Polypharmacy and medicines optimisation

Making it safe and sound

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Acknowledgements

Foreword

Medical advances offer the hope of bringing benefits to patients but also have the potential to do harm if not used appropriately. Knowing when and how to treat patients is particularly important in the prescribing of drugs as populations age and multi-morbidity becomes more prevalent. The challenge for clinicians is keeping up to date with new drugs as they come on the market and being aware of the interaction between them in patients being treated for a number of medical conditions.

In an analysis of more than 300,000 patients, a Scottish study found that the mean number of drugs dispensed increased from 3.3 in 1995 to 4.4 in 2010. As the authors of this paper explain, this meant that the proportion of patients receiving 5 or more drugs increased from 12 to 22 per cent, and the proportion of patients receiving 10 or more drugs increased from 1.9 to 5.8 per cent. This matters because unless the drugs prescribed to patients are reviewed regularly by clinicians with up-to-date knowledge there is a risk that treatment may be ineffective at best and harmful at worst.

A desire to increase awareness of the importance of polypharmacy prompted The King's Fund to commission this paper with the aim of bringing together what is known about this topic and to identify the implications for policy and practice. The Fund's interest derives from work on the care of people with long-term conditions and how this can be improved. Our brief to the authors was to review the evidence on polypharmacy and particularly to highlight how to optimise the contribution that medicines make to enabling informed patient choice and delivering desired outcomes for patients.

The authors have responded to this brief by producing a paper that brings together data from a variety of sources to scope the issues involved and to outline some potential solutions. The paper makes clear that action is needed on several fronts, and must involve patients, doctors, nurses and pharmacists. Avoiding the risks of polypharmacy requires effective team working between clinicians, and in hospitals they argue that there is a role for a generalist clinician able to coordinate the care of patients with complex needs.

In general practice, consultations with patients with multi-morbidity need to be longer to allow sufficient time for the use of drugs to be reviewed. There is also a strong case for reviewing the way in which the quality and outcomes framework focuses on improving the treatment of single diseases rather than the needs of patients with a number of long-term conditions. Although polypharmacy is not exclusively an issue that affects older people, it is particularly important that medication reviews are undertaken regularly for this age group to support scaling back or indeed increasing treatment where appropriate.

It goes without saying that understanding the patient perspective on polypharmacy is essential, not least because patients may not be taking the drugs that clinicians think they are. The practical challenges for some patients of managing their use of multiple medications are well established, adding to the complexity of implementing appropriate prescribing. Although a variety of ways have been developed to help patients deal with this complexity, much more can be done to involve patients as partners in their care, with carers and families engaged where relevant.

In publishing this paper, the Fund hopes both to raise awareness of these issues and to offer practical guidance to clinicians and others in avoiding what the authors describe as 'problematic polypharmacy'. We are grateful to the authors for shining a light on an area of care that deserves more attention.

Chris Ham
Chief Executive, The King's Fund

Key points

Describing and defining polypharmacy

- Polypharmacy is an expression that has been commonly used for many years in medicine. It is generally understood as referring to the concurrent use of multiple medication items by one individual.

- The term has been used both positively and negatively. In the past polypharmacy has been considered something to be avoided. It is now accepted that in many circumstances polypharmacy can be therapeutically beneficial.

- In this report, we propose the terms 'appropriate polypharmacy' and 'problematic polypharmacy'. This recognises that polypharmacy has the potential to be beneficial for some patients, but also harmful if poorly managed.

- **Appropriate polypharmacy** is defined as prescribing for an individual for complex conditions or for multiple conditions in circumstances where medicines use has been optimised and where the medicines are prescribed according to best evidence.

- **Problematic polypharmacy** is defined as the prescribing of multiple medications inappropriately, or where the intended benefit of the medication is not realised.

- Polypharmacy may be harmful in that it can increase the risk of drug interactions and adverse drug reactions, together with impairing medication adherence and quality of life for patients.

- On the other hand, employing many appropriate treatments can theoretically improve outcomes for patients, especially given that there is an increasing evidence base for many drug interventions. However, the evidence base for multiple interventions for several conditions in an individual patient is poor.

- Polypharmacy is widespread and increasingly common, occurring in primary and secondary care, and in care homes for older people. It has become a global issue, particularly, although not exclusively, in Western countries.

- It is driven by the growth of an ageing (and increasingly frail) population and by the increasing prevalence of multi-morbidity (where patients may be living with several long-term conditions, often compounded by disability and/or frailty).

Evidence-based treatment and guidelines

- For many people, appropriate polypharmacy will extend life expectancy and improve their quality of life. Where there is no evidence of benefit from the drugs being prescribed, polypharmacy should be avoided.

- The evidence for choosing treatment where there is polypharmacy should ideally be clearly stated. Prescribers should record the rationale for non-evidence-based prescriptions, for example, through patient choice.

- Many clinical trials and practice guidelines do not consider polypharmacy in the context of multi-morbidity. A single-disease framework prevails in most health care systems, medical research and medical education.

- It is important that pragmatic clinical trials are conducted that include patients with multi-morbidity and polypharmacy.

- Guidelines should be developed that take account of long-term conditions that commonly co-exist, such as diabetes, coronary heart disease, heart failure and chronic obstructive pulmonary disease.

- A pragmatic approach to identifying higher-risk polypharmacy in practice is to focus on patients at particularly high risk: for example, those receiving 10 or more regular medicines, or those receiving 4 to 9 regular medicines together with other unfavourable factors (examples include: a contraindicated drug; where there is potential for drug–drug interaction; or where medicine taking has proved a problem in the past).

Implications of polypharmacy on clinical services and policy

- Multi-morbidity and polypharmacy increase clinical workload. Doctors, nurses and pharmacists need to work coherently as a team, with a carefully balanced clinical skill-mix.

- There should be more training in managing complex multi-morbidity, polypharmacy and other aspects of medicines management. This could include general practitioners (GPs), clinicians who specialise in care of older people, orthogeriatricians, clinical pharmacologists, nurse specialists and clinical pharmacists.

- Rather than attending several disease-specific clinics, patients could have all their long-term conditions reviewed in one visit by a clinical team responsible for co-ordinating their care. Patients with multi-morbidity admitted to hospital under one specialty may require access to a generalist clinician to co-ordinate their overall care.

- There is a need to develop systems that optimise medicines use where there is polypharmacy so that people gain maximum benefit from their medication with the least harm and waste. This may include training programmes, improved electronic decision support for clinicians and/or patients, patient-friendly information systems, judicious use of monitored dose systems and clinical audit.

Implications for clinical practice

- Prescribers may not recognise that symptoms could be iatrogenic and unwittingly prescribe new medication to counter the adverse effects of other drugs. This is known as incremental prescribing or the 'prescribing cascade' and should be avoided.

- Prescribers should consider whether interactions between drugs where medication is combined will undermine therapeutic benefit.

- Many people stay on medicines beyond the point where they are deriving optimal benefit from an intervention. When reviewing medications, health care professionals should consider if treatment can be stopped and recognise that 'end-of-life' considerations apply to many chronic diseases as well as cancer-related conditions.

■ People often do not take medicines in the way that prescribers intend and there is considerable evidence that many dispensed medicines remain unused or are wasted. These problems increase as drug regimens become more complex.

■ The patient perspective on medicine-taking needs to be determined. Compromise may be needed between the view of the prescriber and the patient's informed choice.

We dislike polypharmacy as much as it is possible, and we would never exhibit a remedy of any kind unless we had a scientific reason for so doing and unless we were prepared to defend our method of treatment.

W Newnham, Provincial Medical and Surgical Journal, 1848

Introduction

What is polypharmacy?

In simple terms polypharmacy is the prescribing of multiple items to one individual. Usually this relates to medication use, but in the United Kingdom NHS prescriptions are also used for dressings, appliances and sometimes blood-testing equipment or nutritional preparations. This report concentrates on the prescribing of medication. There has been no consensus on whether polypharmacy applies only to simultaneous prescribing of several drugs at a time, or if it applies to short-term as well as long-term medication. Often the term polypharmacy implies criticism of the way several medicines have been prescribed but sometimes it is necessary for patients to be taking large numbers of medicines. This report proposes a classification based on prescribing multiple medications where the treatment may be *either* appropriate *or* problematic.

Appropriate polypharmacy 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.

Problematic polypharmacy 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:

- the drug combination is hazardous because of interactions

- the overall demands of medicine-taking, or 'pill burden', are unacceptable to the patient

- 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)

- medicines are being prescribed to treat the side effects of other medicines where alternative solutions are available to reduce the number of medicines prescribed.

Measures of polypharmacy are often used to assist assessment of higher risk and to guide audits. For example, some studies have looked at the concurrent prescribing of five or more medicines as a threshold to identify people selected for medication review. Given the growth in prescribing, such a threshold may now be too low.

Patient involvement in decisions on drug use is fundamental in prescribing and particularly in polypharmacy. Patients may not want to take multiple medicines, or prefer one treatment over another. Advice should be given on which interventions may be most likely to minimise side effects, reduce symptoms and improve outcomes. Regimens may

need to be tailored to fit with patient preferences and 'compromise' may be required. Polypharmacy is likely to be futile if medicines are not taken as the prescriber intends.

Medicines optimisation, or robust medicines management, helps to ensure more appropriate polypharmacy so that the various trade-offs of harm, benefit and patient acceptability and choice have been considered and an explicit decision on the drug to use has been made with the patient.

Why polypharmacy is an important challenge

Polypharmacy is becoming increasingly common. In the past decade, the average number of items prescribed for each person per year in England has increased by 53.8 per cent, from 11.9 (in 2001) to 18.3 (in 2011) (NHS Information Centre 2012) (see Figure 1 below and 2, opposite). A large Scottish study has confirmed the considerable and increasing prevalence of polypharmacy: 12 per cent of patients were dispensed 5 or more drugs in 1995, rising to 22 per cent in 2010; and 1.9 per cent of patients were dispensed 10 or more drugs in 1995, rising to 5.8 per cent in 2010 (Figure 3, opposite).

Figure 1 Prescription items dispensed per head of population in UK countries, 2011/12
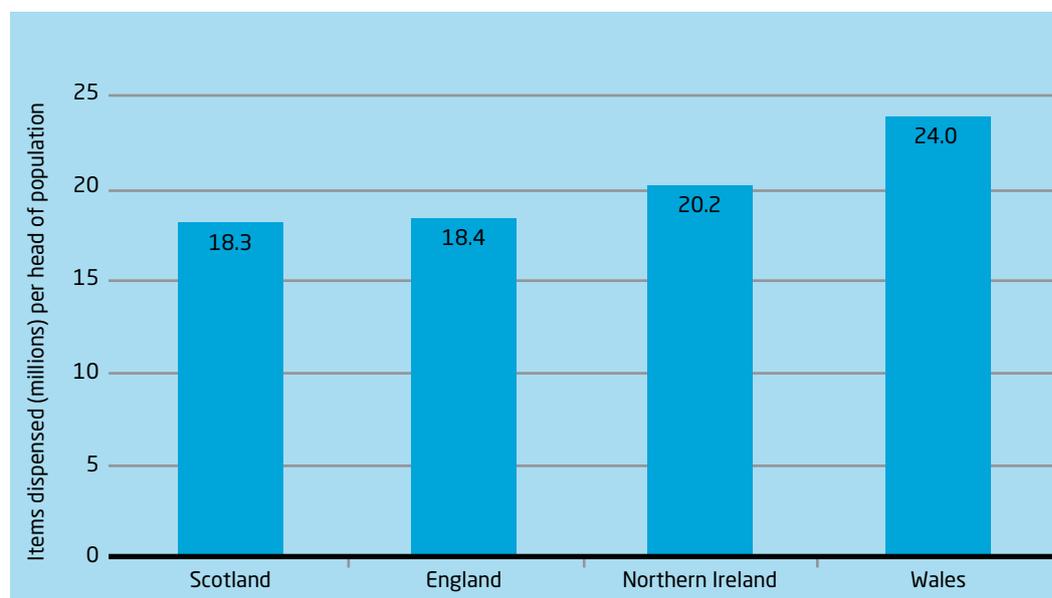
Note: These figures are based on dispensing in the community and do not include hospital-initiated prescriptions. These are not the numbers of specific drugs prescribed per patient; for example, if a patient receives the same drug each month on a repeat prescription this would count as 12 items.

Source: Statistics for Wales (2012)

There are several explanations for this rise. Asymptomatic people are increasingly treated with preventive interventions to reduce their future risk of mortality and disease. This is seen particularly with cardiovascular disease and medicines to reduce stroke and acute myocardial infarction events. Many 'well' people are being prescribed complicated preventive drug regimens, and as a result they are being put at risk of adverse events and harm from drug interaction. The population is also ageing and the prevalence of chronic disease increasing. Already, many patients have several co-morbidities. If each one of these is treated according to national guidelines, patients may end up taking a complicated cocktail of drugs.

Figure 2 Trends in prescription items dispensed, England, 2001 to 2011

Analgesics —
Antiepileptics ⋯
Corticosteroids (respiratory) —
Lipid-regulating drugs ⋯
Drugs used in diabetes —
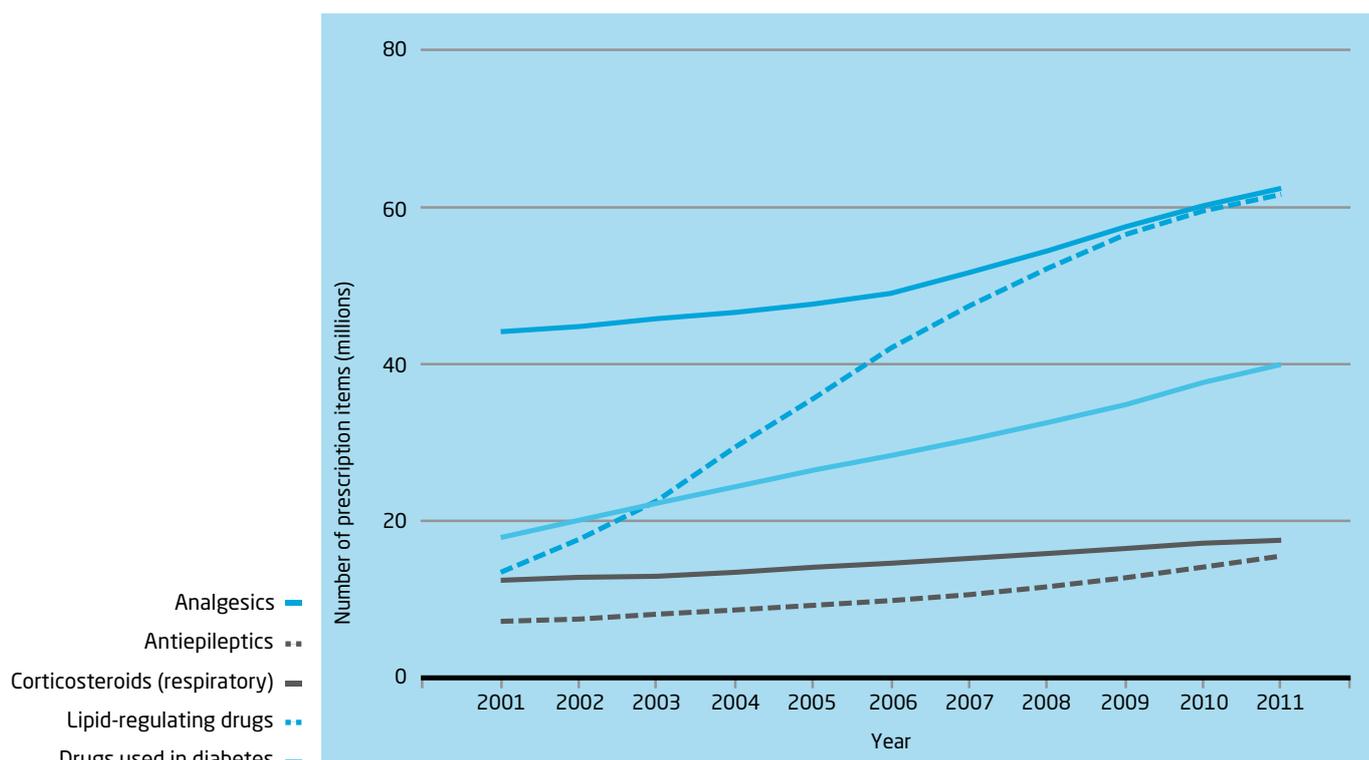
Note: This graph shows items dispensed for the five British National Formulary sections that had the greatest net ingredient cost in 2011.

