Frequency of and Risk Factors for Preventable Medication-Related Hospital Admissions in the Netherlands

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Background: Medication-related problems that lead to hospitalization have been the subject of many studies, many of which were limited to 1 hospital or lacked patient follow-up. Furthermore, little information exists on potential risk factors associated with preventable medication-related hospitalizations.

Methods: A prospective multicenter study was conducted to determine the frequency and patient outcomes of medication-related hospital admissions. A case-control design was used to determine risk factors for potentially preventable admissions. All unplanned admissions in 21 hospitals were assessed during 40 days. Controls were patients admitted for elective surgery. Cases and controls were followed up until hospital discharge. The frequency of medication-related hospital admissions, potential preventability, and outcomes were assessed. For potentially preventable medication-related admissions, risk factors were identified in the case-control study.

Results: Almost 13 000 unplanned admissions were screened, of which 714 (5.6%) were medication related. Almost half (46.5%) of these admissions were potentially preventable, resulting in 332 case patients matched with 332 controls. Outcomes were favorable in most patients. The main determinants of preventable medication-related hospital admissions were impaired cognition (odds ratio, 11.9; 95% confidence interval, 3.9-36.3), 4 or more comorbidities (8.1; 3.1-21.7), dependent living situation (3.0; 1.4-6.5), impaired renal function (2.6; 1.6-4.2), nonadherence to medication regimen (2.3; 1.4-3.8), and polypharmacy (2.7; 1.6-4.4).

Conclusions: Adverse drug events are an important cause of hospitalizations, and almost half are potentially preventable. The identified risk factors provide a starting point for preventing medication-related hospital admissions.

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Group Information: A list of the HARM Study Group members appears on page 1896.

PATIENT SAFETY IS CONSIDered an essential element of high-quality health care systems. This notion has grown in recent years, especially since publication of *To Err Is Human* by the Institute of Medicine.[1] Medications can be an important source of unintended patient harm, which may be caused by either nonpreventable adverse effects of medication use or by medication errors (potentially preventable).

Medication-related problems can cause serious adverse drug effects (ADEs) that may lead to hospitalization of the patient. These have been the subject of many published studies, which have been summarized in 2 meta-analyses[2,3] and in some more recent studies.[4,5] Many of these studies were limited to one hospital or to one specific type of ward,[6-9] had a retrospective design,[10,11] or provided no information on preventability.[2] Furthermore, little information exists on the risk factors associated with preventable medication-related hospital admissions in a general population. Given these limitations and the need for information on potential risk factors, we conducted a multicenter study aimed at identifying the frequency and preventability of medication-related hospitalizations in the Netherlands and risk factors for the preventable hospitalizations.

METHODS

DESIGN

The multicenter, observational Hospital Admissions Related to Medication (HARM) Study, with a prospective follow-up, was conducted between September 1, 2005, and June 30, 2006. Medication-related hospitalizations were defined as hospitalizations due to ADEs: harm due to adverse effects of medication use (as defined by the World Health Organization[12]) or due to medication errors (ie, preventable medi-

cation-related hospitalizations). A medication error was defined as any error in the process of prescribing, dispensing, or administering the medication.[13]

A case-control design was used to identify potential risk factors for the subset of preventable admissions. Conceptually, control patients should be a representative sample from those at risk for an ADE that would necessitate hospital admission. This would imply sampling control patients from the community. The disadvantage of such sampling would be the risk of information bias; for example, nonhospitalized patients have fewer renal function tests available and, therefore, decreased renal function as a risk factor may be oversampled in the case group, leading to inflated risk estimates. This can be dealt with by prospectively performing additional diagnostic tests in control patients, but this was considered unfeasible.

The problem of information bias is largely overcome by using hospital-based controls. However, the potential for selection bias is the main problem in using hospital-based controls. We considered selecting only unplanned admissions not related to an ADE, but we believed that we could never be sure that the admission was definitely unrelated to an ADE (and the same problem arises when selecting controls from all admissions). Therefore, we decided to select controls from the planned surgery population (reason for admission definitely unrelated to ADEs) and to match on age and sex (thereby increasing the comparability of cases and controls regarding the use of medications). The study protocol was approved by a medical ethics committee (Medisch-Ethische Toetsing Onderzoek Patiënten en Proefpersonen, Tillburg, the Netherlands.

