# Risk of adverse drug events by patient destination after hospital discharge

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W ith an estimated 3 billion prescriptions dispensed in 2001,[1] and with 81% of Americans over 18 years of age receiving prescription medications annually,[2] drug therapy has become the predominant method of treating disease in America. The recent passage of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003[3] is intended to further enhance the access of seniors to medication therapies, and seniors are the subpopulation of Americans most likely to take multiple medications[2] and are at highest risk from medication use.[4,5] While the use of pharmaceuticals has positively affected important patient outcomes, resulting in generally accepted evidence-based guidelines for medication therapies,[6-8] drug use carries inherent dangers that can result in patient harm.[9]

The Institute of Medicine in 1999 identified medical errors as a major public health problem and indicated that a large proportion of such errors are related to medications.[10] Medica-

**Purpose.** The prevalence of risk factors for adverse drug events (ADEs) in patients discharged from the hospital to various care settings was studied.
**Methods.** Data on patient risk characteristics for ADEs were collected for hospital discharges for 2000. Differences in the prevalence of 10 risk characteristics among home health care (HHC), self-care (SC), and long-term-care (LTC) patients at the point of discharge were determined.
**Results.** Data for 4250 discharges were analyzed. The three groups differed significantly in the distribution of risk characteristics. HHC patients had the highest prevalence of heart failure, cardiovascular

medication use, and polypharmacy, and LTC patients had the highest prevalence of hypoalbuminemia, cognitive impairment, and psychiatric drug use.
**Conclusion.** The risk of ADEs in patients discharged to HHC appeared to be comparable to or higher than that in patients discharged to LTC.

**Index terms:** Ambulatory care; Cardiac drugs; Cognition disorders; Drugs, adverse reactions; Health care; Heart failure; Hypoproteinemia; Long-term-care facilities; Psychotherapeutic agents; Rational therapy; Reports
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tion errors often result in adverse drug events (ADEs)[4,11-13] (i.e., adverse health events [AHEs][14,15] caused by drug-related problems [DRPs][16]) and may be preventable[17-20]; thus, reducing their frequency has become a national priority.[21] In addition to overt error-related harm,[1,22] the inherent toxicity of drugs and the hazards inherent to health systems also contribute to ADEs,[23] further increasing

the risks associated with medication use.

While DRPs have been identified in institutional settings and steps have been taken to develop systems to avoid them,[24] little has been done in the ambulatory care setting to systematically address this public health issue. Reports show that the recorded prevalence of fatal medication errors in the inpatient environment has

been relatively stable as a percentage of doses dispensed, while their recorded prevalence in the outpatient environment has increased dramatically.[25,26] Likewise, inappropriate prescribing, monitoring, and medication use continue to be identified as problems in the outpatient setting,[16,27,28] and treatment of ADEs routinely requires unplanned physician visits, emergency department visits, and hospitalization.[12,18,29] Since far more individuals receive health care services in the outpatient setting, and since this setting is the arena of choice for providing health care, it is important that any new efforts to reduce ADEs consider the outpatient medication-use system.

Bates et al.[30] have described an increased role of technology, such as better linkages among systems and process simplification, to help reduce medical errors. Recognizing patients at risk for ADEs by using explicit criteria is necessary for implementing a technology-based surveillance system to find and correct DRPs before they result in harm. However, this set of explicit criteria does not exist. Fick et al.[31] and Beers[32] have come closest to this goal by identifying medications that are generally considered to be inappropriate for routine use in the elderly because they either are ineffective or pose too high a risk in such patients. However, outpatient screening with these criteria has not been implemented, perhaps because of the low physician acceptance of the DRPs identified by this process in the ambulatory care environment.[33,34]

Because the health care system operates under budgetary restraints and available resources are limited, action aimed at reducing DRPs would be most effective if it targeted patients at highest risk of ADEs. While certain characteristics (e.g., illness and drug burdens) have been shown to contribute to the risk of an ADE, such characteristics have not been widely employed as a means of allo-

cating pharmaceutical care resources, with levels of pharmaceutical care historically being determined entirely by the physical location of the patient (i.e., outpatient, nursing home, or hospital). While intensive pharmaceutical care services are undoubtedly of value to patients in institutions,[35-38] the failure to provide comparable levels of care to the highest-risk ambulatory care patient results in unacceptably high rates of ADEs.[4,11,12,17-20]

Home health care (HHC) agencies and other providers now offer high-acuity home clinical services previously available only in the inpatient setting. Wound care, respiratory therapy, physical therapy, occupational therapy, enteral nutrition, and parenteral sterile products are frequently provided to patients residing at home, creating a population of high-risk outpatients who frequently experience DRPs and ADEs. This transfer of high-acuity patients into the outpatient arena creates a highly heterogeneous population, encompassing individuals ranging from the healthy to the terminally ill. It is increasingly clear that the present outpatient medication-use system is not equipped either to identify or respond to the special needs of the most burdened outpatients. Therefore, an outpatient medication-use system that can allocate pharmaceutical care resources on the basis of patient risk of ADEs, rather than patient residence within the system, may be helpful.

