Detection of medication-related problems in hospital practice: a review

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Keywords

clinical risk management, error detection,
medication errors, medication-related
problems, methodology, patient safety

Received

10 April 2012

Accepted

26 November 2012

Accepted Article Published Online

30 November 2012

This review examines the effectiveness of detection methods in terms of their ability to identify and accurately determine medication-related problems in hospitals. A search was conducted of databases from inception to June 2012. The following keywords were used in combination: medication error or adverse drug event or adverse drug reaction, comparison, detection, hospital and method. Seven detection methods were considered: chart review, claims data review, computer monitoring, direct care observation, interviews, prospective data collection and incident reporting. Forty relevant studies were located. Detection methods that were better able to identify medication-related problems compared with other methods tested in the same study included chart review, computer monitoring, direct care observation and prospective data collection. However, only small numbers of studies were involved in comparisons with direct care observation ($n = 5$) and prospective data collection ($n = 6$). There was little focus on detecting medication-related problems during various stages of the medication process, and comparisons associated with the seriousness of medication-related problems were examined in 19 studies. Only 17 studies involved appropriate comparisons with a gold standard, which provided details about sensitivities and specificities. In view of the relatively low identification of medication-related problems with incident reporting, use of this method in tracking trends over time should be met with some scepticism. Greater attention should be placed on combining methods, such as chart review and computer monitoring in examining trends. More research is needed on the use of claims data, direct care observation, interviews and prospective data collection as detection methods.

Introduction

Medication-related problems can lead to increased hospitalization, additional use of resources and interventions to deal with deterioration in health and increased costs [1]. Detection of medication-related problems is vital for identifying causes and types of problems as well as developing strategies for improvement. Various detection methods have been used to determine medication-related problems, which can be grouped into seven areas: chart review, claims data, computer monitoring, direct care observation, interview, prospective data collection and incident reporting. There has been very little critical appraisal of the ability of detection methods to identify medication-related problems. In a systematic review conducted on this topic, only four detection methods were compared, and attention was placed on general analysis of adverse events such

as hospital-acquired infections, diagnostic errors and post-operative haemorrhage rather than specific analysis of medication-related problems [2].

The aims of this review are to consider how various detection methods compare in terms of their ability to identify medication-related problems in hospitals and to determine their accuracy of detection.

Methods

A search was conducted of PubMed, CINAHL, EMBASE, Journals@Ovid, International Pharmaceutical Abstract Series via Ovid, Science Direct, Scopus, Web of Science, and PsycInfo from inception to June 2012. The following keywords were used: medication error or adverse drug event or adverse drug reaction, in combination with comparison,

detection, hospital and method. A key inclusion criterion of papers is that they involved a comparison of at least two detection methods. Reference lists of articles were examined manually to identify additional papers.

For the purpose of this review, medication-related problems encompass medication errors, adverse drug reactions and adverse drug events [3]. Medication errors are mistakes that occur during prescribing, transcribing, supplying, administering or monitoring a medication. Most medication errors do not cause patient harm. Adverse drug reactions relate to the intrinsic properties of the medication, whereby harm occurs at doses normally used in patients. Adverse drug events include medication errors and adverse drug reactions, which are associated with harm [4]. Effectiveness was defined as the ability of a particular detection method to identify more medication-related problems compared with other methods in the same study, and to demonstrate good sensitivity and specificity.

Results

Initial searching identified 720 papers. The abstracts of these papers were independently examined by the author and an independent reviewer for potential relevance. A total of 62 papers were selected for further examination and another six papers were added from hand searching references, leading to a total of 68 papers. From these studies, 40 relevant papers were obtained.

Ability of detection methods to identify medication-related problems

Table 1 shows information about studies that provided direct comparisons between detection methods to identify medication-related problems. Most studies involved comparisons with two or three detection methods. The most commonly examined detection methods investigated were chart review and incident reporting.

Chart review There were 32 studies that included comparisons with chart review [5–36]. Of these studies, 18 (56.3%) showed that chart review demonstrated a higher incidence of medication-related problems compared with other methods in each study [5–8, 10, 11, 14–17, 24, 26, 27, 29, 31–33, 35]. Only five studies provided a breakdown of medication-related problems according to stages of the medication process [16, 17, 25, 26, 30]. While greater proportions of prescribing rather than administration problems were found in some studies [16, 25, 30], only small numbers of cases were involved. On the other hand, Grasso *et al.* [17] found a wide diversity of medication-related problems according to stages, with 10.9% occurring at the prescribing stage and 65.8% occurring at the administering stage. Kunac *et al.* [26] did not undertake a breakdown of medication-related problems identified by chart review

according to stages. However, in their study, 83.0% of identified medication-related problems were associated with chart review and 60.8% involved prescribing and 44.6% involved administration problems. Seriousness of medication-related problems was examined in nine studies [5, 11, 13, 15, 19, 20, 24, 27, 33]. Of these studies, four showed the chart review method detected problems of major clinical significance in between 22.5 and 88.5% of cases while the remaining five studies showed chart review detected problems of major significance in between 0 and 9.0% of cases.

Claims data Claims data and variations of this method through analysis of complaints and inquest data have been examined in one study [19]. Hogan *et al.* demonstrated wide variability in detection using these forms of data collection, ranging from 0 medication-related problems with the use of a claims database to 100 medication-related problems with the use of a clinical incident database. These detection levels were much lower than those obtained by case notes or by the patient administration system, which are forms of chart review, and by incident reporting in the same study. No details were given about the stages of the medication process or about the seriousness of medication-related problems in the use of claims data.

