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Medicines management

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There is no widely accepted definition of medicines management, although the term is widely used. The National Prescribing Centre in England defines it as: 'a system of processes and behaviours that determines how medicines are used by patients and by the NHS.'[1] When first described in 2002, medicines management encompassed 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 formularies and guidelines. Some of these topics are covered elsewhere in this book. Recent developments in the UK have resulted in considerable changes in the ways medicines are used, hence medicines management has also changed. These important developments include non-medical prescribing, increasing clinical roles of community pharmacists, changes in the way that GPs and pharmacists are remunerated for their NHS work, electronic prescribing, early discharge from hospital, hospital at home services, minor ailments services, pharmacy public health services and more standards for care quality. Similar changes are going on in many countries.

Many medicines management activities as listed above are aimed at individuals. However, many are also targeted at populations and are designed to improve the overall health of a population, hence form part of public health. This chapter focuses on these activities, in particular, tools for managing, monitoring and improving the use of medicines in populations, such as formularies, guidelines and prescribing indicators, which are similar in many countries. These topics consider the cost-effective use of medicines, which form part of public health activities related to health and social care (clinical effectiveness) (see Box 1.1) Safety of medicines in use is just as important and forms part of health protection (Box 1.1). Key public health activities here are policies on safe handling of medicines, pharmacovigilance and risk management.

Ensuring cost-effective use of medicines within populations

Everywhere in the world, purchasing and supplying medicines (often regarded as pharmacists' core function) constitutes a major component of health costs. In the UK, as in many European countries, pharmaceutical expenditure is already or is approaching the largest cost component of healthcare. Pharmaceutical expenditure is set to rise more rapidly than other components unless addressed.[2] The reasons for this are well known and include demographic changes leading to greater prevalence of chronic diseases, rising patient expectations, stricter clinical targets and the continued launch of new premium priced products. Resources are however, finite and there is a need to maximise the efficiency with which medicines are utilised as a resource. The World Health Organization emphasises the need for rational prescribing, which is based on efficacy, safety, patient acceptability and cost.[3] To ensure rational prescribing, both prescribers and patients need to be aware of why this is beneficial. However, in practice, medicines are frequently not prescribed appropriately or used appropriately by patients. Many reports from various sources have stated that that improvements in prescribing are possible, which could improve cost-effectiveness without compromising efficacy.[3,4] Improving the use of medicines in individuals also has the potential to improve cost-effectiveness, by reducing waste and improving health outcomes, including minimising adverse drug reactions and drug–drug interactions. All require interventions designed to influence behaviour, in both health professionals and patients. The main strategies currently used to achieve this can be described as the 'four Es': education, engineering, economics and enforcement.[5] Examples of these are given in Table 14.1.

Although all have strengths and may help to rationalise prescribing, they often have weaknesses too. For example, the extent to which clinical guidance is followed may be variable and the pharmaceutical industry will seek alternative ways to influence prescribers, since this is necessary for industry to achieve increased sales, just as clinicians will seek ways to get around restrictions on prescribing. Initiatives designed to improve patients' use of medicines are usually targeted at individuals, although the strategic provision of such services forms part of the overall medicines management approach to rationalising medicines use.

Tools for influencing prescribing

Pharmacists have, for many years, been instrumental in developing tools for reducing the range of drugs prescribed and assisting in implementing these in practice.[6] A variety of tools, policies and incentives are used in many countries

Table 14.1 Examples of the 'four E' approach to influencing prescribing		
Measure	**Methods**	**Examples**
Education	Distribute guidelines	NICE clinical guidelines
	Educational outreach visits	Practice-based pharmacist activities
	Public campaigns	Campaign on antibiotics for viral infections
Engineering	Setting prescribing targets	Prescribing quality indicators
	Formulary management systems	Limiting pharmaceutical company representative activities
Economics	Incentive schemes	Payments for non-dispensing
	Payment methods	Quality and outcomes framework (QOF)
Enforcement	Generic substitution	Contract purchasing in secondary care
	Restrictions on prescribing	Authorisation to prescribe non-formulary medicines
Adapted from reference 5.		

to try to influence prescribing. The three main tools which pharmacists routinely use for improving prescribing are:

- formularies, which recommend specific drugs and exclude others
- clinical guidelines, which help to ensure that treatment of patients is based on evidence of best practice
- prescribing policies/treatment protocols, which assist prescribers in using the drugs in a formulary or implementing clinical guidelines.

Used together, formularies, clinical guidelines and treatment policies/protocols can ensure that standards of prescribing are uniform, high quality and cost-effective and there are many of these tools available. Internationally, many countries have, often with the technical advice of the World Health Organization, produced essential medicines lists and national treatment guidelines. These frequently include information about how to use medicines and are particularly important in developing countries, since this provides information for local health workers, who may not always be highly qualified and procurement of medicines can focus around the essential medicines lists.[7]

At a national level within the UK, NICE, Scottish Intercollegiate Guidelines Network (SIGN), the All Wales Medicines Strategy Group and the Scottish Medicines Consortium (SMC) provide advice, guidelines and directions. In addition, various groups such as Royal Colleges produce guidelines for national use. Individual medicines are approved for NHS use in

Scotland by the SMC, so prescribing of those not approved is regularly questioned. To achieve this, SMC reviews all new products shortly after marketing. There is currently no similar process in England, however, NICE issues single or multiple technology appraisals. These cover medicines, as well as other technologies, usually involving novel products for conditions with a high disease burden or high cost or policy implications or when there is evidence of variation in availability or use of the medicines across the country. If medicines are recommended by a NICE technology appraisal, the NHS is then legally obliged to fund them.

