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LA		✓	✓	✓	✓	✓
PL		✓	✓	✓	✓	✓
DL		✓	✓	✓	✓	✓
DS		✓	✓	✓	✓	✓
RS		✓	✓	✓	✓	✓
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Comprehensive identification of medication-related problems occurring prior to, during and after leaving the emergency department: an Australian multicentre, prospective, observational study.

Abstract

Background:

Patients present to Emergency Departments (ED) with various medication-related problems (MRPs). MRPs are also associated with ED care, occurring during ED presentation or shortly afterwards.

Objective:

To describe the prevalence and nature of MRPs that occur prior to, during or shortly after leaving ED.

Methods:

We undertook a prospective, observational study in nine Australian EDs. Blocks of 10 consecutive adult patients who were not seen by a pharmacist in ED and who presented at pre-specified times were identified. Within one week of ED discharge, a pharmacist interviewed patients and undertook a medical record review to determine their medication history, patients' understanding of treatment, potential MRP risk factors and manage any identified MRPs.

Results:

904 patients were recruited: 14.8% aged ≥80 years, 18.9% taking >8 regular medications. 581 MRPs were identified; 287 (49.4%, 95%CI 45.3-53.5%) of moderate-high significance. Most highly significant MRPs involved high risk medications, particularly strong opioids, insulin and anticoagulants. The most common types of MRPs were prescribing errors (46.8%), patient adherence/knowledge issues (31.2%) and adverse drug reactions (7.4%). Of all patients, 381 (42.1%, 95%CI % 38.9-45.5) had at least one MRP; 31.4% (95%CI 28.4-34.6%) had MRPs that could be identified or managed by screening at ED presentation and 12.4% (95%CI 10.4-14.8%) had MRPs that could be identified or managed by screening at ED discharge.

Conclusions:

Patients experienced a range of MRPs throughout the ED continuum of care. From these data, screening tools will be developed so that ED clinicians may identify patients at greatest risk of MRPs.

Key words:

Medication-related problems, adverse drug events, emergency department, continuum of care

Introduction

It is well established that moving from one clinical setting to another is a high risk time for medication-related problems (MRPs); more than one half of MRPs occur at transitions of care.[1,2] It has been estimated that each year in Australia, 250,000 hospital admissions and 400,000 emergency department (ED) presentations are likely to be due to MRPs.[3,4] Medication-related hospital admissions in Australia have been estimated to cost $1.4 billion annually.[3] Medication safety has been identified by peak national and international bodies to be a high priority.[5,6]

Many ED patients present with a range of MRPs, but in 20-50% of cases these are neither identified nor addressed by ED medical staff.[7] Patients are at risk of developing MRPs across the continuum of care, from initial presentation, during their ED stay and following discharge from the ED. They may develop MRPs after they enter the ED, associated with the ED care;[8,9] such as new medications being initiated without full knowledge of which medications are already taken. Patients may also develop MRPs during their ED stay due to failure to continue time-critical regular medications taken prior to the ED presentation, including anti-Parkinsonian or antidiabetic medications. Failure to continue such medications may result in delayed ED discharge. Finally, after patients leave the ED and return home, they may develop MRPs due to a lack of adequate explanation about medications started in ED or regimens changed during the presentation. Prescribing errors are common when patients are admitted to hospital and a major contributing factor to such errors is failure to accurately identify what medications a patient took prior to presentation.[10]

Minimising medication related harm in ED can be time consuming and complex.[11,12] There are several reasons for this complexity. In a study of older patients, only 15% of those interviewed could list their

medications (including doses, frequencies and indications).[13] Most sources of medication regimen information available in ED have several discrepancies and cannot be relied upon in isolation.[14] ED doctors have been reported to obtain correct medication histories in only 12.5% of cases.[15]

Several studies have evaluated the prevalence of MRPs resulting in presentation to ED or occurring at the time of hospital inpatient admission.[1-4, 7-9, 11, 12] These studies have not included MRPs occurring during an ED presentation or shortly after discharge back to the community. This gap in our comprehensive understanding of MRPs occurring across the ED continuum of care exists partly because these data are very labour intensive to collect and need to be undertaken by investigators with detailed medication management expertise. Such data cannot be reliably collected using retrospective chart review given so many MRPs are not identified, managed and therefore documented during routine ED care. The aim of this study was to comprehensively describe the prevalence and nature of MRPs occurring prior to, during the ED stay or shortly after leaving the ED and returning to the community or after leaving the ED and being admitted to a hospital ward.