Computer monitoring Computer monitoring has been examined in 25 studies [5, 8–12, 15, 16, 20–22, 24, 27–29, 34, 37–44]. When compared with other methods, computer monitoring was more effective in identifying medication-related problems in 16 studies (64.0%) [9, 10, 16, 20, 22, 23, 28, 29, 34, 37, 38, 40–43]. Signal types in computer monitoring were either by alert ($n = 11$ studies) where rules were developed to inform prescribers to modify treatment, by detection ($n = 13$ studies) where rules were developed to detect medication-related problems retrospectively for quality control, or by using both types of signals ($n = 1$ study). Neither signal type demonstrated a greater propensity to determine medication-related problems. In 16 studies, the rule type for determining a medication-related problem was based on a single criterion (e.g. patient with an international normalized ratio (INR) of greater than 5) and in eight studies, the rule type was based on combined criteria (e.g. patient with an INR greater than 5 and receiving warfarin). One study involved the use of both single and combined rule types [23]. Stages of the medication process were only examined in two studies [16, 43] and only small numbers of cases were involved. Schade *et al.* [43] found 23 out of 29 medication-related problems of a preventative nature occurred during administration while the remainder occurred with prescription. Franklin *et al.* [16] showed two medication-related problems occurred during prescribing and none occurred during administration. Seriousness of medication-related problems was examined in 15 studies [5, 10, 11, 15, 23, 24, 27, 29, 34, 37–40,

Table 1

Studies comparing the use of different detection methods for medication-related problems

Reference, country and design	Detection methods used	Type of medication-related problem detected, incidence, stages of medication process and severity
Azaz-Livshits <i>et al.</i> [5] Israel Retrospective observational study	Chart review. Computerized monitoring (laboratory data signal, single rule type, detection).	Type of medication-related problems: adverse drug reactions (ADRs). Chart review: 40 ADRs. Computerized laboratory data: 26 ADRs. Stages of medication process: not relevant for ADRs. Seriousness – chart review: 9/40 (22.5%) ADRs were severe; computerized monitoring: 6/40 (15.0%) ADRs were severe.
Bates <i>et al.</i> [6] USA Prospective cohort study	Chart review. Incident reporting (nurses' and pharmacists' logs for recording drug-related incidents). Incident reporting (trained nurse visit to solicit verbal reports from nurses, pharmacists and clerical staff).	Type of medication-related problems: drug-related incidents involving a combination of adverse drug events (ADEs), potential ADEs and problem orders. Study nurse identified 73 medication-related incidents in 2967 patient-days. Chart review: 41% of medication-related incidents. Log: 37% of medication-related incidents. Solicited verbal report: 22% of medication-related incidents. No details about stages of medication process. Seriousness – of 73 medication-related incidents, 27 were ADEs. Of 27 ADEs, five were life-threatening, nine were serious and 13 were significant. No breakdown of seriousness given for each detection group.
Bennett <i>et al.</i> [47] USA Prospective observational study	Prospective data collection by pharmacist. Incident reporting (voluntary).	Type of medication-related problems: ADRs. Prospective data collection by pharmacist: 11/152 patients had ADRs (7.2%). Incident reporting: 8 patients had ADRs (0.08% for total population of admitted patients). Stages of medication process: not relevant for ADRs. Seriousness – 2/11 ADRs (18.1%) from pharmacy surveillance were severe; no details about severity of ADRs from incident reporting.
Berry <i>et al.</i> [7] USA Observational study	Chart review (screening of charts by physician or pharmacist). Chart review (laboratory report screening). Incident reporting (voluntary).	Type of medication-related problems: ADRs for aminophylline, digoxin or gentamicin therapy. Chart review by primary investigator and physician: 13 ADRs. Screening charts by pharmacist: six ADRs (16 false ADRs detected). Chart review (laboratory report screening): 11 ADRs (38 false ADRs detected). Incident reporting: No ADRs detected. Stages of medication process: not relevant for ADRs. Seriousness data of detection methods not addressed.
Brvar <i>et al.</i> [8] Slovenia Retrospective cohort study	Chart review by study team. Chart review by treating physicians. Computer monitoring (detection system through ICD-10 coding, single rule type, detection). Incident reporting (national voluntary).	Type of medication-related problems: ADRs. Chart review by study team: 30/520 admissions related to ADRs (5.8%). Chart review by treating physicians: 30/520 admissions related to ADRs (5.8%). Computer monitoring: 1/520 admissions related to ADRs (0.2%). Incident reporting: 0/520 admissions related to ADRs (0%). Stages of medication process: not relevant for ADRs. Seriousness data of detection methods not presented.
Capuzzo <i>et al.</i> [45] Italy Prospective cohort study	Direct care observation (independent observer). Incident reporting (spontaneous by staff).	Type of medication-related problems: medication errors. Direct care observation: five medication errors. Incident reporting: three medication errors. No details about stages of medication process. Seriousness data of detection methods not presented.
Classen <i>et al.</i> [41] USA Prospective cohort study	Computer monitoring (automated incident reporting through a trigger tool, single rule type, alert). Incident reporting (voluntary using automatic system). Incident reporting (voluntary).	Type of medication-related problems: ADEs. 731 verified ADEs in 648 patients by hospital pharmacist. Computer monitoring: 631/731 ADEs (86.3%). Incident reporting (automatic): 92/731 ADEs (12.6%). Incident reporting (voluntary): 9/731 ADEs (1.2%). No details about stages of medication process. Seriousness – 101 were severe, 600 were moderate and 30 were mild events. Seriousness data of detection methods not presented.
Dalton-Bunnow <i>et al.</i> [9] USA Prospective and retrospective cohort study	Chart review (retrospective review). Computer monitoring (prospective review, single rule type, alert and detection). Incident reporting.	Type of medication –related problems: ADRs. Chart review: 17 ADRs (retrospective random selection of 99 patients), 23 ADRs (retrospective selective review of patients receiving clozapine, thrombolytic agents and anti-arrhythmics). Computer monitoring: 93 ADRs. Incident reporting: 39 ADRs. Stages of medication process: not relevant for ADRs. Seriousness data of detection methods not presented.
Dormann <i>et al.</i> [37] Germany Prospective cohort study	Computer monitoring (single rule type, alert). Incident reporting (stimulated spontaneous reporting: alert).	Type of medication-related problems: ADRs. Computer monitoring: 34 ADRs out of 379 patients (9.0%). Incident reporting: 17 ADRs out of 379 patients (4.5%). Five ADRs were detected by both methods. Stages of medication process: not relevant for ADRs. Seriousness – computer monitoring: three severe, 13 moderate and 18 mild effects; incident reporting: two severe, eight moderate and seven mild effects.

