Although medicines play an important role in the management of chronic and acute illnesses, they can also be a significant source of unintended harm. It has been estimated that at least 5% of all hospital admissions are medicines-related,\(^1,2\) with adverse drug reactions (ADRs) directly leading to admission in 80% of cases, and an overall fatality rate of 0.15%.\(^1,3\)

Medicines-related admissions (MRAs) are estimated to account for 4% of hospital bed capacity, and almost half are potentially preventable.\(^1,2\) This raises important patient safety and economic considerations.

This bulletin discusses the issue of MRAs including their detection, cross-sector reporting, contributory factors, and initiatives aimed at reducing those deemed to be avoidable.

**What is a medicines-related admission?**

Medicines-related admission is the term given to the hospitalisation of a patient that results from harm related to a medicine. There are several ways in which the use of medicines can cause harm to a patient. Firstly, medicines can cause unwanted side-effects (ADRs, including allergic reactions). These can occur even when a medicine is prescribed appropriately and used correctly, and may occur if the patient has been taking the medicine long-term, e.g., angioedema secondary to ACE inhibitors. Secondly, the potential for patient harm may arise due to errors or incidents involving prescribing (including inappropriate or over-treatment, and failure to prescribe the indicated treatment or under-treatment), dispensing, administering, reconciling, or monitoring of medicines. Lastly, harm may arise from poor adherence (incorrect or non-use by the patient, which may be intentional or non-intentional). Many studies of MRAs focus only on those related to ADRs and therefore, may underestimate their prevalence.

**How are MRAs detected and reported?**

According to data from NHS Wales, MRAs accounted for 0.6% of hospital admissions from 2012 to 2013.\(^4\)

This represents a considerably lower prevalence than that of around 5% estimated from large observational studies and systematic reviews.\(^1,2,5,6\) This difference is likely to be due to MRAs not being consistently documented, coded, and reported as such in routine practice in the NHS.

The reasons for this under-recognition and under-reporting of MRAs may be multifactorial. Determining whether an admission is medicines-related can be complex and it may not be immediately recognised as such. Identification of an MRA will usually require a degree of clinical judgement, or perhaps background information to which hospital practitioners may not be party. One study found that the documentation of MRAs in inpatient records, including the discharge summary, were inconsistent and had communication gaps.\(^7\) Furthermore, International Classification of Diseases (ICD) codes related to medicines-related harm were rarely used, thus any work reporting a rate of MRAs based on collecting ICD-10 codes is likely to underestimate the true occurrence.
A project is currently underway at Wrexham Maelor Hospital, Betsi Cadwaladr University Health Board (BCUHB) to actively identify MRAs and follow patients through their hospital stay, aiding accurate coding and discharge information.8 If rolled out across the rest of Wales, this project could improve awareness and understanding of the true scale of MRAs.

Under-reporting of MRAs may be due to a lack of awareness.9 For example, the prescriber may not be aware that the harm has occurred if it is subsequently reported to another health professional or treated in another care setting.

“We track the fate of parcels put in the post a hundred times more accurately than we track the extent to which our medicines may be causing injuries.”10

If a health professional is unaware that patient harm has resulted from their prescribing or dispensing practice, the need to reflect upon, and change his or her current practice may not be identified. Methods of providing meaningful feedback about suspected MRAs to GPs, hospital doctors, pharmacists, and non-medical prescribers are being investigated.8

Which medicines are likely to be involved?

Any medicine has the potential to harm as well as benefit a patient. However, there is evidence that certain medicines, or groups of medicines are more likely to be related to a hospital admission.1,5,11 A systematic review found that just four classes of medicine – antiplatelets (including aspirin), anticoagulants, NSAIDs, and diuretics – are associated with around half of preventable MRAs.5

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Incident</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>Taken at same time of day as calcium tablets</td>
<td>Reduced ciprofloxacin absorption; treatment failure</td>
</tr>
<tr>
<td>Various</td>
<td>Serial use of non-evidence-based dose/choice of antibiotic</td>
<td>Clostridium difficile infection</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Prescribed for a warfarinised patient with no extra monitoring arrangements</td>
<td>Increased INR and subsequent cerebrovascular accident</td>
</tr>
</tbody>
</table>

Table 1. Examples of antibiotic-associated admissions

Are some patients at greater risk of MRAs?

Some groups of patients are at greater risk of an MRA. Studies have highlighted several patient-related and medication-related factors that may help to identify those patients at greatest risk (see Box 2).