MRPs were defined as 'all circumstances involving a patient's drug treatment that actually, or potentially, interfered with the achievement of an optimal outcome'.[16,17] MRPs included prescribing errors, demonstrated non-adherence, significant knowledge deficits, and/or adverse drug reactions, as detailed in box 1. This study sought to include different types of EDs (metropolitan and regional) from a range of states to optimise generalisability. Patients were identified retrospectively, but followed up prospectively after leaving ED to allow the natural course of events to occur without the pharmacists collecting data being ethically compelled to intervene to prevent MRPs during the ED presentation. This also allowed patients who presented to ED across all times and days to be recruited, rather than solely during pharmacists' working hours.

This paper describes the prevalence of a variety of potential risk factors for MRPs. It is part of a larger piece of work that will use these data in regression analyses to develop screening tools to target patients at risk for MRPs. As the pharmacist workforce is unable to review all ED patients, the identification of patients at risk will allow these patients to be targeted by ED pharmacists. The data in this paper may also be used to determine whether the screening tools, once developed, are generalizable to specific EDs.

Methods

We undertook a prospective, observational study in nine Australian EDs across Victoria (Austin Hospital, Casey Hospital, Dandenong Hospital, The Northern Hospital, University Hospital Geelong), New South Wales (Manly Hospital and Prince of Wales Hospital) and Tasmania (Launceston General Hospital). Hospitals were a mix of metropolitan and regional institutions with an annual census range in 2016-17 of 25 – 92 thousand presentations (further details available in Appendix 1). An expression of interest to participate in the study was posted on the Society of Hospital Pharmacists of Australia Emergency Medicine Discussion Forum. Sites who expressed interest needed to be able to achieve local governance approval and have pharmacist(s) available to collect the data. The lead hospital was Austin Health and their ethics committee approved the study for all sites, whilst each participating hospital provided governance approval. Data collection commenced once governance approval was obtained and at a time when staff were available to undertake patient recruitment. Patients were recruited between July 2016 and August 2017.

At each site, blocks of ten consecutive adult patients presenting to the ED at pre-specified times across all days of the week, were identified retrospectively by an investigator pharmacist. The times were identified from a random number table and covered the entire 24-hour period. Investigators started at the specified time and continued identifying consecutive eligible patients until ten patients were recruited for the time-period. Patients were excluded if they were aged less than 18 years, did not wait to be seen by an ED clinician, were seen by a pharmacist in ED, were deemed inappropriate to interview within seven days of presentation (e.g. documented severe aggression or mental health crisis), were transferred from ED to another hospital, or died in the ED. Patients seen by a pharmacist in ED were excluded, as a core role of these pharmacists is to identify and prevent MRPs associated with the ED continuum of care.

Within 24-48 hours after ED discharge, the investigator pharmacist collected data from the hospital medical record using an explicit data collection tool and standardised instructions. For patients admitted to an inpatient ward, a face-to-face patient and/or carer interview was undertaken by an investigator or hospital ward pharmacist. For patients discharged from ED to the community, a telephone interview was undertaken by an investigator pharmacist. Where possible, this interview was conducted 24-48 hours after leaving the ED. If this interview could not be undertaken within seven days of ED discharge, the patient was deemed lost to follow-up. For patients whose data were collected as part of a telephone interview, verbal patient consent was required. Interviews conducted by ward pharmacists formed part of the pharmacists' routine patient admission process, therefore verbal consent to be involved in the study was not required. During the interview, data extracted from the medical record were verified, a best possible medication history was determined, the patient's understanding of any new medication therapy was assessed and any potential MRPs were identified.

