ORIGINAL ARTICLES

Adverse Drug Events Occurring Following Hospital Discharge

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OBJECTIVE: To describe the incidence of adverse drug events (ADEs), preventable ADEs, and ameliorable ADEs occurring after hospital discharge and their associated risk factors.

DESIGN: Prospective cohort study.

SETTING: Urban academic health sciences center.

PATIENTS: Consecutive patients discharged home from the general medical service.

INTERVENTIONS: We determined posthospital outcomes approximately 24 days following discharge by performing a chart review and telephone interview. Using the telephone interview, we identified new or worsening symptoms, the patient's health system use, and recollection of processes of care. Posthospital outcomes were judged by 2 internists independently.

RESULTS: Four hundred of 581 potentially eligible patients were evaluated. Of the 400 patients, 45 developed an ADE (incidence, 11%; 95% confidence interval [CI], 8% to 14%). Of these, 27% were preventable and 33% were ameliorable. Injuries were significant in 32 patients, serious in 6, and life threatening in 7. Patients were less likely to experience an ADE if they recalled having side effects of prescribed medications explained (OR, 0.4; 95% CI, 0.2 to 0.8). The risk of ADE per prescription was highest for corticosteroids, anticoagulants, antibiotics, analgesics, and cardiovascular medications. Risk increased with prescription number. Failure to monitor was an especially common cause of preventable and ameliorable ADEs.

CONCLUSION: Following discharge, ADEs were common and many were preventable or ameliorable. Medication side effects should be discussed, and interventions should include better monitoring and target patients receiving specific drug classes or multiple medications.

KEY WORDS: patient safety; adverse drug reactions; medical errors; hospital care.
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Patient safety is an area of significant public concern. Data from the Harvard Medical Practice Study[1] and other research[2,3] have demonstrated that a significant proportion of patients experience adverse outcomes which are attributable to their health care. When these adverse events are caused by medications, they are termed adverse drug events (ADEs).[4] They are the most common type of adverse event for inpatients and ambulatory patients.[5,6]

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Most research evaluating ADEs has focused on hospitalized patients[4,7–15] and there are a few publications evaluating care in the ambulatory setting.[5,6] In contrast, very little work has been published evaluating the risk of ADEs during the transition home from hospital. The first few weeks following discharge may be a particularly high-risk interval for ADEs because patients have often experienced a recent change in health state[16] and they have frequently had several prescription changes.[17–19] There may also be incomplete communication with community care providers reflecting these changes.[20]

We recently published the results of a cohort study evaluating all types of adverse events affecting patients following discharge.[21] We determined that 19% of patients experience an adverse event within 5 weeks of discharge. One third of these were preventable, that is, they were caused by an error in management. Another third were ameliorable, that is, their severity could have been significantly reduced if health care delivery had been optimal.

As in other research, ADEs were the most common type of adverse event and accounted for almost two thirds of them.[21] The purpose of this current study was to evaluate these ADEs and their associated risk factors in patients recently discharged from hospital so that we could develop strategies to prevent them.

METHODS

We are reporting on a secondary analysis of a previously published study.[21] The objectives of the previous study were to determine the incidence, type, and severity of adverse events occurring following discharge from hospital. This current study focuses specifically on those adverse events caused by medication use, which occurred following discharge. The Institutional Review Board of the study hospital approved the protocol.

Patients

Consecutive patients discharged from the medical service of a large urban academic hospital in Boston, MA over a 3-month period were eligible. We excluded patients if they were not discharged to home, if they did not speak English, or if they did not have a telephone.

Consent was obtained in a two-stage process. First, we mailed every patient a letter describing the study on the day of his or her hospital discharge. The letter contained a preaddressed, prepaid postcard, which the patient was to return if they did *not* consent to the study. Approximately 2 weeks following discharge, we telephoned all eligible patients who had not returned cards to us. At the time of the phone call, we

described the study again and asked the patient whether they were willing to participate in the study.

Case Summary Preparation

We created a case summary for every patient in the study by integrating complementary information from a chart review and a telephone survey. First, we reviewed each patient's electronic medical record to determine the in-hospital diagnoses and treatments. This computerized clinical record contains the prescriptions for each hospital discharge, "hand-over" notes from the hospitalization, discharge summaries, previous orders and written instructions, emergency room and clinic notes, operative and procedure notes, and all laboratory results including radiography, electrocardiograms, and pathology. Hand-over notes were free-text narratives entered into the clinical record by house staff which describe the patient's problem list. "Prescriptions for each hospital discharge" refer to prescriptions written when the patient was leaving the hospital, whereas "previous orders" were all orders for the patient during the hospitalization. We used the former to determine which medications the patients were prescribed at the time of discharge and the latter to determine the treatments and tests ordered for the patient while they were in hospital. "Written instructions" were computer-generated instructions provided to the patient at the time of discharge.

