The incidence and nature of in-hospital adverse events: a systematic review

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ABSTRACT

Introduction: Adverse events in hospitals constitute a serious problem with grave consequences. Many studies have been conducted to gain an insight into this problem, but a general overview of the data is lacking. We performed a systematic review of the literature on in-hospital adverse events.

Methods: A formal search of Embase, Cochrane and Medline was performed. Studies were reviewed independently for methodology, inclusion and exclusion criteria and endpoints. Primary endpoints were incidence of in-hospital adverse events and percentage of preventability. Secondary endpoints were adverse event outcome and subdivision by provider of care, location and type of event.

Results: Eight studies including a total of 74 485 patient records were selected. The median overall incidence of in-hospital adverse events was 9.2%, with a median percentage of preventability of 43.5%. More than half (56.3%) of patients experienced no or minor disability, whereas 7.4% of events were lethal. Operational (39.6%) and medication-related (15.1%) events constituted the majority. We present a summary of evidence-based interventions aimed at these categories of events.

Conclusions: Adverse events during hospital admission affect nearly one out of 10 patients. A substantial part of these events are preventable. Since a large proportion of the in-hospital events are operation- or drug-related, interventions aimed at preventing these events have the potential to make a substantial difference.

Adverse events (AEs) in hospitals are now widely agreed to be a serious problem, annually killing more people than breast cancer or AIDS.1 An AE is usually defined as an unintended injury or complication resulting in prolonged hospital stay, disability at the time of discharge or death and caused by healthcare management rather than by the patient’s underlying disease process.2,3 Aside from the direct harm to the patient, AEs are a considerable financial burden to the healthcare system. In 1999, it was estimated that the total costs of preventable AEs in the USA lie between $17 billion and $29 billion annually.4

In recent years, the focus in thinking about AEs has shifted from the person approach—blaming individuals for errors—to the systems approach. The systems approach assumes that people will make mistakes, and that the system that surrounds them should provide a safety net for these mistakes. Therefore, efforts to eliminate AEs should be directed towards a particular system.5 This new approach has shifted the focus of the debate on AEs from the legal consequences associated with personal responsibility, to a more constructive point of view, clearing the way for thinking about solutions.

In the aftermath of the 2001 Institute of Medicine report “To err is human,”1 many large studies have been performed concerning AEs, some of them nationwide. Although many of these studies used similar methods, they report substantially different incidences. A general overview of data on in-hospital AEs is lacking.

To make the important step towards solutions, it is necessary to gain a more detailed understanding of this problem: what percentage of events is preventable, where do the majority of events happen and which type of event is the most frequent? This will enable identification of categories of AEs that are most susceptible to interventions to improve patient safety.

To gain an insight into the overall incidence, preventability, outcome and subdivision by location, provider and type of in-hospital AEs and the evidence related to relevant patient safety interventions, we conducted a systematic review of available data from the literature.

METHODS

Literature search

Two authors (ENV, MAB) independently performed a formal computer-assisted search of the medical databases Medline (January 1966 to February 2007), Cochrane and Embase (January 1980 to February 2007). Keywords used were “adverse events” and “preventable.” Clinical studies published in peer-reviewed journals in the English language were identified. A manual cross-reference search of the eligible papers was performed to identify additional relevant articles.

Selection

In order to be able to reliably compare the data, we defined an AE as follows: an unintended injury or complication resulting in prolonged hospital stay, disability at the time of discharge or death and caused by healthcare management rather than by the patient’s underlying disease process. All studies that used this or a similar definition to evaluate the incidence of AEs in adult hospital patients and that included a minimum of 1000 patient records were eligible for inclusion. Studies that evaluated errors without linking them to outcomes and studies relying only on computerised screening data were excluded. Studies that evaluated specific types of AEs only (for example, adverse drug events only) and studies that evaluated specific populations (for example, ICU patients only) were excluded. No abstract publications without subsequent full-text
published data were used. Disagreements about inclusion were resolved in a consensus meeting.

Validity assessment
Two authors (ENV, MAB) independently assessed selected studies for methodology and endpoints. Information was extracted on the methods of data collection (prospective or retrospective), record selection and review, the time frame of included AEs and recorded interobserver variability. Primary endpoints were the incidence of AEs and the percentage of preventability. Secondary endpoints were adverse event outcome and subdivision by provider of care, location and type of event.