Data were collected on the nature of MRPs identified and a number of potential risk factors affecting the study outcome measure including patient, medication-related and ED presentation/environmental factors. Patient variables included age, gender, presenting complaint, benefit card status, private insurance status, language/s spoken at home, need for an interpreter, social status such as living alone or with others, and cognitive and sensory problems. Medication-related variables included the number and nature of regular medications taken prior to ED presentation, prescription of high risk medications prior to and during the ED presentation, allergy status, the number and nature of medications prescribed in the ED, complex medication initiation in ED, the person who organised the medications at home, medication adherence, use of dose administration aids and whether prescriptions were dispensed at more than one pharmacy. ED presentation and environmental variables included triage

category, mode of presentation, day and time of presentation, presenting complaint, time of discharge, disposition, duration of stay in ED and whether the patient's care was handed over during a change of ED medical shift. Data collection sheets were reviewed for completeness by a lead investigator; site investigators were asked to provide missing data and to clarify any ambiguities.

The primary study outcome was the presence of MRPs. If an MRP was identified during the interview, the patient's usual doctor or specialist was advised by the patient or pharmacist, as appropriate. Two senior emergency medicine pharmacists not involved in the patient's ED care independently reviewed all MRPs. This review confirmed or excluded potential MRPs, determined their clinical significance and classified them according to whether there were problems that could have been identified, managed or prevented by screening at the time of ED presentation or at the time of ED discharge, as detailed in box 2. Where there was a discrepancy of opinion, this was resolved by consensus between the two assessors. Significance of MRPs were assessed as 'low', 'moderate' and 'high' using the Society of Hospital Pharmacists of Australia consequence-probability matrix.[18]

The sample size for this prospective study was calculated to adequately inform the development of screening tools to be used early in the ED presentation and at the time of ED discharge. Given the resources of the 9 participating EDs, we believed that each site was likely able to recruit an average of at least 100 patients. With a target sample size of 900, we would be 95% certain that the incidence of MRPs would lie +/- 1.8% of an incidence of 7.5% obtained in our pilot study. This precision (+/- 1.8%) was thought to be more than adequate in order to obtain meaningful results. The precise number of patients recruited by each site varied according to each site's capability (see Appendix 1 for further details).

Statistical analysis was undertaken at the patient and the medication level. Descriptive statistics were used for continuous variables and frequencies for categorical variables. Data were analysed using IBM Statistical Package for the Social Sciences (SPSS, version 25).

Results

Overall, 904 adult ED patients were recruited (figure 1). Proportion of patients lost to follow-up did not differ from those recruited in terms of gender or triage category ($p>0.05$), but a significantly greater proportion of patients discharged directly from ED and those in the younger 18-49 year old age group were lost to follow-up. Patient, medication and ED environment specific characteristics are summarised in table 1 (comprehensive details are included in Appendix 2). Approximately one third of patients were aged over 65 years of age. Almost one half held a pharmaceutical benefit entitlement card, whilst one quarter had private health insurance. Over three quarters of patients lived at home with family or in supported accommodation, while 1 in 20 were from a residential care facility. Half were discharged home directly from ED, while one third were admitted to an inpatient ward and the remainder to a short stay unit.

The ED presentation was medication related for 68 (7.5%, 95% CI 5.9-9.5%) patients. These included adverse drug reactions (20 patients), medication adherence issues (17), complications of recreational drug use (8), intentional or unintentional overdoses (6) and other adverse medication events (17). In only 13 of the 68 (19.1%) cases were all of these patients' MRPs identified in ED.

One or more MRPs were identified during the pharmacist medication review in 381 (42.1%, 95% CI 38.9-45.5%) patients (table 2). One or more MRPs that could have been identified or managed by screening early in the ED presentation were identified in 284 (31.4%, 95% CI 28.4-34.6%) patients. One or more MRPs that could have been identified or managed by screening at the time of ED discharge were identified in 112 (12.4% 95% 10.4-14.8%) patients.

