EXHIBIT 2

Hospital Admissions Associated with Adverse Drug Reactions: A Systematic Review of Prospective Observational Studies

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OBJECTIVE: To determine the prevalence of hospital admissions associated with ADRs and examine differences in prevalence rates between population groups and methods of ADR detection.

DATA SOURCES: Studies were identified through electronic searches of Cumulative Index to Nursing and Allied Health Literature, EMBASE, and MEDLINE to August 2007. There were no language restrictions.

STUDY SELECTION AND DATA EXTRACTION: A systematic review was conducted of prospective observational studies that used the World Health Organization ADR definition. Subgroup analysis examined the influence of patient age groups and methods of ADR detection on reported ADR admission rates. All statistical analyses were performed using STATA v 9.0.

DATA SYNTHESIS: Twenty-five studies were identified including 106,586 patients who were hospitalized; 2143 of these patients had experienced ADRs. The prevalence rates of ADRs ranged from 0.16% to 15.7%, with an overall median of 5.3% (interquartile range [IQR] 2.7–9.0%). Median ADR prevalence rates varied between age groups; for children, the ADR admission rate was 4.1% (IQR 0.16–5.3%), while the corresponding rates for adults and elderly patients were 6.3% (IQR 3.9–9.0%) and 10.7% (IQR 9.6–13.3%), respectively. ADR rates also varied depending on the methods of ADR detection employed in the different studies. Studies that employed multiple ADR detection methods, such as medical record review and patient interview, reported higher ADR admission rates compared with studies that used medical record review alone. Antiinfective drugs were most often associated with ADR admissions in children; cardiovascular drugs were most often associated with ADR admissions in adults and elderly patients.

CONCLUSIONS: Approximately 5.3% of hospital admissions were associated with ADRs. Higher rates were found in elderly patients who are likely to be receiving multiple medications for long-term illnesses. The methods used to detect ADRs are also likely to explain much of the variation in the reported ADR prevalence rates between different studies.

KEY WORDS: adverse drug event, adverse drug reaction, hospital admission.

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Medications are the most commonly used clinical intervention and complications associated with their use constitute one of the most common causes of adverse events in health care.[1,2] Adverse drug reactions (ADRs) are a major cause of morbidity and pose a substantial burden on limited healthcare resources.[3] In Western countries, it has been estimated that serious ADRs occur in 6.7% of hospitalized patients and are responsible for approximately 5–9% of inpatient costs.[4,5]

Previous systematic reviews have explored the magnitude, nature, and prevalence of ADRs causing hospital admissions.[6-8] However, these earlier reviews have a number of limitations in that they have focused on a specific patient group,[7] not used a standardized definition of ADRs,[7,8] or combined the results from retrospective and prospective studies.[6] Kvasz et al.[9] have previously argued for the need to ensure consistency in the ADR definition used, population studied, and methods of ADR detection in comparing results across studies. However, limited attention has been given to these issues in earlier systematic reviews. The aims of this study were to estimate the prevalence of hospital admissions asso-

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ciated with ADRs using a standardized definition proposed by the World Health Organization (WHO) and examine how the prevalence varied between different population groups and the methods of ADR detection.

Data Sources and Study Selection

INCLUSION CRITERIA

The following criteria were used for inclusion of studies into our systematic review.

1. Studies were included if they were prospective and observational and provided sufficient data (ie, number of patients who had an ADR requiring hospital admission as the numerator, number of patients admitted to hospital during study period as the denominator) to calculate the prevalence of hospital admissions associated with ADRs.
2. Patients had been admitted to any hospital department, including through emergency departments.
3. Studies explicitly stated that they had used the WHO ADR definition or the ADR definition reported in the paper mapped directly onto the WHO ADR definition, namely that "an adverse reaction to a drug is one that is noxious, unintended, and occurs at doses normally used in man."[10-12]

EXCLUSION CRITERIA

Studies that addressed only specific types of ADRs or ADRs in patients with a particular disease were excluded.