SETTING AND PARTICIPANTS

The data were collected in 21 of the 104 Dutch hospitals.[14] The hospitals (university, teaching, and general hospitals) were selected from all regions of the Netherlands to obtain a representative sample of hospitalizations.

In each hospital, a specially trained researcher screened all unplanned admissions for a potentially medication-related cause of hospitalization during 40 days in 2 consecutive months. The exclusion criteria were age younger than 18 years and admission for obstetric indications, to a psychiatric ward, or for self-poisoning.

For all remaining admissions, the documented reason for admission and medication use before admission were assessed by means of a trigger list. This trigger list consisted of 537 combinations of symptoms and medicines, that have been mentioned in the literature[15] as possible causes of ADEs that may lead to medication-related hospitalizations. Examples of symptom/medication combinations on the list are asthma exacerbation and nonsteroidal anti-inflammatory drugs (NSAIDs)/aspirin, thrombocytopenia and antiepileptic medication, and hyponatremia and selective serotonin reuptake inhibitors (asthma exacerbation, thrombocytopenia, and hyponatremia were, of course, related to a variety of other medicines as well on the trigger list). In addition, some symptoms on the trigger list referred to no particular medication, for example, trauma as a symptom referred to "check whether any medicines used have sedating potential."

Any admission that matched this list was discussed with the hospital physician of the patient. If a relation with medication use was deemed possible, the patient was included as a case and was followed up during admission. Hospital physicians were also asked to report potential cases not identified by the trigger list. For each case, 1 control was selected in the same hospital matched on age (by 5-year age group) and sex. Cases and controls provided written informed consent to use their medical information for research purposes.

DATA COLLECTION

For included cases and controls, relevant information from the medical record (medical history, diagnostic procedures, and outcomes) was collected. The medical record abstracters were not blinded to the nature of the study or to whether the patient was a case. All clinical laboratory data from 1 year before the present admission were recorded. On the basis of serum creatinine values nearest to the hospitalization, renal function before admission was calculated using the Cockcroft-Gault formula.[16] Medications dispensed for 1 year before admission were obtained from the patient's community pharmacy records. From this medication history, adherence to the regimen (compliance) was estimated for all oral medicines by calculating the refill rate for 1 year before hospitalization. The refill rate is defined as the number of daily doses dispensed divided by the total number of days between the first and last prescription in this period. Only medicines indicated for long-term use and dispensed at least 3 times during the year were considered. Patients were classified as adherent to the medication regimen if the refill rates of all these medicines were between 0.8 and 1.2.[17] Information about the living situation (independent vs dependent [ie, in a nursing home, in a care home, or at home with nursing care]), sex, and age was obtained from the patient's medical record. Cognitive function before admission was obtained from the medical record or was discussed with the physician and assessed as "normal" or "impaired" (this is the way cognitive function is assessed in everyday practice in the Netherlands; formal tests, such as the Mini-Mental State Examination, are not routinely used). Information about the number of previous admissions and the number of physicians was obtained from the hospital information system. Previous admissions are mentioned in the medical history of the patient in the hospital information system, even when the admissions took place in other hospitals. The duration of the hospital admission and the outcome were recorded for each case.

ASSESSMENT OF CAUSALITY AND PREVENTABILITY

Two clinical pharmacists (A.J.L. and P.M.L.A.v.d.B) independently assessed all the patients initially included as cases with respect to the causal relationship between the suspected medicine and the reason for hospitalization, according to an adjusted version of the algorithm by Kramer et al.[18] In this version, 3 questions need to be answered (in contrast to 6 questions in the original algorithm): whether the reason for admission is known to be an adverse event of the suspected medicine, whether alternative causes can explain the relationship between the suspected medicine and the adverse event, and whether a plausible time relationship exists between the adverse event and the start of medication administration (or the occurrence of the medication error). On the basis of the answers, causality is classified as "possible," "probable," or "unlikely." Cases with an assessment of unlikely were excluded.