Table 1

Continued

Reference, country and design	Detection methods used	Type of medication-related problem detected, incidence, stages of medication process and severity
Dormann <i>et al.</i> [10] Germany Prospective cohort study	Chart review. Computer monitoring (single rule type, alert).	Type of medication-related problems: ADRs. Chart review: 109 ADRs identified. Computer monitoring: 385 new automatic laboratory signals were associated with 100 (91.7%) ADRs. Stages of medication process: not relevant for ADRs. Seriousness – 66 were mild, 42 were moderate and one was severe, seriousness data of detection methods not presented.
Egger <i>et al.</i> [11] Germany Prospective observational study	Chart review. Computer monitoring (single rule type, detection).	Type of medication-related problems: ADRs. Chart review: 153 ADRs. Computer monitoring: 64 ADRs. Stages of medication process: not relevant for ADRs. Seriousness – only mild (60.8%) and moderate (39.2%) ADRs were recognised by chart review. Mostly mild ADRs detected by computer monitoring (number not stated).
Ferranti <i>et al.</i> [38] USA Retrospective study	Computer monitoring (ADE surveillance, single rule type, alert). Incident reporting (voluntary).	Type of medication-related problems: ADEs. Computer monitoring: 1537 ADEs, 34.9 ADEs/100 admissions (no details about stages of medication process). Incident reporting: 849 ADEs, 18.0 ADEs/100 admissions (stages – 66.7% relate to administration, including dose rate, drug administered, route, intravenous problems and pump malfunction, 31.9% relate to prescribing, including allergy issues, dose omission, 1.4% relate to transcribing). Seriousness – computer monitoring: 1459 (94.9%) had severity score ≤ 2 , 78 (5.1%) had severity score ≥ 3 . Seriousness – incident reporting: 756 events (89.0%) had severity score ≤ 2 , 93 (11.0%) had severity score ≥ 3 .
Field <i>et al.</i> [12] USA Cohort study	Chart review (automated review of electronic clinic notes). Chart review (manual review of hospital discharge summaries). Chart review (manual review of notes from emergency department visits). Computer monitoring: (generated signals, combined rule type, alert). Chart review (progress reports from providers). Incident reporting (manual review).	Type of medication-related problems: drug-related incidents and ADEs. Initial medical record review by pharmacist investigators identified 2266 drug-related incidents and 1523 ADEs. Electronic notes: 591/1523 ADEs (38.9%). Discharge summaries: 169/1523 ADEs (11.1%). Review of emergency department visits: 193/1523 ADEs (12.7%). Computer monitoring: 466/1523 ADEs (30.6%). Provider reports: 173/1523 ADEs (11.3%). Incident reporting: 5/1523 ADEs (0.3%). No details about stages of medication process. Seriousness data of detection methods not presented.
Flynn <i>et al.</i> [13] USA Descriptive study	Chart review. Direct observation. Incident reporting.	Type of medication-related problems: medication administration errors. Research pharmacist confirmed 457 medication administration errors. Chart review: 17/457 medication administration errors (3.7%), 7/457 errors were false positives, 440 errors were missed. Direct observation: 300/457 medication administration errors (65.6%), 73/457 errors were false positives, 157 errors were missed. Incident reporting: 1/457 medication administration errors (0.2%), 456 errors were missed. Stages of medication process: only medication administration errors detected. Seriousness – physician panel: 35 medication administration errors were clinically significant; direct observation: 25 (71%) were clinically significant; chart review: 3 (9%) were clinically significant; incident reporting: none were clinically significant.
Franklin <i>et al.</i> [14] UK Descriptive study	Chart review (ward pharmacist recording medication errors from chart audit). Incident reporting.	Type of medication-related problems: medication prescribing errors. Chart review: 474/4995 prescribing errors (9.5%). What ward pharmacist would have recorded in an incident report: 19/474 prescribing errors (4.0%). Incident reporting: Eight prescribing errors. Stages of medication process: only medication prescribing errors detected. Seriousness data of detection methods not presented.
Franklin <i>et al.</i> [15] UK Pre-post intervention study	Chart review (retrospective medical notes). Prospective data collection. Computer monitoring (retrospective use of trigger tool, single rule type, detection). Incident reporting (spontaneous).	Type of medication-related problems: medication prescribing errors. Pre intervention – 135 prescription errors identified by all methods. Chart review alone: 86/135 prescribing errors (63.7%). Prospective data collection alone: 41/135 prescribing errors (30.4%). Computer monitoring alone: 0/135 prescribing errors (0.0%). Incident reporting alone: 1/135 prescribing errors (0.7%). Prospective data collection and chart review: 7/135 prescribing errors (5.2%). Post intervention – 127 prescribing errors identified by all methods. Chart review alone: 96/127 prescribing errors (75.6%). Prospective data collection alone: 21/127 prescribing errors (16.5%).

