

# **Literature Review: Medication Safety in Australia**

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**Prepared for the**

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## Foreword

Medicines are the most common treatment used in health care and contribute to significant improvements in health when used appropriately. However, medicine use can also be associated with harm and the common use of medicines means they are associated with more errors and adverse events than any other aspect of health care. While rates of serious harm are low, errors do affect health outcomes for people and healthcare costs. The prevalence of medication errors is of particular concern because the majority of these errors are preventable.

Knowing how adverse medication events occur and how they can be prevented is important for understanding how we can improve the safety and quality of medicines use, at the level of both individual practice and within systems for managing medicines.

Literature Review: Medication Safety in Australia 2013 is the third in a series surveying the available literature and information on medication safety in Australian health care. The first was published in 2002, and the second in 2008. Since the second review was published, the evidence base for medication-related problems and medication safety activities in Australia has expanded considerably.

The 2013 review provides important new information on the:

- extent and nature of medication errors in Australia;
- effectiveness of strategies to prevent medication errors.

The review is presented in three parts:

- Part 1: The extent of medication-related problems in Australia
- Part 2: Strategies for improving medication safety in the Australian healthcare setting
- Part 3: Medication safety intervention strategies: the international evidence

The data on the extent of medication-related problems in Australia reported in the 2013 review needs to be interpreted within the context of an increasingly complex health system and increasingly complex health care. The first substantial evidence of the extent of medication safety problems in Australia was collected in the 1990s. Since that time, new treatments have been developed and more intensive treatments of diseases are now recommended. The consequence of this is that multiple medicine use is now much more prevalent leading to the potential for many more problems. Within that context, it is encouraging to note that there is no evidence that the rate of medication-related hospital admissions is increasing. It remains at about 2% to 3% of all admissions. Similarly, data collected across ten years shows the percent of patients seeing a general practitioner who experienced an adverse medication event in the previous six months has remained constant at around 10%.

This review includes data on medication error rates where previously data were limited. There is further evidence for high rates of adverse events and unplanned presentations to hospitals among patients receiving chemotherapy. There is new evidence on medication-related problems and adverse events associated with hospital-in-the-home, palliative care and residential aged care. There is further evidence that consumers who see multiple doctors, have multiple conditions and do not have a regular doctor report a higher incidence of medication errors.

Evidence for successful strategies to reduce prescribing, administration and dispensing errors supports the use of standardised medication charts, improved medicine distribution systems and technology, including smart infusion pumps for intravenous medicine administration and electronic medication management systems for prescribing medicines.

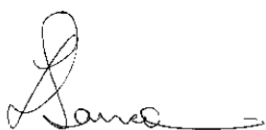
There is Australian evidence that medication errors at transitions of care between community and acute care settings can be reduced through the process of medication reconciliation and the use of an interim medication chart when patients move from hospital to residential aged care.

In the community there is growing evidence for multidisciplinary approaches to improving medication management including collaborative home medicines reviews.

The 2013 review provides further evidence on who is most at risk of an adverse medicines event, where the errors are occurring and what interventions are more successful in reducing the risk of adverse events. This information can be used by individual practitioners, healthcare facilities and policy makers to improve the quality and safety of medicines use in all healthcare settings. The review also highlights areas where evidence is lacking, including data on the effectiveness of interventions in terms of patient outcomes and quality of life. This evidence is critical to those responsible for making decisions on the funding and delivery of health care in Australia.

Future improvements to national medication safety and quality will require an ongoing national focus and coordinated effort by funders, regulators, health professionals, consumers, researchers and health services. An ageing population with increasing co-morbidities will continue to be exposed to the risk of medication misadventure unless improved multidisciplinary systems and processes are developed, evaluated and implemented and then integrated across the range of healthcare settings. The role of e-health in improving medication safety will be fundamental, and the uptake and utilisation of the personally-controlled electronic health record will offer a national basis for an electronic health future and improved health outcomes and efficiencies.

This review is another important step in addressing the ongoing challenges of medication safety and will help guide future work. I commend it to you.



Professor Lloyd Sansom AO  
Chairman, Medication Reference Group  
Australian Commission on Safety and Quality in Health Care

## Executive Summary

This report for the Australian Commission on Safety and Quality in Health Care reviews Australian studies about medication safety, updating work previously undertaken on medication safety in Australia. The report is in three parts:

- part one reviews evidence on the extent and type of medication-related problems in Australia
- part two examines Australian evidence of interventions implemented to improve medicine safety
- part three reviews the international evidence for medication safety intervention strategies.

### *Medication safety in the hospital setting*

#### *Medication-related hospital admissions*

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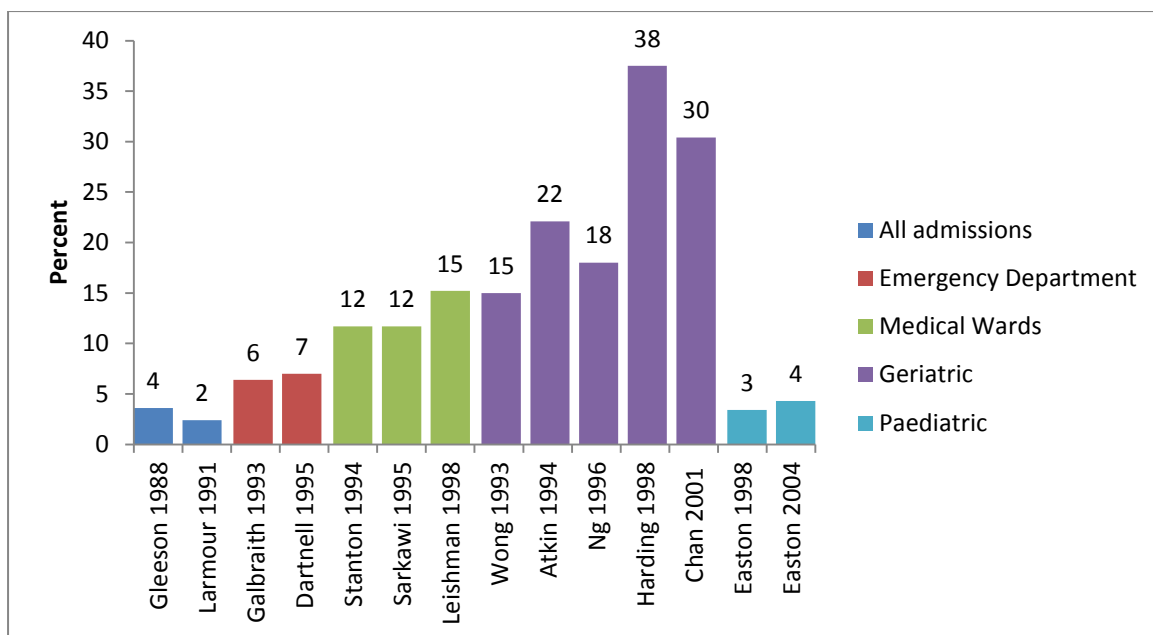
Medication-related hospital admissions have previously been estimated to comprise 2% to 3% of all Australian hospital admissions, with rising estimates of prevalence when sub-populations are studied. For example, 12% of all medical admissions and 20% to 30% of all admissions in the population aged 65 years and over are estimated to be medication-related.

No new studies were located that assessed the overall rate of medication-related hospital admissions. Three studies were located that assessed the rate of adverse drug reactions or accidental overdose associated with hospitalisation, either as a cause of admission or occurring during hospital stay. Two of the studies were undertaken in cohorts of patients that had a hospitalisation involving an overnight stay, the third in a cohort of patients with diabetes.

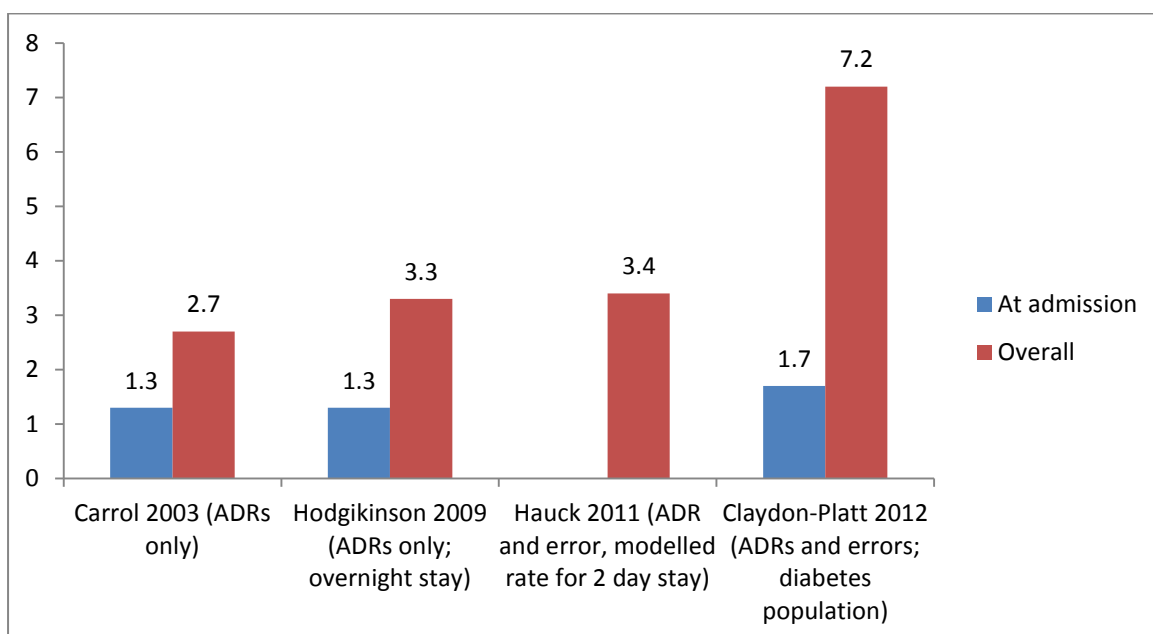
When considering the Australian literature collectively across the three reviews of medication safety (2002, 2008 and 2013), the proportion of all hospital admissions that are medication-related is between 2% and 3%. There were 9.3 million separations from Australian hospitals in 2011-2012, which would suggest a medication hospital admission rate of 230,000 annually. With an average cost per separation in 2011-12 of \$5,204, this suggests the annual cost of medication-related admissions is \$1.2 billion.

The International Classification of Diseases (ICD) coding used in routine administrative data, while likely to under-report the true extent of the problem, provides estimates that 1.4% of admissions are likely to be due to adverse drug reactions. This estimate rises to 3% when considering adverse drug reactions that occur either on admission or during hospital stays. Admissions to oncology units appear to be associated with high rates of adverse reactions. In the previous review, we reported that one study found 74% of hospitalisations for oncology patients were associated with an adverse drug reaction that occurred either as a cause of admission or during hospital stay. One additional study suggests as many as 45% of patients receiving outpatient chemotherapy may have unplanned presentations to hospital, the majority of which result in admission. The extent to which unplanned presentations were medication-related was not reported, however most presentations occurred within four weeks of treatment and involved symptoms that could be associated with chemotherapy.





**Figure 1: Results of previous studies assessing medication-related hospital admissions in Australia**



**Figure 2: Rates of adverse drug reactions associated with hospitalisation identified from routinely collected data in Australia**

### *The accuracy of medication history on admission*

Previous Australian research on the accuracy of medication charts on admission to hospital had shown that there was one omitted medicine from the medication history among every two people admitted. This research was undertaken prior to medication reconciliation being routinely

employed. Four more recently published studies provide further support for this level of error with medication charts on admission where medication reconciliation is not undertaken.

Medication histories taken at the time of admission to hospital are still a point of vulnerability for medication error, particularly where there is no routine practice of medication reconciliation. In studies where initial medication histories were compared with reconciled histories, high levels of error with medication histories at admission were observed where medication reconciliation was not undertaken. Two studies showed that between 60% and 80% of patients were noted to have a discrepancy with their medication history and their reconciled history, while three studies reported error rates ranging from 1 to 2.5 per patient on the initial history. Omission of therapy was the most common discrepancy, accounting for between 40% and 60% of errors. One study found that medication histories were less likely to be accurate if the patients presenting to emergency departments had not brought in their own medicines. Poorer documentation of allergies on charts was observed where pharmacists had not reviewed the charts.

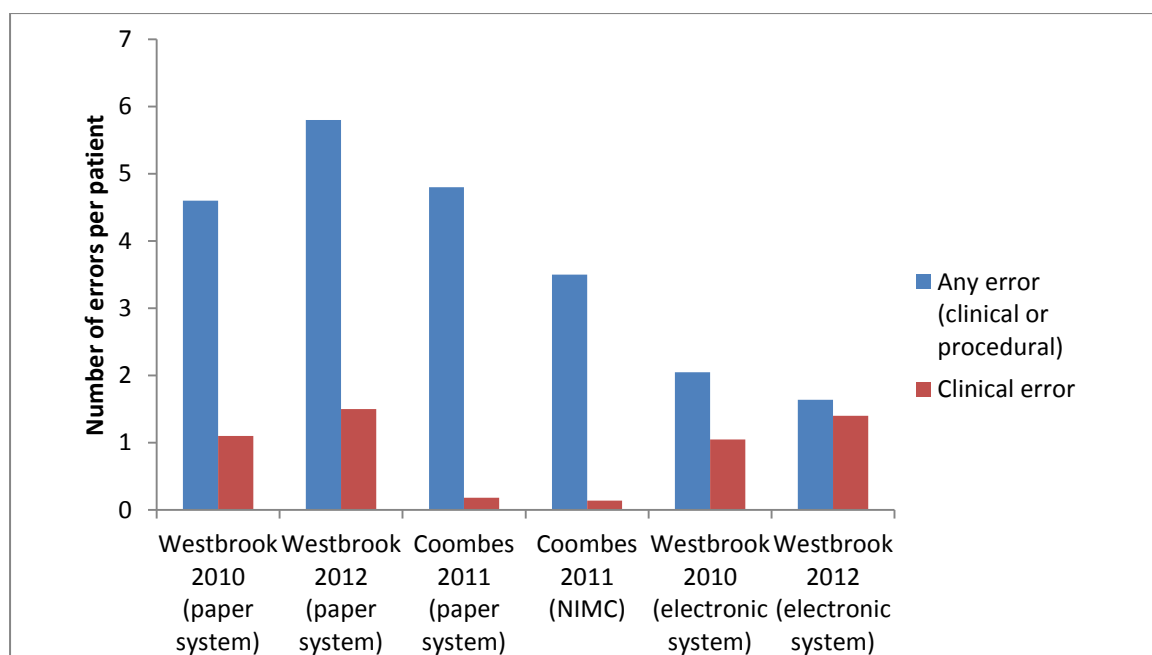
### *Prescribing errors in the hospital setting*

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The definition of prescribing errors may vary from errors that cause harm to patients, to errors that cause administration of the wrong therapy with or without harm. The definition may also extend to errors of documentation, often referred to as procedural errors. Examples of these include unclear prescriptions, lack of documentation of route of administration or signature missing.

When considering prescribing errors that result in harm to patients, one previous Australian study from 2001 estimated the rate was 2.5% of medicine orders. When defining errors more broadly, previous research reported error rates between 5% and 11% of medicine orders. However these estimates were from studies with small sample sizes. A number of additional studies were located that have documented rates of prescribing errors with the estimates generated as part of an intervention assessment. Studies assessing error rates for prescribing by paper-based systems and by electronic prescribing systems were located.

Clinical errors with prescribing were observed at a rate of 0.2 per patient in the largest study undertaken across 22 sites. In smaller studies within wards of major teaching hospitals, the clinical error rate was one per patient. This difference may reflect variation in patient mix, such as greater numbers of sicker patients in major teaching hospitals. The rate of clinical errors was similar for paper-based and electronic systems when compared within the same institutions. Procedural errors for prescribing are common, occurring at a rate of 4 to 5 per patient. Procedural or documentation errors are much less common in studies where electronic prescribing was used compared to paper-based systems. Standardised prescribing charts had slightly lower rates of procedural error than paper-based systems and had better rates of allergy history documentation. Electronic prescribing systems were associated with system-based errors (i.e. those attributed to the software) which occurred at a rate of 0.5 and 0.7 per admission in the two sites where this was assessed. The impact of electronic prescribing on serious errors was only reported in one study, where electronic prescribing included decision support, suggesting decreased serious error rates.



**Figure 3: Prescribing errors from paper-based and electronic systems**

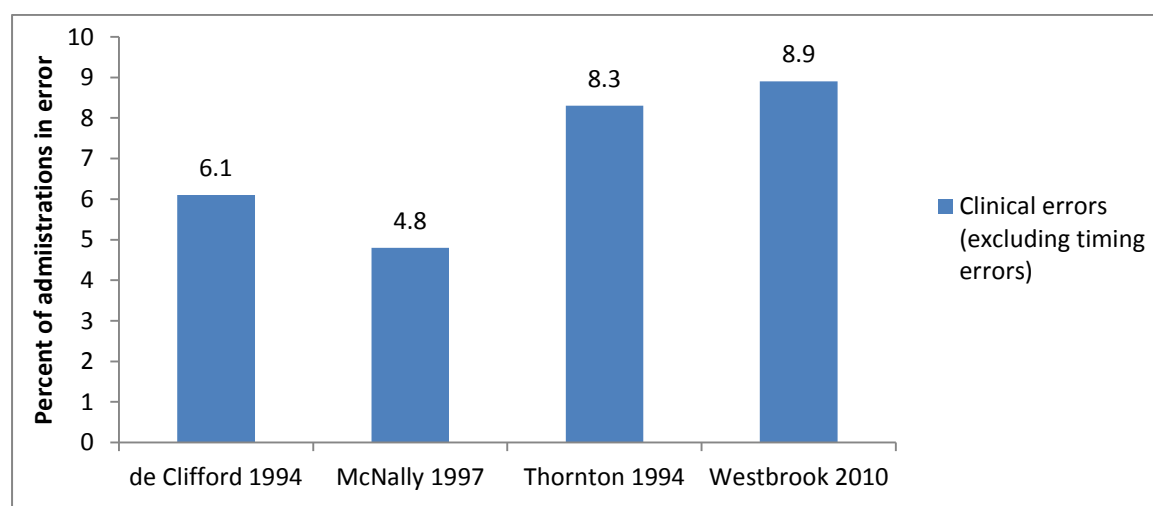
### *Administration errors in the hospital setting*

In the previous report of medication safety in Australia, we found that administration errors varied with the type of system in place. When errors of timing were excluded, we found the clinical administration error rate (e.g. omission of therapy, wrong dose) was between 5% and 8% of medicine administrations where individual patient supply systems were in use, and rose to 15% to 18% of medicine administrations when ward stock systems were in place. The majority of this evidence was from studies undertaken in the 1990s. Prior evidence for errors with intravenous fluid administration was limited to one study, with an error rate of 18%. Three new studies were located that provide further insight into error rates associated with medicine administration, one study providing insight into errors for IV fluids and one providing insight into error rates with any IV administration.

The new studies provide further support for a clinical error rate for medicine administration in the hospital setting of between 5% and 10% of medicine administrations. Interruptions of the nurse during administration were associated with increased risk of error. Factors found to contribute to administration errors included interruptions or distraction of nurses during medicine administration. Interruptions were common, occurring on 58% of occasions when nurses were administering medicines to patients. One study demonstrated that there was a 13% increased chance of error with each interruption. Error-prone abbreviations, which may also contribute to administration error, were also found to be frequently used, occurring on 8.4% of all medicine orders in one study undertaken across three hospital sites.

One new study provides evidence of the high rates of error with intravenous medication administration of any type. It found clinical errors occurred in 70% of administrations. The wrong mixture, wrong volume, wrong rate or medicine incompatibility accounted for 92% of all clinical

errors. One quarter of clinical errors were rated as serious, meaning they led to increased length of stay, surgical intervention or permanent harm. Bolus administrations were associated with a four-fold risk in error and were also associated with more serious error. Nurse experience was also a factor contributing to errors, with errors occurring most frequently among less experienced nurses and reducing by 11% per annum for each additional year of experience up to the first six years of experience.



**Figure 4: Medicine administration errors in hospitals (individual patient supply systems)**

### *The accuracy of hospital discharge summaries*

Previous Australian studies assessing the accuracy of medication discharge summaries undertaken in the late 1990s revealed that, on average, one medicine was omitted on the discharge summary<sup>1</sup>. Three additional studies were located that compared discharge summaries with discharge prescriptions. Two studies from a small metropolitan hospital suggest that 12% of discharge summaries contained discrepancies, while the study from a large teaching hospital assessing patients discharged to aged care found 80% of discharge summaries contained a discrepancy, which is similar to the proportion reported in previous Australian literature. It may be that discrepancies are more common in large teaching hospitals where sicker patients are more likely to be admitted and where more changes in therapy may be made. There is insufficient evidence to draw a solid conclusion.

### *Medication safety and transitions of care*

Transitions of care are known to be a point of vulnerability for medication management. Two studies were located that demonstrated problems occurring on admission or readmission to aged care. These studies demonstrate problems with timely medicine administration on transition from hospital or the community to aged care in both metropolitan and rural settings, with both studies showing approximately 20% of patients experienced a significant delay in medicine administration upon arrival at the facility. The lack of a written medicine order within the aged care facility was a

contributor to delayed medicine administration. The large metropolitan study highlighted that 12% of missed doses were considered high risk and that, while not directly attributable to missed doses, patients with missed doses were more likely to represent to hospital within seven days of discharge. Larger studies would need to be undertaken to confirm this result.

### *Medication safety within hospital in the home*

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Medication-related problems associated with hospital in the home have not been the focus of extensive study. However studies of adverse events of any kind associated with hospital in the home provide some insight into areas of concern. Five small studies of adverse events associated with hospital in the home in Australia included different patient groups, those with bacterial endocarditis, those with cellulitis or deep vein thrombosis and those with bone or joint infections. The studies also varied by location and method of assessment. Studies using retrospective assessment methods suggest adverse medication events rates of up to 5%. Prospective studies suggested higher rates, with adverse medication event rates occurring in up to 17% of all admissions. These studies are small in size and the majority did not have adverse medication events as their primary focus, thus larger studies are required to confirm the extent and type of problems associated with hospital in the home.

### *Medication safety within palliative care*

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One small study gives some insight into adverse events in palliative care. The retrospective study involving 65 patients included a review of case-notes, medication charts and hospital incident reports. Eleven percent had an adverse drug reaction on admission and 30% had an adverse drug reaction documented during admission. More studies are needed to draw conclusions about the level of harm in palliative care. In a small study of patients receiving community-based palliative care, medicine review services were piloted. On average, 2.2 problems per person were identified, with under-treatment and the need for additional information the main issues in this population.

## **Medication safety within residential aged care**

### *Medication-related problems among residents of aged care facilities*

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There are high levels of medicine use in the residential aged care setting and the previous review of medication safety in the community identified problems with supply, problems with administration including inappropriate alteration of dose forms, and errors of documentation. Potentially inappropriate medicine use is often assessed using a pre-defined list of medicines considered inappropriate in specified age-groups or conditions. The Beers Criteria and McLeod's Criteria were developed for the USA and Canada, respectively, and have been adapted for the Australian setting. Prior reviews of medication safety have reported the prevalence of potentially inappropriate medicine use in the aged care population at 20%. Two more recent studies which were located were

based on the population that receive a medicines review and reported higher levels of potentially inappropriate medicine use in the aged care population. These studies showed that between 40% and 50% of residents in aged care facilities were prescribed potentially inappropriate medicine use, as defined by explicit criteria such as the Beers or McLeod's Criteria.

Medication-related problems in people living in aged care are also commonly identified during medicines reviews. One study that reviewed case notes prepared during residential medicine reviews found over 90% of residents had at least one problem, with an average of three problems per person. A second study, also analysing medication review case notes, identified, on average, four medication-related problems per person for those in aged care.

### *The accuracy of dose administration aid packing*

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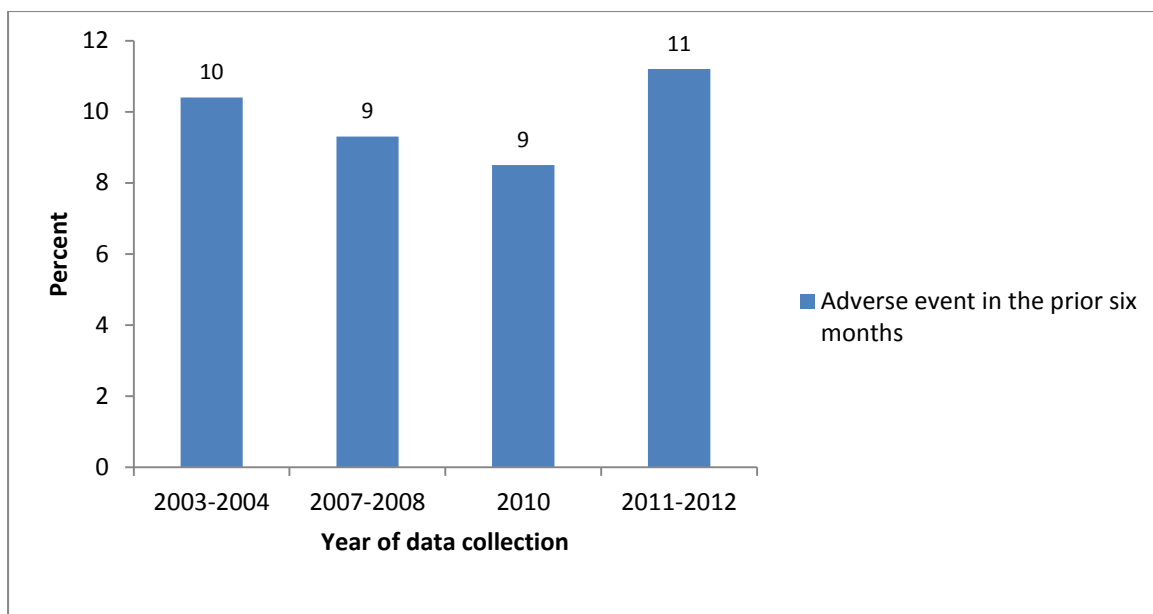
Dose administration aids are routinely used in residential aged care facilities to support medicine administration. One study assessing the accuracy of packing of dose administration aids detected an error rate of four incidents per 100 dose administration aids packed. Thirty-five percent of incidents were omitted medicine, 12% supply of a ceased medicine, 11% wrong strength dispensed and 11% incorrect dosage instructions. Error rates varied by pharmacy responsible for packing the dose administration aids.

## *Medication safety in the community*

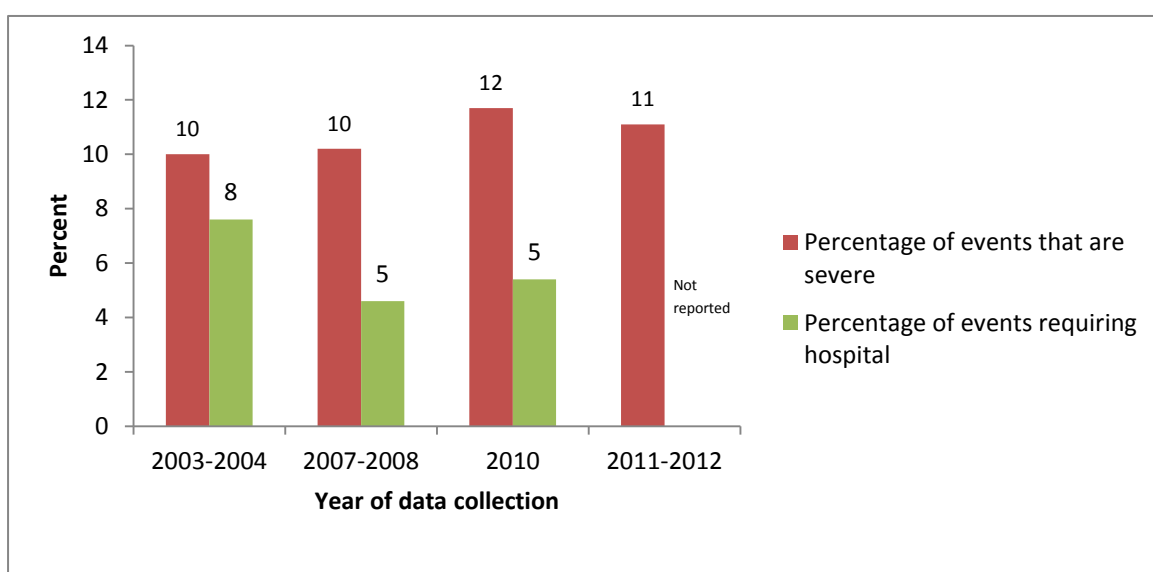
### *Adverse medication events in general practice*

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Prior Australian research found that 10% of patients seeing a general practitioner had had an adverse medication event in the previous six months. Three additional surveys confirm this result, with the surveys showing that between 8.5% and 12% of people attending general practice had experienced an adverse medication event in the previous six months. Eleven to twelve percent of these adverse events were considered severe and approximately 5% required hospitalisation. The accuracy of medication histories in general practice may be a factor contributing to medication-related problems. One study found only 68% of medicines taken by patients were considered correctly recorded in the electronic general practice medical record.



**Figure 5: Percentage of people attending general practice experiencing an adverse medication event in prior six months**



**Figure 6: Proportion of severe adverse events for those attending general practice who had experienced an adverse event in the previous six months**

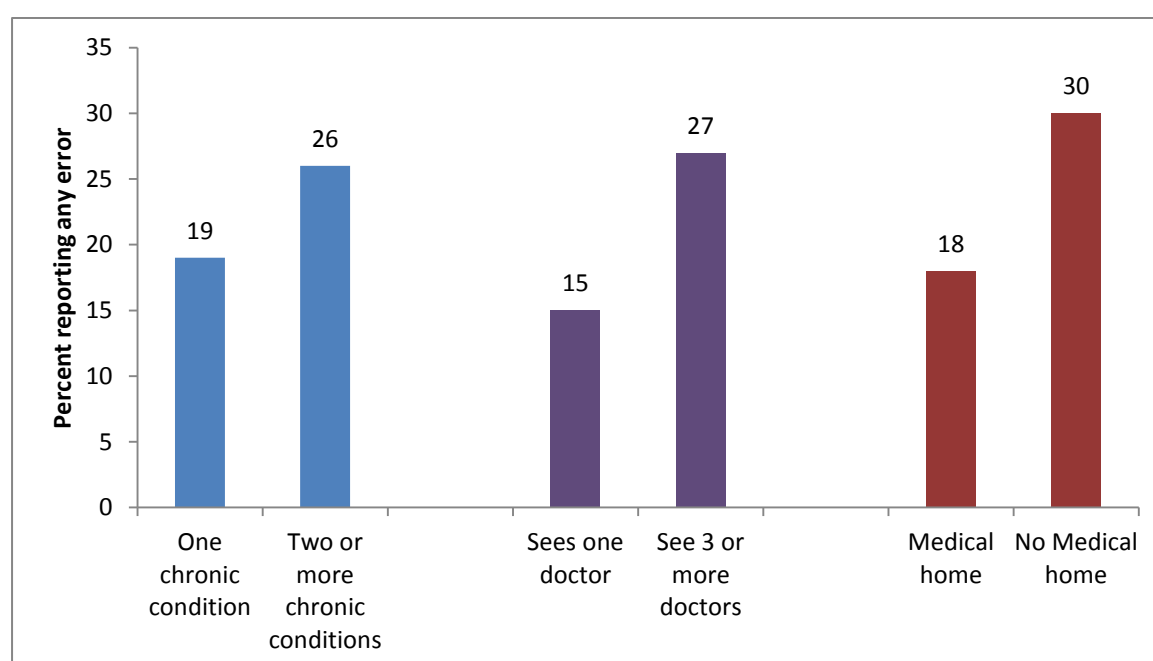
### *Medication-related problems in the community*

In prior medication safety reports, we reported the extent of medication-related problems in the community. A rate of 2.8 problems per person was identified through a review of case notes of people considered to be at high risk of medication problems. More recent studies, which have also used case notes prepared during home medicines reviews to identify problems, highlight that medication-related problems for those at risk of medication misadventure remain significant. The

four more recent studies demonstrate that people who participate in home medicines reviews have between 2.5 to 5 medication-related problems per person identified as part of the review. Medication-related problems are significant in the population with mental health problems, where medicine selection issues are most common. One study undertaken in an outpatients department included medication reconciliation prior to the review. It found 85% of patients had omission of therapy in the medical record to that documented in medication reconciliation, and 45% had dose discrepancies. These results are similar to studies undertaken at time of hospital admission where the hospital studies found 60% to 80% of patients have discrepancies between their medication history and a reconciled history.

Using adapted versions of the Beers and McLeod's Criteria, previous Australian research reported the level of potentially inappropriate medicine use nationally at 21% when assessed retrospectively using the Department of Veterans' Affairs administrative claims data. Two more recently published studies provide further evidence of high levels of potentially inappropriate medicine use in the community. More recent studies have reported between 40% and 50% of people in the community are prescribed potentially inappropriate medicines. These studies have been limited to older adults and, in one study, to those considered at risk of medication misadventure.

Self-reported information from consumers on adverse medication events also provides insight into potential problems. Data were available from six surveys assessing the extent of side effects or errors consumers experience with their medicines. Collectively, the self-reported data from consumers suggest that between 9% and 14% report experiencing side effects and approximately 8% of all consumers and 13% of those with chronic conditions may have been given the wrong medicine or dose in the prior twelve months. Those with chronic conditions, who see multiple doctors and who have no "medical home" more commonly report experiencing errors. Difficulty reading prescription labels, which has been identified as a factor in past reports, was also found to be a problem in a small study undertaken in patients with glaucoma.



**Figure 7: Percentage of patients with self-reported medication or medical error in the previous twelve months**



### *Adverse reactions and complementary therapies*

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There is very limited literature available assessing the extent of error or medication safety issues with over-the-counter and complementary therapies. One Australian study provides some insight into this issue. A survey of customers from community pharmacies in three Australian states found 72% reported using a complementary medicine in the previous twelve months, of which 7% reported experiencing an adverse reaction. Of those who reported experiencing an adverse reaction, the majority indicated the reaction was mild, however 22% considered it moderate or required advice from a health care professional, while 7% reported a severe reaction requiring hospitalisation.

### *Strategies to improve medication safety*

#### *Systems to improve medicine administration and dispensing*

##### *Standardised medication charts*

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There has been a number of studies assessing the impact of standardised medication charts, including one large national, multi-site study undertaken in Australia. All studies were uncontrolled pre-and post-test designs. These results, while limited to Level III evidence, collectively suggest that standardised medication charts lead to reductions in prescribing errors, and result in improved documentation. The study of the National Inpatient Medication Chart (NIMC) found that it reduced prescribing errors, predominantly procedural errors, and improved ADR documentation. The study used surrogate measures of patient harm rather than direct measures. Further controlled trial evaluation of the NIMC and supporting educational programs should be considered in the future, including measurement of impacts on patient harm.

All three studies where standardised charts were used to improve management of a particular pharmacological therapy (insulin, venous thromboembolism (VTE) prophylaxis, warfarin, and N-acetylcysteine) demonstrated improvements in prescribing practice. The modified NIMC intervention improved pharmacological VTE prophylaxis prescribing in a timely manner for high-risk patients, however the incidence of VTE was not shown to change significantly following implementation of the intervention. The warfarin chart resulted in a reduction in INR results of greater than five. The N-acetylcysteine chart led to a reduction in prescribing errors.

#### *Systems to improve medicine administration and dispensing*

##### *Electronic prescribing*

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Since the 2008 review of medication safety in the Australian acute care setting, a number of studies have been published describing the implementation of electronic prescribing (e-prescribing) in acute care and assessing its impact on prescribing errors. The studies, Level III-2 and III-3 evidence, support

the effectiveness of electronic prescribing systems in reducing prescribing errors, particularly procedural errors. The impact on actual clinical errors is less clear, with the level III-2 study showing no difference in clinical errors, although a significant reduction in serious errors was observed. A Level III-3 study where the electronic prescribing system had very limited decision support reported an increase in average error severity, however this study was uncontrolled and thus the findings less robust. The e-prescribing systems did not have the substantial clinical decision support that may be needed to see further reductions in clinical errors. System-related errors were a significant contributor to error with electronic prescribing, but did not out-weigh the number of errors prevented. System-related errors need to be considered in the further refinement of system design and in the user-training and implementation of these systems in Australian hospitals.