The same pharmacists also assessed the preventability of the admissions, according to a modified version of the algorithm by Schumock and Thornton.[19] In this algorithm, an admission was assessed as preventable when a medication error was made with the medication that caused the hospital admission. The original Schumock-Thornton algorithm assesses prescribing errors, which can be defined as dosing errors or therapeutic errors, such as medication not indicated (based on patient history), medication contraindicated, recorded medication allergies, drug-drug interaction (included only if the interaction is inadequately monitored or if the medication involved in the interaction may never be combined [absolute contraindication
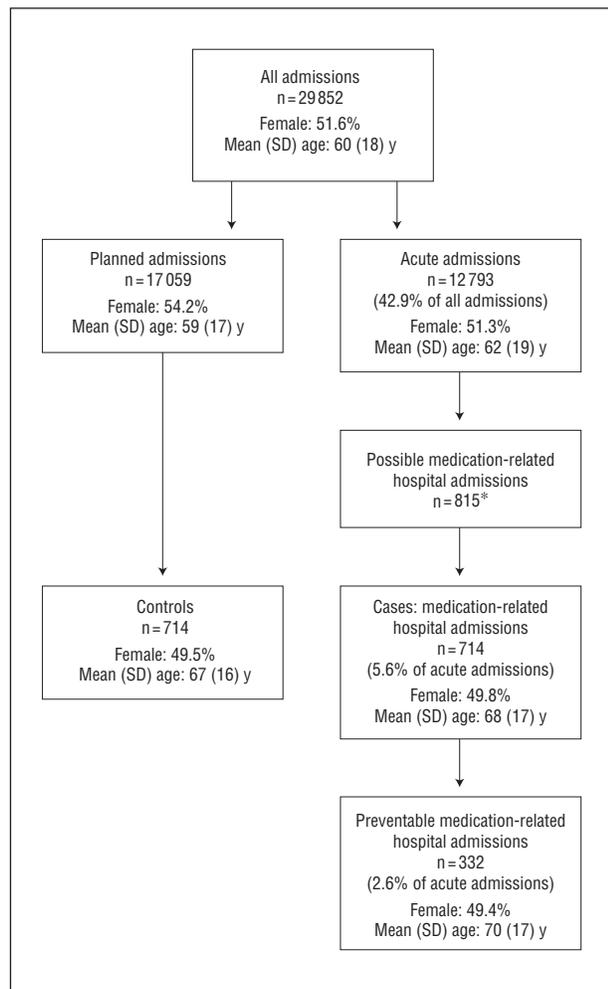
Figure. Study design and main outcomes. *Of 815 admissions assessed by the physician as medication related, 72 refused to participate in the study and 29 were assessed centrally as unlikely to be medication related.

for the combination]), inadequate monitoring of therapy, therapeutic duplication medication, and underprescribing (defined as an essential medicine not being prescribed).[20] The algorithm was expanded to include dispensing errors (errors at the dispensing stage in the pharmacy) and administration errors (errors when administering medication to the patient either by caretakers or by the patient, eg, nonadherence to the medication regimen). If the assessments of the pharmacists disagreed, they met to reach consensus (2.5% of the cases for the causality assessment and 26% of the cases for the preventability assessment).

MAIN OUTCOME MEASURES

The frequency of medication-related hospitalizations was the main outcome measure, defined as the number of medication-related hospitalizations divided by the number of all unplanned admissions of persons older than 18 years (excluding obstetric admissions, self-poisonings, and psychiatric admissions). In addition, the percentage of potentially preventable medication-related admissions and patient outcomes was determined.

The following determinants were assessed as potential risk factors in the case-control part of the study: medication regimen adherence (determined by calculation of the refill rate[17]), patient living situation (independent or dependent), cognition, renal function before admission, number of diseases in

the medical history, number of previous admissions (in the year before the present admission), polypharmacy (defined as ≥5 medicines in long-term use at the time of admission[21]), and number of prescribing physicians.