Since patients receiving home nursing services reimbursable by Medicare must be sufficiently ill to qualify for nursing services and must also be home bound, home care recipients may be clearly distinguished from other outpatient groups. If actual ADEs can be shown to be more prevalent in this group, or if the HHC recipients display a higher prevalence of ADE risk characteristics, the designation "home care recipient" may serve as a useful means

of screening and allocating additional pharmaceutical care services to patients in the outpatient environment.

A growing body of evidence shows that DRPs are quite common in the population of patients receiving HHC services,[39-43] and Triller et al.[27] have developed and implemented a clinical pharmacy service model to identify HHC patients at high risk for AHEs resulting from DRPs. This model identified an average of 3.4 DRPs per patient referred for pharmacy services. Using the Home Health Criteria, which identify patterns of medication use and clinical signs and symptoms suggestive of DRPs, and the Beers criteria, Meredith et al.[41] estimated (by chart review) that up to one third of HHC patients could have DRPs, but Triller et al.[27] documented discovery and correction of a DRP for every HHC patient seen over nine months and discovered 32% of DRPs in their sample of HHC patients only after an in-home medication assessment. These results indicate that 33–100% of HHC patients may have DRPs with the potential of progressing to AHEs.

Multiple studies have identified characteristics that are related to the risk of AHEs.[4,18,44-53] If the total burden of DRPs in patients' medication therapies contributes to their risk of an AHE, and if the HHC population develops a large number of DRPs in the outpatient environment, then it is likely that patients receiving HHC services will also display many of these AHE-risk characteristics. To assess the characteristics of risk for an AHE after hospitalization by using routinely available and easily accessible information, we performed a retrospective cohort analysis. The objective was to compare the distribution of patient risk characteristics associated with AHEs among patients discharged from the hospital to long-term care (LTC), HHC, or self-care (SC). The a priori hypothesis was that HHC patients would display risk characteristics for ADEs compa-

rable to those of LTC patients and in excess of those of patients discharged to SC.

## Methods

To identify previously reported characteristics associated with ADEs or AHEs resulting in emergency-room visits, extended hospitalizations, or death, we reviewed the literature (MEDLINE for "adverse drug event" in title for the period from 1998 to present). With the addition of other selected studies, 23 risk characteristics for ADEs or AHEs were identified (Table 1), 10 of which were represented sufficiently in the available data set for analysis.[4,18,44-53]

Following approval by the Northeast Health institutional review board, we performed a retrospective analysis of records in the master clinical and financial database (Meditech 4.9, Medical Information Technology Inc., Westwood, MA, with MSM-Picis 9.0, Wakefield, MA) for patients discharged from both hospitals in the Northeast Health system between January 1, 2000, and December 31, 2000. Northeast Health is an integrated health system consisting of two community hospitals and a continuum of residential and care services for seniors. The data query captured selected laboratory test values, diagnoses, discharge destinations, medications active upon hospital discharge, and demographics necessary to adequately describe the patient populations and assess the presence of the identified risk characteristics for ADEs or AHEs among the patient groups (i.e., SC, HHC, and LTC patients). Patient data were deidentified and compliant with Health Insurance Portability and Accountability Act (HIPAA) regulations.

Excluded from analysis were individuals who had a length of stay (LOS) of less than 24 hours, who were less than 21 years of age, who were admitted to maternity or same-day surgery units, or who had an actual or implied diagnosis of HIV infection or AIDS. Likewise, patients whose discharge was due to transfer to a different acute care facility or who died during the index hospitalization were excluded. A more detailed description of the data query and data-set compilation, structure, and content has been previously reported.[54]

The number of medications was calculated as the count of all oral medications with active orders on the day of hospital discharge and discontinued by discharge assignment (i.e., active until the moment of discharge). The presence of nine or more such medication orders was considered a risk factor. Medication classes were determined according to the categories given in the online Thompson Micromedex Healthcare Series Databases (volume 116, expiration June 2003), and the number of medication classes was calculated from the medication orders active at the time of discharge. The presence of more than six such classes was considered to be a risk factor.