Many other regional or local health organisations are also involved in providing guidance. For example, in the UK, regional health organisations may have priority setting committees, PCTs may have area prescribing committees (APCs), hospitals have drug and therapeutics committees (DTCs), all of which provide more local formularies and guidance. Even more specific formularies and policies may be produced by individual departments/wards and general practices.

Other European countries have adopted similar approaches. In Austria, a 'medicines and reasons' initiative was introduced in 1999 to enhance rational prescribing, through the production and dissemination of one guideline per year, which are well accepted and have impacted positively on prescribing.[8] Pharmacists are involved in the production of these and patient versions are available in community pharmacies. Pharmacist involvement in Swedish formularies and guidance extends to monitoring drug utilisation and providing educational input.[9] In France, 243 guidelines were introduced between 1994 and 1999 which included penalties for non-compliance. However, the large number produced resulted in limited awareness among physicians, who were reluctant to implement these guidelines.[10] Subsequently, specific campaigns using guidelines targeted towards improving prescribing for selected groups of drugs have begun to influence prescribing.

Much effort goes into the development, production and distribution of these tools, which aim to achieve standardisation in healthcare provision. In general most are based on evidence (see Chapter 7) and some have considerable ownership among the stakeholders expected to use them, which is an essential component of effective guidance. Their effectiveness in influencing prescribing is however, variable. There is little robust evidence of the benefits of formularies in the form of randomised controlled trials.[11] However, controlled studies have shown that active promotion of a formulary can both change prescribing behaviour and prevent rising drug expenditure.[6,8,11] In addition, a recent ecological study conducted in Sweden studied the association between surrogate markers for hypertension, diabetes and hypercholesterolaemia and adherence to formulary drugs.[12] This study found that although there were no significant associations between adherence and outcomes, following guidelines did results in significant cost savings.

Formularies

A formulary is a list of drugs/medicinal products recommended for use and available for use in a given population.[13] It needs to be owned by those required to prescribe from it, hence representatives of all prescribers need to have input into its development and it must be regularly revised to keep it up to date. Increasingly local formularies are developed for joint use between primary and secondary care, since these facilitate better continuity of care. A formulary management system is usually needed to initiate, develop, monitor, manage and review a local formulary and any prescribing policies contained within it. Key factors in this system are the mechanisms for including new products and deleting products, changes in indication, processes for prescribing of non-formulary medicines and monitoring of adherence to the formulary.

Use of a restricted medicines list is influenced by the number of medicines it contains. To ensure adherence, regular reminders of the restricted range of medicines selected are important, as is feedback on their use. Feedback on adherence should provide information about the cost implications of non-adherence, plus percentage of non-formulary medicines prescribed. As with other prescribing information, such feedback is particularly useful when comparisons with peer groups are included. It is facilitated by computerised prescribing data and likely to be enhanced by educational, face-to-face delivery.[5,6,13] Health organisations may also provide financial incentives to encourage prescribing of approved products.[5,10,14]

Guidelines

A clinical guideline is 'a series of systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances'.[15] Guidelines may not indicate which specific drug or product to use in any given circumstance, often recommending a therapeutic class. Smaller local groups such as DTCs may develop their own guidelines or adapt national guidelines for local use. In developing guidelines, the strength of the evidence, derived from critical appraisal of the design and quality of the studies, influences the grade of the recommendations made. This therefore differentiates those based on strong evidence from those based on weaker evidence, providing an indication of the likelihood that the predicted outcome will be achieved if a recommendation is implemented. Guideline users must be able to form an opinion about how the guideline was developed, and international consensus is available on best practice in guideline development (Box 14.1).[16]

Prescribing policies

Prescribing policies are more detailed than a formulary, giving details of medicines which should be selected for use in specific medical conditions, but are not as wide ranging in scope as clinical guidelines. Important prescribing policies designed to protect health include antibiotic policies, head lice

Box 14.1 *AGREE II (Appraisal of Guidelines for Research and Evaluation) criteria for appraising clinical guideline*[*16]

Scope and purpose

1   The overall objective(s) of the guideline should be specifically described.
2   The clinical question(s) covered by the guideline should be specifically described.
3   The patients to whom the guideline is meant to apply should be specifically described.

Stakeholder involvement

4   The guideline development group should include individuals from all the relevant professional groups.
5   The patients' views and preferences should be sought.
6   The target users of the guideline are clearly defined.
7   The guideline has been piloted among target users.

Rigour of development

8   Systematic methods should be used to search for evidence.
9   The criteria for selecting the evidence should be clearly described.
10   The methods used for formulating the recommendations should be clearly described.
11   The health benefits, side effects and risks should be considered in formulating the recommendations.
12   There should be an explicit link between the recommendations and the supporting evidence.
13   The guideline should be externally reviewed by experts prior to publication.
14   A procedure for updating the guideline should be provided.

Clarity and presentation

15   The recommendations should be specific and unambiguous.
16   The different options for management of the condition should be clearly presented.
17   Key recommendations should be easily identifiable.
18   The guideline should be supported with tools for application.

Applicability

19   The potential organizational barriers in applying the recommendations should be discussed.

> **20** The potential cost implications of applying the recommendations should be considered.
>
> **21** The guideline should present key review criteria for monitoring and audit purposes.
>
> *Editorial independence*
>
> **22** The guideline should be editorially independent from the funding body.
>
> **23** Conflicts of interest of guideline development members should be recorded.
>
> *Items from the AGREE Instrument are kindly reproduced with permission from the AGREE Research Trust (www.agreetrust.org).

eradication policies and malarial prophylaxis policies. Treatment protocols go even further in that they specify exactly what should happen to patients throughout their journey of care. This can involve information about diagnosis, processes for recall and review, investigations, detailed instructions about prescribing, non-drug treatments, monitoring, recording and information requirements.