Amongst the 381 patients who had one or more MRPs identified, a total of 581 MRPs were identified. The most common MRPs were prescribing errors, which comprised almost half. Approximately one third related to adherence issues or an inadequate patient understanding of how to manage medications prescribed in ED that needed to be taken after discharge. Adverse drug reactions comprised 7.4% of MRPs and affected 4.4% of patients. Of the 381 patients who had one or more MRPs identified, 25 (6.6%) patients had all of their MRPs identified during the ED presentation. In contrast, 356 (93.4%) patients had one or more MRPs identified after the ED presentation – these were not identified or anticipated in ED.

Highly significant MRPs comprised 12.7% (95% CI 10.6-15.1%) of MRPs and most often involved high risk medications, particularly anticoagulants, strong opioids and insulin (see Appendix 3). Approximately one third of MRPs were of moderate significance, while half were of low significance for patient harm if not identified in ED; these mostly comprised omission of regular medications that could be inadvertently omitted for up to a week without significant patient harm. Of the 74 highly significant MRPs, 61 (82.4%) could have been identified, managed or prevented at the time of ED presentation.

Discussion

Several studies have reported medication related adverse events that have caused presentation to ED or medication errors occurring as patients are admitted from ED to hospital.[1-4, 7-9, 11,12] However, to our knowledge, our study is the first that has described the spectrum of MRPs; those associated with presentation to ED, occurring during the ED presentation and those occurring within the first week after ED discharge. We also believe it is the first to follow-up both patients hospitalised from ED and those discharged back to the community.

Across the spectrum of the continuum of care, MRPs are common, with at least one such problem being identified in 42.1% of patients. The majority of problems could be identified, managed or prevented by screening early in the ED presentation, for example during the initial nursing cubicle assessment. A smaller number arose from decisions made as patients were discharged from ED and could be managed or prevented by screening at the time of ED discharge or follow-up in the days after the ED presentation.

Just over one quarter of patients had one or more MRPs that were moderately or highly clinically significant. Whilst half of the MRPs were assessed to be of low significance for patient harm, these are still important to minimise, for their propensity to cause patient confusion regarding their medication taking routine.[19] When health professionals are keen to encourage their patients to be adherent, inadvertent omissions of regular medications as patients present to hospital may send mixed messages about the importance of meticulously continuing prescribed medications.

In our study, 39.4% of patients had one or more MRPs identified during the pharmacist review that were not identified during the ED presentation. This finding is consistent with other studies that

showed in up to half of cases where patients presented to ED with MRPs, ED medical staff did not identify or manage these as part of the presentation.[8] To comprehensively identify MRPs across the community-hospital continuum of care is labour intensive and is best documented by those with a specific medication focus, such as pharmacists.[8] Currently available national data are incomplete, as these data only include those problems *identified* during an ED or hospital presentation.[20]

Limitations

Strengths of this study are that multiple sites and states were included. A further strength was that MRPs were identified for patients admitted to hospital as well as those discharged back to the community from ED. Additionally, we attempted to recruit consecutive patients across the 24-hour period and seven days per week. However, the study had limitations. The variability of governance requirements across states and individualised requirements of specific sites precluded more sites being involved. In addition, delays at several participating sites meant that staff availability had evolved by the time approval was achieved, which precluded some sites recruiting their target number of patients. Although we identified a consecutive sample of patients, approximately one fifth of eligible patients were lost to follow-up. Those discharged home were more likely to be uncontactable within seven days and those in the younger age group were more likely to decline consent as the study was less relevant to them. Loss of these patients has the potential to over-estimate the prevalence of MRPs. Our sample may not be generalisable to the specific medication issues encountered in Aboriginal and/or Torres Strait Islander communities, private hospital EDs and those with limited hospital pharmacist availability. As we were unable to conduct a home visit or face-to-face interview for patients discharged directly from ED, relying instead on telephone interviews, we may have under-estimated the prevalence of MRPs. Although some authors have suggested roles for ED pharmacists in minimising time to administer critical medications, such as thrombolysis in stroke,[21] our study did

not include such delays as MRPs, because we were unable to systematically identify these delays, with our methodology. Similarly, our methodology has likely under-estimated the prevalence of administration and dispensing errors, due to difficulties in identifying these errors after the ED presentation if they were not identified and documented during the presentation.

