

Review

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Medication errors: what they are, how they happen, and how to avoid them

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Summary

A medication error is a failure in the treatment process that leads to, or has the potential to lead to, harm to the patient. Medication errors can occur in deciding which medicine and dosage regimen to use (prescribing faults—irrational, inappropriate, and ineffective prescribing, underprescribing, overprescribing); writing the prescription (prescription errors); manufacturing the formulation (wrong strength, contaminants or adulterants, wrong or misleading packaging); dispensing the formulation (wrong drug, wrong formulation, wrong label); administering or taking the medicine (wrong dose, wrong route, wrong frequency, wrong duration); monitoring therapy (failing to alter therapy when required, erroneous alteration). They can be classified, using a psychological classification of errors, as knowledge-, rule-, action- and memory-based errors. Although medication errors can occasionally

be serious, they are not commonly so and are often trivial. However, it is important to detect them, since system failures that result in minor errors can later lead to serious errors. Reporting of errors should be encouraged by creating a blame-free, non-punitive environment. Errors in prescribing include irrational, inappropriate, and ineffective prescribing, underprescribing and overprescribing (collectively called prescribing faults) and errors in writing the prescription (including illegibility). Avoiding medication errors is important in balanced prescribing, which is the use of a medicine that is appropriate to the patient's condition and, within the limits created by the uncertainty that attends therapeutic decisions, in a dosage regimen that optimizes the balance of benefit to harm. In balanced prescribing the mechanism of action of the drug should be married to the pathophysiology of the disease.

Introduction

In 2000, an expert group on learning from adverse events in the NHS, chaired by the Chief Medical Officer, reported that since 1985 there had been at least 13 episodes in which people (usually children) had been killed or paralysed because of wrong administration of drugs by spinal injection; 12 involved vinca alkaloids; 10 were fatal.¹ Serious medication errors are uncommon, but it is salutary that it took so long to recognize that

remedial action was needed in this case.² Even so, this error continues to be made.³

Some basic definitions

A medication

A medication (a medicinal product) is 'a product that contains a compound with proven biological effects,

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plus excipients or excipients only; it may also contain contaminants; the active compound is usually a drug or prodrug, but may be a cellular element'.⁴

A codicil to this definition stipulates that a medicinal product is one that is intended to be taken by or administered to a person or animal for one or more of the following reasons: as a placebo; to prevent a disease; to make a diagnosis; to test for the possibility of an adverse effect; to modify a physiological, biochemical or anatomical function or abnormality; to replace a missing factor; to ameliorate a symptom; to treat a disease; to induce anaesthesia. Medication (the process) is the act of giving a medication (the object) to a patient for any of these purposes.

This definition reminds us of the distinction between the drug itself (the active component) and the whole product, which also contains supposedly inactive excipients. The definition of a medication encompasses not only chemical compounds—drugs, prodrugs (which may themselves have no pharmacological activity), stereoisomers that may have only adverse effects, or compounds that are used for diagnostic purposes (such as contrast media); it also includes cellular elements, such as inactivated or attenuated viruses for immunization, blood products (such as platelets), viruses for gene therapy, and embryonic stem cells; 'contaminants' includes chemical and biological contaminants and adulterants, the former being accidentally present the latter deliberately added.

Although the definition covers a wide range of compounds, it does not include medications when they are used to probe systems for non-diagnostic purposes, such as the use of phenylephrine to study baroreceptor reflexes in a physiological or pharmacological experiment.

An error

An error is 'something incorrectly done through ignorance or inadvertence; a mistake, e.g. in calculation, judgement, speech, writing, action, etc.'⁵ or 'a failure to complete a planned action as intended, or the use of an incorrect plan of action to achieve a given aim'.⁶ Other definitions have been published.⁷

A medication error

With these definitions in mind, a medication error can be defined as 'a failure in the treatment process that leads to, or has the potential to lead to, harm to the patient'.^{8,9} The 'treatment process' involves all medications, as defined above.