Data collection
Data on incidence of AEs, preventability, outcome, location, provider of care and type of event were extracted. Whenever possible, raw data were used, and percentages were calculated. Extrapolations to state or country levels were not reproduced. Data on outcome, provider of care, location and type of event were grouped into common categories that the majority of articles used.

Interventions
After analysis of the data yielded the categories of events that were responsible for the majority of adverse events, a computer-assisted search of Medline was performed to identify interventions relating to these categories of events. Only studies with a level of evidence of one or two were included.

Statistical analysis
Medians and interquartile ranges (IQR) of incidence, preventability, and the different categories of outcome, location, provider of care and type of event were calculated using Statistical Package for the Social Sciences version 12.0 (SPSS, Chicago).

RESULTS
Article retrieval
The initial search yielded 257 articles (fig 1). After reviewing the titles and abstracts, 228 articles were excluded. These articles included reviews, studies on specific types of AEs only, for example adverse drug events, and studies in specific populations, for example children or ICU patients. Of the remaining 29 studies, another 17 were excluded after reviewing the full article. Three of these studies applied a different definition of an AE; one study used an observational approach and recorded only errors without linking them to outcomes; the other two studies used a computer-assisted approach to screen a large number of patient records for certain codes denoting complications. Three studies were excluded because of an insufficient number of patient records; one of these studies used retrospective record review; the other studies would otherwise have been excluded due to methodological designs that differed from the large record review studies. Five studies presented data of patient populations already included in other publications, and six studies presented insufficient data on the primary endpoint.

Included studies
We included 12 articles in the review. Of these articles, four reported additional data of patient populations that were already included. In this review, these articles were considered as one study together with the article first published, resulting in eight reviewed studies.

Study characteristics
Characteristics of included studies are presented in tables 1 and 2. A total of 74 485 patient records were derived from the included studies. The number of hospitals per study ranged from 1 to 51 and the median number of patient records reviewed per study was 5162 (IQR 1542–14 569). All studies used a two-stage retrospective record review technique. Records were first screened by trained nurses; when positive for certain

Figure 1  Flow chart of article retrieval.
AE, adverse event.

Potentially relevant articles identified and screened (n = 257)

Articles retrieved for more detailed information (n = 29)

Articles included in systematic review (n = 12)

Studies included for data extraction (n = 8)

Articles excluded because of failure to meet inclusion criteria (n = 228)

Articles excluded because of different definition of AE (n = 3), low number (< 1000) of patient records (n = 3), publications of population data already included (n = 5) or insufficient data on primary outcome (n = 6)

Articles considered together with article first published because of already included patient populations (n = 4)
trigger criteria\textsuperscript{27} (for example an unplanned readmission, an adverse drug reaction or a hospital-acquired infection), the records were then reviewed by a physician to determine whether or not an AE had occurred. In two studies, the data from this approach were compared with voluntary reporting data.\textsuperscript{28,29} Whether or not an event was caused by healthcare management (causality judgement) was measured on a six-point scale in six studies; a score of ≥2\textsuperscript{30} or ≥4\textsuperscript{31–33} was considered positive. The other two studies did not specify the details of the causality judgement.\textsuperscript{28,29} Of the six studies that gave a judgement on preventability, four used a similar six-point scale; a score of ≥4 was considered preventable.\textsuperscript{24,28,30} The other two studies did not specify the details of the preventability judgement.\textsuperscript{29,33}

\begin{table}[h]
\centering
\caption{Included studies}
\begin{tabular}{|l|l|l|l|l|l|l|}
\hline
Reference & Year of publication & Country & No. of hospitals & No. of records & Inclusion period & Study design \\
\hline
1. Brennan et al\textsuperscript{3} & 1991 & USA & 51 & 30 121 & 1984 & Retrospective record review \\
2. O'Neil et al\textsuperscript{4} & 1993 & USA & 1 & 3141 & 1990–1991 & Retrospective record review and review of voluntary reporting data \\
3. Wilson et al\textsuperscript{5} & 1995 & Australia & 28 & 14 179 & 1992 & Retrospective record review \\
4. Thomas et al\textsuperscript{6} & 2000 & USA & 28 & 14 700 & 1992 & Retrospective record review \\
5. Vincent et al\textsuperscript{7} & 2001 & UK & 2 & 1014 & 1998 & Retrospective record review \\
6. Davis et al\textsuperscript{8} & 2002 & New Zealand & 13 & 6579 & 1998 & Retrospective record review \\
7. Baker et al\textsuperscript{9} & 2004 & Canada & 20 & 3745 & 2000 & Retrospective record review \\
8. Sari et al\textsuperscript{10} & 2006 & UK & 1 & 1006 & 2004 & Retrospective record review and review of voluntary reporting data \\
\hline
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\end{table}

