and after drug withdrawal
- **Manage anxiety** and explain that anxiety is the most common withdrawal symptom. Reassure that anxiety is likely to be temporary. Consider slowing or suspending withdrawal until symptoms become manageable. Consider additional use of non-drug treatments
- **Adjunct drug therapy should not be routinely prescribed.** May be considered *only* if other measures fail (e.g. propranolol for severe symptoms, such as palpitations, tremor, and sweating)
- **Manage depression** with antidepressants if required. Consider suspending withdrawal until depression resolves or stabilises. See the NICE CKS topic on Depression
- **Do *not* prescribe antipsychotics** which may aggravate withdrawal symptoms
- **Manage insomnia.** See NICE CKS topic on Insomnia

Advice to people undergoing withdrawal

- **Gradual** withdrawal minimizes the risk of withdrawal effects
- **Reassure** that the person will be in control of the rate of drug withdrawal. This can take 3-12 months or longer. Some people take less time
- **Difficult points** can be managed with maintaining the current dose for a few weeks. Try to avoid increasing the dosage if possible
- **Avoid** compensating for withdrawal by the use of alcohol, other drugs (prescription, non-prescription, or illicit drugs) or smoking
- **Stopping the last few milligrams is often seen as being particularly difficult.** Warn against prolonging the drug withdrawal to an extremely slow rate towards the end (e.g. reducing by 0.25 mg diazepam each month). Advise the person to consider stopping completely when they reach an appropriate low dose (e.g. diazepam 1 mg daily)
- **withdrawal symptom advice**:
  - With slow tapering, many people experience few or no withdrawal symptoms
  - If withdrawal symptoms are present with slow tapering then symptoms will disappear within a few months
  - Rarely some people will suffer from protracted withdrawal symptoms which will gradually improve over a year or longer
  - The acute symptoms of withdrawal are those of anxiety
  - Explain that some of the withdrawal symptoms may be similar to the original complaint and do not indicate a return of this
  - It is not possible to estimate the severity and duration of withdrawal symptoms for the individual
  - For information on managing withdrawal symptoms, see Managing withdrawal symptoms

Advice to people who do not want to stop taking benzodiazepines or z-drugs?

- **Do not pressurize the person to stop** if they are not motivated to do so
- **Listen to the person,** and address any concerns they have about stopping
- Explain that for most people who withdraw from treatment slowly, symptoms are mild and can usually be effectively managed by other means
- Reassure the person that they will be in control of the drug withdrawal and that they can proceed at their rate
- **Discuss the benefits of stopping the drug.** The discussion should include an explanation of tolerance, adverse effects, and the risks of continuing the drug. See Reasons for stopping for further information
- **Review at a later date** if appropriate, and reassess the person's motivation to stop
- **In people who remain concerned** about stopping treatment despite explanation and reassurance, persuading them to try a small reduction in dose may help them realize that their concerns are unfounded

3.5 Management of Constipation

Reproduced from NICE.

Drugs commonly cause constipation in adults, the most common are:

- Aluminium antacids
- Antimuscarinics (e.g. procyclidine, oxybutynin)
- Antidepressants (most commonly tricyclic antidepressants, but others may cause constipation)
- Some antiepileptics (e.g. carbamazepine, gabapentin, oxcarbazepine, pregabalin, phenytoin)
- Sedating antihistamines
- Antipsychotics
- Antispasmodics (e.g. dicycloverine, hyoscine)
- Calcium supplements
- Diuretics
- Iron supplements
- Opioids
- Verapamil

Managing chronic constipation in adults

- Begin by relieving faecal loading/impaction, if present
- Set realistic expectations for the treatment of chronic constipation
- Advise about lifestyle measures: increasing dietary fibre (including regular meals), adequate fluid intake, and exercise
- Adjust any constipating medication, if possible

Laxatives are recommended:

- If lifestyle measures are insufficient, or whilst waiting for them to take effect
- For people taking a constipating drug that cannot be stopped
- For people with other secondary causes of constipation
- As 'rescue' medicines for episodes of faecal loading

If laxative treatment is indicated

- Start treatment with a bulk-forming laxative
- It is important to maintain good hydration when taking bulk-forming laxatives. This may be difficult in the elderly
- If stools remain hard, add or switch to an osmotic laxative (use macrogols as first choice and lactulose if macrogols are not effective, or not tolerated)
- If stools are soft but the person still finds them difficult to pass or complains of inadequate emptying, add a stimulant laxative
- Adjust the dose, choice, and combination of laxative according to symptoms, speed with which relief is required, response to treatment, and individual preference
- The dose of laxative should be gradually titrated upwards (or downwards) to produce one or two soft, formed stools per day
- If at least two laxatives (from different classes) have been tried at the highest tolerated recommended doses for at least 6 months, consider the use of 5-HT_4-receptor agonist or guanylate cyclase-C receptor agonist as per their recommended place in therapy

If the person has opioid-induced constipation

- Advise them to increase the intake of fluid and fruit and vegetables if necessary
- **Avoid bulk-forming laxatives**
- Use an osmotic laxative and a stimulant laxative
- Adjust the laxative dose to optimise the response
- More information on the pros and cons of the various laxatives, is available within NICE CKS topic on Constipation.

Stopping laxatives

If patients is taking more than one laxative, do not stop treatment abruptly. Reduce stimulant first and monitor effect before stopping other laxatives.

3.6 Management of glycaemic control

See this link for Quality Prescribing for Diabetes – A guide for improvement

What is the optimal level of blood glucose control?

There are some important principles to consider when managing diabetes in people who are older and/or frailer, and especially when they have co-morbidities. Tight glycaemic control ($HbA1_c$ <53mmol/mol) may be appropriate in patients who are relatively healthy, with long life expectancy, and will live long enough to derive the benefits, such as reducing microvascular events. However, intensive glycaemic control strategies markedly increase the risk of hypoglycaemia. In turn hypoglycaemia has been associated with poor outcomes such as increased mortality, cardiovascular disease, falls and accidents.[23] There is likely to be a time for each individual when the harm caused by managing glycaemic control starts to outweigh any potential benefits. The challenge is to identify when this happens, which is why these evidence based factors below should be considered at patient review.

The *Hemoglobin A_{1c} Targets for Glycaemic Control With Pharmacologic Therapy for Nonpregnant Adults With Type 2 Diabetes Mellitus* provides clear advice and direction informed by rigorous evidence review and a consensus of key guidelines, including SIGN 116.[23]

- **Guidance Statement 1:** *Clinicians should personalize goals for glycaemic control.*

  The fine balance of benefits and risks of different intensities of glycaemic control are affected by many factors. The individuals glycaemic target should consider the risk of hypoglycaemia, weight gain and other adverse drug events, as well as the patients age, life expectancy, comorbidities, functional and cognitive impairment, fall risk, ability to adhere, medication burden and cost

- **Guidance Statement 2:** *Clinicians should aim to achieve an HbA_{1c} level between 53 and 64 mmol/mol in most patients with type 2 diabetes.*

  Trials show that treating to targets of 53 or less compared with targets of around 64 did not reduce death or macrovascular events over 10 years of treatment, but did result in harm, including hypoglycaemia. Risk of harm was greatest for older patients with comorbidities.

- **Guidance Statement 3:** *Clinicians should consider deintensifying pharmacologic therapy in patients with type 2 diabetes who achieve HbA_{1c} less than 48 mmol/mol*.

  The ACCORD trial, which targeted treatment of HbA_{1c} to less than *48 mmol/mol* was discontinued early due to an increase in all-cause and cardiovascular mortality and severe hypoglycaemic events

- **Guidance Statement 4:** *Clinicians should treat patients with type 2 diabetes to **minimise symptoms related to hyperglycaemia and avoid targeting an HbA_{1c} level** in patients with a life expectancy less than 10 years due to advanced age (80 years or older), residence in a nursing home, or chronic conditions (such as dementia, cancer, end-stage kidney disease, or severe chronic obstructive pulmonary disease or congestive heart failure because the harms outweigh the benefits in this population*.

  For these populations the use of sulfonylureas and insulin carry the greatest risk of harm.

For all patients with type 2 diabetes clinicians should provide counselling and emphasise the importance of lifestyle interventions, including exercise, dietary changes, and weight loss, to achieve good glycaemic control. Smoking cessation, adequate blood pressure control, and lipid management are also indicated in patients with type 2 diabetes and, for many patients, may take priority over achieving glycaemic control, especially for preventing macrovascular complications.

There remains clear evidence of benefit from tight glycaemic control in younger people (<55 years) with type 2 diabetes. The clinical benefits take ten years to be realised, but once established are shown to last a further seven years, even if the tight glycaemic control is not maintained, which is termed the 'Legacy Effect'. Each individual will reach a tipping point when tight glycaemic control does more harm than good, and it is these patients that should be targeted for review.

3.7 Management of Chronic Pain

Reproduced from *Quality Prescribing for Chronic Pain – A guide for improvement*

The Scottish Government, in collaboration with NHS Scotland, has produced a guide on the Management of Chronic Pain which includes both pharmaceutical and non-pharmaceutical interventions in the management of chronic pain. The prescribing for people with chronic pain is clearly defined in SIGN 136. NICE have also produced a number of guidelines on management of chronic pain. However, clinicians in NHS Scotland should refer to SIGN in the first instance which remains the only comprehensive evidence based guideline for managing chronic pain in the non-specialist setting.

Why is this important?

1 in 5 people in Europe suffer from chronic pain which is comparable to the proportion of the population suffering heart disease, diabetes and major depression combined. 1 in 20 people in Scotland suffer severe, disabling chronic pain.[24] Prescribing for chronic pain increased by 66% over the ten years from 2006.[25]

Key Principles

There are a number of key principles which should be considered as part of the management of chronic pain:

- Chronic pain is a condition which is individual to the patient and any therapeutic management plan needs to place the patient at the centre. The approach should be based on assisting the patient to achieve goals which have been identified in partnership with the prescriber
- Goals of therapy should be decided in a partnership with the patient adopting the *what matters to me* principle
- Prescribers should work with patients to develop an understanding of the importance of self-management and non-pharmaceutical approaches to the successful achievement of goals. Patients should be aware that therapeutic options which do not involve medicines, or which are offered in conjunction with prescribed medicines, may result in better achievement of goals and result in less harm than the prescription of medicines alone
- Prescribers should work with patients to develop their understanding of chronic pain, how it differs from acute pain and the impact this may have on goals of therapy. Difficult and honest conversations may be required to establish an understanding with the patient that it is highly unlikely that the therapeutic management plan will result in full resolution of their pain symptoms (>30%), but it may assist them with coping
- Assessment Treatment pathways for chronic pain are available on the SIGN website
- A robust plan for ongoing review of treatment should at the centre of care for every patient

Problems with Pharmacological therapies

There is increasing evidence that many analgesics, including opioids, gabapentin and pregabalin, have the potential for harm and abuse. Cases of dependency have been described and there are reports of an increasing street value risk of drug misuse.[26 27 28] There are a number of pharmacological therapies available for the management of chronic pain.