Source: NHS Information Centre (2012) [1]

Figure 3 Multiple drug use, Scotland, 1995 and 2010

>= 1 drug ■
>= 5 drugs ■
>= 10 drugs ■
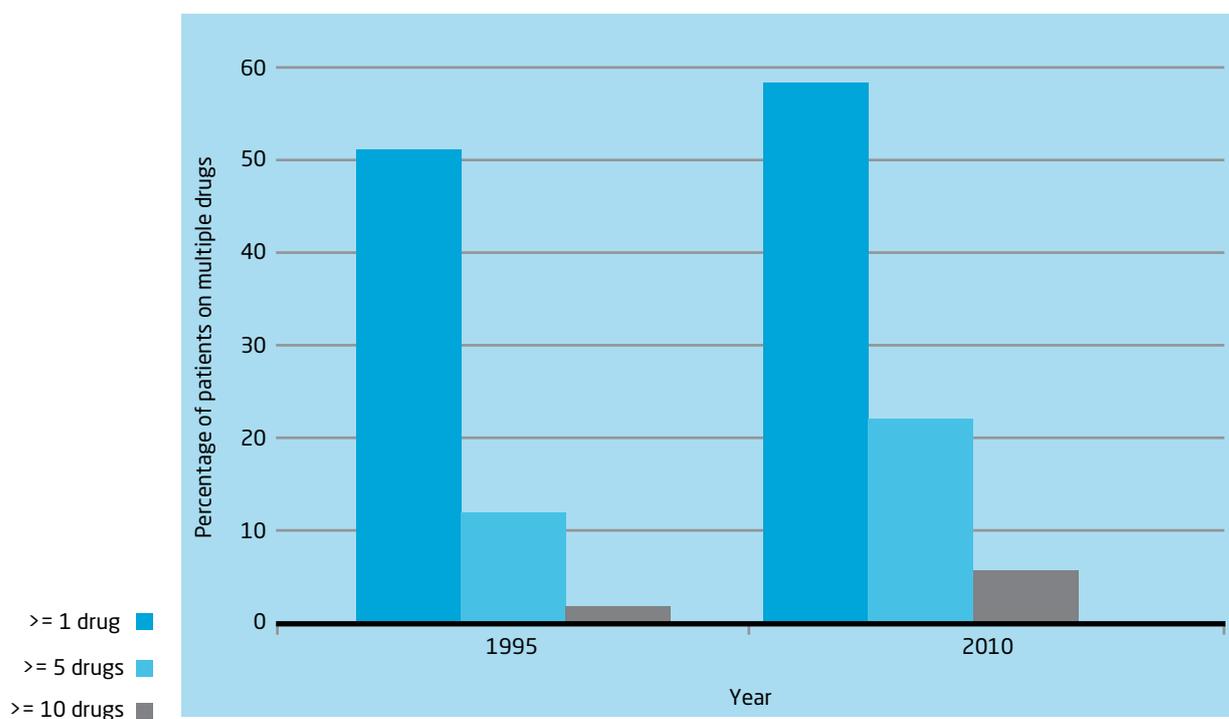
Source: Guthrie and Makubate (2012) [2]

Adverse reactions to medicines are implicated in up to 6.5 per cent of hospital admissions. Patients admitted with one drug side effect are more than twice as likely to be admitted with another (Pirmohamed *et al* 2004). Patients on multiple medications are more likely to suffer drug side effects; this is related more to the number of co-morbidities a patient has than to the patient's age (Pirmohamed *et al* 2004).

Patients are often prescribed (and may remain on) drugs that cause adverse effects and where the harm of the drug outweighs the benefit (Guthrie *et al* 2011). It is also recognised that people who once derived benefit from prescribed drugs may not continue to do so but their treatments are not always stopped once this point is reached. For example, polypharmacy may be a particular problem in people with multiple morbidities and limited life expectancy as they may gain little further benefit from treatments aimed at preventing future disease.

It is worth considering clinical guidelines in relation to multi-morbidity and co-morbidity. Multi-morbidity is generally considered to be the presence of more than one long-term condition; a co-morbidity is a long-term condition that exists in the presence of another long-term condition. Guidelines are often based on evidence from studies of patients with single conditions and guideline developers do not take into account patients with multi-morbidity (Guthrie *et al* 2012a; Hughes *et al* 2013) to whom general principles may not apply (Masoudi *et al* 2003; Travers 2007; Van Spall *et al* 2007; Saunders *et al* 2013). Such guidelines rarely modify or discuss the applicability of their recommendations for patients with multiple co-morbidities or for older patients; nor do they take account of patient preferences. They may also fail to comment on the quality of the evidence underpinning the guideline (Boyd *et al* 2005). Furthermore, guidelines often fail to acknowledge the potential problems of multiple medicines use. Use of clinical guidelines may therefore inadvertently promote problematic polypharmacy and increase the risk of adverse events such as drug–drug and drug–disease interactions. Falls and other complications such as urinary incontinence are well-recognised adverse effects in older or frail people that may not have been considered during guideline development.

For many patients polypharmacy might be entirely appropriate (Aronson 2004). There are many conditions in which the combined use of two, three or more drugs is beneficial and can improve outcomes especially in older people with multiple co-morbidities (for example, type 2 diabetes complicated by coronary heart disease and hypertension). However, it is important to consider whether each drug has been prescribed appropriately or inappropriately, both individually and in the context of all the drugs being prescribed (Aronson 2006). Optimising prescribing in polypharmacy involves encouraging the use of appropriate drugs, in a way that the patient is willing and able to comply with, to treat the right diseases. In certain circumstances, this may include the removal of unnecessary drugs, those that the patient feels unable to take or comply with, or those with no valid clinical indication, as well as the addition of useful ones.

Under-prescribing in older people has also gained recognition as a concern. Paradoxically in some cases, drugs that are recommended for some conditions are actually not prescribed by doctors because of fears of causing polypharmacy-related problems in the patient. There can be a reluctance to prescribe additional drugs to patients with polypharmacy due to a perceived complexity of drug regimens, fear of adverse drug reactions, and concerns about drug–drug interactions or poor adherence (Kuijpers *et al* 2007). It may be that those at highest risk for complications have the lowest probability of receiving recommended medications.

In summary, polypharmacy can refer to the prescribing of many drugs appropriately or too many drugs problematically. What constitutes 'too many' drugs is a prescribing dilemma, and choosing the best interventions aimed at ensuring appropriate polypharmacy is a challenge for all prescribers and health care organisations, but particularly in general practice (Payne and Avery 2011). Prescribing should be done in a way that explicitly considers the overall effects of the total drug regimen.

1 'Measuring' polypharmacy

Defining polypharmacy according to numbers of medicines

The term polypharmacy does not in itself imply whether it is appropriate to prescribe several medications, although it is often assumed that it is inappropriate to do so. This is reflected in the two most common approaches used to define or measure polypharmacy in the literature: the use of a specific threshold for the number of drugs, or alternatively a measure of the number of inappropriate drugs or combinations of drugs according to pre-defined criteria.

The use of a specific numeric threshold is widespread in the literature. It has the advantage of being simple and easily identified in clinical practice. Often these thresholds are arbitrarily chosen, with more than three or four medicines commonly used as the cut-off value. Since the number of drugs that patients receive has been rising in recent years, it is possible that the utility of a specific threshold may change over time. For example, four or more drugs was considered high a decade ago, but this is now commonplace and a threshold of ten or more might be more appropriate. This could potentially provide greater specificity for problematic prescribing and offer a more pragmatic means of identifying those patients most in need of medication reviews. However, these patients may not be readily identified by general practice computer systems. There is evidence that when polypharmacy is defined through use of a threshold it is associated with adverse outcomes (Jyrkka *et al* 2009; Cherubini *et al* 2012). Such definitions are used in admission prediction models where the prescribing of a certain number of drugs can be included as a predictive factor for hospitalisation (Wennberg *et al* 2006). There is also clear evidence of an increasing risk of prescribing errors, high-risk prescribing and adverse drug events the greater the number of drugs prescribed (Bourgeois *et al* 2010; Guthrie *et al* 2011), with ten or more drugs conveying a higher risk than four to nine (Avery *et al* 2012b).

An alternative method of identifying problematic prescribing is to quantify the number of specific inappropriate drugs or combinations of drugs. Examples are shown in Table 1, overleaf. These approaches are not designed specifically to measure polypharmacy. Nonetheless, they are widely used, both in research and clinical practice, to identify potentially hazardous prescribing, and they have proven face-validity.

Tools to assess appropriateness of prescribing in polypharmacy

Various strategies have recently been developed to identify older patients at risk from adverse effects and to reduce the risk of initiating drugs likely to cause adverse events. Several tools have been developed specifically to help identify inappropriate prescribing in older patients (Spinewine *et al* 2007). Examples from North America include the Improved Prescribing in the Elderly Tool (IPET), and the widely cited Beers criteria, which has undergone several revisions, the last in 2012 (Beers 2012). These criteria have been adapted for use in several countries with some improvements that enable clinical medication reviews to be undertaken more consistently and efficiently (Levy *et al* 2010).

Table 1 Prescribing indicators used to identify problematic or inappropriate polypharmacy

Name of indicator set	Description	Reference
Beers criteria for potentially inappropriate medication use in older adults	The original prescribing indicator reference. In some respects the 66 indicators are US-specific. There are regular updates of the 1991 indicators; the indicators have been tested in a variety of situations worldwide.	Beers (2012). 'The American Geriatrics Society Beers criteria update expert panel. American Geriatrics Society Updated Beers criteria for potentially inappropriate medication use in older adults'. *Journal of the American Geriatrics Society*, vol 60, no 4, pp 616–31.
French consensus panel list	36 indicators specific to France, largely based on McLeod and Beers.	Laroche ML *et al* (2007). 'Potentially inappropriate medications in the elderly: a French consensus panel list'. *European Journal of Clinical Pharmacology*, vol 63, no 8, pp 725–31.
HIC Indicators – ePACT style data analysis	52 Australian indicators of a very different style. Rates of prescribing are compared to a national standard. In some cases high rates may be good – eg, prescribing plain penicillin as compared to broad spectrum antibiotics.	Robertson HA and MacKinnon NJ (2002). 'Development of a list of consensus-approved clinical indicators of preventable drug-related morbidity in older adults'. *Clinical Therapeutics*, vol 24, no 10, pp 1595–613.
IPET (constructed from McLeod)	14 indicators which were drawn entirely from the McLeod criteria (*see* below).	Naugler CT *et al* (2000). 'Development and validation of an improving prescribing in the elderly tool'. *Canadian Journal of Clinical Pharmacology*, vol 7, no 2, pp 103–7.
Irish survey indicators	16 indicators developed from an Irish survey of GPs. Emphasis is on quality rather than safety.	Williams D *et al* (2005). 'The application of prescribing indicators to a primary care prescription database in Ireland'. *European Journal of Clinical Pharmacology*, vol 61, no 2, pp 127–33.
Lab safety monitoring in ambulatory patients	Nine US monitoring indicators from a computerised tool. The indicators lack a strong evidence base but significant differences were made using the tool in the monitoring of lithium, amiodarone, theophylline, carbemazapine, phenytoin and metformin.	Raebel MA *et al* (2006). 'Randomized trial to improve laboratory safety monitoring of on-going drug therapy in ambulatory patients'. *Pharmacotherapy*, vol 26, no 5, pp 619–26.
McLeod criteria	71 Canadian indicators, many of which are now outdated (due to new pharmacological evidence).	McLeod PJ *et al* (1997). 'Defining inappropriate practices in prescribing for elderly people: a national consensus panel'. *Canadian Medical Association Journal*, vol 156, no 3, pp 385–91.
NORGEP criteria	36 indicators developed in Norway by consensus. Many drugs are not relevant to the United Kingdom or are no longer prescribed.	Rognstad S *et al* (2009). 'The Norwegian General Practice (NORGEP) criteria for assessing potentially inappropriate prescriptions to elderly patients. A modified Delphi study'. *Scandinavian Journal of Primary Health Care*, vol 27, no 3, pp 153–9.
PINCER Indicators	10 UK indicators validated in general practice and included in the PINCER trial. This trial demonstrated the effectiveness of a pharmacist-led IT-based intervention to reduce hazardous prescribing. Odds ratios for error were significantly lower in the intervention group (0.51 to 0.73).	Avery AJ *et al* (2012a). 'A pharmacist-led information technology intervention for medication errors (PINCER): a multicentre, cluster randomised, controlled trial and cost-effectiveness analysis'. *The Lancet*, vol 379, pp 1310–9.
Potentially harmful drug–drug and drug–disease combinations	This US team developed 50 drug–disease and 6 drug–drug combinations that were considered to represent poor quality prescribing. The indicators were tested in order to determine the prevalence of their occurrence in ambulatory care.	Zhan C *et al* (2005). 'Suboptimal prescribing in elderly outpatients: potentially harmful drug–drug and drug–disease combinations'. *Journal of the American Geriatrics Society*, vol 53, no 2, pp 262–7.

Table 1 (continued)

Name of indicator set	Description	Reference
Prescribing and monitoring error indicators	Of the 30 indicators developed by this US consensus panel some drug–disease combinations represent quality rather than safety. Using the indicators, errors were avoided 88 per cent of the time.	Wessell AM *et al* (2010). 'Medication prescribing and monitoring errors in primary care: a report from the Practice Partner Research Network'. *Quality & Safety in Health Care*, vol 19, no 5, e21-e21.
Prescribing Indicators Tool for Elderly Australians	48 indicators, many of which reflect quality rather than safety, especially in the secondary prevention of CVD. Unusual development process involving prescribing and diagnostic frequencies.	Basger BJ *et al* (2008). 'Inappropriate medication use and prescribing indicators in elderly Australians: development of a prescribing indicators tool'. *Drugs Aging*, vol 25, no 9, pp 777–93.
RCGP indicators	34 prescribing safety indicators developed (using RAND UCLA consensus process) and designed for use in UK general practice. Using a similar process, an updated list of 56 indicators has recently been identified (currently unpublished).	Avery AJ *et al* (2011). 'Development of prescribing-safety indicators for GPs using the RAND Appropriateness Method'. *British Journal of General Practice,* vol 61, no 589, pp 526–36.
Scottish indicators – inappropriate prescribing to vulnerable patients	15 RAND UCLA-derived indicators that were developed in Scotland and tested on general practice data from 1.7 million patients. A composite indicator was found to be the most reliable measure of a practice's performance.	Guthrie B *et al* (2011). 'High risk prescribing in primary care patients particularly vulnerable to adverse drug events: cross sectional population database analysis in Scottish general practice'. *British Medical Journal*, vol 342, d3514.
STOPP/START criteria	A detailed set of 87 indicators developed by consensus methods in Ireland. They have been validated extensively in the UK setting. Many of the STOPP criteria were included in the RCGP indicator set.	Gallagher P *et al* (2008). 'STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation'. *International Journal of Clinical Pharmacology and Therapeutics*, vol 46, pp 72–83.

Source: Compiled by Prof Anthony Avery and Dr Rachel Spencer

In the Irish Republic, two sets of criteria have been developed to assess whether medicines have been inappropriately prescribed or omitted (Gallagher *et al* 2008): The Screening Tool of Older Person's Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START). STOPP comprises 65 clinically significant criteria for potentially inappropriate prescribing in older people. Each criterion is accompanied by a concise explanation as to why the prescribing practice is potentially inappropriate. START consists of 22 evidence-based prescribing indicators for commonly encountered diseases in older people. In the United Kingdom, a set of prescribing safety indicators has been developed specifically for use in general practice (Avery *et al* 2011).

One study of prescriptions issued to a population of Irish patients over the age of 70, using 30 STOPP indicators, found that 36 per cent of patients received a prescription which was deemed potentially inappropriate (Cahir *et al* 2010).

As with any tools, however, their validity is affected by the local availability and cost of medicines, relevant clinical practice guidelines, and the emergence of new evidence and treatments.

Proposed pragmatic approach for identifying higher-risk polypharmacy

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. Nonetheless, there is potential benefit

to be gained from having a simple means of identifying those individuals at particular risk of inappropriate prescribing and adverse drug events. This may be achieved by using a combination of the methods detailed above. A pragmatic approach might focus on the following groups of 'at-risk' patients:

- all patients with 10 or more regular medicines (for example, those medicines taken every day or every week)

- patients receiving between four and nine regular medicines who also:
    - have at least one prescribing issue that meets criteria for potentially inappropriate prescribing
    - have evidence of being at risk of a well-recognised potential drug–drug interaction or have a clinical contraindication
    - have evidence from clinical records of difficulties with medicine-taking, including problems with adherence
    - have no or only one major diagnosis recorded in the clinical record (it might be expected that large numbers of medicines are unlikely to be justified in patients without multiple clinical conditions)
    - are receiving end-of-life or palliative care (where this has been explicitly recognised).