\begin{table}[h]
\centering
\caption{Study characteristics}
\begin{tabular}{|l|l|l|l|l|l|l|}
\hline
Reference & Population & Method of record selection & Method of review & More than one adverse event per patient? & Time frame of included events & Kappa value for interobserver agreement & Endpoints \\
\hline
1. Brennan et al\textsuperscript{3} & Acute-care hospital patients (no psychiatric patients) & Random sample of hospitalisations from 51 hospitals & Two-stage record review: first, screening for one of 18 criteria by trained nurses; second, review by two physicians & Not specified & Occurred before and during and detected during index admission & 0.61 & Incidence, negligence, outcome, location, type of event \\
2. O'Neil et al\textsuperscript{4} & Hospital patients & All admissions to the medical service of one hospital over a 4-month period & 1. Two-stage record review: first, screening for one of 15 criteria by medical-record analysts; second, review by physician & No & Not specified & 0.57 & Incidence, preventability \\
3. Wilson et al\textsuperscript{5} & Acute-care hospital patients (no psychiatric or day-care patients) & Random sample of admissions from 28 hospitals & Two-stage record review: first, screening for one of 18 criteria by trained nurses; second, review by two medical officers & No & Occurred before\textsuperscript{*} and during and detected during or after index admission & 0.55 & Incidence, preventability, outcome, provider of care, type of event \\
4. Thomas et al\textsuperscript{6} & Hospital patients (no psychiatric, rehabilitation or drug/alcohol treatment patients) & Random sample of discharges from 28 hospitals & Two-stage record review: first, screening for one of 15 criteria by trained nurses; second, review by physician & No & Occurred before and during and detected during index admission & 0.4 & Incidence, negligence, outcome, provider of care, type of event \\
5. Vincent et al\textsuperscript{7} & Acute hospital patients (general medicine, general surgery, orthopaedic surgery, obstetrics) & Records randomly drawn from two hospitals & Two-stage record review: first, screening for one of 18 criteria by trained nurses; second, review by clinician & Yes & Not specified & Not specified & Incidence, preventability, outcome, provider of care, type of event \\
6. Davis et al\textsuperscript{8} & Hospital patients (no psychiatric, day-care or rehabilitation patients) & Random sample of admissions from 13 hospitals & Two-stage record review: first, screening for one of 18 criteria by trained nurses; second, review by medical officer & Not specified & Occurred before\textsuperscript{*} and during and detected during index admission & 0.47 & Incidence, preventability, outcome, provider of care, location, type of event \\
7. Baker et al\textsuperscript{9} & Hospital patients (no paediatric, psychiatric, obstetric or rehabilitative) & Random sample of admissions from 20 hospitals & Two-stage record review: first, screening for one of 18 criteria by trained nurses; second, review by physician & Yes & Occurred before and during and detected during or after index admission\textsuperscript{†} & 0.47/0.45/0.69\textsuperscript{†} & Incidence, preventability, outcome, provider of care, type of event \\
8. Sari et al\textsuperscript{10} & Hospital patients (surgery, general medicine, elderly care, orthopaedics, urology, oncology, ENT, ophthalmology) & Random sample of admissions in one hospital & 1. Two-stage record review: first, screening for one of 18 criteria by trained nurses; second, review by physician & Yes & Not specified & 0.76 & Incidence \\
\hline
\end{tabular}
\end{table}

\*Only included if (partly) responsible for index admission.
\footnote{Only included if occurred/was detected during a hospital admission.}
\footnote{Kappa values for interobserver agreement of judgement on injury/causation/preventability.}
Incidence, preventability and outcome

The data on incidence, preventability and outcome of case record review studies are shown in table 3. The median incidence of AEs was 9.2% (IQR 4.6–12.4%). The median percentage of AEs that was judged preventable was 43.5% (IQR 39.4–49.6%). Two studies judged negligence instead of preventability, which was defined as AEs caused by a failure to meet standards reasonably expected of the average physician or institution. Negligence data were not considered in the calculation of the median percentage of preventability.