Medication errors can occur in:

- choosing a medicine—irrational, inappropriate, and ineffective prescribing, underprescribing and overprescribing;
- writing the prescription—prescription errors, including illegibility;
- manufacturing the formulation to be used—wrong strength, contaminants or adulterants, wrong or misleading packaging;
- dispensing the formulation—wrong drug, wrong formulation, wrong label;
- administering or taking the drug—wrong dose, wrong route, wrong frequency, wrong duration;
- monitoring therapy—failing to alter therapy when required, erroneous alteration.

The term 'failure' in the definition implies that certain standards should be set, against which failure can be judged. All those who deal with medicines should establish or be familiar with such standards. They should institute or observe measures to ensure that failure to meet the standards does not occur or is unlikely. Everybody involved in the treatment process is responsible for their part of the process.

Adverse events and adverse drug reactions

An adverse event is 'any abnormal sign, symptom or laboratory test, or any syndromic combination of such abnormalities, any untoward or unplanned occurrence (e.g. an accident or unplanned pregnancy), or any unexpected deterioration in a concurrent illness'.⁴ If an adverse event occurs while an individual is taking a drug it could be an adverse drug reaction (ADR). The term 'adverse drug event' is sometimes used to describe this, but it is a bad term and should be avoided.⁴ If an adverse event is not attributable to a drug it remains an adverse event; if it may be attributable to a drug it becomes a suspected ADR.

An ADR is 'an appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product'.⁴

Some medication errors result in ADRs but many do not; occasionally a medication error can result in an adverse event that is not an ADR (for example, when a cannula penetrates a blood vessel and a haematoma results). The overlap between adverse events, ADRs, and medication errors is illustrated in the Venn diagram in Figure 1.⁸

Frequency and outcomes of medication errors

The precise frequencies of medication errors are not known. The method of detection can affect the estimated frequency.¹⁰ Probably most errors go

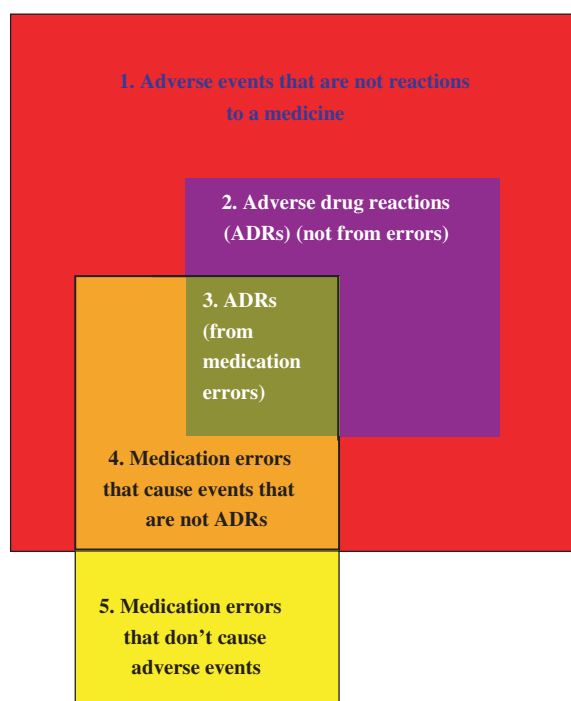


Figure 1. A Venn diagram showing the relation among adverse events, ADRs and medication errors; the sizes of the boxes do not reflect the relative frequencies of the events illustrated (Reproduced from reference 8, with permission from Wolters Kluwer Health/Adis ©; Adis Data Information BV (2006); all rights reserved).

unnoticed (the error iceberg¹¹); of those that are detected a minority actually result in ADRs, or at least serious ones. For example, in a UK hospital study of 36 200 medication orders, a prescribing error was identified in 1.5% and most (54%) were associated with the choice of dose; errors were potentially serious in 0.4%.¹² In a survey of 40 000 medication errors in 173 hospital trusts in England and Wales in the 12 months to July 2006, collected by the National Patient Safety Agency, ~15% caused slight harm and 5% moderate or severe harm.¹³ In a US study, 1.7% of prescriptions dispensed from community pharmacies contained errors.¹⁴ Since ~3 billion prescriptions are dispensed each year in the USA, ~50 million would contain errors. Of those, only ~0.1% were thought to be clinically important, giving an annual incidence of such errors of about 50 000. Wrong label information and instructions were the most common types of errors.

