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Adverse drug events in the elderly

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Background: Increasing recognition of the burden associated with iatrogenic disease has led to international interest into how best to promote patient safety. Within this field, the subject of adverse drug events (ADEs) has received particular attention, this reflecting the known high frequency with which such events occur, particularly in the elderly.

Methods: We conducted a narrative review summarizing epidemiological data on medication-related adverse events in elderly people, considering various known causes of such events and suggesting practical ways in which prescribing can be made safer for high-risk populations.

Results: There is an increasing recognition that a relatively high proportion of ADEs in the elderly may be preventable. Systems issues have been found to play a particularly powerful role in this context, resulting in several promising approaches to address the problem.

Conclusions: Relatively simple system changes have the potential to reduce the burden associated with medication-related adverse events in the elderly.

Keywords: adverse event/elderly/incident reporting/intervention/medicines management/systems approach/taxonomy

> Lord, deliver me from the man who never makes a mistake, and also from the man who makes the same mistake twice. (William J. Mayo)

Introduction

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Adverse drug events (ADEs) in the elderly are an increasingly important problem in healthcare today, these increases being fuelled by a combination of ageing populations and the tendency to prescribe for an ever-increasing range of disorders. Not only these adverse events have important implications for patients (e.g. loss of trust, morbidity and mortality) and healthcare professionals (e.g. stress), but they also pose an enormous financial burden on society.

The elderly (i.e. those aged 65 or older) are at increased risk of ADEs due to a combination of physiological decline (e.g. reduced renal and

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hepatic clearance), co-morbidity resulting in the possibility of drug-disease interactions and in the case of polypharmacy drug–drug interactions, and problems with adherence due to, among other things, frailty, reduced dexterity and memory problems.[1]

At their most basic, these medication-related adverse events can be seen as resulting from commission or omission of medication, but important conceptual work has allowed a more nuanced taxonomy of medication-related adverse events to emerge. These new frameworks have the particular advantage of helping to develop approaches for reducing these adverse events.

It has, however, to be kept in mind that by definition an adverse drug reaction differs from an ADE in that the former is an outcome attributable to a drug, whereas the latter, while occurring during medication intake, is not necessarily so (see Table 1 for a summary of key terms).

An important subgroup of ADEs are *preventable drug-related events* [also known as *preventable drug-related morbidity* (PDRM)]. These can be due to predictable medication side effects (Type A reactions),

Table 1 Glossary of key terms.

Active errors	Errors attributable to frontline professionals who prescribe, dispense or monitor medication
ADE	An unwanted occurrence after exposure to a drug that is not necessarily caused by the drug
Adverse drug reaction (ADR)	Any undesirable effect of a drug beyond its anticipated therapeutic effects occurring during clinical use
Emergent behaviours	Patterns generated from complex systems which cannot be predicted from study of the simpler elements from which they emerge
Lapse	A glitch in cognition, e.g. failing to recall a drug name or a dose
Latent errors	Errors which lie dormant in the system until conditions are right for their expression
Medication process	Five steps in medication management: prescribing, dispensing, administering, monitoring and systems control
Medication use review	These may be planned (e.g. for patients on multiple medicines) or intervention (conducted at time of dispensing) and are interventions aimed at both the administering and monitoring stages of the medication process checking patients' need for and understanding of their medicines
Root cause analysis	A technique involving a retrospective review of a patient safety incident to identify what, how and why it happened
Slip	An unintended act such as writing the wrong dosage schedule perhaps as a result of diversion of attention of the prescriber
Type A ADR	Drug reactions related to dose and pharmacological effect and are potentially preventable
Type B ADR	Drug reactions, which are idiosyncratic and were occurring after initial use of a drug, are not predictable and thus not preventable

Source: Reproduced with kind permission from Fernando *et al.*,[54] p. 2.

medication errors, problems with adherence, professional negligence or frank criminality. Though operating through disparate mechanism, what these different types of PDRM share is that, as the name suggests, these are all in theory preventable. Not all ADEs are, however, preventable; some side effects are, for example, unpredictable (Type B idiosyncratic reactions) and these cannot therefore be currently prevented.