Outcome data were divided into five categories: no or minor disability (resolved within 1 month), temporary disability (resolved within 1 year), permanent disability, death and unknown. The median percentage of AEs that led to no or minor disability was 56.3% (IQR 51.4–62.8%). Permanent disability was found in 7.0% (IQR 6.1–11.0%) of patients experiencing an AE, while 7.4% (IQR 4.7–14.2%) of AEs caused the death of the patient.

Providers of care

Providers of care were divided into three groups (table 4): surgical, containing all surgical professions, anaesthesiology, gynaecology and obstetrics; medicine, containing all internal specialties and paediatrics; and “other,” containing for example family practice, nursing and emergency medicine. The median proportion of AEs associated with surgical providers was 58.4% (IQR 54.5–70.9%) versus 24.1% (IQR 18.7–40.4%) for medical providers.

Table 3: Adverse events, preventability and outcome

| Reference | Brennan et al | O’Neil et al | Wilson et al | Thomas et al | Vincent et al | Davis et al | Baker et al | Sari et al | Median percentage (interquartile range) |
|-----------|---------------|-------------|-------------|-------------|--------------|------------|------------|----------|----------------------------------------|
| No. of records | 30 121 | 3141 | 14 179 | 14 700 | 1014 | 6579 | 3745 | 1006 | – |
| No. of patients with at least one adverse event | 1133 (3.8) | 237* (7.5) | 2353 (16.6) | 475 (3.2) | 110 (10.8) | 850 (12.9) | 255 (6.8) | 110 (10.9) | 9.2 (4.6 to 12.4) |
| No. of adverse events (if >1 adverse event per patient) | – | – | – | – | 119 (11.7) | – | 289 (7.7) | 136 (13.5) | 11.7 (7.7 to 13.5) |
| No. of preventable adverse events | – | 103* (43.5) | 1205 (51.2) | – | 57 (47.9) | 315 (37.1) | 106 (41.6) | – | 43.5 (39.4 to 49.6) |

Outcome

| Categories | No or minor disability† | Temporary disability‡ | Permanent disability§ | Death | Unknown |
|------------|------------------------|-----------------------|-----------------------|--------|---------|
| Numbers (percentages) except last column, Interquartile range = 25th to 75th percentile. | 56.3 (51.4 to 62.8) | 19.1 (15.5 to 30.3) | 7.0 (6.1 to 11.0) | 7.4 (4.7 to 14.2) | 6.5 (5.1 to 9.7) |

| Reference | Brennan et al | O’Neil et al | Wilson et al | Thomas et al | Vincent et al | Davis et al | Baker et al | Sari et al | Median percentage (interquartile range) |
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Locations

Table 5 shows the various locations where AEs took place. For all AEs, 80.8% (IQR 75.6–83.2%) were encountered in hospital, versus 14.9% (IQR 12.9–18.7%) out of hospital before admission or after discharge. The majority of events were seen in the operating room (41.0% (IQR 39.5–45.8%)) or the patient’s room (24.5% (IQR 21.6–26.5%)). By contrast, only 3.1% (IQR 2.7–3.5%) of AEs were located in the complex environment of the intensive care unit. The emergency room accounted for 3.0% (IQR 2.9–3.0%) of AEs.

Type of event

Finally, the AEs were classified according to type of event (table 6). In three studies an AE could be attributed to more than one category, whereas in the other studies, the types of events were mutually exclusive. Importantly, approximately 50% of AEs are operation- or drug-related: 39.6% (IQR 31.5–50.2%) and 15.1% (11.9–20.4%), respectively. By contrast, anaesthesia-related events formed only 2.0% (IQR 1.2–3.7%) of AEs.