However, it is important to detect medication errors, whether important or not, since doing so may reveal a failure in the treatment process that could on another occasion lead to harm. There is also evidence that the death rate from medication errors is increasing. From 1983 to 1993 the numbers of deaths from medication errors and adverse

reactions to medicines used in US hospitals increased from 2876 to 7391¹⁵ and from 1990 to 2000 the annual number of deaths from medication errors in the UK increased from about 20 to just under 200.¹⁶ These increases are not surprising—in recent years hospitals have seen increased throughput of patients, new drugs have emerged that are increasingly difficult to use safely and effectively, medical care has become more complex and specialized, and the population has aged, factors that tend to increase the risk of medication errors.¹⁷

When errors are detected, they can cause much dissatisfaction. According to a 2000 report citing UK medical defence organizations,¹ 25% of all litigation claims in general medical practice were due to medication errors and involved the following errors:

- prescribing and dispensing errors (including a wrong, contraindicated or unlicensed drug, a wrong dosage, or wrong administration);
- repeat prescribing without proper checks;
- failure to monitor progress; and
- failure to warn about adverse effects (which might, however, not be regarded as a medication error).

Types of medication error and prevention

The best way to understand how medication errors happen and how to avoid them is to consider their classification, which can be contextual, modal, or psychological. Contextual classification deals with the specific time, place, medicines and people involved. Modal classification examines the ways in which errors occur (for example, by omission, repetition or substitution). Psychological classification is to be preferred, as it explains events rather than merely describing them. Its disadvantage is that it concentrates on human rather than systems sources of errors. The following psychological classification is based on the work of Reason on errors in general.¹⁸

There are four broad types of medication errors (labelled 1–4 in Figure 2).⁸

- Knowledge-based errors (through lack of knowledge)—for example, giving penicillin, without having established whether the patient is allergic. In an Australian study, communication problems with senior staff and difficulty in accessing appropriate drug-dosing information contributed to knowledge-based prescription errors.¹⁹ These types of errors should be avoidable by being well informed about the drug being prescribed and the patient to whom it is being given. Computerized prescribing systems, bar-coded medication systems, and cross-checking by others (for example, pharmacists and nurses) can help to intercept such errors.²⁰ Education is important.²¹

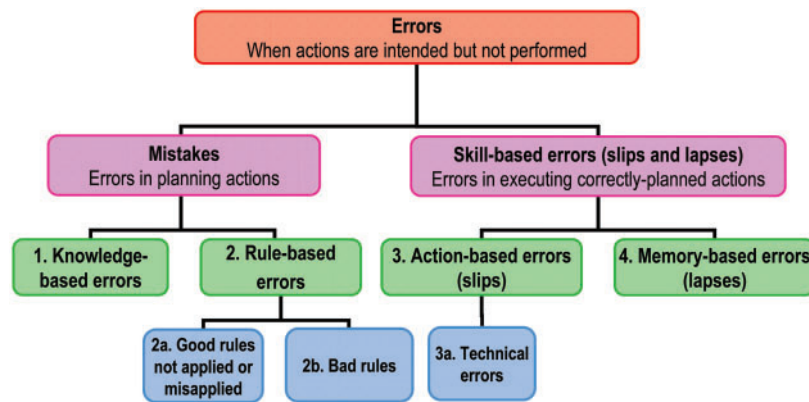


Figure 2. A classification of types of medication errors based on psychological principles. For examples of prescription errors in each category see the text and Table 1 (Reproduced from reference 8, with permission from Wolters Kluwer Health/Adis ©; Adis Data Information BV (2006); all rights reserved).