The medication process is commonly conceptualized as consisting of several stages including prescribing, transmitting, dispensing, administering and monitoring.[2] The majority of medication errors has been found to occur at the prescribing stage.[3] Therefore, prescribing has been the focus of recent efforts to reduce PDRM. Indicators for preventable drug-related morbidity have been identified.[4]

In this paper, we focus on PDRM and, in particular, on the contribution of medication errors as these are in theory preventable. We aim to summarize key considerations in relation to medication safety in the elderly. We begin by describing the scale of the problem, following which we consider contemporary approaches to classifying, defining and learning from medication-related patient safety incidents, and consider strategies for enhancing prescribing safety. We conclude with practical advice to clinicians that should enhance prescribing safety when prescribing for these high-risk patients.

The scale of the problem

Numerous randomized controlled trials and systematic reviews of these studies demonstrate the benefits of medicines in curing and reducing the symptoms of a number of illnesses. However, these benefits have to be weighed against possible risks. It is estimated that there are around 850 000 adverse events in UK hospitals each year, costing the NHS approximately £100 million in increased hospital stays.[5] Meta-analyses indicate that the proportion of drug-related hospitalizations is between 2.4 and 6.2%[6,7] and many of these are considered preventable.[8] A recent study in the Netherlands[9] found that around 41 000 hospital admissions per year are related to ADEs with about half being potentially preventable. The risk was doubled if the patient was 65 or older. Pirmohamed *et al.*[10] found in a prospective observational study conducted in two hospitals in England that adverse drug reactions cost £466 million annually and result in the deaths of around 5700 patients. The frequency with which these errors occur in primary care is unknown.

The elderly are particularly at risk for drug-related problems.[11] A key risk factor in this group of patients is polypharmacy (Fig. 1). Around 30% of hospital admissions of patients aged 65 and over are due to

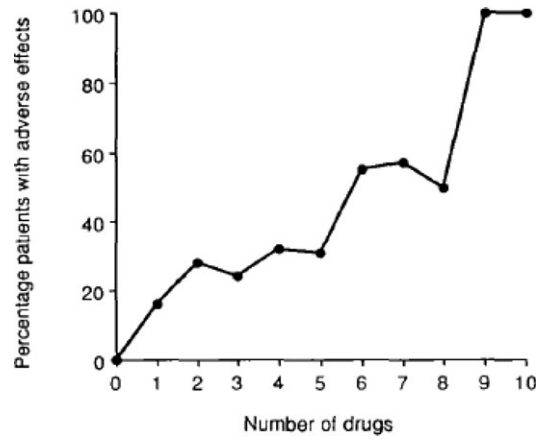

Fig. 1 The relationship between adverse drug reactions and polypharmacy. Reproduced with kind permission from Denham.[55]

ADEs, most of which are preventable.[12] Also of concern is that the likelihood of severe long-term sequelae such as disability and death following ADEs is significantly higher in the elderly population.[13]

Epidemiological studies have found that the classes of drugs most commonly associated with adverse drug reactions in the elderly include diuretics, warfarin, non-steroidal anti-inflammatory drugs (NSAIDs), selective serotonin reuptake inhibitors, beta-blockers and angiotensin-converting enzyme (ACE)-inhibitors.[10,11,14] These treatments are frequently co-prescribed in these populations, thereby greatly increasing the risk (Table 2).

Why do errors occur?

Considering person-centred and systems-based approaches

There are two main approaches to minimizing medical errors: the person-centred approach and the systems approach.[15] The former still dominates in medicine and has a focus on individual accountability. For example, in the case of a patient who experiences an ADE due to a drug–drug interaction, the response from senior colleagues might be to exhort their junior colleague to learn more about the drugs being prescribed, and through taking these steps not to repeat the same mistake again[16] (Table 1). However, this person-centred approach has been associated with avoidance of reporting errors (due to fear of litigation, disciplinary action, etc.) and inhibits both personal and organizational learning.

Table 2 Drug groups most commonly associated with preventable drug-related admissions relating to adverse drug reactions and over-treatment, under-treatment and problems with patient adherence.