We reviewed all the information from the index hospitalization. We also reviewed the clinic notes and other encounter information for visits occurring after the index hospitalization. Last, we reviewed discharge summaries for hospitalizations at the study hospital occurring before the index encounter, if there were any.

Then starting at 2 weeks, we administered a telephone survey to determine posthospital course for all consenting patients. We asked about any new or worsening symptoms since discharge and whether there were any physician visits, emergency department visits, or hospital readmissions. If there were any such outcomes, we asked patients to elaborate on timing, severity, etiology (if known), and resolution. We asked 4 medication-related questions to determine the patient's preparations for discharge. These questions included: 1) "Did someone discuss the medications you were prescribed before discharge?" 2) "Did someone discuss your medications' side effects before discharge?" 3) "Were you provided with a written list of your medications at the time of discharge?" and 4) "Did you experience any problems obtaining your prescriptions at the time you were discharged?" Each survey took approximately 15 minutes to complete.

If we could not reach a patient by telephone, we made up to 20 attempts at several times of the day and week. If we were still not able to contact the patient with these attempts or if 5 weeks had passed, we classified the patient as a nonresponder.

We used the information obtained from the chart review and telephone interview to create case summaries. If a patient experienced any new or worsening symptoms or if they had any visits to health facilities, then we described this outcome's severity, health services used during its treatment, the timing of its onset, and its resolution.

Outcomes

An *ADE* was any adverse outcome or patient injury that was caused by medication use. A *preventable ADE* was any ADE judged to be due to a medication error. An *ameliorable ADE* was a nonpreventable ADE whose severity could have been substantially reduced if there had been an appropriate response by the health system. These are widely accepted definitions that have been used in many studies evaluating medication safety, including the Institute of Medicine's *To Err is Human* report.[4–6,14,15,21–26]

Outcome Ascertainment

Two board-certified internists (HJM, JFP) who were not involved in preparation of case summaries rated each case summary independently to determine whether the case met one of the outcome definitions. They used a standard technique that has been validated and used in many studies and populations.[1–6,14,15,21–25]

Reviewers first rated whether an injury occurred. If so, then they rated their confidence that the injury was caused by medication use on a 6-point scale (1: outcome definitely caused by the patient's disease, 2: outcome probably caused by the patient's disease, 3: outcome more than likely caused by the patient's disease, 4: outcome more than likely caused by the patient's medication, 5: outcome probably caused by the patient's medication, 6: outcome definitely caused by the patient's medication). If their rating was 5 or 6 (injury is probably or definitely caused by medication use), the event was considered an ADE.

If it was an ADE, the internists determined preventability and ameliorability using implicit criteria. It was necessary to use implicit criteria, as it was almost impossible to develop and apply explicit criteria, given the large number of medications and diseases we were studying. In making these judgments, the reviewers considered the expected benefit of the therapy, whether there was an apparent failure to appropriately monitor the patient or therapy, and whether the patient had important contraindications for the particular therapy.

If there was disagreement on any of the ratings, then the two reviewers discussed the case to achieve consensus. If they could not agree, a third board-certified internist (DWB) rated the event independently to determine the final rating. The validity of the method has been demonstrated by excellent interrater reliability and high face validity in a large number of studies.[1–6,14,15,21–25]

Next, reviewers rated injury severity. Injury severity was categorized in 3 different ways. First, we used a classification scheme defined by Bates et al. and subsequently used in several other studies.[4–6,14,15,22–25] This scheme classifies outcome severity into *significant*, *serious*, *life-threatening*, and *fatal*. To guide severity judgments, reviewers were instructed to rate an ADE *significant* if it caused minimal symptoms or it was associated with a low risk of long-term consequences to the patient; *serious* if it caused a temporary or permanent disability or it was associated with a high risk of long-term consequences to the patient; and *life-threatening* if it had the potential to lead to a fatality. Because this rating system method is subjective, we also rated the ADE in terms of the extent of the injury and the associated health system use.[21,27] With respect to extent of the injury, we rated the outcome as *laboratory abnormalities only*, *symptoms only*, *nonpermanent disability*, and *permanent disability*. With respect to health service use, we categorized the outcome as *none*, *additional visit to a physician*, *additional visit for laboratory testing in ad-*

dition to a physician visit, visit to an emergency room, or *readmission to hospital.*[21,27]

Statistical Analysis

We present 4 sets of analyses. The first is descriptive and includes the percentage of patients who developed an ADE following discharge, as well as the percentage of those patients whose ADE was preventable or ameliorable. We also determined the proportion of patients with ADEs caused by medications within specific drug classes. We present the injury severity, and the health services used to manage the ADE.