Conclusions

MRPs occurring prior to, during and shortly after ED presentation are common amongst patients presenting to ED. Often such MRPs are not identified during the ED presentation, therefore the opportunity to prevent or address such problems is missed. These data will be used to develop screening tools to identify patients at greatest risk for MRPs across the continuum of ED care to ensure that these patients receive particular attention to minimise the risk of such problems.

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Box 1: Definition of types of medication related problems

1. Prescribing errors:

- May occur on the admission medication chart.
  - Detection of such errors by a pharmacist led to a change to the patient's medication regimen in collaboration with the inpatient medical team.
- May occur when patients are discharged directly from the ED to the community.
  - Such errors were defined as those identified or corrected by the pharmacist during the telephone follow-up, in collaboration with the patient, community pharmacist and/or general practitioner (GP).
- Prescribing errors comprised wrong or omitted medication, dose or frequency; unnecessary treatment (ceased medication charted); wrong form or route of administration, and wrong patient.

2. Adverse drug reactions:

- Defined as a response to a medication, which was harmful and unintended and occurred at normal doses, i.e. the right medication was used for the right indication in the right dose and route but the patient still suffered harm.

3. Administration errors:

- The correct regimen was prescribed but an incorrect regimen was administered. These included an omitted dose or an extra dose, wrong time, administering to the wrong patient, wrong infusion rate, route (different from that prescribed), technique, dosage-form or preparation.

4. Drug-drug interactions:

- These were those interactions deemed clinically significant or having the probability of harm according to the evidence-based guidelines specified in the Australian Medicines Handbook,[22] Lexicomp Online[23] and/or Stockley's Drug Interactions.[24]

5. Significant knowledge deficit:

- Patients were asked to state the name, dose regimen or how to take/administer the medication and the indication for any newly prescribed medication.
- Where the patient taking the medication regimen, or the carer responsible for giving the regimen after ED discharge, was unaware of the significant aspects of the medication taking process for a new medication prescribed in ED, this was defined as an MRP. Significant aspects were those deficits were patients could experience harm due to their lack of knowledge, e.g. incorrect number of doses of glyceryl trinitrate prior to calling an ambulance.
- Knowledge was not assessed for patients admitted to an inpatient ward who were prescribed medications in ED, as these medications could change during the inpatient admission and the ED was not considered the optimal time to teach patients being admitted to a ward about new medications.

6. Demonstrated non-adherence:

- Where non-adherence to the medication regimen was identified, that could potentially have contributed to the need for an ED presentation or other medical follow-up, this was deemed an MRP.

7. Clinical handover issue:

- Where a significant change was made to a patient's medication regimen in ED that the GP should be aware of so that they can provide optimal ongoing care, the ED doctor should document this in the ED discharge summary.
- If an ED doctor failed to inform the GP that a short-term, minor symptomatic treatment was started, such as a simple analgesic or antacid, this was not considered significant. Those that were considered significant were failure to notify that an antibiotic or strong opioid was prescribed, or a medication was initiated or dose changed that the GP may need to further titrate, such as insulin or an antihypertensive.

Box 2: Classification of medication related problems according to when they could be managed or prevented

ED presentation:

- MRPs that occurred prior to ED presentation, or occurred in ED that could have been prevented had a medication review occurred early in the ED presentation.
- Examples:
    - Failure to continue time critical regular medications during the ED presentation, such as insulin or antihypertensives.