SEARCH STRATEGY

We systematically searched the Cumulative Index to Nursing and Allied Health Literature, EMBASE, and MEDLINE from their inception dates to August 2007 using the following key words: adverse drug reaction, adverse reaction, adverse drug event, adverse event, drug-related problem, meta-analysis, and hospital admission. MeSH terms were used, where appropriate, in combination with key words. The literature retrieval was supplemented by manually searching the reference list of all identified articles. There were no language restrictions.

DATA EXTRACTION

Data were extracted on the study design and ADR prevalence rate onto a data extraction form, which was developed prior to the study. Other information obtained from the identified studies included medications involved in the ADR admissions, method of ADR detection, study setting, duration of the study, and study population.

DATA ANALYSIS

ADR prevalence rates were calculated for each study as the number of patients admitted to the hospital with at least one ADR divided by the total number of patients admitted to the hospital during the study period. Heterogeneity between the different ADR prevalence rates was assessed using χ^2 and I^2 tests to determine whether it would be appropriate to compute a meta-analytic summary estimate.[13] Given the high levels of heterogeneity between the different studies (χ^2 1626, df 24; $p < 0.001$; I^2 98.5%), results across the studies were summarized using the median rate and interquartile range (IQR).

To explore possible reasons for heterogeneity, subgroup analyses were performed to examine the impact of population age groups and methods of ADR detection on the reported ADR prevalence rates. Where possible, studies were classified into 3 age groups: children (≤16 y), adults (17–60 y), or elderly patients (>60 y). Since heterogeneity between studies within the children subgroup (χ^2 73.06; df 2; $p < 0.001$; I^2 97.3%), adult subgroup (χ^2 102.17; df 9; $p < 0.001$; I^2 91.2%), and elderly subgroup (χ^2 13.34; df 4; $p = 0.010$; I^2 70.0%) was very high, the prevalence rates within the subgroups were presented using the median and IQR. In addition, the median ADR prevalence rates between studies using only medical record review to detect ADRs were compared against those using medical record review and patient interview within each of the age groups. All calculations were performed using STATA v 9.0 (StataCorp LP, College Station, TX) statistical software.

Data Synthesis

SEARCH RESULTS

Of the 33 studies identified, 25 that had been published between 1987 and 2003 were eligible for inclusion (Figure 1). Three studies were excluded, as they provided insufficient data to calculate ADR prevalence rates,[14-16] and 5 studies had used retrospective designs.[17-21] Seventeen studies were conducted in Europe,[22-38] 3 in Asia,[39-41] 2 in Australia,[42,43] 2 in North America,[44,45] and 1 in South America.[46] Across the 25 studies, 106,586 patients were admitted to the hospital; 2143 patient admissions were associated with ADRs. The prevalence rate of ADR admissions ranged from 0.16% to 15.7%, as shown in Table 1. The overall median ADR prevalence rate was 5.3% (IQR 2.7–9.0%).

Seven studies included patients of all ages,[24,26,28,30,34,39,40] 3 focused on children,[33,38,41] 10 focused on adults,[22,23,27,29,31,32,35,36,42,46] and 5 included elderly patients.[25,37,43-45] Several methods were used to detect ADRs, including medical record review (9 studies[23,25-28,31,35,41,44]), medical record review combined with patient interviews (13 studies[22,24,29,30,32,34,36-39,43,45,46]), or medical record review combined with spontaneous reporting of ADRs within the hospital (3 studies[33,40,42]). One study compared methods of ADR detection between

medical record review and computer-assisted surveillance of ADRs.[23]

Only 2 studies reported on the severity of ADRs requiring hospital admission.[31,38] Different scales were applied for each study. Dormann et al.[31] found that 51.8% of ADRs were mild, 44.9% were moderate, and 3.3% were severe, whereas Martinez-Mir et al.[38] reported that 4.8% of ADRs were mild, 57.1% were moderate, 38.1% were severe, and no fatal ADR was found.