Second, we present data describing the patient's recollection of preparation for discharge. For this, we report the percentage of people responding "yes" to our questions, and the proportion of these patients experiencing an ADE.

Third, we describe the number of prescriptions in total and within separate medication classes. Using these values as denominators, we determined the ADE rate per prescription within specific medication classes.

Last, we performed exploratory analyses to determine whether clinical factors, discharge preparations, or prescription number were associated with ADE occurrence. The clinical factors we assessed were age, gender, Charlson comorbidity index,[28] and the number of admissions to the study hospital in the 6 months prior to the index hospitalization. With respect to number of prescriptions, we divided the cohort into 4 groups based on quartiles. If any factor was significantly associated with the outcome using univariate methods at $P<.20$, then the variable was included in a multivariable logistic regression model.

We did not perform a formal sample size calculation. We had no data on which to base our risk estimates, as there had been no previous studies evaluating adverse events following hospitalization. Thus, we chose our sample size based on a desired level of precision (range of 95% confidence limits no greater than 10%) and an upper limit of estimated adverse event prevalence (20%). SAS version 8.1 was used for all analyses (SAS Institute, Cary, NC).

RESULTS

During the study period, 677 patients were discharged home and 581 were eligible for our study. Patients were ineligible because they could not speak English (n=47) or did not have a valid telephone number (n=49). We were able to complete interviews for 400 eligible patients (response rate, 69%). It took us, on average, two attempts to contact these patients by telephone (interquartile range [IQR], 1–3).

One hundred eighty-one people were eligible for the study but were not included in our results. Of these, 121 patients did not consent to the study (62 patients returned "refuse to consent cards" and 59 patients refused at the time of the follow-up call). We could not contact 60 patients after several attempts (median 8 telephone calls; IQR, 6–10) or after 5 weeks following discharge.

Of the 400 patients who participated in the study, 61% were female, the mean age was 57 years, and 64% described their race as white. The most common discharge diagnoses were pulmonary (17%) and cardiovascular disorders (15%). Within these categories, the primary diagnosis was most often pneumonia (6%) and congestive heart failure (5%), respectively. Most patients had at least 1 chronic medical condition, as indicated by a median Charlson index of 1 (IQR, 0–2). Although 52% of patients had not been admitted to the study hospital in the previous 6 months, 22% had 1 and 26% had more than 1 hospitalization. Most patients' health insurance was with a managed care plan or was covered by Medicare. Very few patients received Medicaid or free care (Table 1).

Table 1. Patient Population

Characteristic	Population	Nonparticipants*
N	400	181
Female, %	61	57
Age, y	57 ± 17	57 ± 17
Race, %		
White	64	59
African American	24	29
Hispanic	7	8
Other	5	4
Discharge diagnosis, %		
Pulmonary disorders	17	17
Pneumonia	6	8
Obstructive lung disease	6	5
Cardiovascular disorders	15	15
Congestive heart failure	5	6
Coronary artery disease	4	6
Arrhythmia and other	6	4
Payer, %		
Medicare	45	37
Managed care	38	39
Medicaid	10	11
Fee for service	6	10
Free care	2	3

**Participants and nonparticipants did not differ;* $P<.10$.

Incidence and Severity of ADEs

In total, 45 patients experienced an ADE following discharge (incidence, 11%; 95% confidence interval [CI], 8% to 14%). Overall, 27% of ADEs were preventable and 33% were ameliorable. ADEs were rated as significant in 71% of patients, serious in 13%, and life-threatening in 16%. Among patients with an ADE, 7% required additional laboratory testing, 78% experienced new symptoms of at least 1 day's duration, 13% had a nonpermanent disability, and 2% had a permanent disability. In addition, 42% sought additional health care as a result of their ADE: 11% visited a physician's office, 4% required additional laboratory testing in addition to visiting a physician's office, 11% attended an emergency department, and 16% were readmitted to hospital.

Six medication classes were associated with 87% of the ADEs. Anti-infective agents were the cause of the ADE in 31% of patients. Other frequently implicated medications include corticosteroids (16%), cardiovascular medications (16%), analgesic medications including narcotics (11%), anticoagulants (9%), and antiepileptic drugs (4%).