Recommendations

- Follow a clinically appropriate approach to initiation of analgesia, discussing expectations, risks and benefits and incorporating agreed criteria for stopping or continuing medication
- Review effectiveness, tolerability and compliance on an on-going basis. The burden of medicines should be reduced where possible. Electronic tools to assist with this are currently under development and will be hosted on the Effective Prescribing and Therapeutics website

3.8 Medication in the frailest adults

There are some frequently asked questions that come up in discussions around what medications to prescribe and which to withhold in the frailest group of adults. These adults are at high risk of medication side effects due to reduced physiological reserve, and with a limited lifespan are unlikely to derive any of the intended long term benefits. Treatment targets should also be reviewed and the following targets are believed to be more appropriate:

- Blood pressure - **avoid blood pressure < 130 systolic and or < 65 diastolic**
- Blood sugar control - **avoid lowering HbA_{1c} < 65**
- Treatments to maintain renal function and avoid progression of proteinuria - **avoid treating unless considered to have sufficient life expectancy to see benefit**
- Use of blood thinners - **avoid the use of combination blood thinners**
- Heart rate control - **reduce or stop heart rate limiting medication if pulse < 60**

As with all targets an individualised approach should be adopted to include giving clear information to allow an informed decision.

Blood pressure

Lowering blood pressure is an effective strategy to reduce the risk of cardiovascular events across a range of ages including the elderly. The benefits are greatest with reduction from very high blood pressure, and less impact from reducing moderately raised blood pressure. There is increased risk of harm when reducing blood pressure to very low levels in the frail elderly.[28] Study evidence demonstrated an increase in mortality for nursing home residents (mean age 87.5 years) when blood pressure ran at <130 with two or more antihypertensives. The number needed to harm was 10. It is important to note that antihypertensives may be prescribed for another condition, most notably left ventricular systolic dysfunction, which should influence deprescribing decisions

Blood sugar control

Tight glycaemic control takes a long time (10 years) to derive positive outcomes, and there is increased risk of harm below an HbA_{1c} of 65, especially in the frail elderly. Having recognised these facts, the overriding principle is to individualise targets for each patient.

Treatments to preserve renal function

ACE inhibitors and A2R blockers have an established role in slowing the progression of albuminuria to proteinuria to end stage renal failure. This progression takes time (years) even untreated. This is a treatment target that is hard to achieve within the lifespan of a frail adult. Unrealistic benefits of treatment are compounded by increased risk of acute kidney injury with intercurrent illness.

Blood thinners

Anticoagulants and antiplatelets to reduce the risk of stroke are effective even in the very frail. Caution is needed to avoid combining blood thinners. There are few long term indications for this and prescribing > 1 agent in observational studies in the non-frail increase bleeding rates steeply. The risk of bleeding with combination anticoagulants in adults discharge from hospital with atrial fibrillation, taking **warfarin** as baseline (ie 1) risk of bleeding

- Aspirin 0.93 [0.88 - 0.98]
- Clopidogrel 1.06 [0.87 - 1.29]
- Aspirin + Clopidogrel 1.66 [1.34 -2.04]
- Warfarin + Aspirin 1.83 [1.72-1.96]
- Warfarin + Clopidogrel 3.08 [2.32 - 3.91] *13.9% bleed risk /patient year*
- Warfarin + Aspirin + Clopidogrel 3.7 [2.89 - 4.76] *15.7% bleed risk /patient year*

It should be noted that the lowest stroke risk was in the warfarin group.[30]

Heart rate control

Drugs to lower heart rate are commonly prescribed, and as an adult gets frailer the clearance of many of these medications reduces leading to an increase in the heart rate lowering effect. This can often allow them to be steadily reduced or stopped. In particular if heart rate < 60 BPM serious consideration should be given to reducing or stopping.

Appendix A: General Medication Review Leaflet

The patient information leaflet shown below is available to download from this website.

Visiting the GP practice can be daunting for a patient, especially when they are unsure of what to expect. The leaflet below has been produced to help patients understand what happens during a polypharmacy review, why they need a review and it also highlights to patients that they can also use the review as an opportunity to ask any questions or share any concerns they have about their medicines. This leaflet was designed in partnership with a patient focus group.

Questions you may want to ask

If you and your doctor or pharmacist decide that one or more of your medicines should change, you may want to ask some of the following questions:

- What is the medicine for?
- How and when do I take it and how long for?
- Are there any side effects?
- What should I do if I become ill while taking this medicine?
- Do I need regular check-ups once I

Do I need to bring anything with me?

It would helpful if you could bring all of your medicines with you, including any you might have bought (this includes vitamins or herbal remedies).

Can I bring somebody with me?

You are welcome to bring along a family member or a trusted friend to your medicines review if you feel it would be helpful.

Where can I get further information about my medicines?

- Your local pharmacy
- Your GP Practice
- NHS Inform www.nhsinform.scot or phone: 0800 224 488

You can also download the Polypharmacy App from the App Store or Google Play Store, search for 'Polypharmacy'

Produced by the Effective Prescribing and Therapeutics Branch, Scottish Government

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Polypharmacy (Medicines) Review: Information for Patients and Carers

NHS SCOTLAND

Healthier Scotland Scottish Government

What is Polypharmacy?

You might've heard people referring to Polypharmacy. It means lots of medicines.

A review is useful for people who take a lot of medicines, for these people their medicines review may be called a Polypharmacy Review.

What is a medicines review?

A medicines review is a meeting with a doctor or a pharmacist to talk about the medicines you are currently taking.

Why do I need a review?

When you are first prescribed a medicine it is usually the best one for you, however, things change:

- You might have developed a side effect
- Your health may have changed, such as developing a long term condition or a change in a long term condition you already have

Any of these reasons, as well as others can mean the medicine might not be right for you anymore.

What happens at a medicines review?

The review will be carried out by a doctor or a pharmacist. They will ask you some questions and also look at your medical record, this will allow them to check you are on the medication which is right for you.

The review will be between 15 and 30 minutes long. You will have the chance to ask any questions or raise any concerns you have about your medicines.

The doctor or pharmacist may suggest some changes to your medicines. They will explain these changes and why the change will benefit you.

These changes may include: a change to a new or different version of a medicine, changing the dose, changing the time of day you take your medicine or stopping a medicine.

How will my review be carried out?

The doctor or pharmacist will carry out your review around some main themes:

Patient Centredness - what matters to you?

Aims - Do you think the medicine is making you feel better? Think about what is important to you about your treatment

Need - is the medicine essential? Could lifestyle changes mean the treatment objectives are achieved?

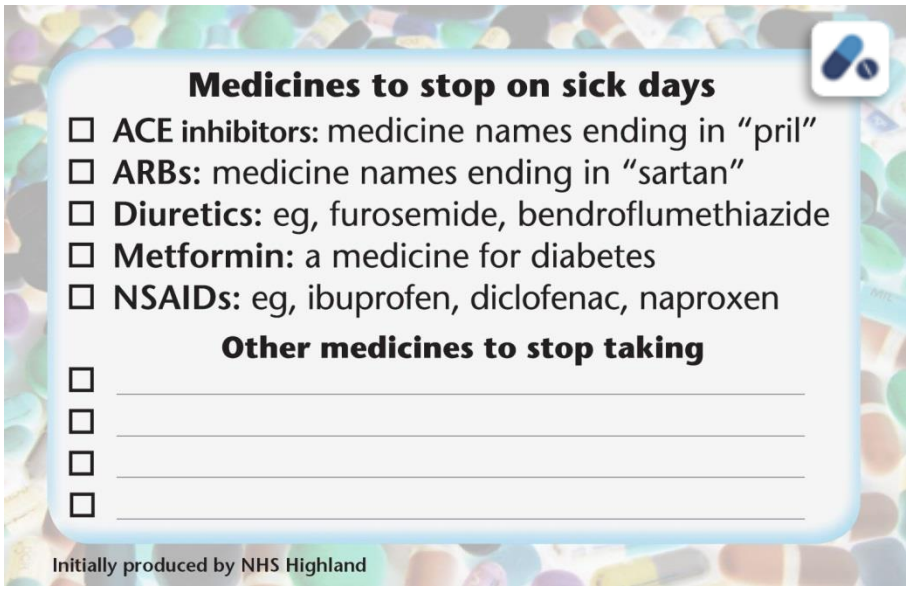
Effectiveness - is the medicine controlling your symptoms?

Safety - is the medicine making you unwell (side effects)?

Appendix B: *Sick Day Rules* Guidance: Information for healthcare professionals and patients

The *Sick Day Rules* guidance is a useful resource for patients, carers and health professionals as it promotes better management of long-term conditions through safer, more effective and person-centred use of medicines. The cards highlight the potential harms which could be caused if patients continue to take certain medicines whilst suffering from illnesses where dehydration can occur.

The Scottish Patient Safety Programme (SPSP) has produced a briefing for professionals and one for patients. The briefing leaflet for professionals provides some examples of what advice to give to patients to ensure that they understand the importance of stopping certain medicines when sick. An example of the *Sick Day Rules* Card is displayed below, copies of these can be downloaded from the SPSP website.



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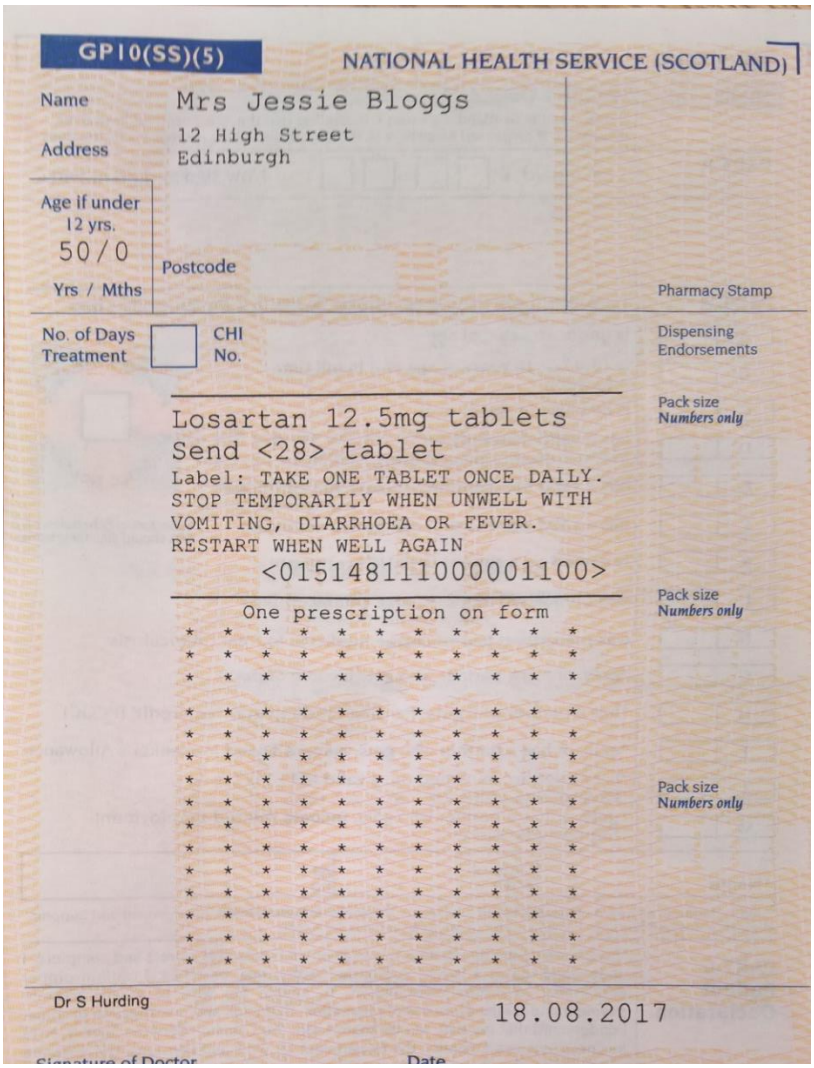
Autopopulation of electronic prescription dosing instructions

One method to implement the *Sick Day Rule* guidance is to include the advice within the dosing instruction on the prescription. This provides a number of triggers to discuss with the patient the importance of temporarily stopping these medicines during a potentially dehydrating illness: when issuing the prescription at consultation; when the medicine is dispensed and when referring to the dosing instruction on the medicine pack.