Academic detailing was assessed in one study to facilitate implementation of a clinical decision support system and improve dosing of medicines that are cleared renally. The evaluation showed that improvements in dosing resulted.

### *Smart pumps*

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One Australian study, using a pre- and post-intervention design in a single institution, assessed the impact of smart pumps on infusion error rates. The error rate decreased from 18% when volumetric infusions were used, to 3.6% when the smart pump combined with software that included hard alerts which could not be overridden was used.

### *Pharmacy services*

#### *Medication reconciliation*

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A number of Australian studies have now assessed medication reconciliation by pharmacists. There is multi-centre randomised controlled trial evidence evaluating medication reconciliation services on admission to hospital. Patients receiving medication reconciliation had discrepancies in their medicine orders resolved more quickly and more discrepancies resolved across their hospital stay. There was a weak but statistically significant positive correlation between the number of unresolved discrepancies and length of hospital stay.

A small, uncontrolled, pre- and post-intervention study examining the effectiveness of medication reconciliation by a clinical pharmacist in an emergency department on prescribing errors showed significant outcomes. Of the 'unintentional discrepancies' between the history obtained by the pharmacist and the medication chart in the usual care arm, 6% were deemed by an expert panel to have a very significant impact on patient health outcomes, and 52% were deemed to have a significant impact. One study provides support for pharmacist chart review, the multi-site study compared medication charts reviewed by a pharmacist with those with no pharmacist review. Charts that had been reviewed by a pharmacist were significantly less likely to have inadequate documentation of allergy.

Collectively these studies provide support for the effectiveness of medication reconciliation services in improving the accuracy of the medication history. Larger studies assessing the impact on adverse events and patient outcomes are yet to be undertaken.

### *Medication reconciliation and pharmacist prescribing*

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A randomised controlled trial assessed pharmacist reconciliation and pharmacist prescribing services in the perioperative setting. The pharmacist wrote up the medication chart for current medicines using standard protocols; medical practitioners wrote up any new orders. The study found less omission of therapy during hospital stays as a result of pharmacist medication reconciliation and prescribing services.

### *Pharmacist prescribing*

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Pharmacist prescribing in the inpatient setting was also assessed in a randomised controlled trial. The pharmacist, who was an accredited pharmacist prescriber in the UK, prepared the medication chart, planned perioperative medicines and ordered venous thrombo-embolism prophylaxis. The orders were counter-signed by the resident medical officer. There was a significant reduction in the likelihood of medicine omission. Independent panel assessment considered 52% of omissions in the control arm had the potential for patient harm or ward inconvenience; only one of the six panel members rated the one omission in the intervention arm sample as significant.

Two Australian randomised controlled trial studies (Level II) have shown significant improvements in prescribing in the perioperative setting in Australian hospitals with an intervention involving pharmacist prescribing. These studies have used surrogate endpoints of medicine charting error and communication error. Further studies examining actual patient outcomes including adverse medication events and application in a larger sample of patients and hospital sites are needed.

One other small study provides insight into pharmacist prescribing. The uncontrolled, pre- and post-intervention design assessed a pharmacist anticoagulant dosing service. The pharmacist managed dosing according to the hospital guidelines and communicated treatment recommendations to the medical unit. The primary outcome measure was the number of days to achieve two consecutive therapeutic INR values, which was significantly reduced in the post-intervention period.

### *Pharmacist handover*

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There is uncontrolled, pre- and post-intervention evidence for the effectiveness of pharmacist handover services for oncology patients transferring between oncology and critical care units. The study found a statistically significant reduction in errors or omission of therapy on transfer and a reduction in delays in treatment associated with service delivery.

### *Discharge services to the community*

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The previous review of medication safety in Australian acute care included controlled studies undertaken in Australia to assess the impact of discharge medication management services implemented by pharmacists or by pharmacists and nurses. These services were shown to improve patient outcomes and reduce undesirable medication events.

An additional non-randomised controlled trial (Level III-2) examined the provision of a post-discharge warfarin management service for adult patients discharged from hospital newly initiated on warfarin or on continuing warfarin therapy. A significantly higher percentage of patients in the usual care group experienced a haemorrhagic event compared to the intervention group.

One randomised control trial was undertaken which found no changes in numbers of medicines used or medication knowledge between the two groups. The study did not assess the rate of medication-related problems between groups.

### *Transition to aged care*

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A pre- and post-intervention study assessed the impact of pharmacist prepared interim residential care medication administration charts on the timeliness of medicine administration on transfer to aged-care. Previous studies had shown many patients missed doses or had significant delays in medicine administration on transfer to aged care facilities. The chart resulted in significantly less patients having delayed doses of medicines, significantly less patients requiring charts written by locum staff and significantly less workaround practices by residential aged care staff to avoid missed doses.

### *Medicines review in the community*

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The Home Medicines Review (HMR) service is an Australian Government funded initiative conducted by accredited pharmacists in collaboration with a patient's general practitioner (GP) and regular community pharmacy.<sup>2</sup> The accredited pharmacist conducts a comprehensive medicines review with the patient in their home, identifies medication-related problems and provides the GP with a report. The GP and patient then agree on a medication management plan.

Two studies published since 2008 have examined how the HMR service has been translated into practice in Australia. Both were retrospective cohort studies using the Department of Veterans' Affairs administrative claims data. Together, the two studies in veterans (Level III-2) provide evidence for the effectiveness of collaborative HMR in the community setting in Australia. The studies suggest that HMR can reduce hospitalisation rates for older people living in the community at high risk of medication-related hospital admissions; those with heart failure taking heart failure medicines and those taking warfarin.

Plan-Do-Study-Act (PDSA) cycles are a cornerstone method in continuous quality improvement processes that have been used by healthcare organisations as a method to improve patient safety. Three papers published since 2008 were located that described medication safety initiatives in Australian acute care settings underpinned by the use of PDSA cycles. Together the studies in adult ICU and in paediatric acute care (both Level III-3 studies) provide evidence for clinical practice improvement projects incorporating PDSA cycles in reducing medication errors, adverse medication events and improving documentation. The study undertaken in the paediatric hospital setting is one of the few studies in Australian healthcare settings to examine adverse medication events and actual severity of harm as an outcome measure.

Controlled studies would improve the evidence base, but controlled studies for systems approaches such as this in a whole unit or hospital may not be achievable.

# Literature Review: Medication Safety in Australia

## Background

This report for the Australian Commission on Safety and Quality in Health Care reviews Australian studies about medication safety, updating work previously undertaken on medication safety in Australia.<sup>1-5</sup> The report is in three parts:

- part one reviews evidence on the extent and type of medication-related problems in Australia
- part two examines Australian evidence of interventions implemented to improve medicine safety
- part three reviews the international evidence for medication safety intervention strategies.

## Scope

The Review covers Australian literature on medication safety published from 2008 to August 2013 and international evidence for studies that have assessed impacts on health outcomes published between 2002 and August 2013. Details of the search strategy, including databases searched and search terms are located in Appendix I.

## Part 1: The extent of medication-related problems

### Medication-related hospital admissions

Medication-related hospital admissions have previously been estimated to comprise 2% to 3% of all Australian hospital admissions, with rising estimates of prevalence when sub-populations are studied. For example, 12% of all medical admissions and 20% to 30% of all admissions in the population aged 65 years and over are estimated to be medication-related.<sup>6</sup>

No new studies were located that have assessed the overall rate of medication-related hospital admissions. Three studies were located that assessed the rate of adverse drug reactions (ADR) or accidental overdose associated with hospitalisation, either as a cause of admission or occurring during hospital stay. Two of the studies were undertaken in cohorts of patients that had a hospitalisation involving an overnight stay,<sup>7,8</sup> the third in a cohort of patients with diabetes.<sup>9</sup>

The proportion of hospitalisations associated with an ADR was assessed in a retrospective observational study among three Victorian public hospitals between March and May 2004.<sup>7</sup> Data were collected from administrative records, supported by medical record review of the discharged patients and review of the adverse reaction spontaneous reports. Same-day admissions were excluded, as were administrative records that could not be verified by medical record review or were judged not to be an ADR after medical record review. In all, 12,414 hospitalisations were assessed. ADR-related codes were included on 4.5% of hospitalisations. However, after comparison with ADR spontaneous reports and patient medical records it was concluded that 3.3% of

hospitalisations involving an overnight stay were associated with an adverse drug reaction that occurred as a cause of or during admission. In 34% of cases the ADR was considered the cause of admission giving an overall ADR hospital admission rate of 1.3% of non-same day hospital separations. The ADR was considered life-threatening in 12% of cases, to have caused death in 0.7% (three cases), disability in 1% (four cases) and resulted in prolonged hospitalisation in 5.6% of cases. In three cases the ADR was considered a definite reaction, in 57% of cases causality was considered probable, and in 42% of cases a possible reaction. In 86% of cases the ADR was considered dose-related. Consistent with prior Australian literature,<sup>1</sup> the medicine classes most commonly implicated were anti-bacterials, opioids, diuretics, antineoplastic agents, antithrombotics and cardiac therapy.<sup>7</sup> While 1.3% of hospital admissions involving overnight stay were estimated to be due to adverse drug reactions, this is likely to be an under-estimate of the true rate. In this study 44 spontaneous adverse drug reaction reports were lodged with the Australian Committee on Safety of Medicines during the study period, of which 29 were not recorded in the ICD codes. Further, in 15 cases the medicine was found to be omitted from the ICD codes, despite being documented in the medical record and on some occasions combination products led to one of the medicines being omitted.<sup>7</sup>

A second Victorian study supports these results. Undertaken in 2005-2006, the study employed econometric modelling with administrative claims data to determine the extent of hospitalisations associated with adverse events, including adverse drug reactions.<sup>8</sup> The group of codes used to define adverse drug reactions included the ICD Y codes indicative of adverse drug reactions, as well as codes indicative of errors in medicine administration, infusion errors and blood mismatches. The definition did not include accidental overdose. The study included all hospitalisations with an overnight stay, excluding maternity, paediatric, dialysis, chemotherapy, radiology and rehabilitation stays. In all, 206,489 hospitalisations were included. The study found that for an average five night hospital stay there was a 5.5% risk of an ADR. The risk was 3.4% for an overnight (two day) stay and increasing to 6.1% for an eight day stay. This study's estimates include those that contributed to the cause of admission as well as those that occurred during hospital stay. The results showed that for every additional day in hospital, the risk of an adverse drug reaction increased by 0.5%. The risk was found to be higher for patients admitted via the emergency department compared to those with elective admissions. This may reflect the medication-related admission rate, as planned admissions are less likely to be medication-related.

A similar study using hospital administrative claims records was undertaken within the diabetes population. The retrospective cohort study of medication-related problems in people with diabetes was conducted between January 2005 and December 2006 using the medication problems, predominantly accidental overdose and adverse drug reactions, that are coded in routinely collected administrative data from a Melbourne public teaching hospital.<sup>9</sup> Of the 9530 admissions assessed, involving 5205 individuals, medication-related problems were documented as the cause of admission in 1.7% of cases, and as a secondary diagnosis, which may have occurred during hospital stay, in 5.5% of admissions. Thus, overall 7.2% of hospitalisations were associated with medication-related problems. Medication error, which included accidental overdose or hypoglycaemia, accounted for 64% of problems, while adverse drug reactions accounted for 36%. This study is likely to under-estimate the true extent of medication-related problems in this population as it relied on previously collected data that was routinely coded.

The estimate of the proportion of hospitalisations associated with adverse drug reactions in these studies, whilst using slightly different definitions, is similar to other studies that have used administrative claims data for identifying the association between hospitalisations and adverse drug reactions. When limited to ICD codes that are indicative of ADRs only, the estimates are consistent at 3%,<sup>7 10</sup> but rise to 5% and 7% when definitions include errors, overdoses, or blood product errors. As with other studies that have used administrative claims data, the result is likely to under-estimate the true incidence of adverse drug reactions because of significant under-reporting in the data.

Two other studies were located that, while not assessing the incidence of medication-related hospital admissions, do provide insight into potential areas of focus for preventive activity. One study examined unplanned presentations to the emergency department or to hospital amongst patients receiving chemotherapy.<sup>11</sup> However, this study did not provide an assessment of the proportion of presentations that were medication-related. The second study assessed hospital admissions for specified conditions and determined whether recommended practice was implemented or known medication-related problems existed in the period prior to admission. For example, with hospitalisations for renal failure, the extent of monitoring of renal function was assessed for those prescribed a specific medicine that may cause renal failure. This study reported the prevalence of hospital admissions where the process of care was not implemented.<sup>12</sup>

Unplanned presentations or admissions to a large metropolitan hospital for patients who had received chemotherapy in the prior six months were assessed retrospectively between Oct 2006 and Sep 2007 using cancer and emergency department database records, as well as medical record review.<sup>11</sup> Haematology outpatients and those under 18 years of age were excluded. There were 363 unplanned presentations involving 233 people within six months of receiving chemotherapy. The proportion of people treated with chemotherapy across this time frame was not reported, however the authors note that the cancer centre treated approximately 518 patients per year, which suggests as many as 45% of patients may have made an unplanned presentation. Eighty-eight percent of presentations (97% of patients) resulted in hospital admission, and the median length of stay was five days. No overall assessment of the rate of medication-related admissions was made. Forty-five percent of presentations involved nausea and or vomiting, 27% pain, 23% fever and or febrile neutropenia, 19% shortness of breath, 12% dehydration, 9% anaemia, 9% fatigue, 9% diarrhoea and 5.5% anxiety or depression. While many of these symptoms are potentially related to chemotherapy, the extent to which these symptoms were medication-related or disease-related was not reported. The majority of presentations (70%) occurred within one month of receiving chemotherapy, which suggests many may have been medication-related. It was also reported that people had been “frequently suffering these side effects for between two to seven days before presenting to hospital”, however, the proportions were not reported. Of those who did have an unplanned admission, the median length of stay was five days (IQR 2-11).<sup>11</sup>

One Australian study examined the proportion of hospitalisations for specified conditions where recommended processes of care were not implemented prior to the admission as a marker of potentially preventable medication-related hospitalisation.<sup>12</sup> The retrospective observational study employed 45 clinical indicators identified from the literature as markers of potentially preventable admissions. The proportion of hospital admissions consistent with the indicator was assessed using the Department of Veterans’ Affairs administrative claims database between Jan 2004 and Dec 2008. There were 216,527 hospitalisations defined by the clinical indicators (representing 13% of all

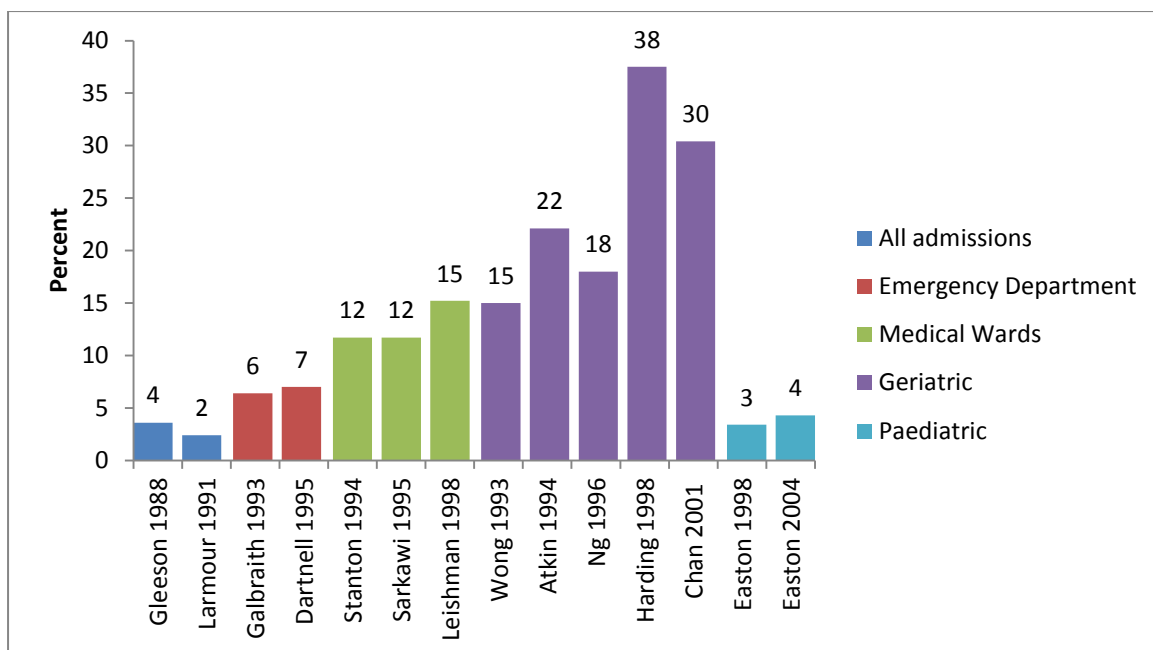


hospitalisations) and of these 20% did not have a recommended process of care implemented prior to the admission. While not providing an estimate of overall numbers of medication-related hospitalisations, this study provides contextual information about care processes that, if utilised, may have reduced the chance of a hospital admission. It did so by linking hospital admission data with Medicare and PBS data. The findings included:

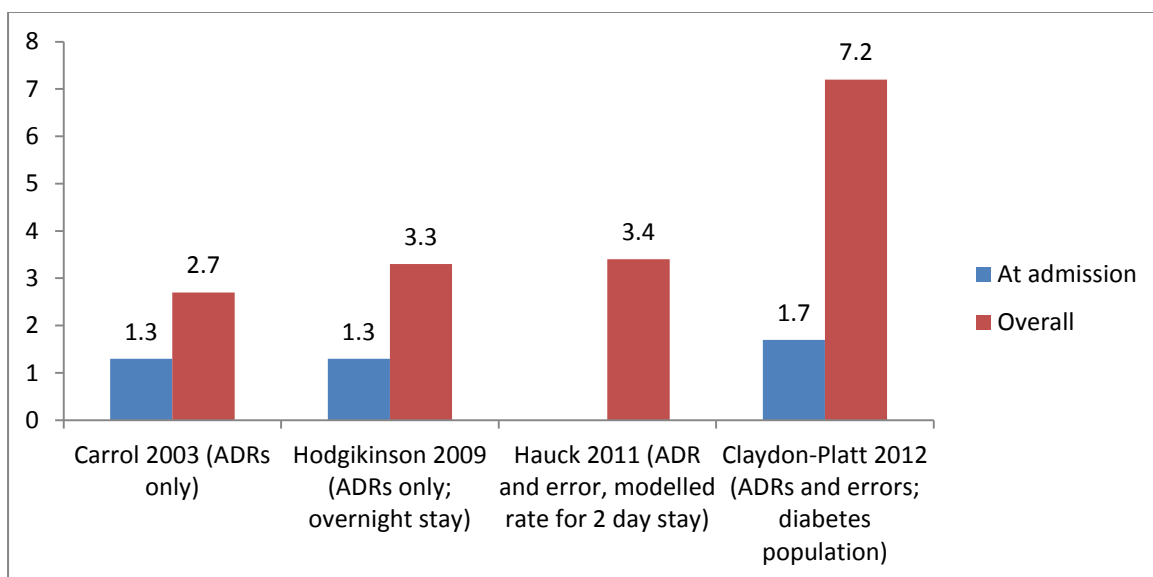
- 61% of those admitted for acute confusion (n= 2,852) were dispensed multiple psychotropic medicines in the three months prior to admission
- 51% of those admitted for hyperkalaemia (n=413) were dispensed a medicine acting on the rennin angiotensinogen system and had not had an electrolyte test in the prior six months
- 40% of those admitted for renal failure (n=6585 ) were dispensed a medicine acting on the rennin angiotensinogen system and had not had a blood urea nitrogen or serum creatinine test in the prior three months
- 31% of those admitted for faecal impaction (n=6851) were dispensed highly anti-cholinergic agents, multiple anti-cholinergic agents or opioids at the time of the admission
- 22% of those admitted for seizure (n=1456) were on an anti-convulsant requiring therapeutic medicine monitoring but had not had a medicine level test in the six months prior to admission
- 23% of those admitted for asthma or chronic obstructive pulmonary disease (n=33,831) had had a prior diagnosis of the condition, were using a bronchodilator, but were not on maintenance therapy
- 18% of those admitted for a thrombo-embolic cerebrovascular event (n=14,544) had a prior diagnosis of atrial fibrillation but were not on warfarin in the three months prior to admission
- 15% of women and 18% of men admitted for hip fracture had had a prior fall from standing resulting in a fracture but were not using a medicine for osteoporosis within the six months prior to the admission.<sup>12</sup>

When considering the Australian literature collectively across the three reviews of medication safety (2002, 2008 and 2013), the proportion of all hospital admissions that are medication-related is between 2% and 3% (Figure 1). There were 9.3 million separations from Australian hospitals in 2011-2012,<sup>13</sup> which would suggest a medication hospital admission rate of 230,000 annually. With an average cost per separation in 2011-12 of \$5,204,<sup>13</sup> this suggests the annual cost of medication-related admissions is \$1.2 billion.

The ICD coding used in routine administrative data, while likely to under-report the true extent of the problems, provides estimates that 1.4% of admissions are likely to be due to adverse drug reactions and this rises to 3% when considering both adverse drug reactions that occur either on admission or during hospital stays (Figure 2).



**Figure 1: Results of previous studies assessing medication-related hospital admissions in Australia**



**Figure 2: Rates of adverse drug reactions associated with hospitalisation identified from routinely collected data in Australia**

## The accuracy of medication history on admission

Previous Australian research on the accuracy of medication charts on admission to hospital had shown that there was one omitted medicine from the medication history among every two people admitted.<sup>1</sup> This research was undertaken prior to medication reconciliation being routinely employed. Four more recently published studies provide further support for this level of error with medication charts on admission where medication reconciliation is not undertaken.

One study, undertaken in five Australian hospitals across three states, assessed discrepancies between the admission medication chart and a reconciled medication list.<sup>14</sup> The study was limited to patients aged over 50 years, with at least two chronic conditions, and who took at least three medicines regularly. A hospital pharmacist compiled a reconciled medicines list using patient interview and review of the patient's available medicines, as well as the patient's community pharmacy dispensing history over the prior six months, the available general practice (GP) information and the hospital doctor's medication history. The reconciled medicines list was compared to the initial medication chart. Discrepancies were defined as omissions of medicines, wrong medicines and dosing errors. Intentional changes by the doctor were not considered discrepancies. Of the 792 patients meeting the criteria, 487 participated. Sixty-six percent of patients had at least one discrepancy between their reconciled list of medicines on admission and their initial medication chart, with a median of one (range 0 to 14) discrepancy per patient.<sup>14</sup> This is a slightly higher estimate than previously reported, however these findings relate to the subset of patients who may be considered at high-risk of medication misadventure, which is those with multiple illnesses on multiple medicines. The authors noted that access to a six-month community pharmacy dispensing history was very helpful in producing the final reconciled list.<sup>14</sup>

Similar results were observed in a South Australian study undertaken between April and July 2007.<sup>15</sup> As part of an intervention, an observational study of patients presenting to an emergency department in a South Australian teaching hospital during normal working hours was undertaken. Patients were included if they were admitted to hospital from the emergency department, aged over 60 years, took four or more regular medicines, and had three or more conditions or had been admitted within the previous three months. Once the patients had seen the doctor and had a medication history recorded, the pharmacist compiled a medication history based on patient interview, as well as information from the community pharmacist. Where necessary the patients' general practitioner was also consulted. Discrepancies between the medication chart and the pharmacist medication history were determined. Intentional changes by the doctor were not considered discrepancies. Forty-five patients participated in the baseline arm of the study, and 76% were found to have one or more unintentional discrepancies, an average of 2.5 per patient. Omission of medicine accounted for 57% of discrepancies identified. Most discrepancies were resolved within a day, however, 13% were only resolved at discharge and 19% appeared unresolved at discharge.

An observational study comparing patients presenting to a metropolitan emergency department over a 19 day period in March 2006 was undertaken at a large Melbourne teaching hospital.<sup>16</sup> Patients were included if they were over 18 years, brought to the emergency department by ambulance, were taking four or more regular medicines, were subsequently admitted to hospital and had not seen the emergency department pharmacist prior to the medication chart being written. Patients from institutional care were excluded. The emergency department pharmacist

compiled a medication history based on patient interview, as well as information from the patient's carer, general practitioner, community pharmacist or community nurse. Discrepancies between the medication chart and the reconciled list were determined. Intentional changes by the doctor were not considered discrepancies. One hundred patients were recruited, and 151 discrepancies were identified with an average of 1.5 discrepancies per patient or 0.2 discrepancies per medicine. Forty percent of problems were omission of the medicine, with a further 28.5% due to documentation of the wrong dose, and 13% due to documentation of the wrong frequency. Less discrepancies were noted when paramedics brought in patient medicines at the time of presentation, with 87% of medicines correctly recorded as opposed to 75% when medicines were not presented with the patient (95% CI;  $P < 0.001$ ).

A South Australian study undertaken in a large teaching hospital in March 2009 also provides insight into the level of prescription errors on admission to hospital.<sup>17</sup> The prospective study assessed 200 consecutive admissions for patients admitted through the acute assessment unit prior to admission to a medical ward. Medication charts created in the acute assessment unit are used after transfer to the medical wards and thus, if not identified, errors may persist throughout admission. Medication charts and admission records were reviewed within 24 hours of admission by the researchers, who were not involved in patient care. Where necessary, medication histories were also collected from family members, carers, GPs, community pharmacists or residential aged care facilities. Study measures included excessive polypharmacy, defined as concurrent use of ten or more medicines daily and prescription errors. Errors were categorised as of no significant consequence, causing temporary harm or requiring intervention, and causing permanent harm or death. Of the 200 patients, 158 were 65 years and over. The prevalence of excessive polypharmacy in those aged 65 years and over was 44%. The overall prescription error rate or the type of error (e.g. omission) was not reported. Twenty-four percent of patients had a prescription error serious enough to cause temporary harm or require intervention and 17% had a potential adverse medicine-medicine interaction. Thirty-seven percent of patients admitted on ten or more medicines had an error serious enough to cause temporary harm or require intervention, compared to 10% of patients on five or more medicines at admission and 3% of patients on less than five medicines. ( $P=0.02$ ). No errors causing permanent harm or death were identified.

Consistent with previous research,<sup>1</sup> these studies show high levels of error with medication histories at admission where medication reconciliation is not undertaken. Two studies showed that between 60% and 80% of patients were noted to have a discrepancy with their medication history, while three studies reported error rates ranging from 1 to 2.5 per patient. Omission of therapy was the most common discrepancy, accounting for between 40% and 60% of errors.

### **Prescribing errors in the hospital setting**

The definition of prescribing errors may vary from errors that cause harm to patients, to errors that cause administration of the wrong therapy with or without harm. The definition may also extend to include errors of documentation, often referred to as procedural errors. Examples of these include where the prescription is unclear, route of administration not documented or signature missing.

When considering prescribing errors that result in harm to patients, one previous Australian study from 2001 estimated the rate was 2.5% of medicine orders.<sup>18</sup> When defining errors more broadly, previous research reported error rates between 5% and 11% of medicine orders. However these estimates were from studies with small sample sizes.<sup>3</sup> A number of additional studies were located that have documented rates of prescribing errors with the estimates generated as part of an intervention assessment. Studies assessing error rates for prescribing by paper-based systems and by electronic prescribing systems were located.

### **Prescribing errors for paper-based systems**

Prescribing error rates for paper-based systems were documented as part of baseline data for an intervention study assessing the impact of e-prescribing systems in two major teaching hospitals in Sydney.<sup>19</sup> Data were collected between May and August 2006 in one hospital and between November 2007 and March 2008 in the second hospital. Pharmacists independent of the hospital reviewed charts daily. Both procedural and clinical errors were documented. There were 11,168 prescribing errors for 1923 admissions or 5.8 prescribing errors per admission. There were 4.3 procedural errors per admission and 1.5 clinical errors per admission. Serious errors, those leading to increased length of stay, permanent harm or death, occurred at a rate of 0.27 per admission. The rates of error varied by hospital site, however, the rate of serious errors was similar at both hospitals.<sup>19</sup>

Prescribing errors for paper-based systems were also documented as part of baseline data for an intervention study assessing the impact of an “off the shelf” e-prescribing system in a 27 bed mental health inpatient unit of a major teaching hospital.<sup>20</sup> Three clinical pharmacists prospectively reviewed all patient medication charts over the two month period, November-December 2007. Prescribing errors included procedural and clinical errors. There were 4.68 errors (95% CI 3.54-5.82) per patient, which were predominantly documentation errors. Clinical errors averaged 1.06 per patient. The prescribing error rate per 100 patient bed-days was 22.5 (95% CI 19.9- 24.1). Overall 70.8% of patients had one or more prescribing errors. Of the 337 errors, 31.5% were considered insignificant, 62.3% were rated of minor severity, 6% were rated of moderate severity, and no major or serious prescribing errors were recorded. Moderate errors occurred at a rate of 0.29 per patient. The most common clinical error was wrong route (0.36 per patient), wrong dose or volume (0.29 per patient) and duplicate therapy order (0.28 per patient).

Prescribing errors for paper-based systems were also documented as part of the baseline data for an intervention study assessing the impact of the National Medication Inpatient Chart, a standardised medication chart.<sup>21</sup> The study was conducted over 22 hospital sites and employed trained pharmacists and nurses who audited charts in medical, surgical, paediatric and mental health wards during November 2004. The study included procedural and clinical errors. In all, 15,557 medicine orders were reviewed at baseline and 6383 prescribing errors identified giving a rate of 4.8 errors per patient. Eighty-five percent of patients’ charts were considered to contain at least one prescribing error. When limited to clinical errors, 1.5% of all prescribing orders were considered to be a clinical error, equating to 0.18 clinical errors per patient. Medication charts also enable documentation of adverse drug reaction history. Seventy-five percent of patients had all their prior

adverse drug reactions documented and 14.1% of patients with a prior adverse drug reaction (ADRs) were re-exposed to a medicine from the same class.

Collectively, these studies show that prescribing errors when prescribing by paper-based systems in hospitals are common, at a rate of approximately five per patient, however, this is predominantly procedural errors or errors of documentation. The clinical error rate from the largest study undertaken across multiple sites suggests a clinical error rate of 0.2 per patient.

### **Prescribing errors for paper-based systems with standardised medication charts**

Prescribing errors for paper-based systems using standardised documentation were recorded in the post-evaluation data collection of the National Medication Inpatient Chart evaluation.<sup>21</sup> The study was conducted over 22 hospital sites and employed trained pharmacists and nurses who audited charts in medical, surgical, paediatric and mental health wards in June 2005, six months after the chart had been implemented. The study included procedural and clinical errors. In all 15,416 medicine orders for 1234 patients were reviewed. Seventy-four percent of patients' charts were considered to contain a prescribing error giving a rate of 3.5 errors per patient. Overall, 1.1% of orders were considered to be clinical errors or 0.14 per patient. Eighty-seven percent of patients had all their prior adverse drug reactions recorded and 7.7% of patients with a prior adverse drug reaction (ADRs) were re-exposed to a medicine from the same class post-implementation of the standardised chart.

Prescribing error rates for paper-based systems were also examined by prospectively auditing medical charts of 200 patients consecutively admitted within 24 hours of emergency department presentation to medical units in one New Zealand and three Australian hospitals in April 2010.<sup>22</sup> All Australian sites used the National Inpatient Medication Chart (NIMC) and all sites employed hand-written prescribing. The study assessed documentation errors only. Documentation errors included:

- lack of prescription by generic name
- illegible medicine name
- illegible prescriber name
- absence of a printed prescriber name
- absence of prescriber signature
- undated prescription
- inadequate allergy documentation.

This study did not assess clinical errors. Overall, 715 medication charts were assessed and 94% (672/715) contained at least one documentation error. The most common documentation errors were:

- lack of prescription by generic name, which occurred on 57.8% of medication charts
- at least one medicine name was illegible on 6.6% of medication charts
- a signature was missing on 20.7% of medication charts
- the prescriber name was illegible on 30.5% of medication charts
- the medication chart was undated on 37.3% of medication charts
- allergy documentation was considered inadequate on 24.3% of medication charts.

Prescribing error rates were found to vary by site, but we were unable to locate the primary data so it was not possible to document Australian results only.

These studies show high levels of procedural errors consistent with other studies of prescribing error rates for paper-based systems. However, slightly lower levels of error were reported with the standardised charts.

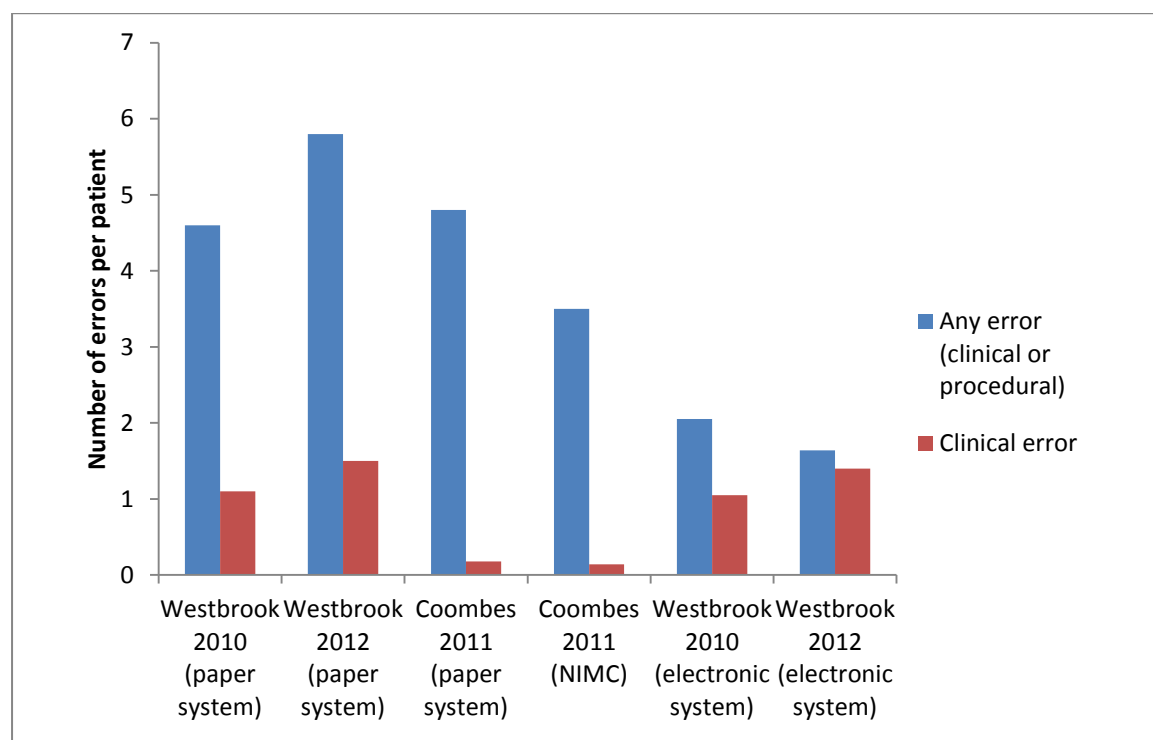
### Prescribing errors for e-prescribing systems

Prescribing error rates for e-prescribing systems have been documented as part of intervention studies assessing e-prescribing systems. In one study in two major teaching hospitals in Sydney, pharmacists independent of the hospital reviewed charts daily during May to August 2008 in the first hospital and during March 2008 and February 2010 in the second hospital.<sup>19</sup> The e-prescribing systems both included some level of decision support. Both procedural and clinical errors were documented. Systems errors (i.e. errors arising from the prescribing software) were also documented. The number of admissions and number of patients assessed post-intervention were not reported in the paper, only the rates of error per admission were reported. There were 1.6 prescribing errors per admission of which 0.25 per admission were procedural errors and 1.4 per admission were clinical errors. Serious errors occurred at a rate of 0.14 per admission. System-based errors (i.e. those attributed to the software) occurred at a rate of 0.5 and 0.7 per admission at the two sites.<sup>19</sup> While system-based errors occurred, there were more errors prevented than created by the system.<sup>23</sup>

Prescribing error rates for e-prescribing systems were also documented as part of an intervention study of an off-the-shelf e-prescribing system that did not include decision support in a 27 bed mental health inpatient unit at a major teaching hospital in April 2008<sup>20</sup>. Three clinical pharmacists prospectively reviewed all patient medication charts over a two month period. Prescribing errors included procedural and clinical errors. Overall there were 2.05 errors per patient. The clinical error rate was similar to the error rate for the paper-based prescribing at 1.05 per patient. Overall, 72.4% of patients experienced at least one error, which was similar to the rate for paper-based prescribing. The results for moderate errors were 0.40 per patient. In this study the clinical prescribing error rates associated with e-prescribing tools were similar to the clinical error rate when using the paper-based prescribing system. It should be noted, however, that the e-prescribing system did not include decision support.