Most of the ADEs resulted directly from the specific pharmacological activity of the drug. These are described in the Appendix (available online at http://www.blackwellpublishing.com/products/journals/suppmat/jgi/jgi30390/jgi30390sm.htm). The most common ADEs related to anti-infective agents included gastrointestinal or cutaneous complications. Common ADEs related to corticosteroid use included hyperglycemia and neuropsychiatric complications. Cardiovascular medications caused a number of problems including, for example, wheezing in a patient prescribed a beta-blocker, acute renal failure in

a patient receiving an angiotensin converting enzyme inhibitor, and urinary retention in a patient receiving clonidine. Common ADEs related to analgesic agents include constipation and somnolence due to narcotics. With antiepileptic drugs the most frequent ADEs occurred when drug-drug interactions led to subtherapeutic drug levels and seizures.

The most common reason for preventable ADEs was the failure to implement appropriate drug monitoring. For example, one patient was sent home on potassium supplements and spironolactone and had no monitoring of electrolytes arranged. This patient was readmitted with dangerously elevated potassium levels within 2 weeks of discharge. Another patient was sent home on IV gentamicin and had no monitoring of drug levels. This patient developed ototoxicity. The most common reason for ameliorable ADEs was failure to evaluate for, and act on, predictable medication side effects. For example one asthmatic patient was sent home on a beta-blocker for coronary artery disease and developed wheezing and coughing. This patient experienced these symptoms for several weeks before seeing the cardiologist and being instructed to stop the medication. The patient did not know that wheezing was a common side effect of beta-blockers. Therefore, the patient did not contact the physician when the symptoms first developed. This ADE was felt to be ameliorable because the duration of the symptoms could have been reduced if the patient had known to contact the physician earlier.

Preparations for Discharge and Association with Adverse Event Occurrence

We asked patients about their recollection of 4 processes of care at the time of discharge (Table 2). In all, 4% of the study participants were unable to answer these specific survey questions because they did not understand the questions. These patients were excluded from this portion of the analysis. For the most part, patients reported exemplary practices related to preparation for discharge. Among patients, 83% recalled discussing their medications with a health provider prior to discharge; 90% of patients recalled being provided with a written list describing the medications; and 88% of patients recalled that they had no problem obtaining their prescribed medications immediately after discharge. However, only 62% of patients could recall a discussion about medication side effects.

The risk of an ADE in patients who recalled having the side effects of their medications described was less than half of the risk in patients who had no such recollection. The risk of ADEs was not related to patient recollection of discussions about medications in general, difficulty obtaining prescriptions, or being provided with a written list of the medications.

Prescription Characteristics and ADE Occurrence

In total, 3,311 prescriptions were written for the 400 study patients at the time of discharge (Table 3). The median number of prescriptions written per patient was 8 (IQR, 5–11). One patient received 26 prescriptions at the time of discharge. The top 5 most commonly prescribed classes of medications at the time of discharge were cardiovascular agents (1.2 prescriptions per patient), nutrient agents (including electrolyte and vitamin supplements; 1.1 prescriptions per patient), gastrointestinal agents (0.9 prescriptions per patient), respiratory agents (0.7 prescriptions per patient), and anti-infective agents (0.7 prescriptions per patient).

The risk of ADE per prescription was highest for corticosteroids (7%; 95% CI, 4% to 14%), anticoagulants (7%; 95% CI, 3% to 17%), antibiotics (5%; 95% CI, 3% to 8%), analgesics (3%; 95% CI, 1% to 7%), and cardiovascular medications (1%; 95% CI, 1% to 3%) (Table 4).

The risk of an ADE increased with the number of medications prescribed. The risk of an ADE was similar in the first, second, and third quartiles of prescribed medications. The ADE rates in these groupings were 7% (95% CI, 4% to 15%), 8% (95% CI, 4% to 16%), and 11% (95% CI, 7% to 18%), respectively. However, the rate increased dramatically to 18% (95% CI, 11% to 27%) in patients prescribed 12 or more medications at discharge. The odds ratio for experiencing an ADE if a patient was prescribed 12 or more medications compared to a patient prescribed 4 or fewer is 2.7 (95% CI, 1.1 to 6.8).

We reviewed each case summary in which there was an ADE to determine whether it was old or new medications that accounted for the ADE. In all but 1 of the 45 ADEs, the ADE was secondary to a new medication being started (41 ADEs) or a dose change (3 ADEs).