GP10(SS)(5)

NATIONAL HEALTH SERVICE (SCOTLAND)

Name Mrs Jessie Bloggs

Address 12 High Street
Edinburgh

Age if under 12 yrs. 50/0 Yrs / Mths

Postcode

Pharmacy Stamp

No. of Days Treatment

CHI No.

Dispensing Endorsements

Losartan 12.5mg tablets
Send <28> tablet
Label: TAKE ONE TABLET ONCE DAILY.
STOP TEMPORARILY WHEN UNWELL WITH
VOMITING, DIARRHOEA OR FEVER.
RESTART WHEN WELL AGAIN
<01514811100000110O>

Pack size Numbers only

One prescription on form

Pack size Numbers only

Pack size Numbers only

Dr S Hurding

18.08.2017

Signature of Doctor

Date

Each GP IT system has a way to autopopulate the prescription with the *Sick Day Rules* guidance, e.g. in EMIS, the formulary EFM-file can be edited to include this dosing instruction which will be installed in each practice as the file is updated; in Vision the dosing instruction can be set by each practice using the default doses functionality. NHS Lothian has an advanced clinically driven electronic formulary called eLJF-CLINICAL, built as a guideline in Vision, which uses the above dosing instruction to autopopulate each relevant prescription. The suggested dosing schedule above, also prints on community pharmacy labels without further editing.

Appendix C: Developing and Maintaining Numbers Needed to Treat (NNT) – Standard Operating Procedure (SOP)

Originally described by Laupacis et al (1988)[31] and cited in Cook (1995)[32], NNT was introduced as an approach to summarise the effect of treatment in terms of the number of patients a clinician needs to treat with a particular therapy to expect to prevent one adverse event over a specified time period.

Background

The Scottish Government *Polypharmacy Guidance – Realistic Prescribing 2018* is intended as a practical tool to help prescribers decide when it is appropriate to initiate and continue long-term medicines. In some circumstances it may be appropriate to discontinue treatments. Presentation of NNT for a range of medicines is one tool that prescribers may use to aid discussions with patients about the likely benefit.

The NNT is defined as the expected number of people who need to receive the experimental rather than the comparator intervention for one additional person to either incur or avoid an event in a given time frame. An NNT of 10 can be interpreted that one additional (or less) person will incur an event for every 10 participants receiving the experimental intervention rather than control over a given time frame.

Scope

This SOP is intended to describe the roles of the Association of Scottish Medicines Information Practitioners (ASMIP) in the development and maintenance of the NNTs and to describe a systematic approach to their calculation.

1. Defining NNTs

1.1 Defining the medicine, intervention and the clinical outcome of relevance

The medicines used in previous editions of the *Scottish Government Polypharmacy Guidance 2012* and *2015* should be included. These will be reviewed to ensure that they are both specific and measurable. Consideration also needs to be given to their relevance to clinical practice, e.g. is the medicine likely to be used in this clinical context and is the comparator described the most relevant to clinical practice?

1.2 Identifying relevant medical literature

The following principles should be applied:

- Cochrane reviews where available should be used
- Systematic reviews should generally be used in preference to individual randomised controlled clinical trials (RCT), unless the RCT includes a greater number of patients
- Where systematic reviews are not available individual randomised controlled trials may be used

The MI pharmacist should carry out a standard Medline® or Embase® search using relevant Medical Subject Heading (MeSH) terms and Boolean operators. In particular the following should be identified:

- Cochrane systematic reviews
- Other high quality systematic reviews
- Pivotal trials for the medicine in the relevant indication

Ideally studies should be identified from the previous five years, but in exceptional circumstances, e.g. where only a single pivotal trial has been published, or no newer systematic reviews have been published, older clinical trials or systematic reviews may be used.

1.3 Dealing with multiple trials and meta-analyses

Where more than one review or trial is identified for the relevant indication and intervention the following criteria should be assessed:

- Relevance to the defined medicine and intervention
- Size of the study or review
- Similarity of review and study cohort to the Scottish population

A judgement can then be made, using the criteria above to identify the most relevant trial or review from which the NNT can be calculated. Where the studies are very similar, the NNT should be calculated for each individual study and the mean taken for inclusion in the table.

2. Calculating NNTs

The NNT can be calculated from the absolute risk reduction (ARR) taken from a clinical trial or systematic review. ARR = $p_1 - p_2$, where p_1 is the baseline or placebo rate and p_2 is response rate in the intervention group in a clinical trial.

> The NNT can be calculated as $1/(p_1-p_2)$.[33] Where the benefit is accrued over a number of years, the annual NNT can be calculated by multiplying the NNT by the number of years over which the study was conducted.

3. Recording research

The MiDatabank® project management function should be used to record all research. The following information should be recorded:

- The literature search
- Trials and reviews identified
- Absolute risk reduction figures taken from the study(ies)
- The calculation used to define the NNT

4. Presenting the NNT data

All NNT data should be tabulated to include the following:

- Intervention - the medicine or other intervention of interest
- Comparator
- Outcome - the desired outcome from the proposed treatment
- NNT - calculated using standard methodology
- Duration of study and intervention
- Demographics of population - age, sex (where relevant), co-morbidities
- Reference - main reference used to calculate the NNT

7. Referencing

Vancouver style should be used to reference all trials and reviews used in the calculation of NNTs. Where data has been taken from websites, the web address and the date accessed should be recorded.

8. Checking and Peer Review

A peer check should be undertaken by another MI or clinical pharmacist prior to publication. The check should include:

- Clarity and completeness
- Any obvious gaps in the information concerning the patient demographics
- A calculation check for the NNT

Drug Efficacy (NNT) table

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Hypertension								
Blood Pressure control (<140/90mmHg)	No treatment	Patients with hypertension and age > 80 years	Total mortality	2 years	333	666	High risk is defined as patients with a previous history of stroke Cardiovascular mortality and morbidity includes fatal and non-fatal MI, sudden cardiac death, aneurysms, congestive heart failure, fatal and non-fatal stroke and transient ischaemic attacks Total mortality is death from all causes NB the evidence base to support the NNT for impact on mortality in the over 80 years is very limited	34
			Cardiovascular mortality and morbidity	2 years	35	70		
Blood Pressure control (<140/90mmHg)	No treatment	Patients with hypertension and high risk* and age > 80 years	Total mortality	2 years	333	666		
			Cardiovascular mortality and morbidity	2 years	16	32		
Blood Pressure control (<140/90mmHg)	No treatment	Patients with hypertension and age > 60 years	Total mortality	4.5 years	83	374		
			Cardiovascular mortality and morbidity	4.5 years	23	104		
Blood Pressure control (<140/90mmHg)	No treatment	Patients with hypertension and high risk* and age > 60 years	Total mortality	4.5 years	33	149		
			Cardiovascular mortality and morbidity	4.5 years	9	41		

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Heart Failure								
Spironolactone 25 mg daily	Placebo	Patients with heart failure Patients had NYHA class IV heart failure in the 6 months prior to enrolment, but were NYHA class III or IV at the time of enrolment	Prevent one death (all causes)	24 months (mean duration of follow-up)	9	18	Mean age of patients was 65 years. Spironolactone also reduced the frequency of hospitalisation for heart failure and produced a significant improvement in the symptoms of heart failure. Patients in the trial were on an ACE inhibitor (if tolerated) and a diuretic. 10% of patients were also on a beta-blocker.	35
Beta-blocker (bisoprolol titrated to target dose of 10 mg/day)	Placebo	Patients with moderate to severe heart failure NYHA class III or IV and LVEF </=0.35	Prevent one death (all causes)	1.3 years (mean duration of follow-up)	18	24	Mean age of patients was 61 years, 83% of whom were NYHA class III. Current treatment had to include a diuretic and an ACE inhibitor although other vasodilators were allowed if patients were intolerant of ACE inhibitors. 96% of patients were on ACE inhibitors.	36
Beta-blocker (carvedilol titrated to target dose of 25 mg twice daily)	Placebo	Patients with severe heart failure NYHA class IV and LVEF < 0.25	Prevent one death (any cause)	10.4 months (mean duration of follow-up)	18	16	Mean age of patients was 63 years. Conventional therapy included diuretics and an ACEI or ARB. 97% of patients were on ACE inhibitor or ARB.	37

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Beta-blocker (Metoprolol modified-release titrated to a target dose of 200 mg/day)	Placebo	Patients with mild to severe heart failure NYHA class II to IV and LVEF </=0.40	Prevent one death (all causes)	12 months (mean duration of follow-up)	28	28	Mean age of patients was 64 years. Optimum standard therapy was defined as any combination of ACE inhibitors, Angiotensin receptor blockers and diuretics. 97% of patients were on an ACE inhibitor or Angiotensin receptor blocker.	38
Beta-blocker (nebivolol titrated to a target dose of 10 mg/day)	Placebo	Patients >70 years old with mild-severe heart failure NYHA class I to IV irrespective of LVEF	Prevent one death (all causes)	21 months (mean duration of follow-up)	44	78	Median age of patients was 75 years. 64% of patients had a LVEF of </=0.35. >95% of enrolled patients were NYHA class II or III. 87% of patients were on an ACE inhibitor or Angiotensin receptor blocker.	39
ACE inhibitor (ramipril 10 mg/day)	Placebo	Patients at high-risk of cardiovascular disease without LVSD or heart failure High-risk of cardiovascular disease defined as: history of coronary heart disease, stroke, peripheral vascular disease or diabetes plus one other cardiovascular risk factor (see comments)	Prevent one death (any cause)	60 months	54	270	Mean age of enrolled patients was 66 years. >50% of patients had a history of MI. Cardiovascular risk factors: hypertension, elevated total cholesterol, low HDL, smoker, microalbuminuria. Ramipril reduced the risk of myocardial infarction, stroke, coronary revascularisation and heart failure. There are no data to support ARBs for this indication.	40

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Angiotensin II receptor antagonist (telmisartan 80 mg/day)	Placebo	Patients intolerant of ACE Inhibitors with established cardiovascular disease: coronary artery, peripheral vascular or cerebrovascular disease, or diabetes with end organ damage Patients with heart failure were excluded	Prevent one of a composite of cardiovascular death, MI or stroke	56 months (median duration of follow-up)	55	258	Mean age of patients was approximately 67 years. Death rate (of any cause) was higher in treatment group than placebo group. When hospitalisations for cardiac failure were added to the composite endpoint as a primary outcome, the results were non-significant. Study concluded that telmisartan did not significantly reduce cardiovascular death.	41
ACE inhibitor (enalapril 2.5 to– 40 mg/day (up-titrated as tolerated))	Placebo	Patients with severe heart failure NYHA class IV Co-morbidities included coronary heart disease, previous MI , hypertension and diabetes	Prevent one death (any cause)	188 days (mean follow-up)	7	3	Mean age of patients was 70 years. Symptomatic improvement was observed i.e. a significant improvement in NYHA classification. NB Patient numbers in the study were low (n=253).	42
ACE inhibitor (enalapril 2.5 to 20 mg/day (up-titrated as tolerated))	Placebo	Patients with heart failure NYHA class I – IV and LVEF ≤0.35	Prevent one death (any cause)	41.4 months (mean follow-up)	22	76	Mean age of patients was 61 years, approximately 80% were male. Less than 2% were NYHA Class IV. Treatment also reduced hospital admissions for heart failure. Mortality benefit appears to be most marked in the first 24 months.	43