ED discharge:

- Those MRPs that could be managed or prevented by screening the patient at discharge.
- Examples:
    - Changes were made to the medication regimen that the patient was to take after leaving ED, but the patient did not implement the change. This lack of implementation may have been due to inadequate patient education or inadequate continuum of care planning, such as notifying a community pharmacy that the regimen in the dose administration aid that they filled had changed.

Figure 1 – Patient recruitment

Table 1 – Patient, medication related and ED presentation characteristics

	Number (%, 95%CI) n=904
i. Patient characteristics	
Age category	
18 – 39 years	288 (31.9, 28.9-35.0)
40 – 64 years	279 (30.9, 27.9-34.0)
65 – 79 years	203 (22.5, 19.8-25.4)
80 years and older	134 (14.8, 12.6-17.4)
Gender, male	457 (50.6, 47.2-53.9)
Pharmaceutical benefits entitlement card holder (Pension/concession)	407 (45.0, 41.8-48.3)
Private Health Insurance	239 (26.4, 23.6-29.5)
Communication difficulties for medical or language reasons - patient unable to describe their medication history in English	207 (22.9, 20.2-25.8)
Living arrangement prior to presentation	
Home alone, homeless	147 (16.3, 14.0-18.9)
Home with family, friends, supported accommodation	713 (78.9, 76.0-81.5)
Residential care facility	44 (4.9, 3.6-6.5)
ii. Medication characteristics	
Medication-related reason for ED presentation	68 (7.5, 5.9-9.5)
Number of regularly scheduled medications taken prior to presentation	
No medications	241 (26.7, 23.8-29.7)
1-3 medications	254 (28.1, 25.2-31.2)
4-8 medications	238 (26.3, 23.5-29.4)
More than 8 medications	171 (18.9, 16.4-21.7)
Taking a high risk medication prior to presentation	230 (25.4, 22.7-28.4)
Anticoagulant	68 (7.5, 5.9-9.5)
Insulin	48 (5.3, 4.0-7.0)
Regular strong opioid	70 (7.7, 6.1-9.7)
Other	44 (4.9, 3.6-6.5)
Person who organises the medications at home	
No medications taken prior to presentation	238 (26.3, 23.5-29.4)
Patient	519 (57.4, 54.1-60.7)
Carer (sometimes with some patient involvement)	103 (11.4, 9.4-13.7)
Health professional	44 (4.9, 3.6-6.5)
iii. ED presentation/environmental characteristics	
Australasian Triage Category	
Category 1, 2	134 (14.8, 12.6-17.4)
Category 3	418 (46.2, 43.0-49.6)
Category 4, 5	352 (38.9, 35.8-42.2)
Mode of presentation	
Self/private vehicle	612 (67.7, 64.5-70.7)
Ambulance	290 (32.1, 29.1-35.3)

Police	2 (0.2, 0.04-0.89)
Disposition from ED	
Home	451 (49.9, 46.6-53.2)
Short stay unit	165 (18.3, 15.8-21.0)
Ward	281 (31.1, 28.1-34.2)
Intensive care unit	7 (0.8, 0.3-1.7)

Table 2 – Nature of medication-related problems identified during pharmacist medication review