- Rule-based errors (using a bad rule or misapplying a good rule)—for example, injecting diclofenac into the lateral thigh rather than the buttock. Proper rules and education help to avoid these types of error, as do computerized prescribing systems.
- Action-based errors (called slips)—for example, picking up a bottle containing diazepam from the pharmacy shelf when intending to take one containing diltiazem. In the Australian study mentioned above most errors were due to slips in attention that occurred during routine prescribing, dispensing or drug administration. These can be minimized by creating conditions in which they are unlikely (for example, by avoiding distractions, by cross-checking, by labelling medicines clearly and by using identifiers, such as bar-codes);²² so-called ‘Tall Man’ lettering (mixing upper- and lower-case letters in the same word) has been proposed as a way to avoid misreading of labels,²³ but this method has not been tested in real conditions. A subset of action-based errors is the technical error—for example, putting the wrong amount of potassium chloride into an infusion bottle. This type of error can be prevented by the use of checklists, fail-safe systems and computerized reminders.
- Memory-based errors (called lapses)—for example, giving penicillin, knowing the patient to be allergic, but forgetting. These are hard to avoid; they can be intercepted by computerized prescribing systems and by cross-checking.

For some examples of prescription errors see Table 1. Examples of other types of medication errors under the same headings are given in reference 8.

Latent factors

Mistakes (knowledge- and rule-based errors), slips (action-based errors) and lapses (memory-based errors) have been called ‘active failures’.¹⁸ However, there are several properties of systems

(so-called ‘latent factors’) that make prescribers susceptible to error. For example, working overtime with inadequate resources, poor support, and low job security all contributed to an increased risk of medication errors by nurses.²⁴ Among doctors depression and exhaustion are important.^{25,26} Errors are more likely to occur when tasks are carried out after hours by busy, distracted staff, often in relation to unfamiliar patients.¹⁹ There is a particular risk of errors when doctors first arrive in hospital, because of shortcomings in their knowledge,¹⁶ and presumably also because they are unfamiliar with local prescription charts and other systems. Improved education and improved working conditions, including better induction processes, should reduce the risk of errors that are due to these factors; a national prescription form would help.

Detecting and reporting errors

One difficulty in detecting errors is that those who make them fear disciplinary procedures and do not want to report them.²⁷ The establishment of a blame-free, non-punitive environment can obviate this.²⁸ The reporting of errors, including near-misses, should be encouraged, using error reports to identify areas of likeliest occurrence and simplifying and standardizing the steps in the treatment process. However, some systems for voluntarily reporting medical errors are of limited usefulness, because reports often lack details and there is incomplete reporting and under-reporting.²⁹ A medication error reporting system should be readily accessible, with clear information on how to report a medication error, and reporting should be followed by feedback; detection may be improved by using a combination of methods.³⁰

Prescribing faults and prescription errors

Errors in prescribing can be divided into irrational prescribing, inappropriate prescribing, ineffective prescribing, underprescribing and overprescribing, and errors in writing the prescription. The inadequacy of the term 'error' to describe all of these is obvious. Failing to prescribe an anticoagulant for a patient in whom it is indicated (underprescribing) or prescribing one when it is not indicated (overprescribing) are different types of error from errors that are made when writing a prescription. I therefore prefer to use the terms 'prescribing faults' and 'prescription errors'.⁹ The term 'prescribing errors' ambiguously encompasses both types.

Prescribing faults

Irrational and inappropriate prescribing

'Rational' is defined in the *Oxford English Dictionary* as 'based on, derived from, reason or reasoning' and 'appropriate' as 'specially fitted or suitable, proper'.⁵ One would expect rational prescribing to be appropriate, but that is not always the case. A rational approach can result in inappropriate prescribing, if it is based on missing or incorrect information. If, for example, one does not know that another prescriber has already prescribed paracetamol unsuccessfully for a headache, a prescription for paracetamol might be rational but inappropriate. Consider an example from my own practice.³¹

- A woman with Liddle's syndrome presented with severe symptomatic hypokalaemia. Her doctor reasoned as follows:
 - she has potassium depletion;
 - spironolactone is a potassium-sparing drug;
 - spironolactone will cause her to retain potassium;
 - her serum potassium concentration will normalize.
- She took a full dose of spironolactone for several days, based on this logical reasoning, but still had severe hypokalaemia. Her doctor should have reasoned as follows:
 - she has potassium depletion due to Liddle's syndrome, a channelopathy that affects epithelial sodium channels;
 - there is a choice of potassium-sparing drugs;
 - spironolactone acts via aldosterone receptors, amiloride and triamterene via sodium channels;
 - in Liddle's syndrome an action via sodium channels is required.

