Polypharmacy – appropriate, problematic or both?

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In the second article of our polypharmacy series the authors explore the difference between appropriate and problematic polypharmacy, and illustrate how in some circumstances these two states can co-exist.

The first article in this series introduced The King’s Fund Report on Polypharmacy and Medicines Optimisation. This report defined polypharmacy and outlined some of what is known of the epidemiology of multimorbidity and associated polypharmacy in the UK. The need for a clearer definition of polypharmacy was a key aim of the King’s Fund report and, following considerable deliberation, including input from a seminar attended by clinicians, policy makers and academics, a definition was published (see Table 1).

When is polypharmacy appropriate?
Prescribing is normally done with the best intention of improving outcome for patients, and of course there is a substantial evidence base for many drug interventions. One might thus expect that employing several appropriate treatments would be of even greater benefit. Yet the evidence base for multiple interventions for several conditions in an individual patient is generally rather poor, and most clinical trials and practice guidelines do not consider polypharmacy in the context of multimorbidity. In reality a single-disease framework prevails in most healthcare systems, medical research and medical education, rather than one centred on the needs of complex patients and the old and the frail. Despite this, the

Table 1. The definition of polypharmacy used in the King’s Fund report

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<th>Appropriate polypharmacy</th>
<th>Problematic polypharmacy</th>
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<td>is prescribing for an individual for complex conditions or for multiple conditions in circumstances where medicines use has been optimised and the medicines are prescribed according to best evidence. The overall intent for the combination of medicines prescribed should be to maintain good quality of life, improve longevity and minimise harm from drugs.</td>
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<td>is where multiple medications are prescribed inappropriately, or where the intended benefit of the medication is not realised. The reasons why prescribing may be problematic may be that the treatments are not evidence based, or the risk of harm from treatments is likely to outweigh benefit, or where one or more of the following apply:</td>
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<td>• The drug combination is hazardous because of interactions</td>
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<td>• The overall demands of medicine-taking, or ‘pill burden’, are unacceptable to the patient</td>
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<td>• These demands make it difficult to achieve clinically useful medication adherence (reducing the ‘pill burden’ to the most essential medicines is likely to be more beneficial)</td>
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<td>• Medicines are being prescribed to treat the side-effects of other medicines where alternative solutions are available to reduce the number of medicines prescribed.</td>
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hope is that for many people appropriate polypharmacy will extend life expectancy and improve their quality of life. However, where there is no evidence of benefit for a particular drug regimen, polypharmacy should be avoided whenever possible.

Caution is needed, however, as under-prescribing in older people has also gained recognition as a concern. In some cases, recommended drugs are not prescribed by doctors because of fears of causing polypharmacy-related problems in the patient. A good example of this is in treating hypertension in older people where, for many, the benefits in reducing stroke or all-cause death outweigh the adverse effects of treatment. One way to assess benefit (and harm) is to pay regard to information derived from evidence-based medicine, which often uses absolute risk and benefit expressed in ‘numbers needed to treat’ (NNT) and ‘numbers needed to harm’ (NNH). To illustrate using the case of statins for primary prevention of cardiovascular disease the
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inflammation. Several resources are available to help guide this assessment; one example is prescribing guidance from NHS Scotland, which also provides useful information on drugs that are most associated with harm in frail, older people.

These estimates of benefit versus harm can also be shared with patients so that a joint decision can be made when optimising medication regimens. As well as maximising benefit and reducing harm, this may also reduce the risk of poor adherence, often seen when there is a significant ‘pill burden’ or complex drug regimen. It is also important to recognise that patient and health professional concerns may differ, and these views need to be determined. A good example is in atrial fibrillation, where the patient might dread the threat of stroke but the doctor might be concerned about anticoagulation-induced bleeding.

**How to identify problematic polypharmacy?**

On a day-to-day level things that might make the adverse consequences of polypharmacy apparent are when there is confusion over which drugs are being taken, or where waste of drugs becomes evident. A set of practical tips to improving prescribing in polypharmacy, and to make prescribing less problematic, is given in Table 2.

One of the questions we were asked in preparing The King’s Fund report was whether there are simple ways to identify those people most at risk from polypharmacy. This has been done in the past by looking at the number of medicines a patient receives; historically, the GP QOF required regular medication review to be undertaken for all people taking four or more regular drugs. However, using the number of medicines prescribed may be too simple and any measure of polypharmacy should be interpreted according to the clinical context. It makes sense to consider potential problems from polypharmacy even in patients on small numbers of medicines.

In this respect, there is no ideal ‘one-size-fits-all’ definition that can be applied for identifying polypharmacy. In any case, as we indicated in the first article, using the ‘greater than four’ threshold is now so commonplace as to be too non-specific and would apply to the majority of patients over the age of 65 years, meaning the resulting medication reviews might be inadequate or unfocussed.