Tools for monitoring prescribing

Methods of assessing how medicines are used are numerous, but those most commonly used include analysis of prescribing data, drug utilisation reviews, prescribing indicators and clinical audit. These require differing levels of effort and the value of the data they provide may reflect that effort. One may lead to another, for example, analysis of prescribing data or a prescribing indicator may provide a prompt to investigate a particular area further using clinical audit.

Studying patterns of medicines use requires data acquired from measures of drug purchase, drug distribution or prescriptions. Evaluating medicines use, also known as drug use evaluation, involves assessing the appropriateness of prescribing and the outcomes achieved, so requires more detailed data which can be derived from medical records or patients. Either can be carried out in specific contexts, such as in a single general practice or a hospital ward, a clinical condition or a particular group of patients.

Monitoring activities often assume some form of standards, against which practice is evaluated, such as a formulary, guidelines or prescribing indicator. As with formularies, increasingly monitoring of indicators is linked to financial incentives and payment. For example, in the UK, GPs income for providing NHS services is in part calculated using a quality and outcomes framework (QOF).[17] This identifies standards of good clinical practice, covering important

diseases, but also good management practice, including how medicines are prescribed. Some examples of QOF indicators are given in Table 14.2. Another example is found in Sweden where two indicators are used. These are the number of different drugs prescribed by an individual GP and the overall adherence to the recommended prescribing guidance measured as the proportion of recommend drugs among those drugs accounting for 90% of prescribed volumes in defined daily doses (DDDs – see page 254).[9,14]

Table 14.2 Examples of indicators taken from various sources

Indicator	Unit	Source
Generic prescribing for drug items (i.e. BNF Chapters 1–15)	Percentage	Audit commission
Benzodiazepines	ADQs per STAR-PU	Audit commission
Ulcer healing drugs	ADQs per STAR-PU	Prescribing indicator group
Prescribing rates of antibacterial drugs	Items per STAR-PU	Healthcare commission
Prescribing of low cost statins	Percentage of items of low cost statins (simvastatin and pravastatin) compared with all items for statins, excluding combinations with ezetimibe	Better care, better value indicators
Patients with non-haemorrhagic stroke or TIA taking aspirin, other antiplatelet drug or anticoagulant (unless contraindication recorded)	Percentage of total registered patients with condition	QOF
Patients with diabetes immunised against influenza in preceding winter	Percentage of total registered patients with condition	QOF

TIA = transient ischaemic attack; ADQ = average daily quantity; QOF = quality and outcomes framework.

Monitoring prescribing is not simply an end in itself, but a means of identifying actions to improve prescribing. A wide variety of information sources are used in monitoring medicines use. These include medicines distribution data, prescribing data, patient medication records within community pharmacies and medical records. Analysing prescribing data can show trends over time, illustrate the impact of changes in availability or highlight unexplained variation between groups of prescribers or between populations. The subsequent activities undertaken to address these issues may include clinical medication review, a lower level of review such as medicine use review or prescription review, therapeutic switching programmes, clinical audit, drug utilisation reviews and drug use evaluation.

A variety of numerators and denominators have been developed to enable comparisons in prescribing patterns to be made over time and between

populations. International systems for classifying drugs (the anatomical therapeutic chemical system (ATC)), and for quantifying drug use (the defined daily dose (DDD)) have facilitated such comparisons. A DDD is available for every drug on the market, based on the average recommended daily maintenance dose for the drug when used for its most common indication in adults. DDDs are often used as a numerator in prescribing analysis. More sophisticated methods of quantifying prescribing data are also used in the UK primary care setting. The 'average daily quantity' has been developed for a number of drugs to reflect typical prescribing in England. Data can also be expressed in terms of cost, rather than quantity.

The most commonly used denominator is 1000 patients. For example, the DDD of diazepam is 10 mg. If used with a DDD of 2000/1000/year, this means that for every 1000 people, 2000 doses of diazepam were prescribed in a year, equivalent to two doses per person per year. Often DDDs per thousand inhabitants per day is used as a standard quantity: DDD/TID. The use of DDDs enables account to be taken of quantities prescribed and frequency of administration. Using a denominator that takes account of the differing needs of populations enhances this further. Examples of this are the ASTRO-PU (which accounts for the age, sex and temporary residential status of a population) and the STAR-PU which also accounts for variability within therapeutic groups.

Data are used to enable identification of prescribing that is higher or lower than the 'norm' for the actual population served, either in terms of quantity and cost. It is important to use other data to support analysis of prescribing data, to ensure that possible reasons for deviation from 'norms' are considered. For example, in an area with higher than usual prevalence of cardiovascular disease, higher than average levels of prescribing of relevant medicines would be expected, indeed encouraged. It is also important to recognise that average prescribing can still be below or above the 'norm' if disease prevalence deviates substantially from average.