This may in part depend on adequate diagnostic coding to enable automated assessments of clinical notes to be made. However, much of the required technology is already incorporated into standard clinical computer systems used in general practice (and increasingly available in hospitals), such as existing databases of drug interactions and contraindications. An alternative approach is to stratify risk based solely on the number of drugs, but to avoid the use of fixed cut-off values. Work should therefore be carried out to develop models to predict adverse consequences (eg, hospitalisation, adverse drug events, prescribing errors, specific drug classes).

2 The epidemiology of polypharmacy

Polypharmacy occurs in both primary and secondary care, and is a global phenomenon. It is associated with a number of adverse consequences, and is becoming increasingly common, driven by an ageing population affected by increasing multi-morbidity.

Polypharmacy in primary care

In the United Kingdom, the central role of general practice in the organisation of health services means that management of long-term prescribing is predominantly carried out in the primary care setting. The predominant use of electronic prescribing and the large databases used in general practice mean that there are considerable amounts of data on prescribing in primary care. There is also extensive primary care pharmacy dispensing data that documents the patterns of medication use in the community. The Prescribing Cost Analysis in England confirms a clear year-on-year increase in the number of medications dispensed in primary care (*see* Figure 2, p 3). The total number of items dispensed has increased by 64 per cent from 587 million in 2001 to 962 million in 2011. This corresponds to an average of 11.9 medications per patient per annum in 2001, and 18.3 medications per patient per annum in 2011. It should be noted, however, that national UK dispensing data does not provide individual patient-level data. It is only able to provide limited demographic information at prescriber-level, and is unable to supply information about the concurrent use of multiple medications, clinical indication or potentially hazardous prescribing behaviour.

An analysis of more than 300,000 patients in Scotland found an increase in the mean number of drugs dispensed, from 3.3 in 1995 to 4.4 in 2010. This corresponded to 1.8-fold and 3.1-fold increases in the numbers of patients receiving respectively 5 or more medications (12 per cent to 22 per cent) and 10 or more medications (1.9 per cent to 5.8 per cent) (*see* Figure 3, p 3). The proportion of older patients (65 years and above) receiving 10 or more medications was particularly high at 16.4 per cent in 2010 (Guthrie and Makubate 2012). The PRACtICe Study, funded by the General Medical Council (GMC), conducted a detailed examination of the prescribing records of 1,777 patients in English general practice. It found 299 patients (17 per cent) were receiving between 5 and 9 medications, and an additional 172 (9.7 per cent) were receiving more than 10 medications (Avery *et al* 2012b). These figures are comparable to data on medication use in the community in other countries. In Sweden in 2008, the average number of medicines was 3.4 per individual, increasing to 5 in those aged 70 to 79 years (Hovstadius *et al* 2010b). In the United States, 29 per cent of patients in the community aged 57 to 85 years received 5 or more concurrent prescription medications, increasing with age and female gender (Qato *et al* 2008).

These high rates of concurrent prescribing were also associated with high rates of hazardous prescribing. The PRACtICe Study found that 30.1 per cent and 47 per cent of patients receiving respectively 5 or more and 10 or more medications had prescribing or monitoring errors in the 12-month study period. After adjusting for other factors, each additional unique medication item increased the odds of an error occurring by a

further 16 per cent (Avery *et al* 2012b). A further Scottish study of primary care patients considered vulnerable to adverse drug events, based on age, co-morbidity and co-prescription, found 13.9 per cent of patients to have received a high-risk prescription in the past year. Among these, the patient characteristic most strongly associated with high-risk prescribing was found to be the number of drugs prescribed: patients on more than 10 medications had 2.9-fold higher odds of high-risk prescribing compared with those receiving 1 or 2 medications (Guthrie *et al* 2011).

Polypharmacy in hospitals

The prevalence of multiple medication use in secondary care is also significant; adverse consequences either directly or indirectly related to prescribing may result in hospitalisation, and initiation and changes of medications will often occur in a hospital setting. However, the data on such use is generally lacking in comparison with that on general practice in the United Kingdom.

Polypharmacy is common in the hospital setting. A study of 6 different centres across western Europe found the median number of medications in an older hospitalised population (median age 82 years) to be 6 (interquartile range 4 to 9). The authors also found that higher numbers of medicines were associated with a higher likelihood of potentially inappropriate prescribing (Gallagher *et al* 2011). Furthermore, the number of medicines has been shown to be the strongest predictor of hospitalisation for adverse drug reactions (Davies *et al* 2009). Indeed, adverse drug reactions are a major cause of morbidity, contributing to 6.5 per cent of hospital admissions in a study in north-west England (Pirmohamed *et al* 2004).

A number of studies have examined the impact of a hospital stay on the number of medicines prescribed. A US study of an acute medical service found an average increase in medicines of 2.9 from admission to discharge (Smith *et al* 1996). In the Italian Gruppo Italiano di Farmacovigilanza nell'Anziano (GIFA) study, there was an increase in the median number of prescribed drugs, from 3 before admission to 4 at discharge, driven by multi-morbidity and a number of specific clinical conditions such as diabetes (Corsonello 2007). The increase observed in an older Slovakian population was relatively small, from 6.0 to 6.2 (Wawruch *et al* 2008). In an older Australian population, Gonski *et al* found an average increase in the number of medications from 4.1 before admission to 4.7 at discharge. They also noted considerable discrepancies between the lists of medications described by patients, hospital doctors and GPs (Gonski *et al* 1993). Another Australian study found the number of long-term medications to increase from 6.6 to 7.7 following acute admission to an elderly care unit, with the change most marked in younger patients (65 to 75 years) (Betteridge *et al* 2012). In a study of patients admitted to general medical wards in Germany only half of long-term drugs prescribed by GPs were continued unchanged. A total of 96 per cent of patients experienced changes to the drug regimen, with 3 or more changes in 61 per cent of individuals (Himmel *et al* 2004). This large change in medications during hospitalisation is supported by other studies: Viktil *et al* found an average of 4.4 drug changes per patient during admission in a Norwegian cohort, with an increase from 5.6 to 7.6 medicines at discharge. Furthermore, 86 per cent of patients had further changes in the immediate few months after leaving hospital (an average of 3.4) (Viktil *et al* 2012). Grimmsmann *et al* have also found in-patient changes in medication to be extremely common in Germany (98.1 per cent), with 60 per cent of patients having 5 or more changes and newer, more costly drugs often being prescribed, although the total number of prescriptions did not change (Grimmsmann *et al* 2007). Analyses have been conducted in specific clinical areas. An increase in medications from 3.6 drugs at admission to 5.0 drugs at discharge was observed in patients admitted for

surgical intervention in a German tertiary care centre, although this decreased back to 3.8 drugs after 3 months (Hach *et al* 2005).

In general, these results demonstrate a consistent increase in the number of drugs a patient receives at discharge from hospital compared with admission, although studies are limited to developed nations and do not focus on younger populations. The size of the increase observed varies considerably, reflecting in part the different patient populations and health care systems studied.

Medication use in care homes

In the United Kingdom an important study highlighted problems in the use of medicines in care homes (Barber *et al* 2009). This project employed both qualitative and quantitative analyses to evaluate medication errors, and made some carefully reasoned recommendations for improving care. The researchers examined the experience of 256 residents from 55 care homes (residential, nursing and mixed), with a mean age of 85 years, in England. The residents were taking an average of eight medicines each – a sign of the complexity of their clinical conditions. Errors were identified by experienced clinical pharmacists who interviewed patients, looked at medical records, observed care and examined the dispensing pathway. Of these 256 residents, 178 (69 per cent) had one or more medication error (mean 1.9). The most common prescribing errors were no strength or route being stated on a prescription or chart when there was more than one option (38 per cent); an unnecessary drug being prescribed (24 per cent); the wrong dose or strength being prescribed (14 per cent); and not prescribing a drug (12 per cent) when it should have been prescribed. Administration errors are probably of greater consequence and 57 residents were given the wrong drug or dose, or not given a drug (116 errors). A drug that required monitoring was prescribed to 147 residents and 27 (18 per cent) of these had an error, the most common one being the failure to carry out blood tests for monitoring purposes.

A similar study also concluded that the incidence of medication administration errors is high in long-term residential care in England (Szczepura *et al* 2011). This was a prospective study conducted in 13 care homes (9 residential and 4 nursing). Data on all medication administrations for a cohort of 345 older residents was recorded. Every attempt by social care and nursing staff to administer medication during a three-month observation period was analysed for potential medication administration errors. A total of 188,249 medication administration attempts were analysed using a barcode administration system. Typically each resident was receiving 9 different drugs and was exposed to 206 medication administration episodes every month. During the observation period, 2,289 potential administration errors were recorded for the 345 residents and 90 per cent of residents were exposed to at least one error. The most common (n = 1,021, 45 per cent of errors) was attempting to give medication at the wrong time. During the three-month observation period, half of residents (52 per cent) were exposed to a serious error such as attempting to give medication to the wrong resident. The study highlighted the use of technology to improve medicines management in the care home setting and proposed that barcode medication administration systems could capture medication administration errors and prevent these from occurring.

Polypharmacy in other countries

Multiple use of medicines is a global phenomenon. However, there are wide variations in health care systems and data sources, as well as numerous definitions of polypharmacy, so comparisons across countries is challenging. Many studies are also limited to older patients.

A number of studies have been conducted in developed nations. In Sweden, substantial national prescribing data for the community is available. During the period 2005 to 2008, Hovstadius and colleagues found an 8.2 per cent increase in the rates of prescribing of 5 or more medicines, and a 15.7 per cent increase in the prescribing of 10 or more medicines, with these increases most marked in men and older patients. In the Swedish population as a whole in 2008, the average number of medicines was 3.4 per individual, but increasing to 5.0 among those aged 70 to 79 years, and 6.6 among those aged 90 and above (*see* Figure 4, below) (Hovstadius *et al* 2010b). Similar data for the United Kingdom is scarce. Some variations have also been observed by geographical region, although this is partly accounted for by age variation (Hovstadius *et al* 2010a). Although this data is based on a three-month prescribing period, and captures both regular and acute prescriptions, the findings are similar to UK observations (Guthrie and Makubate 2012a), and they can likely be generalised to other developed countries. A US survey of medication use in the community found 29 per cent of patients in the age range 57 to 85 years were receiving 5 or more concurrent prescription medications. This figure increased with age and female gender (Qato *et al* 2008).

Analyses have also been carried out in secondary care. One study examined the prevalence of potentially inappropriate prescribing in six acute geriatric medicine units in centres across Europe (Gallagher *et al* 2011). Overall, among patients aged 65 years and above, 39 per cent received 1 to 5 medications; 44 per cent received 6 to 10; and 14 per cent received more than 10. There was some geographical variation, most notably in those with very high levels of polypharmacy (more than 10 medications), ranging from 4 per cent of patients in Perugia in central Italy to 21 per cent in the Swiss city of Geneva, a finding reflected in the differences in potentially inappropriate medicines and not accounted for age variations (Gallagher *et al* 2011). The Italian REPOSI study has shown that age, number of admission medications, various cardiovascular conditions and chronic obstructive pulmonary disease are all independently associated with polypharmacy as determined at hospital discharge (Nobili *et al* 2011). Work in

Figure 4 Polypharmacy, Sweden, 2005 to 2008
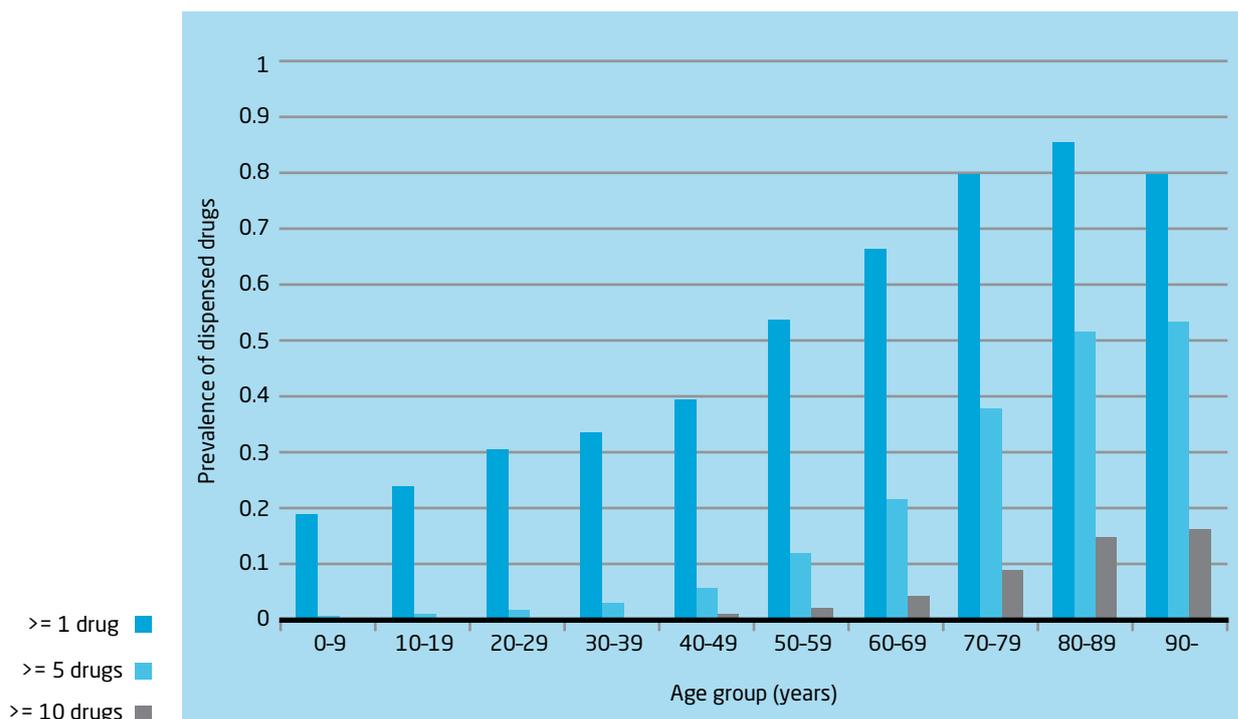
Source: Hovstadius *et al,* (2010b)

Switzerland has also shown widespread use of multiple medicines among hospitalised patients, with adverse drug events a common problem (Fattinger *et al* 2000).

Although fewer studies appear to have been conducted in non-Western countries, polypharmacy certainly appears to be a recognised issue. Furthermore, with increased longevity, prevalence of chronic diseases and improved access to health care and medicines, polypharmacy is likely to increase around the world. In a study of a teaching hospital in New Delhi, patients were found to be receiving an average of 3.9 medicines, with antimicrobials the most frequently prescribed drugs – a contrast to trends observed in Western nations, where treatment for non-communicable diseases prevail (Aqil *et al* 2012). A small questionnaire study in the Bhopal region of India observed over-prescribing of medication in 2.4 per cent of patients, with a further 4.0 per cent experiencing repetition of drugs (Rambhade *et al* 2012). A large analysis of prescribing in rural western China found the average number of drugs per prescription to be 2.4, with 5.8 per cent of patients receiving 5 or more medicines. Patients' age and gender were associated with the number of medicines, as were doctors' workload and the availability of government subsidies (Dong *et al* 2010). A further study of potentially inappropriate medication use by older patients (aged 60 years and above) in Brazilian primary care found around two-thirds were receiving four or more medications, with a strong association with potentially inappropriate medication use (Oliveira *et al* 2012). All these studies underline polypharmacy as a global issue, although arguably less so in poorer populations where access to health care may be limited, and with variations in the types of medicines involved.

Multi-morbidity and ageing as driving factors

Polypharmacy is often closely associated with multi-morbidity. There has recently been considerable interest in recognising the extent of multi-morbidity and understanding its implications. Management of patients with several diseases is a major undertaking. A study from Scotland showed that among older people, patients with multi-morbidity are the norm rather than the exception (Barnett *et al* 2012). This was a cross-sectional analysis based on medical records of 1,751,841 people registered with 314 medical practices in Scotland. Multi-morbidity was defined as the presence in an individual of two or more disorders from a list of 40 specified long-term disorders. The distribution of this multi-morbidity was explored in relation to age, sex and socio-economic deprivation. Perhaps an unexpected finding is that there are greater numbers of younger people (aged less than 65 years) with multi-morbidity than there are older people; although prevalence of disease is less, there are considerably more people under this age (Barnett *et al* 2012). Almost a quarter of all patients, and more than half of those with a chronic disorder, had multi-morbidity. Multi-morbidity is strongly related to age (*see* Figure 5, overleaf).