Patient safety interventions

Table 7 gives an overview of the top level (level of evidence 1 and 2) of evidence-based interventions directed towards the major types of adverse events: operation- and medication-related events. The operation-related interventions include a number of medical interventions such as peroperative beta-blockade and antibiotic prophylaxis. In addition, interventions...
Table 4  Adverse events classified by providers of care

| Reference                  | Wilson et al | Thomas et al | Vincent et al | Davis et al | Baker et al | Median percentage (interquartile range) |
|----------------------------|--------------|--------------|---------------|-------------|-------------|-----------------------------------------|
| No. of adverse event/total no. of records | 2353/14 179  | 475/14 700  | 119/1 014  | 850/6 579  | 289/3 745  | –                                      |
| Surgical                   | 1375 (58.4)  | 298 (62.7)  | 94 (79.0)    | 489 (55.7)  | 149 (51.4)  | 58.4 (54.5 to 70.9)                    |
| Surgery not otherwise specified | –            | –            | –            | –           | –           | –                                      |
| General surgery            | 317 (13.5)   | –            | 47 (39.5)    | –           | –           | 26.5 (13.5 to 39.5)                    |
| Orthopaedic surgery        | 285 (12.1)   | –            | 40 (33.8)    | –           | –           | 22.9 (12.1 to 33.8)                    |
| Obstetrics                 | 140 (5.9)    | 44 (9.2)     | 7 (5.9)      | –           | –           | 5.9 (5.9 to 9.2)                       |
| Gynaecology                | 134 (5.7)    | 32 (6.7)     | –            | –           | –           | 6.2 (5.7 to 6.7)                       |
| Urology                    | 86 (3.7)     | –            | –            | –           | –           | –                                      |
| Cardiac surgery            | 77 (3.3)     | –            | –            | –           | –           | –                                      |
| Vascular surgery           | 71 (3.0)     | –            | –            | –           | –           | –                                      |
| Otolaryngology             | 59 (2.5)     | –            | –            | –           | –           | –                                      |
| Neurosurgery               | 57 (2.4)     | –            | –            | –           | –           | –                                      |
| Colorectal surgery         | 53 (2.3)     | –            | –            | –           | –           | –                                      |
| Plastic surgery            | 49 (2.1)     | –            | –            | –           | –           | –                                      |
| Anaesthesiology            | 47 (2.0)     | 3 (0.7)      | –            | –           | –           | 1.4 (0.7 to 2.0)                       |
| Medicine                   | 385 (16.4)   | 114 (21.4)   | 25 (21.0)    | 303 (35.7)  | 130 (45.0)  | 24.1 (18.7 to 40.4)                    |
| Internal medicine          | 150 (6.4)    | 110 (23.2)   | –            | –           | –           | 14.8 (6.4 to 23.2)                     |
| Cardiology                 | 116 (5.0)    | –            | –            | –           | –           | –                                      |
| Paediatrics                | 49 (2.1)     | 4 (0.9)      | –            | –           | –           | 1.5 (0.9 to 2.1)                       |
| Gastroenterology           | 43 (1.8)     | –            | –            | –           | –           | –                                      |
| Medical oncology           | 25 (1.1)     | –            | –            | –           | –           | –                                      |
| Other                      | 542 (23.0)   | 57 (11.9)    | –            | 58 (6.8)    | 10 (3.6)    | 9.4 (4.4 to 20.2)                      |
| Family practice            | 147 (6.2)    | 21 (4.4)     | –            | –           | –           | 5.3 (4.4 to 6.2)                       |
| Nursing                    | 85 (3.6)     | 8 (1.7)      | –            | –           | –           | 2.7 (1.7 to 3.6)                       |
| Emergency medicine         | 34 (1.4)     | 8 (1.7)      | –            | –           | –           | 1.6 (1.4 to 1.7)                       |
| Ophthalmology              | 28 (1.2)     | –            | –            | –           | –           | –                                      |
| Radiology                  | –            | 5 (1)        | –            | –           | –           | –                                      |
| Other                      | 248 (10.5)   | 15 (3.1)     | –            | –           | –           | 6.8 (3.1 to 10.5)                      |
| Unknown                    | 51 (2.2)     | –            | –            | –           | –           | –                                      |

Numbers (percentages) except last column. Interquartile range = 25th to 75th percentile. Wilson: numbers and percentages were given. Thomas: percentages were given, and numbers were calculated. Vincent: numbers were given, and percentages were calculated. Davis: numbers and percentages were given. Baker: numbers were given in a crosstable with type of event. Because AEs could be attributed to more than one type of event, the total was 360. Numbers and percentages in this table were calculated as a percentage of the total number of AEs.