Table 1

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Reference, country and design	Detection methods used	Type of medication-related problem detected, incidence, stages of medication process and severity
		<p>Computer monitoring alone: 0/127 prescribing errors (0%).</p> <p>Incident reporting alone: 1/127 prescribing errors (0.8%).</p> <p>Prospective data collection and chart review: 9/127 prescribing errors (7.1%).</p> <p>Chart review and computer monitoring: 2/127 prescribing errors (0.8%).</p> <p>84 false positives identified by computer monitoring.</p> <p>Stages of medication process: only medication prescribing errors detected.</p> <p>Seriousness – mean clinical severity scores using scale [0 (no harm) to 10 (death)] – chart review: 4.4; prospective data collection: 4.4; computer monitoring: 6.0; incident reporting: 4.2; severity not affected by CPOE.</p>
Franklin <i>et al.</i> [16] UK Descriptive study	Chart review (retrospective health record). Computer monitoring (trigger tool, single rule type, detection).	<p>Type of medication-related problems: medication prescribing and administration errors, and ADRs.</p> <p>Chart review: four prescribing errors, one medication administration error.</p> <p>Computer monitoring: five ADRs, two prescribing errors, no medication administration errors.</p> <p>Seriousness data of detection methods not presented.</p>
Grasso <i>et al.</i> [17] USA Descriptive study	Chart review (retrospective for prescription, transcription and administration, and concurrent for dispensing errors). Incident reporting.	<p>Type of medication-related problems: medication errors.</p> <p>Chart review: 2194 medication errors (stages: prescription: 239/2194 (10.9%), transcription 498/2194 (22.7%), administration: 1443/2194 (65.8%), dispensing: 14/2194 (0.6%).</p> <p>Incident reporting: 9 medication errors (Stages of medication process not stated).</p> <p>Seriousness overall – 19% of error had low risk of harm, 23% had moderate risk and 58% had high risk. Seriousness data of detection methods not presented.</p>
Haffner <i>et al.</i> [39] Germany Prospective study	Prospective data collection (intensified surveillance by physician). Computer monitoring (screening of laboratory parameters, single rule type, detection).	<p>Type of medication-related problems: ADRs.</p> <p>Prospective data collection: 101 ADRs in 84 patients (84/703, 11.9%).</p> <p>Computer monitoring: 45 ADRs in 36 patients (36/636, 5.7%).</p> <p>Seriousness – direct care observation for score ≥ 3 (moderate physical or psychological impairment): 35.7%; computer monitoring for score ≥ 3: 22.2%.</p>
Haw <i>et al.</i> [18] UK Cross sectional observational study	Chart review. Direct observation. Incident reporting.	<p>Type of medication-related problems: medication administration errors.</p> <p>Chart review: 148/1423 medication administration errors compared with opportunities for error (10.4%).</p> <p>Direct observation: 369/1423 medication administration errors (25.9%).</p> <p>Incident reporting: 0/1423 medication administration errors (0%).</p> <p>All errors detected by chart review were identified by direct observation. Of the 133 dose omissions detected by chart review, direct observation found they were clerical errors where the nurse failed to document the administration.</p> <p>Stages of medication process: only medication administration errors detected.</p> <p>Seriousness of errors overall – 69.1% of errors were negligible, 7.3% were minor, 0.3% were serious, 0% were likely to lead to fatality, 23.3% were unrateable. Seriousness data of detection methods not presented.</p>
Hogan <i>et al.</i> [56] UK Retrospective study	Chart review (case notes). Chart review (patient administration system). Claims database. Clinical incident. Claims data (complaint). Incident report (health and safety incident database). Claims data (inquest database).	<p>Type of medication-related problems: medication errors.</p> <p>Case notes: 15 medication errors.</p> <p>Patient administration system: 13 medication errors.</p> <p>Claims: No medication errors.</p> <p>Clinical incident: 100 medication errors.</p> <p>Complaint: four medication errors.</p> <p>Health and Safety incident database: No medication errors.</p> <p>Inquest: one medication error.</p> <p>No details about stages of medication process.</p> <p>Seriousness data of detection methods not presented.</p>
Honigman <i>et al.</i> [20] USA Retrospective study	Chart review. Computer monitoring (screening for diagnosis codes, allergy rules, computer event monitoring rules, and text searching, combined rule type, detection).	<p>Type of medication-related problems: ADEs.</p> <p>Chart review: 121 ADEs.</p> <p>Computer monitoring: 864 ADEs.</p> <p>No details about stages of medication process.</p> <p>Seriousness – chart review: no ADE was fatal, seven (5.8%) were life threatening; 21 (17.4%); were serious and 93 (76.9%) were significant.</p>
Hope <i>et al.</i> [21] USA Comparative study	Chart review (traditional pharmacist review). Computer monitoring (generated signal, combined rule type, detection).	<p>Type of medication-related problems: ADEs and medication errors.</p> <p>Total number of signals generated from computer monitoring: 11 602 signals, 5859 duplicates occurred.</p> <p>Chart review: Boston – 242 ADEs, 104 medication errors, Indianapolis – 535 ADEs, 562 medication errors.</p> <p>Computer generated signal: Boston – 2492 signals.</p> <p>Indianapolis – 5824 signals.</p> <p>No details about stages of medication process.</p> <p>Seriousness data of detection methods not presented.</p>

Table 1

Continued

Reference, country and design	Detection methods used	Type of medication-related problem detected, incidence, stages of medication process and severity
Huang <i>et al.</i> [22] USA Retrospective cohort review	Chart review. Computer monitoring (automated screening of spironolactone events, combined rule type, detection). Incident reporting (voluntary).	Type of medication-related problems: adverse events from spironolactone. Chart review: 33 adverse events confirmed from automatic review (4.98%). Computer monitoring: 52 adverse events relating to hypokalaemia from spironolactone (7.85%). Incident reporting: One adverse event relating to hypokalaemia from spironolactone. Chart review detected five adverse events not identified from computer monitoring. No details about stages of medication process. Seriousness data of detection methods not presented.
Hwang <i>et al.</i> [23] USA Retrospective cohort study	Chart review. Computer monitoring (single and combined rule type, detection).	Type of medication-related problems: ADEs. 187 adverse drug events identified by both methods. Chart review: 39 computer-unrecognised ADEs (20.9%). Computer monitoring: 148 ADEs (79.1%). No details about stages of medication process. Seriousness – only 10% of the computer-unrecognized ADEs from chart review were severe ADEs; 32% of computer recognized events were severe ADEs.
Jha <i>et al.</i> [24] USA Prospective cohort study	Chart review. Computer monitoring (combined rule type, alert). Incident reporting (stimulated voluntary).	Type of medication-related problems: ADEs. 617 ADEs identified by all methods. Chart review: 398/617 ADEs (64.5%). Computer monitoring: 275/617 ADEs (44.6%). Incident reporting: 23/617 ADEs (0.7%). Only 76 (12%) of the 617 ADEs were identified by both chart review and computer monitoring, 3 (0.5%) were identified by both computer monitoring and incident report. No details about stages of medication process. Seriousness – chart review: 57.5% were not severe, 42.5% were severe; computer monitoring: 49.5% were not severe, 50.5% were severe; incident reporting: 52.2% were not severe, 47.8% were severe.
Kilbridge <i>et al.</i> [42] USA Prospective cohort study	Computer monitoring (automated surveillance system with a trigger tool, combined rule type, alert). Incident reporting (voluntary).	Type of medication-related problems: ADEs. Computer monitoring: university hospital – 520 ADEs, community hospital – 283 ADEs. Incident reporting: university hospital – 144 ADEs, community hospital – 23 ADEs. No details about stages of medication process. Seriousness of ADEs overall – 86.1% had transient effects requiring corrective therapy; 13.5% had significant effects requiring aggressive intervention; 0.1% had permanent effects; 0.2% related to patient death. Seriousness data of detection methods not presented.
Kozer <i>et al.</i> [25] Canada Descriptive study	Chart review. Prospective data collection (mock code in emergency department). Incident reporting.	Type of medication-related problems: 10-fold medication errors. Chart review: two 10-fold errors/1678 orders (0.12%) (stages of medication process: two errors related to prescription). Prospective data collection: four 10-fold errors/125 orders (3.2%) (stages of medication process: three related to prescription, 1 related to administration). Incident reporting: 20 10-fold medication errors (stages of medication process: 18/20 related to prescription, 2/20 related to dispensing). Seriousness data of detection methods not presented.
Kunac & Reith [26] New Zealand Prospective observational cohort study	Chart review. Interview (parents). Incident reporting (voluntary following education). Incident reporting (routine).	Type of medication-related problems: medication-related events. 761 medication-related events detected by all methods. Chart review: 630/761 medication-related events (83.3%). Interview with parents: 16/761 medication-related events (2.1%). Incident reporting (following education): 111/761 medication-related events (14.6%). Incident reporting (routine): 4/761 medication-related events (0.53%). Of 368 preventable events, 224 involved the prescribing stage, 34 involved the dispensing stage, 164 the administration stage, and 55 the monitoring stage. No details about stages of medication process for type of detection method. Seriousness – 9.6% caused patient injury, 11.1% had the potential for patient injury; and 79.3% caused no patient injury. Seriousness data of detection methods not presented.
Levy <i>et al.</i> [27] Israel Prospective observational study	Chart review. Computer monitoring (laboratory data, single rule type, alert).	Type of medication-related problems: ADRs. Chart review: 71 ADRs were detected in 64 (32%) of the 199 admissions. Computer monitoring: 43 ADRs. Stages of medication process: not relevant for ADRs. Seriousness – chart review: 20 serious (28%), 19 (27%) moderate and 32 (45%) mild ADRs; computer monitoring: 10 serious, nine moderate and 24 mild ADRs.