Collectively, these studies show prescribing error rates with electronic prescribing systems of approximately two per admission, about half of that which was observed with paper-based systems (Figure 3). Procedural errors were less common in studies where electronic prescribing was used compared to paper-based systems. The rate of clinical errors was similar for paper-based and electronic systems when compared in the same institutions (Figure 3). The largest study, across 22 sites using paper-based systems, reported lower clinical error rates. This may be due to differences in patient mix, such as illness severity. The studies with higher clinical error rates were located in wards of major teaching hospitals.

The impact of electronic prescribing systems on serious errors was only reported in one study where the system included decision support, the results suggesting electronic prescribing systems with decision support decreased serious error rates.



**Figure 3: Prescribing errors from paper-based and electronic systems**

### Administration errors in the hospital setting

In the previous report of medication safety in Australia,<sup>3</sup> we found that administration errors varied with the type of system in place. When errors of timing were excluded, we found the clinical administration error rate (e.g. omission of therapy, wrong dose) was between 5% and 8% of medicine administrations where individual patient supply systems were in use and rose to 15% to 18% of medicine administrations when ward stock systems were in place.<sup>3</sup> The majority of this evidence was from studies undertaken in the 1990s. Prior evidence for errors with IV fluid administration was limited to one study, with an error rate of 18%.<sup>3</sup> Three new studies were located that provide further insight into error rates associated with medicine administration and one that provides insight into errors for IV fluids.

In 2006-2007, a direct observational study of administration errors was undertaken across six medical or surgical wards in two major NSW teaching hospitals.<sup>24</sup> In total, 98 nurses administering 4271 medicines to 720 adult patients were observed. Observations were subsequently compared with the medication chart to determine errors. Observers were registered nurses or physicians. Comparisons between observations and medication charts were undertaken by an independent nurse and clinical pharmacist. Errors were classified as procedural errors (e.g. failure to check patient



identification) or clinical errors (e.g. wrong medicine administered). The errors were also rated according to their actual or potential severity.

Overall, 80% of medicine administrations were associated with either a procedural or clinical error, with 74% of medicine administrations associated with a procedural error and 25% associated with a clinical error. Timing errors (e.g. administration delayed more than 30 minutes or one hour from ordered administration time) were included as a clinical error and were the most common type of clinical error, accounting for 64.5% of clinical errors. Clinical errors, excluding timing errors, occurred in 8.9% of all medicine administrations,<sup>24</sup> a similar finding to previous administration error rates for individual patient supply,<sup>3</sup> which were between 5% and 8% of administrations. The most common procedural failure, occurring in 59% of medicine administration occasions, was not checking the patient's identification against the medication chart. Wrong IV administration rate was reported as the second most common cause of error, occurring on 207 occasions. However, the overall number of IV administrations observed was not reported, thus an error rate per IV administrations observed could not be calculated. Of the 1067 administrations associated with a clinical error, 11% were considered to have a major severity rating, causing increased length of stay, permanent harm or death. Fifty-seven percent of clinical errors associated with extra dosing were considered severe errors (i.e. result in harm), as were 50% of errors where an unprescribed medicine was administered. In 46% of cases where the wrong medicine was administered the error was considered serious, as were 36% of cases where the wrong IV administration rate occurred.

Procedures where there was high adherence included:

- reading the medicine label, which was followed on 96% of occasions
- recording of medicine administration, which was followed on 96% of occasions
- checking preparation of a dangerous medicine, which was followed 99% of the time
- signing the dangerous medicines register, where the procedure was followed 94% of the time
- use of an aseptic technique, which was followed in 83% of occasions when required.

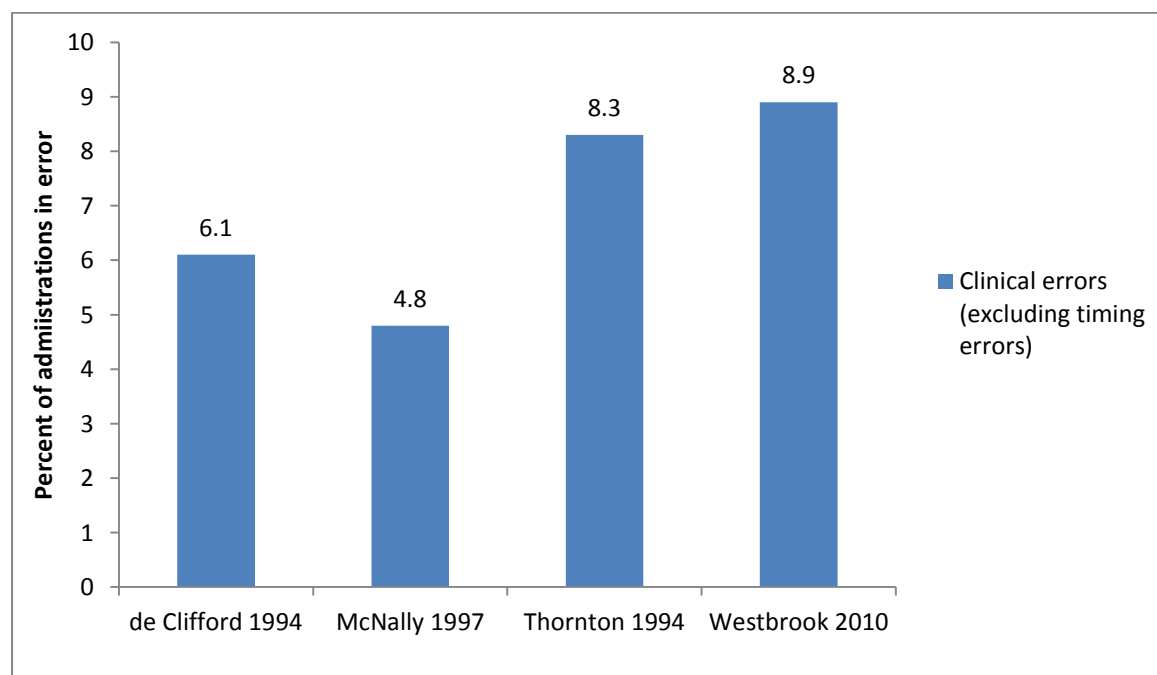
This study also assessed how the medication error rate varied according to interruptions at the time of administration. With each interruption, there was a 12% increase in the likelihood of a procedural error and a 13% increase in the likelihood of a clinical error. Interruptions were calculated per patient per medicine administration round. Of the 1671 occasions where nurses administered medicines to a patient, the nurses were interrupted during 58% of the occasions. On 20% of occasions, there were two or more interruptions. The risk of error where no interruption occurred was 75% for procedural errors and 39% for clinical errors. This rose to 81% for procedural errors and 44% for clinical errors when there was one interruption, increasing to over 90% for procedural errors and over 50% for clinical errors if there were more than two interruptions.

Another Queensland study, undertaken in 2008-2009, used retrospective medication chart review to identify medicine omission rates.<sup>25</sup> The study included 288 adults who were prescribed at least one regular medicine and admitted to any of two medical or two surgical wards at a Queensland hospital. Medicine omission was defined as medicine dose not administered before the next due dose with no documented medical reason for the omission. Medicine omission was identified by the absence of a signature on the medication chart. The presence of a tick, rather than a signature, was also defined as an omission. Medicines administered "as required" or by variable dose were excluded. There were 15,020 medicine administration episodes, of which 11% were considered

medicine omissions. At the patient level, 76% of patients experienced an omission and there were, on average, 5.8 omissions per patient identified. The characteristics of the first omission per patient were identified (n=220) and it was found that 5.5% of omissions identified were due to a tick instead of a signature being recorded (thus, potentially not an omission), the absence of a signature or an National Medication Inpatient Chart code accounted for 30% of omissions identified. Patient refusal accounted for 25% of omissions and medicine unavailability accounted for 17% of omissions.<sup>25</sup> Analgesics and alimentary medicines were the medicines most commonly identified as omissions. The retrospective nature of this study limits any conclusions that can be drawn about the overall rate of medicine omission. The extent to which lack of a signature correlates with actual omission of the medicine is unknown. Further, it is possible that signatures were documented and medicines not administered, which this study could not detect.

A New South Wales study, undertaken in 80 nursing units across 19 hospitals in 2004-05, used prospective patient record review and adverse event or incident reporting software to identify medicine administration errors.<sup>26</sup> This study was part of a larger intervention study. The study found that medication errors occurred in 16% of patients, with the main error being a timing error. The study reported an average of 28.5 (SD 4.98) time-based medication errors per nursing unit per seven days. Unlike studies of administration errors that had used participant observer to document errors, this study was limited to detecting medication errors that were recognised and had been documented in patient record or incident systems and, thus, it is likely to under-estimate the true error rate. It should be noted that the error rate reported was per patient or per nursing unit over time and so is not directly comparable to error rates reported in previous studies.

These studies provide further support that the clinical error rate for medicine administration in the hospital setting is between 5% and 10% of medicine administrations. Interruptions for the nurse during administration were associated with increased risk of error.



**Figure 4: Medicine administration errors in hospitals (individual patient supply systems)**

### ***Intravenous administrations***

In the previous medication safety report, intravenous (IV) infusion errors were reported in only one study within a single hospital and found to be 18%<sup>3</sup>. One additional study evaluating a medication safety intervention in an intensive care unit in NSW collected data in 2009.<sup>27</sup> The study found that in the baseline audit of 330 IV infusions, there was an error rate of 11.5%, with half of these errors being due to incorrect infusion rate, and one quarter being due to incompatible infusions being administered via the same lumen. The other errors related to labelling issues. Both estimates are limited by sample sizes and single locations and are limited to IV infusions.

A larger study of medication administration errors undertaken within four wards of one NSW major teaching hospital between September 2006 and February 2007 and within two wards of a second NSW major teaching hospital between November 2007 and March 2008 reported error rates occurring as a result of any type of intravenous medication administration.<sup>28</sup> Data were collected by direct observation with registered nurses or doctors acting as the observers. Procedural and clinical errors were determined. Procedural errors were identified at the time of observation, while clinical errors were identified subsequently, based on the observational data as well as a review of the Australian Injectable Drugs Handbook. This review was undertaken by a clinical pharmacist and registered nurse, both of whom were independent of the hospitals. In total, observations of 107 nurses preparing and administering 568 intravenous medications were assessed. Procedural errors occurred in 74% of administrations, while clinical errors occurred in 70% of administrations. The wrong mixture, wrong volume, wrong rate or medicine incompatibility accounted for 92% of all clinical errors. One quarter of clinical errors were rated as serious, meaning they led to increased length of stay, surgical intervention or permanent harm. Bolus administrations were associated with the highest rate of error (77% compared with 48% for other intravenous administration,  $p < 0.0001$ ). Bolus administrations were also more likely to be associated with more serious error (23% compared with 10.6% for other types of intravenous administration,  $p < 0.0001$ ). Error rates with infusion pumps were similar to error rates by other methods, however, no detail was provided on error rates with infusion pumps that included software that had hard alerts (eg did not let the operator override maximum doses or flow rates). Nurse experience was associated with error, the risk of error was highest for newly registered nurses, with error rates declining by 11% with each successive year of experience up to six years of experience, after which no further reduction in error rates was observed.

### **Medication incidents within hospital units**

Medication incidents are commonly collected as part of routine hospital incident reporting. Medication incidents may include actual errors or “near misses”, the latter being potential errors recognised and avoided before they are implemented. In this section, we describe studies of incident reports from specific areas of the hospital. Incident reports may under-estimate the true rate of adverse events as they rely on recognition of the event and the motivation of staff to report the event.

### Hospital emergency departments

One study was located that assessed patient-related incidents within the emergency department.<sup>29</sup> The study was a retrospective analysis of incident reports within a Melbourne metropolitan hospital emergency department between January and December 2008. The hospital had no definition of reportable incidents, with individual staff deciding when and what to report. Thus, the incident reports are not likely to include all incidents that occurred. Over the study period there were 61,093 emergency department presentations and 984 incident reports, with 6.5% of the incidents considered medication-related. The definition of medication-related incidents in this study included blood transfusion complications. Medication-related incidents were the third most common incident. Half of the medication-related incidents were associated with dispensing errors, one-third with administration errors and one-sixth with blood transfusion complications.<sup>29</sup> Care should be taken in interpreting these proportions as they reflect what staff felt were reportable incidents and are unlikely to reflect the prevalence of events, nor perhaps the types of errors most commonly occurring. For example, nursing staff may have been in a position, as a third party observer, to identify dispensing errors more commonly than they might identify administration errors where they were a participant. Patients with medication-related incidents were found to be slightly older, more likely to arrive by ambulance, more likely to see medical staff early, have a longer emergency department stay and be more likely to be admitted to hospital.<sup>29</sup> These findings may reflect differences in the patients' under-lying health and cannot be directly attributed to the incident.

### Palliative care

One small study gives some insight into adverse events in palliative care. A retrospective pilot study of patients consecutively admitted to a South Australian palliative care service was undertaken over a four month period at the end of 2008 to assess the incidence of symptomatic adverse events. The retrospective study involving 65 patients included a review of case-notes, medication charts and hospital incident reporting documents.<sup>30</sup> Documentation showed seven people (11%) with an adverse drug reaction on admission and 19 with documented adverse drug reactions during admission (30%). No medicine-medicine interactions or medication errors were documented, which is more likely to reflect absence of documentation or under-recognition of the events rather than absence of events.

In a Victorian study, undertaken between Feb 2009 and Jun 2010, a pharmacist service within a community palliative care team was piloted.<sup>31</sup> Medicine reviews were undertaken by the pharmacist either on admission to the community-based service or within seven to ten days of discharge from hospital-based care to palliative care at home. A total of 52 home visits were undertaken with 113 medication-related problems identified; 2.2 per person. The patient requesting further medicine information accounted for 25% of problems and the need for additional treatment accounted for 22% of problems.

### Anaesthesia

In the previous medication safety literature review, we reported anaesthesia incident rates of 0.2% of procedures.<sup>3</sup> While no new studies providing rates were located, the Victorian Consultative Council on Anaesthetic Mortality and Morbidity report for the two years 2003-2005 found that in

the 40 cases of anaesthesia-related mortality, medicines were implicated as a causal factor in 13 (32.5%), while of the 179 cases of morbidity, medicines were implicated in 49 (27%).<sup>32</sup> In a review of NSW data from 2006-2010, 167 deaths were considered related to anaesthesia and inappropriate medicine dose was considered a problem in 23 (14%) cases.<sup>33</sup>

### **Factors associated with medication-related errors during admission**

There were a number of findings from studies that identify the factors that contribute to medication error in the hospital setting or highlight preventive actions.

With regards to the accuracy of medication history, it was found that patients who presented to the emergency department with their own medicines were less likely to have medication chart errors than those who presented without their medicines.<sup>16</sup> The lack of medication chart review by a pharmacist may also contribute to inadequate documentation. A number of studies demonstrated inaccurate medication histories compared with pharmacist reconciled medication histories.<sup>14-16</sup> A study undertaken in Apr 2010 across three Australian and one New Zealand hospital found patients who had their medication charts reviewed by a clinical pharmacist within 24 hours of hospital admission were less likely to have inadequate allergy documentation.<sup>22</sup> Weekend admissions, when pharmacists may be unavailable, may pose a risk for medication errors. In one study, medication charts were less likely to be reviewed if patients were admitted on weekends as opposed to weekdays. Patients admitted overnight during the week were just as likely to have their charts reviewed as those admitted during the day.<sup>22</sup> Lack of allergy documentation is also a potential risk factor for prescribing error. A study, undertaken in 2010 at large hospital in regional Victoria, retrospectively assessed the adequacy of medicine allergy documentation on the front cover of the patient notes, in admission notes and on the medication chart for a random sample of patients.<sup>34</sup> In all, 521 patients were included, of which 48% had some kind of allergy. Less than 1% of patients had their allergy documented in all three places, however documentation was found in the admission notes for 70%. Of those with an allergy, 85% had the allergy record on the medication chart completed to some extent. However, the front cover of the medical record was poorly documented with only 28% of patients having a written explanation of their allergy recorded. For the majority of patients, the adverse drug reaction itself was poorly described; 35% of patients with medicine allergies had no details listed in their record and 16% were ticked as “unknown”.

Medicine administration errors were increased when nurses were interrupted during the medicine round.<sup>24</sup> A pilot study was undertaken in a major Sydney teaching hospital between July 2005 and February 2006 to test a technique for monitoring nurse interruptions. Fifty-two nurses working in four wards were observed.<sup>35</sup> This study found that nurses were interrupted, on average, every 49 minutes and that a quarter of all interruptions occurred during medication-related tasks. Nurses were found to have spent 12% of their time multi-tasking,<sup>35</sup> another potential risk for medication error.

The impact of nurse staffing levels, workload and environment on medication errors was assessed in a NSW study undertaken from July 2004 to June 2005.<sup>26</sup> The medication errors assessed were those documented in the patient record or reported via the incident reporting system. The study included 80 randomly selected medical or surgical units from 19 public hospitals. Medication errors, excluding

time-based errors, were found to decrease when nurses worked on their usual unit, the units were larger and there was more overtime. Errors were also less likely when greater numbers of patients had planned admissions and when nurse educators or technical assistants were present. Errors were found to increase when threats of violence or abuse occurred or workloads were heavy (e.g. tasks delayed). Time-based errors were more common with heavier workloads as evidenced by additional time needed for patient care per shift. A high turnover of patients and patients waiting for a care facility were also associated with time-based errors. Factors associated with reduction of time-based medication errors included additional staff and additional house-keeping support.

A 2007 Western Australian study of self-reported medicine administration practices of nurses working in either surgical or paediatric intensive care wards provides insight into the factors contributing to nurse non-compliance with medicine administration protocols.<sup>36</sup> Data were collected via questionnaire and focus groups. Of the 131 nurses eligible, 72 (55%) returned questionnaires. As found in the quantitative study of nurse administration errors,<sup>24</sup> nurses self-reported that verifying medicine name, dose, and route were performed most often, with more than 95% of nurses indicating they always or almost always undertook this practice.<sup>36</sup> Only 65% reported always or almost always checking the patient identification. Experienced nurses were more likely to report that they administered medicines on time than graduate nurses ( $p=0.01$ ). However, these data are self-reported so the actual difference in practice is unknown. Protocol violation was the most-common self-reported reason for medicine administration errors. Other reasons cited were prescribing errors, documentation errors, fatigue and interruptions. Patient familiarity was cited as a reason for not following the protocol. Perceived risk was also cited as a factor affecting protocol compliance, with higher risk situations encouraging compliance including the perceived potential risk of administering medicines to younger children and risks associated with dangerous medicines or blood products. Cited examples of “dangerous” medicines included anti-convulsants or anti-arrhythmics. Ward culture and confidence in other nurses involved in the checking process were both cited as reasons affecting compliance, as was the practicality of complying with the protocol, such as requirements for double-checking, particularly during night shift. Other means of checking were cited as alternatives to protocol compliance. A particular issue for graduate nurses was time management as they reported tasks took longer, and that for medicines with which they were unfamiliar they required time to access information. Graduate nurses also cited being influenced by their senior colleagues. Factors nurses thought helpful for reducing error included legible prescriptions, clearly identifying multiple orders for the same medicine where prescribed and specific instructions for medicines not commonly used.<sup>36</sup>

While not an assessment of error, a Victorian study undertaken in April 2008 assessed the frequency of use of error-prone abbreviations.<sup>37</sup> Medication charts of patients who had an overnight stay were audited on a single day using a structured data collection form at three hospitals; a large 350 bed teaching hospital, a 182 bed rehabilitation and aged care hospital and an 80 bed community hospital. Overall, 480 patient medication charts involving 8296 medicine orders were audited, with 8.4% of orders containing error-prone abbreviations. Seventy-seven percent of patients’ charts contained at least one error-prone abbreviation with, on average, 2.4 error-prone abbreviations per patient. The most common error-prone abbreviations were reported for communicating frequency or duration which accounted for 60%, for example “5/52” instead of “five weeks”. Fourteen percent of abbreviations were the use of “mcg” rather than “microgram” and 2.5% were the use of “U” or “IU” rather than unit or international unit. Seven percent were an abbreviation of the medicine

name, for example “GTN” for “glyceryl-trinitrate”. Six percent related to dose abbreviations, for example “½” instead of “half”. In total, 29% were considered high risk abbreviations.

With regards to infusion errors, the type of infusion pump used has been shown to be associated with administration errors.<sup>38</sup> A study, undertaken in a Melbourne metropolitan teaching hospital, assessed concordance between IV administration and the prescribed order at baseline, which was when the hospital was using a volumetric infusion pump and, subsequently, when smart pumps had been introduced to the hospital. Errors were identified where the administration rate or the concentration set differed to the order. The data were collected by pharmacy trainees with baseline data collected during November and December 2007 and intervention data collected in January and February 2010. Of the 432 infusions assessed at baseline, 18% were associated with error. Forty percent of the errors were considered of high clinical significance with one considered of extreme significance. Use of the smart pumps was associated with a 4% error rate. This study was uncontrolled and located in one hospital only which limits the interpretation of the results.

A West Australian study assessed risk factors for patients with more than one hospital admission where an adverse drug reaction was recorded within a three year period.<sup>39</sup> Using the Western Australian hospital administrative claims data, adverse drug reactions were identified by the ICD codes. All records were included where the patient was 60 years or over and an adverse drug reaction was documented between 1980 and 2003. In total, 28,548 patients were included of which 17.7% had a second hospitalisation where an adverse drug reaction was recorded within three years of the first. When compared with patients with no comorbidity, as identified by the Charlson comorbidity index, patients with comorbidity were more likely to have a second hospitalisation where an ADR was documented<sup>39</sup>. These results should be interpreted cautiously as there were a number of confounding factors that were not taken into account. Medicine use was not adjusted for in the study, thus it remains unclear whether the comorbidity itself was associated with the second hospitalisation or whether the treatments for comorbidity were responsible. Similarly, the results were not adjusted for the number of hospitalisations that individuals had across the time period, thus it is difficult to determine if there were similar rates of second hospitalisations amongst both groups. Time between hospitalisations was also not reported, thus it is unclear to what extent some hospitalisations may have been related to the same adverse event.

## The accuracy of discharge summaries

Previous Australian studies assessing the accuracy of medication discharge summaries undertaken in the late 1990s revealed that, on average, one medicine was omitted on the discharge summary.<sup>1</sup> Three additional studies were located that compared discharge summaries with discharge prescriptions.

The accuracy of discharge medication summaries was assessed in a study conducted in a 78 bed Sydney metropolitan hospital.<sup>40</sup> Data were collected during March 2003 to February 2004 when the hospital had hand-written discharge summaries which required doctors to transcribe medicines from the medication chart, and during March 2006 to February 2007 when the hospital had electronic discharge summaries. The electronic discharge summaries still required manual typing of prescriptions by the doctor as the hospital did not have an electronic medication management

system linked to the discharge summary system. Patients discharged to private homes or to nursing homes were included. There were 966 hand-written and 842 electronic discharge summaries which were checked against those ordered for discharge on the inpatient medication chart. Differences identified without explanation were considered an error. Overall, 12% of hand written summaries and 13% of electronic summaries were found to contain an error. The most common type of error in both systems was medicine omitted. While not as frequent, an additional medicine listed was the next most frequently detected error. Error rates were equally common whether the discharge summary was written by the intern, resident medical officer or registrar. The authors noted two phenomena associated with errors appeared to be when changes were made to medicine orders after the discharge summary had been prepared, and when discharge medicines were ordered on more than one sheet of the chart.

A smaller study conducted at the same hospital for patients admitted during April to June 2005,<sup>41</sup> which was six months after the introduction of the electronic discharge summary system, also compared hand-written and electronic discharge summaries. Only doctors trained in using the system were able to create electronic summaries. Doctors not trained in using the system produced handwritten summaries. Discharge summaries were compared with the pharmacy discharge prescription. Overall, 272 discharge summaries were reviewed; 94 handwritten and 151 electronic summaries. Errors were detected for discharge medicines in 6% of handwritten discharge summaries and 13% of electronic discharge summaries. Two doctors contributed disproportionately to the number of electronic summaries compared to the handwritten summaries, the latter which were more evenly distributed amongst prescribing doctors, thus, the significance of the difference in results is unclear. Collectively these studies suggest similar error rates occur where transcription is required regardless of whether transcription was to a handwritten or electronic summary.

Further evidence for errors with discharge summaries comes from a Melbourne study, undertaken during January to April 2009, which compared patient discharge summaries with the discharge prescriptions.<sup>42</sup> This study was undertaken as part of a study assessing transition from hospital or sub-acute aged care to residential aged care, thus all participants were elderly and discharging to residential aged care. Seventy-one discharge summaries were reviewed of which 83% included a discharge medication list. Eighty percent of the discharge medication lists contained one or more discrepancies when compared with the discharge prescription, a median of two discrepancies per patient. A review of medicine change communications that occurred during the hospital stay found only half of the changes to regularly scheduled medicines, and only a quarter of the changes to medicines scheduled “as required” were documented in the discharge summary. Discharge summaries were written by the hospital doctor.

The two studies from a small metropolitan hospital suggest that 12% of summaries contained a discrepancy while the study from a large teaching hospital assessing patients discharged to aged care found 80% of discharge summaries contained a discrepancy, which is similar to the proportion reported in previous Australian literature.<sup>1</sup> It may be that discrepancies are more common in large teaching hospitals where sicker patients are more likely to be admitted and, perhaps, greater changes in therapy occur. There is insufficient evidence to draw a solid conclusion.



## Medication safety and transition to aged care

Transitions of care are known to be a point of vulnerability for medication management.<sup>1</sup> Two studies were located that demonstrated problems occurring on admission or readmission to aged care.

An observational study conducted over a three month period in 2007 assessed transfer of medication information and timing of medicine administration following admission to aged care facilities in rural Victoria.<sup>43</sup> Patients were admitted from either home, acute care hospital, rehabilitation facility or other residential aged care facility. Data were collected by a questionnaire that was completed by nurses in the aged care facility. Data for 59 patients admitted to 14 aged care facilities were collected. Medication information was available for the majority of patients on transfer, although no information was reported to be available for 7%. The majority of patients (64%) arrived with handwritten medication information. Sixty-nine percent of patients received their medicine without delay, 20% experienced a delay of up to four hours and 3% experienced a delay of more than seven hours. The most common reason for delayed administration was that the medicines had not been written on the chart used by the aged care facility. Following admission, most patients' charts were completed by their GP. However, in eight instances (14%), either a staff member or the patient's family member was reported to have taken the medication chart to the GP clinic for a signature. While this is a small study and relies on nurse self-reporting, it does highlight potential medication-related problems when transitioning to aged care and the potential for delayed medicine administration.

Further insight into problems with transition into aged care is provided by a study assessing transition from a 400 bed acute care hospital or discharge from an 80 bed sub-acute aged care hospital to residential aged care.<sup>42</sup> The Melbourne study was conducted over a three month period in 2009. Eligible patients were those who had an overnight inpatient stay in hospital. For those transitioning to an aged care facility for the first time, the hospital provided all prescribed medicines. However, for those returning to a facility that was their usual place of residence, only new or changed medicines were provided. The patient's community pharmacy was provided with a medication summary and fax of the discharge prescriptions prior to discharge by the hospital pharmacy. Medication management summaries were also faxed to the patient's general practitioner. Within a day of discharge, a telephone interview was conducted with the residential care facility staff member responsible for the patient's medication management. In all, 202 patients discharged to 90 residential care facilities were included. Eighteen percent of patients experienced a missed or significantly delayed dose of their medicine within 24 hours of discharge. In 93% of cases the medicine dose was completely missed and in the majority of cases this was for regularly scheduled medicines. Twelve percent of missed doses were considered high risk and 53% moderate risk. Medication charts were not written or updated in time for the first dose for 62% of patients and medicines were not suitably packed for 38%. Missed doses were more common when the medication chart was not written up, rather than when medicines were unavailable. Staff reported using procedures that were not usual practice to avoid missed doses. However, this sometimes resulted in error, with six administration errors being considered to be associated with this practice, for example, administration of a pre-hospital admission dose of medicine rather than the changed dose. Patients who missed doses were more likely to represent to the hospital within seven days of discharge, although this could not be directly attributed to missed doses.

These studies demonstrate problems with timely medicine administration on transition from hospital or the community to aged care in both metropolitan and rural settings, with both studies showing approximately 20% of patients experienced a significant delay in medicine administration upon arrival at the facility. The lack of a written medicine order within the aged care facility was a contributor to delayed medicine administration. The large metropolitan study highlighted that 12% of missed doses were considered high risk and, that while not directly attributable to missed doses, patients with missed doses were more likely to represent to hospital within seven days of discharge. Larger studies would need to be undertaken to confirm this result.

### **Medication-related problems after discharge**

Previous Australian controlled trials have shown that medicines review as part of a discharge liaison service is effective in reducing medicine-related problems.<sup>1</sup> One new study documented the extent of medicine-related problems identified by home medicines review that was implemented as part of a discharge service for cardiology patients.

The retrospective Sydney-based study was undertaken between 2004 and 2007.<sup>44</sup> Patients included were those discharged to home from a hospital cardiology unit with a request to the patient's general practitioner for referral to the home medicines review service and who received the review service after discharge. Hospital discharge summaries, general practitioner referral forms for a home medicines review and home medicines review reports were assessed. Home medicines review reports were available for 76 patients. No medicine-related problems were recorded for five patients, while 398 medicine-related problems were identified among the remaining 71 patients. The average number of medicine-related problems was 5.6 per patient. Uncertainty regarding the aim of the medicine accounted for 32% of the identified problems, medicine interactions accounted for 22% and adverse drug reactions accounted for 15%. Under-use of medicines accounted for 12% of problems. There were differences in medicines listed on the discharge summaries, GP referral forms and home medicines review reports. However, the average time between when these documents were written was not reported so the import of these differences is unclear.

### **Medication safety within hospital in the home**

Medication-related problems associated with hospital in the home have not been the focus of extensive studies, however studies of adverse events of any kind associated with hospital in the home provide some insight into areas of concern.

A retrospective chart review study assessed adverse events among patients admitted to hospital in the home from the emergency department of a Melbourne hospital between 1995 and 2000. In all, 357 patient records were assessed, and 55 adverse events and 118 complications identified. Six adverse events were considered directly attributable to hospital in the home care, four of which were due to medication issues.<sup>45</sup>

A prospective multi-site Victorian study assessed adverse events amongst a cohort of patients with bacterial endocarditis who received at least part of their care through hospital in the home.<sup>46</sup> Forty patients were included, of whom nine experienced an adverse event. There were eleven adverse

events recorded in total, of which seven appeared to be associated with side effects of the antibiotic.

A Northern Territory study assessed outcomes for patients who received outpatient parenteral antimicrobial therapy for bone or joint infections between January 2006 and September 2007.<sup>47</sup> Fifty-five patients were included and all received intravenous antibiotics, with 80% also prescribed oral antibiotics. Thirteen percent of patients experienced adverse medication events.

A Melbourne study assessed the difference in outcomes for patients with deep vein thrombosis or cellulitis treated by hospital in the home during March 2002 to March 2006.<sup>48</sup> A nurse-led model was in place for the first two years, while a medical model was in place from the end of March 2004 to March 2006. For the initial two year period, patients were randomly selected from the hospital records with a matched cohort being used for the subsequent two year period. Outcomes were assessed using independent medical record review. In all, 318 patients were included (159 from each time period). Adverse medication events did not differ between periods and occurred at a rate of 3%. All events were related to over-anticoagulation. This study was limited to detecting adverse medication events that were recognised and documented in the record and, thus, may underestimate events.

A Sydney study assessed the occurrence of adverse drug reactions for patients requiring intravenous therapy consecutively admitted to hospital in the home between June 2002 and November 2004.<sup>49</sup> Overall, 673 patients were assessed, with 714 treatment courses administered. Adverse drug reactions occurred in 5.3% of administered courses.

These small studies of adverse events associated with hospital in the home included different patient groups, those with bacterial endocarditis, those with cellulitis or deep vein thrombosis and those with bone or joint infections. The studies also varied by location and method of assessment. Studies using retrospective assessment methods suggest adverse events rates of up to 5%, however prospective studies suggest adverse medication event rates of up to 17% of all admissions. These studies are small in size and the majority did not have adverse medication events as their primary focus, thus larger studies are required to confirm the extent and type of problems associated with hospital in the home.

## Medication-related problems in aged care

### Medication-related problems

There are high levels of medicine use in the residential aged care setting and the previous review of medication safety in the community identified problems with supply, problems with administration including inappropriate alteration of dose forms, and errors of documentation.<sup>5</sup> Further studies which provide insight into problems with medicines in aged care have been undertaken based on reviews of case notes from residential medicines management reviews.

A NSW study retrospectively assessed the extent of medication-related problems in aged care amongst residents from 62 aged care facilities across metropolitan Sydney.<sup>50</sup> Facilities included both high and low care needs residents. One in five residents receiving a residential medication management review between January and June 2008 were included. Medication-related problems

were identified from the pharmacist-created case notes developed as part of the review service. In all there were 500 participants of which 96% were considered to have a least one medication-related problem. In total, 1433 medication-related problems were identified, an average of three per resident. The most frequent type of medication-related problem was need for additional therapy. While the overall proportion of medication-related problems by type was not reported, a breakdown of problems by medicine class revealed risk of adverse drug reaction was the most common problem with antidepressants, antipsychotics, hypnotics and sedatives, loop diuretics, and agents acting on the rennin angiotensin system. The need for additional therapy was the most common problem associated with analgesics and for persons needing calcium and vitamin D. The retrospective nature of this study limits the findings to those problems that were recognised and documented by the pharmacist at the time of the review.

### Potentially inappropriate medicine use

Potentially inappropriate medicine use is often assessed using a predefined list of medicines considered inappropriate in specified age groups or conditions. The Beers criteria and McLeod's criteria were developed for the USA and Canada, respectively, and have been adapted for the Australian setting. Prior reviews of medication safety have reported the prevalence of potentially inappropriate medicine use in the aged care population at 20%.<sup>5</sup> Two more recent studies were based on the population that received a medicines review and reported higher levels of potentially inappropriate medicine use in the aged care population.

A Tasmanian study assessed the level of potentially inappropriate medicine use in the aged care population using medication records collected as part of medicines reviews undertaken between 2006 and 2007.<sup>51</sup> Potentially inappropriate medicines were defined by the Beers or McLeod criteria. Overall, 2345 residents aged 65 years or over from 41 residential aged care facilities were assessed. Forty-four percent of patients were prescribed at least one potentially inappropriate medicine according to either criteria; 35% according to the Beers criteria and 19% according to McLeod's criteria.

A Western Australian study assessed potentially inappropriate medicines use in the elderly with dementia resident in aged care facilities.<sup>52</sup> Data assessed were baseline data for a larger intervention trial. Inappropriate medicine use was defined by the modified Beers criteria and anti-cholinergic burden was assessed using the anticholinergic medicine scale. In total, 351 people were included, with 50% considered to be prescribed at least one potentially inappropriate medicine. Anticholinergic medicine use, which is not recommended in those with dementia, was common. Eighty-two percent of patients were using at least one medicine that had some anticholinergic effect.

These studies show that between 40% and 50% of residents in aged care facilities are prescribed potentially inappropriate medicine use, as defined by explicit criteria such as the Beers or McLeod's criteria. Medication-related problems are also commonly identified during medication management reviews, with one study showing over 90% of residents had at least one problem with, on average, three problems per resident.