Drug group	All preventable drug-related admissions, number (%) ($n = 1406$)	Adverse drug reactions and overtreatment, number (%) ($n = 1263$)	Patient adherence problems, number (%) ($n = 98$)	Undertreatment, number (%) ($n = 45$)
Antiplatelets (including aspirin when used as an antiplatelet)	225 (16.0)	219 (17.3)	2 (2.0)	4 (8.9)
Diuretics	223 (15.9)	202 (16.0)	20 (20.4)	3 (2.2)
NSAIDs	155 (11.0)	151 (12.0)	4 (4.1)	0
Anticoagulants	117 (8.3)	113 (8.9)	4 (4.1)	0
Opioid analgesics	69 (4.9)	68 (5.4)	1 (1.0)	0
Beta-blockers	65 (4.6)	56 (4.4)	4 (4.1)	5 (11.1)
Drugs affecting the renin–angiotensin system (e.g. ACE-inhibitors)	62 (4.4)	58 (4.6)	4 (4.1)	0
Drugs used in diabetes	49 (3.5)	40 (3.2)	9 (9.2)	0
Positive inotropes	45 (3.2)	41 (3.2)	3 (3.1)	1 (2.2)
Corticosteroids	44 (3.1)	41 (3.2)	2 (2.0)	1 (2.2)
Antidepressant	42 (3.0)	41 (3.2)	1 (1.0)	0
Calcium channel blockers	39 (2.8)	34 (2.7)	1 (1.0)	4 (8.9)
Anti-epileptics	32 (2.3)	11 (0.9)	8 (8.2)	13 (28.9)
Nitrates	24 (1.7)	15 (1.2)	5 (5.1)	4 (8.9)
Inhaled corticosteroids	8 (0.6)	0	7 (7.1)	1 (2.2)
Potassium channel activators	7 (0.5)	1 (0.1)	2 (2.1)	4 (8.9)
Anti-asthmatics*	5 (0.4)	0	5 (5.1)	0
Total	1211 (86.1)	1091 (86.4)	82 (83.7)	40 (88.9)

*Inhaled and oral bronchodilators and corticosteroids and other anti-asthmatic drugs.
Source: Reproduced with kind permission from Howard *et al.*,[56] p. 144.

The systems approach is in contrast based on the assumption that errors are by definition unintentional and happen in all organizations. Here, importance is placed on the system in which individuals work (organizational context) and how this may result in error-producing conditions and processes. This approach distinguishes between active errors (individual contributory factors, e.g. slips, lapses) and latent errors (organizational contributory conditions, e.g. heavy workload, long hours). It is supported by studies identifying stress, fatigue and workload in healthcare professionals as increasig the risk of errors.[17] The systems approach is proactive and non-punitive and is advocated by the UK National Patient Safety Agency. It promotes the use of

incident reporting systems (which are discussed later in this paper) in order to achieve organizational learning and prevent errors. Of particular interest in this context is the recording and analysis of 'near misses', which are more common than actual adverse events, and as such represent a valuable source of personal and organizational learning.

The systems approach is based on Reason's Swiss cheese model of system failures.[15] This model emphasizes the important role of system defences and illustrates how defences, barriers and safeguards (represented by aligned slices of Swiss cheese) within an organization may be breached by an error such as the issuing of a prescription to the wrong patient. Although in most cases this will be picked up by safeguards in the system, in some cases, the 'holes in the Swiss cheese' align and may result in the wrong medication being dispensed and administered resulting in iatrogenic harm. Organizational factors affecting errors have been found to be communication, work environment, workload, training and supervision.[18]

Taxonomies of error and patient safety

In order to help make sense of the data generated through incident reports and the associated conceptual work being undertaken, patient safety taxonomies have emerged as classification systems attempting to encode and organize patient safety data. These often go hand-in-hand with *incident reporting systems*, which will be discussed subsequently. Despite the progress that has been achieved in recent years, the UK Department of Health has concluded that there is still no agreed definition of 'incident' as none of the existing taxonomies adequately incorporate near misses, which is of concern given the need to spread learning throughout the NHS.[5] Spurned on by the inadequacies of existing taxonomies and the lack of agreement on which to use, the World Health Organization (WHO) is currently developing an International Patient Safety Event Taxonomy (IPSET).[19] The aim is to record medical errors, adverse events and near misses globally in order to gain a better insight into causes and ultimately to prevent such events from occurring.