Table 1

Continued

Reference, country and design	Detection methods used	Type of medication-related problem detected, incidence, stages of medication process and severity
Nebeker <i>et al.</i> [28] USA Retrospective cohort study	Chart review. Computer monitoring (algorithm, single rule type, detection).	Type of medication-related problems: bleeding and anticoagulation ADEs and drug-induced delirium and psychosis ADEs. Chart review: not stated. Computer monitoring: prevalence for bleeding and anticoagulation ADEs varied between 1 and 69%, prevalence for drug-induced delirium and psychosis ADEs varied between <1 and 77%. No details about stages of medication process. Seriousness data of detection methods not presented.
Neubert <i>et al.</i> [29] Germany Prospective cohort study	Chart review. Computer monitoring (automatic laboratory signals, single rule type, alert). Incident reporting (spontaneous).	Type of medication-related problems: ADRs. Chart review: 73 ADRs were identified in 439 admissions (396 patients). Computer monitoring: 31/73 (42.4%) ADRs. Incident reporting: 23/73 (31.5%) ADRs. Of all ADRs, 19 were only found by chart review. Stages of medication process: not relevant for ADRs. Seriousness – chart review: not stated; computer monitoring: 24 mild and seven moderate ADRs; incident reporting: 10 mild and 21 moderate.
Olsen <i>et al.</i> [30] UK Descriptive study	Chart review. Prospective data collection (pharmacy surveillance in wards). Incident reporting.	Type of medication-related problems: medication errors. Chart review: 14 medication errors/288 patients (4.9%) (stages: 10/14 prescribing errors, 4/14 administration errors). Prospective data collection: 30/288 medication errors (10.4%) (stages: 24/30 prescribing errors, 6/30 administration errors). Incident reporting: 0/288 medication errors (0%). Seriousness data of detection methods not presented.
O'Neil <i>et al.</i> [31] USA Cohort study	Chart review. Incident reporting (physician reporting system by email).	Type of medication-related problems: medication-related injuries (prolongation of hospital stay or disability caused by medication). Chart review: 37 medication-related injuries. Incident reporting: 33 medication-related injuries. No details about stages of medication process. Seriousness data of detection methods not presented.
Sari <i>et al.</i> [32] UK Two stage retrospective review	Chart review (case note review). Incident reporting (voluntary).	Type of medication-related problems: drug problems. 24 drug problems detected by all methods. Chart review: 19/24 drug problems (79%). Incident reporting: 7/24 drug problems (29%). Drug problems detected by both methods: 2/24 (8%). No details about stages of medication process. Seriousness (only available for all patient incidents) – 42% of incidents led to patient harm, which were all detected by chart and 5% were detected by incident reporting. In all, 21 incidents were missed by chart review, which were minor, but 44.7% of incidents missed by incident reporting led to patient harm. Breakdown of seriousness for drug problems not given.
Savage <i>et al.</i> [33] UK Post evaluation comparative study	Chart review. Interview (staff and patient).	Type of medication-related problems: medication errors. Chart review: 85 medication errors (stages of medication process: not stated). Interview: 72 medication errors (stages of medication process: electronic prescribing interface: 6/72, prescribing: 38/72, supplying: 1/72, administering: 20/72, monitoring: 7/72). Seriousness – chart review: three medication errors leading to harm; interview: one medication error leading to harm.
Schade <i>et al.</i> [43] USA Prospective cohort study	Computer monitoring (targeted audit for use of rescue medication to treat ADEs with trigger tool, single rule type, detection). Incident reporting (use of any medication that led to an adverse outcome for a patient).	Type of medication-related problems: ADEs. Computer monitoring: 109 ADEs, 29/109 ADEs were preventable, 23/29 related to an administration error, 6/29 were a prescription error. Incident reporting: four ADEs. Seriousness – chart review: 33.0% causing no effect, 53.2% caused a mild to moderate effect, 13.8% caused a severe effect; incident reporting: 25% (1/4) causing mild effect, 50% (2/4) caused moderate effect, 25% (1/4) caused severe effect.
Seeger <i>et al.</i> [34] USA Retrospective review	Chart review. Computer monitoring (combined rule type, alert).	Type of medication-related problem: ADEs. Chart review (of only 11% of selected high priority alerts obtained from computer monitoring): 5 non-preventable and 2 non-preventable ADEs. Computer monitoring: 528 high priority alerts, 664 medium priority alerts, 2355 low priority alerts. No details about stages of medication process. Seriousness: Of 3547 alerts, 528 were of high or critical priority, 664 were of medium priority and 2355 were of low priority.