TYPES OF MEDICATIONS INVOLVING CHILDREN

Three studies examined the prevalence of ADRs in children (n = 41,056), with 133 admissions associated with ADRs leading to hospitalization. The median ADR prevalence rate was 4.1% (IQR 0.16–5.3%). Two studies reported on the main types of medications involved in ADRs, which were antiinfective drugs (42.6%), respiratory drugs (17.5%), and vaccines (8.4%)[38,41] (Table 2).

TYPES OF MEDICATIONS INVOLVING ADULTS

Ten studies examined the ADR prevalence rate in adults (n = 11,477); 620 patients experienced ADRs that necessitated hospitalization. Across the adult studies, the median ADR prevalence rate was 6.3% (IQR 3.9–9.0%). Eight of these studies reported types of medications.[27,29,31,32,35,36,42,46] Cardiovascular drugs (45.7%), nonsteroidal antiinflammatory drugs (NSAIDs) (14.6%), and central nervous system agents (9.7%) were the main medications reported to be involved in the ADR reports (Table 2).

TYPES OF MEDICATIONS INVOLVING ELDERLY PATIENTS

Five studies examined the ADR prevalence rate in elderly patients (n = 2029) in which 201 patients were admitted to the hospital because of ADRs. Across the 5 studies, the median ADR prevalence rate was 10.7% (IQR 9.6–13.3%). Four studies reported ADR-related medications (Table 2).[25,37,44,45] The main types of medications involved were cardiovascular drugs (42.5%), NSAIDs (18.8%), and central nervous system drugs (13.8%).

Table 3 shows that higher median ADR prevalence rates were found in studies that used combined methods of medical record review and patient interview rather than medical record review alone for each of the 3 age groups.

Discussion

The findings from this systematic review suggest that ADRs represent a significant burden on health care. On average, 5.3% of hospital admissions were associated with ADRs. Our results suggest higher prevalence rates than were shown in 2 earlier systematic reviews. Lazarou et al.[4] reviewed 21 prospective studies published between 1966 and 1996 and estimated that 4.7% (weighted meta-analytic estimate) of hospital admissions were associated with ADRs. More recently, Wiffen et al.[8] suggested the proportion of admissions associated with ADRs to be 3.1%. These differences are likely due to the fact that we have focused our review on prospective observational studies that have used a well-established and consistent ADR definition. In contrast, the Wiffen et al. study results were derived from prospective and retrospective studies that had used a variety of different ADR definitions. Likewise, many of the studies included in the Lazarou et al. review either did not explicitly state an ADR definition or the definition used did not map onto that proposed by the WHO. Caution is therefore warranted in comparing our results with those of the earlier reviews, especially reviews that calculated meta-analytic summary estimates despite very

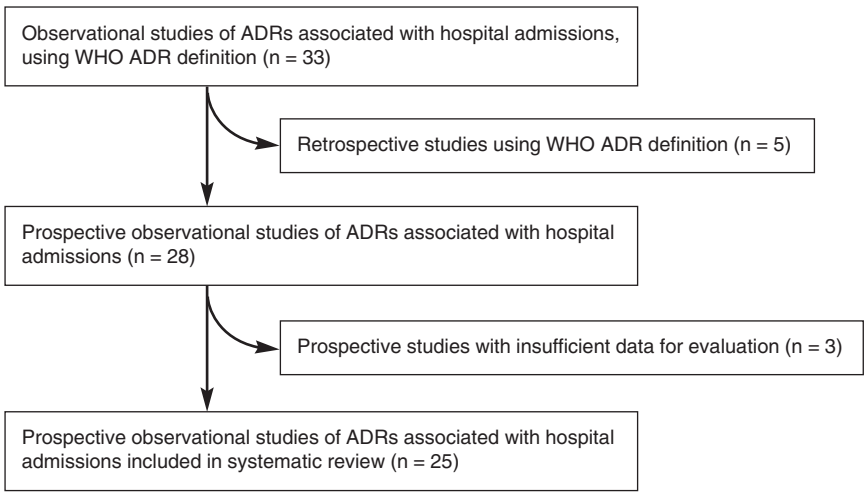

Figure 1. Flowchart of ADR studies included in the systematic review. ADR = adverse drug reaction; WHO = World Health Organization.