Prescribing indicators

Prescribing indicators are quantitative measures of prescribing that can be used to estimate the quality of prescribing and again enable comparisons to be made between prescribers, regions and countries. One of the main ways in which prescribing indictors are used is to enable peer pressure to influence prescribers' behaviour, such that they are encouraged to work towards the average or norm of prescribing. The applicability of indicators must be reviewed regularly, as new medicines become available and opinions about what constitutes 'high quality prescribing' change with emerging evidence. Other factors that may influence the applicability of an indicator are improvements in performance over time (for example, in the proportion of patients prescribed aspirin for secondary prevention of cardiovascular events), new drugs that may supersede

older ones and changes in morbidity within the population. A variety of indicators have been developed which are used nationally in England to assess the quality of prescribing. Some examples of these are given in Table 14.2. Similar indicators, especially those that focus on the prescribing of low cost alternatives versus premium priced, single sourced products in a class or related classes, are also used in other European countries.[9,10]

Using the basic variables outlined above, simple indicators such as the number of prescriptions for isosorbide mononitrate modified release per 1000 adjusted population can illustrate the extent to which these premium priced products are being used. Minimising the prescribing of such products and replacing them with generically prescribed standard release products enables therapeutic goals to be achieved while reducing costs. Having identified an issue such as this, pharmacists may develop a programme to switch patients on to the cheaper alternative and subsequently to monitor any change achieved using the same indicators. Indicators can also be used to identify areas where education or policy development may be needed, such as those relating to antibiotics. However, evaluating the effect of such programmes or developments requires intensive effort to collect data from the records of patients actually prescribed these drugs. Prescribing indicators can provide some data about whether prescribing practices have changed, but they are simply derived from information about what has been prescribed, not why. In other words prescribing indicators lack any association with clinical data, such as diagnosis, co-morbidity and response to the medicine prescribed. Therefore, although they may have been agreed by 'experts' as indicators of prescribing quality, their use does have limitations. As computerisation of medical records increases, the ease with which clinical data can be captured routinely increases. This enables more realistic indicators of quality prescribing to be developed and tested, which incorporate diagnosis and monitoring (see Table 14.2). Indeed the QOF has also resulted in a substantial increase in routine recording of indicators of quality medical practice, many of which include prescribing.

Ensuring high quality prescribing

One of the main ways of improving the quality of prescribing is to ensure that all the formularies, guidance and policies, developed with so much effort, are followed. NICE provides a range of tools to help with implementing its guidance.[18,19] Interventions which are mostly effective include reminders, education outreach (also known as academic detailing) and interactive educational workshops.[6] Simple audit and feedback, use of opinion leaders, local consensus conferences and patient-mediated interventions are less effective.[15] However, multiple or multi-faceted interventions are probably most effective.[6,9,15]

Review of repeat prescribing

In the UK, a system has developed in medical practices to enable patients requiring regular medicines to obtain a prescription without the need to see a doctor, the repeat prescribing system. This is so extensive that around 75% of all prescriptions written are repeats, which are generated by staff using computer systems. The repeat prescribing system is made up of three components: production, management control and clinical control.[20] There is though evidence that repeat prescribing systems are not effectively controlled, resulting in patients requesting items unnecessarily and inappropriately. Consequently, systems should be regularly assessed to ensure that effective controls are in place to minimise the risk of this occurring.[21]

Further developments in primary care within the UK and elsewhere include electronic transfer of prescriptions between medical practices and community pharmacies and repeat dispensing systems. In the latter system, the repeat prescription is valid for several months and the pharmacist is responsible for ensuring continued need, efficacy and safety of each drug at every dispensing. This provides pharmacists with an opportunity to exercise some clinical control over repeat prescribing since they should be seeing patients regularly. It may be appropriate for a pharmacist to undertake a more substantial review of an individual patient's medicines periodically and a nationally agreed service is now increasingly provided by community pharmacists, the medicine use review service.

At an individual level, repeat dispensing and medicine use reviews can help to minimise inappropriate medicines use and reduce waste. Clinical medication reviews, using medical records, and clinical audit activities can help to implement evidence-based formularies and guidelines. Pharmacists frequently provide these services, but GPs and nurses also review patients' medicines, and increasingly so since the introduction of medication review standards in the QOF in the UK. QOF standards relate to specific conditions, but also to patients taking repeat medicines, hence could include medicine use review and holistic clinical reviews. Pharmacists could be involved in developing templates for GPs and nurses to use and in training them in review techniques to improve the quality of reviews in the overall population.[22,23]

Therapeutic switching programmes

As highlighted above, ensuring cost-effective and evidence-based prescribing may involve changing patients from one medicine to another. When carried out for a population, this has become known as a switch. Switches may be of varying types, including:

- changes to generic medicine
- changes to a different drug within the therapeutic group, e.g. proton pump inhibitors or statins, to reduce costs

- changes to the dose, e.g. from a treatment dose of proton pump inhibitors to a maintenance dose
- changes to the formulation, e.g. from dry powder inhaler to a metered dose inhaler
- changes to the formulation and dose, e.g. from modified release to standard diclofenac
- changes to the product because of lack of efficacy, e.g. from a topical non-steroidal anti-inflammatory drug to a rubifacient.

Usually such switches are done using medical records but without seeing the patient. A systematic method of carrying out this activity is required. An example is shown in Box 14.2.

In hospitals, generic prescribing is encouraged, but regardless of whether brand or generic names are used, only one brand of a particular medicine is usually stocked. Switching to generic prescribing in primary care, however, has resulted in large cost savings and the proportion of generic prescribing is in fact a prescribing indicator (see Table 14.2). There is currently the possibility of generic substitution being permitted in primary care in England, which may

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Box 14.2 *Example of processes required for a therapeutic switching programme*

- Decide on criteria for including patients in the switch and exclusions.
- Ensure community pharmacists are aware of plans to ensure adequate stocks and minimise waste.
- Identify all patients prescribed relevant product.
- Identify who initiated product.
- Review medical records to determine suitability for switching products.
- Confirm with community pharmacist product being dispensed.
- Confirm that appropriate monitoring is being carried out.
- Draft letter to be sent to patients and either attach to next prescription or send by post.
- Contact patients by telephone to confirm their use of the product and receipt of letter.
- Document the switch in records.
- Make changes to repeat prescriptions.
- Record any responses from patients and reasons for reverting back to original product.
- Assess effectiveness of switching protocol by measuring proportion of successful switches.