Cardiovascular medications included any diuretics, potassium supplements, β-adrenergic-receptor antagonists, angiotensin active agents, calcium-channel antagonists, antiarrhythmics, or other antihypertensives. Antiinfectives included any systemically administered antibiotics or antifungals. Antivirals were excluded from analysis by protocol to avoid implying a diagnosis of HIV infection or AIDS. Psychiatric medications included all available typical and atypical antipsychotic agents, while the category of central-nervous-system (CNS) medications included any tricyclic or tetracyclic antidepressants, selective serotonin-reuptake inhibitors, or benzodiazepines but did not include narcotic analgesics or other medication classes with CNS adverse effects.

Cognitive impairment included the presence of a diagnosis of dementia as defined by the *International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM)*, codes of 290.xx, 294.xx, or 331 or by the presence of any commercially available antidementia agent (e.g., donepezil). Renal insufficiency

Table 1.
**Characteristics Associated with Adverse Drug Events (ADEs)[a]**

| Risk Characteristic | Measured Outcome(s) | Reference(s) |
|---|---|---|
| 5 or 6 drug orders | Panel-determined ADE | 44–46 |
| 7 or 8 drug orders | Panel-determined ADE | 46 |
| >9 drug orders | Panel-determined ADE | 46 |
| >2 drug classes | Increased hospital LOS | 47 |
| >4 drug classes | Increased hospital LOS | 47 |
| >6 drug classes | Increased hospital LOS | 47 |
| Any newly prescribed drug | Panel-determined ADE | 47 |
| Any newly discontinued drug | Panel-determined ADE | 45 |
| Cardiovascular drugs | Panel-determined ADE | 17, 44, 48 |
| Antiinfective drugs | Panel-determined ADE | 45, 46, 48 |
| Psychiatric drugs | Panel-determined ADE | 46, 48 |
| CNS drugs | Panel-determined ADE | 17, 44–46, 48 |
| Gastrointestinal drugs | Panel-determined ADE | 17, 45, 48 |
| Heart failure | ER visit | 53 |
| Cognitive impairment | Self-reported ADE | 4, 49 |
| Renal impairment | ER visit | 49 |
| Hepatic impairment | ER visit | 49 |
| Serum albumin conc., <3.4 g/dL | Increased LOS and death | 50 |
| Inadequate monitoring | Investigator-determined ADE | 18, 51, 52 |
| Toxic drug concentration | Investigator-determined ADE | 51, 52 |
| Inappropriate dosage | Investigator-determined ADE | 51, 52 |
| Drug–drug interaction | Investigator-determined ADE | 51, 52 |
| Patient noncompliance | Investigator-determined ADE | 18, 51 |

[a]LOS = length of stay, CNS = central nervous system, ER = emergency room.

was considered to be an estimated glomerular filtration rate of less than 60 mL/min (i.e., stage 3 chronic kidney disease); calculations were performed with the modification of diet in renal disease equation by using the serum creatinine measurement obtained closest to the discharge date. The presence of heart failure was also identified by all *ICD-9-CM* codes identifying heart failure.

Risk characteristics were tested for significant differences of prevalence across the three groups (LTC, HHC, and SC patients) by chi-square analysis for binary counts of the presence or absence of a characteristic and by analysis of variance (ANOVA) for continuous variables, such as patient age and LOS. Minitab, version 13.30 (Minitab Inc., State College, PA), was used for all statistical analysis, and the level of significance for the statistical procedures was set at <0.05 for the initial analysis and ≤0.01 for subanalyses. Data are presented as means and standard deviations or (for dichotomous variables) percentages.

## Results

Following the application of inclusion and exclusion criteria, data from 4250 episodes were analyzed, consisting of 2420 patient discharges to SC, 1057 to HHC, and 773 to LTC. Patient demographics are presented in Table 2. Patients were predominantly white and female, and the LTC group was significantly older, had more medical diagnoses, and had a longer average LOS than the other groups.