Table 5  Adverse events classified by location

| Reference          | Brennan et al | Wilson et al | Thomas et al | Davis et al | Median percentage (interquartile range) |
|--------------------|---------------|--------------|--------------|-------------|-----------------------------------------|
| No. of adverse events/total no. of records | 1133/30 121 | 2353/14 179 | 475/14 700 | 850/6 579 | –                                      |
| In hospital        | 920 (81.2)    | 1741 (74.0)  | 396 (83.8)   | 683 (80.4)  | 80.8 (75.6 to 83.2)                      |
| Operating room     | 465 (41.0)    | 1077 (45.8)  | 188 (39.5)   | –           | 41.0 (39.5 to 45.8)                      |
| Patient’s room     | 300 (26.5)    | 577 (24.5)   | 103 (21.6)   | –           | 24.5 (21.6 to 26.5)                      |
| Emergency room     | 33 (2.9)      | –            | 14 (3.0)     | –           | 3.0 (2.9 to 3.0)                        |
| Labour and delivery room | 32 (2.8)   | 87 (3.7)     | 31 (6.5)     | –           | 3.7 (2.8 to 6.5)                        |
| Intensive care unit | 31 (2.7)     | –            | 17 (3.5)     | –           | 3.1 (2.7 to 3.5)                        |
| Radiology          | 23 (2.0)      | –            | –            | –           | –                                      |
| Cardiac catheterisation laboratory | 10 (0.9)     | –            | 20 (4.2)     | –           | 2.6 (0.9 to 4.2)                        |
| Ambulatory care unit | 9 (0.8)      | –            | –            | –           | –                                      |
| Procedure room     | –             | –            | 16 (3.4)     | –           | –                                      |
| Other              | 19 (1.7)      | –            | 10 (2.2)     | –           | 2.0 (1.7 to 2.2)                        |
| Out of hospital    | 156 (13.8)    | 297 (12.6)   | 76 (16.0)    | 167 (19.6)  | 14.9 (12.9 to 18.7)                     |
| Physician’s office  | 87 (7.7)      | 200 (8.5)    | 33 (7.0)     | 54 (6.4)    | 7.4 (6.6 to 8.3)                        |
| Patient’s home     | 31 (2.7)      | 56 (2.4)     | 16 (3.4)     | 45 (5.3)    | 3.1 (2.5 to 4.8)                        |
| Ambulatory care unit | 16 (1.4)  | –            | –            | 11 (1.3)    | 1.4 (1.3 to 1.4)                        |
| Nursing home       | 10 (0.9)      | 41 (1.7)     | 3 (0.6)      | 32 (3.8)    | 1.3 (0.7 to 3.3)                        |
| Day surgery        | –             | –            | 6 (1.2)      | –           | –                                      |
| Private hospital   | –             | –            | –            | 17 (2.0)    | –                                      |
| Other              | 12 (1.1)      | –            | 18 (3.8)     | 8 (0.9)     | 1.1 (0.9 to 3.8)                        |
| Unknown            | 58 (5.1)      | 315 (13.4)   | 1 (0.3)      | –           | 5.1 (0.3 to 13.4)                       |

Numbers (percentages) except last column. Interquartile range = 25th to 75th percentile. Brennan: percentages were given, and numbers were calculated. Wilson: numbers and percentages were given. Thomas: percentages were given, and numbers were calculated. Davis: percentages were given, and numbers were calculated.
such as training programmes for laparoscopy and a medical emergency team are mentioned. The medication-related practices include bar code technology and computerised physician order entry systems.

**DISCUSSION**

We conducted a systematic review to gain an insight into the overall incidence, preventability and outcome of adverse events and added information about location, provider and type of events. Despite the enormous amount of recent attention for patient safety, such systematic compiling of all available evidence on the subject is lacking to date.

This systematic review included eight studies from the USA, Canada, the UK, Australia and New Zealand. The median overall incidence of adverse events was 9.2%, and almost half of these events were regarded as preventable. The majority of