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have the potential for further savings although, of course, for some medicines there is a need for brand retention in individual patients, and the risk of differing adverse reaction profiles caused by varying excipients must not be forgotten.

Managing high cost medicines

Increasingly new medicines are often expensive and well publicised to the public, particularly if they involve major therapeutic advances. Often they require specialist medical knowledge to use effectively and as such may be initiated in secondary care. The introduction of a novel, expensive product can easily put pressure on a restricted prescribing budget, therefore managing this becomes an imperative. Indeed, the continued introduction of new, premium priced drugs is seen as the biggest threat to continued and comprehensive healthcare in Europe.[2] Systems need to be in place to ensure that prescribing of high cost products is controlled and budgeted for, but such systems must also ensure equity of access for patients.[2] This is already happening in the UK and other European countries. Although often initiated in hospitals, where long term use is required, ultimately these products will be prescribed in primary care settings. If not managed properly, with clear financial accountability agreed, tensions can arise between the acute and primary care providers especially following budget devolution. For some products, guidance is available from NICE on when they should be used. For all such technology appraisals, NICE also produces costing tools to enable the calculation of the likely financial impact of the product's introduction.[24] This information can be used to estimate costs locally, based on data derived from the local population. The National Prescribing Centre also produces information on the likely budget impact of new products in primary care. Other national organisations produce information for use in the other home countries.

One consequence of the escalating cost of medicines and the need to restrict availability of high cost products is frequently highlighted by the media, as 'postcode prescribing'. This is the apparent inequitable access to medicines arising when one locality or hospital approves a product for use which a neighbouring locality or hospital does not. It is essential that robust, processes are in place so that any decisions about whether or not to fund individual high cost products are consistent, rational and defensible. The DoH has produced guidance on the processes which should be in place to support decision making about medicines availability.[25,26]

Area prescribing committees

It is clear from the above that patients may obtain different medicines from various sources at different times; some may be supplied by community pharmacists, others by secondary care. Furthermore they may require support

with medicines taking from a wider range of services, including social care. It is therefore essential that medicines provision and support are coordinated. Area prescribing committees bring together representatives from all local organisations which have a role in managing medicines. Their role as described by the National Prescribing Centre[27] includes 'coordinating the safe and cost-effective use of medicines across a health community to improve outcomes for patients'. It is often the committee that makes decisions about which medicines to fund locally. Other functions that may be carried out by the committee with the potential to affect the quality of prescribing are: identifying the need for and/or developing shared care protocols and treatment guidelines, contributing to 'traffic light' systems for shared care (see page 259), developing formularies and local guidance, developing incentive schemes, providing guidance on working with the pharmaceutical industry and facilitating public campaigns.

Ensuring safe use of medicines within populations

Role of the National Patient Safety Agency

As described in Chapter 10, the NPSA, a special health authority of the NHS, created in 2001, plays a very important role in minimising the risks associated with medicines supply and administration. As well as coordinating learning from errors, the NPSA issues alerts that are designed to ensure that appropriate action is taken when safety issues with medicines become apparent through this system. An example is *Safer Lithium Therapy*, which was issued in December 2009,[28] requesting healthcare organisations to ensure that patients are monitored in accordance with NICE guidance, results of monitoring are shared appropriately, patients receive all relevant information, and systems are in place to identify and address use of interacting medicines. Alerts such as this also carry a date by which time organisations are expected to have implemented the guidance, in this case, 31 December 2010. To support this, the NPSA produce information leaflets and booklets for patients to record their serum lithium levels.

Medicines safety across the interface

When patients move from one healthcare setting to another, or between healthcare and other settings, information about their medicines needs to move with them. There are many situations when this does not occur and a proportion of these can result in harm. An example of this is the failure to reconcile medicines prescribed on hospital admission with those being taken prior to the admission. The NPSA and NICE issued a joint alert in December 2007, requiring pharmacists to be involved in medicines reconciliation as

soon as possible after admission, with all staff having clear responsibilities about obtaining information to facilitate this.[29] Hence policies and procedures must be developed to ensure that these requirements are achieved. This may be undertaken by multi-disciplinary staff working together in the individual hospital. However, in general, it is an APC or DTC which has responsibility for ensuring that NPSA alerts are implemented locally.

Clearly discharge from hospital is another situation where errors can occur with medicines. Indeed, a recent report by the Care Quality Commission indicated that 81% of GP practices surveyed reported that details of medicines prescribed by hospitals were incomplete or inaccurate all or most of the time.[30] From April 2010, all NHS trusts in England are required by law to register with the Commission and must meet standards, including effective medicines management, as a requirement of registration. Electronic discharge summaries, populated with patient and medication information from electronic prescribing systems, have the potential to reduce errors occurring through transcription or illegibility.[31] These can be transmitted electronically to GPs, reducing delays, but obviously a clinical check will still be required to ensure that all medicines are in fact required after discharge. Another initiative with the potential to reduce problems is the Summary Care Record, which has been piloted in several areas of England. This is an electronic record which is web-based, but very securely protected and can thus be accessed by any health professional providing care to an individual patient, with the patient's permission.[32]

For some medicines, safety concerns arise because of their inherent toxicity or the need for invasive monitoring, resulting in the need for continued secondary care involvement in prescribing. Sometimes prescribing may also be restricted to initiating and continuing supply by hospital clinicians only for other reasons. Such medicines often require a shared care approach to prescribing, since patients will almost inevitably be resident in the community most of the time and may be highly inconvenienced by the need for frequent hospital visits to obtain medicines supplies. Shared care protocols are routinely developed for medicines such as these and others, usually by an APC. Many areas use a 'traffic light system' to classify medicines which are used entirely by secondary care specialists (red), those which require shared care and may need a specific protocol (amber) and those which are prescribed freely (green). They may also highlight medicines which are not recommended at all, because of lack of evidence of efficacy, or no benefits over other therapies. Hence the system also supports the local formulary. Several examples are available via the internet.