Table 1. Characteristics of Prospective Studies Examining the Prevalence of ADR Admissions

Reference	Country	Study Duration, mo	Study Year	Study Ward	Type of Hospital	Population	Study Method	Prevalence Rate
Alcalde Tirado (2001)[25]	Spain	9	1998/1999	acute geriatric care unit	general	elderly	medical record review	44/610 (7.2%)
Buajordet (2002)[33]	Norway	5	1996	general pediatric department	university	children (<16 y)	medical record review, spontaneous reporting	49/919 (5.3%)
Chan (2001)[43]	Australia	2	1998	all medical wards	public	elderly (≥75 y)	medical record review, interview	32/240 (13.3%)
Courtman (1995)[44]	Canada	5	1992/1993	medical ward	tertiary teaching	elderly (range 65–108 y)	medical record review	16/150 (10.6%)
Dartnell (1996)[42]	Australia	1	1994	emergency department	tertiary teaching	adults (range 15–91 y)	medical record review, spontaneous reporting	26/965 (2.7%)
Davidsen (1988)[36]	Denmark	2	1986	department of cardiology	university	adults	medical record review, interview	49/426 (11.5%)
Dormann (2004)[31]	Germany	18	NS	department of internal medicine	university	adults (range 18–97 y)	medical record review	39/ 630 (6.2%)
Garijo (1991)[35]	Spain	5	NS	medicinal emergency department	university	adults	medical record review	72/1847 (3.9%)
Green (2000)[27]	UK	NS	NS	acute medical assessment unit	university	adults (range 18–89 y)	medical record review	18/200 (7.5%)
Grymonpre (1988)[45]	Canada	4	1983	department of medicine	tertiary referral center, primary care	elderly	medical record review, interview	83/863 (9.6%)
Guemes (1999)[28]	Canary Islands	3	NS	emergency department	general	all pts.	medical record review	9/219 (4.1%)
Howard (2003)[22]	UK	6	2001	medical admissions unit	teaching	adults (>16 y)	medical record review, interview	178/4093 (4.3%)
Kjustad (1987)[37]	Norway	2	1984	medical and surgical ward	regional	elderly (>70 y)	medical record review, interview	26/166 (15.7%)
Lamabadusuriya (2003)[41]	Sri Lanka	11	2002	medical units	university pediatric	children	medical record review	63/39,625 (0.16%)
Lepori (1999)[29]	Switzerland	12	1996/1997	medical clinics	regional	adults (≥17 y)	medical record review, interview	138/2168 (6.4%)
Malhotra (2001)[39]	India	8	1999	emergency department	tertiary care	all pts.	medical record review, interview	5/1072 (0.5%)
Martinez Mir (1996)[38]	Spain	6.8	NS	all wards	university pediatric	children (≤2 y)	medical record review, interview	21/512 (4.1%)
Mjorndal (2002)[32]	Sweden	9	1997/1998	departments of medical and cardiology	university	adults (range 21–92 y)	medical record review, interview	82/681 (12.04%)
Olivier (2001)[26]	France	1	1998	medical admission ward	university	all pts.	medical record review	41/671 (6.1%)
Pfaffenbach (2002)[46]	Brazil	4	1997/1999	internal medicine ward	university	adults (≥13 y)	medical record review, interview	9/135 (6.6%)
Pouyanne (2000)[34]	France	0.5	1998	medical wards	teaching general	all pts.	medical record review, interview	100/3137 (3.2%)
Ramesh (2003)[40]	India	7	2001/2002	all inpatient wards	tertiary	all pts.	medical record review, spontaneous reporting	26/3717 (0.7%)
Raschetti (1999)[30]	Italy	3	1994/1995	emergency department	public	all pts.	medical record review, interview	15/1833 (0.8%)

ADR = adverse drug reaction; NS = not stated.

(continued on page 1021)

high levels of heterogeneity being present among the studies evaluated.