Table 6  Adverse events classified by type of event

| Reference          | Brennan et al | Wilson et al | Thomas et al | Vincent et al | Davis et al | Baker et al | Median percentage (interquartile range) |
|--------------------|---------------|--------------|--------------|---------------|-------------|------------|----------------------------------------|
| No. of adverse events/total no. of records | 1133/30 121 | 2952/14 179 | 475/14 700 | 118/1 014 | 1080/6 579 | 360/3 745 | –                                      |
| Operation-related  | 599 (52.9)    | 1159 (49.3)  | 213 (44.9)   | 40 (33.9)    | 258 (24.3)  | 123 (34.2) | 39.6 (31.5 to 50.2)                     |
| Drug-related       | 178 (15.7)    | 249 (10.6)   | 92 (19.3)    | 17 (14.4)    | 130 (12.3)  | 85 (23.6)  | 15.1 (11.9 to 20.4)                     |
| Diagnostic         | 79 (7.0)      | 314 (13.3)   | 33 (8.9)     | 5 (4.2)      | 85 (8.0)    | 38 (10.6)  | 7.5 (6.2 to 11.3)                       |
| Therapeutic        | 62 (5.5)      | 276 (11.7)   | 21 (4.4)     | –            | 89 (8.4)    | –          | 7.0 (4.7 to 10.9)                       |
| Procedure*         | 88 (7.8)      | 197 (8.4)    | 64 (13.5)    | 6 (5.1)      | 82 (7.7)    | 26 (7.2)   | 7.8 (6.7 to 9.7)                       |
| Fall/fracture      | 38 (3.4)      | 192 (8.2)    | 8 (1.7)      | –            | –          | 8 (2.2)    | 2.8 (1.8 to 7.0)                       |
| Postpartum/obstetric | 18 (1.6)      | 126 (5.4)    | 17 (3.6)     | –            | –          | 1 (0.3)    | 2.6 (0.6 to 5.0)                       |
| Anaesthesia-related | 13 (1.1)      | 51 (2.2)     | 6 (1.3)      | 6 (5.1)      | –          | 7 (2.0)    | 2.0 (1.2 to 3.7)                       |
| Neonatal           | 29 (3.0)      | 30 (1.3)     | 15 (3.1)     | –            | –          | –          | 3.0 (1.3 to 3.1)                       |
| System/f/other     | 29 (3.0)      | 358 (15.2)   | 7 (1.5)      | –            | 416 (39.3)  | 29 (8.1)   | 8.1 (2.3 to 27.3)                      |
| Ward management    | –             | –            | –           | 30 (25.4)    | –          | –          | –                                      |
| Discharge           | –             | –            | –           | 14 (11.9)    | –          | –          | –                                      |
| Other clinical management | – | – | – | – | 43 (11.9) | – | – |

Brennan: numbers were given, percentages were calculated. Wilson: numbers and percentages were given. Thomas: percentages were given, and numbers were calculated. Vincent: numbers were given, and percentages were calculated. Davis: numbers and percentages were given. Baker: numbers were given, and percentages were calculated.

Numbers (percentages) except last column. Interquartile range = 25th to 75th percentile.

*Medical procedure such as coronary angiography or endoscopy.

†Contains: defective equipment or supplies, inadequate reporting or communication, inadequate staffing, training or supervision, no protocol/failure to implement protocol.

Table 7  Interventions related to operation- and drug-related events

| Type of event       | Intervention                                      | Highest-level study example                                                                 | Level of evidence |
|---------------------|---------------------------------------------------|---------------------------------------------------------------------------------------------|------------------|
| Operation-related   | Localising care to high-volume centres            | Halm et al. Is volume related to outcome in health care? A systematic review and methodologic critique of the literature. Ann Intern Med 200226 | 2A               |
|                     | Training programmes for laparoscopic procedures   | Scheeres et al. Animate advanced laparoscopic courses improve resident operative performance. Am J Surg 200424 | 2B               |
|                     | Medical emergency team                            | Bellomo et al. Prospective controlled trial of effect of medical emergency team on postoperative morbidity and mortality rates. Crit Care Med 200428 | 2B               |
|                     | Ultrasound guidance of central vein catheterisation| Randolph et al. Ultrasound guidance for placement of central venous catheters: a meta-analysis of the literature. Crit Care Med 199646 | 1A               |
| Prevention of surgical site infections: | Antibiotic prophylaxis                            | Song et al. Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomized controlled trials. Br J Surg 199840 | 1A               |
| Peri-operative normothermia |                                    | Kurz et al. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. N Engl J Med 199637 | 1B               |
| Supplemental oxygen |                                    | Greif et al. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. N Engl J Med 200030 | 1B               |
| Glucose control in diabetics |                                    | Fumary et al. Clinical effects of hyperglycaemia in the cardiac surgery population: the portland diabetic project. Endocr Pract 200641 | 2B               |
| Perioperative beta blockers |                                    | Devereaux et al. How strong is the evidence for the use of perioperative beta blockers in non-cardiac surgery? Systematic review and meta-analysis of randomised controlled trials. BMJ 200542 | 1A               |
| Drug-related        | Computerised Physician Order Entry (CPOE) and Clinical Decision Support System (CDSS) | Overhage et al. A randomized trial of “corollary orders” to prevent errors of omission. J Am Med Inform Assoc 199343 | 1B               |
|                     | Clinical pharmacist consultation services          | Leape et al. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. JAMA 199944 | 2B               |
|                     | Bar code technology in pharmacy                   | Poon et al. Medication dispensing errors and potential adverse drug events before and after implementing bar code technology in the pharmacy. Ann Intern Med 200645 | 2B               |
| Patient self-management of anticoagulation |                                    | Cromheecke et al. Oral anticoagulation self-management and management by a specialist anticoagulation clinic: a randomized crossover comparison. Lancet 200047 | 1B               |
events were associated with a surgical care provider, and more than half of events were operation- or drug-related.