Population projections produced by the Office for National Statistics point towards significant increases in the population of older people in the next two decades, as the current 'bulge' of people aged between 40 and 60 grow older. Also because of increased longevity, the number of people who are older than 85 is projected to increase dramatically (*see* Figures 6 and 7, pp 15–16). This is clearly likely to have important implications for the prevalence of multi-morbidity. This prevalence also increases with socio-economic deprivation, with people in deprived areas experiencing the same prevalence of multi-morbidity as more affluent patients who are 10 to 15 years older (Barnett *et al* 2012) (*see* Figure 8, p 16).

Studies show that people with multi-morbidity have a reduced quality of life and worse health outcomes than those with a single disease. Salisbury points out that patients with multi-morbidity are also the main consumers of health care, including prescribed

Figure 5 Number of chronic disorders by age group
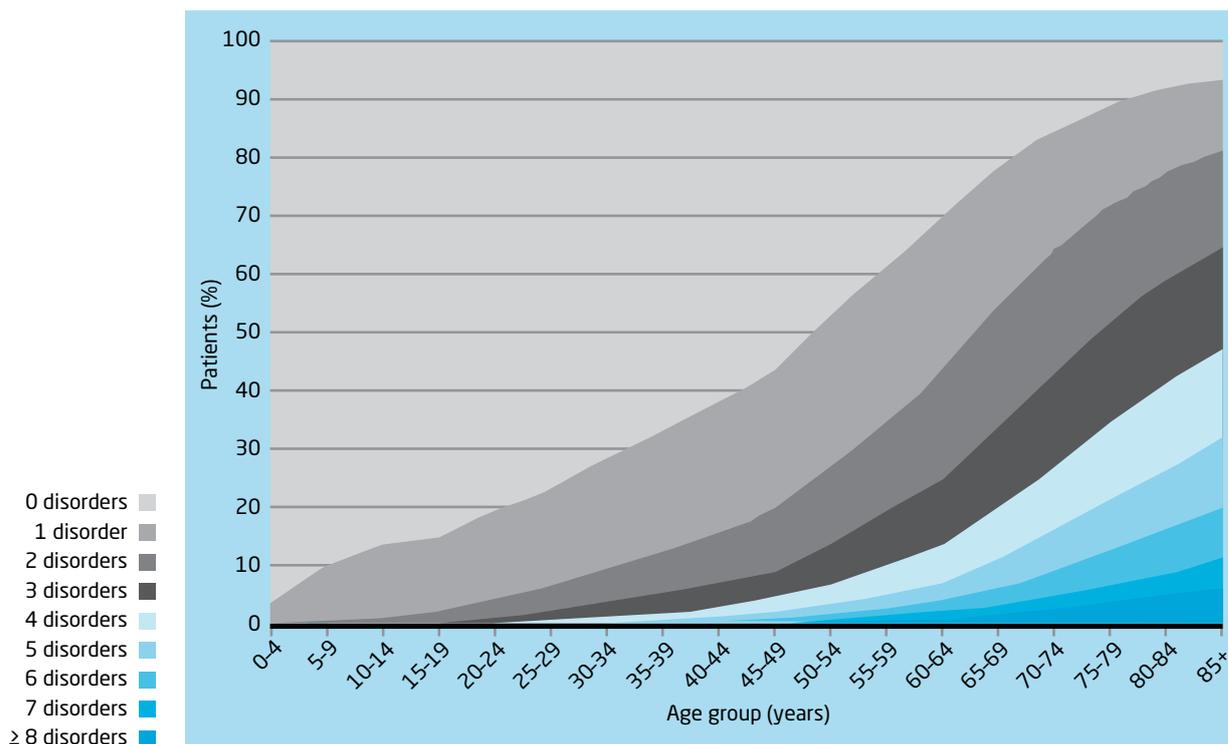
Note: This figure shows how common it is to have significant long-term conditions in relation to age. Few people (fewer than 30 per cent) do not have at least one condition by the age of 60, and many people will have two or three.

Source: Barnett *et al* (2012)[3]

Table 2 Year-on-year change for drugs used to treat diabetes, England, 2005/6 to 2011/12

Financial year	Total items (millions)	Change in number of items on previous year (millions)	Percentage change on pevious year
2005/6	27.1	2.3	9.3
2006/7	28.9	1.8	6.6
2007/8	30.8	1.9	6.7
2008/9	32.9	2.1	6.9
2009/10	35.5	2.6	7.8
2010/11	38.3	2.8	7.8
2011/12	40.6	2.3	6.1

Note: This table indicates how prescribing for people with diabetes has rapidly increased between 2005 and 2012.

Source: NHS Information Centre (2012)

medicines (Salisbury 2012). In one study, 58 per cent of patients attending general practices had multi-morbidity, but they accounted for 78 per cent of all consultations (Huntley *et al* 2012). Expenditure on health care rises very rapidly with the number of chronic diseases so it may be that the potential for waste is greatest in this context (Salisbury *et al* 2011). These are important reasons for challenging the single-disease framework seen in most health care systems, medical research and medical education (*see* Figure 8, p 16) (Guthrie *et al* 2012a; Hughes *et al* 2013).

3   Reprinted from *The Lancet*, vol 380, pp 37–43, © 2012, with permission from Elesevier.

Alongside these demographic changes, it is clear that prescribing is also growing rapidly (*see* Figures 1, 2, 3 on pp 2–3 and Table 2 opposite). One reason is the increasing amount of prescribing for chronic conditions such as diabetes (Table 2). The Quality and Outcomes Framework for general practice in the United Kingdom has resulted in much more consistent use of evidence-based interventions. This has potentially driven growth in prescribing, with more coherent adherence to evidence-based guidelines resulting in much greater use of drugs. There is also data that clearly shows that the number of prescriptions an individual receives increases with age (see Figure 4, p 12), fitting with the pattern of acquiring more morbidities with age.

Figure 6 Estimated and projected age structure, UK population, mid-2010 and mid-2035
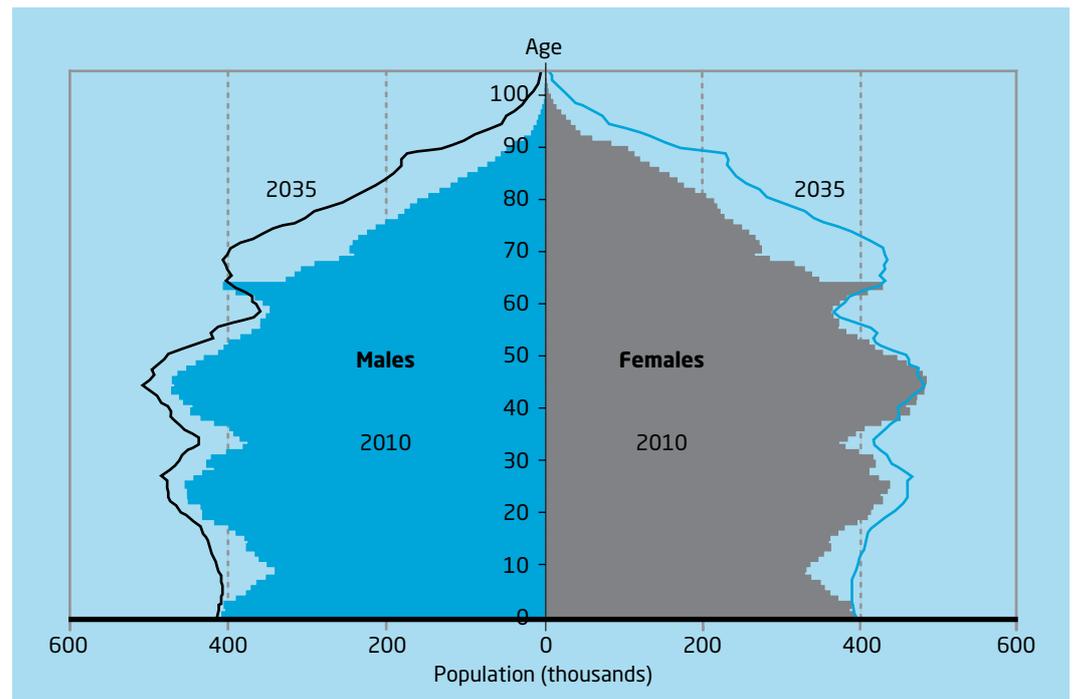
Notes:

- The UK population is projected to increase by 4.9 million from an estimated 62.3 million in 2010 to 67.2 million over the 10-year period to 2020.

- Projected natural increase (more births than deaths) accounts for 56 per cent of the projected increase over the next decade.

- The UK population is projected to increase to 73.2 million over the 25-year period to mid-2035, which is equivalent to an average annual growth rate of 0.6 per cent.

- The UK population is projected to reach 70 million by mid-2027.

- The population is projected to continue ageing with the average (median) age rising from 39.7 years in 2010 to 39.9 years in 2020 and 42.2 by 2035.

- As the population ages, the numbers in the oldest age groups will increase the fastest. In 2010, there were 1.4 million people aged 85 and over; this number is projected to increase to 1.9 million by 2020 and to 3.5 million by 2035, more than doubling over 25 years.

Source: Office for National Statistics (2011)

Figure 7 Estimated and projected population aged 85 and over, United Kingdom, 2010 and 2035
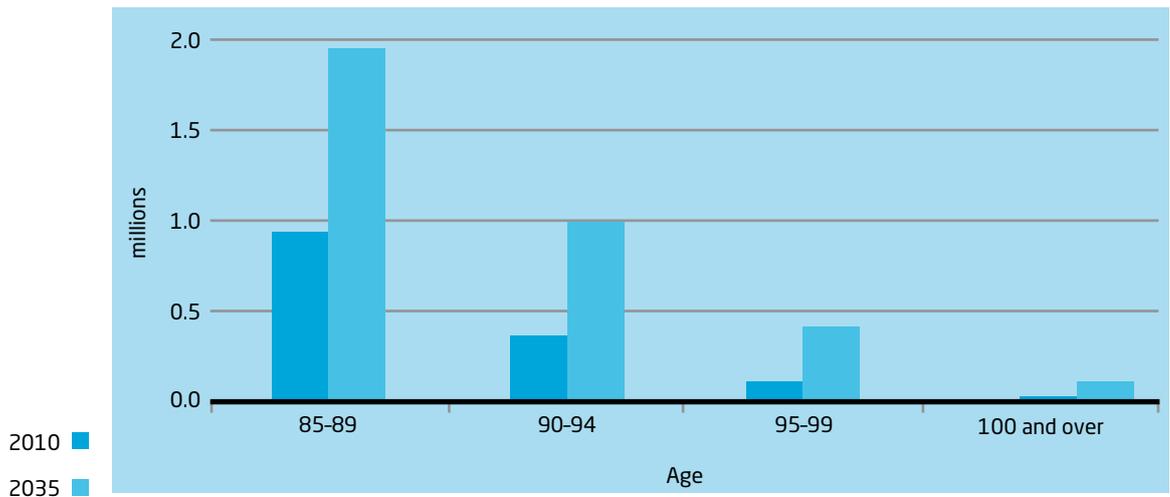
2010 ■
2035 ■

Note: The number of people aged 90 and above is projected to more than triple by 2035; the number of people aged 95 and above is projected to more than quadruple; and the number of centenarians is projected to rise from 13,000 in 2010 to 110,000 in 2035, a more than eightfold increase.

Source: Office for National Statistics (2011)

Figure 8 Selected co-morbidities in people with coronary heart disease, diabetes, COPD or cancer in the most affluent and most deprived areas of Scotland
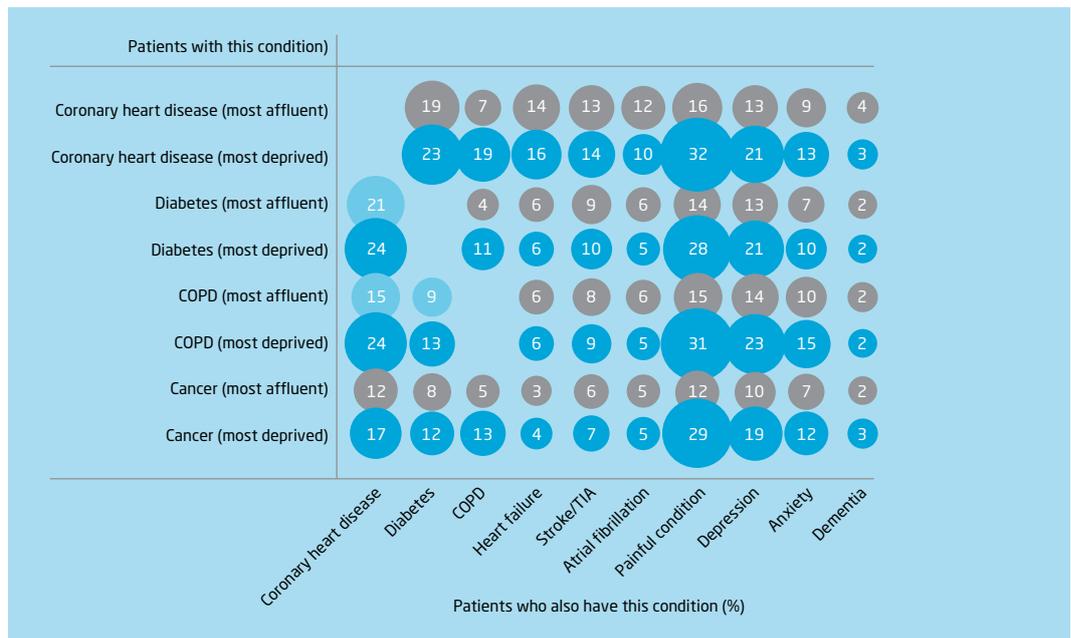
COPD = chronic obstructive pulmonary disease; TIA = transient ischaemic attack; most deprived = the 10% highest (decile); most deprived = the 10% lowest (decile).

Note: this figure looks at the percentage of people in the left-hand column with these four common conditions who also have other co-morbidities. In this study these were more common in people living in deprived areas. For example, it demonstrates that for this dataset, in the most deprived areas 23% of people with coronary heart disease will also have diabetes, and in the most affluent areas this percentage is 19%. People living in deprived areas were much more likely to have COPD, depression, and painful disorders as co-morbidities than other disorders. Most people had some major co-morbidity: for coronary heart disease overall only 9% had no other major co-morbidity. For diabetes this percentage is 14%, for COPD it is 18% and for cancer 23%.

Sources: Barnett *et al*, (2012) [4]

4 Reprinted from *The Lancet*, vol 380, pp 37–43, © 2012, with permission from Elesevier.

3 Medicines optimisation and polypharmacy

Medicines optimisation encompasses many aspects of improving medication use, and is fundamental to addressing the challenges posed by polypharmacy. These aspects had previously come under the banner of medicines management but there is an increasing trend towards using the term medicines optimisation. The former National Prescribing Centre (now incorporated into the National Institute for Health and Care Excellence (NICE) as the Medicines and Prescribing Centre) defines medicines management as '...*a system of processes and behaviours that determines how medicines are used by patients and healthcare services*' (NPC 2002).

A wider definition might encompass the entire way medicines are selected, procured, delivered, prescribed, administered and reviewed to optimise the contribution that medicines make to enabling informed patient choice and delivering desired outcomes for patients. This includes clinical assessment, monitoring and review in individual patients, medicines delivery services, review of repeat prescribing systems, clinical audit, health education, risk management, disease prevention and the development and use of formularies and guidelines.

To encompass this wider definition, alongside the drive to more patient-centred care, the focus has changed in the United Kingdom towards the concept of medicines optimisation. A definition of medicines optimisation is that it, '...requires evidence-informed decision making about medicines, involving effective patient engagement and professional collaboration to provide an individualised, person-centred approach to medicines use, within the available resources' (NICE 2013). NICE are in the process of developing a guideline based on these principles.

Medication management and optimisation processes to address both polypharmacy and the potential problems it may cause are discussed below.

Evidence for improving medicines management in polypharmacy

Developments in the United Kingdom in the past decade have resulted in considerable changes in the ways medicines are used and consequently in medicines management. These changes include the increasing role of non-medical prescribing, the changing role of community pharmacists, changes in the way that GPs and pharmacists are remunerated for their NHS work, the advent of electronic prescribing, the move towards early discharge from hospital, hospital at home services, and minor ailments services. Similar changes are going on in many countries.