- When she was given amiloride instead of spironolactone her serum potassium concentration rapidly rose to within the reference range.

This stresses the importance of understanding the relation between the pathophysiology of the problem and the mechanism of action of the drug (see below).

Ineffective prescribing

Ineffective prescribing is prescribing a drug that is not effective for the indication in general or for the specific patient; it is distinct from underprescribing (see below). In a study of 212 patients, 6% of 1621 medications were rated as ineffective.³² Of 196 US out-patients aged 65 and older who were taking five or more medications, 112 (57%) were taking a medication that was ineffective, not indicated, or duplicative.³³ And in a Scottish study, 49% of general practices prescribed homoeopathic remedies, 5% of practices accounting for 50% of the remedies prescribed.³⁴

One would expect ineffective prescribing to be minimized by the use of guidelines, but there is conflicting evidence; prescribing guidelines may be ineffective unless accompanied by education or financial incentives.³⁵

Underprescribing

Underprescribing is failure to prescribe a drug that is indicated and appropriate, or the use of too low a dose of an appropriate drug. The true extent of underprescribing is not known, but there is evidence of significant underprescribing of some effective treatments, such as angiotensin converting-enzyme inhibitors for patients with heart failure³⁶ and statins for hyperlipidaemia.³⁷

The sources of underprescribing include fear of adverse effects or interactions, failure to recognize the appropriateness of therapy, and doubts or ignorance about likely efficacy. Cost may play a part.³⁸ There is a tendency to avoid treatment in older people,^{39,40} and this can lead to unwanted effects,²⁸ including the so-called risk-treatment mismatch, in which those who are at greatest risk are less aggressively treated, an effect that may be partly associated with age.⁴¹ However, other factors may contribute to this type of mismatch, such as distraction by co-morbidities, miscalculation of the true benefit to harm balance and a reluctance to undertake or exacerbate polypharmacy.⁴²

In a study of the relation of underprescribing to polypharmacy in 150 elderly patients, the probability of underprescribing increased significantly with the prescribed number of drugs.⁴³ This resulted

in failure to use β -adrenoceptor antagonists after myocardial infarction, ACE inhibitors for heart failure, anticoagulants in atrial fibrillation and bisphosphonates in osteoporosis.

Overprescribing

Overprescribing is prescribing a drug in too high a dosage (too much, too often or for too long). In some cases treatment is not necessary at all. For example, among hospital patients who were given a proton pump inhibitor treatment was indicated in only half.⁴⁴ Polypharmacy, defined as the use of five or more drugs, occurs in >10% of people aged over 65 years in the UK.⁴⁵ And although not all polypharmacy is inappropriate,⁴⁶ some undoubtedly leads to ADRs and drug-drug interactions.

Overuse of antibiotics is well known and much discussed. A systematic review of 55 trials showed that no single strategy or combination of strategies was better than any other and none was highly effective, although the authors singled out active education of clinicians as a strategy to pursue.⁴⁷

In a Spanish study, those who overprescribed were more likely to be in rural practices, further from specialist centres, caring for children, lacking postgraduate education and in part-time or short-term work.⁴⁸ In some countries, doctors' income may have an effect.⁴⁹

Prescription errors

All the factors that lead to medication errors in general contribute towards prescription errors. They include lack of knowledge, using the wrong drug name, dosage form, or abbreviation, and incorrect dosage calculations.⁵⁰ In a US study of about 900 medication errors in children, ~30% were

prescription errors, 25% were dispensing errors and 40% were administration errors.⁵¹ In one study the most common form of prescription error was writing the wrong dose.¹² In six Oxford hospitals the most common errors on prescription charts were writing the patient's name incorrectly and writing the wrong dose, which together accounted for ~50% of all errors.¹⁶ In a hospital study of 192 prescription charts, only 7% were correctly filled; 79% had errors that posed minor potential health risks and 14% had errors that could have led to serious harm.⁵²

Table 1 lists some examples of prescribing faults and prescription errors under the headings of the four types of error. The remedies are as outlined above.