The JCAHO Patient Safety Event Taxonomy (PSET)[20] is an attempt to develop a multi-dimensional standardized taxonomy by extracting elements of existing taxonomies and integrating these (Fig. 2). The PSET includes the definition of terms as well as the classification of events. It also takes into account the impact (of the incident on the patient), type (observable processes of incident), domain (setting and individuals involved), cause (factors/agents that led to incident) and prevention (proposed or actual actions to prevent incidence from

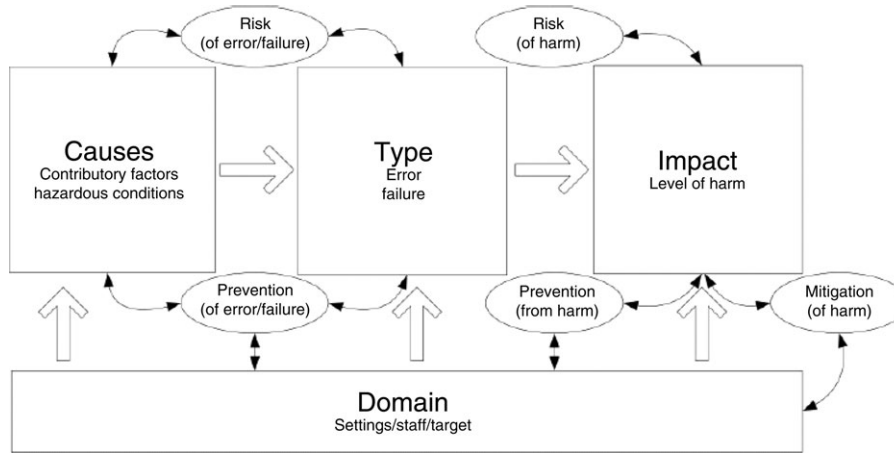

Fig. 2 Analytical framework of the JCAHO patient safety event taxonomy. Reproduced with kind permission from Chang *et al.*[20]

occurring again and/or to minimize negative impact). These domains are further divided into 21 secondary categories, 200 subcategories and an infinite number of fields containing narrative information. A major advantage of this taxonomy is its wider applicability to different healthcare settings.

Approaches to improving patient safety: interventions

Incident reporting systems

One approach to address the issues surrounding patient safety in healthcare is the development of incident reporting systems. These involve self-reporting adverse events and near misses into a database as they take place. The aim is to understand how and why adverse events occur in order to facilitate learning from such events and then to try and prevent them from occurring in the future. This involves attempting to identify similarities, differences, causes and contributing factors of incidents and to use this information for developing strategies for prevention. Incident reporting systems target organizational culture and promote culture of safety to encourage the reporting of errors.[15] There is thus a shift from blaming individuals to the recognition that organizational circumstances can contribute to covering up errors.[21] Central to this idea is the concept of reflexivity—the reflexive healthcare professional is crucial for organizational learning to take place.

Although reporting systems are more common in secondary care, their potential for primary care has been highlighted.[22] In the UK, a

National Reporting and Learning System (NRLS) has been developed by the UK National Patient Safety Agency (NPSA) and was launched in 2004.[23] It is derived from the existing taxonomies and designed to 'collect information on patient safety incidents' across several NHS services in England and Wales. The aim is to gradually roll out the system across the whole NHS including both primary and secondary care. In a pilot study, implemented at 28 pilot sites, detailed incident data were reported through an anonymous electronic form directly to the NPSA where it was analysed on the basis of six standardized categories: details of the incident, patient information, medication, medical devices, information about the staff and other contributing factors. Other data gathered addressed the usability of the taxonomy. Analysis by the NPSA has indicated that the number of incident reports and trusts involved has been steadily increasing since its launch—by June 2006, the system had collected almost 800 000 incident reports.