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
ACE inhibitor (enalapril 2.5 to 20 mg/day (up-titrated as tolerated))	Placebo	Patients with heart failure and chronic kidney disease NYHA class I - IV and LVEF ≤0.35 and eGFR <60 mL /min /1.73m2	Prevent one death (any cause)	41.4 months (mean follow-up)	29	101	Mean age of patients was 64 years. Approximately 75% were male.	44
ACE inhibitor (enalapril 2.5 to 20 mg/day (up-titrated as tolerated))	Placebo	Patients with asymptomatic heart failure NYHA class I and LVEF ≤0.35	Prevent one death (any cause)	34 months (mean follow-up)	88	251	Mean age of enrolled patients was 60 years. Treatment reduced the incidence of congestive heart failure and related hospital admissions.	45
Angiotensin receptor blocker (candesartan 4 to 32 mg/day)	Placebo	Patients with intolerance to ACE inhibitors with symptomatic heart failure NYHA Class II-IV and ejection fraction ≤0.4	Prevent one death (cardiovascular cause) or hospital admission for chronic heart failure	33.7 months	14	40	Mean age of enrolled patients was approximately 66 years. Patients were already taking other drugs as part of therapy for heart failure. Approximately 70% had heart failure of ischaemic cause.	46
			Prevent one death		34	94		
ACE inhibitor and indapamide (perindopril 4 mg/day and idapamide 2.5 mg/day)	Placebo	Patients who had a history of stroke or TIA in the last 5 years	Prevent one stroke (any cause)	3.9 years (mean duration of follow-up)	17	68	Mean age of patients was 64 years. 70% of patients in the trial had ischaemic stroke. There were similar reductions in the risk of stroke in hypertensive v. non-hypertensive patients.	47

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Cerebrovascular/ Cardiovascular Disease								
Warfarin (target INR 2 - 3)	Aspirin 75 mg daily	Age > 75 years with AF	1st occurrence of fatal or non-fatal disabling stroke (ischaemic or haemorrhagic), other intracranial haemorrhage or clinically significant arterial embolism	2.7 years (mean duration of follow-up)	20	54	Mean age of patients prescribed warfarin was 81.5 years. 73% of patients had a CHADS2 score of 1-2. 67% of patients on warfarin remained on this treatment for the complete duration of the trial.	48
Direct Acting Oral Anticoagulants (DOACs) There are no studies comparing DOACs against placebo. The NNT and NNH data in the table are based on comparative studies against warfarin, not against placebo. Great care is required in interpreting this data. It is of limited use to guide a decision on whether or not to continue with a DOAC. In addition it should be noted that these studies were equivalence/non-inferiority studies against warfarin, so the validity of extrapolating the results could be questioned. However, these data are included as a useful representation of the potential relative risks and benefits between warfarin and the individual agents.								
Apixaban 5 mg twice daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 2.1 (CHADS2 score > 3 (30%))	Stroke or systemic embolism	1.8 years	167	301	Median age 70yrs (63-76). Treating 167 patients with apixaban instead of warfarin for 1.8 years might prevent one stroke or systemic embolism **Note: warfarin group were within therapeutic range only 66% of the time.**	49
Apixaban 5 mg twice daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 2.1 (CHADS2 score > 3 (30%))	Major bleeding	1.8 years			NNH of 67 with respect to major bleeding, so treating 67 patients with apixaban instead of warfarin for 1.8 years might prevent one major bleeding episode.	

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Dabigatran 110 mg or 150 mg twice daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 2.1 (CHADS2 score 3-6 (33%)) Approx age 71 years	Stroke or systemic embolism	2 years	**333** (for 110 mg twice daily dose) **91** (for 150 mg twice daily dose)	**666** (for 110 mg twice daily dose) **182** (for 150 mg twice daily dose)	Approximate average age 71 yrs. This means that treating 333 (110mg) or 91 (150mg) patients with dabigatran instead of warfarin for 2 years might prevent one stroke or systemic embolism (depending on the dose used). **Note: warfarin group were within therapeutic range only 64% of the time.**	50
Dabigatran 110 mg or 150 mg twice daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 2.1 (CHADS2 score 3-6 (33%))	Major bleeding	2 years			NNH, with respect to major bleeding, treating 83 (110mg) or 250 (150mg) patients with dabigatran instead of warfarin for 2 years might prevent one major bleeding episode (depending on the dose used).	
Edoxaban 30 mg or 60 mg daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 2.8 (CHADS2 score 4-6 (23%))	Stroke or systemic embolism	2.8 years	**167** (for 60 mg daily dose)	**468** (for 60 mg daily dose)	Median age 72 years (range 64-78) This means that treating 167 patients with edoxaban instead of warfarin for 2.8 years might prevent one stroke or systemic embolism. **Note, however, that the warfarin group were within**	51

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Edoxaban 30 mg or 60 mg daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 2.8 (CHADS2 score 4-6 (23%))	Major bleeding	2.8 years			**therapeutic range only 68% of the time.** NNH, with respect to major bleeding, treating 67 patients with edoxaban instead of warfarin for 2.8 years might prevent one major bleeding episode.	
Rivaroxaban 20 mg daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 3.5 (CHADS2 score > 3 (10%)) Median age 73 years (range 65-78)	Stroke or systemic embolism	1.9 years	**200**	**380**	Median age 73 years (range 65-78) This means that treating 200 patients with rivaroxaban instead of warfarin for 1.9 years might prevent one stroke or systemic embolism. **Note, however, that the warfarin group were within therapeutic range only 55% of the time.** NNH, with respect to major bleeding, treating 260 (in favour of warfarin) patients with rivaroxaban instead of warfarin for 1.9 years might cause one major bleeding episode.	52
Rivaroxaban 20 mg daily	Warfarin (to maintain an INR of 2-3)	Patients with non valvular AF Mean CHADS2 score 3.5 (CHADS2 score > 3 (10%))	Major or clinically relevant non major bleeding	1.9 years				

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Aspirin	Placebo or no treatment	Primary prevention of CVD Individuals without history of occlusive disease	Serious vascular event (MI, stroke or vascular death).	Mean 5.8 years	246	1428	Age range in trials was 19-94 years Patients had hypertension or coronary risk factors without overt disease.	53
Aspirin or other antiplatelet*	Placebo or no treatment	Secondary prevention of CVD in patients with history of stroke or TIA	Serious vascular event (non-fatal MI, non-fatal stroke or vascular death).	29 -31 months	28-40	68 – 94	*Antiplatelets included aspirin (most widely studied), clopidogrel, dipyridamole, and other antiplatelets not commonly used in UK practice.	54, 55
Antiplatelet*	Placebo or no treatment	Secondary prevention in patients at high risk of cardiovascular events (previous MI, acute MI, previous stroke/TIA, and other high risk (excluding acute stroke)).	Serious vascular event (non-fatal MI, non-fatal stroke or vascular death).	26 months	15	32	*Antiplatelets include aspirin (most widely studied), clopidogrel, dipyridamole, and other antiplatelets not commonly used in UK practice.	54
Aspirin & dipyridamole	Placebo	Secondary prevention of CVD in patients with arterial vascular disease (coronary artery disease, MI, angina, retinopathy, nephropathy, PAD, stroke, TIA, amaurosis fugax)	Vascular event (non-fatal MI, non-fatal stroke or vascular death).	30 months	25	163	Mean age of patients 54 years.	56

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Aspirin & dipyridamole	Aspirin	Secondary prevention of CVD in patients with arterial vascular disease (coronary artery disease, MI, angina, retinopathy, nephropathy, PAD, stroke, TIA, amaurosis fugax)	Vascular event (non-fatal MI, non-fatal stroke or vascular death).	29 months	50	121	Mean age of patients 55 years	57
Clopidogrel or ticlopidine	Aspirin	Secondary prevention of CVD in patients with history of ischaemic stroke or TIA.	Stroke (all types)	22 months	100	184	Mean age of patients was 63 years Ticlopidine is not available in the UK but has similar mode of action to clopidogrel	58
			Stroke, MI or vascular death	28 months	100	223		
Statin (Simvastatin 40 mg daily, atorvastatin 80 mg daily, pravastatin 40 mg daily)	Placebo	Secondary prevention of CVD in patients with history of ischaemic or haemorrhagic stroke or TIA.	Ischaemic or haemorrhagic stroke	48 months	100	400-420		59
			Serious vascular events (non-fatal stroke, non-fatal myocardial infarction, vascular death) and all-cause mortality including sudden deaths	41- 44 months	20	68-74		

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Diabetes								
Intensive sulphonylurea with insulin to achieve fasting plasma glucose less than 6.0mmol/L	Conventional treatment with diet to aim for fasting blood glucose less than 15mmol/L (Metformin and/or sulphonyl-urea could be added, or patients changed to insulin if target not achieved)	Newly diagnosed type 2 diabetes patients between 25-65 years	Any diabetes end point	10 years (median duration of follow-up)	20	200	Mean age of patients was 54 years (range 25-65). Any diabetes-related endpoint: sudden death, death from hyperglycaemia or hypoglycaemia, fatal or non-fatal myocardial infarction, angina, heart failure, stroke, renal failure, digital amputation, vitreous haemorrhage, retinopathy requiring photocoagulation, blindness in one eye, or cataract extraction. Diabetes related death was death due to: myocardial infarction, stroke, peripheral vascular disease, renal disease, hyperglycaemia or hypoglycaemia, and sudden death. Reduction in micro-vascular events were mostly retinal. Median HbA_{1c} over 10 years 7.0% in intensive group versus 7.9% in conventional group. Intensive group had more hypo-glycaemic episodes per year and higher weight gain than conventional group.	60
			Diabetes related death		91	910		
			Micro-vascular complications		36	360		

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)	Annualised NNT	Comments	Ref
Metformin to achieve fasting blood glucose <6.0mmol/l (maximum dose 2550mg) Glibenclamide added if target not achieved and changed to insulin if required	Diet alone to achieve fasting blood glucose <15mmol/l. sulphonyl-urea or metformin or insulin could be added	Newly diagnosed type 2 diabetes patients - between 25-65 years Overweight defined as >120% ideal body weight	Any diabetes end point	10.7 years (median duration of follow-up)	7	80	Mean age of patients was 53 years; mean weight 87kg ; BMI 31. Any diabetes-related endpoint: As above. Median HbA_{1c} during 10 years was 7.4% in metformin group and 8.0% in conventional group. Hypoglycaemic episodes were higher in metformin group but lower than the sulfonylureas group. Hypoglycaemia rates increased over time in insulin group as higher doses were required.	61
			Diabetes related death		19	203		
			Microvascular disease		45	481		
Intensive control of glucose by including Gliclazide mr to existing medication to achieve a HbA_{1c} of 6.5% or less.	Hypo-glycaemia agents chosen by the treating physician	Patients with type 2 diabetes mellitus at least 55 years old with a history of major macro-vascular or micro-vascular disease or at least one other risk factor for vascular disease	Major microvascular or macrovascular events (death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke)	5 years (median)	53	263	Mean HbA_{1c} in control group was 7.3% and intensive (gliclazide mr) arm was 6.5% after 5 years follow up. Microvascular benefits were mostly due to reduction in nephropathy. No significant effect on major macrovascular events alone. Severe hypoglycaemia occurred in 2.7% of patients on intensive therapy compared with 1.5% of patients in the standard therapy group (NNH=80).	62
			Major micro-vascular events (new or worsening nephropathy or retinopathy).		67	333		