### **Dose administration aid errors**

Dose administration aids are used by many aged care facilities and one study provides insight into the extent of errors that occur with their packing.<sup>53</sup> The study, undertaken between May and August 2006, assessed the accuracy of dose administration aid packing among 42 residential aged care facilities in regional NSW. Registered nurses in the facility audited one dose administration aid for every resident using a standard audit form and compared the audit to the patient's general practitioner-completed medication chart. Discrepancies between the two were noted, with incidents counted at the unit of each medicine, not at the unit of each dose. For example, if a daily medicine was missing from the pack for the week, it was counted as one incident not seven. In total, 6972 packs for 2480 residents were audited, with 297 incidents detected giving an incident rate of 4.3% of all dose administration aids packed. Incidents were of the following types:

- omitted medicines were 33% of incidents
- supply of a ceased medicines were 12%
- wrong strength dispensed were 11%
- incorrect dosage instructions were 11%.

Incident frequency varied by facility, as well as by the pharmacy responsible for packing the dose administration aid, and by general practitioners. Multivariate analysis was not undertaken so independent associations were not reported. Medicine omission was common at one low care facility, and the supply of ceased medicines was thought to be associated with the pharmacy practice of packing in advance of the time required. Twelve pharmacies supplied the dose administration aids. While no incidents were found in dose administration aids packed by two pharmacies, incident rates varied from 2% to 22% for the other pharmacies.

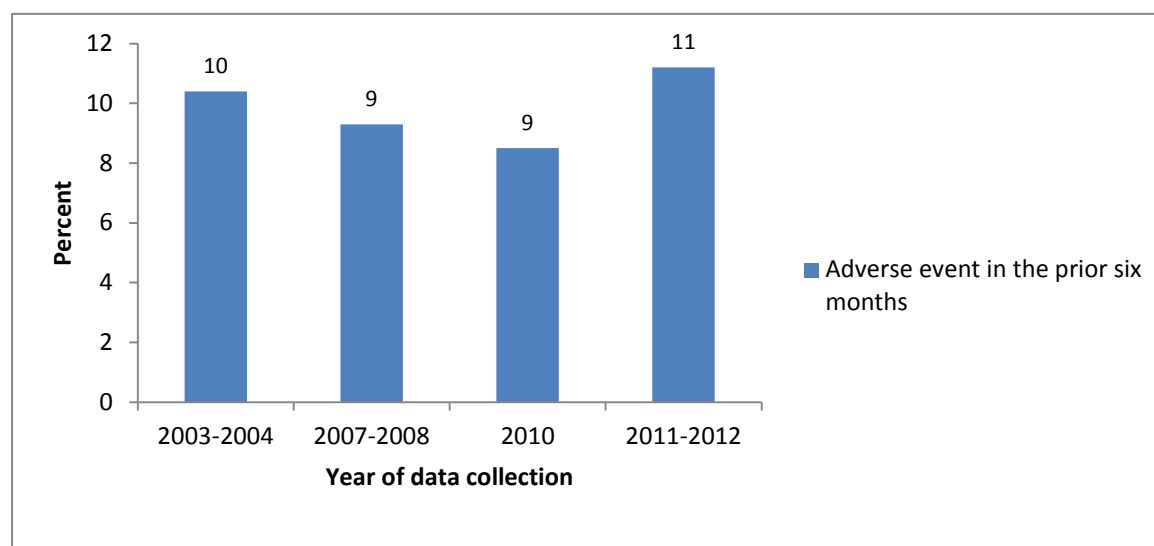
## **Medication-related problems in the community**

### **Adverse medication events in general practice**

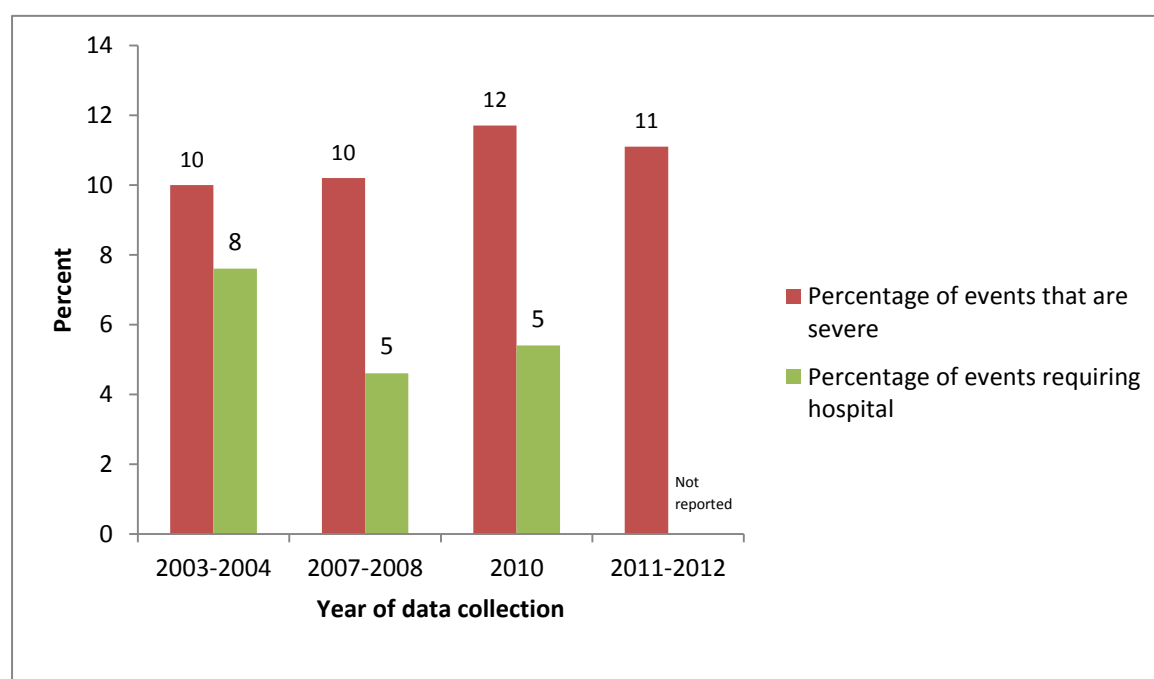
Prior Australian research found that 10% of patients seeing a general practitioner had had an adverse medication event in the previous six months.<sup>54</sup> Three additional surveys confirm this result.

In 2007-08, the Bettering Evaluation And Care of Health, or BEACH, Program repeated data collection on this topic. Data from 294 general practitioners and 8602 encounters were included. Overall, 9% of patients had experienced an adverse event as a consequence of medicine use in the prior six months. The majority of the reported events were known side effects of medicines and 10.5% were classified as severe. In 4.6% of cases hospitalisation resulted.<sup>55</sup> In a similar survey collected in 2010, data were available from 189 general practitioners for 5497 encounters. Overall, 8.5% were reported to have experienced an adverse medication event in the previous six months. In all, 12% were classified as severe and 5.4% of events resulted in hospitalisation.<sup>56</sup> These results were confirmed in a third survey undertaken during 2011 and 2012. Data were available from 293 general practitioners covering 4468 patients. Similarly to the previous survey results, 11% were found to have experienced an adverse medication event in the previous six months. In this survey, 11% were classified as severe. Hospitalisation results were not reported.<sup>57</sup>

Collectively, these results confirm that between 8.5% and 12% of people attending general practice have experienced an adverse medication event in the previous six months (Figure 5). Eleven to twelve percent of these adverse events are considered severe and approximately 5% require hospitalisation (Figure 6).



**Figure 5: Percentage of people attending general practice experiencing an adverse medication event in prior six months**



**Figure 6: Proportion of severe adverse events for those attending general practice who had experienced an adverse event in the previous six months**

### Medication-related problems

In prior medication safety reports, we reported the extent of medication-related problems in the community. A rate of 2.8 problems per person was identified through a review of case notes of

people considered at high risk of medication problems.<sup>1</sup> More recent studies, which have also used medicine review case notes to identify problems, highlight that medication-related problems for those at risk of medication misadventure remain significant.

The extent of medication-related problems was assessed during July 2007 to January 2008 in a community dwelling population aged 65 years or over who attended a Victorian metropolitan aged care assessment clinic or memory clinic.<sup>58</sup> Participants were a convenience sample of 46 patients (23 from each clinic) who attended the clinic on days when the pharmacist was present. After the patient's medical consultation, the pharmacist took a medication history, interviewed patients using a structured questionnaire with validated questions to identify medication management issues, medication adherence and adverse drug reactions, and where necessary contacted the patient's community pharmacies to clarify the medication history. By comparison with the pharmacist's history, it was found that patients were using a median of nine medicines (range 3 to 21) and a median of six medicines were recorded in the medical record ( $P<0.0001$ ). Omissions occurred for 85% of patients and dose discrepancies were found for 43%. There was a median of 2.5 (range 0-9) medication-related problems per patient identified by either the pharmacist or doctor. Of the 34 problems identified by the doctor, 44% were need for additional therapy, 12% an adverse drug reaction, 12% too low a dose and 12% unnecessary medicine use. The pharmacist identified that 41% of patients were using an inappropriate medicine, 35% had an untreated indication, 32% had a potentially unnecessary medicine and 33% had adherence issues. Overall, 26% of patients had a possible current adverse drug reaction. Risks were evaluated independently by a geriatrician and consulting clinical pharmacist, with 35% of pharmacist-identified problems being considered high or extreme risk. One third of the pharmacist identified problems related to medicines not found in the medical record, of which one quarter were considered high or extreme risk.

The extent of medication-related problems was also measured by review of case notes, which had been prepared by accredited pharmacists as part of the home medicines review service and subsequently provided to the accreditation body as part of the reaccreditation process.<sup>59</sup> Pharmacists self-selected which cases were submitted, which may have introduced some bias into the results. An alphabetically sequential subset of reviews undertaken between 1998 and 2005 (80% in 2004 or 2005) were selected for analysis. In total, 234 reviews from 200 accredited pharmacists across Australia were assessed. On average, 4.8 medication-related problems were identified per patient for those who had a home medicines review and 3.9 per patient for those who had a residential medicines management review. The most common problem was an adverse drug reaction accounting for 20% of all problems, with untreated indication accounting for 16%. Medicine interactions accounted for 11% of problems, as did compliance problems, with dosage problems accounting for 9%. Thirty percent of problems were considered to be of moderate or major significance.

Further insight into medication-related problems occurring in the community is provided by a NSW study that retrospectively assessed the home medicines review case notes developed by seven accredited pharmacists between February 2006 and October 2008.<sup>60</sup> In all, 224 cases involving community dwelling older people were included. Medication-related problems were identified in 98% of patients. In total, 1110 medication-related problems were identified or five per patient. Need for additional therapy accounted for 16% of problems. Ten percent of problems were due to adverse

drug reactions. Too low a dose accounted for 7% of problems, too high a dose for 6% and the wrong medicine for 5.5%.

Data collected by accredited pharmacists in NSW between February 2006 and October 2009 when undertaking home medicines reviews were also used for assessing medicine appropriateness, as defined by the medicine appropriateness tool.<sup>61</sup> A purposive sample of cases from seven accredited pharmacists was used. All scores were calculated retrospectively based on documentation in the case notes for the home medicines review. Of the 270 cases assessed, 99% were considered to have one inappropriate rating prior to the review. Medicines with no indication accounted for 22% of problems, while medicine-medicine interactions accounted for 14% and dosage issues 13%.

A New South Wales study provides insight into the level of medication-related problems in people with mental health problems.<sup>62</sup> Case notes from medicines reviews were reviewed for 48 patients of a mental health service in Sydney. In total, 209 problems were identified from the case notes; an average of 4.4 medication-related problems per person. There were 2.3 medication-related problems per person, on average, specifically relating to mental health. The most common problem, accounting for 39% of problems, was medicine selection. This grouping included adverse drug reaction problems. Twenty-two percent of problems were for management issues and 17% related to the medicine regimen.

Collectively these studies demonstrate that people who participate in medicines review services have between 2.5 to 5 medication-related problems per person identified as part of the review. Medication-related problems are significant in the population with mental health problems, where medicine selection issues are most common. A medication reconciliation study in the outpatient setting suggests problems with medication histories, with omission of therapy in the medical record occurring for 85% of patients and dose discrepancies occurring for 45%. The outpatient study results are similar to studies undertaken at time of hospital admission, where the hospital studies found 60% to 80% of patients have discrepancies between their medication history and a reconciled history.

### Potentially inappropriate medicine use

Previous Australian research reported the level of potentially inappropriate medicine use in the community at 21%, when assessed using Department of Veterans' Affairs administrative claims data and adapted versions of the Beers and McLeod's criteria.<sup>63</sup> Two more recently published studies provide further evidence of high levels of potentially inappropriate medicine use in the community.

A prospective cohort study undertaken in Western Australia enrolled 12,203 men between 1996 and 1999 who were selected from the electoral role and aged between 65 and 83 years.<sup>64</sup> Follow-up data for 4260 men were collected between 2001 and 2004. This study was part of a trial assessing screening for abdominal aortic aneurysms. Medicine use was collected at baseline and follow-up. Modified Beers criteria were used to assess potentially inappropriate medicine use while potential over-use and under-use were also assessed. Of the 4260 men, 49% were considered to be taking a potentially inappropriate medicine. Non-steroidal anti-inflammatory agents which were included as potentially inappropriate medicines were taken by 26%. Potential under-use of medicines was identified for 86% of men with peripheral arterial disease, 84% with coronary heart disease, 73%



with cerebrovascular disease, 39% with hypertension and 14% with atrial fibrillation. Potentially inappropriate medicine use was associated with a history of self-reported falls (RR 1.23, 95%CI 1.04-1.45). Under-utilisation of medicines was associated with a 20% increase in subsequent cardiovascular risk (RR 1.20 95%CI 1.03-1.40) and potentially inappropriate medicine use associated with a 16% increase in admission to hospital (RR 1.16, 95%CI 1.08-1.24).

Data collected by accredited pharmacists in NSW when undertaking home medicines reviews were reviewed retrospectively to determine the level of potentially inappropriate medicine use and the level of sedative and anticholinergic burden.<sup>65</sup> Data were obtained from both the Australian Association of Accredited Pharmacists (148 cases) and from seven individual accredited pharmacists (n=224). The sample of cases from the Australian Association of Accredited Pharmacists represented those self-selected for submission as part of reaccreditation processes, thus some bias may be introduced by the self-selection process. Of the 372 cases assessed, 40% were found to be prescribed one or more potentially inappropriate medicine. The most commonly prescribed potentially inappropriate medicines were long acting benzodiazepines, amiodarone, amitriptyline, dextropropoxyphene and bisacodyl. Anticholinergic medicine use was common, prescribed for 25.5% of the population. This study was limited to those who were referred for home medicines review, which represents a community dwelling population considered at risk of medication misadventure. Further, some of the sample included case notes purposively submitted for the purpose of re-accreditation. For this reason, the representativeness of the data is unclear.

These studies assessing the prevalence of potentially inappropriate medicine use in the community suggest between 40% and 50% of people in the community are prescribed potentially inappropriate medicines. These studies have been limited to older adults and, in one study, those considered at risk of medication misadventure.

### *Calls to the poisons centre*

Further insight into the types of errors occurring in the community is provided in a Victorian study that assessed cases reported to the Victorian Poisons Information Centre.<sup>66</sup> Of the 40,000 calls annually received by the centre, 4% were considered due to therapeutic errors such as wrong dose and missed dose. Case information for adults in residential aged care or living in the community was collected at the time of the call, with follow-up information collected two days later for those who agreed to participate. Cases were stratified to community or residential-aged care. Of the 1204 calls made between January 2006 and March 2007, 708 cases with follow-up data were assessed. Eighty-six percent of calls from the community sample concerned error with a single medicine, usually a double dose (34% of errors) or an incorrect dose (26% of errors). Thirteen percent of errors in the community sample involved the ingestion of an incorrect medicine, 10% involved the ingestion of another person's medicine, 10% were timing errors and 8% involved administration by the incorrect route. By contrast, only 35% of errors from residential care were for one medicine, while in 65% of cases the error involved two or more medicines. The most common types of error in the residential care sample were administration of the incorrect medicine (30% of errors) or administration of another person's medicines (27% of errors). Double dose accounted for 20% of errors, timing errors 16.5%, incorrect dose 6% and incorrect route in only one case. Four percent of the residential care cases and 2.6% of the community care cases were referred to hospital. Human factors were

considered the most common reason for errors in the community, such as distraction, while staffing issues were the most common reason for residential aged care errors, such as staff not following protocol or new staff. This study is not a measure of the extent of error, but is limited to errors that participants recognised and were sufficiently concerned about to seek further advice.

A similar analysis was undertaken of calls to the poisons line concerning therapeutic error in children.<sup>67</sup> The prospective study included consecutive calls between January 2006 and March 2007, with follow-up at 48 hours. In total 491 cases were assessed, with incorrect dose accounting for 57% of calls and double dose accounting for 26%. Eleven percent of calls involved the incorrect medicine being taken. Most of the errors occurred with analgesics or cough and cold preparations. Human factors, such as distraction, accounted for 38% of errors. Packaging was found to be associated with 17% and poor communication between carers accounted for 13%. In 97% of cases the caller was advised to observe the child at home, and in 2.6% of cases to proceed to hospital, with the remaining case being referred to the general practitioner.

### **Adverse reactions and complementary therapies**

There is very limited literature available assessing the extent of error or medication safety issues with over-the-counter and complementary therapies. One Australian study provides some insight into this issue.<sup>68</sup> A survey of customers randomly selected from 60 community pharmacies in three Australian states was undertaken between August 2008 and February 2009. A self-administered questionnaire was employed to determine the prevalence of patient reported adverse reactions to over-the-counter and complementary therapies, whether patients reported the adverse reactions they experienced and their understanding of the AUST L (listed medicine) term. In total, 1121 persons responded, with 72% reporting using a complementary medicine in the previous twelve months, of which 7% reported experiencing an adverse reaction. Of those who reported experiencing an adverse reaction, the majority indicated the reaction was mild. However 22% considered it moderate or required advice from a healthcare professional while 7% reported a severe reaction requiring hospitalisation. In response to the reaction, 78% stopped using the product, 13% changed products and 7% reduced the dose. Only 27.5% of those who experienced a reaction reported notifying their doctor, with 16% notifying the pharmacist, and 14.5% notifying the complementary medicine practitioner. Most respondents were unaware of the meaning of the AUST L listing.

### **Medication-related problems for specific medicines or conditions**

There are a number of Australian studies that have identified issues with specific medicines or conditions. In general these studies were outside the scope of this review. Some examples include studies finding high levels of psychotropic medicine use among nursing home residents,<sup>69 70</sup> treatment conflicts in those with diabetes,<sup>71</sup> heart failure,<sup>72</sup> on antidepressants,<sup>73</sup> and medication-related problems associated with warfarin use<sup>74</sup> or management of atrial fibrillation.<sup>75</sup>

### Patient self-reported problems with medicines

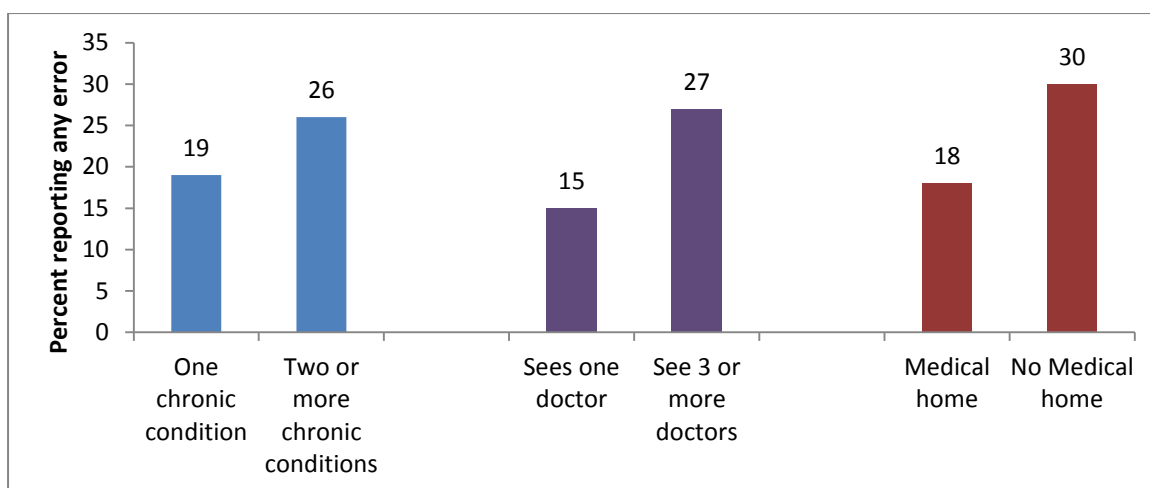
Self-reported information from consumers on adverse medication events also provides insight into potential problems. A NSW study to determine patient-reported risk factors for medication misadventure provides some insight into patient self-reported problems.<sup>76</sup> In all, 849 participants aged 65 years and over and living in the community were recruited by 20 general practitioners from 16 general practices. Fourteen percent of participants reported experiencing side-effects from their medicines, 9% reported problems reading labels, 9% reported difficulty remembering to take the medicine, 8% did not know what the medicine was prescribed for, 6% had trouble understanding the label and 10% had difficulty opening the bottle or packaging.

Insight into patient self-reported side effects is also provided by a Victorian study that assessed the baseline data collected in 1994 from the Melbourne Longitudinal Study on Healthy Ageing.<sup>77</sup> The study sample included 1000 English speaking persons aged 65 years and over and living in the community. Overall, 76% of the cohort reported taking medicines and 6.7% of the entire cohort (8.5% of those on medicines) reported medicine side effects.

Analysis of patient self-reported adverse events associated with health care was assessed with the North West Adelaide Health Study, a longitudinal cohort study of a representative sample of adults living in the north-western suburbs of Adelaide.<sup>78</sup> In 2000, baseline measures for 4060 adults were undertaken, with follow-up measures in 2004-2005, the latter which were completed by 3522 people. Four percent of the respondents reported experiencing an adverse event causing harm in the previous 12 months. Medication error was the type of event causing harm in 46% of cases.

A series of international multi-country surveys, which includes Australia, also provide insight into patient self-reported errors.<sup>79-81</sup> The 2007 survey involving 1009 Australian adults found that 8% indicated they had been given the wrong medicine or dose in the previous year, with 15% reporting either a medical or a medication error.<sup>79</sup> Rates of self-reported errors were higher for those who saw multiple doctors, had multiple conditions and did not report having a regular doctor (Figure 7). The 2008 survey, which included 750 Australian adults with at least one chronic condition or poor self-rated health, found 13% reported having been given the wrong medicine or dose in the previous year, rising to 22% when considering a medication or medical error.<sup>80</sup> The 2011 survey, which included 1500 Australian adults with complex care needs, found 19% reported a medication, medical or laboratory error.<sup>81</sup>

Collectively, the self-reported data from consumers suggest that between nine and fourteen percent report experiencing side effects and approximately 8% of all consumers and 13% of those with chronic conditions may have been given the wrong medicine or dose in the prior twelve months. Those with chronic conditions, who see multiple doctors and who have no “medical home” more commonly report experiencing errors.



**Figure 7: Percentage of patients with self-reported medication or medical error in the previous twelve months** (Source: Schoen et al. 2007<sup>79</sup>)

## Factors contributing to problems in the community

A number of studies were located that provide some insight into factors that may contribute to medication-related problems in the community.

### Accuracy of electronic medication histories in general practice

Errors in electronic health record medication histories in general practice were explored in a pilot study undertaken in Victoria.<sup>82</sup> Patients were recruited over nine sessions from a single general practice that had six general practitioners. Patients were recruited prior to seeing the general practitioner and subsequently interviewed after the consultation. Data were compared with the electronic health record. Thirty-three records were assessed. Allergy documentation was correct for 61%, incorrect for 3% and not recorded for the remaining. Medicines were reported as incorrect by 51.5%, with the majority indicating the electronic health record included medicines they were no longer taking. Nine percent indicated a medicine was missing from the record. Of the medicines recorded in the electronic health record, 68% were considered correctly recorded.

### Reading prescription labels

Previous Australian literature has demonstrated that patients have difficulty reading or interpreting prescription labels, with a small pilot study finding that 20% of consumers have difficulty reading the label, and 20% report having difficulty understanding the label.<sup>83</sup> A prospective study undertaken with patients with glaucoma attending an outpatient clinic at a Melbourne teaching hospital between September 2007 and January 2008 provides further evidence that errors may be associated with difficulty reading the label.<sup>84</sup> Participants were asked about the name and dosage regimen of their eye medicines and provided with four sample dispensing labels and asked to answer questions on the medicine name and directions for use. In total, 200 patients were recruited of which 12% were unable to read the dispensing labels. One third of patients could not report their own medicine accurately and this correlated with their ability to read the printed label.

### Patient reported risk factors

An international multi-country survey that included Australian adults asked participants about errors in their care in the previous 12 months. The 2007 survey, involving 1009 Australian adults, found that 8% indicated they had been given the wrong medicine or dose in the previous year, with 15% reporting either a medical or a medication error.<sup>79</sup> A secondary analysis of these data assessed factors associated with increased rates of error and found that poor care coordination and cost-related barriers were both associated with a doubling in risk of reporting an error in care. Hospitalisation, seeing two or more specialists and attendance at the emergency department were also associated with a doubling in the risk of reporting error.<sup>85</sup> These results are based on a survey of self-reported factors which may be affected by memory or recall bias.

## Part 2: Strategies for improving medication safety in the Australian healthcare setting

This review of published studies examining strategies to improve medication safety in the Australian health care setting included studies conducted in the community, hospital outpatient or ambulatory care setting. Studies were included if they implemented a medication safety intervention and measured an endpoint that included at least one patient outcome, which could include any of the following: hospital admissions, adverse events, mortality, quality of life, symptoms or surrogate health endpoints (e.g. blood pressure control, blood glucose level, medication errors, medication knowledge or changes in the quality of medicine use). Studies that implemented strategies to improve the quality of medication management only were excluded.

In summarising the studies, the National Health and Medical Research Council (NHMRC) Evidence Hierarchy, designations of 'levels of evidence' for intervention studies, has been used to indicate the level of the study design<sup>86</sup> (See Appendix II). Most studies included in this review are pre- and post-intervention studies without control, where outcomes for a group of subjects exposed to the intervention are compared with previously treated subjects at the same institutions (Level III-3 design). Some studies involved the use of randomised controlled trial (Level II) or non-randomised controlled trial (Level III-2) designs.

### Systems to improve medicine administration and dispensing

#### Improved medicines packaging, storage and administration equipment

##### *Smart infusion pumps for intravenous administration*

Errors in intravenous (IV) medicine administration can result in significant patient harm or treatment failure. A pre and post-intervention study (Level III-3) examining the impact of a smart infusion pump<sup>38</sup> on IV administration errors was undertaken in an acute hospital in Melbourne in 2008. In the pre-intervention stage an audit undertaken by an independent observer over 41 working days recorded prescribing and administration details for medicine infusions when conventional pumps (IMED Gemini Volumetric Infusion) were used in the hospital. The smart pump intervention used in the study was an Alaris GP Volumetric Pump with software called Guardrails which includes a medicine library. The medicine library included standard concentrations, dosing units and maximum and minimum infusion rates and was developed for local requirements of the hospital. The software provided 'soft' and 'hard' alerts in under-dose and overdose scenarios. In the case of 'hard' alerts, the user would be notified that the dose was above the maximum level in the medicine library and the infusion would not be allowed to proceed until re-programmed to an acceptable dose level.

Twenty months after the introduction of the smart pumps, IV medicine administration errors (defined as any deviation of the rate or concentration set on the pump when compared to the medication chart) and clinical significance were audited for a period of 27 days. The clinical significance of errors was assessed independently by an emergency physician and clinical pharmacist. There were 432 infusions audited in the pre-intervention period and 266 in the post-intervention period. In the post-intervention, period 62% of infusions (165/ 266) were administered using the Guardrails software.

Major findings of the study included:

- during the pre-intervention period, 18% of infusions (76/432) had one or more errors recorded compared to 9.4% of infusions (25/266) following the introduction of the smart pumps ( $p=0.003$ )
- of the 165 infusions administered using Guardrails software, only 3.6% (six infusions) had errors identified ( $p<0.001$  compared to pre-intervention)
- when medicines were infused using the Alaris GP pumps without Guardrails, 19% (19/101) had errors which was no different from the pre-intervention ( $p = 0.8$ )
- the error rates were significantly lower when the smart pump was used with the Guardrails software compared to the pump without the software ( $p<0.001$ )
- when Alaris GP pumps with Guardrails were used there were no errors of 'extreme' clinical significance or 'high' clinical significance compared to the pre-intervention period where there was one error of 'extreme' clinical significance and 30 errors of 'high' clinical significance
- there was a statistically significant reduction in errors of 'high' or 'extreme' clinical significance between the two study periods ( $p=0.03$ ).

This study (Level III-3) suggests that the Alaris GP smart pump with Guardrails can significantly reduce intravenous administration errors in an Australian acute care setting. The study findings also suggest that use of the software containing a medicine library and alert system (tailored to the local requirements) must be used with the pump for the error reduction to occur.

### *Tall Man lettering to reduce medicine selection errors*

Confusion between medicine names has been identified as significant cause of medication error in Australia and internationally.<sup>87</sup> Tall Man lettering has been suggested as one strategy to reduce these types of errors for medicine names that sound or look-alike. Tall Man lettering is a technique of using selective capitalisation of parts of a medicine name to differentiate similar looking medicine names more easily (e.g. cefUROXime and cefOTAXime).<sup>87</sup>

Two studies published since 2008 were identified that examined the use of Tall Man lettering in Australia. One study was a laboratory-based study that examined the rates of errors in identification of medicine names by pharmacists and junior medical officers when names were presented in one of three formats: natural case, Tall Man and random capitalisation<sup>1</sup>. This study found no significant differences in errors with any one type of format. A second study described the successful introduction of Tall Man letters as a safety strategy in a hospital network in Victoria.<sup>88</sup> Labels using Tall Man lettering were added to dispensary shelves and ward medicine storage areas and Tall Man lettering was introduced into the pharmacy dispensing software. However, no studies were located that examined the impact of Tall Man lettering on error rates or patient outcomes.

### *Medicine delivery and storage in hospital wards*

A pre- and post-intervention study (Level III-3) undertaken in 2008/09 in a Tasmanian rural/regional hospital assessed the impact of a ward pharmacy technician service to facilitate medicine delivery to a medical ward.<sup>89</sup> In the pre-intervention period, the medicine distribution system on the ward consisted of imprest and individual dispensing with medicines administered to patients from

medicine trolleys. In the post-intervention period, the pharmacy technician serviced the medical ward's imprest and individual dispensing and stored medicine in individual bedside drawers. They also contacted the clinical pharmacist if they identified discrepancies between items in bedside drawers and medicine orders or found incomplete or ambiguous medicine orders. Two audits examining missed doses were conducted pre-intervention (May and December 2008) and two further audits (including missed doses) were conducted post-intervention (February and June 2009). There was a high rate of missed doses pre-intervention with 8.9% of regular doses (72/811) and 7.9% of regular doses (52/657) missed in the first and second pre-intervention audit, respectively. In both post-intervention audits there were no missed doses detected ( $p < 0.01$ ).

### Standardising medication charts

A study undertaken in Queensland to improve insulin management in hospitals<sup>90</sup> examined the effect of form redesign and standardisation to improve the prescription and administration of insulin (details of this study relating to prescribing errors are described below in the section Systems to improve prescription writing: Standardising Medication Charts). The study was undertaken in four tertiary and regional hospitals and used a pre- and post-intervention design (Level III-3). A state-wide expert panel, including endocrinologists, physicians, pharmacists, diabetes educators and medication safety nurses, was involved in the design of two standardised charts, one for intravenous insulin and one for subcutaneous insulin. Consensus and available evidence were used to guide the development process. The forms were also assessed using prescribing and administration scenarios and then piloted with format changes applied where required. The charts were designed to allow all documentation for prescribing and administration of insulin to be included on the one chart. They also included prompts for prescribers to reduce unsafe documentation (such as the elimination of the abbreviation 'u' for units). A decision support tool for managing hypoglycaemic episodes was also developed and incorporated. The forms were implemented with education for hospital staff from site-based project officers over a period of eight weeks.

Insulin management was measured through an audit of documentation and blood glucose control before, and three months after, the implementation of the charts. There were a total of 117 patients in the pre-intervention audit and 82 patients post-intervention. In an audit of intravenous insulin administration documentation the following significant improvements were seen following the intervention:

- the proportion of administration forms in which insulin infusion rates were correctly recorded (hourly recording expected) by nursing staff increased from 56% (644/1151) of forms pre-intervention to 69% (455/661) post-intervention ( $p < 0.0002$ )
- the proportion of administration forms in which the infusion rate was incorrectly documented decreased from 10.4% (120/1151) pre-intervention to 5.6% (37/661) post-intervention ( $p = 0.0004$ )
- the proportion of administration charts in which the documentation was unclear decreased from 30.9% (356/1151) pre-intervention to 0.9% (6/661) post-intervention ( $p < 0.0002$ )
- the proportion of administration forms in which the infusion rate was missing (hourly expected recording) decreased from 40.1% (461/1151) pre-intervention to 30.6% (202/661) post-intervention ( $p < 0.0002$ ).



In an audit of subcutaneous insulin administration documentation, the proportion of administration charts with unclear dose documentation decreased significantly from 10.1% (21/208) pre-intervention to 2.9% (7/245) post-intervention ( $p=0.0014$ ). There were no significant changes in the proportion of charts with dose incorrectly documented or missing.

This study (Level III-3) provides evidence that form design implemented with staff education can improve the documentation of insulin therapy administration in the acute care setting.

## Systems to improve prescription writing

### Standardising medication charts

A national medication chart for inpatients common to all hospitals in Australia arose from the Medication Safety Breakthrough Collaborative. The National Inpatient Medication Chart was adopted for national roll-out following a requirement by the Australian Health Ministers' Conference in April 2004 that the chart be used in all Australian public hospitals by June 2006. Prior to this, multiple different medication charts were used within each state across Australia.

In the previous review of medication safety in the Australian acute care setting,<sup>4</sup> three studies examining the piloting and implementation of the National Inpatient Medication Chart (NIMC) in hospitals were included. Five studies published since 2008 were located that examined the impact of standardising medication charts on prescribing.

Two studies were undertaken in Queensland hospitals that examined the impact of medication charts, which were subsequently rolled out on a statewide basis; these charts were developed as part of the NIMC initiative. Another study piloted the NIMC in hospital sites across Australia. All studies used a pre- and post-intervention methodology (Level III-3) and examined effects on prescribing error, opportunity for error and documentation. A further study examined a modification of the NIMC to incorporate support tools for venous thromboembolism (VTE) prophylaxis prescribing. One study examined the use of a weight-based dosing chart for improving prescribing of a particular high-risk medicine, N-acetylcysteine, used to treat paracetamol toxicity.

A study published by Coombes et al. in 2009<sup>91</sup> which was undertaken in 2002/03 involved the development of a standardised paper-based medication chart for use in public hospitals in Queensland. The impact of the chart on the frequency and type of prescribing errors, ADR documentation and warfarin prescribing was examined. The chart was developed by a multidisciplinary panel incorporating recommendations from the literature and information obtained from previous Australian studies of medicine prescribing and administration, as well as an analysis of local medication incidents. The chart was designed to improve the visibility of previous ADR information, to improve entry of dosing times for regular medicines and also incorporated a warfarin section to improve prescribing of this high-risk medicine. The warfarin section ensured that information about the current and target international normalised ratio (INR) was clearly visible at the time of prescribing and administration of the medicine. The chart was piloted with medical, nursing and pharmacy staff during its development. Implementation and training sessions for staff were held at all hospital sites involved in the study.

An audit of all available prescriptions for four months before, and six months after, implementation of the standardised chart was undertaken at five hospital sites by study and local nurse/ pharmacist pairs. Inpatient INR results for 12 months before and after implementation were collected. Charts were assessed for 730 patients pre-intervention and 751 post-intervention, representing 9772 orders pre- and 10,352 orders post-intervention. Major findings included:

- the prescribing error rate decreased from 20.0% of orders per patient pre-intervention to 15.8% post-intervention ( $p=0.03$ ) with an absolute error reduction of 4.2%
- previous ADRs were not documented for 19.5% of 185 patients pre-intervention and 11.2% of 197 patients post-intervention ( $p=0.032$ )
- prescribing errors involving selection of a medicine for which a patient had a previous ADR decreased from 11.3% of patients pre-intervention to 4.6% post-intervention ( $p=0.021$ )
- INRs greater than 5 (data from four sites) decreased from 1.9% of 14,405 INRs pre-intervention to 1.45% of 15,090 INRs post-intervention ( $p=0.004$ ).