A Cochrane Review published in 2012 examined the evidence behind interventions to improve the appropriate use of polypharmacy for older people (Patterson *et al* 2012). However, its findings may be relevant to medication management and polypharmacy for younger patients too. The review notes that inappropriate polypharmacy is a particular concern in older people and is associated with negative health outcomes.

Studies were carefully screened and selected for incorporation into the review. Several types of study were eligible for inclusion. Eligible studies were those aimed at improving appropriate polypharmacy in people aged 65 years and older where a validated measure of appropriateness was used (eg, Beers criteria (Beers 2012) or Medication Appropriateness Index – MAI (Hanlon *et al* 1992)) (*see* box below). Initial electronic searches identified 2,200 potentially relevant citations, of which 139 were examined in detail. Following this assessment, only 10 studies were included. These inclusion criteria somewhat limit the generalisability of these findings to current UK practice, given that there are now other well-validated measures of prescribing quality. However, the review is useful to help delineate the current evidence. It also identifies areas of uncertainty and the context where future research is most likely to be informative.

One intervention described in the review used computerised decision support to help the doctor decide on the right treatment. Nine studies involved complex, multi-faceted pharmaceutical care provided in a variety of settings. These were services provided by pharmacists, which involved identifying, preventing and resolving medication-related problems, as well as promoting the correct use of medications and encouraging health promotion and education. The review concluded that there is limited evidence to show that these interventions may be successful in ensuring older people receive the right medicines and thereby reduce medication-related problems. It was not clear if such interventions always result in clinical improvements.

The Medication Appropriateness Index (MAI)

The MAI was designed to assist clinicians and pharmacists in assessing the appropriateness of a medication for a given patient. The MAI requires clinicians to rate 10 explicit criteria to determine whether a given medication is appropriate for an individual. For each criterion, the index has operational definitions, explicit instructions and examples along with evaluator rates about whether the particular medication is 'appropriate', 'marginally appropriate', or 'inappropriate'.

The 10 explicit criteria are:

1   Indication: the sign, symptom, disease or condition for which the medication is prescribed.

2   Effectiveness: producing a beneficial result.

3   Dosage: total amount of medication taken per 24-hour period.

4   Directions: instructions to the patient for the proper use of a medication.

5   Practicality: capability of being used or being put into practice.

6   Drug–drug interaction: the effect that the administration of one medication has on another drug; clinical significance connotes a harmful interaction.

7   Drug–disease interaction: the effect that the drug has on a pre-existing disease or condition; clinical significance connotes a harmful interaction.

8   Unnecessary duplication: non-beneficial or risky prescribing of two or more drugs from the same chemical or pharmacological class.

9   Duration: length of therapy.

10 Expensiveness: cost of drug in comparison to other agents of equal efficacy and safety.

Reducing medication errors

Medication errors are a common consequence of using multiple medications. A number of studies have looked at methods to reduce the risk of harmful prescribing decisions and these are highly relevant to polypharmacy. One of these, the PINCER trial, was undertaken to evaluate whether a complex pharmacist-led IT-based intervention was more effective than simple feedback in reducing medication error rates in general practices (Avery *et al* 2012a). The study involved at-risk patients in 72 general practices who were being prescribed drugs commonly associated with medication errors. GP practices were randomised to receive either the PINCER intervention or simple feedback. Those allocated to receive simple feedback were provided with computerised feedback on patients identified to be at risk from medication errors along with brief written information on the importance of each type of error. GP practices allocated to the PINCER intervention were also provided with computerised feedback on patients identified to be at risk from medication errors. In addition, they met with a pharmacist to discuss the problems identified from the computerised feedback and to agree on an action plan. The pharmacist then spent up to three days per week for the next 12 weeks working in the practice to resolve the problems identified and improve medicine management systems to avoid future errors using the principles of educational outreach and root-cause analysis to bring about change.

The results of the trial showed that the PINCER intervention is an effective method for reducing a range of clinically important and commonly made medication errors in primary care (Avery *et al* 2012a). At six-months' follow-up, the general practices receiving computerised feedback and pharmacist support had significantly fewer prescribing errors than the general practices that received computerised feedback alone. For example, patients in the PINCER group were 42 per cent less likely to have been prescribed a non-selective NSAID if they had a history of peptic ulcer without gastro-protection, 27 per cent less likely to be given a beta-blocker if they had asthma, and almost 50 per cent less likely to be prescribed an ACE inhibitor or loop diuretic without appropriate monitoring. The intervention also improved composite prescribing and monitoring outcomes.

The GMC's PRACtICe Study also explored the causes of prescribing errors, as well as trying to identify defences against such mistakes (Avery *et al* 2012b). A wide range of underlying causes of error was identified. Those relevant to the problem of polypharmacy include lack of training in undertaking complex medication reviews and lack of time to undertake these reviews in routine consultations. Defences against error identified included strategies employed by individual prescribers and primary care teams, and making best use of health information technology. The conclusions from the study were that prescribing errors in general practices are common, although severe errors are unusual; and that strategies for reducing the prevalence of error associated with polypharmacy should focus on GP training, continuing professional development for GPs, clinical governance, effective use of clinical computer systems, and improving safety systems within general practices and at the interface with secondary care.

Polypharmacy and use of monitored dose systems

The purpose of reminder systems for the day (and time) of the week included with medications packaging is to help people take long-term medications. Their effectiveness has been explored by a Cochrane Review (Mahtani *et al* 2011). Twelve studies containing data on 2,196 participants were included in the analysis. Six intervention groups in four of these trials provided data on the percentage of pills taken, and found reminder packaging to increase the percentage of pills taken. Two further trials provided data for the proportion of self-reported adherent patients, and provided weak evidence for

a reduction in adherence in that intervention group. The researchers also conducted a meta-analysis on data from two trials assessing the effect of reminder packaging on blood pressure measurements, and found that reminder packaging significantly decreased diastolic blood pressure but had no effect on systolic blood pressure. Two trials looked at change in HbA1c and found that reminder packaging significantly reduced glycated haemoglobin levels. In one study, it was found that patients with low literacy levels preferred the presence of a reminder packaging aid. The authors concluded that reminder packaging may represent a simple method for improving adherence for patients with selected conditions, but that further research is warranted to improve the design and targeting of these devices.

A study of medications use in care homes by Barber and colleagues (Barber *et al* 2009) produced striking findings after it analysed the 86 per cent of residents on monitored dose systems (MDS), using blister packs or cassettes. Although intended to improve medication use, these systems often appeared to make matters worse. The authors point out that more research is urgently needed in this area. These problems arise because to prepare MDS, many tablets need to be repackaged, which immediately introduces the chance of mixing up tablets removed from their original container and of losing the specific instructions required for administration. If an acute treatment is added, or a change made in the four-week cycle, the MDS system can be rigid and cause confusion.

Medication review and repeat prescribing

It is important for patients' medications to be reviewed periodically to ensure that essential laboratory tests are undertaken, side effects are detected, patients are given essential information and are involved in decisions about their medicines, and that therapy is optimised. Where things are relatively straightforward, reviews can be done as part of normal follow-up consultations. In more complex cases, it is important to find ways of ensuring that adequate time is given to medication review so that discussion around medicines does not get squeezed into the final couple of minutes of the consultation. One option is to make it clear to patients that the consultation is primarily for the purposes of reviewing medications.

Another option is to involve clinical pharmacists in helping with the more complex medication reviews. Where the prescribing has been more complex, the medication review may be more difficult. Pharmacists are suited to focused medication reviews, as in the context of the PINCER study (Avery *et al* 2012a). However, there is not much evidence for pharmacist-led medication review in the context of complex polypharmacy (Holland *et al* 2006; Holland *et al* 2007). Nor is there much evidence for doctor-led medication review. Close collaboration of pharmacists and doctors in both prescribing and subsequent medication review seems a sensible approach (Holland *et al* 2005; Salter *et al* 2007). Possibly, particular training will be needed in this regard and clinical pharmacologists may also have a specific role in complex drug decisions involving polypharmacy.

The National Prescribing Centre guide to medication review outlines good practice (NPC 2008). The guide describes three types of medication review: prescription review, compliance and concordance review, and clinical medication review.

Repeat prescribing brings benefits of convenience to both doctors and patients and plays a significant part in the delivery of medicines to patients in primary care in the United Kingdom. However this area is remarkably under-researched considering the sheer scale of prescribing 'on repeats'. The last published estimates of the number of repeat prescriptions dates back to 1969. A recent analysis from Leeds University has attempted to update our knowledge based on 29 practices and prescribing in 2012 (Petty, personal communication 2013). In this study the median proportion of repeated prescriptions

(compared to acute prescribing) was 77 per cent (interquartile range 73 to 80 per cent). Forty-three per cent of people received at least one repeat prescription, increasing to 75 per cent of those over the age of 60 years. If this is representative of GP prescribing across the United Kingdom then more than 75 per cent of prescriptions generated in primary care are for patients who have requested a repeat supply of the medicines they regularly take. More than 2 million prescriptions are issued each day in England, meaning that it is likely that 1.5 million prescriptions are issued each day for repeat items; this overall figure rises by around 5 per cent per year. It is therefore important that an efficient and effective repeat prescribing process is in place, not just for general practice staff, but also for patients. This has greater importance for patients on multiple treatments.

However, repeat prescribing systems are complex and there are safety risks at various points in the process. In England, rapid change is affecting repeat prescribing systems with the introduction of the Electronic Prescriptions Service, being implemented in stages across England. This system allows for electronic transfer of prescriptions between general practices and community pharmacies. This is happening alongside 'repeat dispensing' arrangements whereby the pharmacy requests and monitors repeat prescriptions. Unless there is a robust check of the necessity and continuation of drug use by individual patients, the whole system could be responsible for significant drug waste (York 2010).

A final point is that drug interactions or clinical contraindications may not be flagged up by prescribing IT systems at the point of repeat prescribing. Tools for medication review could possibly be developed to enable this.

Some of these aspects of medicines management are considered at greater length in The King's Fund research paper on the *Quality of GP Prescribing* (Duerden *et al* 2011).

Polypharmacy at discharge and medicines reconciliation

How primary and secondary care providers communicate about medication prescribed also merits attention. Medication discrepancies at discharge are more common as numbers of medicines prescribed increase (Hu *et al* 2012). Glintborg and colleagues found that Danish hospitals failed to obtain a complete record of current prescriptions for around a fifth of patients. Less than a half of prescriptions were documented in discharge letters (Glintborg *et al* 2007). Accuracy of medication information on discharge summaries is poor, with a New Zealand study finding on average 1.4 and 0.8 errors for medical and surgical discharges respectively (McMillan *et al* 2006). It is likely the findings of both these latter studies are generalisable to other developed countries. A number of medicine reconciliation systems have also been examined. These are systems for ensuring that any changes made during a recent hospital admission are updated accordingly in primary care after the patient is discharged, with attention paid to new medication changes, deletions and additions. A recent systematic review found that interventions reduced medication discrepancies and potential and actual adverse drug events, although this had an inconsistent impact in terms of subsequent reductions in utilisation of health care services following discharge (Mueller *et al* 2012). Although electronic systems have been shown to provide better agreement between care providers at both admission and discharge, they are still not ideal (Van der Kam *et al* 2001; Moore *et al* 2011).

The Care Quality Commission (CQC) evaluated discharge medicines management in a number of English primary care trusts. It noted a number of important areas for improvement, including quality of discharge summaries, recording of whether appropriate information is sent across the primary–secondary care interface, and ensuring adequate medication review once patients return to primary care (Care Quality Commission 2009).

As well as issues of communicating with professional colleagues, the discharge process has important implications in terms of patients' experiences. Older patients discharged on four or more medicines have been found to be generally dissatisfied with the discharge process. Their carers report similar dissatisfaction. In particular, patients and carers report receiving poor explanations about their medicines, resulting in anxiety, confusion and omission or incorrect doses of drugs (Knight *et al* 2011). This problem has also been noted by the CQC.

The CQC report indicates that there is significant room for improvement; for example, 81 per cent of GP practices surveyed said that when hospitals sent them summaries of the care they had provided to patients, details of medicines prescribed were incomplete or inaccurate 'all of the time' or 'most of the time'. In Scotland a set of standards has been agreed for discharge documentation (SIGN 2012). This states that the accurate recording of medicines is an essential component of discharge documentation as it has a direct impact on patient care and management and is an important factor in improving patient safety. It advises that medicines reconciliation should include the accurate recording and comparison of all medicines a patient was taking on admission to hospital with those they are taking at the time of discharge from hospital, documenting all changes that have taken place. Sharing the discharge document with the patient's community pharmacist is considered to be an important step in improving medicines reconciliation at discharge and enhancing patient safety regarding medicines. A template of the expected content is provided by SIGN and sets a standard for this important component of care (SIGN 2012). This seems to be an ideal framework that could be adopted across the United Kingdom, particularly given the burgeoning problem of polypharmacy described in this review.

In addition, a recent Royal Pharmaceutical Society report on patients' safety regarding medication when they transfer between care highlights current pitfalls within and between the NHS and other 'provider' systems. It describes a 'pathfinder' project to address these and makes some aspirational recommendations based on this early project work (RPS 2012). Among other elements, it suggests that all suppliers of IT systems to hospitals and general practice should ensure that their systems are able to effectively transfer the recommended core content of records for medicines; that all community pharmacies should have an NHS.net website address to enable secure communications between secondary and primary care (this applies to the NHS in England); and that in future all clinical records should be structured in a recognised and nationally agreed format to assist interoperability and the transfer of information.

Suggestions for improving care in the context of multi-morbidity

It is clear that multi-morbidity is an important factor driving polypharmacy. It is thus important to consider approaches to medicines management designed to address the issue of multiple co-existing long-term conditions.

Chronic disease management is increasingly being provided within disease-specific clinics by clinicians working to checklists based on national guidelines. The role of the GP Quality and Outcomes Framework (QOF) has been deliberately to drive consistent application of such guidance as a marker of quality. The guidelines behind this framework look at only one condition at a time although the weakness of this approach is now recognised by NICE, which is looking at how best to consider multi-morbidity within its guidance (NICE 2012).

Treatment of diseases in isolation may be less efficient and lead to duplication of care or inconvenience; for example, the same patient may attend several clinics in a short space of time when a single visit would be easier and more productive.

These are some changes that we propose.

- Primary care consultations for multi-morbidity may need to be longer to tackle the many problems that arise (Kadam 2012).

- The clinical skill-mix needs careful consideration with clearly defined roles for doctors, nurses and pharmacists working coherently as a team.

- Doctors working in deprived areas may need smaller caseloads and longer consultations because of the increased complexity of their patients' medical needs.

- Instead of attending several disease-specific clinics, patients could have all of their chronic diseases reviewed in one visit by a team of health care workers. Ideally one team should have responsibility for co-ordinating their care. This may require training and development of 'generalists' skilled in the complexity of multiple diseases.

- The role of individual doctors as generalists and 'gatekeepers' to specialist care should be encouraged and developed (Haggerty 2012; RCGP 2012). The trend and current political policy has been for the patient to be a consumer and encouraged to move around between doctors, expressing choice; this may be counterproductive in the context of multi-morbidity and polypharmacy.

- In hospital, patients with multi-morbidity also require access to generalist clinicians who can co-ordinate their care, rather than having the outcome of their stay defined by which specialty they happen to be admitted under. The trend in recent years has been to increase the development of sub-specialties that may detract from seeing the overall or holistic needs of the patient. Geriatricians and orthogeriatricians have a valuable role to play here.

- The roles of the clinical pharmacologist in overseeing complicated drug treatments and doctors specialising in complex co-morbidity should be further enhanced.

- There is a place for care of the elderly specialists working at the interface between community and specialist care, in order to provide improved co-ordination of care and to ensure polypharmacy is appropriate.

These proposals are supported by a small qualitative study that explored the health care priorities of 26 patients with multi-morbidity (Bayliss *et al* 2008). Patients wanted convenient access to health care, individualised care plans, support from one co-ordinator of care, and continuity of relationships with health professionals. They also wanted health care providers who had a caring attitude and listened to them, appreciating that their needs were unique and fluctuating.

Patients tend to be fairly resistant to moving between doctors. This is in spite of changes towards systems that allow fairly ready change of registration with different practices in the NHS. It may be that this reluctance is appropriate and justified and that people recognise the benefits of continuity of care within a practice that has developed an understanding of their and their families' needs over a period of time.