Medicines safety in non-healthcare settings

Wherever people live or spend time, they may use medicines, for example, in care homes, prisons, respite care or schools. In these situations, staff are not

trained health professionals but may be involved in administering or advising people about how to use their medicines. Therefore safety can only be assured by having policies and procedures in place to manage medicines properly. Safe and secure handling policies are frequently developed by pharmacists or by the local APC/DTC for use in these settings. Care homes are regularly inspected by the Care Quality Commission and medicines policies and practices are an important aspect of this inspection. The RPSGB has produced guidance for the safe handling of medicines in care settings.[33]
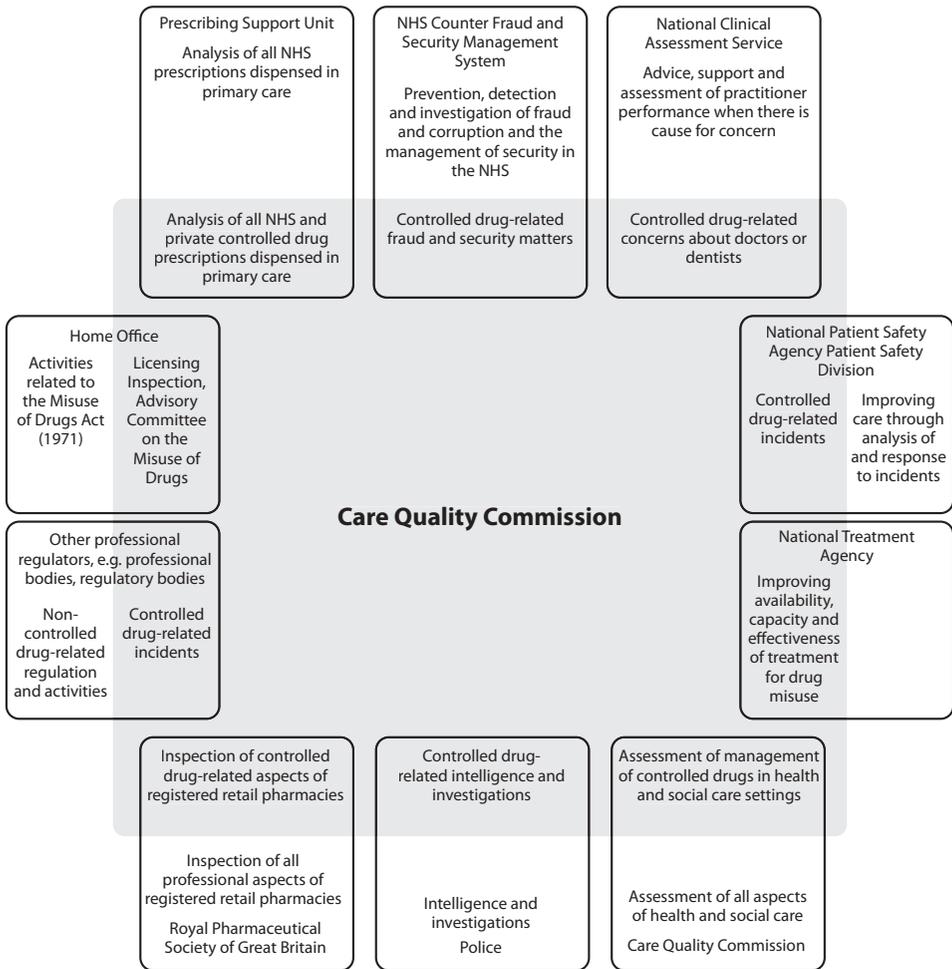
Controlled drugs

The Care Quality Commission is also responsible for assessing and overseeing how health and social care providers manage controlled drugs.[34] The Commission, together with a wide range of organisations, are involved in managing controlled drugs to ensure their safety in use (Figure 14.1).

The Commission maintains a register of accountable officers, who are employees of NHS organisations or private hospitals, with designated responsibility for ensuring that safe systems are in place for managing and using controlled drugs. These officers are often pharmacists. Another of their responsibilities is to establish local intelligence networks involving all the key local organisations with involvement in controlled drug use to enable information to be shared. This facilitates appropriate action in the event of incidents involving these drugs.

Pharmacovigilance

Pharmacovigilance is defined by the World Health Organization as the 'science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems'. The need for continuous pharmacovigilance arises because of the nature of pre-marketing requirements for medicines, which frequently involve short term studies, in relatively small number of patients who may be highly selected. Indeed clinical trials are capable of identifying only type A adverse drug reactions (ADRs) (predictable by the pharmacological action of the drug) that affect 1 in 250 or more patients studied. After marketing, medicines will subsequently be used in much larger populations, with characteristics often unlike those included in pre-marketing studies such as greater co-morbidity, and for longer periods of time. Hence the opportunity for ADRs to develop is increased, particularly those that have a long latency, are rare or involve interaction with other medicines or conditions.

ADRs are a major public health problem, estimated to be between the fourth and sixth leading cause of death in the USA and a source of cost to healthcare providers. A large UK cross-sectional study estimated that ADRs

Figure 14.1 The agencies that are involved in different aspects of the regulation and control of controlled drugs. Reproduced with permission from the CQC, 2009.[34]

may be responsible for the deaths of 0.15% of all patients admitted to hospital.[35] Pharmacovigilance involves identifying a potential ADR that may be associated with a medicine, characterising it, evaluating the risks and benefits of the medicine, assessing the risks of taking action to change the availability of the medicine or information about it, then making a decision on action and communicating this to health professionals and the public. Most countries have some scheme in place and many send data from these schemes to a central monitoring centre in Sweden, the WHO Uppsala Monitoring Centre (WHO-UMC).