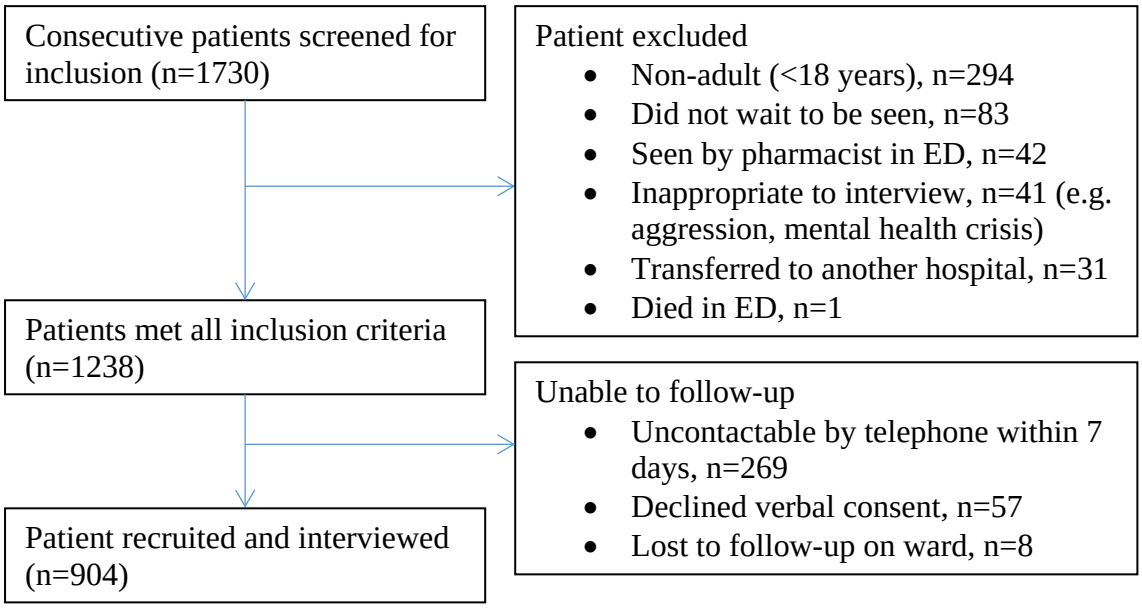
	Number of patients with one or more such problems (n=904)	**Number of such medication related problems (n=581)**
Type of medication related problem, n (%) [range per patient] †		
Prescribing error	171 (18.9)	272 (46.8) [0-6]
Adherence/knowledge issue	155 (17.1)	181 (31.2) [0-2]
Adverse Drug Reaction	40 (4.4)	43 (7.4) [0-1]
Drug-drug interactions	14 (1.5)	15 (2.6) [0-2]
Medication administration errors in ED	10 (1.1)	10 (1.7) [0-4]
Other*	58 (6.4)	60 (10.3) [0-2]
Significance of medication related problems, n (%) [range per patient]†		
Low significance	220 (24.3)	294 (50.6) [0-4]
Moderate significance	179 (19.8)	213 (36.7) [0-5]
High significance	60 (6.6)	74 (12.7) [0-4]
Time point in ED presentation when medication related problem could be identified or managed, n (%) [range per patient]		
ED presentation/cubicle assessment	284 (31.4)	455 (78.3) [0-6]
ED discharge	112 (12.4)	126 (21.7) [0-2]
Medication related problem/s identified *during* the ED presentation, n (%)		
All MRPs identified in ED	25 (2.8)	
Not all MRPs identified in ED	356 (39.4)	

No MRPs identified during pharmacist review after ED presentation	523 (57.9)

* unable to determine whether prescribing or patient knowledge issue; swallowing difficulty; failure to inform general practitioner of significant prescription in ED that patient was to take after discharge such as insulin, oxycodone, antibiotic, antiarrhythmic, anticoagulation; dispensing error; failure to have ED discharge prescription dispensed

† Some patients experienced more than one type of problem or had problems of more than one level of significance.

Figure 1 – Patient recruitment



Title: Comprehensive identification of medication-related problems occurring prior to, during and after emergency department presentation: an Australian multicentre, prospective, observational study.

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AH		✓	✓	✓	✓	✓
DT	✓		✓	✓	✓	✓
AW		✓	✓	✓	✓	✓
LA		✓	✓	✓	✓	✓
PL		✓	✓	✓	✓	✓
DL		✓	✓	✓	✓	✓
DS		✓	✓	✓	✓	✓
RS		✓	✓	✓	✓	✓
SL		✓	✓	✓	✓	✓
HC		✓	✓	✓	✓	✓
ET			✓	✓	✓	✓
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Figure 1 – Patient recruitment