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)		Annualised NNT		Comments	Ref
Osteoporosis										
Alendronate 10 mg tablets	Placebo	Post-menopausal women a) For primary prevention average T-score was within 2 standard deviations of the mean for bone density b) For secondary prevention in women who had experienced previous vertebral compression fractures	Rate of vertebral, non-vertebral or hip fractures (as below) over a 5 year period	60 months (5 years)	As per age range (left column) below		As per age range (left column) below		Age range 42-85 but >62 for secondary prevention These NNTs apply to the first 5 years of treatment only.	63
			Vertebral secondary prevention		65-74	16	65-69	80		
					70-74	13	70-74	65		
					75-79	9	75-79	45		
					80-84	12	80-84	60		
					85-89	11	85-89	55		
					90+	8	90+	40		
			Non-vertebral secondary prevention		65-69	52	65-69	260		
					70-74	39	70-74	195		
					75-79	36	75-79	180		
					80-84	27	80-84	135		
					85-89	24	85-89	120		
					90+	12	90+	60		
			Hip secondary prevention		65-69	21	65-69	105		
					70-74	86	70-74	430		
					75-79	36	75-79	180		
					80-84	21	80-84	105		
					85-89	9	85-89	45		
					90+	8	90+	40		

Medicine / intervention	Comparator	Study population	Outcome	Duration of trial	Number needed to treat (NNT)		Annualised NNT		Comments	Ref
Alendronate	Placebo	Postmenopausal women a) For primary prevention average T-score was within 2 standard deviations of the mean for bone density b) For secondary prevention women who had experienced previous vertebral compression fractures	Rate of vertebral, non-vertebral or hip fractures (as below) over a 5 year period Vertebral primary prevention	60 months (5 years)					Age range 42-85 but >62 for secondary prevention. These NNTs apply to the first 5 years of treatment only. All patients received calcium and vitamin D.	63
					65-69	14	65-69	740		
					70-74	12	70-74	615		
					75-79	67	75-79	335		
					80-84	97	80-84	485		
					85-89	89	85-89	445		
					90+	47	90+	235		
			Non-vertebral primary prevention		65-69	10	65-69	520		
					70-74	67	70-74	335		
					75-79	59	75-79	295		
					80-84	42	80-84	210		
					85-89	32	85-89	160		
					90+	12	90+	60		
			Hip primary prevention		65-69	23	65-69	118		
					70-74	11	70-74	590		
					75-79	50	75-79	250		
					80-84	27	80-84	135		
					85-89	11	85-89	55		
					90+	9	90+	45		

Appendix D: Health Economics Analysis of Polypharmacy

Introduction and overview

Although the primary purpose of polypharmacy reviews is in deriving clinical benefits, they also deliver long-term direct and indirect economic benefits. A direct reduction in the cost of prescribing, and reduction in medicines waste is anticipated. In terms of indirect economic benefits, a patient stabilised on fewer medicines will likely require less contact with health professionals, thereby freeing up capacity. Of prime aim is the indirect economic benefit of fewer unscheduled hospital admissions due to adverse drug reactions (ADRs). [64 65]

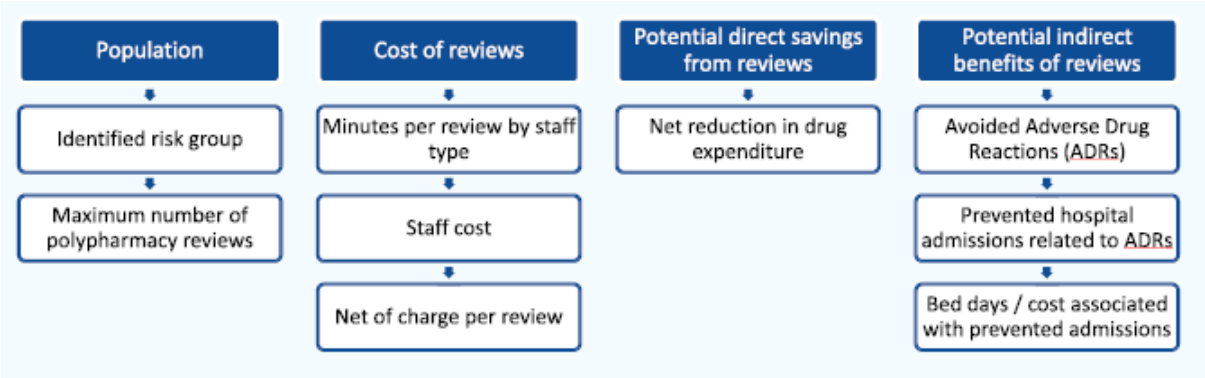
SIMPATHY Economic Analysis Tool

The goal of the SIMPATHY Economic Analysis tool [66], developed as part of the EC SIMPATHY project, was to provide a high-level analysis of the economic costs and benefits associated with carrying out polypharmacy reviews. The analysis follows a top-down approach and estimates maximum costs and benefits associated with activity. Activity is driven by the selected population for whom reviews are intended to be carried out.

Costs of reviews are based on the resource (staff) cost of carrying out a review, net of any potential review charge. The direct potential financial benefit of reviews will consist of the net reduction in drugs prescribed, and associated expenditure. Potential indirect benefits (non-cash releasing) centre around potentially avoided Adverse Drug Reactions (ADRs), preventable hospital admissions associated with these ADRs, and the associated number of hospital bed days avoided. The costs of medicines stopped and reduced are cash releasing, whereas avoided admissions are a capacity release productive opportunity.

Ultimately, the tool was intended to add to the package of SIMPATHY change management tools by offering a bespoke analysis of the micro-economic impacts, the costs and benefits of introducing and carrying out reviews. It is thought that this will give a broad overview around resource needs and potential benefits to interested users.

Structure of the SIMPATHY model



Implementation cost – review cost

Table D1 provides an overview of estimated activity and associated costs per review for Scotland. A range of different models and estimates are provided with some variation in the way that this information was provided. Renewed estimates range from £24.36 to just over £67 per review, which is a reduction on earlier work. It should also be noted that these cost estimates are a monetisation of assumed core clinical activity, and will therefore not pose an additional cost.

Cost avoidance – number of drugs stopped

Net reductions in the number of items stopped over one year were estimated to be in a range of between 4.9 and 18.2 items, and an average of 11.9 items (number of reviews per annum, applied to the net of the number of drugs stopped/decreased minus those started/increased, and their average number of repeats). That range is then applied to a lower and an upper estimate of costs per item (£10.17 and £10.90)[A] to give a full range of the potential direct savings from net reductions in drugs, ranging from £50 to £200.

Indirect impacts – Adverse Drug Reactions

Pirmohamed (2004) estimate a prevalence of 6.5% (95% C.I. 6.2% to 6.9%) of admissions judged as being due to an ADR. The study determined avoidability of admissions related to an ADR. Only 28% (25% to 30%) of the ADRs were assessed as unavoidable, while 9% (7% to 10%) were classified as definitely avoidable and 63% (60% to 66%) as possibly avoidable.

Applying these parameters, and an additional conservative assumption that 10% of avoided admissions (and associated bed days) are avoided due to polypharmacy reviews, to a population of 1,000 gives the associated indirect benefits presented in Table D4 (central estimates only). Note that this also gives a variation in results depending on different types of population groups, each stratified by their level of risk of admission or readmission via Scottish Patients at Risk of Readmission and Admission (SPARRA) database.

Scottish SPARRA population groups

Tables 1a and 1b in Appendix G summarise SPARRA population groups. Applying the estimated ranges of costs, and direct and indirect benefits (central estimates) to the population of, e.g. the 75+ SPARRA group (and underlying admissions data) generates the set of results summarised in table D3.[B]

Net value of direct and indirect costs and benefits

Table D4 shows the net benefit of deducting the range of costs from savings from all benefits. If all indirect benefits are taken into account, the net benefit is positive throughout. Note that, in the most pessimistic scenario with maximum costs and minimum drug savings, the balance is tipped and can become negative if only direct benefits are taken into consideration.

Notes

[A] Item cost estimates are quarter 3, 2016/17 only, to acknowledge more accurately the current cost of prescriptions, but not ta king seasonality into consideration. Includes items prescribed on GP10 forms only, excludes prescribed by pharmacists, nurses, etc, to avoid inclusion of stock orders and medicines supplied from hospital and CPU forms. Excludes appliances and vaccines as these are not therapeutic treatments considered in polypharmacy reviews

Lower estimate includes BNF chapters: 01;02;03;04;05;06;07;09;10;11;12
Upper estimate includes all BNF chapters

[B] Cost and benefit are per annum, given the assumption that these are derived as a follow on from the first review

Table D1: Cost of polypharmacy reviews (per patient)

Different models of review staff time allocation	Staff type	AfC Band (where appropriate)	Preparation (work-up)		Face to Face review		Follow-up and Related activities[1]		Total time taken		Total cost per review[2]	
	Type	Band	min minutes	max minutes	min minutes	max minutes	min minutes	max minutes	min minutes	max minutes	min £	max £
2015 guidance	Clinical Pharmacist	8a			60	60	15	15	75	75	£40.61	£40.61
	GP	n/a			15	15	15	15	30	30	£26.40	£26.40
	Total cost										**£67.01**	**£67.01**
Highland												
Model 1 - First review	Clinical Pharmacist	8a	5	5	15	15	40	40	60	60	£32.48	£32.48
	Total cost										**£32.48**	**£32.48**
Model 2 - Follow-up review	Clinical Pharmacist	8a	5	5	10	10	35	35	50	50	£27.07	£27.07
	Total cost										**£27.07**	**£27.07**
Tayside												
Model 1 - independent Pharm prescriber	Clinical Pharmacist	8a	15	30	30	30			45	60	£24.36	£32.48
	Total cost										**£24.36**	**£32.48**
Model 2 - non -independent prescriber, With GP review	Clinical Pharmacist	7	15	30			15	30	30	60	£14.15	£28.30
	GP	n/a					15	15	15	15	£13.20	£13.20
	Total cost										**£27.35**	**£41.51**
Model 3 - consultant clinic, with GP follow-up	GP	n/a					15	15	15	15	£13.20	£13.20
	Geriatric consultant	n/a			30	30			30	30	£42.00	£42.00
	Total cost										**£55.20**	**£55.20**
Ayrshire and Arran[3]	Clinical Pharmacist	8a							80	120	£43.31	£64.97
	Total cost										**£43.31**	**£64.97**
GG&C[4]												
Model 1 - non -independent prescriber, with GP review	Clinical Pharmacist	7	30	30	30	30			60	60	£28.30	£28.30
	GP	n/a					5	10	5	10	£4.40	£8.80
	Total cost										**£32.70**	**£37.10**
Model 2 - independent pharm. prescriber, With tech. support	Clinical Pharmacist	8a	10	30	30	30			40	60	£21.66	£32.48
	Pharmacy tech.	5	15	5					15	5	£5.26	£1.75
	Total cost										**£26.91**	**£34.24**

[1] Follow-up and related activities include: Follow-up; MDT meetings; practice meetings; travel; other activities
[2] Estimated Weighted Total Cost including on-cost, AfC 2015-16
[3] based on Advisers carrying out 2-3 reviews during half-day sessions (4hrs)
[4] models for AfC band 7 and band 8a led reviews. Local variation around tech support, less tech support requires more pharmacist preparation time