The prevalence rate of ADRs varied between the different age groups, with elderly patients experiencing far more ADRs compared with children or adults. As noted by Pham and Dickman,[47] elderly patients are particularly vulnerable to adverse drug events because of multiple drug regimens and age-associated changes in pharmacokinetics and pharmacodynamics. Medications commonly reported to be involved in ADRs in elderly patients included those used to treat cardiovascular and central nervous system disorders, as well as NSAIDs. Similar findings were recently reported in a systematic review of 9 studies examining preventable drug-related hospital admissions, in which approximately half of the admissions involved antiplatelets (16%), diuretics (16%), NSAIDs (11%), or anticoagulants (8%).[48]

Our systematic review has also shown that studies using more intensive methods for ADR detection consistently found higher prevalence rates for ADR admissions across all 3 age groups. Specifically, studies that used medical record review and patient interview provided the highest prevalence rates. This finding is in line with the conclusions of Field et al.,[49] who found that voluntary reporting by healthcare professionals had several major limitations and suggested that multiple strategies for detection of adverse drug events are required. Furthermore, studies that included pharmacists as chart reviewers have been shown to detect higher rates of adverse drug events than those that included other healthcare professionals as chart reviewers.[50]

Given the high level of morbidity associated with ADRs, there is a need for large-scale, rigorously designed prospective intervention studies using clinically relevant outcome measures. In terms of clinical interventions, recent systematic reviews have found that pharmacist-led medication reviews can reduce polypharmacy and improve patient knowledge and adherence to treatment, but have limited effect on reducing hospital admissions.[51,52] No evidence to support the effectiveness of other interventions (including those led by other primary healthcare professionals) was found.[52] Interventions that target specific high-risk drug groups, such as cardiovascular drugs, NSAIDs, and drugs used to treat central nervous system disorders, are likely to achieve the greatest benefits in reducing the number of drug-related hospital admissions. The use of more intensive methods for ADR detection, such as medical record review combined with patient interview, and particularly the role of pharmacists as medical chart reviewers, will also be important in the design of future studies. Only 2 of our included studies reported on the severity of ADR admission; this is an important knowledge gap that should be addressed as part of future research in this field.

Strengths and Limitations of the Review

To minimize publication bias, a broad range of electronic databases were searched and supplemented by manually checking the reference lists of all included studies. Strict inclusion criteria were applied when appraising the different studies. The systematic review was limited to studies that used the WHO ADR definition to control for some of the marked variation in the definitions employed in this broad field of research. The review was also limited to prospective observational studies to avoid the risks of recall bias and problems related to incomplete documentation. In addition, the differences in reported ADR rates between different population groups and the methods used to identify ADRs accounted for substantial variation among the studies.

Despite these strengths, several important limitations remain that need to be taken into consideration when interpreting the findings of this systematic review. Given the observed heterogeneity between the studies, it was not appropriate to calculate a meta-analytic summary estimate. Instead, we provided median rates and their corresponding IQR for each of the predefined subgroups. However, dif-

Table 1. Characteristics of Prospective Studies Examining the Prevalence of ADR Admissions (continued)

Reference	Country	Study Duration, mo	Study Year	Study Ward	Type of Hospital	Population	Study Method	Prevalence Rate
Schneeweiss (2002)[24]	Germany	30	2000	departments of internal medicine and emergency	in urban regions	all pts.	medical record review, interview	993/41,375 (2.4%)
Thuermann (2002)[23,a]	Germany	3	1999	department of neurology	teaching	adults (range 16–93 y)	medical record review	9/332 (2.7%)[b]

ADR = adverse drug reaction.
[a]This study compared methods of ADR detection between an intensified surveillance and computer-assisted surveillance.
[b]ADRs were identified by medical record review (intensified surveillance).