DATA ANALYSIS

Data were entered into local databases, which were merged. Before data analysis, all electronic case report forms were verified centrally on missing values, extreme values, and coding of the medical history. For validation purposes, a random sample of cases was assessed completely on correct input into the database. Data were analyzed using statistical software (SPSS, version 11; SPSS Inc, Chicago, Illinois).

The mean age of the potentially preventable cases was compared with that of all patients admitted in the same period in the same hospitals using the Mann-Whitney test. The sex of these cases was compared with that of all admissions using a χ^2 test. Cases were compared with all hospitalized patients for these patient characteristics because cases and controls were matched on age and sex and, therefore, could not be compared with each other.

Duration of hospitalization was tested against the national mean after logarithmic transformation of the length of hospitalization of the potentially preventable medication-related admissions. In this case, national data were used because duration of hospitalization of all hospitalized patients in the 21 hospitals was not available (in contrast to age and sex). Cases were not compared with controls regarding length of hospitalization because only cases were prospectively followed up.

For the analysis of potential risk factors for preventable admissions, a univariate conditional logistic regression analysis was performed, with stratification on matching variables. Determinants identified in the univariate analysis as being statistically significantly associated with the outcome ($P<.05$) were considered confounding variables that were included in a stepwise multivariate conditional logistic regression analysis.

RESULTS

FREQUENCY

During the study, 29 852 patients were admitted to the 21 participating hospitals, of which 12 793 were unplanned admissions. Seventy-two patients refused participation, mostly because they did not understand the questions asked or did not speak the Dutch language. Initially, 743 admissions were considered to be medication related but, after central causality assessment, 714 admissions were included as possibly or probably medication related, representing a frequency of 5.6% of unplanned admissions. A total of 332 of these cases (46.5%) were assessed as potentially preventable (**Figure**).

The median length of hospital stay of the 332 potentially preventable medication-related cases was 8 days, and 24 (7.2%) of these cases were admitted to an intensive care unit. Of the 332 potentially preventable medication-related admissions, 233 patients (70.2%) recovered completely, but 21 (6.3%) died and 31 (9.3%) experienced a disability after discharge; for 47 cases (14.2%), the outcome was uncertain at the time of discharge. Whether patients died of the actual ADE leading to hospitalization or of other causes (eg, hospital-acquired infection and comorbidities) was not assessed.

Table 1. Reasons for Potentially Preventable Medication-Related Hospital Admissions and the Associated Drugs

Reason for Admission	Preventable Admissions, No. (%) (n=332)	Associated Drugs (No. of Admissions[a])
Digestive system		
GI tract bleeding	48 (14.5)	Antiplatelets (34), NSAIDs (14), anticoagulants (12), oral corticosteroids (4)
GI tract symptoms (eg, diarrhea, constipation)	22 (6.6)	Oral antidiabetics (4), laxatives (4), diuretics (4), opiates (3), loperamide (3), statins (3), antibacterial drugs (3)
Circulatory system: cardiovascular symptoms (eg, dysrhythmias, heart failure)	35 (10.5)	β-Blockers (15), drugs affecting the RAAS (9), calcium antagonist (9), diuretics (9), anticoagulants (7)
Respiratory symptoms (eg, dyspnea)	26 (7.8)	Diuretics (12), respiratory drugs (6), β-blockers (6), NSAIDs (5)
Endocrine system: hypoglycemia or hyperglycemia	20 (6.0)	Insulin (18), oral antidiabetics (12), corticosteroids (3), diuretics (3)

Abbreviations: GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs; RAAS, renin angiotensin aldosterone system.
[a] An admission can be associated with more than 1 drug and is then mentioned more than once in the list.

The most common reasons for hospitalization of the potentially preventable cases were gastrointestinal tract problems: 14.5% (48 of 332) of these cases were admitted for gastrointestinal bleeding and 6.6% (22 of 332) for other gastrointestinal tract symptoms, such as constipation and diarrhea. Other common problems were cardiovascular symptoms (10.5% [35 of 332]), respiratory symptoms (7.8% [26 of 332]), and poor glycemic control (6.0% [20 of 332]) (**Table 1**).