Table 1

Continued

Reference, country and design	Detection methods used	Type of medication-related problem detected, incidence, stages of medication process and severity
Stanhope <i>et al.</i> [35] UK Retrospective review	Chart review. Incident reporting (by staff to maternity risk manager). Detection by risk manager but not reported.	Type of medication-related problems: drug errors (documentation, prescribing and administering errors). Chart review: 46 medication errors. Medication omissions were not recorded in notes, thus chart review likely to underestimate true rate. Incident reporting by staff to maternity risk manager: One medication error. Detection by risk manager but not reported: two medication errors. No details about stages of medication process. Seriousness – 65.2% were minor; 34.8% were moderate. Seriousness data of detection methods not presented.
Takata <i>et al.</i> [44] USA Descriptive surveillance study	Direct observation (pharmacist intervention). Computer monitoring (trigger tool, single rule type, alert). Incident reporting (voluntary).	Type of medication-related problems: ADEs (injury caused by medication). Direct observation: 2.67 ADEs per 1000 patient days (349 ADEs). Computer monitoring: 22.3 ADEs per 1000 patient days (79 ADEs). Incident reporting: 1.7 ADEs per 1000 patient days (278 ADEs). No details about stages of medication process. Seriousness – direct observation: 100% of events rated as at least causing significant permanent harm; computer monitoring: 93.7% causing temporary harm, 1.3% causing life threatening event, 1.3% caused death, 3.7% caused no harm; incident reporting: 90.6% causing temporary harm, 2.5% causing life threatening event, 0.4% caused death, 6.1% caused no harm.
Viktil <i>et al.</i> [46] Norway Prospective cohort study	Prospective data collection (pharmacy surveillance in wards). Interview (patient).	Type of medication-related problems: drug-related problems (ADRs, medical chart error, problems with formulation, dosing, or timing, need for medication, adherence, drug interactions, monitoring and patient education). Prospective data collection: 1533 drug-related problems/631 patients = 2.4 drug related problems per patient (stages of medication process: prescribing: 1056/1533, 68.9%, administering: 405/1533, 26.4%, ADRs: 56/1533, 3.7%). Interview: 421 drug-related problems/96 patients = 4.4 drug related problems per patient (stages of medication process: prescribing: 277/421, 65.8%, administering: 126/421, 29.9%, ADRs: 14/421, 3.3%). Seriousness – prospective data collection: 37/94 (39.4%) of drug-related problems were extremely important or of major clinical significance; patient interview: 19/30 (63.3%) of drug-related problems were extremely important or of major clinical significance.
Weissman <i>et al.</i> [36] USA Randomized sample survey	Chart review (medical record). Interview (post discharge patient).	Type of medication-related problems: ADEs – unintended harm to the patient by an act of commission or omission of medications. Chart review: 32 ADEs. Interview: 135 ADEs. Interview and chart review: 21 ADEs. No details about stages of medication process. Seriousness – chart review: 1.2% adverse events were life threatening, 39.0% were serious, 50.0% were clinically significant; interview: 0.8% adverse events were life threatening, 13.4% were serious, 62.5% were clinically significant. Breakdown of seriousness of ADEs not given.
Whipple <i>et al.</i> [40] USA Retrospective cohort study	Computer monitoring (combined rule type, detection). Incident reporting (voluntary).	Type of medication-related problems: ADEs (detection of narcotic overdoses with patient controlled analgesia). Computer monitoring: 14 ADEs for narcotic overdoses. Incident reporting: seven ADEs for narcotic overdoses. No details about stages of medication process. Seriousness – computer monitoring: One ADE leading to death, one ADE leading to admission to intensive care; incident report: one ADE leading to death; one ADE leading to admission to intensive care.

43, 44]. Of these studies, there was large variability in the proportions of medication-related problems that were detected as being severe, ranging from 0 to 50.5%.

Direct care observation Direct care observation was utilized in five studies [13, 18, 25, 44, 45]. Three out of five studies (60.0%) showed that this method identified more

medication-related problems compared with other examined methods [13, 18, 45]. Generally, this method was used to examine medication administration problems. Conversely, Kozer *et al.* undertook a breakdown of medication-related problems occurring at various stages of the medication process but only small numbers of cases were involved [25]. In examining 10-fold dosing errors, Kozer

et al. found problems in three prescriptions and one administration. Seriousness of medication-related problems was provided in two studies [13, 44], which showed the proportion of severe problems of clinical significance, varied between 71.4 and 100%.

Interview Interviews were used as a detection method in four studies [26, 33, 36, 46]. Three out of the four studies showed that interviews identified fewer medication-related problems than other compared methods [26, 33, 46]. Conversely, Weissman and colleagues [36] showed post-discharge interviews with patients revealed a greater number of adverse drug events ($n = 135$) compared with the number obtained using medical record review ($n = 32$). Information about the stage in medication process was provided in two studies [33, 46]. Savage *et al.* [33] showed prescribing and administration comprised 52.8% and 27.8% of cases, respectively, while other stages affected included monitoring (9.7%), interface (8.3%) and supply (1.4%). Similarly, Viktil *et al.* [46] found prescribing and administration were affected by 65.5% and 29.9% of cases respectively with the remainder involving adverse drug reactions. Seriousness was examined in three studies [33, 36, 46], whereby in two studies between 63.3 and 76.7% of medication-related problems were clinically significant [36, 46]. Savage *et al.* [33] found one medication-related problem out of 72 problems identified by interview led to patient harm.

Prospective data collection Prospective data collection by pharmacists or physicians has been investigated in six studies [15, 21, 30, 39, 46, 47]. Four studies showed that this method detected more medication-related problems [30, 39, 46, 47] and the remainder showed fewer medication-related problems than other compared methods in the same study [15, 21]. Two studies had data about stages of the medication process. Olsen *et al.* showed 80.0% of prescribing and 20.0% of administration problems were identified [30]. Similarly, Viktil *et al.* showed 68.9% of problems involved prescription, 26.4% involved administration, while 3.7% involved adverse drug reactions [46]. Of the four studies that provided data on seriousness of medication-related problems, in three studies, between 35.7% and 44.0% of problems were of major significance [15, 39, 46], while in one study, 81.3% of problems were moderately significant [47].

