The polypharmacy programme in Scotland: realistic prescribing

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Since 2012, NHS Scotland has published a series of polypharmacy guidelines to help clinicians address the many medication-related problems arising from multimorbidity. Here, Alpana Mair, Chair of the guideline group, Martin Wilson and Tobias Dreischulte explain how the third and latest edition of the polypharmacy guidance has been updated to place a greater emphasis on what matters to the patient.

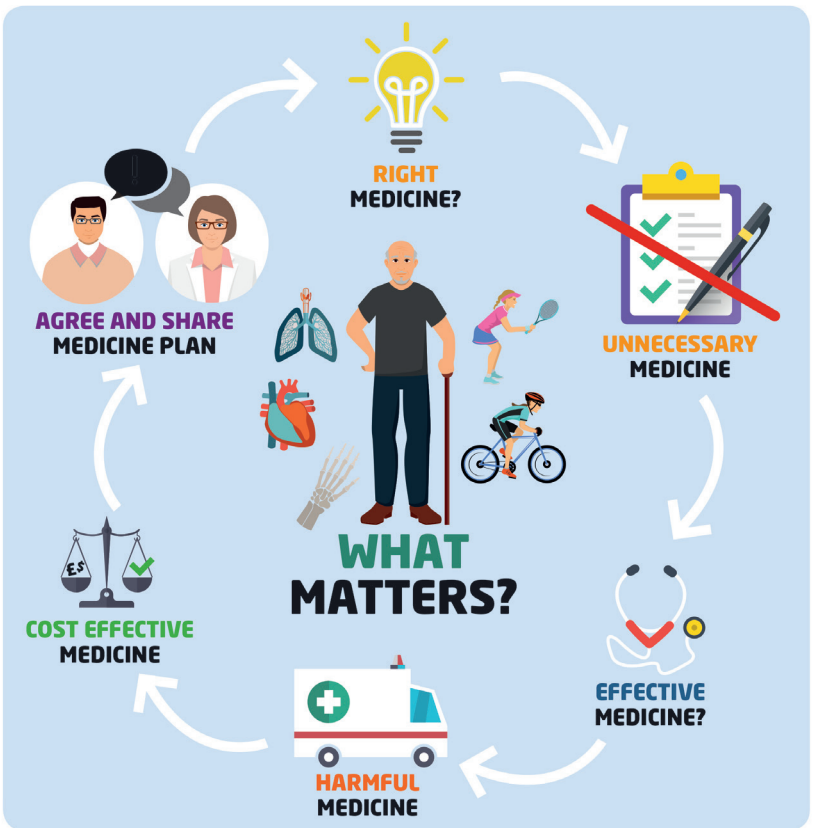


Figure 1. The 7-Steps to appropriate polypharmacy. From: Scottish Government Polypharmacy Model of Care Group. *Polypharmacy Guidance, Realistic Prescribing*, 3rd edn[5]

The care of patients with multimorbidity (multiple medical conditions) is a major challenge now faced by health services across the world. Medical research and guidelines to date, together with contractual agreements, have focused on single disease states, whereas in reality most patients with one long-term condition suffer from another, requiring multiple treatments.[1,2] In addition, higher proportions of adults with multiple morbidities live in the most deprived communities, which compounds the complexity.[1]

Medication plays a major role in the prevention and management of long-term conditions, and prescription of medicine is the single most common healthcare intervention in primary care, with medicines ranking third among the highest cost healthcare expenditure items.[3] As a consequence, patients with multiple conditions typically take multiple medicines (polypharmacy). Polypharmacy has now become the rule rather than the exception[4] and can be appropriate or inappropriate.[5,6] The key challenge for healthcare providers and patients is to optimise treatments in order to maximise benefit while minimising treatment burden and risk of medication-related harm.[3,4]

In the UK, it is estimated that up to 11% of unplanned hospital admissions are attributable to medication-related adverse events, of which 70% occur in elderly patients on multiple medicines, and of which 50% are deemed preventable.[7] If these figures were extrapolated across the EU, 8.6 million unplanned admissions each year would be attributable to medicines, of which half would be preventable.[8]

There are therefore significant opportunities to reduce this burden by timely and effective interventions, as highlighted by IMS Health and more recently the Royal Pharmaceutical Society (RPS) polypharmacy report.[9,10] The IMS Health report estimated that globally 0.4% of the total health expenditure, 18 billion US dollars, could be saved per annum if inappropriate polypharmacy were addressed.[9] In England in 2015, NICE also published guidance (NG5) on the safe and effective use of medicines for people in health and care settings to ensure that benefits from medicines were optimised while minimising harm.[11]