Table 2. Drug Groups Associated with ADRs Requiring Hospital Admission[a]

Reference	GI System	CVS[b]	Respiratory	CNS[c]	Antiinfectives	Endocrine	Contraceptives	Immuno-suppression	Nutrition and Blood	NSAIDs	Eye	Skin	Vaccines	Anesthesia	Other
Children															
Lamabadusuriya (2003)[41]	0.0	0.0	0.0	17.5	60.3	0.0	0.0	0.0	0.0	7.9	0.0	0.0	14.3	0.0	0.0
Martinez-Mir (1996)[38]	5.0	5.0	35.0	15.0	25.0	0.0	0.0	0.0	0.0	0.0	0.0	10.0	2.5	0.0	2.5
Median (range)	2.5 (0.0–5.0)	2.5 (0.0–5.0)	17.5 (0.0–35.0)	16.2 (15.0–17.5)	42.6 (25.0–60.3)	0.0 NA	0.0 NA	0.0 NA	0.0 NA	4.0 (0.0–7.9)	0.0 NA	5.0 (0.0–10.0)	8.4 (2.5–14.3)	0.0 NA	1.2 (0.0–2.5)
Adults															
Dartnell (1996)[42]	0.0	30.8	0.0	0.0	0.0	30.8	0.0	19.2	0.0	19.2	0.0	0.0	0.0	0.0	0.0
Davidsen (1988)[36]	0.0	81.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	18.4
Dormann (2004)[31]	11.2	18.8	0.9[d]	23.1	13.2	0.0	0.0	0.6	15.8[e]	0.0	0.0	0.0	0.3	3.3[f]	4.3
Garijo (1991)[35]	0.0	10.0	2.9[d]	2.9	0.0	14.3	0.0	1.4	0.0	67.1	1.4	0.0	0.0	0.0	0.0
Green (2000)[27]	0.0	43.8	0.0	12.5	6.2	0.0	0.0	0.0	0.0	37.5	0.0	0.0	0.0	0.0	0.0
Lepori (1999)[29]	0.0	65.0	0.0	9.0	0.0	0.0	0.0	0.0	0.0	18.0[g]	0.0	0.0	0.0	0.0	8.0
Mjorndal (2002)[32]	9.7	47.6	0.0	10.4	4.0	8.1	4.0[h]	5.6	0.0	4.8[i]	0.0	0.0	0.0	0.0	5.6
Pfaffenbach (2002)[46]	0.0	66.7	0.0	11.1	0.0	11.1	0.0	0.0	0.0	11.1[j]	0.0	0.0	0.0	0.0	0.0
Median (range)	0.0 (0.0–11.2)	45.7 (10.0–81.6)	0 (0.0–2.9)	9.7 (0.0–23.1)	0.0 (0.0–6.2)	4.0 (0.0–30.8)	0.0 (0.0–4.0)	0.3 (0.0–19.2)	0.0 (0.0–15.8)	14.6 (0.0–67.1)	0.0 (0.0–1.4)	0.0 NA	0.0 (0.0–0.3)	0.0 (0.0–3.3)	2.2 (0.0–18.4)
Elderly															
Alcalde Tirado (2001)[25]	0.0	47.4	5.3[d]	0.0	5.3	5.3	0.0	15.8	0.0	21.0	0.0	0.0	0.0	0.0	0.0
Courtman (1995)[44]	0.0	37.5	6.2[d]	18.8	6.2	0.0	0.0	0.0	0.0	31.2	0.0	0.0	0.0	0.0	0.0
Grymonpre (1988)[45]	0.0	65.2	0.0	8.7	0.0	15.9	0.0	0.0	0.0	10.1	0.0	0.0	0.0	0.0	0.0
Kjustad (1987)[37,k]	NA	5.4	5.3[l]	66.0	15.0	NA	NA	NA	NA	16.6	NA	NA	NA	NA	NA
Median (range)	0.0 NA	42.5 (5.4–65.2)	5.3 (0.0–6.2)	13.8 (0.0–66.0)	5.8 (0.0–15.0)	5.3 (0.0–15.9)	0.0 NA	0.0 (0.0–15.8)	0.0 NA	18.8 (10.1–31.2)	0.0 NA	0.0 NA	0.0 NA	0.0 NA	0.0 NA

ADR = adverse drug reaction; CNS = central nervous system; CVS = cardiovascular system; GI = gastrointestinal; NA = not applicable; NSAIDs = nonsteroidal antiinflammatory drugs.