Of course, overly complicated methods of identifying problematic polypharmacy may be difficult to understand or implement. A more pragmatic approach to identifying individuals potentially subject to higher-risk polypharmacy was therefore suggested in The King’s Fund report, looking not only at numbers of regularly prescribed items but also clinical context and other evidence of inappropriate prescribing (see Table 3).

Using such a model would hopefully help identify those patients at greatest risk of problematic prescribing, meaning that limited medication review resources could be better targeted, and reviews could be conducted in a more timely, focussed and effective manner. Implementing such a model in practice will depend on adequate and reliable diagnostic coding, having the ability to interrogate prescribing records to determine medication use, and availability of suitable drug safety databases. This would enable automated assessments of clinical notes to be made.

Much of the required technology is already incorporated into the standard general practice clinical computer systems, but still relies in part on clinicians recording accurate clinical information such as diagnoses and contraindications.

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**Table 2. Practical tips to medicines optimisation: avoiding problematic polypharmacy**

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<td>• Never assume your patient is taking what you think they are taking. Regular review is essential. Brown bag reviews (ask the patient to bring all the medicines they are taking to the clinic) or reviews in the patient’s home can be illuminating.</td>
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<td>• Keep medication regimens as simple as possible – ideally with once or twice daily dosages. The number of pills or ‘pill burden’ should be kept to the minimum necessary to provide effective treatment.</td>
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<td>• Provide clear written instructions and a dosing schedule.</td>
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<td>• Ensure that the directions on each prescription item identify the problem it is intended to treat.</td>
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<td>• Be aware of the known pitfalls with specific drugs and recognised drug interactions. You should carefully consider and avoid hazardous prescribing wherever possible.</td>
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<td>• It is important to put systems in place to ensure consistent and appropriate biochemical monitoring takes place for high-risk medicines, e.g. lithium, DMARDs, warfarin.</td>
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<td>• Consider the use of compliance aids such as monitored dosage boxes or ‘pill organisers’ to improve medicine-taking but be aware that they can also have disadvantages.</td>
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<td>• Discuss complex repeat medication regimens with clinical pharmacy colleagues (both in the community and hospital setting). They can advise on safety, check for hazardous interactions, guide on formulations appropriate to the patient’s needs and help in checking patient understanding.</td>
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<td>• Try to ensure that quantities of medication are synchronised so that patients can order their repeat items at the same time and thus avoid potential missed doses and waste.</td>
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<td>• Avoid use of the term ‘as directed’ rather than specific dosage instructions on prescriptions.</td>
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<td>• Always ask your patient if they are using home remedies, such as herbal products or ‘over-the-counter’ products. Also, could the patient be using somebody else’s treatment?</td>
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<td>• Try to substitute rather than add to medication regimens.</td>
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<td>• Think of introducing drugs as a trial: do not forget to stop treatment that is unnecessary or ineffective.</td>
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NNT is low – 49 to prevent a cardiovascular event over five years, compared with relatively high NNHs – 198 to cause diagnosis of type two diabetes over five years and several thousand to cause muscle inflammation. Several resources are available to help guide this assessment; one example is prescribing guidance from NHS Scotland, which also provides useful information on drugs that are most associated with harm in frail, older people.
Case history: making problematic polypharmacy more appropriate

Grace is a 67-year-old woman with osteoporosis (she had a Colle’s fracture several years ago), a long history of dyspepsia, generalised osteoarthritis and hypertension. She also had a Clostridium difficile infection following antibiotic treatment for ‘acute bronchitis’ two months ago. She smokes 20 cigarettes per day and admits to drinking 0.5–1 bottle of wine on most days. She takes:

- alendronate 70mg once a week (to strengthen bones)
- calcium and vitamin D effervescent tablets, two tablets daily (to strengthen bones)
- omeprazole 20mg daily (for indigestion)
- ramipril 5mg daily (for high blood pressure)
- amlodipine 10mg daily (for high blood pressure)
- ventolin inhaler two puffs as required (for breathlessness)
- simvastatin 40mg at night (for elevated CV risk)
- ibuprofen 400mg, one to two tablets three times a day (for joint pains).

She says she dislikes her fizzy tablets but her main concern at present is swollen ankles. She admits to often forgetting her simvastatin as taking it at night is inconvenient. She takes gingko biloba bought from the herbalist to help with her mood.