Although all included studies used the same definition, incidences of adverse events varied considerably. In 2000, a comparison was made between the Utah/Colorado study (incidence 3.2%) and the Australian study (incidence 16.6%), and a number of possible reasons for this difference were provided.47–49 There were a number of methodological differences between the studies, such as a lower threshold for defining causation in the Australian study and inclusion of some types of events in one study that were excluded in the other. Aside from these differences, the authors suggest that the disparity might be due to differences in quantity and methods of documentation between Australia and the USA, and different perspectives of the two studies (medicolegal versus quality-improvement). These considerations may also apply to the other studies included in this review. For example, both studies that were performed from a medicolegal point of view47–49 reported considerably lower incidences than the other studies, performed from a quality-improvement point of view.50–52 Furthermore, not all studies employed the same time frame for included events. Out-of-hospital events were included in only a few studies. Some studies only recorded one adverse event per patient record, whereas others did not enforce this restriction. These methodological differences may well, at least in part, account for the difference between the recorded incidences.

Retrospective record review has been criticised for a number of reasons. As it relies heavily on patient records, it is dependent on the quality of documentation. If adverse events are not documented properly, they will not be detected by this method. Furthermore, only those adverse events are detected that result in one of the trigger criteria of the review method. Finally, in retrospective record review, the interobserver variability is very high, especially with regard to the judgements on causality and preventability.49 The studies included in this review show moderate interobserver agreement scores, illustrating this drawback of retrospective record review.

Aside from the fact that the conclusions from this review are based solely on retrospective record review studies, and as such, most likely represent an underestimation of the problem, there are a number of other limitations of this systematic review, the most important one being the heterogeneity of the included studies. Although most studies used roughly the same methods, the details differed considerably. For example, the studies from Australia and New Zealand applied a lower threshold for causation than the other studies. The time frame of included events also differed between studies: the studies from the United States did not include events discovered after discharge, whereas the other included studies did. Because differences in methodology and perspective may lead to different numbers of recorded AEs,47–49 we must proceed with caution when drawing conclusions from the combined data from these studies. Apart from differences in methodology between the included studies, our strict inclusion criteria potentially may have caused us to exclude interesting studies. The three studies we excluded because of an insufficient number of patient records evaluated, when combined, 1607 records, amounting to 2% of all records included in this systematic review (more than 74 000 records). The two excluded studies that used a computer-assisted approach15 reported incidences of adverse events that were slightly lower (8.3% and 6.9%) than the median incidence of the studies included in the present review. This approach is much less time-consuming than the retrospective record review, but a drawback is that it cannot make judgements on causation or preventability.

Much attention is being devoted to finding solutions to improve patient safety. In 2005, the authors of some of the largest adverse event studies advocated the implementation of selected evidence-based practices that have a potential for large impact.53 When looking at the classification of events as demonstrated in this review, operation-related and drug-related events together comprise the majority. It would thus be logical to concentrate funds and efforts on evidence-based interventions aimed at reducing these events. In addition to the evidence-based interventions reviewed here, there are a number of other interventions that seem promising but warrant further research to prove their value. This includes interventions derived from the aviation industry, such as crew resource management and the use of checklists in the operating room.

In conclusion, adverse events during hospital admission are a serious problem, occurring in approximately 9% of all admitted patients and leading to a lethal outcome in 7% of cases. Since a large portion of the adverse events are operation- or drug-related, and almost half of these events are preventable, funds and efforts should be concentrated on interventions aimed at reducing these types of events.

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