Medicines management in care homes

Studies on polypharmacy in care homes help identify aspects of medicines management that may improve patient safety and quality of prescribing in this environment (Barber *et al,* 2009; Szczepura *et al,* 2011). Suggested approaches include:

- a lead GP for each care home

- appropriate monitoring of patients on riskier medicines and all patient's medication to be reviewed by a pharmacist

- one person (possibly a pharmacist) having overall responsibility for medicines use in the care home

- constant review of the use and accuracy of medication administration records (lack of protocols and adequate staff training is an issue)

- prescribing medicines for different times to ease busy morning drug rounds which can often be interrupted

- monitoring of omitted doses and ordering systems

- electronic administration systems

- prescribing audits.

Polypharmacy and stopping medicines

Most medicines do not need to be used lifelong. Primary care and specialist prescribers both should frequently reassess the risk-benefit profile of medications. There is much advice on when to initiate a medicine, but there is far less information and evidence to help support decisions to stop therapy. This is something that clinical guidelines need to address. It is also something to be tackled during training of clinicians, in order to help empower them to make what they may feel are clinically and ethically challenging decisions.

There are many reasons why withdrawing a medicine might be beneficial, ranging from a serious adverse reaction to a lack of clinical response. However, there may be a reluctance or indifference towards changing treatment, and 'stepping down' medication can be neglected. A change in the circumstances of a patient or their disease state may make the risk-benefit profile of certain medicines unfavourable. New evidence and changing guidelines may also affect the desirability of using a particular medicine. In cases where the risks of treatment outweigh the benefits it would obviously be prudent to review the medicine in question.

Stopping Medicines, a report by the Welsh Medicines Support Centre, suggested various questions a clinician could ask regarding continuation of prescribed medicines (WeMeReC 2010).

- Is the drug still needed?

- Has the condition changed?

- Can the patient continue to benefit?

- Has the evidence changed?

- Have the guidelines changed?

- Is the drug being used to treat an iatrogenic problem?

- What are the ethical issues about withholding care?

- Would discontinuation cause problems? Some therapies should not be stopped abruptly following long-term use.

As patients with multi-morbidity age and become frail, and preventive treatments become less meaningful, prescribers must identify when it is appropriate to broach the subject of scaling back or stopping treatment. They must then decide in what particular order to taper or eliminate treatments. This transition from disease-modifying treatment towards a palliative approach to care is a challenge (Burge 2012). Burge describes the hypothetical case of an older woman with five illnesses who lives alone. She has heart disease, severe osteoarthritis and rheumatoid arthritis, hypertension, and a foot ulcer; she is also poor

and socially isolated, with no children living nearby. One approach to this circumstance is to ask the 'Would I be surprised' question; in this case, 'Would I be surprised if this person were to die in the next 12 months?' (Boyd and Murray 2010). If the answer is 'no' it should trigger a discussion with the patient and caregivers about beginning a review of goals of care, with consequent revision of treatments and limitations on investigations. Burge points out that for patients who have borne a large burden of multiple drug treatments, frequent diagnostic testing, and numerous health care appointments, making this transition to care which is simpler and easier is often a relief.

An approach to identifying those who may benefit from scaling back treatment, assessing their needs and goals, and planning and communicating care is outlined in the Gold Standard Framework for people nearing the end of life (The Gold Standard Framework 2013). Taking this approach ensures a 'palliative approach' to care outside the usual circumstances where palliative care has been traditionally limited to specialised palliative or hospice programmes. Palliative care generally aims to improve the quality of life for people with life-limiting illnesses (and their families), by reducing suffering through early identification, assessment and treatment of pain, as well as meeting their and their families' physical, cultural, psychological, social and spiritual needs (Kristjanson *et al* 2003). Burge and colleagues recommend that such a palliative approach could be taken much earlier in the trajectory of life-limiting illnesses.

A recent study in Scotland estimated that only 29 per cent of all those who die have been identified and placed on a general practice palliative care register (Harrison *et al* 2012). Considering the prevalence of multi-morbidity, particularly with an ageing population, this suggests that only a small proportion of people who may benefit from a palliative approach to care may get it. Tools to support the identification of patients who are at risk of dying within a year are coming into common practice. An example is the Supportive and Palliative Care Indicators Tool (SPICT). The Scottish Patients At Risk of Readmission and Admission (SPARRA) tool uses hospital-based electronic data to assess risk of emergency admission over the next year but may also indicate high mortality risk (NHS Scotland 2009; Scottish Government 2010). Once patients are identified as being suitable for a palliative approach, there needs to be an active strategy to engage patients and families in the process.

Burge and colleagues advise that the transition to a palliative approach to care is not simply a 'transition' from one form of care to another (Burge 2012). Early symptom experience, diagnosis, patient education, and chronic disease self-management are all phases through which people progress. The palliative approach should be considered the last phase in the continuum of good care for patients with multi-morbidity in whom multiple active treatments are no longer appropriate.

Medication waste, medicines management and polypharmacy

A perhaps less often considered aspect of polypharmacy is the potential for medication waste. Appropriate medicines management may help contain this problem. A study commissioned by the Department of Health looked into the scale, causes and cost of medicine waste in 2009. The report found that unused prescription medicines costs the NHS at least £300 million per year in England and £150 million of this waste is avoidable (York 2010). Similar work in Wales indicates that more than 250 tons of out-of-date, surplus and redundant medicines are returned each year to pharmacies and dispensing GP surgeries, representing an estimated annual cost of £50 million. This is an underestimate of waste as many drugs are disposed of in domestic rubbish. Not all medicine waste is avoidable or a result of poor practice. Some waste is caused not by failures on the part of either patients or professionals, but by factors such as progression

in illness and changes in treatment. However, it is clear that there are significant improvements that could be made.

The evaluation identified some of the causes of medicine waste as (York 2010):

- patients recovering before their dispensed medicines have all been taken

- therapies being stopped or changed because of ineffectiveness and unwanted side effects

- patients' conditions progressing so that new treatments are needed

- patients' deaths

- factors relating to repeat prescribing and dispensing processes, which may cause excessive volumes of medicines to be supplied, independently of any patient action

- care system failures to support medicines taken by vulnerable individuals living in the community, who cannot independently adhere fully to their treatment regimens

- medicines prescribed during a hospital stay continued unnecessarily when the patient returns home

- patients stockpiling 'just in case' medicines and re-ordering repeat medication that they do not need.

It is clear that the potential for waste is much greater if many medicines are being prescribed together, particularly if the regimens are not synchronised or are overly complex. Suggestions identified in the report for reducing waste of prescribed medicines include:

- providing targeted support for patients starting new therapies and for those on unusually costly and/or difficult-to-take treatments

- supporting high-quality prescribing, and ensuring that medication and associated treatment regimens are effectively reviewed

- caring better for people who may not be taking their medicines correctly (often described as 'treatment-resistant')

- providing better support for isolated patients and other vulnerable groups of patients

- undertaking audits of the supply and use of monitored dosage systems

- enhancing hospital and primary care liaison, for example improving the quality of care at the time of hospital discharge

- delivering better-integrated terminal care in the domestic home setting

- developing more effective returns of waste medicines at national or local level and related public information campaigns.

4 Evidence-based polypharmacy

Clinicians practice in an environment where evidence-based medicine is the accepted practice. It is worth noting that the majority of clinical trials focus on single therapies. The impact of combining multiple interventions is rarely examined, nor is the effect outside the relatively artificial clinical trial environment.

In an editorial on the implications of the Heart Protection Study, Yusuf pointed out that aspirin, beta-blockers, ACE inhibitors and lipid-lowering therapies all lower the risk of future vascular events by about a quarter each in high-risk patients (for example, those who have established coronary heart disease) (Yusuf 2002). The benefits of each intervention appear to be largely independent, so that when used together in appropriate patients it is reasonable to expect that about two-thirds to three-quarters of future vascular events could be prevented. Added to this are the potential benefits of blood-pressure lowering (a 10mm Hg reduction in systolic blood pressure for example reduces the risk of vascular events by a quarter) and lifestyle intervention (for example, quitting smoking lowers the risk of myocardial infarction by a half). Yusuf points out that there are potentially large gains from combining currently known preventive strategies but this would also possibly entail multiple pill-taking. This was one of the early papers to propose a 'polypill' with multiple ingredients of relatively safe cardiovascular risk-lowering ingredients (Yusuf 2002) (*see* Table 3 below).

However this paper also notes the 'law of diminishing returns', in that each additional drug gives a smaller absolute reduction in risk. Ideally, the most important interventions should be maximised and treatments chosen that give greatest benefit with smallest harm.

Table 3 Reducing relative and absolute risk through polypharmacy

	Relative-risk reduction (per cent)	2-year event rate (per cent)
None	–	8
Aspirin	25	6
ß-blockers	25	4.5
Lipid lowering (by 1,5 mmol)	30	3
ACE inhibitors	25	2.3
Cumulative relative-risk reduction if all four drugs are used is about 75%		

Notes: The table shows the reductions achieved in relative and absolute risk by adding drugs to reduce risk of subsequent events in cardiovascular disease (secondary prevention).

Events=cardiovascular death, myocardial infarction, or strokes.

To calculate cumulative risk-reduction, multiplicative scale was used – eg, two interventions each reducing the risk of event by 30% would be expected to have about 50% relative risk-reduction [$1-(0.70 \times 0.70)$].
No interactions in treatment effects are observed in trials suggesting that proportionate risk-reduction of specific drug in presence or absence of other effective interventions would be expected to be similar. Smoking cessation lowers risk of recurrent myocardial infarction by about one-half after about two years. So, in smoker with vascualr disease, quitting smoking and use of four simple preventive strategies could theoretically have large potential benefit (say around 80% relative-risk reduction).

Source: Yusuf (2002)

In this way the pill burden can be reduced, with the potential for greater concordance, but with greatest gain. Several resources produced in Scotland have looked at this in more detail. To aid choice of treatments they give tables of absolute risk and benefit expressed in 'numbers needed to treat' and 'numbers needed to harm' (Wilson 2011; NHS Scotland 2012). They also provide useful information on drugs that are most associated with harm (*see* Resources section pp 34–44).

There is certainly a clear need for further research to improve quantification of the risk-benefit ratio of different drug interventions in the context of polypharmacy and in relation to real-life applications.

5 Prescribing and polypharmacy in older people

The issue of polypharmacy in relation to older patients is worth considering. Approximately one-fifth of people in the United Kingdom are now aged 65 or older, and this proportion is rising. In a Welsh Health Survey conducted in 2009, 86 per cent of respondents reported taking regular prescribed medication for a year or more, and in those aged over 75 the percentage was even higher (Welsh Health Survey 2009). Polypharmacy is commonplace and generally more problematic in older people; ageing is associated with a greater burden of disease. On the other hand there are examples of underuse of appropriate treatments in older people (Cancer Services Report 2012). In many instances the benefits of therapy can be greater than in younger people because baseline risk is higher (the absolute benefit is greater or numbers needed to treat (NNT) are lower).

Are drugs for older people effective?

There has been considerable reticence or resistance to actively treat cardiovascular risk factors in older patients, with specific concerns that it causes more harm than good and general concerns over polypharmacy and the medicalisation of old age (Oliver 2009). However, the clear reduction in overall mortality seen in the Hypertension in the Very Elderly Trial may put this into question (HYVET) (Beckett *et al* 2008) (*see* Table 4 overleaf). It demonstrates that where the baseline risk of an event is very high, the absolute gains can be considerable and exceed potential harm from treatment. Caveats are that relatively fit older people were selected in this trial and a Cochrane Review of hypertension in older people, which incorporated this study, did not show an overall benefit (Musini *et al* 2009). Similar gains are seen with statins, with patients recruited up to the age of 80 years in the Heart Protection Study of simvastatin (HPS 2002; Yusuf 2002) and the PROSPER study of pravastatin (Shepherd *et al* 2002).

Trials like these are unusual however; evidence of benefit for most medicines is obtained from clinical trials where subjects with more than one morbidity, those taking other medicines, or older people are often excluded. Many clinical guidelines and standards recommending use of medicines are routinely applied in practice to older people, despite weaker supporting evidence for such use. It could be argued that specific guidelines are required for older people. Unfortunately, clinical trials may fail to identify adverse drug events (ADEs) and drug interactions in older patients (Cresswell *et al* 2007). The way that clinical trials are conducted is also unsuccessful in evaluating the impact that a medication regimen has on quality of life, and on personal and social factors, such as support needs; this is a general failing, although it is probably particularly relevant for old persons. For these reasons it can be difficult to assess the burden of treatment and to gauge overall benefit compared to harm in older people.

Prescribing for older patients therefore presents particular challenges. The risk of under-treatment needs to be balanced against that of over-treatment and unrealistic expectation. There is a possibility of positive discrimination because of concerns about equalities and age discrimination. Being too focused on one aspect of risk, such as hypertension, may

Table 4 The Hypertension in the Very Elderly Trial (HYVET)

| | Rate per 1000 patient-yr (no. of events) | | Unadjusted hazard ratio | |
| | Indapamide | Placebo | | |
	No. (%)		95% CI	p-value
Primary outcome Fatal/nonfatal stroke	12.4 (51)	17.7 (69)	0.70 (0.49-1.01)	0.06
Death from stroke	6.5 (27)	10.7 (42)	0.61 (0.38-0.99)	0.046
Death from any cause	47.2 (196)	59.6 (235)	0.79 (0.65-0.95)	0.02
Death from non-CV/unknown causes	23.4 (97)	28.9 (114)	0.81 (0.62-1.06)	0.12
Death from CV cause	23.9 (99)	30.7 (121)	0.77 (0.60-1.01)	0.06

Notes: 'HYVET's goal was to evaluate the benefits and risks of providing medical care to very elderly individuals presenting with hypertension'.

■ 3,845 patients: age >80 years, systolic BP>160 mmHg, 12 per cent history of CVD, 7 per cent DM

■ Median follow-up 1.8yrs

■ Target BP 150/80 – indapamide +/- perindopril vs. placebo +/- placebo

Primary endpoint: fatal and non-fatal strokes

'There have been no conclusive results suggesting benefit in treating patients with hypertension over 80 years of age.'

Source: Beckett *et al* (2008)

NICE guidelines on managing hypertension
1. Offer people aged 80 years and over the same antihypertensive drug treatment as people aged 55 to 80 years, taking into account any co-morbidities.

2. Aim for a target clinic blood pressure below 140/90 mmHg in people aged under 80 years with treated hypertension. Aim for a target clinic blood pressure below 150/90 mmHg in people aged 80 years and over, with treated hypertension.

Source: NICE (2011)

lead to decisions to treat disease or to try to prevent future disease when the treatment is unnecessary or unwelcomed by the patient. Providing treatments for some diseases can be viewed as selecting for other causes of death (Mangin and Jamoulee 2012), highlighting the importance of doctors communicating risks and benefits with patients in the decision-making process. A recent review on frailty notes that we need to develop more efficient methods to detect frailty in older people and to measure its severity in routine clinical practice, particularly in primary care. To do this would inform the appropriate selection of older people for invasive procedures or drug treatments and could be the basis for a shift in the care of frail older people towards more appropriate goal-directed care (Clegg *et al* 2013). Perhaps what should be the over-riding issue is the wishes of the individual patient, once fully informed of the risks, benefits and uncertainties of treatment based on their own personal circumstances.

Medication reviews, polypharmacy and older people

Doctors may not be aware of all the drugs their older patients are taking. Frank and colleagues reported that in a study in Canada 37 per cent of patients were taking drugs without their doctors' knowledge, and 6 per cent of patients were not taking medications that were on their doctors' lists. When past medical history and a patient's active drug profile are incomplete, doctors may not consider drug interactions as a possible cause for the presenting complaints of older patients (Frank *et al* 2001). As this study was conducted more than a decade ago it may not reflect current practice. Another study also from more than a decade ago noted that atypical presentation of disease or vague presenting complaints such as confusion, falls, urinary incontinence and weakness could

mask or confuse the detection of drug interactions (Gaeta *et al* 2002) – a finding that intuitively seems still to be relevant.

Several different doctors may be involved in prescribing treatment for older patients although this may occur more in countries where the role of the GP as co-ordinator of care and provider of subsequent prescriptions is less well defined. In one study the risk of receiving an inappropriate drug combination was directly related to the number of doctors who were prescribing drugs for that older patient (Tamblyn *et al* 1996).