The authors reported that following some minor modifications, the chart was rolled out in hospitals across Queensland and which enabled standardised medication training across the state. The chart also formed the basis for the NIMC described further below.

Another study undertaken in Queensland to improve insulin management in hospitals<sup>90</sup> examined the effect of form redesign and standardisation to improve the prescription and administration of insulin. The study was undertaken in four tertiary and regional hospitals and used a pre- and post-intervention design (Level III-3). A state-wide expert panel, including endocrinologists, physicians, pharmacists, diabetes educators and medication safety nurses, was involved in the design of two standardised charts; one for intravenous insulin and one for subcutaneous insulin. Consensus and available evidence were used to guide the development process. The forms were also assessed using prescribing and administration scenarios, then piloted with format changes applied where required. The charts were designed to allow all documentation for prescribing and administration of insulin to be included on the one chart. They included prompts for prescribers to reduce unsafe documentation (such as the elimination of the abbreviation 'u' for units). A decision support tool for managing hypoglycaemic episodes was also developed and incorporated. The forms were implemented with education for hospital staff from site-based project officers over a period of eight weeks.

Insulin management was measured through an audit of documentation and blood glucose control before and three months after the implementation of the charts. There were a total of 117 patients in the pre-intervention audit and 82 patients post-intervention. In an audit of intravenous insulin prescribing documentation, the following significant improvements were seen following the intervention:

- there was a clear prescribing regimen documented in 52.5% (21/40) of forms pre-intervention versus 92.3% (24/26) post-intervention ( $p=0.0009$ )
- the start time was documented in 12.5% (5/40) of forms pre-intervention versus 73.1%, (19/26) post-intervention ( $p<0.0002$ ).

Regarding the audit of subcutaneous prescribing documentation, the following significant improvements were seen following the intervention:

- the opportunity for administration error as the result of an unclear order occurred in 41.8% (87/208) of forms pre-intervention versus 12.2% (30/245) post-intervention ( $p < 0.0002$ )
- an unclear route occurred in 75.5% (157/208) of forms pre-intervention versus 4.9% (12/245) post-intervention ( $p < 0.0002$ )
- unclear frequency occurred in 65.9% (137/208) of forms pre-intervention versus 6.5% (16/245) post-intervention ( $p < 0.0002$ ).

There were no significant differences in blood glucose control pre- and post-intervention. At the time of study publication the forms were being rolled out across the Queensland public hospital system.

A paper published in 2011 by Coombes et al.<sup>21</sup> describes the piloting of the NIMC in 22 public hospitals across Australia. The chart was a modification of that used in hospitals across Queensland as described above<sup>91</sup>. Modifications to the previously used chart were made following a Delphi process of piloting, evaluating error rates and seeking clinician feedback from across Australia. In 2005 a pilot version of the NIMC was approved. Workshops were held in major capital cities around Australia to explain the background and rationale for the chart to doctors, nurses and pharmacists from the participating pilot sites.

Pre- and post-intervention audits of medication charts were undertaken by trained nurse/pharmacist teams. The study examined errors in orders for stat, variable dose, regular and 'as required' medicines. Pre-intervention data were collected in November 2004 and post-intervention data were collected in June 2005, six months after implementation of the chart. There were 1328 patients included in the pre-intervention audit and 1234 in the post-intervention audit. Major findings for the combined results from the various sites included:

- decreased prescribing errors from a median (range) 3 (0-48) per patient in the pre-intervention audit (6383 errors in 15,557 orders), to 2 (0-45) per patient post-intervention (4293 errors in 15,416 orders), ( $p < 0.001$ )
- decreased errors per order per patient from 33.3% of orders pre-intervention to 16.7% post-intervention ( $p < 0.001$ )
- increased documentation of medicines causing previous ADRs from 81.9% of medicines pre-intervention to 88.9% of medicines post-intervention ( $p < 0.001$ )
- decreased proportion of patients with at least one previous ADR re-exposed to the same class of medicine from 14.1% (57/403) of patients pre-intervention to 7.7% (28/363) post-intervention
- increased documentation of the indication for warfarin from 12.1% pre-intervention to 34.3% post-intervention ( $p = 0.001$ )
- increased documentation of target INR from 10.8% pre-intervention to 70.0% post-intervention ( $p < 0.001$ ).

Another study conducted in a regional Victorian hospital examined an intervention using the NIMC to improve the use of venous thromboembolism (VTE) prophylaxis in a hospital setting.<sup>92</sup> VTE prophylaxis includes use of low-dose unfractionated heparin, low molecular weight heparin or graduated compression stockings. This intervention was introduced in response to the under-utilisation of VTE prophylaxis in hospitals to prevent complications such as deep vein thrombosis and pulmonary embolism. This retrospective cohort study (Level III-3 evidence) was conducted over a 25 month period (2007/09). The study population included inpatients  $\geq 16$  years consecutively admitted

under medical and surgical wards of the hospital who were not pregnant and who had a hospital stay of  $\geq 3$  days. Data were collected for one year before and one year after the implementation of the intervention. The intervention used the NIMC and modified it to incorporate three elements: a) a VTE risk stratification and prophylaxis guidance tool, b) an instrument for screening for contraindications to VTE prophylaxis, c) a VTE prophylaxis prescription prompt. These three elements were developed in accordance with best practice guidelines. The chart intervention was launched in the hospital along with a hospital-wide forum to educate medical and other relevant allied health staff. Outcome measures included frequency of prophylaxis use, incidence of VTE disease and prophylaxis-related complications. There were 1478 medical patients (806 pre-intervention and 672 post-intervention) and 893 surgical patients (450 pre-intervention and 443 post-intervention). Major findings related to the use of VTE prophylaxis included:

- increased use of pharmacological prophylaxis in medical patients at high risk of VTE with  $> 1$  risk factor, from 48.0% of patients (153/319) pre-intervention to 79.8% (158/198) post-intervention ( $p < 0.001$ )
- increased use in surgical patients at high risk of VTE with  $> 1$  risk factor, from 73.4% of patients (234/319) pre-intervention to 85.4% ( $n = 258/302$ ) post-intervention
- an increased percentage of patients at high risk (with  $> 1$  risk factor) with prophylaxis initiated in a timely fashion (on the day of hospital admission), from 64.1% pre-intervention to 85.8% post-intervention ( $p < 0.001$ ) for medical patients and from 56.9% pre-intervention to 77.2% post-intervention ( $p < 0.001$ ) for surgical patients
- increased adherence to guidelines by 22.1% in the surgical patients post-intervention and by 15.4% in the medical patients ( $p < 0.01$ )
- no significant change in overall or subgroup incidence of VTE following the implementation of the chart intervention - overall risk ratio 0.88 [95% CI 0.48-1.62]; medical RR 0.82 [95% CI 0.39-1.77]; surgical risk ratio 1.02 [95% CI 0.36-2.87]
- no significant change in the incidence of pharmacological prophylaxis-related complications with the intervention, risk ratio 1.13 [95% CI 0.36-3.48].

There is now a suite of different charts available through the NIMC initiative including acute and long-stay inpatient charts, paediatric charts, day surgery and residential aged care facility charts<sup>10</sup>. A national survey of mental health clinicians on the use of the NIMC in psychiatric acute care settings was recently reported.<sup>18</sup> Based on the survey it was recommended that the NIMC be used in these settings with the development of a national chart for titrating clozapine doses and specific educational resources for health professionals working in acute psychiatric care.

The NIMC initiative is also supported by the National Inpatient Medication Chart Online Training Course available through the NPS MedicineWise web site [www.nps.org.au/health-professionals/professional-development/online-learning/nimc](http://www.nps.org.au/health-professionals/professional-development/online-learning/nimc). This course aims to familiarise professionals involved with the prescribing and administration of medicines with the NIMC, and to raise awareness of safe prescribing and administration practices.

Another study concerned with prescription errors for one particular medicine, N-acetylcysteine (NAC), examined the effect of a weight-based dosing chart<sup>93</sup>. NAC is used to treat paracetamol poisoning but when over- or under-dosed it can itself result in significant morbidity or mortality. This pre- and post-intervention study was conducted in the emergency department of a major hospital in Melbourne in 2010/11. Patients included were those  $> 17$  years with paracetamol poisoning

requiring NAC treatment upon hospital presentation. The intervention was a weight-based dosing chart based on previously validated NAC charts and modified for the local working environment. The chart was a fluid/medicine infusion chart with fluid type, volume and rate pre-printed. Doses for each patient weight to the nearest 10kg were specified on the chart. The chart required the prescriber to record the patient's weight and transcribe the appropriate dose. The introduction of the chart was accompanied by intensive staff education and publicity (e.g. reminders to use charts attached to NAC vials). Retrospective chart review was used to gauge rates of NAC prescription error. The pre-intervention phase was 46 months and the post-intervention period was 10 months with a two week 'wash in' period. A total of 123 episodes of paracetamol poisoning met the study criteria (81 pre-intervention, 42 post-intervention). Patient demographic factors were similar between the different periods, however more prescriptions were written by emergency consultant physicians in the post-intervention period (14.8% pre-intervention and 42.9% post-intervention,  $p=0.001$ ) that may have influenced the study outcomes. Major study findings included:

- for the primary outcome measure of overall incidence of NAC errors, the proportion of total prescriptions with any error was 56.8% [95% CI 45.3-67.6] pre-intervention and 14.3% [95% CI 5.9-29.2] post-intervention ( $p<0.001$ )
- the proportion of prescriptions with at least one minor prescription error (including fluid type and volume) was 50.6% [95% CI 39.4-61.8] pre-intervention and 4.8% [95% CI 0.8-17.4] post-intervention ( $p<0.001$ )
- the proportion of prescriptions with at least one major prescription error (including NAC dose, infusion rate, incomplete prescription) was 18.5% [95% CI 11.1-29.0] pre-intervention and 11.9% [95% CI 4.5-26.4] post-intervention, which was not significant ( $p=0.49$ ), however the proportion of dosage errors was significantly lower post-intervention ( $p=0.01$ ).

These results, while limited to Level III evidence, collectively suggest that standardised medication charts lead to reductions in prescribing errors, and result in improved documentation. The pilot study suggested that the NIMC was useful for reducing prescribing errors and improving ADR documentation. The study used surrogate measures of patient harm, rather than direct measures. Further controlled trial evaluation of the NIMC and supporting educational programs should be considered in the future, including measurement of impacts on patient harm.

All three studies where standardised charts were used to improve management of a particular pharmacological therapy (insulin, VTE prophylaxis, warfarin, and N-acetylcysteine) demonstrated improvements in prescribing practice. The modified NIMC intervention improved pharmacological VTE prophylaxis prescribing in a timely manner for high-risk patients, however the incidence of VTE was not shown to change significantly following implementation of the intervention. The warfarin chart resulted in a reduction in INR results of greater than five. The N-acetylcysteine chart led to a reduction in prescribing errors.

### Electronic prescribing/medication management

Since the 2008 review of medication safety in the Australian acute care setting,<sup>4</sup> a number of studies have been published describing the implementation of electronic prescribing (e-prescribing) in acute care and assessing its impact on prescribing errors. Evidence for the effect of this intervention comes from two new studies. One study examining the effect of e-prescribing on prescription errors used a

pre- and post-intervention design<sup>20</sup> (Level III-3) and another assessing two different e-prescribing systems used both a pre- and post-intervention and non-randomised controlled design (Level III-2 and III-3).<sup>94</sup>

A study by Westbrook et al.<sup>20</sup> examined the effect of implementing a commercial electronic medication management system on the incidence, nature and severity of prescribing errors in a NSW public hospital mental health unit. The study, undertaken in 2007/08, used a pre- and post-intervention design. The e-prescribing system used for the intervention was the Hatrix Med Chart. Only limited decision support was used with the system, which included allergy and intolerance warnings, pregnancy warnings, therapeutic duplication (alerts if another medicine from the same class had already been prescribed for the same patient), some dose range checking and local decision support rules (mainly targeting how medicines were administered). The system allowed the prescriber to continue the prescribing process after the warning had been displayed. Medicine information references were made available online. A one month prospective review of all medication charts from the unit was conducted pre-intervention by three clinical pharmacists independent of the hospital. Sixteen weeks after the commencement of the e-prescribing system intervention, a post-intervention chart review was conducted for another one month period. Thirteen categories of prescribing errors were assessed which were collapsed into two main types: errors related to documentation processes (procedural errors), and those related to ordering decisions (e.g. wrong dose or route) (clinical errors). A published five-point severity scale was also applied in the chart review. Charts were reviewed for 72 patients pre-intervention and 58 patients post-intervention.

The major findings of the study included:

- significantly decreased prescribing error rate per patient per 100 days from 22.5 [95% CI 19.9-24.1] pre-intervention to 9.0 [95% CI 8.8-9.2] post-intervention
- a decrease in the mean number of prescribing errors per patient from 4.68 [95% CI 3.54-5.82] pre-intervention to 2.05 [95% CI 1.41-2.69] post-intervention
- little change in the proportion of patients experiencing one or more errors with 70.8% (n=51) pre-intervention and 72.4% post-intervention
- reduced procedural errors, from a mean number of 3.63 per patient (n=261 errors) pre-intervention to 0.17 (n=10 errors) post-intervention (p value not reported), with incomplete or unclear orders eliminated
- no change in clinical errors (related to ordering decisions), with 1.06 errors per patient pre-intervention (n=76 errors) and 1.05 errors per patient post-intervention (p value not reported)
- the average severity of the errors increased significantly following introduction of the system from 1.75 [95% CI 1.7-1.8] pre-intervention to 2.14 [95% CI 2.0-2.2] post-intervention (p<0.001); this represented a large decline in errors rated as 'insignificant' but an increase in errors rated as of 'moderate' or 'major' severity
- moderate/major errors occurred at a rate of 0.29 per patient (1.4 per 100 patient-days) pre-intervention and rose to a rate of 0.41 per patient (1.8 per 100 patient days) post-intervention (p value not reported)
- the average severity for documentation errors did not change significantly after system introduction, however the severity of clinical (ordering decision errors) did increase

significantly from a mean severity score of 1.91 (n=76 errors) pre-intervention to 2.33 (n=61 errors) post-intervention ( $p<0.001$ ).

The authors concluded that the e-prescribing system was effective at targeting documentation-type errors. However it resulted in little change in the rate of clinical errors and there was actually an increase in the mean severity of these errors. It was suggested that some of the clinical errors might be prevented if targeted decision support was used with the system.

A second larger study examining the effect of electronic prescribing on prescribing error rates was conducted by Westbrook et al.<sup>94</sup> between 2006–2010. This study was conducted in two acute care hospitals in Sydney, NSW. At one site (Site A), a non-randomised controlled design was used with one ward (geriatric) receiving the e-prescribing intervention and comparisons were made with three wards (geriatric, renal/vascular and respiratory) not receiving the intervention. At the other site (Site B), a pre- and post-intervention design was used with two wards (psychiatry and cardiology) receiving the intervention with error rates compared before and after.

In the pre-intervention period, all wards used a paper-based prescribing system. At Site A, the Cerner Millennium PowerOrders e-prescribing system was used as the intervention. This system mainly involved the selection of pre-prepared 'order sentences' following medicine selection that could be modified by the prescriber. Decision support activated during the study included allergy alerts and medicine-medicine interaction alerts (set at most severe level). Patient allergy status had to be recorded for the order to be completed. Prescribers could also select other 'passive' decision support such as a medicine information database, pre-defined order sets, and integration of patient laboratory testing and medicine doses. At Site B, the iSoft MedChart system was used. The data entry using this system could be performed using drop-down lists to select prescribing information, pre-written orders or protocols (which were combinations of pre-written orders). This system included alerts for allergy, pregnancy warnings, therapeutic duplication, some dose-range checking and local decision support (e.g. local guidelines). All alerts were displayed as 'pop-ups' on the screen and the prescriber could continue the order by closing the alert box (information only alerts) or clicking an over-ride box. Medicine information resources were made available online. Review of all medication charts from the unit was conducted pre-intervention by three clinical pharmacists independent of the hospitals for at least two months pre- and post-intervention (with the exception of the psychiatry ward with one month in each phase). Errors were classified and rated for severity (with a five-point severity scale, with those  $\geq 3$  categorised as serious).

Major findings of the study included:

- a statistically significant reduction in error rates associated with use of the e-prescribing systems within the three intervention wards at the two sites, with reductions of 66.1% [95% CI 53.9%–78.3%], 57.5% [95% CI 33.8%–81.2%] and 60.5% [95% CI 48.5%–72.4%]
- the control wards at Site A experienced no significant change in error rates (respectively –12.8% [95% CI –41.1% to 15.5%], –11.3% [95% CI –40.1% to 17.5%], –20.1% [95% CI –52.2% to 12.4%])
- at Site A, the use of the Cerner Millennium system resulted in a decline in prescribing errors from 6.25 per admission [95% CI 5.23–7.28] to 2.12 [95% CI 1.71–2.54] ( $p<0.0001$ )
- at Site B the use of the MedChart system resulted in a decrease in prescribing errors from 3.62 per admission [95% CI 3.30–3.93] to 1.46 [95% CI 1.20–1.73] ( $p<0.0001$ )

- the decrease in errors was mainly due to a large reduction in unclear, illegal, and incomplete orders (procedural errors) (90.8% reduction for Site A, 93.6% reduction for Site B,  $p < 0.0001$ )
- there was limited change in clinical error rates, but serious errors decreased by 44% (0.25 per admission to 0.14;  $p = 0.0002$ ) across the intervention wards compared to the control wards (17% reduction; 0.30–0.25;  $p = 0.40$ )
- at both sites there were e-prescribing system-related errors (site A 0.73 and site B 0.51 per admission), which accounted for 35% of post-intervention errors in the intervention wards, with each system associated with different types of errors
- at Site A (Cerner Millennium system) the most common types of system-related errors were wrong route 23% ( $n=27$ ), at a rate of 0.16 per admission and wrong medicine 12% ( $n=14$ ), at a rate of 0.09 per admission
- at Site B (MedChart system) the most common types of system-related errors were wrong strength 44% ( $n=106$ ) at a rate of 0.23 per admission and wrong formulation 13% ( $n=31$ ) at a rate of 0.07 per admission.

Another study conducted in 2005/06 at two hospital sites of a private health service examined the effects of introducing an electronic medication management system on reported medication errors.<sup>95</sup> The study compared the MedChart system in one site with conventional paper-based medication management at the second site. The endpoint of the study was medication-related incident reports submitted through all departments. The use of self-reported incidents, which may be influenced by a number of factors including the introduction of the system, were not considered a valid endpoint for assessment of the effect of the system.

Level III-2 and III-3 Australian evidence supports the effectiveness of electronic prescribing systems in reducing prescribing errors, particularly procedural errors. The impact on actual clinical errors is less clear, with the Level III-2 study showing no difference in clinical errors, although a significant reduction in serious errors was observed. A Level III-3 study, where the electronic prescribing system had very limited decision support, reported an increase in serious errors, however this study was uncontrolled and thus the findings are less robust. The e-prescribing systems did not have the substantial clinical decision support that may be needed to see further reductions in clinical errors. System-related errors were a significant contributor to error with electronic prescribing, but did not out-weigh the number of errors prevented. System-related errors need to be considered in the further refinement of system design and in the training and implementation of these systems in Australian hospitals.

## Education and training

### *Educational strategy based on knowledge translation and consultative education.*

The SCRIPT study<sup>96</sup> examined the effectiveness of an educational intervention to improve prescription practice in the intensive care unit (ICU) setting. The study was conducted in one NSW acute care hospital in 2008/09. The educational strategy was based on the principles of knowledge translation; translating knowledge obtained from research into clinical practice. Consultative education and a systems approach were used to identify barriers occurring in the local practice area and to work with stakeholders to develop and implement solutions. Prior to commencing the



project, a planning phase was implemented which involved two meetings of a senior management advisory committee attended by ICU staff, including medical specialists, senior nurses and the pharmacist. Issues were identified through an analysis of local prescribing practices with medical and nursing staff, including junior staff. Barriers identified included poor communication between medical staff and nursing staff as well as between more senior and more junior doctors, illegible handwriting and inadequate documentation of the reason for giving antibiotics or the targets for certain infusion medicines (e.g. mean arterial pressure for vasoactive medicines). A standardised data collection form based on the NIMC audit form was developed which highlighted the local issues identified.

Baseline prescribing performance was audited for ten weeks before an educational intervention was performed by an ICU specialist and a pharmacist. Education was conducted with all medical and nursing staff in the unit. An intensive eight week phase was performed initially, followed by an ongoing maintenance period (including 'one minute reminders'). Education was provided during bedside teaching of small groups and in more formal forums such as handovers and unit meetings. Educational messages were designed to be simple and time efficient. An audio-visual presentation of 5-10 minutes duration was used to highlight examples of prescribing errors and to discuss local prescribing issues and recommended solutions. The SCRIPT acronym was used to highlight important educational messages and was prominently displayed in various areas in the ICU:

- **S:** Senior doctor cross-check
- **C:** Check allergies
- **R:** wRite indications for antibiotics
- **I:** (Initial Date) of charting medicine in parenthesis
- **P:** PRINT and sign your name
- **T:** Appropriate Targets for infusions.

Following the intensive educational intervention, post-education was audited for another ten weeks. Parameters for which there was a significant improvement post-intervention included:

- decreased number of orders where any component of the prescription was illegible or ambiguous from 39.4% (359/912) pre-intervention to 13.4% (154/1151) post-intervention ( $p < 0.001$ );
- decreased orders with prescriber name absent or illegible from 38.3% (349/912) pre-intervention to 27.0% (311/1151) post-intervention ( $p < 0.001$ )
- decreased antibiotic prescriptions with no indication documented from 64.8% (79/122) pre-intervention to 32.5% (50/154) post-intervention ( $p < 0.001$ )
- decreased infusion orders without a legible prescriber name or signature from 56.9% (78/137) pre-intervention to 14.6% (23/158) post-intervention ( $p < 0.001$ ).

There was no significant difference between the periods for charts with ADR or 'no known medicine allergy' documentation, pages without 100% correct patient identification, infusion prescriptions not legible or infusion goals or targets not written. No serious adverse events resulting from a medication error occurred during the pre-or post-intervention period.

### Academic detailing

A study undertaken in 2004/05 at a teaching hospital in SA specialising in the care of older people examined the use of academic detailing to facilitate the implementation of a clinical decision support system (CDSS).<sup>97</sup> The intervention targeted the prescribing of renally-cleared medicines (medicines predominantly removed from the body via the kidneys) that had a narrow therapeutic index (including enoxaparin, gentamicin, vancomycin, allopurinol, ACE inhibitors, digoxin, metformin and lithium). These medicines have potential for overdosing in older patients if there is inadequate dose adjustment to compensate for declining renal (kidney) function with age. The CDSS system (called GFR+) was introduced independently of computerised provider order entry. The CDSS system was linked to the hospital database and designed to calculate and automatically update estimates of renal function for individual patients (based on laboratory testing results) and calculate an appropriate dose of the renally-cleared medicines (based on 'specific hospital-approved dosing models'). The system would also highlight episodes of acute renal failure in which these medicines should be withheld. Academic detailing was used to introduce and train prescribers in the use of the system. This included a 15 minute one-to-one training session by a trained operator with the prescribing physician. This training was conducted within two weeks of any new prescribers commencing work at the hospital. The training included instruction on how to navigate the CDSS and training about the clinical issues surrounding the dosing of the target medicines. Baseline data was collected for a six month period in the absence of the CDSS. The system was put online and the academic detailing intervention implemented, with a further five months of post-intervention data collected.

Enoxaparin dosing conformity (appropriate dosing according to renal function estimates) improved from 68% of patients (n=44) pre-intervention to 86% (n=58) post-intervention (p=0.03). Gentamicin dosing conformity also improved from 63% (n=73) pre-intervention to 87% (n=38) post-intervention (p=0.01). There was an increase in the dosing conformity with vancomycin from 47% (n=34) pre-intervention to 77% (n=17) post-intervention but this did not reach statistical significance (p=0.07). In the pre-intervention period acute renal failure occurred in 41 patients with 38% of renally-cleared medicines (n=65 medicines) appropriately withheld during these episodes. In the post-intervention period, 32 patients experienced acute renal failure with 62% of renally-cleared medicines (n=52 medicines) appropriately withheld (p=0.01 compared to pre-intervention).

### Systems providing pharmacy services

Pharmacists participate in a number of medicine processes including medicines review, medication reconciliation, ordering, dispensing, monitoring and education. Many pharmacist services are provided as part of collaboration with other healthcare professionals. Interventions were included in this section if the pharmacist was the main provider of the intervention and led the intervention strategy.

### Pharmacy services to improve medication reconciliation and information transfer between different healthcare settings

The previous review of medication safety in Australian acute care<sup>4</sup> included controlled studies undertaken in Australia to assess the impact of discharge medication management services

implemented by pharmacists or by pharmacists and nurses. These services were shown to improve patient outcomes and reduce undesirable medication events. A small, uncontrolled, pre- and post-intervention study examining the effectiveness of a clinical pharmacist in an emergency department on prescribing errors also showed significant outcomes.

A number of the pharmacist service studies, published since 2008, concerned improving transfer of information about a person's medicines as they moved between different health care settings; between the community and acute care setting, as well as between different units within the acute care setting. These studies add considerably to the body of evidence in Australia for pharmacy services and are described below. Components of these services included the provision of medication reconciliation, pharmacist charting or prescribing of medicines, chart review and enhancing communication between healthcare providers in different settings.

### *Emergency department (community to acute care)*

A pre- and post- intervention study (Level III-3), undertaken in 2007 in an acute care hospital, examined a clinical pharmacy service in an emergency department setting.<sup>15</sup> The study aimed to determine the frequency and clinical significance of medication errors occurring when i) a pharmacist obtains a medication history from a patient in the emergency department after the medicines have been charted by a doctor, and ii) when the pharmacist took the medication history and charted the medicines prior to the doctor's approval. Patients aged 60 years or older at high risk of medication misadventure were included. The study compared a usual care period (six weeks) followed by pharmacist intervention arm (five weeks). For patients recruited in the usual care period, the pharmacist interviewed the patient about their medicines after they had been seen by the hospital doctor who prescribed their medicines. A medication history was compiled based on the patient interview, and contact was made with the patient's main community pharmacy and, if necessary, their GP. The medication history was compared with the medicines prescribed by the doctor and any 'unintentional discrepancies' were documented in the patient case notes and communicated to the patient's medical team. For patients recruited in the intervention period, the pharmacist interviewed patients as soon as possible after their admission to the ED, prior to seeing a hospital doctor. The medication history was obtained as for the usual care period, and then the pre-admission medicines were documented on the patient's hospital medication chart. The hospital doctor then reviewed the chart on seeing the patient and signed off on continuing medicine orders or indicated if changes were required or if a medicine was to be ceased. In both arms, the clinical significance of discrepancies was assessed by an expert multidisciplinary panel.

The numbers per patient of unintentional discrepancies on the medication chart, doses missed due to discrepancies and incorrect doses given due to discrepancies were significantly lower in the intervention period compared to the usual care period ( $p < 0.05$  compared to usual care) (Table 1). Of the 111 'unintentional discrepancies' between the history obtained by the pharmacist and the medication chart in the usual care arm, 6% were deemed by an expert panel to have a very significant impact on patient health outcomes, and 52% were deemed to have a significant impact. The majority (57%) were omission errors, 16% incorrect dose errors, 12% incorrect time errors and 11% incorrect frequency errors. Only one discrepancy occurred in the intervention arm, resulting in the omission of a cardiovascular medicine.

Another pharmacist-led intervention in the emergency department (ED) undertaken in 2006 encouraged ambulance paramedics to bring a patient's own medicines to the ED.<sup>16</sup> During the pre-intervention (usual care) period, medical staff in ED wrote up medication charts according to usual procedures. An ED pharmacist conducted a multifaceted intervention program including information sessions for paramedic team managers and dissemination of promotional materials to encourage ambulance paramedics to bring the patient's own medicines to ED so that the medicines would be available at the time of prescribing on the inpatient chart. In both pre- and post- intervention periods the ED pharmacist compiled a medication history from the patient or carer and community health practitioners to detect any potential prescribing errors, then discussed these with the medical team in the admitting unit. The percentage of regular medicines (those used prior to admission) prescribed incorrectly on inpatient medication charts reduced significantly from 18.9% in the usual care period (151 of 800 regular medicines) to 8.8% in the post-intervention period (73 of 834 regular medicines,  $p < 0.001$  compared to usual care). This was accompanied by an increased proportion of patients for whom the paramedics brought some or all of their regular medicines (67.0% pre-intervention to 87% post-intervention).

#### *Elective surgery (community to acute care)*

A randomised controlled trial undertaken in 2008/09 in an acute care hospital examined a clinical pharmacy service in the perioperative setting.<sup>98</sup> The aim of the study was to examine the effect of pharmacist involvement in medication history taking and supplementary prescribing on the rate of medication errors post-operatively. This study was undertaken to overcome problems with the usual care system which meant that the patient's regular medicines were not prescribed on the medication chart before admission, with most medicines being charted post-operatively when limited information was available. Elective surgery patients taking at least one regular medicine and with a post-operative stay of at least one night in hospital were included in the study. In this three-arm study, participants were randomised to receive either usual care ( $n=118$ ), a pharmacist interview and medication history on admission ( $n=119$ ) or the full intervention ( $n=120$ ) which involved the pharmacist interviewing the patient, taking a medication history and prescribing the patient's regular medicines on the medication chart on the day of surgery. Pharmacist prescribing was guided by standard protocols or discussion with the patient's medical team. New medicines were prescribed by the medical officer for all three groups.

The primary outcome measure was the number of inappropriate missed doses of medicine during the inpatient stay. Secondary outcome measures included the number of medicines charted with the incorrect dose or frequency; number of missed doses of significant medicines post-operatively (including beta blockers, HMG-CoA reductase inhibitors, anti-platelet and anticoagulant medicines). When compared to the usual care group, it was found that there was a significant reduction in the number of inappropriately omitted medicines during the hospital stay. In the usual care group, the marginal mean omitted medicines per patient was 3.21 [CI 2.89-3.52], in the medication history group 3.30 [2.98-3.63] and in the pharmacist interview and prescribing group 1.07 [0.9-1.25]. The difference between the full intervention and usual care group was significant ( $p=0.002$ ), but not between the usual care and history only group. This suggested the full intervention, not just medication history taking, was required to ensure that medicines were prescribed appropriately post-operatively. Secondary outcome measures are reported in Table 1

Evidence for the role of a clinical pharmacist in a surgery pre-admission clinic is also provided by the study of Dooley et al. undertaken in 2007.<sup>99</sup> This study compared the accuracy and completeness of a medication history obtained by a clinical pharmacist with that completed by the patient on a pre-admission questionnaire (which had been the previously used strategy in the hospital to obtain a medication history prior to elective surgery admission). Patients included were attending a pre-admission clinic with planned admission to elective surgery short-stay centre or hospital wards post-surgery over a three-week period. Patients and/or their community healthcare provider completed a medication history questionnaire and returned it by post prior to admission. A clinical pharmacist interviewed patients in the clinic consulting room and obtained a comprehensive medicine list documented on a reconciliation form. Information was obtained by the pharmacist from the patient and from community healthcare providers where necessary. The medication history obtained by each method was compared. There was an average of 3.9 medicine discrepancies per patient completed questionnaire. The majority were medicines omitted in error (317 instances, 36% of total medicines recorded by the pharmacist), incorrect doses (24 instances), omitted doses (110 instances), incorrect dosing frequency (24 instances) and dosing frequency omitted (63 instances). Adverse drug reaction history was incomplete or incorrect for 19 patients (13%). This was not a controlled trial and there was no independent assessment of the pharmacist-obtained history. However, it does suggest that a clinical pharmacist in a pre-admission surgery clinic can improve the documentation of medication history.

#### *Hospital inpatient setting within 24 hours of hospital admission (community to acute care)*

The Med eSupport study<sup>14</sup> was a multicentre randomised controlled trial (Level II) undertaken to examine whether a pharmacy-led intervention to improve medication reconciliation on hospital admission would improve the identification and resolution of discrepancies in medication histories. Patients aged 50 years or older at high risk of medication misadventure were included. Within 24 hours of hospital admission, a six-month dispensing history and other relevant information was obtained from the patient's community pharmacist through fax or a secure electronic communication pathway. The patient's GP was also contacted to obtain a medication history. The hospital pharmacist interviewed the patient and reviewed the patient's own medicines where available. The pharmacist compiled medicines lists and documented any discrepancies between the reconciled medicines list and the initial inpatient medication chart. These included omissions, wrong medicines and dosing errors. Suggested solutions to resolve the discrepancies were also documented. The control group (n=284) received usual care with the medication information filed; no discussion with the patient's hospital doctor was undertaken. For the intervention group (n=203) the hospital study pharmacist discussed the discrepancies with the patient's doctor, and any unresolved discrepancies were followed up with medical staff during the inpatient stay. At baseline the number of discrepancies was not significantly different between the groups. The proportion of patients with at least one discrepancy resolved within 48 hour of admission was significantly greater for the intervention group (78.1%) compared to usual care (36.5%,  $p<0.0001$ ). The proportion of patients with at least one discrepancy not resolved during the entire hospital stay was higher in the usual care group (83.2%) compared to the intervention (27.7%,  $p<0.0001$ ). The number of discrepancies per patient not resolved for the usual care was a median of 1 (range 0-12), while for the intervention group it was a median of 0 (range 0-4) ( $p<0.0001$ ). There was a weak but statistically significant positive correlation between the number of unresolved discrepancies and

length of hospital stay (Spearman Rho = 0.1,  $p < 0.01$ ,  $n = 487$ ). There was no independent panel assessment reported for the unresolved discrepancies, therefore the clinical significance of these is unclear.

Another study<sup>22</sup> conducted in four public or private acute care hospitals in Australia (three sites) and New Zealand (one site) provides some additional evidence for the role of clinical pharmacists in improving medication documentation in this setting. While the primary aim of the study was quantification of prescribing error, the medication charts reviewed by a pharmacist were also compared with those with no pharmacist review. In the audit of a total of 715 patients' medication charts within 24 hours of patient admission, those that had been reviewed by a pharmacist (229 patients' charts) were significantly less likely to have inadequate documentation of allergy (13.5% with pharmacist review, versus 29.4% without pharmacist review,  $p < 0.001$ ). Data for individual hospitals was not reported and therefore Australia-only data cannot be presented.

#### *Oncology/haematology unit transferring to critical care (within hospital transfer)*

A pre- and post-intervention study (Level III-3) conducted in 2007/08<sup>100</sup> in a teaching hospital evaluated the effectiveness of a pharmaceutical handover initiated by a pharmacist when patients were transferred from an oncology/haematology unit of the hospital to a critical care unit. This pharmacist handover was developed to address an information gap when patients were transferred to critical care which resulted in prescription errors and delays in administration for mouth-care products, chemotherapy medicines, granulocyte colony-stimulating factors and antimicrobial medicines. The study examined the impact of the handover on the number of interventions relating to the specific medicines (including errors and omissions in prescribing or administration) and the number of specific medicines administered at the correct time. In the pre-implementation period (ten months) patients received usual care, in the post-implementation period (eight months), a pharmacist provided a verbal and written handover at the time the patient was transferred detailing information related to the patient's specific medicines including dosage, frequency and indication. The written component was filed in the medical records.

There was a reduction in the number of errors or omissions for specific medicines (mean per patient transfer):

- 3.97 during the usual care period and 0.45 during the intervention period ( $p < 0.0001$ ).

There was a reduction in delayed medicine administration:

- percentage of doses of specific medicines not administered on time (>6 hours after time due) was 34% ( $n = 28$ ) in the usual care period and 4% ( $n = 2$ ) in the intervention ( $p < 0.0001$ )
- and >12 hours after time due was 9% ( $n = 7$ ) in the usual care period and 0% ( $n = 0$ ) in the intervention period ( $p < 0.0001$ ).