Incident reporting Of the seven detection methods used, incident reporting was consistently least likely to identify medication-related problems. Out of 28 studies [6–9, 12–15, 17, 18, 22, 24–26, 29–32, 35, 37, 38, 40–45, 47], only one study (3.6%) indicated that this method identified more medication-related problems than other methods compared [25]. Some variations in results for incident reporting depended on whether or not a proactive approach was used. Studies involving solicitation [6], an

automated approach [41] or voluntary reporting facilitated by education of health professionals [26], were usually associated with greater rates of reporting than if a proactive approach was not used. However, the incident rate was still low. Stages of the medication process were assessed in two studies. Ferranti *et al.* found the breakdown of stages was 66.7% for administration, 31.9% for prescription and 1.4% for transcription [38]. Kozer *et al.* showed 18/20 problems occurred with prescription and 2/20 occurred with dispensing [25]. Nine studies provided information about seriousness of medication-related problems, demonstrating between 0% and 47.8% were clinically significant [13, 15, 24, 37, 38, 40, 41, 43, 44].

Accuracy of detection methods

Twenty-four studies (60.0%) had information about the accuracy of detection methods (Table 2) and 17 studies involved the use of a gold standard. Of the gold standard studies, 14 (35%) used chart review in every patient independent of the results achieved by other detection methods [4, 5, 7, 8, 10, 11, 16, 22–24, 27, 29, 36, 39]. Two (5%) studies involved the use of chart review in selected patients only [20, 48]. Two studies used a stimulated report method as the gold standard [24, 37].

A process of verification, which included a pharmacist or physician review, was used in seven studies [9, 12, 21, 34, 38, 40, 44]. This process involved determining whether a trigger or alert created by computer monitoring was truly a medication-related problem. By using verification, the absolute number of medication-related problems was unknown, and hence these studies could only provide details about positive predictive values.

Sensitivity was examined in five methods, and demonstrated high variation (chart review 23.1–100%, computer monitoring 0.4–94.4%, interviews 50.5%, prospective data collection 67.2%, incident report 0–37.0%). Similarly, specificity, which was examined in four methods, was also variable (chart review 56.3–93.2%, interview 80.3%, incident report 98–100%). Positive predictive values (PPVs) ranged between 0.02 and 63.5%. For the use of chart review, PPVs ranged from 2% to 54% [12, 36]. In the use of computer monitoring, PPVs were between 4.0% and 16.8% [8–12, 16, 20–24, 28, 34, 36–40, 44]. With regards to interviews, the PPV obtained in one study was 50.5% [36]. PPVs for incident reporting ranged from 4% to 54% [12, 38]. Only three studies provided details about negative predictive values (NPVs), which ranged from 80.3 to 99.2% [20, 22, 36].

Discussion

The review of seven detection methods in determining medication-related incidents in hospital settings revealed important concerns with past research. Chart review and computer monitoring were better able to identify more medication-related problems compared with other

Table 2

Description of studies that assessed accuracy of detecting medication-related problems

	If gold standard used	Application by blind independent reviewer	Detection method for accuracy results	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Azaz-Livshits <i>et al.</i> [5]	Yes, chart review of all patients	Unknown	Computer monitoring (automatic laboratory signals).	65.8	51.3		
Berry <i>et al.</i> [7]	Yes – chart review for all patients	Unknown	Chart review (screening of charts by pharmacist). Chart review (laboratory report screening). Incident reporting (voluntary)	54.4 100 0	81.6 56.3 100		
Bivar <i>et al.</i> [8]	Yes – chart review of all patients	Yes	Computer monitoring (automatic signals).			5.8	
Dalton-Bunnow <i>et al.</i> [9]	No – verification only, pharmacists review	Unknown	Computer monitoring			6	
Dormann <i>et al.</i> [37]	Yes – stimulated voluntary incident reporting	Unknown	Computer monitoring (automatic signals). Incident reporting (stimulated voluntary).	74 37	75 98	13	
Dormann <i>et al.</i> [10]	Yes – chart review of all patients	Unknown	Computer monitoring (automatic signals).	91	23s	25	
Egger <i>et al.</i> [11]	Yes – chart review of all patients	Unknown	Computer monitoring (automatic signals for detecting ADRs). Computerized automatic signals for detecting drug interactions.	47.5 58.3	1.6 1.4	1.8 0.9	
Ferranti <i>et al.</i> [38]	No – verification only, pharmacists review	Unknown	Computer monitoring (automatic signals). Incident reporting (stimulated voluntary).			5.1 11.0	
Field <i>et al.</i> [12]	No – verification only, physician review	No	Chart review (provider reports). Chart review (hospital discharge summaries). Chart review (emergency department visits). Computer monitoring (generated signals). Chart review (electronic clinic notes). Incident reporting.			54 5 2 7 12 4	
Franklin <i>et al.</i> [16]	Yes, chart review of all patients	Yes	Computer monitoring (trigger tool).	0.4		0.04	
Haffner <i>et al.</i> [39]	Yes – chart review by physician of all patients	Unknown	Computer monitoring (screening of laboratory parameters). Prospective data collection.	44.8 67.2	72.8	18.6	
Honigman <i>et al.</i> [20]	Yes – chart review on a sample of rule positive alerts	Unknown	Computer monitoring – trigger tool. Diagnosis codes. Allergy rules. Computer event monitoring rules. Text searching.	58	88	7.5 0.02 0.49 0.03 0.07	99.2
Hope <i>et al.</i> [21]	No – verification only, chart review on a sample of rule positive alerts	No	Computer monitoring (trigger tool); Boston site Indianapolis site			10.2 (adverse drug events). 4.4% (medication errors). 9.6 (adverse drug events) 10.0% (medication errors)	
Huang <i>et al.</i> [22]	Yes – chart review conducted on all patients at one study site	Unknown	Computer monitoring (automated detection tool).			63.5	99.2
Hwang <i>et al.</i> [23]	Yes – chart review of all patients	Unknown	Computer monitoring (adverse drug event monitor).	79.1		21	
Jha <i>et al.</i> [24]	Yes – chart review of all patients, stimulated voluntary report	Yes	Computer monitoring.			17	
Levy <i>et al.</i> [27]	Yes – chart review of all patients	Unknown	Computer monitoring (automatic laboratory signals).	62	42		
Nebeker <i>et al.</i> [28]	Yes – chart review of all patients	Yes	Computer monitoring (model for bleeding). Computer monitoring (model for delirium).	86.4 94.4	89 71	11.5 2.93	
Neubert <i>et al.</i> [29]	Yes – chart review of all patients	Unknown	Computer monitoring.	90.3	19.6		
Seeger <i>et al.</i> [34]	No – verification only, chart review of 11% of high or critical priority alerts	Unknown	Computer monitoring			12.5	
Takata <i>et al.</i> [44]	No – verification only, chart review of rule positive alerts	No	Computer monitoring (trigger tool).			16.8	
Thuermann <i>et al.</i> [48]	Yes – intensified surveillance – chart review of a small number of patients	No	Computer monitoring (surveillance).	45.1	78.9		
Weissman <i>et al.</i> [36]	Yes – chart review of all patients	No	Chart review. Interview (patient).	23.1 50.5	93.2 80.3	50.5 23.1	80.3 93.2
Whipple <i>et al.</i> [40]	No – verification only, chart review of rule positive alerts	No	Computer monitoring (detection tool).			3.7	