<table>
<thead>
<tr>
<th>Box 2. Risk factors for MRAs 2,6,11</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient-related factors</strong></td>
</tr>
<tr>
<td>Impaired cognition</td>
</tr>
<tr>
<td>Four or more diseases in patient’s medical history</td>
</tr>
<tr>
<td>Dependent living situation</td>
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<tr>
<td>Impaired renal function before hospital admission</td>
</tr>
<tr>
<td>Non-adherence to medication regimen</td>
</tr>
<tr>
<td>Age &gt; 65 years (more likely to experience an ADR)</td>
</tr>
<tr>
<td><strong>Medication-related factors</strong></td>
</tr>
<tr>
<td>Polypharmacy (the use of five or more medicines at the time of admission)*</td>
</tr>
<tr>
<td>New medicine started within the last seven days</td>
</tr>
</tbody>
</table>

*Complex medication regimens at hospital admission have also been found to be predictive of re-hospitalisations for adverse drug events.

How can the risk of an MRA be minimised?

The NHS in Wales is moving towards a culture of prudent healthcare.12 Prudent healthcare has been described as “healthcare that fits the needs and circumstances of patients and actively avoids wasteful care that is not to the patient’s benefit”.12 The principles are to:9

- minimise avoidable harm;
- carry out the minimum appropriate intervention;
- promote equity between the people who provide and use services;
- organise the workforce around the “only do what only you can do” principle;
- remodel the relationship between user and provider on the basis of co-production.

All of these principles have relevance to aspects of prescribing practice (‘prudent prescribing’) and some are particularly pertinent to MRAs.

Local tracking of suspected MRAs at Wrexham Maelor Hospital, highlighted the involvement of antimicrobials; a group of medicines not mentioned in previous studies of MRAs.8 Further analysis of these MRAs identified a number of themes including inappropriate choice or dose of antibiotic; timing of advice; lack of extra monitoring arrangements; and avoidable allergy (see Table 1 for examples).8
Minimise avoidable harm

Much harm associated with medicines is avoidable if their pharmacology is considered together with individual patient factors. All medicines have the potential to cause ADRs. Dose-related, or type A ADRs, are most common and are predictable (and potentially avoidable) based on the pharmacology of the medicine. Around 70% of ADRs causing hospital admission are type A. Type B ADRs are less common and less predictable as they are related to individual susceptibility or hypersensitivity. Approximately 20% of patients re-admitted to hospital within one year of discharge from their index admission are re-admitted due to an ADR.13

Very young children and elderly (particularly frail) adults are most prone to experiencing type A ADRs because their means of eliminating the medicine from the body are, respectively, immature or impaired. The effect this will have on the safe and effective dose of medicine in a patient depends on the degree of impairment of these elimination processes and their importance in the elimination of the medicine. Dose-related failure of therapy to manage a condition adequately may be one of the most important reasons for admission of the elderly to hospital. Therefore, age itself should not be a reason for withholding adequate doses of effective therapies.14,15

Avoidable harm from medicines may also arise from prescribing errors. It is estimated that 5% of prescription items are associated with prescribing or monitoring errors.16 The causes of these errors are likely to be multifactorial,16 but might include human error (not knowing enough about the patient or medicine, or a slip or lapse when prescribing); communication problems (with patients or between primary and secondary care); problems in monitoring and review of therapy, or in repeat prescribing.

Ten tips for safer prescribing20

1. Keep therapeutics knowledge up-to-date.
2. Before prescribing, make sure you have all the patient information that you need, e.g. renal function.
3. Before prescribing, make sure you have all the information you need about the medicine, e.g. interactions.
4. Think ‘Do I need to prescribe this medicine at all?’
5. Check computer alerts for missed interactions/allergies.
6. Check the prescription for errors before signing.
7. Involve patient in prescribing decisions and make sure they know how to take the medicine, when to return for monitoring/review, and warning signs of serious ADRs.
8. Have systems in place to ensure essential laboratory monitoring of treatment takes place.
9. Review the safety of your repeat prescribing system regularly, to minimise the risks of harm due to errors in systems and processes.
10. Have safe and effective ways of communicating medicines information between primary and secondary care, and of acting on medication changes suggested or initiated by secondary care clinicians.

Encourage co-production

It is possible for patients to suffer from medication-related adverse events because either they do not have sufficient knowledge of their conditions and medicines, or they have not been given adequate explanation of how to take the medicines, side-effects to look for and what monitoring is needed (for example, see Box 3).17

Research suggests that 11-22% of hospitalisations for exacerbations of chronic disease are a direct result of medication non-adherence.18 For some conditions, it is particularly important to ensure that patients have an understanding of the medicines that they are taking, in order to prevent incorrect, under- or over-use that could result in an MRA. These include asthma, coronary heart disease, diabetes mellitus (particularly if using insulin), epilepsy, and heart failure.