Sample chapter from *Pharmacy in Public Health*

Yellow Card Scheme

The main pharmacovigilance system in the UK is the Yellow Card Scheme (YCS), run by the Medicines and Healthcare products Regulatory Agency (MHRA) to which pharmacists along with doctors, other health professionals and coroners, can submit reports of suspected ADRs identified in patients with whom they have had contact. The general public have also been able to report directly since 2005. It is not essential to be certain that there is an association between the medicine and the reaction to submit a report, only a suspicion. Information from Yellow Card reports is entered into a database ('Sentinel') and further information is sought from reporters if required to enable the report to be assessed. Reactions listed on the forms are categorised using the Medical Dictionary for Regulatory Affairs (MedDRA), a hierarchical method of grouping signs and symptoms, which is used internationally. The WHO also use a subset of adverse reaction terms (ARTs) for serious disease states, which have been regarded as particularly important to monitor, called WHO-ART.

Reports are assessed for causality, i.e. the likelihood that the problem was caused by the medicine, by expert staff at the MHRA. A variety of factors need to be considered in assessing causality.

- *Nature of the reaction:* some clinical events are commonly caused by medicines, such as Stevens Johnson syndrome.
- *Timing of the reaction:* some events occur minutes or hours after taking a single dose and are thus likely to be associated, although other events can be considerably delayed, even by years.
- *Relationship to dose:* if the dose changes, corresponding changes in the severity of the event may indicate an association.
- *Exclusion of other possible causes:* other medicines being taken or symptoms associated with disease states present should be considered as possible causes.

A systematic review has identified 34 different methods for assessing causality,[36] and studies have repeatedly shown that they lack consistency in the probabilities of particular drugs causing particular reactions. The categories used by the WHO-UMC are shown in Table 14.3.[37]

Signal generation, validation and strengthening

The reports are used to generate signals, i.e. the first alerts that there may be a problem with a medicine. A signal is defined by WHO-UMC as: 'reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously. Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the

Table 14.3 World Health Organization categories of causality of suspected adverse drug reactions	
Causality category	**Assessment criteria**
Certain	Event or result with plausible time relationship to drug administration
	Cannot be explained by concurrent disease or other concomitant drugs
	When withdrawn (de-challenge) response is clinically plausible
	Event pharmacologically or phenomenologically definitive on re-challenge
Probable/likely	Event or result with a reasonable time relationship to drug administration
	Unlikely to be explained by concurrent disease or other concomitant drugs
	Follows a clinically reasonable response on withdrawal (dechallenge)
Possible	Event or result with a reasonable time relationship to drug administration
	Could also be explained by concurrent disease or other concomitant drugs
	Information on withdrawal (dechallenge) unclear or lacking
Unlikely	Event or result with a time relationship to drug administration which makes a relationship improbable, but not impossible
	Concurrent disease or other concomitant drugs provide plausible explanations
Conditional/unclassified	More data essential for classification
Unassessable/unclassifiable	Information insufficient or contradictory
	Data cannot be supplemented or verified
Adapted from reference 37.	

information.' Signals are more likely to be generated when events are reported for frequently used medicines, when the event described is normally rare and/ or often drug related, and when events occur in patients with similar characteristics. Many signals are generated automatically by the software each week, which depend on the number of reports submitted, which is constantly increasing. Different methods are used to generate signals, and it is possible for a signal to change as further reports are received. Obviously the length of time it takes for a signal to be generated will depend on the number of reports of the medicine and particular event received. This in turn depends on the frequency with which a medicines is used, as well as the number of people who actually submit reports. Hence the more people who submit reports, the greater the possibility of signals being detected earlier.

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Staff regularly review the signals generated, to consider the extent of further work required. This may include requesting further details from reporters to enable causality assessment, contacting manufacturers to elicit any further information to support the association and reviewing the literature or other reporting databases.

Managing the findings

If a signal is confirmed as a potential ADR, then action may be required. This will vary depending on a number of factors including, the seriousness of the potential ADR, the likely incidence, which will be affected by the use of the medicine and the potential impact on health for the population, which will relate to the type of patient using the medicine. It is also important to consider whether other therapies are available to manage the condition(s) for which the medicine is being used and the risks associated with these conditions themselves. Possible actions which may result from identification of a new ADR are to amend the summary of product characteristics and/or the patient information leaflet for all products containing the drug in question, restricting usage or withdrawing marketing authorisation of the medicine.

Obviously if any of these actions are taken, it is essential to inform both health professionals and the public. The MHRA produces regular bulletins *Drug Safety Update* available on their website.[38] For individual issues, *Dear Doctor* letters are produced. These are published on the internet and also cascaded down through the Chief Medical Officer system, through NHS trusts and public health departments, to reach individual health professionals, including hospital staff, GPs and community pharmacists.

New products

Medicines newly introduced on to the UK market are given 'black triangle' status. These include entirely new drugs, new formulations of existing drugs or sometimes existing medicines that have new indications. All require intensive monitoring by the MHRA to further assess their risk/benefit profile and the time over which black triangle status is maintained varies, depending on how much information is obtained to ensure a product's continued safety. Many countries have similar systems for newly marketed products, which permit authorities to collect information about any problems with the product in their own country, even if the products have been marketed elsewhere.