Medicines associated most often with potentially preventable medication-related hospital admissions were those that affect blood coagulation, such as antiplatelet drugs (8.7% [29 of 332 patients]), oral anticoagulants (6.3% [21 of 332]), NSAIDs (5.1% [17 of 332]), and a combination of these medicines (10.5% [35 of 332]). Antidiabetic drugs were related to the reason for admission in 41 of 332 cases (12.3%). Medications that act on the central nervous system (5.1% [17 of 332 patients]) were most often related to a trauma (Table 1).

A total of 509 medication errors were identified in the 332 potentially preventable medication-related hospitalizations. Lack of a clear indication for the medication (n=84), nonadherence to the medication regimen (n=78), inadequate monitoring (n=71), and drug-drug interactions (n=70) were the most common errors found. Underprescribing of gastroprotective drugs in the case of NSAID or aspirin use (only in high-risk patients) and drug-drug interactions were the most common errors found in patients admitted with gastrointestinal tract bleeding (**Table 2**).

POTENTIAL RISK FACTORS

The mean age of patients admitted with a potentially preventable medication-related cause was 68 years, which differed significantly from the mean age of all unplanned admissions: 60 years (Mann-Whitney test, $P<.001$). The robust mean of the duration of hospitalization (the Hampel M-estimator[22]: 8.2 days; 95% confidence interval [CI] of length of stay in the hospital, 7.3-8.7 days) also differed from the national mean hospital stay (5.6 days). No significant difference was found for sex between cases and the entire patient population admitted during the study period in the participating hospitals (χ^2 test, $P=.73$) (Figure).

The most important patient-related, statistically significant potential risk factors identified were impaired cognition (odds ratio [OR], 13.0; 95% CI, 4.6-36.5), 4 or more diseases in the patient's medical history (11.3; 4.4-29.0), dependent living situation (4.5; 2.4-8.1), impaired renal function before hospital admission (2.6; 1.6-4.2), and nonadherence to the medication regimen (2.6; 1.7-4.0). After adjustment for several confounders, the effect of these risk factors remained statistically significant (**Table 3**).

Polypharmacy was a medication-related determinant that was associated with medication-related hospital admissions. For the use of 5 or more medicines at the time of admission (polypharmacy), a statistically significant effect was found that remained so in the multivariate model (OR, 2.7; 95% CI, 1.6-4.4).

The determinant previous admissions was not statistically significantly associated with risk of preventable medication-related hospitalization (OR, 1.3; 95% CI, 0.9-1.7), and neither was the number of prescribers after correction for the confounding factor polypharmacy (≥4 prescribers: 1.4; 0.6-5.2) (Table 3).

COMMENT

The HARM Study was the first multicenter study of medication-related hospitalizations in the Netherlands. The results of this study show that a considerable proportion (5.6%) of all unplanned admissions is medication related. Almost half (46.5%) of these admissions are potentially preventable. The frequency of 5.6% is comparable to the frequencies of 4.9% and 5.2% reported in a meta-analysis of studies on medication-related hospital admissions[2] and in a large study in the United Kingdom, respectively.[4]

As was shown in a recent systematic review,[23] the HARM Study identified anticoagulant and antiplatelet drugs as major causes of medication-related hospital admissions. Other groups identified in the HARM Study (antidiabetic drugs, NSAIDs, and medications that act on the central nervous system) are also well known from the literature as medications with increased risks.[23]

Impaired cognition, number of comorbidities, impaired renal function, dependent living situation, and non-

Table 2. Medication Errors Associated With Potentially Preventable Medication-Related Hospital Admissions