The hedgehog principle and balanced prescribing

The major barrier to rational, appropriate and effective prescribing is failure to apply what I call the hedgehog principle. The Greek poet Archilochus (seventh century BC) wrote that 'The fox knows many things, the hedgehog one big thing'. What he meant is not clear, since the text is fragmentary, but Isaiah Berlin suggested that it could be interpreted as distinguishing between 'those who relate everything to a single central vision [hedgehogs] ... and those who pursue many ends [foxes]'.⁵³ As a prescriber I am a hedgehog, and the one big idea to which I subscribe is the need to marry the mechanism of action of the drug to the pathophysiology of the disease. Using amiloride to treat hypokalaemia in Liddle's syndrome (as described above) is a perfect example of this principle. If in addition one pays

Table 1 Examples of prescribing faults and prescription errors

Type of error	Example	Outcome
Knowledge based	Being unaware of the interaction between warfarin and erythromycin	Warfarin toxicity
Rule based	Prescribing oral treatment in a patient with dysphagia	Lung aspiration or failure to treat
Action based	Being distracted, writing diazepam for diltiazem	Sedation
Technical	Writing illegibly, so that 'Panadol' (paracetamol) is dispensed instead of 'Priadel' (lithium) ^a	Loss of effect
Memory based	Forgetting to specify a maximum daily dose for an 'as required' drug	Poisoning or unnecessary treatment

^aThis stresses the importance of prescribing by generic name whenever possible, since more errors are made by confusing brand names than generic names; however, in this case 'Priadel' had to be prescribed—modified-release formulations of lithium must be prescribed by brand name because of differences in bioavailability from brand to brand.

attention to the balance of benefit and harm, one achieves 'balanced prescribing', defined as the use of a medicine that is appropriate to the patient's condition and, within the limits created by the uncertainty that attends therapeutic decisions, in a dosage regimen that optimizes the balance of benefit to harm.⁵⁴ Note that this definition includes the two components of the hedgehog principle: the disease and the medicine.

Achieving balanced prescribing

Nine questions should be asked before writing a prescription (adapted from the Medication Appropriateness Index^{55,56}):

Indication: is there an indication for the drug?

Effectiveness: is the medication effective for the condition?

Diseases: are there important co-morbidities that could affect the response to the drug?

Other similar drugs: is the patient already taking another drug with the same action?

Interactions: are there clinically important drug-drug interactions with other drugs that the patient is taking?

Dosage: what is the correct dosage regimen (dose, frequency, route, formulation)?

Orders: what are the correct directions for giving the drug and are they practical?

Period: what is the appropriate duration of therapy?

Economics: is the drug cost-effective?

The mnemonic for this list is 'i.e. do I dope?'. Each item relates to an important process in prescribing, and in the absence of evidence that following this schedule improves prescribing, it makes sense to use it.

Conclusion: a prescription for better prescribing

We all make errors from time to time. There are many sources of medication errors and different ways of avoiding them. However, we must start by being aware that error is possible and take steps to minimize the risks. The essential components of this are monitoring for and identifying errors, reporting them in a blame-free environment, analysis of their root causes,⁵⁷ changing procedures according to the lessons learnt and further monitoring.

How can we improve prescribing and reduce medication errors? Five prescriptions might help^{35,58}:

- R Education, to be taken as often as possible (a repeat prescription—learning should be lifelong).
- R Special study modules for graduates and undergraduates, to be taken as required.
- R Proper assessment: in the final undergraduate examination, to be taken once or twice; in postgraduate appraisal, to be taken occasionally; this could be linked to a licence to prescribe.
- R A national prescription form for hospitals, to be applied uniformly and used as a training tool.
- R Guidelines and computerized prescribing systems, to be taken if indicated (their roles and proper implementation are not yet clear).

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