methods in a relatively large number of studies. Direct observation and prospective data collection were also able to identify more medication-related problems compared with other methods. However, only small numbers of studies have been undertaken with these comparisons. Medication-related problems were generally not classified according to the stages of the medication process. It was difficult to examine accuracy properly because many studies did not involve the use of a gold standard. Seriousness of medication-related problems was analyzed in only a few studies.

Chart review was a widely-examined detection method. Generally, this method demonstrated that it was better able to identify medication-related problems compared with other methods in 56% of studies. This method determined problems at the prescription or administration stage compared with other stages. Contrary to the commonly-held view that chart review is mainly associated with the detection of prescription problems, Grasso *et al.* detected a greater proportion of administration problems compared with prescription problems using the chart review method [17]. Unfortunately, in studies where seriousness of problems was examined, the chart review method tended to detect problems of low clinical significance.

Computer monitoring was able to identify more medication-related problems in over half of the comparisons made with other methods. Over half of the studies utilizing this method were restricted to a single rule type, such as an abnormal laboratory result. Such rule types lack discrimination and may lead to high false positives for medication-related problems. In some studies, signals obtained from alert or detection rules were not fully analyzed to determine the extent to which they were associated with medication-related problems. Stages of medication process were largely not addressed. Large variability was also detected in the seriousness of problems detected. With increasing investment in this method due to ready availability of data and lack of time consumption, greater attention needs to be placed on refining this method to identify problems of increased clinical significance [49].

Aside from chart review, incident reporting was the most highly studied detection method. It is also the one mostly used in determining trends over time [30]. Unfortunately, this method consistently showed under-reporting of medication-related problems. Even in situations where health professionals received regular in-service training about the importance of submitting incident reports, detection rates remained low. Yet, this method continues to be used extensively in national database analysis of medication-related problems occurring in hospitals [50]. Additional strategies that could be implemented to improve reporting rates include the development of time-efficient systems and of resources to provide feedback and action to clinicians [51]. Incident

reporting showed extensive variability in determining the seriousness of medication-related problems, demonstrating clinicians' lack of understanding about the reports they choose to submit or fears about possible reprimand if they put forward problems of enormous clinical significance [52].

Interviews with health professionals, patients or family members, were rarely analyzed as a detection method; yet, of the studies utilizing this method, important information was uncovered. Unfortunately, when examined with other methods, the interview approach usually identified fewer medication-related problems. Of the studies that considered the stages of the medication process, this method was better able to detect problems associated with prescription and administration compared with those relating to monitoring and supply. Generally, problems of high clinical significance were determined using this method. Depending on how interview questions are posed, this method can help to identify medication-related problems that are not readily shown by other methods. While it may be perceived as labour intensive [36], the use of structured forms, satisfaction questionnaires and focus groups involving patients with complex care needs, and randomly selected health professionals from different health care settings [53], can help to identify problems arising from poor communication and difficulties occurring as patients move across transition points of care [54].

Direct observation was consistently shown to identify a greater number of medication-related problems compared with other methods. However, most studies focused on medication administration rather than examining all stages of the medication process. Further work is needed to demonstrate the ability of this method to identify problems across various stages of the medication process. Direct observation has been shown to be effective in determining serious medication-related problems. Unfortunately, this method is resource intensive and time-consuming [55]. It may be more appropriate to use direct observation in providing snapshots of trends over specific periods of time and in combination with other detection methods.

Only 17 studies involved comparisons with a gold standard and wide variability in accuracy results made it difficult to draw conclusions. Reported sensitivities and specificities were generally low, indicating that some medication-related problems went unidentified or demonstrated false positives. Some studies only involved verifying detected medication-related problems using pharmacist or physician review. Examining validity of data without the use of the whole sample is debatable due to the absence of an identified denominator with which to measure the detection method. Future accuracy analyses should ensure that gold standard assessment is carried out by a blinded assessor and the gold standard is applied to all data being examined.

Conclusion

In general, high quality comparative studies examining effectiveness of detection methods were lacking. Insufficient attention has been paid to identifying medication-related problems across different stages of the medication process and to determining high severity problems. Also lacking was determining the accuracy of methods through the appropriate use of a gold standard. In view of the relatively low identification of medication-related problems using incident reporting, employment of this method in tracking trends over time should be met with more scepticism than currently occurs. Greater attention should be placed on combining methods that have consistently identified medication-related problems, such as chart review and computer monitoring to obtain a comprehensive view of trends over time. More work is needed on the use of claims data, direct care observation, interviews and prospective data collection as detection methods.

Competing Interests

The author has completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declares no support from any organization for the submitted work, no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years and no other relationships or activities that could appear to have influenced the submitted work.

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