Table 2. Patient Responses to Survey Determining Recollection of Discharge Preparations and Risk of Adverse Drug Event

Question	Response N = 400 (%)	Response "Yes" (%)	Patients Responding "Yes" Who Experienced ADE (%)	Patients Responding "No" Who Experienced ADE (%)
Did a health provider discuss your medications with you before you left the hospital?	385 (96)	83	12	10
Were you provided with a written list describing your medications?	383 (96)	90	12	14
Did you have any trouble getting your prescriptions filled when you left the hospital?	382 (96)	12	18	11*
Did someone describe the side effects of your medications to you before you left the hospital?	382 (96)	62	8	18%†

**Difference not statistically different;* P = .24.
†Difference statistically different; P < .01.
The table describes the 4 questions we posed to patients to assess their recollection of preparations for discharge. For each question, we identify the number of patients responding appropriately to the question, the proportion responding "Yes" to the question, and the proportions of "Yes" respondents and "No" respondents experiencing an ADE. For each question, approximately 4% of patients did not respond appropriately.
ADE, adverse drug event.

Table 3. Medications Prescribed at Discharge

Drug Class	Prescriptions Within Class (*N*)	Prescriptions per Patient	Interquartile Range	Maximum Prescriptions per Patient
All classes	3,311	8.3	6	26
Cardiovascular	496	1.2	2	6
Nutrients*	422	1.1	2	6
Gastrointestinal	354	0.9	1	5
Respiratory	287	0.7	1	7
Anti-infectives	274	0.7	1	8
Analgesia	159	0.4	1	3
Antiplatelet agents	131	0.3	1	2
Diuretics	114	0.3	1	3
Antidepressants	111	0.3	0	3
Antilipid	110	0.3	1	2
Hypoglycemics	105	0.3	0	3
Corticosteroids	98	0.2	0	2
Sedatives	81	0.2	0	4
Hormone	68	0.2	0	4
Warfarin	56	0.1	0	1
Epilepsy	49	0.1	0	3
Immune-modulating	49	0.1	0	2
NSAIDS	41	0.1	0	1
Antipsychotics	34	0.1	0	2
Heparins	29	0.1	0	2
Gout	23	0.1	0	2
Antihistamine	22	0.1	0	2
Ophthalmics	18	0.0	0	5
Osteoporosis	17	0.0	0	1
Muscle relaxants	9	0.0	0	2
Stimulants	4	0.0	0	1
Antineoplastic	3	0.0	0	2
Anti-Parkinson's	3	0.0	0	1
Alzheimer's	2	0.0	0	1
Other	142	0.4	0	4

*"*Nutrients" refer to electrolyte supplementation and vitamin supplementation.*
NSAIDS, nonsteroidal anti-inflammatory drugs.

Risk Factors for ADE Occurrence

Only the number of medications prescribed and a recollection of having their side effects described were significantly associated with ADE occurrence using univariate methods at $P<.20$ (Table 5). The adjusted OR for the risk of ADE in patients recalling education regarding side effects versus those patients who do not was 0.4 (95% CI, 0.2 to 0.8). The adjusted OR for the risk of an ADE in patients prescribed the highest quartile of medication prescriptions versus those patients receiving the lowest quartile of medication prescriptions was 2.6 (95% CI, 1.0 to 6.8) (Fig. 1).

Table 4. Adverse Drug Event Rate per 100 Prescriptions

Drug Class	ADEs (N)	Prescriptions (N)	ADEs per 100 Prescriptions (95% CI)
All classes	45	3,311	1.4 (1.0 to 1.8)
Corticosteroid	7	98	7.1 (3.5 to 14.0)
Anticoagulants	4	56	7.1 (2.8 to 17.0)
Anti-infectives	14	274	5.1 (3.0 to 8.4)
Analgesics (including narcotics)	5	159	3.1 (1.3 to 7.1)
Cardiovascular	7	496	1.4 (0.7 to 2.9)

This table displays the number of ADEs per prescription. For example, there were 7 ADEs occurring in patients prescribed a corticosteroid at discharge and 98 prescriptions for this type of medication.
ADE, adverse drug event.

Reviewer Agreement

Physician reviewers had moderate to high reliability in their judgments. For adverse event judgments, the reviewers agreed 87% of the time on initial review, with a corresponding κ value of 0.61. For the remaining 13% of cases, consensus was achieved 80% of the time and one third were judged adverse events. A third reviewer reviewed the remaining cases and one third of these were rated adverse events. For preventability there was 82% agreement and a κ of 0.60 and for ameliorability there was 78% agreement and a κ of 0.51.