The prevalence of risk characteristics varied considerably among patient groups, reaching significance across the three groups for 9 of the 10 factors assessed (Table 3). Subanalysis of the significant factors (i.e., $p \leq 0.01$) identified that significant differences also existed between the LTC and HHC groups, with the prevalence of three characteristics (hypoalbuminemia [$p \leq 0.01$], cogni-

tive impairment [$p \leq 0.001$], and psychiatric medication use [$p \leq 0.001$]) being more prevalent in the LTC group and four others in the HHC group (cardiovascular medication use [$p \leq 0.001$], polypharmacy [more than six medication classes], [$p \leq 0.001$], polypharmacy [more than nine medication orders] [$p \leq 0.001$], and heart failure [$p \leq 0.01$]). Significance was maintained for all seven of these factors compared with the SC group.

## Discussion

Nine of 10 patient characteristics that have previously been associated with drug-related emergency-room visits, extended hospitalizations, or death were present in different frequencies among patients discharged from hospitals to LTC, HHC, or SC. While LTC patients, who have been mandated to receive comprehensive pharmacy services since 1974,[35,55,56] did display the highest prevalence of three risk factors (hypoalbuminemia, cognitive impairment, and psychiatric drug use), the HHC population had a significantly higher prevalence of four others, suggesting that outpatients who receive HHC services are at comparable or higher risk of ADEs or AHEs than LTC patients.

From a medication safety perspective, these findings are problematic. The LTC group was federally mandated to receive all medications from a designated pharmacy and to have monthly drug regimen reviews by a pharmacist. In addition, the LTC patients generally were not responsible for their own medication adherence, with nurses administering nearly all doses. In contrast, HHC patients received medications via the same system as the lower-risk SC patients, with no provision of comprehensive medication management services. The contrast in the levels of pharmaceutical services is highlighted by a report in which 27% of patients enrolled in a home LTC program were found to frequently encounter prob-

lems with drug procurement and administration.[39] SC patients, while having a high prevalence of certain AHE-risk characteristics, never exceeded the LTC and HHC groups with respect to any risk characteristic, suggesting that SC patients are, in general, a distinct outpatient population in less need of comprehensive medication management services.

While we did not attempt to weight these AHE-risk factors, other researchers have done so. Gurwitz et al.[18] studied the prevalence of ADEs in 30,397 Medicare enrollees in the outpatient environment and found that cardiovascular drugs, anticoagulants, and diuretics collectively accounted for 56.8% of all preventable ADEs. CNS medications and antipsychotic agents infrequently caused ADEs, and ADEs caused by antibiotics were rarely considered preventable. In view of the prevalence of cardiovascular drug use, heart failure, and polypharmacy (more than nine active medication orders or more than six medication classes) in HHC patients in our study, these patients could be at higher risk of preventable ADEs than residents of an LTC facility.

While the LTC group had the highest rate of cognitive deficits and use of psychiatric medications, these factors combined caused less than 1% of the ADEs identified by Gurwitz et al.[18] Because the Gurwitz et al. trial excluded LTC patients, those results may not be directly applicable to the LTC population. However, if a patient's risk of an ADE is inherent in his or her overall drug and disease burdens, then it is likely that measurement of these risk characteristics would translate across patient locations. Likewise, if the total risk of an AHE is affected by the level of ancillary health care services, then the overall risk of an AHE may increase in populations with comparable prevalences of drug and disease risk characteristics but receiving a lower level of supportive services.

Table 2.
**Patient Demographics[a]**

| Characteristic | SC Group (n = 2420) | HHC Group (n = 1057) | LTC Group (n = 773) | p |
|---|---|---|---|---|
| Age, yr (CI) | 64.5 (63.9–65.2) | 74.1 (73.3–74.8) | 81.9 (81.2–82.5) | ≤0.001 |
| Female, no. (%) | 1193 (49.3) | 635 (60.1) | 512 (66.2) | ≤0.001 |
| Male, no. (%) | 1227 (50.7) | 422 (39.9) | 261 (33.8) | ≤0.001 |
| White, no. (%) | 2202 (91.0) | 974 (92.1) | 727 (94.0) | ≤0.025 |
| LOS, days (CI) | 4.9 (4.7–5.1) | 7.2 (6.8–7.5) | 10.5 (9.7–11.2) | ≤0.001 |
| Diagnoses, no. (CI) | 7.1 (7.0–7.3) | 8.7 (8.5–8.9) | 9.6 (9.4–9.8) | ≤0.001 |

[a]SC = self-care, HHC = home health care, LTC = long-term care, CI = 95% confidence interval.