Barach and Small[24] have reviewed incident reporting systems in other industries and conclude that encouraging individuals to report events is challenging as it involves admitting that one has made a mistake. As a result, incidents tend to be under-reported. The authors conclude that other industries (especially the aviation industry) therefore focus on reporting near misses. Analysis of these can help to prevent errors from occurring and they are reported more readily. Although most existing reporting systems are voluntary, there is an ongoing debate about mandatory versus voluntary reporting. In voluntary reporting, only a small proportion of incidents are actually reported with the added limitation that there is disproportionate reporting of less serious incidents.[25] Despite holding great potential, these reporting systems are therefore not a particularly accurate epidemiological tool.[26] There is also thus far no robust scientific evidence of the effectiveness of such systems.

Organizational factors that can promote incident reporting have been found to be a strong 'safety culture' (i.e. one that is fair and open), anonymity, a clear definition of the range of events to report, the perceived value of incident reporting and feedback.[24] Fear of litigation has been found to be the main barrier to reporting.[27]

Investigating errors

Common techniques to retrospectively identify and analyse adverse events are significant event analysis, root-cause analysis, chart reviews and clinical database studies. Significant event and root-cause analysis involves identifying the conditions that lead to an adverse event with the aim to spot system failures and hazards. Chart reviews entail reviewing medical records (electronic or paper) from different settings

(e.g. hospitals, A&E, primary care), identifying adverse events and judging these events for causality and preventability. Clinical database studies involve computer searching of electronic records from known problems (e.g. prescription of a beta-blocker to a patient with asthma), but computer systems are still uncommon in UK secondary care, which reduces their applicability. Nevertheless, this method is an inexpensive and 'real-time' alternative to chart review techniques.[28]

A prospective method to identify and analyse adverse events is Failure Modes and Effects Analysis, which attempts to identify risk factors potentially leading to patient safety events and aims at decreasing their impact. However, even though this approach has obvious advantages, it has been criticized for relying heavily on individual experiences and for being resource-intensive.[29]

Proactive intervention

Three proactive intervention approaches to reduce medication-related adverse events have yielded promising results. These include pharmacist-led medication reviews, educational outreach interventions and interventions that utilize computer systems. These will be considered in turn.

Pharmacist-led medication review

During this process, patients' medications are re-examined and an assessment is made of what action can be taken to minimize drug-related problems and to maximize drug-related benefits. The patient and the practitioner are then involved in decisions of medication changes and future treatment.

In secondary care, pharmacist's participation during medication rounds has been found to reduce ADEs[30] and clinical pharmacy services have been found to be related to reduced mortality rates.[31] Evidence also points to the financial benefits of such interventions.[32] Pharmacist-led interventions in primary care are less well researched, although evidence points to their effectiveness in reducing hospital admissions (but there is no strong evidence from randomized controlled trials with regard to this)[33] and in improving prescribing behaviour.[34] More convincing evidence of the effectiveness of such interventions in primary care is certainly needed.

Evidence of the effectiveness of pharmacist-led medication review in the elderly is mixed in the UK.[33,35] This might be due to the predominantly small scale of existing investigations in this group and a lack of consistency in outcome measures (hospital admissions, drug-related problems, quality of life, mortality, etc.) The most compelling evidence

appears to come from primary care settings, but a comprehensive analysis of the cost-effectiveness of such interventions in the elderly is yet to be performed.

Educational outreach interventions

Reviews indicate that educational outreach visits are effective in changing professional behaviour (including prescribing behaviour).[36] They have also been found to increase physician reporting of adverse drug reactions.[37] Audit and feedback techniques employed in educational outreach visits appear to be particularly successful in improving professional medical practice.[38] However, data on the cost-effectiveness of such interventions are sparse.

Utilizing computer systems

Another approach involves the use of computer systems. Bates and Gawande[39] outline how computer systems can reduce errors. These include strategies for improving communication, making information accessible, prompting for information, helping with calculations, checking and monitoring and decision support.