DISCUSSION

We identified several aspects of medication safety that could be improved following hospital discharge. Overall, about 1 in 9 medical patients experienced an ADE during this period. Approximately a third of the ADEs were the result of errors and another third were more severe than they might have been if health care delivery had been optimal. While nearly all patients had discussed their medications with a provider before discharge, only about two thirds recalled being warned about their side effects, and these patients were about half as likely to experience an ADE. We also found that patients were prescribed a large number of medications and the more drugs prescribed, the greater the risk of an ADE. The risk increase was not linear, as there was a dramatic increase once patients were prescribed more than 11 medications. Also, all but 1 of the ADEs was due to newly prescribed medications or modifications in previously prescribed medications. The risk per prescription appears to be greatest for corticosteroids, anticoagulants, anti-infective agents, analgesic agents, and cardiovascular medications. Finally, problems with monitoring drug therapies were the most frequent cause of preventable and ameliorable ADEs.

We found that some aspects of preparing patients in anticipation of discharge may help reduce ADEs. Our finding of an association between the recollection of instructions regarding medication side effects and reduced ADE risk is intriguing but does not prove causation. The biologic explanation for this relationship is unknown but it could relate to differences in patient behavior. If a patient is warned about a side effect, then they may stop a medication at an earlier stage and may not even report the problem, as to them it was "expected." Similarly, if they are aware of the need to perform blood testing to avoid complications, then they may be more compliant. An alternative explanation for the association is confounding by unmeasured patient or treatment characteristics. However, in another study by Gandhi et al. this association was also identified.[6] Taken together, these data suggest that clinicians may be wrong in assuming that discussion of medication side effects will actually increase the risk of symptoms, although tailoring for individual patients is likely important.[29]

Our data demonstrate one particular difficulty in improving drug safety. Specifically, patients today receive large numbers of prescriptions that on their own are associated with low risk. The risk associated with each prescription in our study

Table 5. Risk Factors for Adverse Drug Events

Factor	Patients with ADE n=45	Patients Without ADE n=355	OR (Unadjusted)	OR (Adjusted)
Age, y (range)	57 (43–68)	58 (43–71)	1.0 (1.0 to 1.0)	
Gender (% female)	31 (69)	312 (60)	1.4 (0.7 to 2.7)	
Charlson score	1 (0–1)	1 (0–2)	0.9 (0.7 to 1.1)	
Admissions in preceding 6 months (%)				
None	27 (60)	179 (50)	1	
1 or more	18 (40)	176 (50)	0.7 (0.4 to 1.3)	
Length of stay (%)				
1 day or less	11 (24)	88 (25)	1	
2 days	9 (20)	78 (22)	0.9 (0.4 to 2.3)	
3–4 days	9 (20)	101 (28)	0.7 (0.3 to 1.8)	
>5 days	16 (36)	88 (25)	1.5 (0.6 to 3.3)	
Side effects explained (% yes)	19 (42)	218 (65)	0.4 (0.2 to 0.7)	0.4 (0.2 to 0.7)
Trouble getting medications (% yes)	8 (18)	38 (11)	1.7 (0.7 to 4.0)	
No. of medications prescribed (%)				
<5	7 (16)	87 (25)	1	1
5–7	8 (18)	87 (25)	(0.4 to 3.2)	1.1 (0.4 to 3.3)
8–11	13 (29)	10 (29)	1.6 (0.6 to 4.1)	1.5 (0.6 to 4.0)
>12	17 (38)	79 (22)	2.7 (1.1 to 6.8)	2.6 (1.0 to 6.8)

This table demonstrates the results of our analysis to determine risk factors for adverse drug events. We determined that only the number of medications prescribed and whether the patient recalled having the medication side effects explained were associated with ADE occurrence using univariate analyses. These factors remained significant when they were entered into a multivariate model.
ADE, adverse drug event; OR, odds ratio.

was approximately 1 ADE per 100 prescriptions, as opposed to the risk per patient, which was closer to 1 in 10. Given the large number of prescriptions and the potential problems associated with each of these, teaching efforts cannot possibly be inclusive. It is probably better to focus on specific education efforts on high-risk therapies and their most likely side effects, while at the same time improving methods of monitoring every patient postdischarge for problems.