Table 3.
**Prevalence of Risk Characteristics among Patient Groups[a]**

| | No. (%) Patients | | | |
|---|---|---|---|---|
| Risk Characteristic | SC Group (n = 2420) | HHC Group (n = 1057) | LTC Group (n = 773) | p |
| Serum albumin conc., <3.4 g/L[b] | 856 (40.4) | 521 (54.4) | 444 (61.4) | 0 |
| Antiinfective drugs | 1266 (52.3) | 694 (65.7) | 549 (71.0) | 0 |
| Cardiovascular drugs | 1892 (78.2) | 957 (90.5) | 651 (84.2) | 0 |
| CNS drugs | 1242 (51.3) | 511 (48.3) | 416 (53.8) | 0.063 |
| Cognitive impairment | 148 (6.1) | 124 (11.7) | 425 (55.0) | 0 |
| GFR, <60 mL/min[c] | 1194 (52.1) | 709 (69.4) | 522 (69.0) | 0 |
| Drug classes, >6 | 1464 (60.5) | 786 (74.4) | 497 (64.3) | 0 |
| Drug orders, >9 | 1425 (58.9) | 703 (66.5) | 449 (58.1) | 0 |
| Heart-failure diagnosis | 639 (26.4) | 494 (46.7) | 305 (39.5) | 0 |
| Psychiatric drugs | 293 (12.1) | 108 (10.2) | 272 (35.2) | 0 |

[a]SC = self-care, HHC = home health care, LTC = long-term care, CNS = central nervous system, GFR = estimated glomerular filtration rate.
[b]n = 2118, 958, and 723 subjects for groups SC, HHC, and LTC, respectively.
[c]n = 2292, 1021, and 757 subjects for groups SC, HHC, and LTC, respectively.

This study supports the hypothesis that HHC patients display risk characteristics for ADEs comparable to or greater than those of patients residing in LTC facilities. Given these findings, we believe that comparable levels of pharmaceutical care should be made available to HHC patients. While patients in the SC group also had a high prevalence of some risk characteristics, HHC patients appeared to differ in risk from SC patients and to be more similar to LTC patients. Interventions providing pharmaceutical care to high-risk patients in the community have been shown to identify and resolve DRPs[4,5,13,27] and to improve clinical and financial outcomes.[5,57,58] While it would be optimal but infeasible to provide institutional-level pharmaceutical care to all patients exposed to medication therapies, it may be possible to expand the level of pharmaceutical care received by LTC residents into the HHC population.

The task of providing pharmaceutical care to such a large population of patients may appear daunting, but the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 may already have created the reimbursement incentive. The decision to reside in an LTC facility is generally a permanent one, but home care services are typically made available on an episodic basis and are limited to patients for whom the services are deemed medically necessary. The typical home care patient is referred to an agency immediately following an index health event, such as a hospitalization, and such transitions in the level of care have also been iden-

tified as increasing the risk of ADEs.[12] The provision of pharmaceutical care to outpatients who qualify for home nursing may be an ideal method for targeting services to a high-risk population at a key point of transition in their health status.

While our results support the concept of providing pharmaceutical care to home care recipients, the study is not without limitations. The data were collected from two acute care facilities in a limited area of upstate New York and may be subject to geographic influences. The number of active medication orders may be somewhat inflated, since the query was unable to separate orders for scheduled medications from those for drugs to be administered on an as-needed basis. As a result, the absolute number of medications may not be directly comparable to those in other studies, and it is not known if drug counts were biased with respect to any of the three groups.

Because the analysis was performed on a deidentified, HIPAA-compliant data file, multiple encounters for individuals may have been included. While multiple inpatient encounters may affect the reported data, the fact remains that important ADE-risk characteristics can be identified in patients prior to hospital discharge and that HHC patients appear to display a disproportionate prevalence (relative to their disease burden) of these risks. Predischarge screening, automated or otherwise, could provide a reasonable mechanism by which additional phar-

maceutical care services could be effectively allocated to high-risk outpatients.

ADEs are commonly experienced in the outpatient setting, and such events frequently occur in patients with identifiable risk factors. Patients discharged from hospitals to HHC display a high prevalence of such risk factors, suggesting that the designation "HHC recipient" may be an effective means of allocating pharmaceutical care services to high-risk patients in the outpatient environment.

## Conclusion

Patients discharged to HHC had higher rates of certain risk characteristics associated with ADEs (cardiovascular medication use, heart failure, polypharmacy), while patients discharged to LTC had higher rates of other ADE-risk characteristics (hypoalbuminemia, cognitive impairment, psychiatric medication use). These findings suggest that the risk of ADEs in patients discharged to HHC is comparable to or higher than that in patients discharged to LTC.

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