[a]Percent of all ADRs.

[b]Includes diuretics, β-receptor blockers, calcium-channel blockers, angiotensin-converting enzyme inhibitors, nitrates, antithrombotics, anticoagulants, and cardiac glycosides.

[c]Includes analgesics, neuroleptics, antiepileptics, antiparkinsonian drugs, antipsychotics, and antidepressants.

[d]Antihistamine.

[e]Electrolytic, caloric, and water balance.

[f]Includes local anesthetics and smooth muscle relaxants.

[g]Includes NSAIDs and corticosteroids.

[h]Includes contraceptives and hormone replacement therapy.

[i]Includes NSAIDs and analgesics.

[j]Dipyrone.

[k]Some events were associated with drugs in more than one category; therefore, frequencies total more than 100%.

[l]Theophylline.

ferences in the healthcare setting and country may also impact the prevalence of hospitalizations associated with ADRs.[53,54] The studies included in our review were conducted over a period of 19 years in 14 different countries, mostly in the Western hemisphere. As a consequence, the results of the review may not be applicable to all countries, but rather serve as a benchmark for countries in which ADR prevalence rates are poorly characterized.

Summary

ADRs continue to be an important risk to patient safety. This systematic review suggests that approximately 5.3% of hospital admissions are associated with ADRs, with much higher rates reported for elderly patients. ADR rates also varied depending on the method of detection used, with studies using medical record review combined with patient interview reporting the highest rates. Future research should focus on rigorously designed intervention studies to reduce the burden of drug-related hospitalizations, and targeting interventions toward patients using specific drug groups is likely to achieve the greatest impact.

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Table 3. Subgroup Analyses of Prevalence Rates by Age Group and Method of ADR Detection

Subgroup	Studies (n)	Crude ADR Rate (%)	Median ADR Rate (IQR), %
Children (≤16 y)			
Medical record review	1	63/39,625 (0.16)	
Medical record review and patient interview	1	21/512 (4.1)	
Adults (17–60 y)			
Medical record review	4	138/3009 (4.6)	5.05 (3.3-7.6%)
Medical record review and patient interview	5	456/7503 (6.1)	6.7 (6.4-11.5%)
Elderly (>60 y)			
Medical record review	2	60/760 (7.9)	8.95 (7.2-10.7%)
Medical record review and patient interview	3	141/1269 (11.1)	13.3 (9.6-15.7%)

ADR = adverse drug reaction; IQR = interquartile range.

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Admisiones al Hospital Asociadas con Reacciones Adversas: Una Revisión Sistemática de Estudios de Observación Prospectivos

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EXTRACTO

TRASFONDO: Las reacciones adversas a fármacos (ADRs) son una causa principal de morbilidad y representan una carga sustancial sobre los limitados recursos de asistencia de salud.

OBJETIVO: Determinar la prevalencia de las admisiones al hospital asociadas con ADRs y examinar diferencias en los índices de prevalencia entre grupos de población y métodos para detectar ADRs.

MÉTODO: Se realizó una revisión sistemática de estudios de observación prospectivos que utilizaron la definición de ADR de la Organización Mundial para la Salud. Los estudios fueron identificados a través de búsquedas electrónicas de CINAHL, EMBASE, y MEDLINE hasta agosto de 2007. No hubo restricciones de idioma. Un análisis de subgrupo examinó la influencia de grupos de diferentes edades de pacientes y los métodos para detectar ADRs, sobre los índices de admisión debido a ADRs reportados. Todos los análisis estadísticos se realizaron utilizando STATA v 9.0.