As she is taking eight different regular medications and there are potential concerns about medication appropriateness, such as adherence and drug-drug interactions, medication review with a view to optimising therapy would be indicated. There are a number of things worth considering in order to improve the appropriateness of the polypharmacy:

- Smoking obviously aggravates her dyspepsia, may contribute to osteoporosis, and would be a likely cause of suspected COPD and recent ‘acute bronchitis’. Stopping smoking may reduce the need for inhalers and antibiotic courses. Has Grace considered smoking cessation, and has support to do this been offered?
- Alcohol use is excessive. It will contribute to osteoporosis and dyspepsia. Has this been raised with her and is she amenable to support in reducing or stopping consumption? As well as improving her overall health, this may reduce the need for drug treatment.
- Does she know what each treatment is for? Indicating, in layman terms, what the drugs are for on the prescription is good practice and helps with patient understanding, and possibly adherence.
- The ‘fizzy tablets’ are the vitamin D and calcium tablets. As she dislikes them, is she taking them regularly? Are they strictly necessary? If they are, could a more palatable preparation be found?
- Alendronate may aggravate dyspepsia. Is it strictly necessary? Has a DXA scan been performed? Could a ‘bisphosphonate holiday’ or stopping them be indicated – eg after five years of use?
- Should she be taking omeprazole with the recent history of C. difficile infection? This is known to make infection more likely and she is at risk of recurrence. However, stopping it with her high alcohol intake and ibuprofen use will almost certainly aggravate her dyspepsia, and may cause more serious gastric problems.
- The ‘history suggests COPD. Has a formal assessment been carried out: has she had spirometry?
- It is quite likely that amiodipine is the cause of swollen ankles. This is a side-effect not amenable to diuretics because it is due to increased capillary permeability. It is dose dependent, so could the dose of amiodipine be reduced to 5mg to see if this helps. If necessary the dose of ramipril could be subsequently increased to 10mg daily instead. Given her ACE inhibitor treatment, she may need her renal function checking, and certainly if the dose of ramipril is increased.
- Does she really need simvastatin? How keen is she on CV risk reduction? Have the NNT been discussed with her? If this is felt necessary taking it at the same time as her other tablets would be a better option, and more useful than not taking it. Taking it at night enhances its lipid-lowering effect by a small amount, as the effect on blocking cholesterol synthesis is higher when dietary intake is low. Alternatively using different statins (eg atorvastatin), which have longer half-lives and can thus be taken at any time without reduction in effect, could be considered.
- Is ibuprofen wise given its adverse gastric effects coupled with her excessive alcohol intake, plus the potential to aggravate her hypertension and increase CV risk? It can also make her more susceptible to acute kidney injury if taken alongside ramipril. Would paracetamol or a topical NSAID be a better compromise? If an oral NSAID is strictly necessary naproxen has fewer cardiovascular adverse effects, and ‘as required’ use may be adequate if regular paracetamol is also given.
- The herbal remedy gingko biloba may contribute to her dyspepsia and increase her risk of gastrointestinal bleeding. It can interact with various drugs. Preparations vary in their effects. It is worth exploring why she thinks it is necessary; ideally she should be dissuaded from using it.

Reaching concordance: You agree that she should tackle the smoking and alcohol issues with the local support services. You arrange spirometry. For the time being she will stop the alendronate and vitamin D with calcium and you request a further DXA scan. You decrease the amlodipine to 5mg daily and she continues with ramipril with arrangements for a blood pressure check in four weeks’ time. She continues with the omeprazole. As she rarely takes it, it makes sense to stop the simvastatin until the lifestyle issues have been tackled. She agrees to try paracetamol and to only use ibuprofen on the days her osteoarthritis is bad. She is dissuaded from taking gingko biloba and any other herbal remedies. She will still experience polypharmacy, but the medication burden is less than before and the regimen is more appropriate and safer.
However, information such as patient preference is harder to code. Where this approach is not considered possible, the ‘10 or more’ threshold is a reasonable starting point, with case finding employed subsequently.

Another approach may be to use cruder measures such as looking at those people of older age to further narrow the selection of patients. Many practices have clinical pharmacists attached to them who may be able to help with this work, and there is evidence that such input can reduce potentially harmful prescribing.7 The case example provided demonstrates how the appropriateness of polypharmacy might be improved in an older person with a number of chronic conditions.

### Conclusion

With rising levels of multi-morbidity, a rapidly ageing population and increasing numbers of treatments available that can potentially alleviate symptoms, prevent disease events and reduce mortality, polypharmacy seems an inevitable and growing consequence of modern medicine. The identification of those most at risk of harm, distinguishing problematic from appropriate polypharmacy, in order to effectively target medication optimisation systems, is a vital issue for clinicians, policy makers and researchers alike.

It is also important not to forget that polypharmacy can be both appropriate and problematic. Achieving a suitable balance, acceptable to the prescriber and the patient, is clinically challenging and requires an understanding of the patients’ views, and often needs compromise.

### References


### Declaration of interests

None to declare.

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