Medication Error	All Admissions (N=332)	Reasons for Potentially Preventable Medication-Related Hospital Admissions		
		GI Tract Bleeding (n=48)	CVD (n=35)	Respiratory Symptoms (n=26)
Prescribing error, therapeutic error, No. (%)				
Drug not indicated	84 (16.5)	13 (16.7)	4 (9.3)	6 (16.2)
Inadequate monitoring	71 (13.9)	5 (6.4)	8 (18.6)	3 (8.1)
Drug-drug interaction	70 (13.8)	20 (25.6)	6 (14.0)	6 (16.2)
Underprescribing	57 (11.2)	23 (29.5)	3 (7.0)	3 (8.1)
Contraindication	45 (8.8)	8 (10.3)	1 (2.3)	4 (10.8)
Prescribing error, dose too high, No. (%)	29 (5.7)	6 (7.7)	1 (2.3)	0
Administration error, No. (%)				
Nonadherence to medication regimen	78 (15.3)	1 (1.3)	17 (39.5)	12 (32.4)
Incorrect use	36 (7.1)	1 (1.3)	1 (2.3)	1 (2.7)
Other	39 (7.7)	1 (1.3)	2 (4.7)	2 (5.4)
Total[a]	**509** (100.0)	**78** (100.0)	**43** (100.0)	**37** (100.0)

Abbreviations: CVD, cardiovascular disease; GI, gastrointestinal.
[a] Because of rounding, percentages may not total 100.

Table 3. Determinants Associated With Potentially Preventable Medication-Related Hospital Admissions Before and After Adjustment for Confounders

Variable	Frequency, No. (%)[a]		Univariate Odds Ratio (95% CI)	Multivariate Analysis	
	Cases (n=332)	Controls (n=332)		Odds Ratio (95% CI)	Adjusted for
Patient related					
Elderly (>65 y)	226 (68.1)	221 (66.7)	NA[b]	NA[b]	NA[b]
Female sex	164 (49.4)	164 (49.4)	NA[b]	NA[b]	NA[b]
Living situation (dependent)	90 (29.8)	37 (12.3)	4.5 (2.4-8.1)	3.0 (1.4-6.5)	Polypharmacy, cognition, medication regimen adherence, and renal function
Impaired cognition	51 (21.6)	8 (3.3)	13.0 (4.6-36.5)	11.9 (3.9-36.3)	Polypharmacy and living situation
Impaired renal function	124 (40.9)	39 (20.5)	2.6 (1.6-4.2)	2.6 (1.6-4.2)	
Nonadherence to medication regimen	157 (65.1)	102 (45.9)	2.6 (1.7-4.0)	2.3 (1.4-3.8)	Polypharmacy and cognition
No. of diseases					
0	16 (4.8)	56 (16.9)	1 [Reference]	1 [Reference]	
1-3	130 (39.2)	144 (43.4)	7.0 (2.7-17.9)	5.9 (2.2-15.5)	Polypharmacy and medication regimen adherence
≥4	185 (55.7)	132 (39.8)	11.3 (4.4-29.0)	8.1 (3.1-21.7)	
No. of previous admissions					
0	172 (51.8)	192 (57.8)	1 [Reference]	1 [Reference]	
≥1	160 (48.2)	140 (42.2)	1.3 (0.9-1.7)	1.3 (0.9-1.7)	
Physician related					
No. of prescribers (including general practitioner)					
1	159 (47.9)	178 (53.6)	1 [Reference]	1 [Reference]	
2 or 3	147 (44.3)	142 (42.8)	1.2 (0.9-1.7)	1.0 (0.7-1.4)	Polypharmacy
≥4	26 (7.8)	12 (3.6)	2.5 (1.2-5.2)	1.4 (0.6-5.2)	
Medication related					
Polypharmacy (≥5 drugs, chronically used)	180 (54.2)	96 (28.9)	3.0 (2.1-4.3)	2.7 (1.6-4.4)	Medication regimen adherence

Abbreviations: CI, confidence interval; NA, not applicable.
[a] Frequency is calculated without missing values.
[b] Matching variable.

adherence to the medication regimen were identified as the most important patient-related determinants, whereas polypharmacy was the most important medication-related potential risk factor identified. Many of these risk factors have been mentioned in the literature.[24,25]

The HARM Study has several limitations. First, the frequency of medication-related hospitalizations may be underestimated because of the conservative assessment of cases using a 3-step approach (trigger list, confirmation by a physician, and central assessment). On the other hand, this approach is likely to result in high specificity, adding to the reliability of the results. A second limitation is the exclusion of children and psychiatric patients, which may limit the generalizability of the re-

sults. Yet, by excluding these very specific populations, we intended to generate results that are more representative of the general population.