In an attempt to provide usable, patient-centred guidance on how to address the many medication-related problems that arise from multimorbidity, since 2012 NHS Scotland has developed a series of polypharmacy guidelines to aid clinicians.[5,12,13] This article aims to outline the key messages delivered by these guidelines and how these have evolved. The guidance has drawn on key tools such as Medication Appropriateness Index (MAI), STOPP/START and the Beers Criteria, and considers information from the UK and internationally with each revision.[14-16]

From the earliest stages, the development of the polypharmacy programme in Scotland has been an iterative piece of work and lessons have been learned (and continue to be learned) about how best to deliver quality care to adults with multiple conditions.[5] This is in terms of both the clinical guidance and also the targeting and delivery of the programme as a whole.

The third edition of *Polypharmacy Guidance, Realistic Prescribing*, published in 2018, aims to provide guidance on preventing inappropriate polypharmacy at every stage of the patient journey. It contains a clear structure for both the initiation of new treatments and the review of existing treatments, and has been updated to place a greater emphasis on "what matters to the patient?".[5]

Core clinical concepts in polypharmacy management

To aid clinicians and patients with decision making around medication, each edition of the guideline has outlined a '7-Steps' approach to medication review, which has been developed with patient groups, and doctors and pharmacists in primary and secondary care (see Figure 1

Patient details
58-year-old woman

Current medical history
- Diabetes type 2 (diagnosed 5 years ago)
- Coronary heart disease (non-STEMI, diagnosed 1 year ago)
- Hypertension
- Atrial fibrillation
- COPD
- Chronic back pain
- Depression (2 episodes)
- Hypothyroidism

Results
- HbA1c: 86mmol/mol (10%)
- BP: 150/85mmHg
- BMI: 35kg/m^2
- Spirometry shows mild obstruction
- No urinary protein detected
- eGFR: 55ml/min

Lifestyle
- Smoking: 10–15 cigarettes a day
- Alcohol: 20 units/week

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

Current function
Receptionist in local garage. Works six 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 one 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."

Box 1. Multimorbidity without frailty: case summary

Checks	Medication-related risks/problems identified
Step 1: What matters to the patient? • Review diagnoses and identify therapeutic objectives	• Patient reports: "I feel breathless whenever I have to rush or when climbing the stairs; do I really need to take so many pills?; my ankles are getting really swollen" • Consider lifestyle objectives – see step 7 • Therapeutic objectives: Secondary prevention of cardiovascular events (incl. stroke prevention in atrial fibrillation); rate control in atrial fibrillation; management of chronic kidney disease (CKD), COPD, diabetes and depression; pain control
Step 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: To treat type 2 diabetes
Step 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 *vs* paracetamol; is an NSAID required? • Antidepressant: Is the duration acceptable? • High-dose omeprazole: Active peptic ulcer or oesophagitis? Are symptoms of gastric origin? May require endoscopy or trial without NSAID
Step 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: CHA_2DS_2-VASc score 4, so consider replacing aspirin with anticoagulant; check rate control • COPD management: Symptom control (MRC breathlessness scale score); inhaler technique; formulary compliance • Pain control: Discuss symptom control and review expectations; if gabapentin prescribed for back pain then consider withdrawal; review NSAID therapy • Depression management: Discuss symptom control • Hypothyroidism management: Check thyroid function test results • CKD management: Check and monitor for proteinuria • Diabetic control: HbA_{1c} high despite three antidiabetic drugs; check adherence
Step 5: Safety • Identify patient safety risks • Identify adverse effects	• Actual adverse drug reaction: 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 + ACE inhibitor/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 + coronary heart disease – risk with diclofenac (ibuprofen or naproxen preferred); pioglitazone (risk of ankle swelling and ischaemic heart disease) • Risk of arrhythmia: QTc prolongation: omeprazole, citalopram and gabapentin
Step 6: Cost-effectiveness	Opportunities for cost minimisation: generic substitution; formulary compliance; switch from levothyroxine oral solution to tablets
Step 7: Patient centeredness • Are the outcomes of the review clear? • Are changes the patient's preferences? • Agree and communicate plan	Preferences and understanding: • Secondary prevention of cardiovascular disease: Prioritise discussion that the most effective intervention would be stopping smoking followed by anticoagulant for atrial fibrillation; 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, *eg* Alzheimer's Scotland helpline

Table 1. Applying the 7-Steps to the patient described in Box 1

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 is an issue
2. Potential to usefully detect and treat conditions (in this case atrial fibrillation)
3. Potential for high-risk drug combinations, particularly with multiple medications that may need to be stopped
4. Need for direct advice to patient on medication, *eg* 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, focus on medication and deprescribe where appropriate
7. Need for a multidisciplinary approach

Table 1. Applying the 7-Steps to the patient described in Box 1 (cont.)

and Table 1). Both patients and clinicians have access to this, together with shared decision aids.