6 Polypharmacy and the patient experience

Reviews of medicines management often lack approaches on how to incorporate the patient's viewpoint. Considerable work is taking place to improve patient information using patient decision aids; this is not reviewed in detail here but there are some excellent resources available (*see* Resources section, pp 34–44). People taking multiple medicines long term have to develop strategies for fitting these into the routine of daily life. Qualitative research indicates that many people consider that they have little control over whether and how they use their medicines. Prescribers and other health care professionals may not recognise the significant demands placed on patients in managing the use of multiple medicines, and they should endeavour to adopt a style that explores the patient's perceptions and concerns in routine consultations. One recent piece of research indicates that while many patients adapt to long-term medicines use, others find that the demands their regimen places on them is detrimental to their quality of life (Krska, personal communication 2013). For these reasons, the patient perspective on medication-taking needs to be determined and recorded. Compromises may often need to be reached between the view of the prescriber in delivering interventions intended to improve outcome, and the choice made by the patient, based on the demands of the medication regimen. The alternative is the potentially wasteful process of prescribing where the patient does not take the medicines appropriately, or does not take them at all, but the prescriber unwittingly continues to supply prescriptions. Various estimates of long-term drug use indicate that as many as 40 per cent of people on long-term prescriptions do not take them as intended (Department of Health 2001).

7 Summary

Despite the common use of the word 'polypharmacy' for more than 150 years in both British and US medical literature, there is no clearly accepted definition. In the past, it was considered poor practice and frowned on to prescribe several medications at the same time to a patient. Increasingly it is recognised that polypharmacy is a 'necessary evil' that for many patients is required to improve clinical outcome. However, it still remains the case that some people are prescribed multiple medications potentially unnecessarily, when they are unlikely to benefit or where drug interactions are likely to cause harm. For these reasons, this report recommends a definition of polypharmacy where it can be considered either appropriate or problematic. Furthermore, the use of simple thresholds to define polypharmacy may be unhelpful, and less crude methods are recommended.

Polypharmacy is certainly a common and growing global issue, affecting primary and secondary health care settings. This is driven by our ageing population and by the increasing levels of multi-morbidity. Numerous evidence-based guidelines help drive the increase in polypharmacy, yet rarely advise on how to manage multi-morbidity. There is a need to have research and guidance that covers commonly associated co-morbidity together with the associated polypharmacy. It is also necessary to address the increasing specialisation of clinicians, and the need to train clinicians with specific expertise in managing co-morbidity and clinical complexity, in addition to wider generalist skills. This all requires a significant change in policy and poses a considerable challenge. Further research is also required to examine systems and processes designed to improve medicines management in relation to polypharmacy.

Finally, another important challenge in the area of polypharmacy is that of working alongside patients to empower them to make informed choices about treatments and the burden of pills they are expected to consume. Increasingly, it is recognised that many people find their medication regimens an unpleasant chore and this can in its own right detract from their quality of life. If this is not managed well, medicines will not be taken as the prescriber intends, resulting in significant and costly waste, and of course a failure to realise the anticipated benefits of treatment.

8 Case examples and practical tips

Case example 1

An example of uncorrected, potentially problematic polypharmacy

The following table shows the medications prescribed for a 75-year-old woman with multiple morbidities. Four specialists were involved in the care of this lady. She had ischaemic heart disease and paroxysmal atrial fibrillation, and a number of her cardiac medications were initiated following acute hospital admissions. She also had frequent infective exacerbations of chronic obstructive pulmonary disease (COPD) and suffered from various gastrointestinal problems, Parkinson's disease and anxiety.

Indication	Medication	Formulation, dose and frequency
Coronary heart disease with paroxysmal atrial fibrillation and history of myocardial infarction	Aspirin	75 mg dispersible tablets, once daily
	Simvastatin	40 mg tablets, one at night
	Verapamil hydrochloride	240 mg M/R tablets, one in morning
	Digoxin	125 microgram tablets, one at night
	Glyceryl trinitrate	Sublingual spray, 1–2 puffs as required for angina
	Furosemide	40 mg tablets, one in morning
COPD with bronchiectasis	Seretide	250 Evohaler, 2 puffs twice daily
	Ventolin	100 Evohaler, 2 puffs up to 4 times daily
Dyspepsia, previous history of peptic ulcer, biliary reflux, previous history of portal vein thrombosis and portal hypertension with oesophageal varices, irritable bowel syndrome, constipation	Peptac	Liquid, 5–10 ml as required for indigestion
	Omeprazole	20 mg E/C capsules, twice daily
	Domperidone	10 mg tablets, two 3 times daily
	Mebeverine hydrochloride	135 mg tablets, two 3 times daily
	Docusate sodium	100 mg capsules, two twice daily
	Senna	7.5 mg tablets, two as required at night for constipation
	Glycerol	700 mg suppositories, one as required in morning for constipation
Parkinson's disease	Ropinirole hydrochloride	8 mg M/R tablets, three in morning
	Amantadine hydrochloride	100 mg capsules, one at breakfast
	Co-Careldopa	25/100 tablets, one and a half tablets at breakfast, lunch and teatime
	Co-Careldopa	50/200 M/R tablets, one tablet at night
	Co-Beneldopa	12.5/50 dispersible tablets, two in morning
Long-term health anxiety	Amitriptyline Hydrochloride	25 mg tablets, one in morning and two at night

While it is possible that all these drugs were necessary, it is likely that the regimen could have been rationalised based on a multidisciplinary team review.

Case example 2

An example of possible questions to ask when faced with potentially problematic polypharmacy

This case is of a 60-year-old woman, managed by her GP, who had breast cancer diagnosed five years ago which was initially treated with Herceptin (trasuzumab). She developed metastatic disease, with pain in the thoracic spine and right hypochondrium, and experienced a fit probably due to brain metastases. She had been taking tramadol for a few weeks for pain, and was started on a fentanyl transdermal patch a few days ago. She had become increasingly tired and nauseated, and was unable to attend the GP surgery requiring home visits. She had been on a long-term statin for hypercholesterolaemia, took an SSRI antidepressant, and complained of dyspepsia. She also had heart failure attributed to previous Herceptin therapy, and remained short of breath. Her medications were as follows:

Indication	Medication	Formulation, dose and frequency
Pain	Paracetamol	500 mg tablets, four times daily
	Naproxen	250 mg tablets, three times daily
	Ibuprofen	200 mg tablets, three times daily
	Tramadol	50 mg capsules, 1–2 capsules up to 4 times daily as required for pain
	Fentanyl	25 microgram/hr patch, one patch applied every 72 hours
Depression	Fluoxetine	20 mg capsules, one in morning
	St John's Wort	One over-the-counter capsule daily
Heart failure	Furosemide	40 mg tablets, one in morning
	Ramipril	5 mg tablets, twice daily
Primary cardiovascular risk prophylaxis	Simvastatin	40 mg tablets, one at night
	Aspirin	75 mg E/C tablets, once daily
Dyspepsia	Gaviscon Advance	Suspension, 5–10 ml as required for indigestion
	Co-magaldrox	195/220 suspension, 10–20 ml after meals
Breast cancer	Tamoxifen	20 mg tablets, once daily

There are a number of potential problems with her medication regimen, reflecting potential drug interactions, and possible side effects contributing to many of her symptoms. Her regimen may benefit from rationalisation. A number of possible questions may be asked by the clinician:

■ She is on two NSAIDs, but her pain is still not adequately controlled. There is a significant risk of gastrointestinal bleeding, compounded by aspirin and SSRI therapy and lack of gastro-protection. It may also be aggravating the nausea, and any resulting anaemia may be contributing to dyspnoea. Could one or both be stopped, and opioid analgesia optimised?

■ The SSRI and tramadol may lower the seizure threshold resulting in more fits. Does she need to continue the fluoxetine? Can the tramadol be switched to alternative opioid analgesia? There is also an increased risk of developing serotonin syndrome with this combination of medications.

■ Would an alternative opioid analgesic for breakthrough pain be preferable to tramadol, particularly as the patient has been commenced on a long-acting opioid in the form of fentanyl, and given the potential for complications as a consequence of serotonin effects?

- Herbal remedies such as St John's Wort are often not considered. However, this product interacts with a number of conventional medications and may have additional undesirable serotonin effects. Its very use also raises questions about the efficacy and continuing need for the SSRI.

- The combination of NSAID, ACE inhibitor and loop diuretic may lead to renal dysfunction. The NSAID may also counteract her diuretic, aggravating fluid retention and contributing to dyspnoea. Can the NSAID be stopped? Could renal impairment be contributing to fatigue?

- The combination of SSRI and loop diuretic may cause hyponatraemia. This may in turn aggravate seizures. Have the electrolytes been checked? Is there room to stop one of these drugs?

- Is a proton pump inhibitor or H2-receptor antagonist indicated for dyspepsia? The dyspepsia may also resolve if the gastro-irritant medications are stopped.

- Is the dose of fentanyl too high (approximately equivalent to 90mg of oral morphine per day)? This may depend on previous tramadol usage, particularly as it was prescribed 'as required'. Consideration should be given to whether it is necessary to use fentanyl as the opiate of first choice, and whether prescribing by brand might be appropriate. It may be contributing to both tiredness and nausea.

- Is there a clear indication for aspirin? Aspirin is not indicated for primary prevention. It also contributes to gastrointestinal bleeding, particularly in the presence of other NSAIDs. Furthermore, its effect may be antagonised by ibuprofen.

- Similarly, although the patient has a history of raised cholesterol, is she likely to get continued benefit from simvastatin?

- Treatment with two antacids is probably not ideal. Would a proton pump inhibitor or H2 receptor antagonist be appropriate? Or indeed, would there be any symptomatic benefit from stopping the gastro-irritant drugs?

Some or all of these issues could be considered by the GP, depending on their experience, although a multidisciplinary team meeting may be indicated. Consideration should probably be given to discussing end-of-life care, with a view to alleviating her pain, nausea and dyspepsia, and if possible also trying to improve her dyspnoea and fatigue.

Case example 3

An example of how effective medication review can address potentially problematic polypharmacy

This concerned a 90-year-old woman who had a previous history of myocardial infarction, severe aortic stenosis and heart failure. She also suffered from asthma, osteoporosis and hypothyroidism. She underwent aortic valve replacement and was discharged to a care home on the following medicines, where her care was primarily managed by her GP.

Indication	Medication	Formulation, dose and frequency
Coronary heart disease, heart failure	Isosorbide mononitrate	60 mg M/R capsules, once daily
	Digoxin	62.5 microgram tablets, once daily
	Bumetanide	1 mg tablets, four in morning
	Simvastatin	40 mg tablets, one at night
	Clopidogrel	75 mg tablets, once daily
	Captopril	25 mg tablets, twice daily
	Bendroflumethiazide	2.5 mg tablets, one in morning
	Amiodarone	200 mg tablets, once daily
	Glyceryl trinitrate	Sublingual spray, 1–2 puffs as required for angina
Asthma	Salbutamol	CFC-free inhaler 100 micrograms/puff, two puffs up to 4 times daily as required
Osteoporosis	Calcichew D3 Forte	1.25g tablets, twice daily
Prophylaxis against GI bleed	Lansoprazole	30 mg capsules, once daily
Hypothyroidism	Levothyroxine sodium	50 microgram tablets, once daily

Due to improvements in the heart failure following her cardiac surgery, the bendroflumethiazide was stopped and bumetanide reduced. However, her quality of life was poor over the next six months, and she experienced nausea and diarrhoea. The lansoprazole was also recognised as a potential cause for the latter, but the GP was reluctant to stop this because of continued mild iron deficiency anaemia, for which ferrous sulphate was also prescribed.

A domiciliary visit from a care-of-the-elderly specialist was requested, and a decision made to focus on symptomatic treatment and quality of life. The amiodarone, clopidogrel and simvastatin were stopped, the bumetanide further reduced, and lansoprazole changed to ranitidine. The full blood count remained stable and the ferrous sulphate was stopped. The patient's symptoms resolved as a result of these changes. Quality of life improved considerably and was maintained for a further four years. This revised medication regimen, which could be considered 'appropriate polypharmacy', is summarised in the table below.

Indication	Medication	Formulation, dose and frequency
Coronary heart disease, heart failure	Isosorbide mononitrate	60 mg M/R capsules, once daily
	Digoxin	62.5 microgram tablets, once daily
	Bumetanide	1 mg tablets, once daily
	Captopril	25 mg tablets, twice daily
	Glyceryl trinitrate	Sublingual spray, 1–2 puffs as required for angina
Asthma	Salbutamol	CFC-free inhaler 100 micrograms/puff, two puffs up to 4 times daily as required
Osteoporosis	Calcichew D3 Forte	1.25g tablets, twice daily
Prophylaxis against GI bleed	Ranitidine	150 mg tablets, twice daily
Hypothyroidism	Levothyroxine sodium	50 microgram tablets, once daily

Practical tips on medicines management of polypharmacy

■ 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.

■ 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.

■ Provide clear written instructions and a dosing schedule.

■ Ensure that the directions on each prescription item identify the problem it is intended to treat.

■ Be aware of the known pitfalls with specific drugs and recognised drug interactions. You should carefully consider and avoid hazardous prescribing wherever possible.

■ It is important to put systems in place to ensure consistent and appropriate biochemical monitoring takes place for high-risk medicines, eg, lithium, disease-modifying anti-rheumatic drugs (DMARDs), warfarin.

■ 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.

■ 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.

■ 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.

■ Avoid use of the term 'as directed' and put specific dosage instructions on prescriptions.

■ 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?

■ Try to substitute rather than add to medication regimens.

■ Think of introducing drugs as a trial: do not forget to stop treatment that is unnecessary or ineffective.

9 Resources

Resource 1

The Quality Of GP Prescribing, The King's Fund research paper, August 2011.
Summary of recommendations and proposals for quality indicators (Duerden *et al* 2011)

Duerden MG, Avery A, Millson D, and Smart S (2011). *The Quality of GP Prescribing.*
London: The King's Fund. Available at: www.kingsfund.org.uk/sites/files/kf/field/field_
document/quality-gp-prescribing-gp-inquiry-research-paper-mar11.pdf (accessed 26
June 2013)

**Demonstrate use of systems to reduce medication error and potential for
drug interaction**
GPs should be able to demonstrate that they have systems in place to help guard against
medication errors. These include: ensuring that prescribers have access to all necessary
information about the patient and their medication at the point of decision-making; use
of computerised hazard alerts and reference sources such as the *current* British National
Formulary (BNF) when making prescribing decisions; and having robust systems for
repeat prescribing, laboratory test monitoring and medication review.

Evidence of significant event reviews arising from prescribing errors
Significant events relating to medication error should be investigated and lessons learned
within an 'appropriate blame' culture. If there is an obvious theme (ie similar packaging
resulting in two drugs being confused) that might affect other practices, this should be
flagged up to the primary care organisation (PCO) or clinical commissioning group
(CCG) and the National Patient Safety Agency. For individual GPs these events could be
reflected on at the time of appraisal.

**Assess individual GPs' prescribing against safety indicators developed by the Royal
College of General Practitioners**
The intention is that prescribers will be able to use the RCGP prescribing safety indicators
to audit their prescribing and to make improvements. The indicators could be used to
prompt significant event audits and as evidence for discussion at appraisals. In the future,
it is possible that prescribing safety indicators could form part of revalidation of GPs.

Reduce risk of dispensing errors by uptake of electronic transmission of prescriptions
The Electronic Prescribing Service has potential to reduce the risks of dispensing errors
and its continued roll-out and evaluation should be encouraged.

Demonstration of response to National Patient Safety Agency (NPSA) alerts
Each GP and practice should be able to clearly demonstrate the action they have taken in
response to NPSA (or its successor organisation) alerts: recent examples are for warfarin,
lithium and 'loading doses'. Ideally, audit material should be provided as evidence.

**Demonstration that patients' views about medicine-taking are explored and their
choice considered at the point of prescribing**
This could be investigated using patient experience surveys. GPs could develop systems
to record and demonstrate that discussions have taken place, particularly with high-risk

medicines and/or those used for the treatment of long-term conditions. GP training needs to reinforce the communication skills aspect of this.

Suitable, accredited information on medicines and the medical conditions they treat are provided on the Internet (or supplied) for patients to access

Ready access to patient decision aid material can be provided usually via computer. The GP computer system can be configured to indicate when a patient information leaflet has been issued and this can be recorded in the medical record.

Repeat prescribing systems have been audited to ensure accurate and timely supply of medicines in accordance with a written repeat prescribing protocol

Practices should have a written repeat prescribing protocol and should undertake audits to help ensure compliance with this. Patient surveys may also be valuable in assessing patient views on the repeat prescribing system. Practices will need to adapt their repeat prescribing protocols in light of the introduction of electronic transfer of prescriptions from general practices to dispensing contractors.