#### *Home-based post-discharge service (hospital to community)*

A non-randomised controlled trial (Level III-2) undertaken in 2008/09<sup>101</sup> examined the provision of a post-discharge warfarin management service for adult patients discharged from hospital newly initiated on warfarin or on continuing warfarin therapy. The study included patients discharged from eight hospitals to their home in metropolitan, rural and remote regions of Australia. Patients in the usual care arm ( $n = 139$ ) were managed according to the standard warfarin management service

provided by the patient's community healthcare provider without any formal post-discharge outreach program. For patients in the intervention arm (n=129), a summary of the patient's inpatient warfarin therapy was provided to the community healthcare providers. Patients received two or three home-visits from a Home Medicines Review (HMR) accredited pharmacist within eight to ten days of hospital discharge. The intervention included point-of-care INR monitoring, warfarin education and an HMR performed in collaboration with the patient's GP and community pharmacist.

The primary outcome measure was major and minor haemorrhagic events within 90 days of discharge. A significantly higher percentage of patients in the usual care group (14.7%) experienced a haemorrhagic event compared to the intervention group (5.3%) ( $p=0.03$ ). Most were minor haemorrhagic events. Secondary outcomes are summarised in Table 1. The intervention was associated with significantly lower rates of haemorrhagic and thrombotic adverse events. Hospital admissions and mortality were not significantly different between the groups.

A randomised controlled trial (Level II) examining the effectiveness of a pharmacy liaison service<sup>102</sup> to improve continuity of care across the acute care to community interface included medication knowledge as an outcome measure (as well as adherence). This study involved patients discharged from two hospitals in Melbourne to independent living, who were aged 55 or above and at risk of medication misadventure or requiring assistance in the use or monitoring of medicines. Patients randomised to the control group received usual care including counselling upon discharge, provision of compliance aids and communication with community healthcare practitioners where necessary. Patients in the intervention group received usual care plus a home visit from a community liaison pharmacist within five days of discharge. During the home visit the liaison pharmacist assessed the patient's medication management and understanding of their medicines, assessed use of administration devices and provided education and information where appropriate. The pharmacist also examined supplies and storage of medicines, identified medication problems or potential problems and, if possible, resolved these or highlighted them for primary care provider intervention. A report was sent to the patient's primary healthcare providers and contact made with other healthcare providers by phone if a problem required more urgent attention. Outcome measures were assessed for both groups by telephone interview eight to twelve weeks post-discharge which included a standard questionnaire to assess and score the patient's medication understanding. This assessment was not blinded. There were 356 patients randomised (152 intervention, 164 usual care), intervention group patients were on average slightly older ( $74.4 \pm 10.6$  years) compared to usual care patients ( $69.3 \pm 12.1$ ), and a greater proportion were female (53% for intervention, 42.1% for usual care) and had language difficulties (5.9% intervention, 0% usual care) ( $p$  values not reported). Follow-up data were available for 127 patients in the intervention group and 132 in the control group. There was no statistically significant difference in the number of medicines taken at follow-up by the two groups. The intervention had no beneficial effects on the proportion of patients with good medication knowledge at follow-up, with a greater proportion of control patients assessed as having good knowledge of some aspects of their medicines (Table 1). The study did not examine other patient safety outcomes or medication error.

### *Hospital pharmacist prepared interim medication administration chart (hospital to residential care)*

As a part of the MedGap study<sup>103</sup> a pre- and post-intervention study (Level III-3) was undertaken in 2009 to examine the impact of an interim residential care medication administration chart (IRCMAC) prepared by a trained hospital pharmacist on medication errors and use of locum medical services post-discharge from hospital to residential care. The IRCMAC was developed in consultation with various stakeholders including hospital and residential care staff, professional bodies and GPs. In the pre-intervention (control) period (n=202) standard hospital discharge medication policies were followed with seven days supply of discharge medicine for patients discharged to a new residential care facility (RCF) or on new medicines and a copy of the discharge prescription provided in the bag with medicine supply. In the intervention period (n=226), a trained hospital pharmacist prepared an IRCMAC which was included with the discharge prescription in a red plastic sleeve with instructions for use and the RCF was notified. The IRCMAC was generated from the hospital pharmacy dispensing software at the time of dispensing discharge medicines with automatic entry of patient and medicines data. Prior to generating the IRCMAC, a pharmacist checked the discharge prescription, reconciled it with pre-admission and inpatient medicines and corrected any errors. For each medicine the change status (including 'unchanged', 'new' or 'dose changed') was included, as well as a list of ceased medicines. Where possible, the reason for changing or ceasing medicines and date was also provided. For all continuing medicines, the time of the last dose given in hospital was also documented by the pharmacist.

Outcomes were assessed by structured telephone interview with RCF staff 24 to 72 hours after discharge and on day eight post-discharge. One primary outcome measure was the proportion of patients who experienced one or more missed or significantly delayed medicine doses. 'Significantly delayed' was defined as delayed by more than 50% of the prescribed dose interval or for 'when required medicines' delayed by 'any length of time if it was required by the patient'. The proportion of patients with omitted or delayed medicine doses decreased from 18.3% (37 patients) in the pre-intervention usual care period to 2.75% (six patients) in the intervention period ( $p < 0.001$  compared to usual care). Significant reductions were also found for the proportion of patients for whom a locum doctor was required to write the RCF medication chart and the proportion of patients for whom RCF staff used a 'workaround' to avoid a missed or delayed medicine dose when an updated chart was not available (Table 1).



**Table 1: Pre- and post-intervention and controlled trials of pharmacist interventions to improve medication information transfer between different health care settings in Australia**

Ref.	Trial design Evidence level*	Setting Year(s)	Patients/ Intervention studied	No. of patients randomised (completed)	Outcomes
<b>Community to acute care</b>					
<sup>15</sup>	Pre-post study with usual care period (6 weeks) followed by pharmacist intervention arm (5 weeks) Level III-3	One acute care hospital, South Australia, Emergency department setting 2007	Patients aged $\geq 60$ years at high risk of medication misadventure.  Usual care period: patients were prescribed medicines by hospital doctor. Research pharmacist obtained a comprehensive medication history and documented any 'unintentional discrepancies' in the case notes.  Intervention period: patients were seen by the pharmacist in ED prior to seeing a hospital doctor. The medication history was obtained as for the usual care period, and then the pre-admission medicines were documented on the medication chart. The hospital doctor then reviewed the chart after seeing the patient and signed off on continuing medicine orders or indicated any changes/cessation required.  Clinical significance of discrepancies was assessed by an expert panel.	Usual care <b>45</b> Pharmacist intervention <b>29</b> (18 admitted to hospital and included in missed /incorrect dose analysis)	<i>No. unintentional discrepancies on medication chart</i> (mean per patient $\pm$ SD) Usual care: $2.51 \pm 2.37$ Intervention: $0.034 \pm 0.19$ ( $p < 0.05$ compared to usual care)  <i>No. doses missed due to discrepancies</i> (mean per patient $\pm$ SD) Usual care: $2.35 \pm 3.82$ Intervention: $0.24 \pm 0.97$ ( $p < 0.05$ compared to usual care)  <i>Incorrect doses given due to discrepancies</i> (mean per patient $\pm$ SD) Usual care: $1.04 \pm 2.50$ Intervention: $0.00 \pm 0.00$ ( $p < 0.05$ compared to usual care)  Of the 111 'unintentional discrepancies' between the history obtained by the pharmacist and the medication chart in the usual care arm, 6% were deemed to have a very significant impact on patient health outcomes, and 52% were deemed to have a significant impact.

Ref.	Trial design Evidence level*	Setting Year(s)	Patients/ Intervention studied	No. of patients randomised (completed)	Outcomes
<b>Community to acute care (cont.)</b>					
<sup>16</sup>	Pre–post study with usual care period (1 month) followed by pharmacist intervention then post-intervention period (1 month) Level III-3	One acute care hospital, Victoria Emergency department setting 2006	Adult patients brought to ED by ambulance taking four or more regular medicines who were admitted to hospital. Patients from an aged care home were not included.  Pre-intervention: Usual care – medical staff in ED wrote up medication chart according to usual procedures. Intervention ED pharmacist conducted a multifaceted intervention including information sessions and dissemination of promotional materials to encourage ambulance paramedics to bring a patient's own medicines to ED so they would be available at the time of prescribing on the inpatient chart.  In both periods the ED pharmacist compiled a medication history from patient/carer, community health practitioners to detect any potential prescribing errors then discussed these with medical team in the admitting unit.	Usual care <b>100</b> Post-intervention <b>100</b>	<i>Percentage of regular medicines prescribed incorrectly on inpatient medication charts</i> Usual care: 151/800 (18.9%) Post-intervention: 73/834 (8.8%) (p<0.001 compared to usual care)

Ref.	Trial design Evidence level*	Setting Year(s)	Patients/ Intervention studied	No. of patients randomised (completed)	Outcomes
<b>Community to acute care (cont.)</b>					
<sup>98</sup>	RCT Level II	One acute care hospital, NSW Perioperative setting, elective surgery 2008/09	Elective surgery patients taking at least one regular medicine and with a post-operative stay of at least one night in hospital were included in the study  Intervention: pharmacist interviewed the patient, taking a medication history and prescribing the patient's regular medicines on the medication chart on the day of surgery. Pharmacist prescribing was guided by standard protocols or discussion with the patient's medical team. Compared to 1) usual care 2) pharmacist interview and medication history on admission	Usual care 118 (109)  Pharmacist medication history 119 (109)  Pharmacist medication history and prescribing 120 (112)	<p><i>No. of inappropriate missed doses</i> Usual care: marginal mean per patient 3.21 [CI 2.89-3.52]; Medication history: 3.30 [2.98-3.63]; Pharmacist interview &amp; prescribing: 1.07 [0.9-1.25]. The difference between the full intervention and usual care group was significant (p=0.002), but not between the usual care and history only group.</p> <p><i>No. medicines charted at incorrect dose</i> Usual care: marginal mean per patient 0.48 [CI 0.36-0.61]; Medication history: 0.12 [0.05-0.18]; Pharmacist interview &amp; prescribing: 0.02 [0.00-0.04]. The difference between usual care and the history and history plus prescribing group was significant (p&lt;0.001). The number of incorrectly charted doses in the prescribing group was also significantly less than the history only group (p=0.004)</p> <p><i>No. medicines charted at incorrect frequency</i> Usual care: marginal mean per patient 0.29 [CI 0.19-0.39]; Medication history: 0.07 [0.02-0.12]; Pharmacist interview &amp; prescribing: 0.015 [0.00-0.06]. The difference between usual care and the history and history plus prescribing group was significant (p&lt;0.001).</p>

Ref	Trial design Evidence level*	Setting Year(s)	Patients/ Intervention studied	No. of patients randomised (completed)	Outcomes
<b>Community to acute care (cont)</b>					
<sup>14</sup>	RCT Level II	Five hospitals Tasmania (2) Western Australia (2) Victoria (1)	<p>Patients aged 50 years or older at high risk of medication misadventure, not living in an aged care facility.</p> <p>Within 24 hours of admission hospital pharmacist compiled medicines lists and documented any discrepancies (e.g. omissions, wrong medicines and dosing errors) between the reconciled medicines list and the initial inpatient medication chart as well as suggested solutions.</p> <p>Control group: received usual care - medication information filed but no discussion with the patient's hospital doctor.</p> <p>Intervention group: hospital pharmacist discussed the discrepancies with the patient's doctor, and any unresolved discrepancies were actively followed up with medical staff during the inpatient stay</p>	Usual care 307 <b>(284)</b> Intervention 232 <b>(203)</b>	<p><i>Unresolved discrepancies:</i></p> <p><i>Proportion of patients with at least one discrepancy resolved within 48 hour of admission</i></p> <p>Usual care: 36.5%</p> <p>Intervention: 78.1% (p&lt;0.0001 compared to usual care)</p> <p><i>Proportion of patients with at least one discrepancy not resolved during hospital stay</i></p> <p>Usual care: 83.2%</p> <p>Intervention: 27.7% (p&lt;0.0001 compared to usual care)</p> <p><i>No of discrepancies per patient not resolved median (range)</i></p> <p>Usual care: 1 (0-12)</p> <p>Intervention: 0 (0-4) (p&lt;0.0001 compared to usual care)</p> <p><i>Correlation with length of hospital stay</i></p> <p>There was a weak but statistically significant correlation between the number of unresolved discrepancies and length of hospital stay (Spearman Rho = 0.1, p&lt;0.01).</p>

Ref	Trial design Evidence level*	Setting Year(s)	Patients/ Intervention studied	No. of patients randomised (completed)	Outcomes
<b>Acute care within hospital transfer</b>					
<sup>100</sup>	Pre-post study Level III-3 Usual care period of 10 months. Post- intervention period of 8 months	One teaching hospital, Victoria  Transfer from oncology and haematology unit (OHU) to a critical care unit 2007/08	Patients admitted under OHU and transferred to a critical care unit were included. The intervention involved a pharmacist providing a verbal and written handover at the time the patient was transferred from an oncology/haematology unit to a critical care unit. Handover of information related to the patient's specific medicines including dosage, frequency and indication. The written component was filed in the medical records. The impact on prescription errors and delays in administration for mouth care products, chemotherapy medicines, granulocyte colony-stimulating factors and antimicrobial medicines were assessed.	Usual care <b>30</b>  Intervention <b>22</b>	<i>No. of errors or omissions for specific medicines (mean per patient transfer)</i> Usual care period 3.97 Intervention period 0.45 (p<0.0001 compared to usual care)  <i>No. (percentage) of doses of specific medicines not administered on time</i>  <i>&gt;6 hours after time due</i> Usual care: 28 (34%) Intervention: 2 (4%) (p<0.0001 compared to usual care)  <i>&gt;12 hours after time due</i> Usual care: 7 (9%) Intervention: 0 (0%) (p<0.0001 compared to usual care)

Ref	Trial design Evidence level*	Setting Year(s)	Patients/ Intervention studied	No. of patients randomised (completed)	Outcomes
<b>Acute care to community</b>					
<sup>101</sup>	NRCT Level III-2	Home setting: patients discharged from 8 hospitals in metro, rural and remote regions 2008/09	Adult patients discharged from hospital on warfarin therapy.  Usual care: management according to the standard warfarin management service provided by the patient's community healthcare provider.  Intervention arm: patients received 2 or 3 home-visits from a Home Medicines Review (HMR) accredited pharmacist within 8-10 days of hospital discharge and the pharmacist collaborated with the patient's GP and community pharmacist.	Usual care 139 (data available for <b>128</b> )  Intervention: 129 (data available for <b>108</b> )	<i>Primary outcome measure: Major and minor haemorrhagic events to day 90 post-discharge</i> (n (%) of patients) Usual care: 17 (14.7%); Intervention: 5 (5.3%) (p=0.03)  <i>Secondary outcome measures</i>  <i>Combined haemorrhagic and thrombotic events to day 8 post-discharge</i> Usual care: 10 (7.2%); Intervention: 1 (0.9%) (p=0.01)  <i>Major haemorrhagic events to day 90 post-discharge:</i> Usual care: 5 (4.3%); Intervention: 2 (2.2%) (ns, p=0.39)  <i>Minor haemorrhagic events to day 90 post-discharge:</i> Usual care: 14 (11.3%); Intervention: 3 (2.8%) (p=0.01)  <i>Combined haemorrhagic and thrombotic events to day 90 post-discharge:</i> Usual care: 22 (19.0%); Intervention: 6 (6.4%) (p=0.008)  <i>Unplanned hospital readmissions to day 90 post-discharge:</i> Usual care: 33 (27.5%); Intervention: 29 (27.1%) (ns, p=0.95)  <i>Warfarin-related hospital readmissions to day 90 post-discharge:</i> Usual care: 7 (5.6%) Intervention: 3 (2.9%) (ns, p=0.30)  <i>Death to day 90 post-discharge</i> Usual care: 2 (1.6%); Intervention: 3 (2.8%) (ns, p=0.54)

Ref	Trial design Evidence level*	Setting Year(s)	Patients/ Intervention studied	No. of patients randomised (completed)	Outcomes
<b>Acute care to community (cont.)</b>					
<sup>102</sup>	RCT Level II	Home setting: patients discharged from two acute care hospitals, Victoria	<p>Patients 55 years or older at risk of medication misadventure or requiring assistance in the use or monitoring of medicines.</p> <p>Usual care: medication counselling upon discharge, provision of compliance aids and communication with community healthcare practitioners where necessary.</p> <p>Intervention group: usual care plus a home visit from a community liaison pharmacist within 5 days of discharge- including assessment of medication management and medication understanding, use of administration devices and education and information provision where appropriate.</p> <p>Medication problems or potential problems identified and if possible resolved. Report sent to primary healthcare providers and contact made with other healthcare providers if a problem required more urgent attention.</p>	<p>Usual care 164 (data for <b>132</b>)</p> <p>Intervention 152 (data for <b>127</b>)</p>	<p><i>Proportion of patients with good medication knowledge 8-12 weeks post-discharge in the following areas:</i></p> <p><i>Medicine name</i> Usual care 92.3% Intervention 83.3% (p=0.028)</p> <p><i>Medicine strength</i> Usual care 71.5% Intervention 68.3% (ns, p=0.567)</p> <p><i>Dosage</i> Usual care 96.9% Intervention 88.1% (p=0.007)</p> <p><i>Frequency of administration</i> Usual care 96.9% Intervention 87.3% (p=0.004)</p> <p><i>Indication</i> Usual care 83.1% Intervention 69.8% (p=0.012)</p> <p><i>Side effects</i> Usual care 7.7% Intervention 4.8% (ns, p=0.333)</p>

Ref	Trial design Evidence level*	Setting Year(s)	Patients/ Intervention studied	No. of patients randomised (completed)	Outcomes
<b>Acute care to residential care</b>					
<sup>103</sup>	Pre–post- study Level III-3 Control period (12 weeks) followed by pharmacist intervention period (12 weeks)	One acute care hospital and one subacute aged care hospital, 128 residential care facilities (RCFs), Victoria 2009	<p>Patients discharged after inpatient stay to residential care facility</p> <p>Control period: Standard hospital discharge policy - 7 days' supply of discharge medicine for patients discharged to new RCF or on new medicines, copy of discharge prescription provided in bag with medicine supply</p> <p>Intervention period: Trained hospital pharmacist prepared an interim residential care medication administration chart (IRCMAC), included with discharge prescription in red plastic sleeve with instructions for use. RCF notified. Other discharge procedures unchanged.</p>	Usual care <b>202</b> Pharmacist intervention <b>226</b>	<p><i>Primary outcome measure / proportion of patients who experienced one or more missed or significantly delayed medicine doses</i> Usual care: 37 (18.3%) Intervention: 6 (2.75%) (p&lt;0.001 compared to usual care)</p> <p><i>Primary outcome measure / proportion of patients whose RCF medication chart was written/updated by a locum doctor within 24h of discharge</i> Usual care: 66 (32.7%) Intervention: 25 (11.1%) (p&lt;0.001 compared to usual care)</p> <p><i>Secondary outcome measure / proportion of patients for whom a 'workaround' was used by RCF staff to avoid a missed or delayed medicine dose when an updated chart was not available</i> Usual care: 90 (44.6%) Intervention: 22 (9.7%) (p&lt;0.001 compared to usual care)</p>

\*NHMRC Levels of evidence for intervention studies<sup>86</sup>; RCT = randomised controlled trial; NRCT= non-randomised controlled trial; CI = confidence interval; SD = standard deviation; ED = emergency department; ns= not significant



## Pharmacist prescribing and dosing services

### *Pharmacist prescribing in the perioperative acute care setting*

A randomised controlled trial (Level II) describing a new clinical pharmacy service in the perioperative setting in an acute care hospital in Queensland was published by Hale et al.<sup>104</sup> Conducted in 2009, the study evaluated a model of pharmacist service involving inpatient medicine prescribing by the pharmacist. The study pharmacist, with three years of experience in hospital pharmacy and a postgraduate diploma in clinical pharmacy, was trained to be a prescriber in a course accredited in the United Kingdom. The course involved working under the supervision of a 'designated medical practitioner' in the hospital who confirmed the pharmacist's competency to prescribe before the study commenced. An amendment to the *Queensland Health (Drugs and Poisons) Regulation 1996* was facilitated to allow the study to occur.

In the intervention arm of the study, the study pharmacist generated the inpatient medication chart based on an assessment of the patient's regular medicines, made a plan for medication peri-operatively and prescribed venous thromboembolism (VTE) prophylaxis based on guidelines. The pharmacist saw the patient prior to the resident medical officer (RMO). The RMO countersigned the pharmacist prescriptions and undertook their usual duties. In the control (usual care) arm, the medication chart was generated by the RMOs on the unit, and patients received usual care including a pharmacist-generated medication history. Appropriateness of VTE prophylaxis prescribed in both arms was assessed by two assessors. An expert panel (blinded to randomisation) assessed the clinical significance of omissions in a randomly selected sample of patients from both arms of the study. There were 194 patients randomised to the intervention arm and 190 to the control arm. The demographics of the patients randomised into each arm of the trial were similar, except for a higher number of medicines taken by patients in the control arm.

The primary endpoint for the study was the accuracy of medication charts. With respect to this endpoint the following findings were reported:

- total unintentional medicine omissions from medication charts were higher for control patients, 31.5%, (383/1217) compared with intervention patients, 1.2% (11/887)
- after adjustment for the number of medicines per patient, the Odds Ratio for an order in the control group to be omitted, compared with that for the intervention group, was 41.0 [95% CI 20.6 to 81.8;  $p < 0.001$ ].

Omissions from a randomly selected 5% sample of the total study cohort were evaluated for clinical significance by a six member expert panel:

- in the control arm sample, of the 89 regular medicines recorded in the patients' medication histories, 28% (25) were omitted from the medication charts, compared with 2% (1 of 55) in the intervention arm sample
- the average severity ratings across the panel indicated that 52% of omissions in the control arm had 'the potential for patient harm or ward inconvenience' while only one of the six panel members rated the one omission in the intervention arm sample as significant
- in total 53 errors were identified where the medicine strength, dose or frequency prescribed did not match the medication history or perioperative plan; this equated to 6.3% of control orders compared with 0.2% of intervention orders ( $p < 0.001$ )

- communication errors, where prescriptions were rated as 'ambiguous or unclear', were significantly higher in the control arm, 43% of orders (445 communication errors) compared with 23% (208) for the intervention arm ( $p<0.001$ ); prescribing communication errors including ambiguous or unclear medicine name, dose or frequency, administration times incorrect or missing, 'prn' maximum dose missing and slow release dosage form not specified were all significantly higher in the control group compared to the pharmacist prescribing intervention ( $p<0.001$ ).

The secondary endpoint was the appropriateness of prescribing for both chemical and mechanical VTE prophylaxis according to local and national guidelines. Patients in the intervention arm were significantly more likely than controls to have appropriate prophylaxis prescribed on the medication chart in the pre-admission clinic (63.9% control versus 93.8% intervention,  $p<0.001$ ). On admission to the ward there was no significant difference between the two groups, with approximately 90% of both intervention and control patients prescribed appropriate VTE prophylaxis.

As described in the previous section, another randomised controlled trial (Level II) in an acute care perioperative setting<sup>98</sup> involved a pharmacist prescribing the patient's regular medicines on the medication chart on the day of surgery as part of the full intervention. Pharmacist prescribing in that study was guided by standard protocols or discussion with the patient's medical team.

Both the studies of Hale et al.<sup>104</sup> and Marotti et al.<sup>98</sup> (Level II) have shown significant improvements in prescribing in the perioperative setting in Australian hospitals with an intervention involving pharmacist prescribing. These studies have used surrogate endpoints of medicine charting error and communication error. Further studies are needed to examine actual patient outcomes including adverse medication events and application in a larger sample of patients and hospital sites.

### *Dosing service in a hospital in the home program*

A pre- and post-intervention study (Level III-3) conducted in 2009/10 in the hospital in the home (HITH) program of one large Melbourne teaching hospital assessed the effectiveness of a pharmacist anticoagulant medicine dosing service.<sup>105</sup> In the five month pre-intervention phase, patients admitted to the HITH anticoagulation service unit were managed by doctors from the treating unit; doctors prescribed warfarin and reviewed laboratory INR monitoring. In the eight month post-intervention period, patients were enrolled in a pharmacist dosing service. The pharmacists providing the service completed a peer-reviewed training program. Patients were enrolled into the pharmacist service with medical unit consent. The pharmacist managed anticoagulation in accordance with approved hospital anticoagulation guidelines, monitored INR and communicated treatment recommendations to the treating unit. Once two consecutive therapeutic INR values were obtained, patients were eligible to be discharged and managed by their community healthcare practitioner. There were 74 patients included in the pre-intervention phase and 46 in the post-intervention phase, with 53 and 35, respectively, included in the primary outcome analysis. Patient demographics were well matched but significantly more patients in the post-intervention phase were receiving warfarin for the first time ( $p<0.001$ ). The primary outcome measure was the number of days to achieve two consecutive therapeutic INR values. Secondary outcomes included the number of warfarin-related adverse events identified after initiation of warfarin therapy (including thrombo-embolic or bleeding events). With respect to the primary outcome measure, there was a

significant decrease in the number of days taken to achieve two consecutive therapeutic INR values (11.8 days pre-intervention versus 8.8 days post-intervention,  $p=0.002$ ). In the pre-intervention phase, bleeding events were recorded for 16% (12 out of 74 patients) and 14% ( $n=10$ ) were re-hospitalised with 6.8% ( $n=5$ ) of re-hospitalisations a result of warfarin-related adverse events. In the post-intervention period there was one warfarin-related adverse event reported among 46 patients (2%) which was a bleeding event (between group statistical analysis not reported).

This single Level III-3 study demonstrated effective management of warfarin therapy by a pharmacist dosing service. It suggests that there may be potential for pharmacist dosing of anticoagulant therapy and other medicines that require therapeutic monitoring. However, larger controlled studies in more than one centre are required to support these findings.

## Pharmacist services in the community setting

### *Community pharmacist clinical interventions for medicine-related problems*

As part of a community pharmacy study in Australia called the PROMISE study<sup>106</sup> a documentation system was developed for pharmacists to classify and record medication-related problems and record clinical interventions.<sup>107</sup> The DOCUMENT classification system was validated and refined in pilot studies and incorporated into software installed in 185 Australian pharmacies. During a 12 week trial period in the PROMISE III study, the number and nature of medication-related problems detected within Australian community pharmacies was recorded. The clinical significance of the interventions was also assessed by the community pharmacist recording the intervention. A total of 5948 medication-related problems and clinical interventions were documented from 2,013,923 prescriptions dispensed with an intervention frequency 0.3% (three clinical interventions per 1000 prescriptions dispensed). The most common types of interventions were:

- medicine selection-related problems (1829 interventions, 30.7% of interventions) which included incorrect or lack of details about medicine strength ( $n=347$ ), a likely interaction between two medicines ( $n=265$ ), inappropriate use of two medicines from the same class ( $n=232$ ), wrong medicine prescribed or dispensed ( $n=223$ ) and inappropriate dosage form ( $n=211$ )
- educational issues (1412 interventions, 23.7%), most commonly a request from a patient for information about their medicine ( $n=668$ ) or condition ( $n=278$ )
- over- or underdose (1183 interventions, 19.9%) which included prescribed dose too high ( $n=384$ ), incorrect/unclear dose ( $n=392$ ) and dose too low ( $n=316$ )
- patient compliance issues (557 interventions, 9.4%)
- toxicity or ADR (445 interventions, 7.5%), in all cases an ADR likely to be dose-related.

The pharmacists made an average of 1.6 recommendations per intervention, commonly relating to changing therapy (40.1%) and provision of information (34.7%). Almost half of interventions (42.6%) were classified by recording pharmacists as being at a higher level of clinical significance (moderate or high). No independent assessment was made.

While this was not a controlled trial and the clinical significance of the interventions was not independently assessed, it does provide evidence for the role that community pharmacists play in detecting medication-related problems in the Australian community setting.

Another study conducted in the community pharmacy setting in 2004/05 aimed to determine the rate, clinical significance and adverse health consequences avoided by pharmacist interventions for non-prescription medicines (pharmacist-only S3 and pharmacy S2).<sup>5</sup> Non-prescription medicine interventions undertaken by community pharmacy staff were recorded in two studies. The first was a study where all Australian pharmacies with Pharmaceutical Benefits Scheme dispensing were invited to participate, of which 31.6% (1574) pharmacies agreed to participate with 18.8% (934) completing the study. This study was undertaken to determine incidence rates for low-incidence, highly significant interventions. The second study included a sample of pharmacies to collect data on all non-prescription interventions with a total of 101 pharmacies completing this second study. In both studies, pharmacy staff recorded interventions relating to non-prescription medicines on a pre-printed intervention form during a two week allocated study period. Recorded interventions were assessed by a clinical panel for clinical significance, potential adverse health consequence avoided, probability and likely duration of the adverse health consequence.

In this study it was found that:

- the rate of professional intervention for pharmacist-only and pharmacy medicines was 5.66 per 1000 unit sales [95% confidence interval 4.79-6.64]
- there were 310 interventions from the larger study and 189 interventions from the sample study sent to clinical panels for evaluation
- 101 interventions were assessed to have averted emergency medical attention or serious harm or were potentially life-saving (this was calculated as an intervention rate of 1.18 per 1000 units [95% CI 0.96-1.43])
- 50 interventions were assessed to have averted minor symptoms or averted routine medical attention (this was calculated at a rate of 4.48 per 1000 units [95% CI 3.32-5.90]).

The main impact of the interventions was avoidance of urgent GP visits, followed by avoidance of regular GP visits and accident and emergency treatment. The most common adverse health consequences avoided were exacerbations of an existing condition (e.g. hypertension, asthma) and adverse medicine effects.

While this was not a controlled trial, it does provide evidence for the role that community pharmacists play in preventing medication and other harm through intervening at the point of supply.

### *Pharmacists in the general practice setting*

A current study<sup>108</sup> is examining the role of a practice pharmacist located in the general practice setting. This pre-post study is being conducted in two general practice clinics in Melbourne, Victoria. The practice pharmacist intervention will include:

- long patient consultations by the pharmacist for patients at high risk of medication-related problems, including a 30-60 minute consultation with the pharmacist, medication history taking, medication review, medication counselling and education
- short patient consultations (15-30 minutes) for patients with potential medication issues that do not require comprehensive review
- a medicine information and education service for practice clinic staff

- quality assurance activities conducted by the pharmacist such as drug use and evaluation.

Outcomes will include the number, type and severity of medication-related problems identified and resolved by the pharmacist for patients receiving the longer consultations, and effect on patient health and well-being.

### ***Medication management***

A number of studies were located that examined interventions by community pharmacists or pharmacists in the community setting in improving medication management for chronic conditions. While these interventions assessed the impact of the service on patient outcomes such as quality of life, symptom severity and hospitalisations, and surrogate endpoints such as blood pressure and cholesterol levels, they did not specifically use adverse medication events or medication errors as an outcome measure. These papers were considered outside the scope of this review but are listed below.

- Bereznicki et al. 2008<sup>109</sup> “Pharmacist-initiated general practitioner referral of patients with suboptimal asthma management”
- Basheti et al. 2008<sup>110</sup> “Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique”
- Krass et al. 2011<sup>111</sup> “Diabetes Medication Assistance Service Stage 1: impact and sustainability of glycaemic and lipids control in patients with Type 2 diabetes”
- Barker et al. 2012<sup>112</sup> “Pharmacist directed home medication reviews in patients with chronic heart failure: A randomised clinical trial”
- McNamara et al., 2012<sup>113</sup> “A pilot study evaluating multiple risk factor interventions by community pharmacists to prevent cardiovascular disease: the PAART CVD Pilot Project”
- Armour et al., 2013<sup>114</sup> “Feasibility and Effectiveness of an Evidence-Based Asthma Service in Australian Community Pharmacies: A Pragmatic Cluster Randomized Trial”.

## **Systems promoting multidisciplinary care**

### **Medication management review services: the evidence**

#### ***Collaborative Home Medicines Review (HMR) in the community setting***

The Home Medicines Review (HMR) service is an Australian Government-funded initiative conducted by accredited pharmacists in collaboration with a patient’s GP and regular community pharmacy.<sup>2</sup> The accredited pharmacist conducts a comprehensive medication review with the patient in their home, identifies medication-related problems and provides the GP with a report. The GP and patient then agree on a medication management plan.

Two studies published since 2008 have examined how the HMR service has been translated into practice in Australia.<sup>115 116</sup> Both of these studies were retrospective cohort studies (Level III-2). They were conducted using administrative claims data for Australian war veterans and war widows and

which include prescription medicines data, medical and allied health services use (including HMR) and hospitalisations. The studies examined the effectiveness of HMR in groups at high risk of medication-related hospital admissions; those with heart failure and those taking warfarin.

The study examining the effectiveness of HMR in veterans with heart failure<sup>115</sup> examined claims data for veterans and war widows aged 65 years and older receiving a beta-blocker medicine (bisoprolol, carvediol or metoprolol succinate) for heart failure. These medicines were chosen as they were only available under a prior authorisation process where the prescriber had to indicate that the patient had heart failure and it was unlikely they would have been prescribed for another indication. The study was undertaken to cover the period Jan 2004-Jul 2006. The 'exposed' intervention group were veterans who had an HMR, had all health services fully subsidised by the Department of Veterans Affairs (DVA) and had one of the beta-blockers dispensed in the six months prior to the HMR. The 'unexposed' (control) group had had all health services fully subsidised by DVA, had one of the beta-blockers dispensed but had not had an HMR. Eligibility for veterans in the unexposed group was determined at each month through the study period. Eligible veterans were randomly allocated to an index month to match the time of an HMR in the exposed group. The veterans were followed to the time of first hospitalisation for heart failure after the index month (for unexposed group) or after the HMR (for exposed group), or until death or study end. There were 273 individuals in the HMR exposed group and 5444 in the unexposed group. The groups had similar ages and gender ratios but the exposed group had significantly more co-morbidities, more prescriptions, more medicine changes ( $p < 0.0001$ ), and more hospitalisations in the previous year ( $p = 0.03$ ), while the unexposed group had a greater likelihood of high socioeconomic disadvantage scores ( $p = 0.01$ ). For the adjusted results (adjusted for factors including age, comorbidity, socioeconomic index, season, number of prescriptions, number of hospitalisations), in the HMR exposed group there was a 45% reduction in the rate of hospitalisation for heart failure (hazard ratio 0.55 [95%CI 0.30-0.77]). Unadjusted results were also significant with a 37% reduction in the rate of hospitalisation (hazard ratio 0.63 [95% CI 0.44-0.89]).

A second study examining the effectiveness of HMR in veterans taking warfarin<sup>116</sup> used a similar methodology. In this study the exposed (intervention) group were veterans who had an HMR, were aged 65 years or older at the time of the review, were eligible to have all health services fully subsidised by the DVA and had warfarin dispensed at least two times in the six months prior to the HMR. The unexposed (control) group had the same eligibility criteria except they had not received an HMR. The study period was Jan 2004-Jul 2006. Subjects were followed up until the first hospitalisation associated with a bleed, or until study end or death. There were 816 individuals in the exposed group and 16,320 in the unexposed group. The groups had similar ages and gender ratios but the exposed group had significantly more co-morbidities, more prescriptions and prescribers and more prior hospitalisations. Major findings included:

- in the time period two to six months after an HMR, there was a 79% reduction in the likelihood of hospitalisation for bleeding in the exposed group (hazard ratio 0.21 [95% CI 0.05-0.87])
- there was no significant reduction in the rate of hospitalisation in the exposed group in the zero to two month period post-HMR nor in the six to eleven month period
- at greater than 12 months post-HMR the exposed group were found to be at an increased risk of being hospitalised for a bleed hazard ratio 1.61 [95%CI 1.18-2.20]).

The results of the study suggested that, in clinical practice, an HMR service for older people taking warfarin is effective in reducing the likelihood of hospitalisation for bleeding between two to six months after the review. However, the effect does not appear to be sustained, suggesting the HMR may need to be conducted on a six-monthly basis for older patients on warfarin at high risk of bleeding.

Together the two studies using DVA data<sup>115 116</sup> (Level III-2) provide evidence for the effectiveness of collaborative HMR in the practice setting in Australia. The studies suggest that HMR can reduce hospitalisation rates for older people living in the community at high risk of medication-related hospital admissions; those with heart failure taking heart failure medicines and those taking warfarin.