Disadvantages of spontaneous reporting

The YCS, as with most spontaneous reporting systems, suffers from severe under-reporting, estimated by a systematic review as being 82–98%.[39]

Studies have shown a variety of reasons may be involved in under-reporting, including lack of certainty that the medicine caused the symptom, guilt feelings, fear of reprisal and apathy. Many possible methods of increasing reporting have been mooted over the years. One method, which includes ADR reporting as part of the overall quality of prescribing and rewards this with financial incentives, has recently been reported to result in higher than usual reporting rates.[14]

YCS data cannot provide the incidence of any individual ADR from any medicine, partly because of under-reporting, but also because the number of patients prescribed a particular drug is not known. Although data is freely available on the overall number of reports submitted in relation to a particular product, via drug analysis prints, from the MHRA website,[40] the data do not present a full analysis of risks and benefits associated with medicines. Hence health professionals, including pharmacists must be in a position to interpret the data for patients presenting with concerns about suspected ADRs.

Manufacturer responsibilities

MHRA also has a pharmacovigilance inspectorate, which assess the compliance of pharmaceutical manufacturers with legislation relating to the safety of medicines. This legislation is beyond the scope of this book. However, it should be noted that manufacturers are legally obliged to report any serious, unexpected ADR, from any clinical or epidemiological study, drug use or literature report within 15 days. Fatal or life-threatening ADRs must be reported within seven days. In addition, periodic safety update reports must be submitted every six months for the first two years after marketing, then with decreasing frequency to ensure the continued safety of marketed products.

Direct patient reporting

As already mentioned, MHRA accepts reports directly from patients and other members of the public. An evaluation of this has recently been completed which shows that there is limited awareness of the facility by both the public and among health professionals, but that most patient reporters learnt about the facility from pharmacies.[41] The majority of people who reported a suspected ADR identified it as such through issues relating to timing, as outlined in the causality methods used by pharmacovigilance experts, or by accessing information about the medicine, such as their patient information leaflet.[42] There is an increasing number of countries worldwide that accept patients reports. It has been suggested that there are advantages such as faster signal generation, avoiding the filtering effect of interpretation of events by health professionals and not least, maintaining the number of reports at a time when health professional reporting may be reducing.

Other reporting schemes

As outlined above, the WHO-UMC accepts reports from 96 countries, including the UK via the MHRA. Approximately 4.7 million reports are collated in the UMC database. In the USA, the Food and Drug Agency runs the MedWatch system, which, in addition to ADRs, also covers problems with products and medication errors. The MHRA operates the Defective Medicines Report Centre, which accepts reports concerning problems with medicines and also covers problems with medical devices, while, as outlined above, medication errors are reported to the NPSA in the UK. All alerts issued by the MHRA and the DoH, which includes messages from the Chief Medical Officer, and by NPSA are available on a single website, the Central Alerting System.[43] This site therefore has all details of safety alerts, drug recalls, *Dear Doctor* letters and medical device alerts issued.

Prescription event monitoring is a complementary pharmacovigilance system which is operated by the Drug Safety Research Unit at Southampton University.[44] This system involves the distribution of green forms to selected GP prescribers throughout the UK who have issued a prescription for a particular product. Products are selected specifically for monitoring, thus as a system it complements the YCS. GPs are asked to report on the green forms all events that have been reported to them by the patients prescribed the drug being studied since it was initiated over a specified time period, regardless of any suspected association of the event with the medicine. Since the number of patients is available as a denominator, prescription event monitoring has the ability to estimate the incidence of ADRs for these drugs and has been shown to identify new ADRs not previously suspected to be due to the drugs studied.

Pharmacist's role in pharmacovigilance

Pharmacists have many opportunities to identify suspected ADRs themselves and to support patients and other health professionals in doing so. Their role in explaining risks and benefits of medicines to patients (Chapter 10) is important in helping patients to understand the literature about and risks of ADRs. However, pharmacists should also routinely ask patients about problems with medicines including ADRs, and encourage patients to report or report themselves, since pharmacovigilance is a vital public health service.

Communicating medicines management issues

Ensuring the safe and effective use of medicines involves communicating with people, both patients and health professionals. Often this may be for the purpose of encouraging behaviour change. Some types of intervention designed to support behaviour change are described in Chapter 11. However,

achieving change in prescribing behaviour may require other approaches. Involvement in the local development of formularies and treatment protocols encourages their use, but even where there is agreement in principle with these tools, there may still be resistance to change among both prescribers and patients.[5] Pharmacists are often actively involved in persuading prescribers to carry out changes and while the goal of rational, cost-effective prescribing may appeal to some, others may be swayed through such factors as peer pressure, the need to follow expert advice or of having influence themselves on others, personal achievement, financial gain or fear of litigation.

Patients are also increasingly aware of the drive to use cheaper alternative products for the same health gain, and pharmacists may be in a position to influence their behaviour, perhaps when prescriptions that have been changed for this purpose are presented for dispensing. Explaining the concepts of cost-effectiveness and maximising the use of scarce resources is therefore of importance to patients as well as to health professionals.

Understanding that there are many reasons for resistance to change and that people do differ in their drivers for change is important, since techniques needed to influence behaviour will need to vary as a result. Change itself is threatening and can take time. Changing prescribing behaviour, just like helping someone to stop smoking, may take repeated attempts and ensuring that prescribing is in line with local formularies and guidelines also requires constant intervention. An awareness of how to influence behaviour is obviously an asset for any pharmacist involved in public health. Chapter 10 highlights some ways in which pharmacists can help to bring about changes to practice, and there are many more suggestions on the National Institute for Health Research Service Delivery and Organisation website[45] and NICE guidance is also available on how to change practice.[46] However, over 150 systematic reviews have been conducted on behaviour change interventions. Many reviews of relevance are available on the Cochrane database. The message seems to be that there is no simple answer!

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