There is demonstrable co-ordination of prescribing between hospitals and general practice

The Care Quality Commission already requires that, in England, discharge summaries are shared with patients and issued to GPs within 72 hours of discharge. These summaries should contain details of any medication prescribed at the time of discharge along with any adverse reactions or details if the patient experiences an allergy to medication during admission. There should be a regular audit of both admission letters and discharge summaries to determine that they contain accurate and useful information about medicines. General practices need to be able to demonstrate robust systems for medicines reconciliation after patients are discharged from hospital.

Practices should demonstrate that medication review is done regularly and effectively and to a high standard. Clinical pharmacists should be involved where practicable

Careful assessment of medication reviews should be conducted to determine that they are of high quality. This is already required by the Quality and Outcomes Framework but scrutiny has proved difficult. Review by experienced practice pharmacists should flag up areas of concern or significant events, and these should be considered at practice level, and lessons learned.

Close co-operation between the practice and community pharmacy should be demonstrated

This may be difficult where there are many local pharmacies. Ideally each practice should have regular meetings with the pharmacies that are most closely related to them. Where pharmacists flag up significant medication issues they should be given feedback on how these have been dealt with. Likewise, if GPs encounter dispensing errors or inappropriate advice given to patients there should be a frank and open discussion.

Extra support is provided to assess patients who need to take six or more medicines (appropriate polypharmacy)

Six-monthly reviews of patients on four or more medications is already a Quality and Outcomes Framework target. GPs and practices should be able to demonstrate that they have robust systems for review of more complex patients and that this process is clearly recorded and audited.

GPs should have ready access to accredited, concise, high-quality information on drugs. Access to this high-quality information should be demonstrated as part of appraisal and revalidation (linkage at point of access is ideal)

GPs should have systems to demonstrate how they access prescribing support materials and drug information. Ideally a record should be kept of these access events. Examples of the use of these materials should be demonstrated at the time of appraisal; for example,

where an important learning point has been encountered, this can be discussed. Systems for electronically logging access to information could be used.

All prescribers should have ready access to a fast and reliable Internet connection

This should be happening already but we encountered evidence that Internet access could still be a problem for some prescribers. There should be scrutiny to ensure that practice NHS Internet access is 'fit for purpose'.

Multi-faceted systems are used to inform GPs and keep them up-to-date (newsletters, email, events etc)

The PCO/CCG should ensure that sufficient effort is made to supply practices with relevant information and that there is a medication/prescribing communication strategy. Funding may be required for high-quality medicines information. This needs regular review.

Practices should have agreed preferential drugs that they become familiar with (formularies) and demonstrate adherence to. These should be relatively cost-effective to the health care economy

The practice or area should have an agreed formulary. This has important safety implications as well as ensuring cost-effectiveness and consistency. By developing familiarity this ensures quick recognition of problems, such as incorrect doses.

Practices should have agreed policies on their interaction with drug company representatives. GPs should be aware of potential biases in information sources

Having an explicit policy or 'rules of engagement' ensures a consistent approach to drug company representatives and helps in consideration of conflicts of interest. There should be regular training in critical appraisal skills and understanding of sources of bias for all prescribers. Such training could be explored and reflected on at the time of appraisal.

Networks are in place and active between GPs and other informed prescribing advisers

A Quality and Outcomes Framework target already encourages regular meetings with the locality prescribing adviser. Topics like comparative prescribing information or local policies can be discussed with a view to encouraging reflection and, where appropriate, change. GPs should be able to demonstrate that they have regularly attended such meetings. They can give feedback on the usefulness, or otherwise, of these encounters.

Patients accept switching of medicines to reduce costs but there should be careful communication of the reasons and ready access to the prescriber, if required

Patients generally have a preference for face-to-face encounters if medication switches are made. However, we came across evidence that this can be successfully achieved using written communication. If medication switches are made for economic reasons there should be explicit and careful communication of the reasons for such changes, under agreed operating procedures. The programme should be carefully evaluated and there should be collation of information about the success, or otherwise, of the change process. If patients are unhappy or concerned they must have ready access to the prescriber.

Systems to enable GPs to be more cost-aware in prescribing choices should be developed and used. Patients should have greater understanding of the cost of medicines

It is generally agreed that GPs do consider costs when making drug choices. More could be done to flag up cost implications at the time of prescribing. It is also possible that drug wastage by patients would be less if the costs of medication supplied were made explicit. Consideration should be given to research to see if medication adherence can be improved by labelling prescriptions with the cost to the NHS.

Generic prescribing rates are a good indicator of quality and value for money

Generic prescribing is clearly regarded as a marker of quality prescribing in the United Kingdom as long as due regard is given to when generic prescribing may be inappropriate. GPs or practices with low generic prescribing rates should be encouraged to increase their use of generic preparations.

Pricing structure of drugs should ensure that brands are not priced more cheaply than generics

The system that causes branded generics to undercut generic prices in the Category M basket requires urgent revision. It can perversely encourage switching from generic prescribing back to brand prescribing which is counter to years spent encouraging generic prescribing as a principle. This is also confusing for patients.

Use of decision support prescribing systems

Increasingly, prescribing support software (eg ScriptSwitch®) is being commissioned and programmed by primary care. Such software links to GP clinical systems, to provide prescribers with local formulary choices and advice on the latest cost-saving, safety and effectiveness issues relating to medicines. At the point of prescribing, the software will offer alternative prescribing options if these are cheaper than the one initially selected, or messages reminding clinicians of any relevant information. This support software has an important role in offering cost-effective prescribing choices and in keeping prescribers updated and engaged with local decision-making. Appropriate use of these systems seems a valuable intervention and should be supported as an example of intelligent 'decision support'.

Robust training of prescribers-in-making and junior prescribing

Unfortunately the funding for the eLearning for Healthcare *Prescribe* project has now been withdrawn as part of the government's financial cuts. The project has been mothballed. When we prepared The King's Fund research paper on the *Quality of GP Prescribing* our view was that this was a vital development to ensure better education of medical students and young doctors and to encourage them to be better and safer prescribers. By helping doctors to avoid medication errors, and by making junior prescribers cost-aware, it was highly likely to be cost-effective. The *Prescribe* project should be reinstated.

Regular updating on therapeutics demonstrated via appraisal and revalidation

Our review concluded that formal, continuing postgraduate training in prescribing and therapeutics is necessary. PCOs could be measured against how many of their contracted GPs have undergone such training. This training should also be part of the GP appraisal and revalidation process as it is essential that all doctors keep up-to-date in this area of their work.

Transfer of admission medication and discharge medication streamlined

It seems strange that after so many years of concern communication between practices and hospitals remains poor, as pointed out in the recent Care Quality Commission report. Robust systems for electronic transmission of vital medication and other clinical data should be developed rapidly. We are aware of exemplary practice and this should be shared and disseminated.

Transfer of knowledge from exemplary systems demonstrated – implementation of best practice

As with admission and discharge data there are many examples of good practice that can be shared and promulgated. The National Prescribing Centre has been very effective in providing the mechanism for this on a national basis. This promulgation should be maintained and enhanced and should focus on stimulating good prescribing and medicines management practice by GPs, alongside educational support.

Resource 2

Good prescribing practice in older people

Derived from: 'Prescribing For Older People', *WeMeReC Bulletin 2011* (WeMeReC 2011). From: www.wemerec.org/ (accessed 28 June 2013)

- **Use drugs that are familiar.** Prescribers are advised to limit the range of drug preparations they use to those with which they are thoroughly familiar. The British National Formulary (BNF) lists available medicines, and those considered 'less suitable for prescribing' are noted and should be avoided.

- **Use the lowest effective dose.** Titrate up from low doses slowly. Doses in older people are often substantially lower than in younger adults because pharmacokinetics and pharmacodynamics alter with age. Factors such as increased body fat and reduced lean body mass, reduced body water, and lower serum albumin concentration may affect initial drug distribution. Other significant factors that will affect doses of ongoing treatment include:
  - reduced renal function
  - reduced hepatic function
  - reduced haemostatic reserve
  - increased sensitivity/changes in drug receptors.

- **Anticipate drug interactions.** Potential interactions between drugs should be screened for, as should 'drug–food', 'drug–alcohol', and 'drug–herbal' interactions. Be alert to the use of over-the-counter medicines, complementary products, old prescriptions or out-of-date medicines, and 'shared' medication. Although interactions may not always be associated with adverse outcomes, many probably go unrecognised or are attributed to other causes. Polypharmacy can be associated with complex networks of interactions, but many common interactions are identifiable.

- **Be alert to adverse drug events (ADEs).** Adverse drug events can be the result of interactions between drugs or more frequently 'drug–disease' or 'drug–patient' interactions. Common ADEs that are often not attributed to medication include confusion, constipation, hypotension and falls. Some ADEs may occur as a result of one or more contributing factors. The impact of potential harm from ADEs cannot be underestimated. Severe ADEs account for 5 to 17 per cent of hospital admissions for older patients and are associated with significant morbidity and mortality. Less severe ADEs can also be detrimental as they reduce quality of life and may adversely affect patient concordance; they may limit the choice of available therapies, and can cause diagnostic confusion.

- **Monitor therapy.** Prescribing responsibility extends to monitoring medicines use, especially given the potentially harmful effects of medicines commonly prescribed for older people. Several studies have identified anticoagulants, opioids, insulins, thiazide diuretics, NSAIDs and antipsychotics in dementia as the drugs that represent 'areas of greatest harm and potentially, greatest opportunity for improvement'. Drugs which are deemed suitable for prescribing in primary care only under 'shared-care' agreements (eg amiodarone, methotrexate, leflunomide) should have monitoring requirements specified in pre-defined protocols.

- **Initiation of a medicine should be considered as a trial.** Discontinuation is always an option. Stopping medicines is often feasible in older patients with no adverse consequences.

- **Avoid the prescribing cascade.** When ADEs are misinterpreted as a new disease and treated with new medication, a 'prescribing cascade' is established. The additional treatment has the potential to further complicate the patient's clinical picture and

compound their risk. In circumstances where a medicine is not efficacious or ADEs are complicating therapy, a strategy of substitution is preferred.

- **Promote concordance.** Various approaches have been used to optimise prescribing and reduce inappropriate medicines use, but good communication with the patient is vital. Up to half of patients do not take their medicines 'as expected'.

- **Involve carers where reasonable.** Informal (family and friends) or formal carers can play an important role in supporting medicines use. Clarifying roles and lines of communication, and ensuring consistency in the provision of care is an area that frequently presents challenges.

- **Recognise system weaknesses.** Risk factors for inappropriate prescribing that are associated with systems of care include:
  - discharge from hospital/facility in last four weeks
  - multiple doctors/health professionals
  - need for carers/residential care
  - changes to medicines in last three months
  - repeat prescribing.

  These risk factors highlight the **significance of interfaces** between primary care, secondary care, home or residential care, and between individual health professionals – points where care can become fragmented, and where good communication and documentation are most needed, but often lacking.

- **Repeat prescribing and medication review.** Following good practice when issuing repeat prescriptions (ie, making authorisation checks and undertaking medication review) is essential in providing care for older people.

Resource 3

Polypharmacy guidance

Derived from: *Polypharmacy Guidance*, NHS Scotland, October 2012 (NHS Scotland 2012)
www.central.knowledge.scot.nhs.uk/upload/Polypharmacy%20full%20guidance%20v2.pdf
(accessed on 26 June 2013)

The Scottish Government has issued guidance on 'Appropriate prescribing for patients and polypharmacy guidance for review of quality, safe and effective use of long-term medication'.

In Scotland all NHS boards are expected to ensure that they have in place firstly, plans to review patients identified as high-risk by multidisciplinary teams and, secondly, systems to allow for evaluation of the impact of these patient reviews.

A multidisciplinary group from NHS boards across Scotland developed the guidance.

Prescribers are frequently faced with two often overlapping situations where extra thought and consideration are needed:

- when faced with a patient who is either on or has indications to be on multiple medications

- when a patient is 'frail' in a medical sense. 'Frailty' in this guideline is taken to describe a state where a patient has a reduced ability to withstand illness without loss of function.

This guidance aims to:

- provide information about patient groups that NHS boards should consider as a higher priority for polypharmacy review

- outline a robust and pragmatic process of medication review in these patient groups

- provide NHS boards with tools that can then be adapted for local use as guidance for clinicians undertaking the reviews; where possible relevant documentation and guidance has also been provided. It should be stressed to clinicians that this guidance should be read before carrying out reviews, rather than be used as a checklist during reviews. It aims to provide background information to help clinicians conduct this level of medication review.

Resource 3

Resource 4

Use of medicine framework: Australia tool

Scott IA, Gray LC, Martin JH, Mitchell CA (2012). 'Minimizing inappropriate medication in older populations: a 10 step conceptual framework'. *American Journal of Medicine,* vol 125, pp 529–37.

The increasing burden of harm resulting from the use of multiple drugs in older patient populations represents a major health problem in developed countries. Authors estimate that in Australia approximately 1 in 4 older patients admitted to hospitals are prescribed at least 1 inappropriate medication, and up to 20 per cent of all inpatient deaths can be attributable to potentially preventable adverse drug reactions.

To minimise this drug-related harm, this paper proposes a quality use-of-medicine framework that comprises 10 sequential steps:

1 ascertain all current medications

2 identify patients at high risk of or experiencing adverse drug reactions

3 estimate life expectancy in high-risk patients

4 define overall care goals in the context of life expectancy

5 define and confirm current indications for continuing treatment

6 determine the time until benefit is obtained for disease-modifying medications

7 estimate the magnitude of benefit versus harm in relation to each medication

8 review the relative utility of different drugs

9 identify drugs that may be discontinued

10 implement and monitor a drug minimisation plan with ongoing reappraisal of drug utility and patient adherence by a single nominated clinician.

The framework aims to reduce drug use in older patients to the minimum number of essential drugs, and its utility is demonstrated in reference to a hypothetic case study. Further studies are warranted in validating this framework as a means for assisting clinicians to make more appropriate prescribing decisions in at-risk older patients.

Resource 5

NICE guidance on medicines adherence

Derived from: NICE (2009). *Medicines Adherence (CG76)*. National Institute for Health and Clinical Excellence. www.nice.org.uk/CG76 (accessed on 26 June 2013)

In January 2009 NICE produced a clinical guideline on medicines adherence. This guideline points out that it is believed that between a third and a half of all medicines prescribed for long-term conditions are not taken as recommended. It states that if the prescription is appropriate, then this may represent a loss to patients, the health care system and society. The guideline asserts that non-adherence should not be seen as the patient's problem. It represents a fundamental limitation in the delivery of health care, often because of a failure to fully agree the prescription in the first place or to identify and provide the support that patients need later on.

Possibly the most important aspect of this guideline is the explicit recognition that we should be more frank and open about the reality of non-adherence; it should be recognised that non-adherence may be the norm (or is at least very common) and to take a no-blame approach, actively encouraging patients to discuss non-adherence and any doubts or concerns they have about treatment. This 'patient-centred' guideline recommends identification of specific perceptual and practical barriers to adherence for each individual, both at the time of prescribing and during regular review, because perceptions, practical problems and adherence may change over time. It gives advice on how best to communicate with patients and the issues to be addressed at medication review.

Resource 6

Some useful sources of information on patient decision aids and shared decision-making

(links accessed on 26 June 2013)

- Stacey D, Bennett CL, Barry MJ, Col NF *et al.* 'Decision aids for people facing health treatment or screening decisions'. *Cochrane Database of Systematic Reviews 2011,* issue 10.

- National Prescribing Centre database of patient decision aids – www.npc.nhs.uk/patient_decision_aids/pda.php (legacy site)

- Dr Chris Cates' EBM website – www.nntonline.net

- The NNT website – www.thennt.com

- Patient UK: patient information leaflets
  www.patient.co.uk/pils.asp

- Elwyn G, Laitner S, Coulter A *et al.* 'Implementing shared decision making in the NHS'. *British Medical Journal 2010,* vol 341, c5146
  www.bmj.com/content/341/bmj.c5146.full

- Cochrane Inventory of Decision Aids, hosted by University of Ottawa, Canada
  http://decisionaid.ohri.ca/cochinvent.php

- Shared Decision-Making – NHS Right Care and BMJ Group
  http://sdm.rightcare.nhs.uk/pda/
  http://sdm.rightcare.nhs.uk/

- Cardiff University – hosts International Patient Decision Aids Standards Collaboration (IPDAS)
  www.decisionlaboratory.com/

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Bayliss EA, Edwards AE, Steiner JF, Main DS (2008). 'Processes of care desired by elderly patients with multimorbidities'. *Family Practice*, vol 25, pp 287–93.

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