Table D2: Avoidable bed days and present values of avoidable admissions for 1,000 people

Population = 1,000	No risk stratification	Risk stratification			
		BNF10+	BNF10+ & High Risk Med	BNF 5-9	BNF 5-9 & High Risk Med
Definitely avoidable hospital **bed days***	0.9	8.4	7.3	7.6	6.6
Assoc. cost avoidance of **definitely** avoidable **admissions**	£326	£3,110	£2,699	£2,801	£2,421
Possibly avoidable hospital **bed days**	6.2	59.1	51.3	53.2	46.0
Assoc. cost avoidance of **possibly** avoidable **admissions**	£2,280	£21,771	£18,891	£19,604	£16,945

* Including assumption that 10% of avoided bed days are avoided due to polypharmacy reviews

Table D3: Costs and benefits for 75+ SPARRA group, in year one

Total in group	42,882	
Direct costs and benefits	minimum	maximum
Cost of reviews	£1,044,761	£2,873,565
Net drug reduction	£2,137,077	£8,509,982
Indirect benefits: avoidable bed days and admissions		
Definitely avoidable hospital **bed days***	362	
Associated cost avoidance of **definitely** avoidable **admissions**	£133,368	
Possibly avoidable hospital **bed days**	2,535	
Associated cost avoidance of **possibly** avoidable **admissions**	£933,576	

* Including assumption that 10% of avoided bed days are avoided due to polypharmacy reviews

Table D4: Net value of direct and indirect costs and benefits

		Costs of reviews (£m)	
		minimum	maximum
Net drug savings & indirect benefits* (£m)		£1.04	£2.87
minimum	£3.20	£2.16	£0.33
maximum	£9.58	£8.53	£6.70

* indirect benefits of definitely avoidable admissions only

Appendix E: *Case Finding* Indicators to prioritise patients for review

This section is to support prioritising patients for review. The following case finding criteria provide a high level strategic classification:

A. Aged 50 years and older and resident in a care home, regardless of the number of medicines prescribed
B. Prescribed 10 or more medicines (this will identify those from deprived communities where the average age is lower when taking 10 or more medications)
C. On high-risk medication (as defined by the *Case Finding* indicators (see below), regardless of the number of medicines taken
D. Approaching the end of their lives: Adults of any age, approaching the end of their life due to any cause, are likely to have different medication needs, and risk versus benefit discussions will often differ from healthy adults with longer expected life spans

If is not realistic to review all of these patients immediately the above criteria can be further stratified by:

- **Age** (e.g. 75 years and over, then 65 years and over as resource allows)
- **Frailty** (e.g. HIS Frailty / SPARRA score) – use the score which has been agreed by your organisation
- **Dominant condition** (e.g. dementia) – certain conditions dominate patient care as they impact and inform decisions for all other conditions

There has been further development of using high-risk medication measures to develop a suite of 69 *Case Finding* prescribing and monitoring indicators. Many of these measures can be also used as *Clinical Outcomes* indicators, where a fall in the number of patients affected may be seen following intervention (Appendix F). In addition, where the *Case Finding* indicators (27 indicators) utilise patient level prescribing data (PIS) the measures can be used to identify prevalence figures (Table E1).

Table E1: Prevalence from Validated *Case Finding* indicators (PIS Data)

Composite Indicator	Measure	Denominator	2017 Q1	% of Denominator
1. Cardiac decompensation and/or bradycardia	d. Patient prescribed nitrate and phosphodiesterase type-5 inhib.	Of all people prescribed a nitrate	1332	1.58
	h. Patient prescribed beta-blocker and verapamil/diltiazem	Of all people prescribed a beta-blocker	2889	0.72
2. Bleeding	c. Patient prescribed aspirin and another antiplatelet without gastroprotection	Of all people prescribed aspirin	6167	2.25
	d. Patient prescribed oral anticoagulant and antiplatelet	Of all people prescribed an oral anticoagulant	6334	6.51
	i. Patient ≥75 years prescribed an NSAID without gastroprotection	Of all people ≥ 75 years	5421	1.28
	k. Patient prescribed antiplatelet and NSAID	Of all people prescribed an antiplatelet	18992	5.22
	l. Patient prescribed oral anticoagulant and NSAID	Of all people prescribed an anticoagulant	1559	1.60
	m. Patient prescribed oral corticosteroids and NSAID	Of all people prescribed an oral corticosteroid	9577	8.62
3. Bone Marrow Suppression	a. Patient prescribed methotrexate without folic acid	Of all people prescribed methotrexate	2689	11.14
	b. Patient prescribed two different strengths of methotrexate tablets	Of all people prescribed methotrexate	266	1.10
	c. Patient prescribed methotrexate with long-term trimethoprim	Of all people prescribed methotrexate	12	0.05
4 – Acute Kidney Injury	a. Patient prescribed ACEI/ARB **and** diuretic **and** NSAID	Of all people prescribed an ACEI **or** an ARB **and** a diuretic	11499	5.97

Composite Indicator	Measure	Denominator	2017 Q1	% of Denominator
	b. Patient ≥65 years prescribed metformin **and** ACEI/ARB **and** NSAID	Of all people prescribed metformin **and** an ACEI/ARB	2417	4.67
5 - Hyperkalaemia	b. Patient prescribed ACEI or ARB **and** potassium supplement	Of all people prescribed an ACEI **or** an ARB	709	0.12
	c. Patient prescribed ACEI **and** ARB	Of all people prescribed an ACEI **or** an ARB	4764	0.81
	d. Patient prescribed all of: (ACEI or ARB) **and** (spironolactone or eplerenone) **and** (aliskiren or potassium supplement)	Of all people prescribed an ACEI **or** an ARB	78	0.01
	e. Patient prescribed all of: (ACEI or ARA) **and** (triamterene or amiloride) **and** (aliskiren or potassium supplement)	Of all people prescribed an ACEI **or** an ARA	9	0.00
10 – Hypoglycaemia	a. Patient prescribed insulin without glucose test strips	Of all people prescribed insulin	7410	12.69
14 – Falls, Fractures and Delirium	b. Patient ≥65 years prescribed THREE or more drugs with sedating or anticholinergic effects (excluding antiepileptics)	Of all people ≥ 65 years	25802	2.85
	d. Patient prescribed steroid long term without co-prescription of a bone protecting agent	Of all people prescribed a steroid long term	16092	54.90
15 – Opioids and gabapentinoid dependency	a. Patient prescribed opioid at dose equivalent to >180 mg morphine per day over last 6 months	Of all people prescribed an opioid	6016	1.11
	b. Patient prescribed gabapentin at dose of >4800 mg per day over last 6 months (or equivalent dose of pregabalin)	Of all people prescribed a gabapentanoid	964	0.65
16 – Seizures and neurotoxicity	a. Patient on lithium prescribed an NSAID	Of all people prescribed lithium	262	4.17
	b. Patient on lithium recently prescribed a thiazide	Of all people prescribed lithium	6	0.10
17 - Extrapyramidal symptoms	a. Patient prescribed levodopa and metoclopramide long term	Of all people prescribed levodopa	16	0.17
	b. Patient ≥65 years prescribed metoclopramide long term[A]	Of all people ≥ 65 years	3802	0.42
	b.(alt) ≥65 years prescribed metoclopramide long term[B]	Of all people ≥ 65 years	2532	0.28

Notes:

A - Long term metoclopramide defined as ≥ 2 dispensings in the 6 month period

B - Long term metoclopramide defined as ≥ 1 dispensings in the most recent 3 month period and ≥ 1 dispensing's in the 3 month period immediately preceding this.

The remaining 42 *Case Finding* indicators utilise diagnosis, examination signs and laboratory data and so cannot be straightforwardly used to identify prevalence figures. They have been grouped as *Composite* indicators to help linkage with other clinical diagnosis data sets such as hospital admission data:

1. Cardiac decompensation and/or bradycardia
2. Bleeding
3. Bone Marrow Suppression
4. Acute Kidney Injury
5. Hyperkalaemia
6. Hypokalaemia
7. Hyponatraemia
8. Hypercalcaemia
9. Hypocalcaemia
10. Hypoglycaemia and Lactic Acidosis
11. Hypotension
12. Stroke / Vascular Events

13. Respiratory Exacerbation
14. Falls, fractures and delirium
15. Opioid and gabapentinoid dependency
16. Seizures and neurotoxicity
17. Extrapyramidal Symptoms
18. Gynaecological Cancer

All 69 *Case Finding* indicators have been developed within the Scottish Therapeutics Utility (STU) and will enable practices to run searches to identify patients for review. A full list of the case finding indicators can be accessed online.

Indicator selection through a consensus process

The consensus process to define the case finding criteria was conducted in 5 steps:

1. A list of candidate indicators was compiled based on previously published indicator sets
2. In the first round, panel members rated each candidate indicator on a 5 point scale (1=strongly disagree, 2=disagree, 3=neither agree nor disagree, 4=agree, 5=strongly agree) reflecting their level of agreement with the statement *'It is necessary that a patient triggering on the respective indicator receives a medication review as soon as possible and it would be inappropriate to wait until the next routine medication review'*
3. Panel members met in person for a discussion of first round ratings, informed by a presentation of current evidence and guidance, subsequent to which all candidate indicators were rerated
4. Candidate indicators, for which there was disagreement in the second rating round (defined as >30% of panellists agreeing or strongly agreeing and >30% of panellists disagreeing or strongly disagreeing with the statement) were rerated
5. Indicators that achieved a median rating of 4 or higher without disagreement after three rating rounds were accepted as case finding criteria

Appendix F: Monitoring the effect of Polypharmacy medication reviews

1. Outcome measures

The ultimate aims of polypharmacy medication reviews are to reduce drug-related harm and to achieve therapeutic objectives in line with patients' preferences, rather than simply reducing the numbers of medicines patients are taking. However, establishing whether clinical outcomes are attributable to drug therapy or other underlying causes is not realistically possible at scale, and monitoring of the effect of polypharmacy medication reviews therefore requires the use of proxy outcome measures that can be implemented in routine data sources available at national level. These measures fall into two categories: drug utilisation and hospital admissions.