Computerized physician order entry (CPOE) and clinical decision support systems (CDSS) are examples. The former involves physicians entering medication orders into the computer where they are then integrated with information about the patient. Advantages include computerized warnings of possible contraindications (e.g. the use of tetracylines in renal failure), drug–drug interactions (e.g. macrolides with theophylines), a systematic way of data entry as well as integration of the prescription with the patient's history (e.g. allergies). The latter are technological systems that aid clinical decision-making (e.g. in selecting medication, dosing, diagnostic tests). They are usually also linked to patient records and may take the form of computer-based reminder systems.

Reviews have supported the potential of CPOE and CDSS in improving physician performance[40,41] and in reducing medication errors.[42] It has been suggested that these systems are especially effective when targeting high-risk populations and high-risk drugs.[43] For example, a recent study by Smith *et al.*[44] found CPOE and CDSS to be effective in reducing prescribing rates of contraindicated medication in a sample of elderly outpatients.

Other less well-researched areas with potential for the future are Laboratory Information Systems and Bar-Coding Systems. Laboratory Information Systems are computer systems that store data on patient tests and allow hospitals to keep records of results. This can make test results available for both doctors and patients and improves the efficiency. Bar-Coding Systems may involve both barcodes for patients in

the form of wristbands and barcodes for medication packages. This allows for medication information to be easily accessible by means of a portable scanner.

It should also be kept in mind that computer systems can bring their own problems. Unfortunately, such systems often currently lack specificity and generate many spurious warnings (e.g. a spurious warning of a possible adverse drug reaction due to drug doubling when two antihypertensive drugs are prescribed together). We know that 49–96% of safety alerts are over-ridden and alerting systems themselves may contain error-producing conditions.[45] Such warnings have the potential to add to latent errors and lead to clinicians ignoring important warnings. Additionally, there is a potential for over-reliance on warnings. Clinicians may not be aware of failings in prescribing systems (e.g. most will not detect interaction with laboratory results such as raised creatinine).[46] It has also been found that there is a lack of knowledge of systems by GPs and a lack of training.[47] Therefore, computers are unlikely to be able to substitute human judgement, but nonetheless have enormous potential in complementing it.

In the UK, the use of computers is much more common in primary care, which has led governmental efforts to aim at introducing computerized prescribing in NHS hospitals.[48] The NHS has already established the Health Electronic Prescription Service as part of NHS Connecting for Health's Electronic Transmission of Prescriptions (ETP) programme which will eventually be integrated with the NHS Care Records Service. ETP is designed to connect primary care prescribers and dispensers in England by permitting direct electronic transfer of prescriptions. This obviates the need for paper prescriptions and patients carrying prescriptions from the doctor to the pharmacy, which should reduce the potential for errors in transmission of prescriptions between prescriber and dispenser. It is currently in its first stages (in 24% of GP surgeries and 36% of community pharmacies in January 2007) and is planned to be implemented across England.

Multi-faceted interventions

Grimshaw *et al.*[49] have conducted an overview of systematic reviews, which indicated that multi-faceted interventions are more effective than single interventions in bringing about behaviour change in healthcare professionals. In line with this and the evidence of effectiveness of the proactive intervention approaches outlined above, a multi-dimensional intervention with the aim to improve prescribing safety is currently underway in the UK. The PINCER study (Table 3) is a randomized controlled trial rolled out in the general practice environment. The acronym stands for 'a cluster randomised trial comparing the effectiveness of a Pharmacist-led IT-based Intervention with simple feedback in

Table 3 Summary of PINCER trial.

Aim: improving prescribing safety in general practice
Objectives: investigating the effectiveness, costs/benefits and acceptability of a pharmacist-led intervention (using information technology and educational outreach) and a simple feedback intervention (using information technology and educational materials)
Intervention: integration of skill-mix, educational outreach and computer systems
Method: cluster randomized controlled trial
Participants: 'At-risk' expand patients in 68 practices around Nottingham and Stoke
Outcome measures: range of errors in the prescribing and monitoring of medications
Expected completion: March 2009

reducing rates of clinically important Errors in medicines management in general practices'. The trial is investigating whether a pharmacist-led intervention (using information technology and educational outreach) is more effective than a simple feedback intervention (using information technology and educational materials) in reducing medication errors.