“In gymnastics, the dismount may be more important than the rest of the routine. In health care, we often ignore the ‘dismount’ – the handoff of responsibility from healthcare system to patient.”19

Prudent healthcare encourages the relationship between patient and healthcare provider to be based on the concept of ‘co-production’. This involves creating a prescribing partnership where the process of prescribing, dispensing, and administering medicines puts the patient at its centre and encourages shared decision-making.15

All suspected medicines-related admissions should be reported to the Medicines and Healthcare products Regulatory Agency (MHRA) via the Yellow Card Scheme.

www.mhra.gov.uk/yellowcard

Adapted from National Prescribing Centre. 10 Top tips for GPs. Strategies for safer prescribing. 2011
Carry out minimum appropriate intervention

The average number of prescribed items per person in the UK increased by over 50% between 2001 and 2011. Polypharmacy is becoming increasingly common in primary and secondary care, and in care homes for older people. This increase is driven by the growth of an ageing population with increasing prevalence of multi-morbidity, an increase in the range of effective medicines, and also the plethora of disease-specific clinical guidelines (many of which were not developed in the context of multiple morbidity). However, polypharmacy increases the risk of adverse events, especially in the frail elderly, and the toxicity of some medicine combinations may be greater than the sum of the toxicity of either agent used alone, resulting in significant ADRs.15

Certain combinations of medicines and conditions are generally considered high risk for causing harm (see Box 4). These combinations should be avoided if possible and clearly justified if considered necessary.22

In the past, polypharmacy has been considered as something to be avoided. However, it is now recognised that in some circumstances, it can be therapeutically beneficial. For many people, appropriate polypharmacy will improve their quality of life and extend life expectancy. However, because polypharmacy may be harmful — in that it can increase the risk of drug interactions and ADRs, and can impair medication adherence and quality of life — problematic polypharmacy, where there is no evidence of benefit from the prescribed medicines, should be avoided.21

Although polypharmacy is not an issue that affects only older people, it is particularly important that medication reviews are undertaken regularly for this group of patients to support scaling back or increasing treatment where appropriate.

When prescribing any medicine it is important to consider for how long treatment will be required, or even whether it is required at all — is it being given as part of a “prescribing cascade” to treat an iatrogenic illness?24 Increasingly, prescribers are becoming aware of the need to consider deprescribing.25 Guidelines often focus on starting treatments and are not balanced by guidance on when it might be appropriate to stop or reduce the medication, often making decisions on tapering or stopping a medicine difficult. Several tools have been developed to support and assist prescribers and patients in making informed decisions on whether to deprescribe, including NO TEARS and STOPP/START.26,27 Guidance on stopping some specific medicines can be found at www.wemerec.org.

### Box 3. Medicines and acute kidney injury (AKI)

It is estimated that one in five emergency admissions into hospital are associated with AKI.23

Patients taking any of the following medicines are particularly susceptible to AKI:

- ACE inhibitors or ARBs (“sartans”)
- NSAIDs
- metformin
- diuretics

Many patients (excluding those with heart failure or under specialist care, who should seek medical advice) may withhold these medicines temporarily (for up to 48 hrs), when there is a risk of dehydration e.g. if suffering from vomiting and diarrhoea, fever, or infection.

Patient information leaflets should be used as part of a discussion to explain the medicines involved and clarify what level of illness would warrant temporarily stopping medicines, and when they should be re-started.

### Box 4. High-risk combinations 22 (adapted)

- NSAID
  + ACE inhibitor or ARB + diuretic
  + heart failure diagnosis
  + eGFR < 60 ml/min
  + warfarin or non-vitamin K antagonist oral anticoagulants (NOACs)
  + age > 75 years without PPI cover

- Heart failure diagnosis
  + NSAID
  + glitazone
  + tricyclic antidepressant

- Warfarin
  + antiplatelet
  + NSAID
  + NOAC
  + acutely prescribed antibiotics* 
  + oral azole antifungals (including oral gel)*
  + oral antivirals*
  + tramadol*

*may be used with extra monitoring

This list is not exhaustive; consult the BNF for full details of cautions, contraindications, and interactions.

### Conclusion

MRAs are an important patient safety issue. Improved awareness, recognition, recording, coding, reporting, and feedback are needed to help us better understand the problem. The root causes of MRAs are complex and it is likely that successful interventions to reduce the scale of the problem will need to be multi-faceted, involving health professionals from both primary and secondary care, as well as patients.

References available at www.wemerec.org

www.wemerec.org
References


27. Gallagher P et al. STOPP (Screening Tool of Older Person’s Prescriptions) and START (Screening Tool 