1.1 *Clinical Outcome* - drug utilisation measures

It is recommended that the high-risk medication *Case Finding* indicators listed in Appendix E of this guideline are used as a basis to monitor the effect of polypharmacy medication reviews. Given the large number of indicators, it is impractical to consider each indicator separately. The following strategies can be used to reduce the number of drug utilisation measures used:

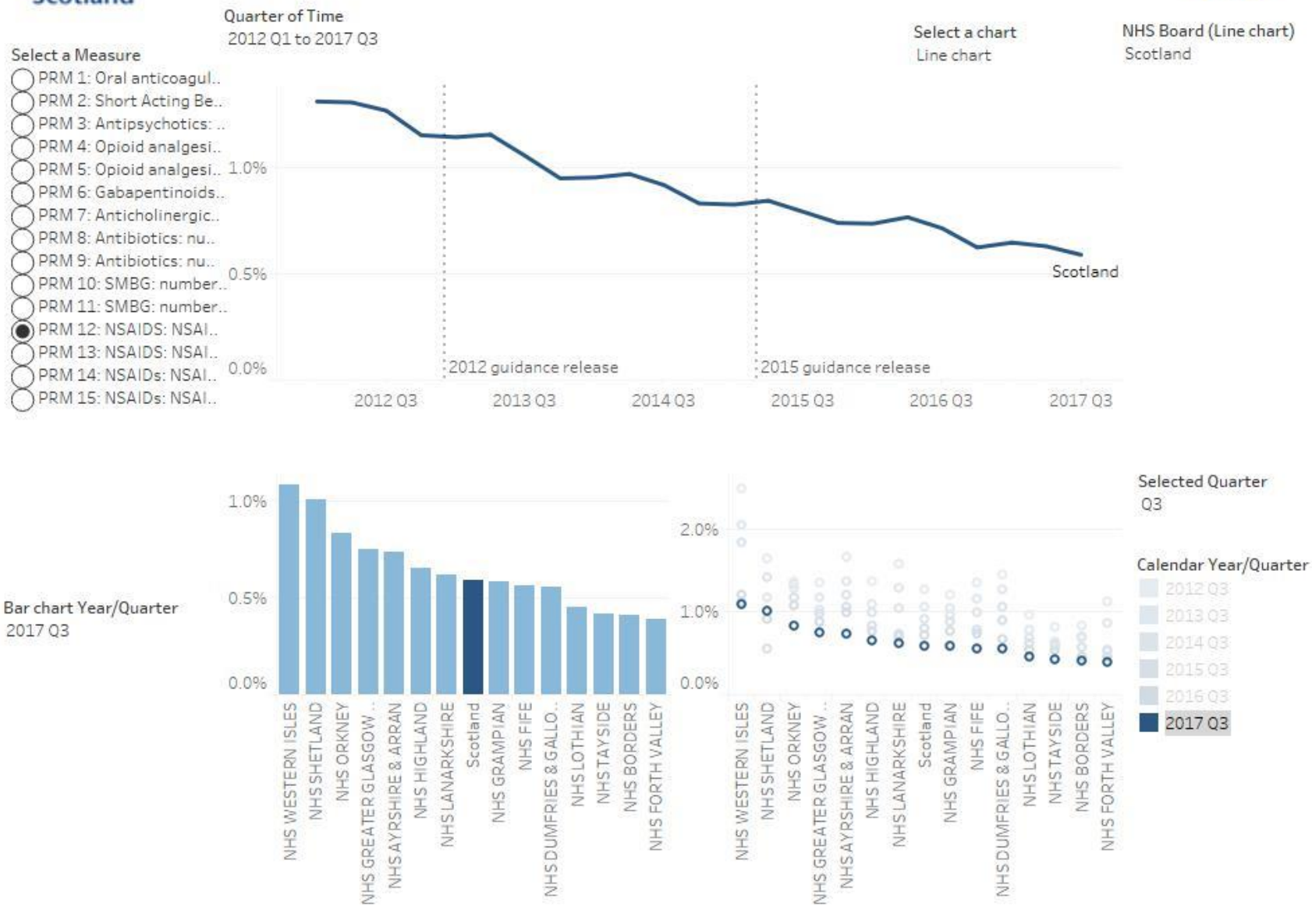
- Measure the average number of high-risk medication *Case Finding* indicators triggered per person in the target population (as defined in Section 1 of this guideline, with further detail in Appendix E)
- Measure the proportion of patients triggering on any high-risk *Case Finding* medication indicator (overall composite)
- Measure the proportion of patients triggering on any high-risk *Case Finding* medication indicator targeting the same adverse event (event specific composites)

17 of the drug utilisation measures that can be used for both *Case Finding* and *Clinical Outcomes* are established indicators. In Scotland the National Therapeutic Indicators provide prescribing measures, which are closely related to the high-risk medication *Case Finding* indicators, and may be used to monitor *Clinical Outcomes.* A clear advantage of taking this approach is that they are mostly already built into the GP clinical systems, prescribing support tools and national dashboards.

The Information Services Division (ISD) prescribing team have produced standard reports on these indicators, which are available to authorised Prescribing Information System (PIS) users and will enable them to run summary and comparator reports. For further details please go to: http://www.isdscotland.org/Health-Topics/Prescribing-and-Medicines/Community-Dispensing/Polypharmacy/ or contact nss.isdprescribing@nhs.net

An example of the dashboard which will be available to authorised PIS users is shown on the next page. The example show the number of patients ≥ 65 years prescribed a NSAID, ACEI/ARB and a diuretic. The dashboard show time series data showing the changes between Q3 of 2012 and Q3 of 2017.

PRM 12: NSAIDS: NSAID prescribing to patients aged ≥65 years prescribed an ACE inhibitor/angiotensin receptor blocker and a diuretic as a percentage of all people aged ≥65 years



Polypharmacy Related Additional Prescribing Measures 2018-19		Desired change in indicator / measure
Cardiovascular	**Oral anticoagulant:** number of patients prescribed an antiplatelet also prescribed an oral anticoagulant but without gastroprotection as percentage of all patients prescribed an oral anticoagulant	↓
Respiratory	**Short Acting Beta-Agonist (SABA) Inhalers:** number of patients prescribed more than 12 SABA inhalers in a year as a percentage of all patients prescribed SABAs	↓
CNS - psychotropic	**Antipsychotics:** antipsychotic prescribing to patients aged ≥75 years as a percentage of all people aged ≥75 years	↓
CNS - analgesic	**Opioid analgesics:** number of patients prescribed average daily dose of opioid equivalent to ≥ 120 mg per day of morphine as a % of all patients prescribed step 2 and strong opioids††	↓↑
	Opioid analgesics: number of patients prescribed strong opioids (including tramadol preparations) long term (>2 years) as a percentage of all patients prescribed strong opioids	↓
	Gabapentinoids: number of people prescribed more than the maximal recommended dose (>2 DDDs) per day of gabapentinoid as a percentage of all people prescribed a gabapentinoids (6 months)	↓↑
CNS - adverse effects	**Anticholinergics:** number of patients aged ≥75 dispensed >10 items of strong or very strong anticholinergics (mARS 3&2) in 12 months as a percentage of all people aged ≥75 years	↓
Antibiotics	**Antibiotics:** number of people > 4 antibiotics per annum per 1,000 LS	↓
	Antibiotics: number of adult women prescribed a 3-day course of acute UTI antibiotics as a percentage of all adult women prescribed acute UTI antibiotics	↑
Antidiabetics	**SMBG**: number of patients prescribed blood glucose test strips who are not prescribed treatments for diabetes (insulins and/or antidiabetic drugs) or are only prescribed metformin as a percentage of all patients prescribed blood glucose test strips	↓
	SMBG: number of patients prescribed insulin not prescribed blood glucose test strips as a percentage of patients prescribed insulin	↓
	Sulfonylureas: number of patients ≥75 years prescribed a sulfonylureas as a percentage of all patients prescribed an antidiabetic drug	↓
	Metformin: number of patients ≥65 years prescribed metformin **and** ACEI/ARB **and** NSAID as a percentage of all patients prescribed metformin and an ACEI/ARB	↓
Musculoskeletal	**NSAIDs:** NSAID prescribing to patients aged ≥65 years prescribed an ACE inhibitor/angiotensin receptor blocker and a diuretic as a percentage of all people aged ≥65 years	↓
	NSAIDs: NSAID prescribing to patients aged ≥65 years prescribed an antiplatelet without gastroprotection as a percentage of all people aged ≥65 years	↓
	NSAIDs: NSAID prescribing to patients aged ≥75 years without gastroprotection as a percentage of all people aged ≥75 years	↓
	NSAIDs: NSAID prescription to patients prescribed an oral anticoagulant without gastroprotection as a percentage of all patients prescribed an oral anticoagulant	↓

1.2 *Clinical Outcomes* - hospital admissions reduction measures

Hospitalisation data is routinely collected at national level in the Scottish (SMR01) record. Although the outcome of interest are hospital admissions that are explicitly drug-related (which is unfeasible to measure at national scale), for some types of hospital admissions, a drug-related aetiology may be sufficiently common to attribute the admission to that cause. Improvements in drug utilisation may be reflected in an overall reduction in these admissions among those targeted for polypharmacy medication reviews. Although the specific criteria used by different health boards to prioritise patients for review may differ, it is suggested that outcomes are measured among the subpopulation of patients aged 75 years older. Since the case finding criteria (nursing home residents, those on 10 or more drugs and those triggering high-risk medication indicators) are most commonly met in this subpopulation, and any effects of polypharmacy medication reviews are therefore likely to be most visible. The following *Clinical Outcome* hospital admission measures are recommended.

Proportion of patients 75 years or older with an emergency admission for:

- gastro-intestinal bleeding
- bleeding of any cause
- heart failure
- acute kidney injury
- falls and fractures
- stroke
- delirium
- clostridium difficile infection
- hypoglycaemia
- hyperglycaemia
- asthma
- COPD

Combining the measurement of specific types of hospital admissions with drug utilisation patterns may enhance the interpretation of any observed changes. For example, if a reduction in hospital admissions for gastro-intestinal bleeding was accompanied by a reduction in the prevalence of patients triggering high-risk medication use indicators targeting gastro-intestinal events, this would increase the confidence that the observed changes in clinical outcomes are attributable to improved medication use processes.

1.3 *Clinical Outcomes* - undesirable increase in specific hospital admissions- balancing measures

All plausibly beneficial health care interventions have the potential to have unintended consequences. Where such potential consequences can be identified, it is good practice to measure them to enable a balanced accounting of intervention effects. As part of polypharmacy medication reviews, patients and practitioners are encouraged to have informed discussions about omitting, discontinuing or de-intensifying prophylactic treatments (such as blood pressure lowering or antidiabetic treatment) that have doubtful benefits over the patient's likely remaining life span. The following balancing measures are therefore recommended to provide reassurance that reviews do not adversely impact on the incidence of cardiovascular events.

Among patients 75 years or older:

- the proportion of patients with an emergency hospital admission for myocardial infarction
- the proportion of patients with an emergency hospital admission for stroke
- the proportion of patients with an emergency hospital admission for diabetes/hyperglycaemia

1.4 *Clinical Outcomes* - reductions in all cause health care utilisation

In addition to reductions in specific hospital admissions it is possible that polypharmacy medication reviews also impact on unscheduled health care utilisation more generally. However, 'all cause health care utilisation' may be more commonly influenced by non-drug-related causes and it is therefore likely to be a measure that is less responsive to the impact of polypharmacy medication reviews than hospital admissions for commonly drug-related causes. Nevertheless, the following outcome measures may usefully supplement the outcome measures specified in sections 1.1 and 1.2:

Among patients 75 years or older:

- the proportion of patients with an emergency hospital admission of any cause
- the number of unscheduled occupied bed days
- the proportion of patients discharged into dependent care

Appendix G: SPARRA Data

What is SPARRA?[66]

Scottish Patients at Risk of Readmission and Admission is a risk prediction tool developed by ISD which predicts an individual's risk of being admitted to hospital as an emergency inpatient within the next year.

What is a SPARRA Score?

Scores are calculated for approximately 4.2 million patients. Information on those whose score indicates that they may be at increased risk of emergency admission are accessed by authorised health care professionals in NHS Boards, CHPs and GP practices. SPARRA scores can range from 1 to 99% for patients in the cohort. Patients with a score of 50%, for example, are generally said to have a 1 in 2 chance of being admitted to hospital in the prediction year.

What is the purpose of SPARRA?

There is growing recognition of the need to shift from a healthcare system geared towards reactive, hospital-based treatment of acute conditions to one that is more community based with a preventative and anticipatory approach.