Another study using a pre- and post-intervention design (Level III-3) examined whether HMR services by pharmacists for community-dwelling older people would lead to an improvement in the use of medicines, as measured by a decrease in the Drug Burden Index (DBI) score and the 'potentially inappropriate medicines' (PIMs) score.<sup>65</sup> The DBI is an evidence-based tool that 'measures a person's total exposure to medicines with sedative and anti-cholinergic properties and has been shown to be independently associated with impairment in cognitive and physical function'. This was a retrospective review of HMR cases and reports pertaining to 372 people aged 65 years or older living in the community. These reports were submitted to the Australian Association of Consultant Pharmacy (reports submitted for re-accreditation purposes by 112 accredited pharmacists) and reports from seven individual service providers in NSW. The scores for DBI and PIMs were calculated pre and post-HMR. The PIMs score was calculated using the published Beers criteria.

With respect to the primary outcome measure of total DBI score, there was a statistically significant reduction in the sum total of DBI scores for all patients observed following pharmacist recommendations during the HMR service (206.9 pre-intervention versus 157.3 post-intervention ( $p < 0.001$ ).

- medicines contributing to the DBI (medicines with sedative or anti-cholinergic properties) were identified in 60.5% of patients (225/372) prior to the HMR, and 51.6% (192/372) of the patients following pharmacist recommendations during the HMR service
- PIMs were identified in 39.8% (148/372) of the patients prior to the HRM, and 28.2% (105/372) of the patients following pharmacist recommendations during the HMR service.

This study relied on documentation in the case notes for home medicines reviews. It is not clear to what extent pharmacist recommendations are acted upon, thus the results may reflect recommended practice rather than actual practice. This study suggests pharmacist recommendations during HMR services, if acted upon, may effect changes in the prescribing of sedative and anti-cholinergic medicines, with the potential to reduce the patient's medicine burden. Further studies are required to examine if the service can improve actual patient outcomes as a result of changes in the prescribing of these medicines.

Less rigorous evidence for the effectiveness of medication review interventions is provided by studies in which interventions undertaken by trained pharmacists have been independently reviewed in order to assess their clinical significance. The evidence obtained from these types of studies is not as strong as that obtained from controlled studies as there is no comparison group, nor

pre- and post-test design. However, one study using this methodology was located which examined medication review for clients of a community mental health team. The study is summarised briefly below because it addresses a neglected area with little research in the Australian setting, examining strategies to reduce medication-related problems amongst psychiatric patients.

Gisev et al.<sup>62</sup> undertook a study in five community mental health teams in NSW. Clients of the service recruited to the study were aged 18 years or older and taking at least one medicine for mental illness. Case managers recruited clients to the intervention who they believed would benefit from a medication review. The reviews were conducted by five trained pharmacists. Pharmacists conducted 30 to 45 minute interviews with clients, identified actual and potential medication-related problems as well as reviewing medication history and community dispensing records. The pharmacist provided a written report, including recommendations, that was presented at face-to-face multidisciplinary case conference meetings. Reviews were conducted with 48 clients. An expert panel independently reviewed and evaluated the findings. Evaluation was conducted on 209 medication review findings and 208 medication review recommendations. The panellists agreed with 76% of findings and considered that 81% of recommendations were appropriate. Collectively, 69% of recommendations were considered likely to be implemented. Seventy-seven percent of reviews (n=37) were deemed potentially to have a positive clinical impact.

Further controlled trials are warranted including actual patient outcomes to assess the impact of comprehensive medication review services for mental health clients in the community.

## Systems-based approaches to understanding and preventing medication errors

### Systems to allow hospitals to assess medication systems and performance

#### *Quality improvement projects incorporating Plan-Do-Study-Act (PDSA) cycles*

Plan-Do-Study-Act cycles are a cornerstone method in continuous quality improvement processes that have been used by healthcare organisations as a method to improve patient safety. The Agency for Healthcare Research and Quality (USA) describes the elements of PDSA cycles as follows:<sup>117</sup>

- **Plan:** Analyse the problem that requires improvement and formulate a plan to address it
- **Do:** Carry out the plan (usually starting with a small scale pilot or simple intervention in the first cycle)
- **Study:** Examine whether the plan was successful in addressing the problem. If not successful examine what went wrong. If partially successful, examine how the plan may be refined.
- **Act:** Adopt the change piloted if successful, abandon if a complete failure, or modify if partially successful, then run through the cycle again. 'Regardless of which action is taken, the PDSA cycle continues, either with the same problem or a new one'.

Three papers published since 2008 were located that described medication safety initiatives in the Australian acute care setting underpinned by the use of PDSA cycles.

A paper describing the first three years (2009-2011) of the Medication Error Minimisation Scheme (MEMS) was published in 2013 by Breeding et al. (Level III-3).<sup>27</sup> This was a quality improvement



initiative in a large NSW teaching hospital adult intensive care unit that aimed to improve medication safety. Goals of this scheme included:

- exploring the barriers and enablers of medication incident reporting
- increasing reporting of medication incidents
- gathering information related to medication safety through surveys of, and focus groups with, staff
- uncovering unreported medication incidents through auditing and chart review
- examining issues related to non-reporting of medication incidents and implementation of interventions to address these
- positively promoting medication safety.

The project was driven by a multidisciplinary team of health professionals from within the intensive care unit. Data were collected before and after the implementation of initiatives and analysed using simple statistical methods. Medication safety was promoted through regular staff meetings as a standing agenda item and through promotional materials such as posters, signs and staff incentives. Education sessions on specific topics for staff were conducted on a monthly basis. Audits were undertaken in areas not usually included in the existing reporting structure, including intravenous (IV) infusion errors and chart reviews of documentation of omitted or withheld medicines according to the symbols provided for the National Inpatient Medication Chart (NIMC). Feedback sessions were provided to staff following audits and ways to improve practices were explored. Repeat audits were undertaken approximately one year later and pre- and post-intervention data were reported back to staff.

With respect to medication incident reporting, pre-intervention (study initiation) the rate of medication incident reporting was 6.2 reports per 1000 patient days. This increased to 14.9 per 1000 patient days at follow-up (post-intervention). Statistical significance was not reported.

The number of errors decreased at the repeat audit following feedback sessions (post-intervention). IV infusions associated with errors were 11.5% (38/330) pre-intervention and reducing to 3.2% (15/468) post-intervention. These included:

- incorrect rate of infusion at 5.5% (18/330) pre-intervention and 0.9% (4/468) post-intervention
- infusion label incorrect or incomplete at 3.0% (10/330) pre-intervention and 1.9% (9/468) post-intervention
- incompatible infusions administered by the same lumen at 3.0% (10/330) pre-intervention and 0.4% (2/468) post-intervention.

Statistical significance was not reported.

Withheld or omitted medicines not documented using the correct NIMC symbols were 30.3% (105/347) pre-intervention and which decreased to 21.4% (104/486) post-intervention. Again, statistical significance was not reported.

This project is ongoing. Results so far indicate that medication incident reporting has increased, rates of error related to intravenous infusions have decreased and documentation of omitted medicines has improved.

PDSA cycles were a key component of another Australian acute care project which examined the development of a model to reduce medication errors and harm in children.<sup>118</sup> This prospective interrupted time series study (Level III-3) involved a multifaceted intervention conducted in stages over four years (2003-2007). The study was undertaken in a NSW major paediatric hospital. The focus of the intervention was to integrate key strategies accessible in most hospitals, focusing on guidelines for safe paediatric prescribing. The project was led by a senior clinician with expertise in paediatric clinical pharmacology and therapeutics, health services research and implementation science.

Data were collected from all inpatients in three representative wards (excluding ICU) over three time periods; baseline, one year and four years post-implementation. Data collection occurred over a period of one month at a similar time of the year. Local guidelines for safe paediatric prescribing were developed by a multidisciplinary team. A separate guideline for paracetamol prescribing was also developed. Following the baseline evaluation, the guidelines were implemented in the hospital using evidence-based guideline implementation strategies and the PDSA model of clinical practice improvement. PDSA was used as an implementation and evaluation tool and was used to identify and address specific barriers.

Initially, intensive education was used through small group sessions, with opinion leaders in the hospital emphasising the potential to reduce patient harm. Promotional materials, mail-outs, newsletters and the intranet were used to disseminate the guidelines. Three PDSA cycles were used to guide this process. An early implementation audit was undertaken after this first year. After the first year, guidelines and associated education were incorporated in the routine orientation program for all clinicians. Data-based feedback was given through newsletters and as part of meetings and PDSA cycles used to address any identified problems.

During the fourth year, as part of a national program, the standardised Paediatric National Inpatient Medication Chart was introduced with accompanying education. Outcome measures included medication errors (medication incidents), adverse medication events and elements of adherence to guidelines. Outcome measures were obtained from voluntary reports from nursing, medical staff and pharmacists (including pharmacist interventions), as well as intensive chart review conducted by a study pharmacist. The data collection tool used in the study included the nature of the event, contributing factors, preventability, severity, likelihood of recurrence and outcome. Data from all sources were reviewed by a multidisciplinary panel.

Results for the primary outcome measures were:

- total errors (medication incidents per 100 orders) reduced at year 1 and year 4; baseline 4.51, 1 year 3.02 ( $p < 0.05$  versus baseline), 4 year 2.78 ( $p < 0.05$  versus baseline)
- prescribing errors (per 100 orders) reduced by year 4; baseline 4.07, 1 year 2.50 (not significant (ns) versus baseline), 4 year 2.05 ( $p < 0.05$  versus baseline)
- paracetamol errors (per 100 orders) reduced at year 1 and year 4; baseline 1.18, 1 year 0.52 ( $p < 0.05$  versus baseline), 4 year 0.54 ( $p < 0.05$  versus baseline)
- adverse medication events (actual and potential per 100 patients) reduced at year 1 and year 4; baseline 19.22, 1 year 10.43 ( $p < 0.05$  versus baseline), 4 year 8.59 ( $p < 0.05$  versus baseline)

- adverse medication events (actual, per 100 patients) reduced at year 1, but not year 4; baseline 6.96, 1 year 3.07 ( $p < 0.05$  versus baseline), 4 year 3.99 (ns versus baseline)
- adverse medication events (preventable, per 100 patients) remained unchanged; baseline 3.62, 1 year 1.84 (ns versus baseline), 4 year 2.15 (ns versus baseline).

The most common medicines involved in errors and adverse medication events (AMEs) were analgesics and anti-infectives. Most preventable and non-preventable actual AMEs were judged to be of minor severity. There were no major or serious actual AMEs seen during the data collection periods. At baseline there were five potential AMEs (of 44) classified as major or serious. These types of AMEs were reduced to zero at the four year follow-up, but small numbers prevent an assessment of the significance of this finding.

Together, the studies of Breeding et al.<sup>27</sup> in adult ICU, and Gazarian and Gaudins<sup>118</sup> in paediatric acute care (both Level III-3), provide evidence for clinical practice improvement projects incorporating PDSA cycles in reducing medication errors, adverse medication events and improving documentation. The study undertaken in the paediatric hospital setting is one of the few studies in the Australian healthcare setting to examine adverse medication events and actual severity of harm as an outcome measure. Controlled studies would improve the evidence base, but controlled studies for systems approaches such as this in a whole unit or hospital may not be achievable.

One further pre- and post-intervention study conducted in a cancer centre aimed to design and test the effectiveness of a consumer-healthcare professional partnership to improve medication reconciliation.<sup>119</sup> The program development was informed by PDSA cycles. The outcomes measured and used to examine effectiveness of the intervention were rates of pharmacist interventions and near-miss medication errors. This was a before and after cohort study with a test and control ward. There was a marked reduction in the pharmacist intervention rates on the control ward after implementation of the intervention ( $p = 0.04$ ), which was attributed to a change in documentation practices with a new pharmacist on duty in the ward. This change in outcome measures in the control ward meant the effects of the intervention could not be clearly interpreted.

### *Multidisciplinary approaches using practice improvement methodology*

A study describing a multidisciplinary intervention to improve the safety and effectiveness of warfarin therapy was conducted in a Sydney acute care private hospital.<sup>63</sup> The practice improvement methodology involved identification of problems associated with warfarin therapy management in the hospital, as well as the quantifying the size and scope of the problems, identifying the most appropriate interventions for the local context, implementing appropriate interventions and measuring process and outcome indicators to examine the effect of the interventions. A multidisciplinary team identified a suite of specific evidence-based interventions to address problems identified. These included decision support tools, audit and feedback, educational initiatives for patients and providers, as well as use of opinion leaders. Warfarin process indicators from the Indicators for Quality Use of Medicines in Australian Hospitals and outcome indicators from the Australian Council of Healthcare Standards (ACHS) clinical indicator set were measured at baseline (for one month) and in monthly retrospective chart audits over a ten month period for all patients on warfarin therapy.

While medicine-related adverse event outcome measures were examined in this study, small numbers meant meaningful pre- and post-intervention comparisons could not be made. At the baseline audit, none of the ACHS adverse warfarin outcomes were identified, including bleeds, cerebral haemorrhage, deaths related to warfarin or INR >5. Continuous monitoring of these outcomes on a monthly basis found that the percentage of patients with INR > 5 varied between 1.1 to 3.7% and the percentage of patients experiencing bleeds varied between 0 to 1.2%, which stayed below the ACHS benchmark of 1.4%. There were no deaths reported.

### *Multidisciplinary approaches using Failure Mode and Effect Analysis*

Failure Mode and Effect Analysis (FMEA) is a process used in some high-risk industries to identify prospectively the error risk for a particular process.<sup>81</sup> It involves mapping out a process and identifying all the steps that must occur for a given process to occur (e.g. ordering and administering a particular medicine). Once the process is mapped out, the analysis is continued to identify ways in which each step can go wrong (failure modes for each step). The probability that each error will be detected (so it can be corrected before causing harm) is also assessed, as are the consequences of the error not being detected. A criticality index is calculated and used to estimate the magnitude of hazard posed by each step. This identifies the steps which should be prioritised for improvement and 'error proofing'.

A pre- and post-intervention study (Level III-3) in the Australian hospital setting and which incorporated FMEA was conducted by Dooley et al.<sup>120</sup> between 2007-2010. The study targeted the processes of prescribing, dispensing and administration of insulin in the hospital setting. In particular, the intervention was aimed at reducing potentially fatal errors associated with high doses of insulin. The study was conducted in three sites of a Victorian hospital network including a tertiary care hospital, a community hospital and a rehabilitation/aged care hospital. Prior to study commencement, several major errors involving the administration of a ten-fold excess dose had occurred as a result of the use of the abbreviation 'u' for units on the prescription which had been misread as a zero. A multidisciplinary working party was convened to lead the project. Factors contributing to the insulin errors were reviewed and a FMEA performed. Possible failures and controls were identified. In consultation with a range of hospital staff, the various controls were prioritised using a scoring system, with a dose validation process for high doses of insulin considered to be the most practical and cost-efficient control. The working party adopted a definition of 'high dose insulin' (> 50 units per dose for intermediate or mixed action insulins, and > 25 units per dose for short acting insulins). A guideline was developed that ensured medical staff validated all high doses by seeking dose confirmation from a source such as the patient's GP, a competent patient or other authorised person. Nursing staff were required to ensure there was documentation of 'dose validated' on the prescription prior to administering the dose or to contact the prescriber. Ward-based pharmacists were required to ensure prescribers were contacted to validate high doses prior to administration. The introduction of the guideline was accompanied by an educational intervention for staff, promotional materials for the study and prominent reminders in relevant areas such as on fridges where insulin was stored and on the insulin products.

Data were collected through continuous prospective audits of patient medication charts for 90 weeks post-intervention and through incident monitoring. Post-intervention data were compared

with incidents reported in the two years prior to the intervention implementation. The analysis of outcomes from this study is limited by the use of only incident report data from the hospital system for the pre-intervention period. It was not possible to undertake an analysis of statistical significance. The major findings were that there were seven major errors resulting in excessive insulin administration identified over the two year pre-intervention period prior to the introduction of the insulin high-dose validation system. In contrast, in the 90 weeks after implementation there were 150 patients identified in which 200 high doses of insulin were prescribed; for these patients there were 8 instances where high doses of insulin were prescribed in error, but were detected and rectified through the new validation process. There were 12 dosing errors that occurred during this time including two major (ten-fold) dosing errors.

### *Other multifaceted interventions*

Two further studies were identified that used multifaceted strategies to improve patient outcomes and surrogate outcomes including medication errors. One examined the use of Transforming Care at the Bedside improvement strategies<sup>121</sup> and another used a Practice Partnership Model of Care.<sup>122</sup> In relation to medication error, the endpoint of these studies was self-reported incidents which may be influenced by a number of factors including the introduction of the intervention. These were not considered a valid endpoint for assessment of the intervention for this particular outcome.

## **Part 3: Medication Safety Intervention Strategies – the International Evidence**

### **USA Agency for Healthcare Research and Quality (AHRQ) systematic review of practices to improve patient safety**

#### **The report**

In March 2013, the USA Agency for Healthcare Research and Quality (AHRQ) published an international systematic review of the evidence for processes and structures aimed at improving patient safety in health care titled Making Health Care Safer II: An Updated Critical Analysis of the Evidence for Patient Safety Practices.<sup>123</sup>

#### **Medication safety topics included in the review**

The 2013 report updated a previous systematic review of patient safety practices undertaken by the Agency in 2001 titled Making Health Care Safer: A Critical Analysis of Patient Safety Practices.<sup>124</sup> The review was undertaken by a project team from the RAND corporation, Stanford University, University of California, San Francisco, Johns Hopkins University, the ECRI Institute and an international panel of stakeholders and methods experts. The review aimed to assess the evidence of the effectiveness and implementation of safety practices.

The strategies that were reviewed specifically for reducing adverse medication events (AMEs) included:

- patient safety practices for intravenous anticoagulants
- clinical pharmacy services in preventing AMEs
- ‘Do Not Use’ list of hazardous abbreviations for reducing abbreviation-related medication errors
- smart pumps and other protocols for infusion pumps.

Other practices reviewed relevant to medication safety included:

- medication reconciliation supported by clinical pharmacists
- promoting engagement by patients and families to reduce adverse events
- monitoring patient safety problems
- human factors and ergonomics – medication safety
- interventions to improve care transitions at hospital discharge
- computerised provider order entry with clinical decision support systems.

#### **Methods used in the AHRQ systematic review**

The project comprised three phases: topic refinement, an evidence review, and a critical review and interpretation of the evidence.

Prior to undertaking the review, the project team refined the topics. This process was undertaken with a Technical Expert Panel which included a large number of patient safety stakeholders. This included key patient safety leaders from the USA, Canada and the United Kingdom. Members of the

panel included experts in specific patient safety practices, experts in evaluation methods and people responsible for implementing patient safety practices in the healthcare system.

Evidence reviews took the form of either in-depth reviews or brief reviews. For in-depth reviews high quality, relevant systematic reviews were reviewed where available and updated where necessary. Where no systematic review existed for a topic or existing reviews were not suitable or of sufficient quality, the team conducted new searches using guidance as outlined in AHRQ's Methods Guide for Effectiveness and Comparative Effectiveness Reviews.

Brief reviews were not full systematic reviews. Brief reviews focused on either information about effectiveness of an emerging safety practice or implementation of an established one. These reviews involved the focused literature searches for evidence relevant to the specific need.

The framework for evaluating the strength of evidence included the strength of evidence assessments, evidence regarding context, implementation, and the use of theory or logic models, in addition to standard criteria on consistency, precision, and the possibility of reporting bias.<sup>125</sup>

### Summary tables for patient safety practices relevant to medication safety from AHRQ review

Intervention	Scope of the problem targeted by the intervention(s) (frequency/severity)	Strength of evidence for effectiveness of the intervention(s)	Evidence or potential for harmful unintended consequences	Estimate of cost	Implementation issues: How much do we know?/How hard is it?
Patient safety practices for IV heparin	Common/moderate	Low	Low to moderate	Low	Little/moderate
Clinical pharmacists in preventing ADEs	Common/low	Moderate to high	Low	High	Little/moderate
'Do not use' lists of abbreviations	Common/low	Low	Negligible	Low	Little/probably not difficult
Smart pumps and other protocols for infusion pumps	Common/low	Low	Low	Moderate	Moderate/moderate
Medication reconciliation	Common/low	Moderate	Low	Moderate	Moderate/moderate
CPOE with CDSS	Common/moderate	Low to moderate	Low to moderate	High	Moderate/Difficult
Promoting engagement by patients and families to reduce AEs	Common	Emerging practice (few studies available)	Uncertain	Low	Little/moderate
Monitoring patient safety problems	Common/low to high	Low	Negligible	High	Moderate/difficult
Incorporation of human factors and ergonomics in the design of healthcare practices	Potentially applicable to all patient safety problems	Not assessed systematically, but moderate-to-high evidence for some	Negligible	Moderate	A lot/moderate
Interventions to improve care transitions at hospital discharge	Common/moderate	Low	Negligible	Moderate to high	Little/difficult



## Strategies considered 'ready for adoption'

The Technical Expert Panel reviewed the results of the evidence review performed by the project team. After analysing 41 patient safety practices, the international panel identified 22 strategies that it considered were 'ready for adoption' based on the strength and quality of evidence available for both effectiveness and implementation. Although some practices had limited published evidence for effectiveness, they were included in this list due to their acceptance, ease of implementation and low cost. For these 22 strategies, it was deemed that enough evidence exists to recommend that health systems and institutions should move forward in implementing these strategies now.<sup>126</sup> Of the 22 strategies, 10 are 'strongly encouraged' for adoption and 12 are 'encouraged'.<sup>126</sup> Of the patient safety practices ready for adoption, four are relevant to medication safety:

### Strongly encouraged

- 'Do Not Use' list for hazardous abbreviations

### Encouraged

- Use of clinical pharmacists to reduce adverse medication events
- Medication reconciliation
- Computerised provider order entry (CPOE)

## Recommendations for future research

The AHRQ review also suggested high priority areas for future research, the four priority areas relevant to medication safety were:

- Interventions to improve post-discharge care transitions
- Medication reconciliation
- Measures to encourage a culture of patient engagement in patient safety
- Use of human factors engineering and ergonomics in the design of healthcare practices.

## Evidence for specific patient safety practices in the AHRQ report to reduce adverse medication events (AMEs)

This section summarises the findings from the AHRQ review relevant to medication safety, as well as cited reports and other relevant studies where appropriate. It should be noted that health systems differ around the world and the structure of the health system may influence whether a practice or strategy is effective.

### *Practices to reduce AMEs for high risk medicines - intravenous heparin*

The US Institute of Safe Medication Practices has identified major high-alert medications subject to administration error. These include insulin, opioids, injectable potassium chloride, intravenous anticoagulants (heparin) and sodium chloride solutions above 0.9 %, due to their common use and significance of associated harm. Intravenous anticoagulant administration is considered high risk because calculating the correct dose is difficult and the therapeutic range is narrow.

In the AHRQ review, interventions for intravenous (IV) heparin were reviewed as IV heparin is the most frequently used IV anticoagulant. The review considered effectiveness studies of any type of intervention that aimed to reduce adverse events associated with IV heparin in the inpatient setting. Studies which included a comparison group and that were not qualitative were included.

### Nomograms

Weight-based nomograms employ patient body weight to calculate an optimum patient-specific dose. Doctors dosing without nomograms often do not account accurately for patient weight.

Five studies published between 2001 and 2005 were identified in the review that examined the effectiveness of weight-based nomograms for IV heparin.

One randomised controlled trial (RCT) (Level II) tested a weight-based nomogram for heparin dosing in transient ischemic attack (TIA) or stroke.<sup>127</sup> In this study of 206 patients:

- total complications were significantly reduced with the nomogram (8.5% [9/105] with the nomogram versus 2% [2/101] without the intervention,  $p=0.04$ )
- time to therapeutic-range APTT (i.e. therapeutic anticoagulation) was significantly less with the nomogram (13.4 hours [SD 17.0] versus 17.9 hours [SD 14.1] without the nomogram,  $p<0.05$ )<sup>1</sup>.

A pre- post-implementation study (Level III-3) assessed the effect of using a weight-based nomogram in 173 patients with acute coronary syndromes.<sup>128</sup> Median time to first therapeutic APTT (the primary outcome measure) was lowered from more than 24 hours to 8.75 hours ( $p<0.001$ ). Four (4.5%) major haemorrhagic events occurred in the non-weight-based heparin nomogram group versus two (2.4%) major haemorrhagic events in the weight-based heparin nomogram group (differences were not statistically significant, but numbers were small).

Another pre- and post-intervention study (Level III-3)<sup>129</sup> involving 419 patients examined the implementation of a computerised nomogram for acute coronary syndromes, finding improved anticoagulation outcomes (PTT in a goal range of 44% with the nomogram vs 27% without nomogram); data on complications were not reported.

Two further small studies ( $n=68$  and  $n=38$ ) of nomograms were also reviewed; one reported no statistical outcomes and the other found no significant difference between the nomogram intervention and control.

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<sup>1</sup> Data presented here were obtained from the original paper due to some errors in the summary provided in the AHRQ review

### **Use of new medication administration, dosing, and monitoring technology**

Two further studies<sup>130 131</sup> examined the impact of smart infusion devices in addition to other interventions supporting heparin administration safety.

A 2011 pre- and post-implementation design (Level III-3) study aimed to improve medication safety through the use of intelligent infusion devices, a barcode-assisted medication administration system, and an electronic medication administration record system. Findings included:

- improved monthly compliance with the telemetry medicine library increasing from 56.5% ( $\pm 1.5\%$ ) pre-intervention to 72.1% ( $\pm 2.1\%$ ) post-intervention ( $p < 0.001$ );
- a reduced number of telemetry manual pump edits decreasing from 56.9 ( $\pm 12.8$ ) pre-intervention to 14.7 ( $\pm 3.9$ ) post-intervention ( $p < 0.001$ ).

Another pre-and post-implementation design study (Level III-3) assessed the impact of a smart infusion device with a locally determined medicine library and programmable software on anticoagulation errors. A total of 14,012 administered doses of heparin in 3,674 patients were reviewed, for which the software generated a total of 501 heparin alerts in 246 patients. No significant difference in anticoagulation errors was found as a result of the intervention (49 pre-versus 48 post-intervention).

### **Conclusions**

Overall the AHRQ reviewers found a low strength of evidence that nomograms and new intelligent medication administration, dosing, and monitoring technology improve outcomes for the use of IV heparin. Only one study was a RCT. Many studies reported process outcomes rather than actual patient outcomes. There were no studies of nomograms published after 2005 and no studies of inpatient anticoagulation services published since 2000, although both the use of protocols and indications for heparin have greatly changed since that time. Only two studies evaluated new technology, and no studies evaluated other types of interventions to improve heparin safety. Study quality was generally low and many studies had small sample sizes, insufficient to demonstrate the impact on complications of heparin administration.

### ***Clinical pharmacist interventions to reduce adverse medication events***

The literature searched by AHRQ covered the years 2001-2011, in which time there have been several systematic reviews of the efficacy of pharmacist-led interventions. Studies included were clinical pharmacist interventions on medication errors and adverse medication events in various healthcare settings.<sup>123</sup> Five systematic reviews and 11 new studies<sup>2</sup> were included. A summary of the AHRQ findings is given below.

#### **General inpatient setting**

One review that was included examined the role of clinical pharmacists in the inpatient setting and included studies with concurrent controls or a time series design published between 1985 to 2005.<sup>132</sup> This was the largest review and included 36 studies (10 of pharmacist participation on ward rounds, 11 of participation in medication reconciliation and 15 of pharmacist involvement in medicine-specific services). This narrative review concluded that there was evidence overall to support the role of pharmacists in improving the quality, safety and efficiency of care in the inpatient

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<sup>2</sup> It is stated in the AHRQ review Ch 4 page 33 that 8 new studies not included in the systematic reviews were identified, however 11 studies are listed in Table 1 of this chapter.

setting although it was noted that many studies were small, that variable endpoints were measured and most studies lacked generalisability having only been conducted in one institution.

### **Elderly patients and nursing home residents**

Two included reviews examined the clinical pharmacist's role in the care of elderly adults and residents in nursing homes. One review found pharmacist services for elderly people to be beneficial in improving quality of care and reducing medicine-related problems but that evidence was minimal for reducing adverse medication events (due to the difficulty in performing studies that are large enough to demonstrate a significant effect on this outcome measure). The review of randomised controlled trials in the nursing home setting found that pharmacist interventions showed inconsistent effects on actual patient or clinical outcomes.

### **Paediatric patients**

A review of pharmacist interventions for paediatric patients found that, while the studies were generally older and of heterogeneous design, the overall effect was generally positive amongst the 18 included studies. The review highlighted the important role of pharmacists in detecting and correcting medication errors including dosing errors in paediatric patients.

### **Emergency department setting**

A review by Cohen et al.<sup>133</sup> included 16 studies of pharmacist involvement in the emergency department setting and found that the interventions performed by pharmacists in this setting were diverse in nature. The review included several studies that reported cost-avoidance and savings data and decreases in medication errors associated with clinical pharmacy services. However, medication safety and patient-specific outcomes were often not the primary outcomes measures, and it was concluded that more studies examining patient outcomes were needed<sup>3</sup>.

### **Newer studies**

As indicated above, 11 additional clinical pharmacist studies were also included in the AHRQ review. These included studies of the general inpatient setting (2), adult, paediatric and neonatal ICUs (4), a hospital paediatric unit (1), outpatient psychiatric setting (1) and emergency departments (3). Overall it was concluded that these newer studies support the role of clinical pharmacists in reducing prescribing mishaps, with some studies showing improvement in patient-level outcomes including adverse drug reactions and mortality.

### **Conclusions**

It was concluded that studies of clinical pharmacist services lacked consistency and comparability, however, systematic reviews and more recent evidence included in the AHRQ review generally support pharmacist services for improving patient safety.

Evidence supports clinical pharmacist involvement in ICUs, in particular their involvement in bedside rounds. Data for other inpatient and outpatient settings was concluded to be less robust, but supportive of a role for clinical pharmacists.

In terms of cost savings, the studies assessed were too methodologically heterogeneous to estimate specific cost savings. Savings also depended on whether existing clinical pharmacy staff could be engaged in provision of the service or whether new pharmacists needed to be employed.

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<sup>3</sup> Summary obtained from original paper by Cohen et al.

### ***'Do Not Use' list of hazardous abbreviations for reducing abbreviation-related medication errors***

Confusion over medication abbreviation is a well described source of medication prescription and administration error,<sup>134</sup> and the use of error-prone abbreviations is relatively common. In the AHRQ review the effectiveness of 'Do Not Use' Lists of hazardous abbreviations was examined.

In 2003 the US Joint Commission on Accreditation of Healthcare Organizations announced nine abbreviations or shorthand notations, a 'Do Not Use list', that should be banned in its accredited hospitals. The list included the following as inappropriate abbreviations:

- U or u instead of unit; IU instead of International Unit
- Q.D. or similar instead of once daily
- Q.O.D or similar instead of every other day
- MS, MSO4 and MgSO4 instead of writing morphine sulfate or magnesium sulphate
- use of trailing zeros (e.g. 1.0 instead of 1) or lack of a zero before a decimal point (.9 instead of 0.9).<sup>135</sup>

In the AHRQ report a narrative literature review was conducted to examine:

- the degree to which healthcare organisations have implemented procedures to prevent the use of inappropriate abbreviations and
- which method(s) have worked well.

A focus was given to studies conducted in the USA. In the review, studies that addressed the primary methods for addressing safety issues associated with abbreviations were considered 'education, enforcement and leadership'.

#### **Education for healthcare providers to reduce the use of unsafe abbreviations**

It was found that it was difficult to gauge patient outcomes relating to implementation of 'Do Not Use' lists as there are few projects specifically assessing the efficacy of implementing such lists on rates of medication error or adverse medication events.

One US educational project included in-service training for hospital staff, and contact with prescribers to clarify orders and explain why certain abbreviations should not be used. Pocket cards, chart dividers separating laboratory and medication orders and stickers were used. Over a period of eight months, over 20,000 orders were reviewed and the incidence of unsafe abbreviation use declined from around 20% at pre-intervention to around 3% by end of study.<sup>136</sup>

Another US study focussing on 'safe prescribing behaviours' in a teaching hospital used a multi-faceted approach including lectures as well as reminders and prompts to encourage desired prescribing practices, including avoiding particular abbreviations that could lead to dosing or frequency errors. There were equivocal findings, with prescribing errors decreasing among surgical staff but increasing among medical staff, and there was no decrease in the use of potentially hazardous abbreviations.

Another study in seven independent healthcare organisations, including 13 hospitals in the US, examined their collaborative effort to ban nine specific abbreviations and shorthand notations. The intervention included educational sessions and information materials as well as feedback to physicians continuing to use banned abbreviations (for in-patient prescribing) and passive education

through newsletters in the outpatient clinic setting. There was a significant improvement in appropriate documentation (not using banned abbreviations or notations) from 62% at baseline to 81% post-intervention ( $p < 0.0001$ ) in the inpatient hospital setting, but no significant change in the outpatient clinic setting.

#### **Leadership and enforcement to reduce unsafe abbreviation use**

No formal studies were located in the AHRQ review.

#### **Electronic prescribing to reduce use of unsafe abbreviations**

In the AHRQ review it was noted that the other group of studies in which reduction of rates of abbreviation error are sometimes demonstrated are studies evaluating computerised prescribing on medication error rates.

A prospective RCT (Level II) provided the highest level of evidence for this strategy. This study examined whether a personal digital assistant-based clinical medicine system affected prescribing by 78 office-based primary care physicians. Practices were randomised to use the personal digital assistant (PDA) system to enter prescriptions or usual handwritten prescriptions. The study findings were limited by the fact that intervention practices could still use handwritten prescriptions if desired. In the PDA-use period, 43% of prescriptions were entered using the PDA. It was found that illegibility decreased from around 9% to 3%. Various abbreviations and short-hand notations decreased but the significance ( $p$  value) was not reported. For example, abbreviations for administration route decreased from 63% to 37% and for frequency from 86% to 51%. Notably, dosing abbreviations rose from 61% to 71% as some dosing abbreviations were allowed in the PDA application.

Another pre- and post-intervention community-based study from a US multi-speciality community clinic (Level III-3) described the frequency of illegible prescriptions decreasing from 3% to less than 0.1% post-intervention after the introduction of a basic computerised order entry system of limited clinical decision support capacity.<sup>137</sup> Use of inappropriate abbreviations decreased from 5% to 0.4% post-intervention.

A small study of 17 physicians in an outpatient setting compared errors when transitioning from an older electronic prescribing system (with some auto-correction of abbreviations) to a newer system that would alert prescribers when they entered an inappropriate abbreviation but did not auto-correct it. It was found that reducing inappropriate abbreviations was the primary factor in reducing overall prescription error rates. Rates of inappropriate abbreviations fell from 24% at baseline to near 11% at six months and 6% at one year ( $p < 0.001$ ).

#### **Conclusions**

In the AHRQ review it was stated that, while various organisations have taken a strong stand against the use of certain abbreviations, evidence on implementation methods is limited and hence no clear implementation method could be recommended. No literature was located in the review that assessed whether reducing hazardous abbreviations leads to less patient harms. It was noted that no obvious harms resulted from use of these lists. It was suggested that a 'low-cost approach of implementation, such as through ongoing education and/or feedback, focused on avoiding selected harmful abbreviations whenever and wherever possible seems reasonable and feasible'.<sup>123</sup>

### *Smart pumps for reducing intravenous infusion pump medication error*

Infusion pumps often deliver high-risk medication rapidly and are inherently prone to administration error. Manufacturers have designed “smart pumps” with various technologies for regulating dosage and creating alert systems to mitigate the rate of medication error; some even recognise bar coding. The evidence for efficacy of smart pumps for prevention of medical errors is limited by the small number of studies and the use of observational study designs.

The AHRQ report authors<sup>123</sup> cited a systematic review of the literature (2003-2008) assessing the use of smart pumps to decrease medication errors. It was found that most published studies have only assessed smart pumps with soft alerts which consist of prompts about dosing, whilst still allowing staff to administer the dose they wish, rather than hard alerts in which the programme precludes staff administering an incorrect dose. Findings vary, ranging from no effect to a limited effect of soft alerts in reducing medical error rate.