Agreeing specific objectives with the patient in terms of both therapeutic objectives and current life priorities (step 1) sets the context within which all further decisions are made, namely on which medicines are essential (step 2) or unnecessary (step 3), whether therapeutic objectives that matter to the patient are achieved (step 4), which medicines are too risky or cause unacceptable adverse effects (step 5), which medicines are not cost effective (step 6), and whether the patient is willing and able to manage their medicines in a way that avoids harm and maximises benefit (step 7).

Core elements that aim to inform and support the review are:

- To highlight areas that are common sources of undertreatment
- To highlight areas that are common sources of medication-related harm (for instance drug-drug interactions or drug-disease interactions)
- The development of a medication effectiveness section, which allows clinicians and patients to gain a better understanding of the likely impact of a medication, including safety and need for the medication.

Reviewing the elements above may therefore result in reduction or stopping medication that is no longer needed, sometimes referred to as deprescribing.

In practice, clinicians will prioritise issues that they want to discuss with the patient and address these issues over a few consultations. Six examples to outline the guideline in practice, which have been based on clinical cases, are provided in the latest edition to support implementation of the 7-Steps. Clinical templates are being developed for GP IT systems that will allow the recording against the 7-Steps of coding to enable evaluation and improvement.

Medication effectiveness

One of the most innovative elements of all editions of the polypharmacy guideline since 2012 has been the development of a section providing numbers needed to treat (NNT) for a range of commonly prescribed medications, together with details of the trials. The NNT is the reciprocal of the absolute risk reduction[17,18] These numbers have been calculated using a set methodology that has been improved upon across the three editions of the guideline.

However, reliable date on number needed to harm (NNH) has been harder to produce in a robust way. Most of the evidence for harms in real-world populations comes from observational data, which is less robust than NNTs, which are produced from randomised trials. More research on actual harm is needed before NNH can be presented in as clear a way as the estimated benefits.

Although the NNTs provided allow a numerical comparison between treatments, it is important that they are not taken in isolation from other issues. For instance:

- *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 six months is more effective than the drug that 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 is the likelihood and severity of harm caused by the drug?* If a medicine saves the life of one patient in 25 but causes debilitating side-effects for the rest then its costs may outweigh its benefits.

Also highlighted in this section are issues around applicability of trial data to individual adults. The closer an individual is to the trial population in terms of characteristics and duration of treatment, the more likely they will achieve the expected benefits. The guidance provides data on the trials that the calculations are based on so that the reviewer can consider how their patient matches the trial population. 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.

Example cases

From the second edition of the guideline onwards, example cases were introduced. This followed feedback from teaching sessions supporting the roll out of the first edition of the guideline. These have been used to highlight common issues but also reinforce concepts. The example case summary in Box 1 and Table 1 highlights that medication-related issues are commonly present in younger adults, often co-existing with deprivation, as well as in more elderly groups.

The revised *Polypharmacy Guidance app* supports patients in shared decision making about their medicines (taking into account health literacy). The app is free and open access and can be found on:
Website:
http://www.polypharmacy.scot.nhs.uk
iOS/Apple App Store:
https://itunes.apple.com/gb/app/polypharmacy-guidance/id1072829127
Android Google Play:
https://play.google.com/store/apps/details?id=com.tactuum.quris.nes.polypharmacy

Box 2. Polypharmacy Guidance app

Educating and supporting medical professionals and patients
To support the polypharmacy programme, an app has been produced that is now in its second version. As a new development, this app now has patient-focused information as well as providing support for professionals (see Box 2).

Getting the guideline into practice: development and delivery

The EU-funded project Stimulating Innovation in the Management of Polypharmacy and Adherence in the Elderly (SIMPATHY) was a two-year study of polypharmacy and adherence management in Europe.[8] This work 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 the third edition of *Polypharmacy Guidance, Realistic Prescribing*. 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.[19,20] The aim is to reduce severe avoidable medication-related harm by 50% over a period of five years, globally. The polypharmacy guidance provides the opportunity to address all three elements of this challenge:
- Medication safety in polypharmacy
- The use of high-risk medicines
- Ensuring that information on appropriateness of medicines is shared across transitions of care.