SPARRA data can help health-care professionals to prioritise patients with complex care needs who are likely to benefit most from anticipatory health care. SPARRA data can also be used in a service planning capacity by locating groups of patients who would benefit from specific interventions or services.

Table 1a. SPARRA[A] patients aged 50 years and older, residing in a care home on 1st May 2017. These patients have any risk score (1%-99%).

The numbers in these groups by NHS Board are shown in Tables 1a and 1b. It should be noted that the two groups overlap, so many patients will be in both groups A and B. (Of the patients included in Table 1a as resident in a care home, **6854** aged 75 and over also appear in Table 1b and **7354** aged 65 and over also appear in Table 1b.)

	Age 50+
NHS Board	Number of People in a Care Home[D]
NHS Ayrshire & Arran	2,577
NHS Borders	551
NHS Dumfries & Galloway	979
NHS Fife	2,387
NHS Forth Valley	1,600
NHS Grampian	3,010
NHS Greater Glasgow & Clyde	6,779
NHS Highland	1,962
NHS Lanarkshire	3,283
NHS Lothian	4,153
NHS Orkney	84
NHS Shetland	71
NHS Tayside	2,869
NHS Western Isles	178
Total	**30,483**

Table 1b. Patients aged 75+ and 65+ in SPARRA[A] on 1st May 2017 with a risk score of 40-60% who were dispensed items from 10 or more BNF sections

	Age 75+					Age 65+				
NHS board	Number of patients dispensed drug items from 10 or more BNF sections	Number of patients with high risk medicines[C]	Number of patients in a care home[D]	Number of patients with high risk medicines and in a care home	Number of patients with dementia[E]	Number of patients dispensed drug items from 10 or more BNF sections	Number of patients dispensed high risk medicines[C]	Number of patients in a care home[D]	Number of patients with high risk medicines and in a care home	Number of patients with dementia[E]
NHS Ayrshire & Arran	3,894	3,808	647	629	556	4,999	4,883	689	670	599
NHS Borders	990	961	134	126	182	1,208	1,169	142	134	190
NHS Dumfries & Galloway	1,546	1,496	245	235	280	1,908	1,849	269	259	304
NHS Fife	2,928	2,828	579	549	641	3,642	3,525	617	587	686
NHS Forth Valley	2,155	2,092	320	312	371	2,738	2,660	344	334	408
NHS Grampian	3,249	3,144	531	514	537	4,052	3,914	572	553	576
NHS Greater Glasgow & Clyde	10,331	10,054	1,632	1,568	1,745	13,338	12,970	1,769	1,699	1,890
NHS Highland	2,480	2,400	403	385	455	3,092	2,990	432	413	491
NHS Lanarkshire	5,630	5,478	716	699	984	7,271	7,077	774	756	1,073
NHS Lothian	5,651	5,469	955	912	1,134	7,061	6,834	1,020	974	1,223
NHS Orkney	147	141	19	16	17	179	171	19	16	18
NHS Shetland	160	156	13	13	25	189	184	13	13	25
NHS Tayside	3,452	3,339	623	592	620	4,170	4,040	652	620	658
NHS Western Isles	269	264	37	37	44	343	334	42	42	49
Total	**42,882**	**41,630**	**6,854**	**6,587**	**7,591**	**54,190**	**52,600**	**7,354**	**7,070**	**8,190**

Notes:

A SPARRA (Scottish Patients At Risk of Re-admission or Admission) is a risk prediction model that estimates the risk of emergency admission to hospital in the next 12 months (1 May 2017 - 30 April 2018).

B The number of different BNF sections from which a patient's drugs were prescribed and dispensed. SPARRA Version 3 uses the most recent 12 months prescribing data available prior to the start of the risk year.

C Defined as medications in any of the following BNF Sections: 2.1, 2.2, 2.4, 2.5, 2.8, 2.9, 4.1, 4.2, 4.3 and 10.1.

D Identified by a CHI institution code of 93 or 98.

E Evidence of dementia has been determined either by prescribing history (dispensed items within BNF Section 4.11) or previous inpatient admission to hospital where diagnosis at discharge includes ICD-10 codes (F00-F03, F051); and ICD-9 codes (2900, 2901, 2902, 2904, 2908, 2909).

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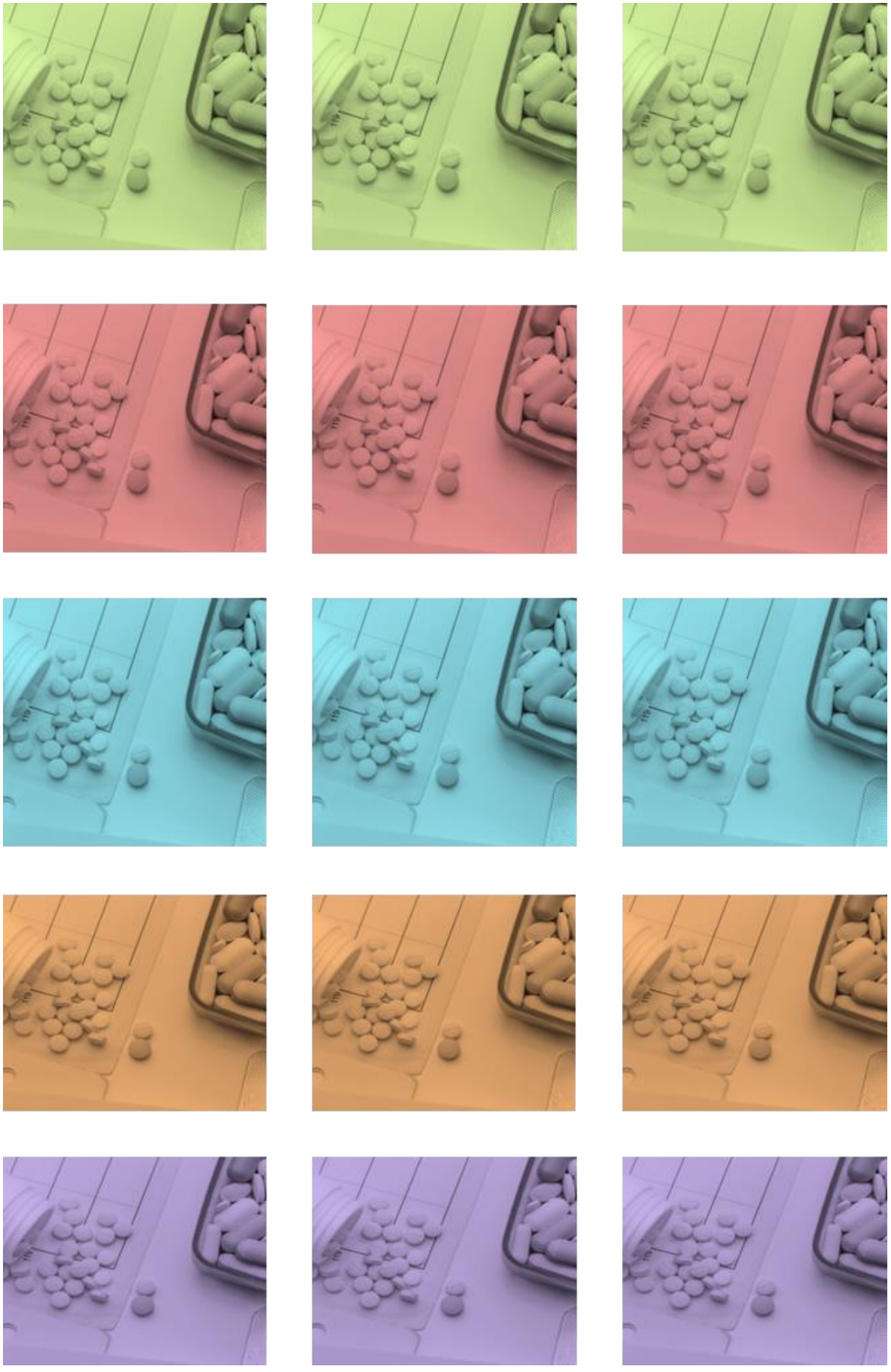
Glossary

ACE	Angiotensin Converting Enzyme
ACEI	Angiotensin Converting Enzyme Inhibitor(s)
ACS	Acute Coronary Syndrome
ADR	Adverse Drug Reaction
AF	Atrial Fibrillation
AKI	Acute Kidney Injury
ARB	Angiotensin II Receptor Antagonist
ASB	Asypmtomatic Bacteriuria
BMI	Body Mass Index
BNF	British National Formulary
BNP	Brain Natriuretic Peptide Test
BP	Blood Pressure
BPM	Beats per Minute
CI or C.I.	Confidence Interval
CCBs	Calcium Channel Blockers
CHA2DS2-VASc	Score for Atrial Fibrillation Stroke Risk
CHD	Coronary Heart Disease
CHF	Congestive Heart Failure
CHI	Community Health Index
CKD	Chronic Kidney Disease
CNS	Central Nervous System
COPD	Chronic Obstructive Pulmonary Disease
CVA	Cerebrovascular Accident
CVD	Cardiovascular Disease
DMARDs	Disease-modifying anti-rheumatic drugs
DM	Diabetes Mellitus
DMT2	Diabetes Mellitus Type 2
DN4	Douleur Neuropathique 4 (Questionnaire used in diagnosis of neuropathic pain)
DOACs	Direct Acting Oral Anticoagulants
ECG	Electrocardiogram
ECHO	Echocardiogram
EFIPPS	Protocol for the Effective Feedback to Improve Primary Care Prescribing Safety
eGFR	Estimated Glomerular Filtration Rate
FEV1	Forced Expiratory Volume-one second
g	Gram (unit of measurement)
GI	Gastro-intestinal
GTN	Glyceryl Trinitrate
HbA_{1C}	[Refers to] glycated haemoglobin
HDL	High-density lipoprotein
HF	Heart Failure
ICD-9	International Classification of Disease (Version 9)
ICD-10	International Classification of Disease (Version 10)
IHD	Ischaemic Heart Disease

INR	International Normalised Ratio
ISD	Information Services Division
L2	2nd Lumbar Vertebrae
LANSS	Leeds Assessment of Neuropathic Symptoms and Signs
LFTs	Liver Function Tests
LVEF	Left Ventricular Ejection Fraction
LVSD	Left Ventricular Systolic Dysfunction
MAOIs	Monoamine oxidase inhibitors
mg	Milligram (unit of measurement)
MI	Myocardial Infarction
MMSE	Mini-Mental State Examination
MRI	Magnetic Resonance Imaging
NICE	The National Institute for Health and Care Excellence
NNH	Number Needed to Harm
NNT	Number Needed to Treat
Non-STEMI	Non ST-elevation myocardial infarction
NSAID	Non-steroidal anti-inflammatory drugs
NYHA	New York Heart Association (Functional Classification)
PIS	Prescribing Information System
POA	Power of Attorney
PPIs	Proton Pump Inhibitors
QTc	Corrected QT Interval
SIGN	Scottish Intercollegiate Guidelines Network
SMBG	Self-Monitoring of Blood Glucose
SMR01	Scottish Morbidity Record (Covers General Acute Inpatient and Day Case)
SPARRA	Scottish Patients at Risk of Re-admission or admission
SSRI	Selective Serotonin Reuptake Inhibitors
STEMI	ST-elevation myocardial infarction
STU	Scottish Therapeutics Utility
TCA	Tricyclic Antidepressants
T Score	Bone Density Score
TFT	Thyroid Function Test
UTI	Urinary Tract Infection
U&E	Urea & Electrolyte Profile



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