Third, although the study used a central assessment of preventability, the proportion of preventable cases may not reflect reality. In real life, medical decisions depend on many circumstances that cannot be extracted from medical records. That is the reason we preferably use the term *potential preventability*. A fourth limitation concerns the use of 21 different researchers, which could have led to variability in the inclusion of cases. By using strict protocols and thorough training, this variability was reduced as much as possible.

Finally, the control patients may not be ideal. In the "Methods" section, we considered the reasons for selecting this group. Despite these considerations, one may still argue that the control patients may be less ill than the unplanned admissions because, to be able to undergo surgery, they need to be reasonably well. However, Table 3 shows that the number of previous admissions is relatively comparable between cases and controls, suggesting that both groups are at equal risk for hospitalization. By matching on age and sex, controls are likely to be equally exposed to medications as are cases. Even when the risks are overestimated in the case group, the ORs are of such a magnitude that taking the overestimation into account would probably still result in identification of the same risk factors.

Notwithstanding these limitations, the HARM Study differs from many other studies of medication-related hospitalizations. Major differences concern its prospective design, the number of hospitals included, and the focus on preventability and risk factors. In this study, patients were prospectively included on admission and were followed up until discharge. Other prospective studies[4,7,26,27] identified frequencies of fatal medication-related hospitalizations of 0.15% to 9%, which are comparable to the present results. One other study[28] reported that this frequency was 19%, but it was conducted among intensive care admissions only and, therefore, reflects the most serious ADEs. The length of stay mentioned in these studies[4,7,27] ranged from 5 to 10 days, which is also comparable to the present results.

Furthermore, the HARM Study was performed in a large representative sample of Dutch hospitals, screening a large number of admissions from all patient groups and wards, thus providing more generalizable outcomes. This study is one of the few multicenter studies on this subject. Other multicenter studies[5,7,29-31] that used comparable methods identified frequencies of medication-related hospital admissions of 2.4% to 17%. However, only 1 of these studies[5] also investigated the aspect of preventability.

Thus, the HARM Study confirms findings from previous studies, thereby strengthening the evidence base of medication-related hospital admissions, and also adds new evidence regarding the frequency, outcome, and risk factors of preventable medication-related admissions. The meta-analysis by Beijer and de Blaey[2] concluded from the available evidence at that time that large-scale studies on preventable medication-related hospital admissions were needed, and this is what the HARM Study provides.

Based on findings from the present study, several recommendations can be made. First, the medication use of high-risk patients (eg, elderly patients with polypharmacy) should be reviewed regularly for potential medication-related problems, such as underprescription and overprescription, interactions, and user convenience. Such an evaluation should also include a cognitive assessment and identification of barriers for medication regimen adherence and should provide tools to facilitate the proper use of medication. The patient should be actively involved in this process and should be given his or her own responsibility in achieving treatment goals.

Second, we recommend that physicians and pharmacists exchange more information relevant to adequate medication surveillance, such as comorbidities and clinical laboratory data (eg, renal function). Third, policy makers should facilitate the development of information technology designed to provide all relevant health care professionals the information necessary for medication assessment and evaluation and to document changes in medication and reasons for these changes.

Finally, when analyzing the ADEs most frequently involved in preventable medication-related hospitalizations, the following medication-specific actions should be taken whenever possible: provide gastroprotection for NSAID and low-dose aspirin users at risk for gastrointestinal events, limit the duration of benzodiazepine use, avoid combinations of psychotropic medications, educate users of diuretics and antidiabetics how to act in periods of low food and fluid intake, and monitor blood glucose levels in patients in whom corticosteroid therapy is initiated.

Further study is needed into the effectiveness of the aforementioned recommendations in reducing the risks of medication-related hospitalizations. Also, confirmation of the risk factors identified in this study and in other large case-control studies with different control selections should be undertaken. In addition, other potential risk factors for preventable medication-related hospitalizations should be studied, such as the dosage of medication taken (eg, in relation to body surface).

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