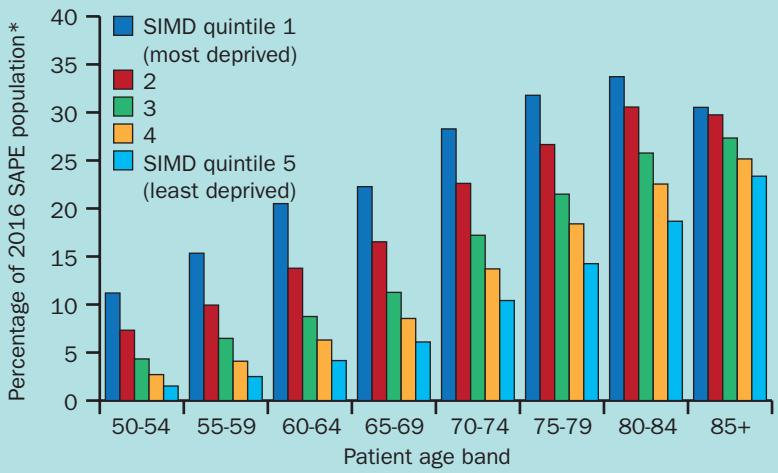
For example, the polypharmacy guidance suggests targeting patients on high-risk medications (a list of which can be found in the guideline) for polypharmacy reviews and ensuring that these reviews are undertaken at transitions of care.

From the outset, the NHS Scotland polypharmacy guideline was intended to support a systems-wide approach to the care of adults with multiple morbidities. Essential to this are the following five questions:

Who should deliver the intervention?
The combined knowledge and experience of physician, pharmacist, nurse and patient are required to ensure that the patient's 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. To be skilled in this complex intervention, training is needed. Pharmacists have played an important role in this and polypharmacy teaching is now included in undergraduate pharmacy courses in Scotland.

How should care be organised to meet the needs of patients with polypharmacy?
An important principle in improving the care of patients with multimorbidities 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.

How should healthcare professionals be encouraged and funded to embed the work in routine practice?
Initially, the work was supported both by a chief executive's letter to all health boards. This, combined with enhanced service payments and later inclusion



*Percentage dispensed 10+ *BNF* paragraphs plus high-risk drug by age group and 2016 Scottish Index of Multiple Deprivation (SIMD) quintile, Scotland Jan–July 2017
SAPE = small area population estimate

Figure 2. Incidence of polypharmacy by age and deprivation[5]

in Quality Outcome Framework (QOF) targets, helped to establish this work. Pharmacists have been funded since 2013 to work in general practice and support the delivery of appropriate polypharmacy management in Scotland.

Given limited health service resources, who should be targeted for review?

The first edition of the polypharmacy guideline focused on older adults who were also frail or adults with very limited life expectancy. However, both clinical experience and population-level data led to an extension of the focus of the programme to take into account the adverse health impact of deprivation. It was found that deprivation had an enormous impact on prescribing patterns (see Figure 2). This led to a clinical as well as strategic change of focus.

The earliest iterations of the guideline (and supporting education) had a focus on what medication to stop (due to risk of side-effects or lack of efficacy): this has been termed deprescribing. Although an important component of polypharmacy review, the focus needs to be wider than on just stopping medication. For example, an ACE inhibitor may need to be started for a patient with heart failure to improve prognosis and also help symptoms of breathlessness. Materials and example cases were therefore developed to help highlight how to support adults taking many essential medications and to identify unmet need for medication (see example case summary in Box 1 and Table 1).

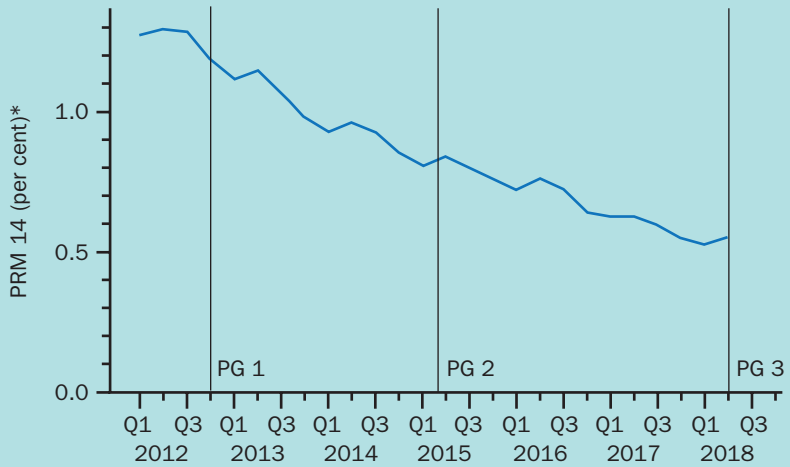
In order to prioritise the people for review, the following case-finding criteria were developed and are provided in the guidance:

A. People aged 50 years and older and resident in a care home, regardless of the number of medicines prescribed

B. Adults of any age approaching the end of their lives with increased frailty score

C. Patients prescribed 10 or more medicines (this will help identify those patients from deprived communities, where the average age of those taking 10 or more medications is lower)

D. Triggering indicators of high-risk medication and combinations regardless of the number of medicines and combinations taken (see appendix E of the guidance).



*PRM 14: NSAID prescribing to patients aged ≥65 years prescribed an ACE inhibitor/angiotensin II-receptor blocker and a diuretic as a percentage of all people aged ≥65 years
PG1, PG2, PG3 = First, second and third edition of *Polypharmacy Guidance, Realistic Prescribing*, respectively, published
PRM = polypharmacy-related measure

Figure 3. National data (Scotland) showing reductions in prescribing of high-risk drug combinations (here NSAIDs with ACE inhibitors/angiotensin II-receptor blockers and diuretics) since publication of the guidance in 2012. Developed as part of the polypharmacy guidance measures. Data source: ISD Scotland, NSS Discovery Database, NHS National Services Scotland by Colin Daly and Gavin MacColl

Examples of high-risk medication indicators (factor D above) are those associated with falls, fractures and delirium, which include: patients aged 65 years or older who are prescribed THREE or more drugs with sedating or anticholinergic effects (excluding antiepileptics); and patients prescribed long-term steroids without co-prescription of a bone-protecting agent.

What outcome measures should be used to determine if the work has been successful?

A health economic analysis of the expected impact of the guidance has been included in all the editions of the polypharmacy guideline. Health economic evaluation has demonstrated that the reviews focused around ensuring appropriate polypharmacy result in one to two medicines stopped per patient. Across Scotland, this has resulted in over 120,000 inappropriate medications being stopped per annum. Using this work, together with work undertaken as part of the EU, SIMPATHY developed an economic tool that can be used by healthcare organisations or countries to build their own economic case.[21] This can be found at http://www.simpathy.eu/resources/change-management.

Seventeen outcome measures have been developed, including monitoring the prevalence of specifically targeted high-risk prescribing. One example would be the use of one or more drugs with high anticholinergic burden. Work in development includes looking at changes in the incidence of admissions that can relate to over- or under-treatment with medication. The targets are focused on improving quality of prescribing appropriateness and safety. Figure 3 is an example of an indicator showing the reduction in the prescribing of a combination of drugs that have been implicated in gastrointestinal bleed and acute kidney injury.

Future steps

The next planned changes to the guidance will be to develop the capability of

patients to hold their own medication lists and also to collect patient-reported outcome measures from the reviews. Work is ongoing to embed the 7-Steps of the polypharmacy guidance into the GP IT prescribing systems, making it easier to deliver the reviews consistently, and also to develop a clinical decision aid tool for the 7-Steps.

Conclusion

The case for effective polypharmacy management is quite clear, but in a complex healthcare setting with many competing priorities, a core feature of its successful roll out in Scotland has been the inclusion of quality and economic reasons why it should be prioritised in each edition of the polypharmacy guideline. Going forward, continuing to demonstrate improvements in these areas will be key.

A holistic polypharmacy patient review has the potential to address all six dimensions of quality: efficacy, safety, efficiency, timeliness, equity and acceptability. Over time, greater emphasis has been placed on shared decision making to actively engage the patient with the 7-Steps medication review.

Although starting with a focus on the frailest older adults, the programme has extended to take into account issues such as deprivation as well as practical issues around taking many medications at any age. A main aim of a holistic polypharmacy review is to optimise patient outcomes from medicines and reduce avoidable harm.

Central to this guidance is the patient, and empowering them to take part in shared decision making about their medications. The consultation should start with "what matters to you?" and clinical decision tools have been developed for patients so that they can take an active role in the review. The final step of the review also ensures that the patient is happy with the changes and is prepared to adhere to the outcomes of the review. We have started to work with patient groups nationally and internationally to get feedback to ensure that this, together with clinical, economic and policy feedback, informs future development of the guidance.

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Declaration of interests

None to declare.

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