Practical advice for clinicians

With the potential of the above approaches in mind, medication-related adverse events in high-risk patients such as the elderly can be reduced by relatively simple system changes.[50] Merely being aware of risk has the potential to protect against possible adverse events. This awareness can permeate the whole experience of being a clinician and can extend from awareness of high-risk situations (e.g. working under time pressure), high-risk patients (e.g. the elderly) to high-risk medications (e.g. those with most commonly associated with preventable events and morbidity). Criteria for safe use of medication in the elderly—for example, avoiding use of anticholinergics in the elderly, which may cause confusion—outlining drugs and/or drug classes which should be avoided in this group, have been developed and are constantly updated.[51]

A patient-centred approach with a focus on patient and carer involvement, patient/carer education, open discussion and shared decision-making also has significant potential in safeguarding against errors.[52] Carers play a particularly powerful role in the care of elderly patients due to their frailty. A working partnership between the physician and the patient/carer can aid safe decision-making and monitoring as well as facilitate the exchange of information and the reporting of problems. In some instances, patients and carers may act as 'error buffers' having extensive knowledge about their history, current medication intake, potential allergies and existing co-morbidities.

The Medicines and Healthcare products Regulatory Agency (MHRA) has published a report with the title *Always read the leaflet* focusing on strategies to improve the quality of information about medicines.[53] The main areas addressed in this context are patient involvement, the quality of patient information leaflets, risk communication and issues surrounding the accessibility of information about medicines. The full report and further practical advice, examples and guidance can be found on the MHRA website (www.mhra.gov.uk).

Conclusions

Potentially preventable medication-related adverse events have received increasing attention, in particular those which are the result of medical errors. We have outlined approaches to understand and address these with a focus on the most vulnerable population in the medication safety arena. The elderly are at elevated risk due to physiological decline, co-morbidity and polypharmacy, resulting in particularly high rates of hospital admissions and death due to potentially preventable medication-related adverse events. However, theoretical and practical approaches to address these issues have not exclusively focussed on the elderly population.

Patient safety taxonomies are still in their infancy and much is to be expected from future developments in this domain. Although a number currently exist, the international focus is on developing a more universal framework to classify and define patient safety incidents. The increasing focus on using a systems-based approach to understand why errors occur is leading to a welcome shift away from the 'culture of blame' and this has in turn led to the development of incident reporting systems. Proactive approaches, especially multi-dimensional interventions that incorporate components of pharmacist-led medication reviews, educational outreach and computer systems, appear promising, particularly in high-risk populations such as the elderly. However, a robust evidence base for these approaches is still lacking and illustrates the need for further interventional studies. While the evidence for (or against) these complex interventions accrues, relatively simple measures can be implemented by all healthcare professionals to safeguard against errors, these including greater risk awareness and patient involvement, both of which have huge potential in relation to prescribing safety.

However, more research is clearly needed and there is still a long way to go to achieve a true 'culture of safety' in healthcare systems internationally. Economically developing countries have, in particular, been somewhat neglected. The wide variety of approaches illustrates the

urgent need for integration—both politically and theoretically. This will also involve investigating how issues of safety are addressed in healthcare professional education. A Department of Health funded study is currently underway to investigate how students from several healthcare professions learn about patient safety. It is hoped that with rising political and academic interest in the patient safety arena, the area will develop further and effective interventions will be increasingly implemented.

Conflict of Interests

Kathrin Cresswell is currently employed on projects funded by the Patient Safety Research Programme supported PINCER study (PS024) and a study to investigate teaching of patient safety in the undergraduate curriculum (PS030). Aziz Sheikh is a grant holder on both these projects and is PI on a study funded by Connecting for Health's Evaluation Programme investigating the role of IT to improve the quality and safety of health care (CfH001). Brian McKinstry is a grant holder on this Connecting for Health Evaluation Programme supported study.

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