Finally, we determined that patients prescribed more drugs, those on new medication regimens, and those prescribed medications within specific classes could be targeted for prevention and amelioration strategies. Given the limited resources available in most hospitals, it might be most cost effective to preferentially target patients receiving high-risk or new medications. Although untested, there are a number of interventions that could be tried following discharge. For example, warfarin clinics may be set up to monitor hospitalized patients sent home on warfarin; other high-risk patients could be seen by the treating hospitalist within a week of discharge; or a pharmacist could meet with patients prior to discharge to discuss medications and phone the patient a few days later to resolve any problems they were having.

Compared to data on inpatients, relatively little data are available regarding ADEs immediately following discharge from the hospital. Although there are several studies evaluating ADEs in hospital and in ambulatory settings, the ADE Prevention Study,[4] which evaluated hospitalized patients, is the most similar to this current study's methodology. Both used a prospective method of ADE detection and then implicit physician judgments to determine whether adverse outcomes were due to medication use. One important difference was that we used first-hand reports from patients to identify posthospital outcomes, whereas the other study used prompted incident reporting by health workers and daily chart reviews.

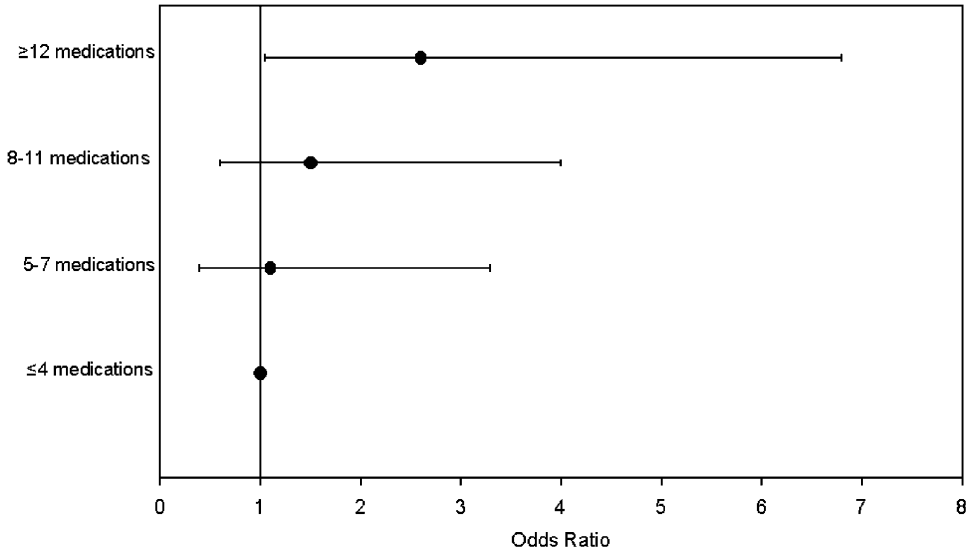

FIGURE 1

The results of the two studies are similar. The ADE rate in the ADE Prevention Study, which included both medical and surgical patients, was 6.5 per 100 admissions, versus 11 per 100 hospital discharges in the current study, which included only medical patients. The proportion of ADEs that were preventable was 28% versus 27% in the two studies. The severity of injuries was similar in the two studies, with approximately 1 in every 7 injuries rated as life-threatening. The types of medications responsible for the ADEs were also very similar.

The slightly higher rate of ADEs following discharge could be related to the fact that patients are not monitored as closely following discharge as is capable in the hospital. It could also relate to the fact that patients were followed for on average 24 days following discharge, which is much longer than the average hospitalization. Taken together, these data suggest that the increased vigilance for ADEs must carry on after a patient's hospital discharge.

Our study had a number of limitations. It is carried out at a single institution and only includes medical patients. Also, in measuring preparation for discharge, we did not observe what actually did occur before discharge but instead relied on a patient's recollection of what occurred. Finally, although we were able to determine for all the ADEs whether the responsible medication was newly prescribed or changed, we do not have such data for all medications.

In conclusion, we identified that a significant number of patients experience ADEs following hospital discharge. We identified a number of risk factors which suggest interventions to improve safety. These interventions include improved teaching regarding medications, especially regarding side effects. Improved monitoring of drug therapies following discharge is also likely necessary. The next step is to test these interventions.