RESULTADOS: Veinticinco estudios fueron identificados incluyendo 106,586 pacientes que fueron admitidos al hospital, de los cuales 2143 pacientes habían experimentado ADRs. Los índices de prevalencia de ADRs variaron de 0.16% a 15.7%, con una mediana total de 5.3% (amplitud inter-cuartil [IQR] 2.7–9.0%). La mediana de los índices de prevalencia de ADRs también varió entre los grupos de diferentes edades; para los niños, el índice de admisión por ADRs fue 4.1% (IQR 0.16–5.3%), mientras que los índices correspondientes para pacientes adultos y ancianos fueron 6.3% (IQR 3.9–9.0%) y 10.7% (IQR 9.6–13.3%) respectivamente. Los índices de ADRs también variaron dependiendo de los métodos utilizados para detectar ADRs en los diferentes estudios. Estudios que emplearon múltiples métodos para la detección de ADRs tales como la revisión de expedientes médicos y entrevistas a pacientes, reportaron

índices de admisión por ADRs mayores que estudios que utilizaron la revisión de expedientes médicos solamente. Los fármacos antiinfecciosos estuvieron asociados más frecuentemente con admisiones por ADRs en niños, mientras que los fármacos cardiovasculares estuvieron asociados más frecuentemente con admisiones por ADRs en pacientes adultos y ancianos.

CONCLUSIONES: Aproximadamente 5.3% de las admisiones al hospital estuvieron asociadas con ADRs. Se encontraron índices mayores en pacientes ancianos, los que es probable que estén recibiendo múltiples medicamentos para enfermedades prolongadas. Es probable que los métodos usados para detectar ADRs también puedan explicar mucha de la variación en los índices de prevalencia de ADRs reportados entre los diferentes estudios.

Traducido por Brenda R Morand

Hospitalisations Reliés aux Effets Indésirables dus aux Médicaments: Revue Systématique des Études Observationnelles

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RÉSUMÉ

OBJECTIF: Déterminer la prévalence des hospitalisations reliées aux effets indésirables et d'examiner le lien entre différents groupes de population et les méthodes de détection de l'ADR.

SOURCES DES DONNÉES: Des études ont été identifiées par des recherches électroniques d'Index Cumulatif de Soins et la Santé Littérature, EMBASE, et MEDLINE à août 2007. Aucune restriction de langue n'a été appliquée.

SELECTION DES ÉTUDES ET EXTRACTION DES DONNEES: Une revue systématique des études observationnelles utilisant la définition de l'Organisation Mondiale de la Santé de ADR. L'influence de l'âge des patients et des méthodes de détection de l'ADR sur l'ADR a signalé des taux d'admission. Toutes les analyses statistiques ont été effectuées à l'aide de STATA v9.0.

SYNTHÈSE DES DONNÉES: Vingt-cinq études ont été identifies. Celles-ci portaient sur 106,586 patients hospitalizes, dont 2143 patients suite à un effet de ADR. LA prévalence de ADR variait de 0.16% à 15,7%, avec une médiane globale de 5.3% (écart interquartile [EIQ] 2.7-9.0%). La prévalence médiane variait aussi selon les groupes d'âge. Chez les enfants, le taux d'hospitalisation pour effet ADR était de 4.1% (EIQ 0.16–5.3%), alors que ceux chex les adultes et les personnes âgées étaient de 6.3% (EIQ 3.9–9.0%) et 10.7% (EIQ 9.6–13.3%), respectivement. Les taux de ADR variaient aussi selon les méthodes de detection. Les études qui utilisaient une combinaison de méthods, telles que la revue du dossier medical et une entrevue avec le patient, rapportaient des taux d'hospitalization (pour ADR) plus élevés en comparasion des etudes qui n'utilisaient que la revue du dossier médical. Chez les enfants, ce sont les agents anti-infectieux qui sont le plus souvent responsables de ces hospitalizations, alors que chez les adultes et les patients âgés, ce sont les medicaments du système cardiovasculaire.

CONCLUSIONS: Environ 5.3% des hospitalisations sont reliées avec ADRs. Des taux plus élevés sont observés chez les patients agées,ces derniers recevant souvent plusieurs médicaments pour le traitement de maladies chroniques. Les méthodes utilisés pour détecter les effets indésirables expliquent vraisemblablement une large part des variations observées entre les études.

Traduit par Suzanne Laplante