Hard alerts and barcode technology should theoretically have more impact on error rates, but too few studies were located in the AHRQ review to evaluate the relative effectiveness of these features.

Two retrospective before-after studies were reviewed that examined smart pumps with soft and hard alerts. A study published in 2011 in a community hospital setting found use of rescue medications and heparin infusions decreased substantially from pre- to post-intervention, and length of stay in patients receiving antimicrobial agents also decreased substantially. Of the alerts, 86.2% were soft alerts (61% of which were over-ridden by users) and 13.8% were hard alerts. Another study published in 2007 evaluated the impact of a smart pump with soft and hard alerts in an academic medical centre. Anticoagulation errors in 3674 patients were reviewed and it was found that there was no significant decrease in errors (49 pre-intervention versus 48 post-intervention). This lack of difference may reflect the fact that only a minority of events were infusion-related errors (19 of the 97 total events).

One study published in 2010 was included in the AHRQ review and involved a simulation (laboratory) study comparing nurses’ ability to avoid medication errors using a traditional pump, a smart pump (with soft and hard alerts), and a pump with an integrated bar code scanner (soft and hard alerts). Wrong medication errors did not differ significantly by pump type. Patient ID errors were reduced when using pumps with barcode scanners (88%) compared to the smart pumps without barcode scanners (58%) or traditional pumps (46%). Significantly more nurses remedied critical overdose errors when using pumps with barcode scanners (79%) and smart pumps without barcode scanners (75%) due to hard alerts than with traditional pumps (38%). While this study provides perspectives on error rates, it was not conducted in the actual clinical environment.

### **Conclusions**

It was concluded that smart pumps have the most potential to reduce medication errors when integrated into a larger medication safety system that connects them with computerised provider order entry systems, barcode enabled point of care and electronic medicine administration records. However, too few studies were located in the AHRQ review which evaluated these features in terms of their relative effectiveness.

Implementation of smart pump technology by health systems and hospitals are described as generally requiring considerable planning including identification of stakeholders, evaluation of



software capabilities, evaluation of hospital-specific practices, decisions regarding standard operating systems and procedures, building of medicine libraries, and education of staff before the pumps can be deployed.<sup>123</sup> Once medicine libraries have been developed, considerable time must also be devoted to maintaining and updating the libraries. Wireless communication technology in an organisation's infrastructure allows easier adjustment or updating of medicine libraries, which otherwise would require manually updating each pump separately.

## **Other practices reviewed by AHRQ relevant to medication safety**

### ***Medication reconciliation supported by pharmacists***

The World Health Organization has prioritised medication reconciliation as one of the top five patient safety strategies. The AHRQ review sought to quantify the impact of medication reconciliation on unintentional medication discrepancies with potential for harm ('clinically significant discrepancies') and unplanned emergency visits and readmission to hospital.<sup>123 138</sup> The review considered 18 medication reconciliation studies in the hospital setting, 15 of which involved pharmacists playing a major role while the other three were delivered by nurses or physicians. All included studies were undertaken in the USA or Canada.

### **Impact of medication reconciliation on clinically significant unintended discrepancies**

Only two RCTs (Level II) conducted by the same research group in the US compared medication reconciliation interventions to usual care, with an explicit focus on AMEs.

One trial (published in 2006) involved randomizing 178 patients being discharged from a teaching hospital to an intervention that included medication reconciliation and counselling by a pharmacist, with a follow-up phone call within five days. Patients in the control arm received discharge counselling from a nurse and pharmacists reviewed medication orders, but did not perform a formal reconciliation process. It was found that significantly fewer patients in the intervention arm experienced preventable AMEs (1%) compared to the control group (11%;  $p=0.01$ ), though total AMEs did not differ between the two groups.

A subsequent trial involved 322 patients and 14 medical teams at two teaching hospitals. The intervention included a web-based application using the hospital's electronic medical record to create a preadmission medication list for 162 intervention arm patients. For patients in the usual care arm, residents compiled medication histories on admission and pharmacists then reviewed the medications histories. The intervention achieved statistical significance at one hospital, with a relative reduction of possible AMEs or clinically significant medication discrepancies of 0.72 [95% CI 0.52-0.99], but not the other 0.87 [95% CI 0.57-1.32]. The difference was attributed to variation in the degree to which the two hospitals integrated the medication reconciliation tool into the computerised order entry applications.

### **Impact of medication reconciliation on unplanned emergency visits and readmission to hospital**

The review examined the impact of medication reconciliation interventions within 30 days of discharge with three RCTs (Level II) meeting the inclusion criteria. A pooled result from these three studies showed that readmissions and emergency department visits were reduced by 23% [95% CI 5%-37%]. However this result was primarily driven by the results from one study. This study including a multifaceted intervention that incorporated several interventions specifically aimed at reducing hospital readmission as well as medication reconciliation.



The authors also cited a Swedish RCT of 400 patients aged 80 years and over that resulted in a statistically significant reduction of 16% in hospital visits in the intervention patients over a 12 month period.<sup>139</sup> This study was excluded from the meta-analysis due to the longer follow-up time. The intervention consisted of clinical pharmacists compiling a list of medicines on admission complementing the list compiled in the emergency department, a medicines review with advice to treating physicians on medicine selection and dosages, patient counselling, communication with primary care clinicians and a follow-up call from pharmacists to patients within two months of discharge. Patients in the control arm received usual care with the pharmacist involved with the ward team.

### **Harms**

The authors of the AHRQ review considered whether there may be any harms associated with medication reconciliation as a strategy. While no studies were reviewed that suggested harm from this intervention, the authors stated that mistakes in a medication reconciliation process could have the potential to become “hardwired” in a patient’s record with carer’s relying on a documented medication history rather than checking the accuracy with the patient or another source. Due to the important role that pharmacists play in preventing AMEs in hospitals, the authors indicated there may be the risk that using pharmacists to conduct medication reconciliation may take pharmacists away from other important patient safety activities (given that they are in short supply in the hospital setting).

### **Costs**

The authors of the AHRQ review concluded that most studies of medication reconciliation determined loose estimates of costs in terms of time spent by pharmacists performing the intervention. One model-based study cited in the AHRQ review<sup>140</sup> used literature values to estimate the cost-effectiveness of a range of interventions with evidence of effectiveness for reducing medication error. Based on their modelling, a pharmacist-led reconciliation intervention has the highest expected net benefits, with a probability of being cost-effective of over 60% by a quality adjusted life year value of £10 000 (\$US 16,272).<sup>123 140</sup>

### **Conclusions**

The AHRQ review authors concluded that the cross-study frequency of “non-trivial” medication errors in medication reconciliation interventions was varied, and that only one study demonstrated a statistically significant reduction of discrepancies resulting in potential AMEs at one study site. The evidence suggests that when considered as a sole intervention, medication reconciliation does not reduce hospitalisation rates within 30 days, though it may do so over longer time frames. The authors indicated that ‘the paramount issue becomes how to target medication reconciliation in order to direct resources most efficiently’.

### **Other reviews of medication reconciliation**

The AHRQ review only included medication reconciliation studies conducted in the hospital setting. It is worth noting another review by Bayoumi et al.<sup>141</sup> that focussed on medication reconciliation in the primary care setting. Four trials met the inclusion criteria. Two pre- and post-intervention studies (Level III-3) in ambulatory care gave conflicting results. One study showed a reduction in the

proportion of medication discrepancies from 88.5% to 49.1% and the other showed no benefit. One RCT (Level II) and pre- and post-intervention study (Level III-3) evaluated pharmacist medication review at hospital discharge. Neither showed a benefit. The authors concluded that all included studies had significant design flaws and there is currently a lack of quality evidence demonstrating the effectiveness of medication reconciliation in the primary care setting. Further research in this setting is required.

### *Human factors and ergonomics: medication safety*

In the AHRQ review, strategies involving changes of work systems and processes to reduce the plethora of physical, cognitive and organisational factors associated with medication safety were considered.<sup>123</sup>

Human factors and ergonomics was reviewed which 'covers a wide range of physical, cognitive and organizational issues involved in system design'.<sup>123</sup> Human factors and ergonomics works on the principle that systems should be designed to fit the characteristics, needs and limitations of the people using it in order to improve well-being as well as the overall performance of the system. As indicated in the AHRQ review, human factors and ergonomics can contribute to different domains of patient safety such as the useability of medical devices and health information technology, understanding human error and healthcare worker performance and their contribution to patient safety and system resilience.

The domain of useability of medical devices and health information technology has been a focus of human factors and ergonomics research in the area of patient safety and has relevance to medication safety. It is recognised that health IT can contribute to reducing patient safety hazards, however it may also create new hazards. The useability of a health IT system may influence whether it produces safety benefits or creates new hazards.

This chapter of the AHRQ review was not a systematic review but rather sought to identify examples of studies that demonstrate how human factors and ergonomics may be beneficial. One example relevant to medication safety was an examination of how human factors and ergonomics can provide information on the useability of computerised physician order entry (CPOE) technology. The review described a framework used to improve the design and implementation of a CPOE system. This framework included four stages:

- Analysis of the medication use process (ordering-dispensing-administration) using a literature review, observation of and interviews with healthcare staff and review of medication order and administration records.
- Co-operative system design in consultation with nursing staff around preparation and administration of medicines.
- Evaluation of a proposed CPOE technology using standardised human factors and ergonomics criteria related to workload, compatibility, control, homogeneity, guidance and error prevention. Laboratory testing in a simulated work environment was also undertaken.
- Redesign of the CPOE system with possible solutions to usability issues proposed and evaluated according to costs and benefits. Mock-ups and prototypes for possible solutions developed, tested and re-designed until all critical useability issues are addressed.

## Conclusions

Further research is needed to demonstrate the value of human factors and ergonomics-based interventions on patient safety outcomes. This should include changes in the work-system, changes in the processes and changes in outcomes (for both patients and healthcare providers). The AHRQ review concluded that “HFE [human factors and ergonomics] is a core element of patient safety improvement; therefore, every effort should be made to support HFE applications in patient safety.”<sup>123</sup>

### *Patient and family engagement to reduce adverse events*

The AHRQ review examined practices centred on patient and family participation in care, including as ‘an overarching philosophy applicable to a number of patient safety practices’<sup>123</sup> or as an implementation in its own right. Studies focussing on the hospital setting were included. Some studies were relevant to the area of medication safety and are discussed below.

The authors cite a systematic review of patient and family-centred strategies to enhance patient safety,<sup>142</sup> most of which related to medication management. They concluded there was limited evidence for the efficacy of patient safety interventions and the studies were generally of limited quality. One RCT (published in 2004) in which the intervention arm patients were provided with a personalised medication list and medication safety education, demonstrated no statistically significant outcome on AMEs or ‘close calls’ compared to general medication safety education only for the control group.<sup>143</sup>

One intervention, the Care Transitions Intervention, has been evaluated in several settings. The Care Transitions Intervention is based on four conceptual domains derived from qualitative studies with patients and care-givers referred to as “four pillars” of medication self-management: a patient-centred record, follow-up and “red flags” which indicate worsening condition and education about how to respond to that exigency. It involves hospital visits to educate patients about medication, a home visit post-discharge to reconcile pre- and post-hospital medication lists and follow-up calls.

Studies included in the AHRQ review assessing the efficacy of the Care Transitions Intervention reported reduced rates of hospital readmission with patients reporting higher levels of confidence in self-management including their understanding of how to take their medications.

In an RCT of Colorado Medicare fee-for-service patients aged 65 years and older, the primary outcome measure was whether the intervention reduced re-hospitalisation rates at 30, 90 and 180 days post-discharge. This study found that intervention patients were statistically significantly less likely to be readmitted for their index condition at 90 and 180 days.<sup>144</sup>

A quasi-experimental, prospective cohort study implemented the Care Transitions Intervention in Medicare patients at six Rhode Island hospitals. Compared with people who did not receive the Care Transitions Intervention, the odds of readmission within 30 days were significantly lower for intervention patients (OR 0.61; 95% CI 0.42-0.88). The difference in absolute readmission rate was 12.8% versus 20.0%.<sup>145</sup> There were no data on cost effectiveness.

## Conclusions

Few studies have been published on the effectiveness of patient and family engagement as a patient safety strategy. The Care Transitions Intervention has been shown to reduce rates of hospital

readmission and to improve patient confidence in medication self-management. Despite the lack of clear evidence of effectiveness for interventions engaging patients and families, the AHRQ review considers this an important emerging area requiring further research.<sup>123</sup> Issues need to be addressed, including the definition of patient and family engagement and the particular safety endpoints that should be measured.

### *Monitoring patient safety problems*

Monitoring Patient Safety is cited by the AHRQ review as a new area of intervention. There are many mechanisms for monitoring patient safety. One commonly adopted is incident reporting systems which the authors assert may well under-estimate the real prevalence of such occurrences. Staff fear litigation, may be too busy to report patient incidents or may be concerned about their professional reputations.<sup>123</sup> In the last decade, computerised physician order entry and clinical decision support systems which flag adverse medication events (AMEs) have become increasingly common.

As an example the review cites a prospective Dutch study providing online medicine-medicine interactions checks and medicine dosing checks, with safety alert information derived from a national medicine information database. The study compared an adverse drug event alerts system (ADEAS) to the conventional medication monitoring system over 31 days. The conventional system generated 177 alerts; in the same time-frame the total of ADEAS alerts was 248. Alerts for different kinds of patients were identified with the ADEAS compared to routine monitoring; the ADEAS alerts were related to laboratory value abnormalities such as a decline in renal function or the absence of a medication protective of an AME, providing additional clinical value.<sup>146</sup> The review refers to a number of reports which examine the efficacy of methods to reduce the rate of AMEs such as chart review, trigger tools and incident reporting.<sup>147</sup>

### **Conclusions**

The AHRQ report concludes that, given the diverse interventions used to monitor, detect and prevent AMEs, all interventions have individual benefits and drawbacks. The authors suggest it may be less important for organisations to choose one method as it is to employ several methods, and the authors reiterate the need for amplified research into efficacy.

### *Interventions to improve care transitions at hospital discharge*

The period post-patient discharge is high risk for medication harms. The AHRQ review included interventions targeted at patients discharged from acute care to any community setting with the goals of optimising continuity of care, and preventing AMEs and re-hospitalisation. The review reported on three components of transitional care:

- pre-discharge interventions
- post-discharge interventions
- 'bridging interventions', that is interventions that have intervention components for the patient both before and after leaving hospital.

The review included RCTs and non-randomised clinical controlled trials which evaluated one or more interventions in the adult general medical population, used at least one pre-discharge intervention and reported rates of re-hospitalisation, emergency department visits, and AMEs post discharge. The caveat offered by the authors is that there is no clear consensus about preventable readmission when assessing interventions,<sup>123</sup> and that readmission rates vary between disease specific and

general medical cohorts. Fourteen studies assessed costs, but no studies evaluated the cost of the intervention implementation.

### **Interventions to prevent adverse events after discharge**

Of the 43 studies identified in a systematic literature review, five specifically focussed on adverse medication events. As reported above, a Swedish RCT of 400 people aged 80 years and older that included comprehensive pharmacist intervention resulted in fewer hospital readmissions in this older cohort.<sup>139</sup> In another Swedish cohort of 210 people aged 65 years and over, a prospective controlled study examining the impact of medication reconciliation post-admission was undertaken. Intervention patients received the Lund Integrated Management Model (LIMM) of medication reconciliation at admission and discharge, and additional medication review and monitoring. Control patients received usual care and medication reconciliation on discharge. The result was a significant decrease in the number of inappropriate medicines taken by intervention patients: 51% (95% CI 43-58%) versus 39% (95% CI 30-48%) of control patients. Within three months of discharge, there were six revisits to hospital where the medicine-related causality was rated as possibly, probably or certainly the case in intervention patients, compared to 12 in the control group ( $p=0.0469$ ).

In a cluster RCT with blinded outcome assessment<sup>148</sup> among 631 patients at high risk for readmission, the intervention was a clinical prescriber order entry software application facilitating communication to community pharmacists and clinicians. A letter to the primary care doctor included diagnoses, medication lists and follow-up information. Control patients received usual care. When comparing intervention to control patients there was no difference in hospital readmission rates within six months (37% versus 37.8% 95% CI -0.074-0.065); ED visits within six months (35.4% versus 40.6% 95% CI -0.115-0.011;  $P=0.018$ ); or adverse events within a month (7.3% versus 7.3% 95% CI -0.037-0.043;  $P=0.884$ ). The result could have been associated with the narrow time period for readmission. The authors suggest another contributing factor may have been limitations of the automated decision support: prompts to physicians did not itemise pending tests; the software did not warn physicians of potential medicine-medicine interactions, therapeutic duplications or missing items.<sup>148</sup>

In a prospective cluster randomised study of patients receiving warfarin, the impact of a Pharmacist-Directed Anticoagulation Service (PDAS) on patient transition of care and safety was assessed.<sup>149</sup> The pharmacist collaborated with outpatient anticoagulation clinics in the intervention group; management of anticoagulation for control patients was through the primary care team. The PDAS group at first follow-up visit required significantly less dosage adjustment than the control group. The International Normalised ratio (INR) greater than five occurred less frequently in the PDAS group but did not reach statistical significance. The impact of PDAS was greater in patients whose length of stay was in excess of five days. These results were gained prior to the hospital using an electronic database designed for the management of inpatient anticoagulation with clinical decision support features.

A British study used the Screening Tool of Older Persons (STOPP) criteria to screen potentially inappropriate medicines. In a prospective study of consecutive acute admissions the authors compared the STOPP's screening efficacy in comparison to the Beers criteria.<sup>150</sup> The STOPP criteria identified a significantly higher proportion of patients hospitalised as a result of an adverse event associated with an inappropriate medicine than the Beers criteria (35% versus 25%); medicines were

considered causal or contributory in 11.5% versus 6% of 715 patients with a median age of 77 years.<sup>151</sup>

## Conclusions

The AHRQ review concluded that pharmacist-led interventions do seem to reduce AME rates post-discharge, but that the numbers of these studies from which to draw definitive conclusions remains small, and only a limited number of resource-intensive studies have resulted in reductions of readmission or ED visits.

### *Computerised provider order entry with clinical decision support systems*

The review of patient safety practice undertaken from AHRQ in 2001<sup>124</sup> found a moderate level of evidence for the effectiveness of clinical provider order entry or computer physician order entry with clinical decision support systems for reducing patients harms. In the recent AHRQ review<sup>123</sup> a brief update review was undertaken to update the evidence base.

There were three systematic reviews of inpatient clinical provider order entry or computer physician order entry (CPOE) with clinical decision support systems (CDSS) since 2008 that were considered in the AHRQ review.

One review of ten studies published from 1994 -2006 (none of them RCTs) concluded that CPOE with clinical decision support systems are effective at reducing rates of AMEs; five of the ten studies reported statistically significant reductions in AMEs and four reported non-statistically significant reductions.<sup>152</sup>

Another review found four RCTs (among 27 studies) published between 1998 and 2007 examining prompts and alerts in CPOEs. The types of alerts were basic, for example, medicine allergy warnings, or medicine-medicine interaction alerts, or advanced medicine alerts such as medicine-laboratory alerts or dosing guides. The review concluded that most studies evaluating the effects of computerised prompts demonstrated positive, even substantial, effects but that additional studies are needed to establish the design features most strongly associated with improved clinical and prescribing outcomes.<sup>153</sup>

The third systematic review, concentrating on paediatrics and intensive care units (ICUs) aimed to evaluate the effectiveness of CPOE on medication prescription error, AMEs and mortality in inpatient paediatric care and neonatal, paediatric or adult ICUs. There were 12 observational studies published from 2004 to 2007, no randomised trials and one controlled cross-sectional trial. Despite substantial heterogeneity of studies, the authors performed a meta-analysis to pool outcome measures, revealing a significant reduction in medication prescription errors (RR: 0.08; 95% CI 0.01-0.77). The number of potential and actual AMEs showed a non-significant decrease with CPOE use (RR 0.65; 95% CI 0.40-1.08). The authors concluded that use of CPOE results in reduction of medication prescription error, and in better structured and more legible prescriptions. The authors advocate a large multicentre randomised controlled before/after study of CPOE efficacy, acknowledging the methodological difficulty of doing so.<sup>154</sup>

There were also two recent studies in outpatient settings. One was a quasi-experimental pre- and post-test study on the impact of CPOE on medication errors in 60 community-based US clinics.<sup>137</sup>

This found a marked improvement in legibility, as would be expected in most e-prescribing systems, and significant reductions in medicine-disease and medicine-medicine interaction errors. In a

prospective study of 12 US adult primary-care practices with 30 ambulatory care providers, baseline paper prescriptions for errors, and errors in e-prescriptions 12 months post implementation of an electronic prescribing tool were assessed. A seven-fold reduction in error rates was found in providers of solo and small group community practices using the e-prescribing system.<sup>155</sup> It was noted in the AHRQ review that these two recent studies achieved reductions in prescribing errors but not in clinical AMEs, reflecting the evidence from the inpatient setting.<sup>123</sup>

### Harms

The AHRQ report also examined the potential harms of the patient safety practices, indicating that the increased use of computerised provider order entry (CPOE) and clinical decision support systems (CDSS) has also resulted in increased recognition of the unintended consequences of this technology. In the review these are summarised as:

- more or new work for prescribers
- unfavourable workload issues
- never-ending system demands
- problems related to persistence of paper orders as well as electronic ones
- unfavourable changes to communication patterns and practices
- negative attitudes to new technology
- new types of errors
- unexpected changes to the organisational culture, power structure
- over-dependence on technology
- 'alert fatigue' leading prescribers to ignore some critical alerts.

### Conclusions

The AHRQ review authors state that a decade ago (2001) the "Making Health Care Safer" Report<sup>124</sup> advised that the evidence for benefits of CPOE with or without CDSS was moderate, and that the position now remains the same. The systems do appear to reduce prescription error rates, but there is no clear evidence yet for clinical reduction of AMEs. There is also potential for CPOE with CDSS to affect clinician workflow and patient care adversely. Close attention to the design and implementation of this technology is required to prevent these unintended consequences.

## Medication safety intervention strategies: the international evidence and implications for the Australian healthcare setting

### Patient safety practices encouraged for adoption now

As described above and following completion of the AHRQ review, an expert international panel considered the strength and quality of evidence for patient safety practices in terms of implementation and effectiveness. Based on these criteria, the panel developed a list of 22 patient safety practices it considered should now be encouraged for adoption.<sup>126</sup> Four of these practices are relevant to medication safety. The implementation of 'Do Not Use' lists for hazardous abbreviations was strongly encouraged and the use of clinical pharmacists to reduce adverse medication events, medication reconciliation and computerised provider order entry were encouraged.



### ***'Do Not Use' lists for hazardous abbreviations***

In the AHRQ review it was stated that while various organisations have taken a strong stand against the use of certain abbreviations used in medication prescribing/ordering, the evidence on implementation methods is limited. It was suggested that a 'low-cost approach of implementation, such as through ongoing educations and/or feedback, focused on avoiding selected harmful abbreviations whenever and wherever possible seems reasonable and feasible'.

As indicated in Part 1 of this report (Factors associated with medication-related errors during patient admission) a study at three Australian hospitals found a high rate of error-prone abbreviations. Overall, 8.4% of orders contained error-prone abbreviations and 77% of patients' charts contained at least one error prone abbreviation. In total, 29% were considered high risk abbreviations.<sup>156</sup>

The Australian Commission on Safety and Quality in Health Care has published recommendations for terminology, abbreviations and symbols used in medication prescribing and administration.<sup>157</sup> The international evidence supports the implementation of this medication safety practice. Future research could focus on the best strategies to implement these recommendations in the Australian healthcare setting and the impact of these on rates of hazardous abbreviations, medication errors and patient harm.

### ***Clinical pharmacists to reduce adverse medication events***

Systematic reviews and more recent studies included in the AHRQ review generally support the role of clinical pharmacists in reducing adverse medication events. International evidence supports clinical pharmacist involvement in ICUs, in particular their involvement in bedside rounds, while evidence for other inpatient and outpatient settings was found to be less robust.

In Australia, clinical pharmacists have an established role in improving patient safety in the acute care setting. Most Australia studies examining the impact of clinical pharmacist services have used uncontrolled pre-and post-intervention designs or have been studies in which interventions undertaken by clinical pharmacists have been independently reviewed in order to assess their clinical significance<sup>4</sup>. More recent studies (Part 2 of this report) of hospital pharmacist services have focussed on the role of the pharmacist in the transition between the hospital and other healthcare settings as well as between different units within the hospital. There are still limited studies assessing actual patient safety outcomes and AMEs in the Australian setting.

### ***Medication reconciliation***

The AHRQ report suggests the strength of evidence for effectiveness of medication reconciliation is moderate. When considered as a sole intervention, medication reconciliation was not found to reduce hospitalisation rates within 30 days, though it may do so over longer time frames or when used as part of a multifaceted intervention. Most studies included in the review of international evidence involved pharmacists as the primary provider of the service. The authors indicated that 'the paramount issue becomes how to target medication reconciliation in order to direct resources most efficiently'.

An international review of medication reconciliation interventions in the primary care setting<sup>141</sup> was published in 2009. It found that included studies had significant design flaws and there was currently



a lack of quality evidence demonstrating the effectiveness of medication reconciliation in primary care.

Medication reconciliation has been recognised as a priority medication safety strategy for Australia. Australia is a partner in the World Health Organisation High 5s Project which focuses on medication reconciliation. This project is targeting medication reconciliation at transition points of care. As detailed in Part 2 of this report, there is now research evidence from a number of studies in the Australian healthcare setting showing that medication reconciliation services involving pharmacists improve the accuracy of the medication history. Larger studies assessing the impact on adverse events and patient outcomes still need to be undertaken in the Australian setting. Medication reconciliation in conjunction with pharmacist prescribing in the perioperative setting in Australian hospitals has shown improvements in surrogate endpoints such as medication charting error and communication error. Further studies are needed examining actual patient outcomes including adverse medication events and application in a larger sample of patients and hospital sites. In keeping with the international findings, there is also a need to examine how best to resource these services and whether other healthcare professionals can also conduct these services. Further studies on medication reconciliation services in the Australian primary care setting are also required.

### *Computerised provider order entry (CPOE)*

The AHRQ review authors found that the strength of the international evidence for effectiveness of computerised provider order entry (CPOE) with or without clinical decision support systems (CDSS) was moderate. A decade of research since the previous AHRQ report in 2001 has not changed the assessment of the evidence base. The systems were found to reduce prescription error rates, but there was no clear evidence for reduction of AMEs. It was also noted that there is significant potential for CPOE with CDSS to adversely affect clinician workflow and patient care with a need for close attention to the design and implementation of this technology.

In the Australian setting (as described in Part 2 of this report), a number of studies have been published since 2008 describing the implementation of electronic prescribing (e-prescribing or CPOE) in acute care and assessing its impact on prescribing errors. The studies provide Level III-2 and III-3 evidence supporting the effectiveness of CPOE in reducing prescribing errors, particularly procedural errors. The impact on clinical errors is less clear. The e-prescribing systems did not have the substantial CDSS that may be needed to see further reductions in clinical errors. In keeping with the international evidence, further research in the Australian setting may need to be undertaken to consider system-related errors and the further refinement of system design and training for these systems in Australian hospitals. One strategy for improving the useability of CPOE systems discussed in the AHRQ report was the use of human factors and ergonomics frameworks.

### *Interventions recommended as priorities for future research*

Following the AHRQ review, high priority areas for future research in patient safety were also identified, and four of the priority areas are relevant to medication safety. In addition to medication reconciliation (already discussed above), the three following areas were considered priorities for research: interventions to improve post-discharge transitions, measures to encourage a culture of patient engagement and the use of human factors engineering and ergonomics in the design of healthcare practices.

### *Interventions to improve post-discharge care transitions*

The AHRQ review recommended further research into interventions that improve transitions between the hospital and community settings. While it was found that pharmacist-led interventions do seem to reduce AME rates following hospital discharge, the number of these studies remains small, with only a limited number of resource-intensive studies showing reductions in readmission or emergency visits.

In the Australian setting, the previous review of medication safety in acute care and Part 2 of this report have included controlled studies undertaken to assess the impact of discharge medication management services implemented by pharmacists or by pharmacists and nurses. These have been shown to improve patient outcomes and reduce undesirable medication events. A recent pre- and post-intervention study to improve the transition from hospital to aged care assessed the impact of pharmacist-prepared interim residential care medication administration charts on the timeliness of medication administration on transfer. The chart resulted in significantly less patients having delayed doses of medicines and significantly less ‘workaround’ practices by residential aged care staff to avoid missed doses. In keeping with the international evidence, there is a need to examine the effect of these services on actual patient outcomes including adverse medication events and its application in a larger sample of patients and hospital, community or aged care sites.

### *Measures to encourage a culture of patient engagement in patient safety*

The international review found that few studies have been published on the effectiveness of patient and family engagement as a patient safety strategy. Despite the lack of clear evidence of effectiveness for interventions engaging patients and families, the AHRQ review and expert panel considered this an important emerging area requiring further research. A particular intervention called the Care Transitions Intervention has been shown to reduce rates of hospital readmission and to improve patients’ confidence in medication self-management.

In the Australian setting some intervention studies with a patient-centred approach have been undertaken, such as small studies of a Practice Partnership Model of Care<sup>122</sup> and patient medication self-administration in hospital.<sup>158</sup> However these have assessed only limited medication safety outcomes. There is a need for further research in the Australian setting on patient-centred approaches to medication safety either alone or in conjunction with other medication safety strategies.

### *Use of human factors engineering and ergonomics in the design of healthcare practices*

The AHRQ review concluded that “HFE [Human Factors Engineering] is a core element of patient safety improvement; therefore, every effort should be made to support HFE applications in patient safety.” Further research is needed to demonstrate the value of HFE-based interventions on patient safety outcomes including in the Australian healthcare setting. This should include changes in the work-system, changes in the processes and changes in outcomes (for both patients and healthcare providers).

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## Appendix I

### Method:

**Method:** Evidence from 2008 to present for Australian data on medication safety was sought from the following databases: Medline (including Pubmed); Embase; Cinahl; Informit; and Joanna Briggs Institute (JBI) Database. Criteria for inclusion of studies are that the studies address adverse medicine events; adverse drug reactions or medication incidents as a result of the therapeutic prescribing, dispensing and or administration of medicine.

To identify publications about incidence the following terms were used (phrase followed by / denotes subject heading, \* denotes a truncation in a keyword search): Medication Errors, Medication Reconciliation;/ Medical Errors, Diagnostic Errors;/ Safety Management, Quality of Health Care ; Drug Toxicity;/ Quality Assurance, Health Care;/patient\* safety; medication\* safety; patient\* safety; Adverse Drug Events;/ adverse drug event\*; adverse drug react\*; medication mishap\*; medica\* incident\*; medica\* mishap\*; medica\* mistake\*; medica\* misadventure\*; drug misadventure\*; drug\* toxicity; medication related harm\*; medication related incident\*; medication related problem\*; medication reporting system\*; pharmaceutical reporting system\*; medic\* prescri\* error\*; drug\* prescri\* error\*; prescri\* error\*; medica\* dispensing error\*; drug\* dispensing error\*; dispensing error\*; medication\* administra\* error\*; drug\* administra\* error\*; administra\* errors\*; medication\* related admission\*; drug related admission\* or patient transfer; key words above and incidence; prevalence; rate\*; Drug Substitution;/ therapeutic shift\*; brand substitution\*; generic substitution.\*

To identify publications for specific intervention strategies the following terms were also been used (phrase followed by / denotes subject heading, \* denotes a truncation in a keyword search):

Clinical Pharmacy Information Systems;/ Medication Errors;/ Medication Systems, Hospital;/ Medical Order Entry Systems;/ Medical Records Systems, Computerized;/ Decision Support Systems, Clinical;/ Electronic Prescribing;/ e-prescri\* ; electronic prescri\*; computer\* decision support\*; Safety Management;/ error reduc\*; bar cod\*; Drug Packaging/ [Adverse Effects, Supply & Distribution]; robot\* distribution or automat\* distribution; individual patient supply; self\* administrat\*; clin\* pharmac\* service\*; Pharmacy Service, Hospital;/ Community Pharmacy Services/ Pharmaceutical Services;/ Medication Therapy Management;/ medicat\* review\*; SMS\*; smart\* device\*; medication reconciliation; Medication Reconciliation;/ automat\* dispens; continuous quality improvement; Quality Improvement/ continuity of care;. Continuity of Patient Care/); Liaison; hospital transfer; hospital to home; hospital to aged care;

The literature was restricted to studies in the Australian healthcare setting using the terms: Australia/ or Australian Capital Territory/ or New South Wales/ or Northern Territory/ or Queensland/ or South Australia/ or Tasmania/ or Victoria/ or Western Australia/ or Australia or Victoria or Tasmania or New South Wales or Queensland or Australian Capital Territory or Australia\*.

Selected international literature was confined to meta-analyses or systematic reviews of controlled trials that measure at least one patient health outcome. In combination with the search terms listed above the following terms have been used (random\* controlled trial\* or control\* trial\* or systematic

review\* or meta-analys\*) AND medicine or medicat\* or drug or prescrib\* or precrip\* or dispens\*.  
The Cochrane database systematic reviews were searched using Cochrane Database MESH headings including medication error, medical order entry systems; medication review.

The database search was supplemented with searches of relevant websites, including:

Australian Commission on Quality and Safety in Health Care [www.safetyandquality.gov.au/](http://www.safetyandquality.gov.au/)

Advanced Incident Management Systems (AIMS) reports, incident reporting systems and or sentinel event reporting systems from Australian jurisdictions including the Victorian Department of Health [www.health.vic.gov.au/clinrisk/publications/sentinel-anrep.htm](http://www.health.vic.gov.au/clinrisk/publications/sentinel-anrep.htm)

Australian Institute of Health Innovation (AIHI) Centre for Health Systems and Safety Research (CHSSR) at the University New South Wales (UNSW) [www.aihi.unsw.edu.au/chssr](http://www.aihi.unsw.edu.au/chssr).

Roadmap of Australian Primary Health Care Research (ROAR) [www.phcris.org.au/roar/index.php](http://www.phcris.org.au/roar/index.php)

The Family Medicine Research Centre Bettering the Evaluation and Care of Health (BEACH) <http://sydney.edu.au/medicine/fmrc/beach/>

The Australian Institute of Health and Welfare (AIHW) [www.aihw.gov.au/sqhc-other-information/](http://www.aihw.gov.au/sqhc-other-information/)

### **Incidence of medication-related harm in Australia**

Papers about incidence of medication safety or harm occurring in Australian hospitals including studies of prescribing errors after emergency department admissions or rates of transcription errors on discharge were included, as were studies of incidence of medication safety or harm incurred during hospital in the home. Papers about medication safety in aged care facilities, including studies of administrative errors found in audits of aged care facility dose administration aid packages were reviewed as were studies assessing the incidence of medication safety issues in the community.

### **Interventions to reduce medication-related harm in Australia**

Australian interventions which met the following criteria were selected: English language; conducted in the community, hospital or ambulatory care settings; and measured at least one patient outcome e.g. medicine-related hospitals admissions; adverse events; mortality; decreased quality of life; symptoms; surrogate health endpoints e.g. BP control; cholesterol; blood glucose level); medication knowledge or changes in the quality of medicine use. Papers which meet these criteria describing strategies to reduce rates of medication adverse events, such as prescribing indicator tools; clinical pharmacist services, computerised decision support measures, electronic prescribing and multifaceted approaches will be included.

### **International Interventions to reduce medication-related harm**

Descriptions of evidence-based international interventions aimed at reducing rates of medication error were obtained from systematic reviews of controlled trials in the international literature, and overseas conducted controlled trials published in English.

## Appendix II

### NHMRC Evidence Hierarchy

Designations of levels of evidence for intervention studies

Level	Intervention
I	A systematic review of level II studies.
II	A randomised controlled trial.
III-1	A pseudo-randomised controlled trial (i.e. alternate allocation or some other method).
III-2	A comparative study with concurrent controls: Non-randomised experimental trial; Cohort study; Case-control study; Interrupted time series with a control group.
III-3	A comparative study without concurrent controls: Historical control study; Two or more single arm study; Interrupted time series without a parallel control group.
IV	Case series with either post-test or pre-test/post-test outcomes.