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REFERENCES

1. **Brennan TA, Leape LL, Laird NM, et al.** Incidence of adverse events and negligence in hospitalized patients. Results of the Harvard Medical Practice Study I. N Engl J Med. 1991;324:370–6.
2. **Wilson RM, Runciman WB, Gibberd RW, Harrison BT, Newby L, Hamilton JD.** The Quality in Australian Health Care Study. Med J Aust. 1995;163:458–71.
3. **Vincent C, Neale G, Woloshynowych M.** Adverse events in British hospitals: preliminary retrospective record review. BMJ. 2001;322:517–9.
4. **Bates DW, Cullen DJ, Laird N, et al.** Incidence of adverse drug events and potential adverse drug events. Implications for prevention. ADE Prevention Study Group. JAMA. 1995;274:29–34.
5. **Gurwitz JH, Field TS, Harrold LR, et al.** Incidence and preventability of adverse drug events among older persons in the ambulatory setting. JAMA. 2003;289:1107–16.
6. **Gandhi TK, Burstin HR, Cook EF, et al.** Drug complications in outpatients. J Gen Intern Med. 2000;15:149–54.
7. **Bates DW.** Drugs and adverse drug reactions: how worried should we be? JAMA. 1998;279:1216–7.
8. **Bates DW, Leape LL, Cullen DJ, et al.** Effect of computerized physician order entry and a team intervention on prevention of serious medication errors. JAMA. 1998;280:1311–6.
9. **Bates DW, Leape LL, Petrycki S.** Incidence and preventability of adverse drug events in hospitalized adults. J Gen Intern Med. 1993;8:289–94.
10. **Bates DW, Boyle DL, Vander Vliet MB, Schneider J, Leape L.** Relationship between medication errors and adverse drug events. J Gen Intern Med. 1995;10:199–205.
11. **Bates DW, Spell N, Cullen DJ, et al.** The costs of adverse drug events in hospitalized patients. Adverse Drug Events Prevention Study Group. JAMA. 1997;277:307–11.
12. **Bates DW.** Using information technology to reduce rates of medication errors in hospitals. BMJ. 2000;320:788–91.
13. **Cullen DJ, Sweitzer BJ, Bates DW, Burdick E, Edmondson A, Leape LL.** Preventable adverse drug events in hospitalized patients: a comparative study of intensive care and general care units. Crit Care Med. 1997;25:1289–97.
14. **Leape LL, Bates DW, Cullen DJ, et al.** Systems analysis of adverse drug events. ADE Prevention Study Group. JAMA. 1995;274:35–43.
15. **Leape LL, Cullen DJ, Clapp MD, et al.** Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. JAMA. 1999;282:267–70.
16. **Brook RH, Appel FA, Avery C, Orman M, Stevenson RL.** Effectiveness of inpatient follow-up care. N Engl J Med. 1971;285:1509–14.
17. **Himmel W, Tabache M, Kochen MM.** What happens to long-term medication when general practice patients are referred to hospital? Eur J Clin Pharmacol. 1996;50:253–7.
18. **Parkin DM, Henney CR, Quirk J, Crooks J.** Deviation from prescribed drug treatment after discharge from hospital. BMJ. 1976;2:686–8.
19. **Katz E, Nicod P, Brunner HR, Waeber B.** Changes in treatment during and after hospitalization in patients taking drugs for cardiovascular diseases. Cardiovasc Drugs Ther. 1996;10:189–92.
20. **van Walraven C, Weinberg AL.** Quality assessment of a discharge summary system. CMAJ. 1995;152:1437–42.
21. **Forster AJ, Murff HJ, Peterson JF, Gandhi TK, Bates DW**. The incidence and severity of adverse events affecting patients following discharge from the hospital. Ann Intern Med. 2003;138:161–7.
22. **Kaushal R, Bates DW, Landrigan C, et al.** Medication errors and adverse drug events in pediatric inpatients. JAMA. 2001;285: 2114–20.
23. **Gandhi TK, Weingart SN, Borus J, et al.** Adverse drug events in ambulatory care. N Engl J Med. 2003;348:1556–64.
24. **Forster AJ, Murff HJ, Peterson JF, Gandhi TK, Bates DW.** Adverse drug events occurring following hospital discharge. J Gen Intern Med. 2003;18(suppl 1):282. Abstract.
25. **Gurwitz JH, Field TS, Avorn J, et al.** Incidence and preventability of adverse drug events in nursing homes. Am J Med. 2000;109: 87–94.
26. The Institute of Medicine. To Err Is Human: Building a Safer Health System. Washington DC: National Academy Press; 2000.
27. **Forster AJ, Clark HD, Menard A, et al.** Adverse events affecting medical patients following discharge from hospital. CMAJ. 2004;170: 345–9.
28. **Deyo RA, Cherkin DC, Ciol MA.** Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol. 1992;45:613–9.
29. **Barsky AJ, Saintfort R, Rogers MP, Borus JF.** Nonspecific medication side effects and the nocebo phenomenon. JAMA. 2002;287:622–7.