Adverse Events Due to Discontinuations in Drug Use and Dose Changes in Patients Transferred Between Acute and Long-term Care Facilities

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Background: Care transitions are commonplace for ill older adults, but no studies to our knowledge have examined the occurrence of iatrogenic harm from medication changes during patient transfer.

Objectives: To identify medication changes during transfer between hospital and nursing home and adverse drug events (ADEs) caused by these changes.

Methods: Participants were residents of 4 nursing homes in the New York City metropolitan area admitted to 2 academic hospitals. Nursing home and hospital medical records were reviewed to identify changes in medication regimens between sites. Medications were matched and compared regarding dosage, route, and frequency of administration. Two physician investigators used structured implicit review to identify ADEs attributable to transfer-related medication changes.

Results: During a total of 122 admissions, the mean numbers of medications altered during transfer from nursing home to hospital and hospital to nursing home were 3.1 and 1.4, respectively ($P<.001$ for comparison). Most changes in drug use were discontinuations, followed by dose changes and class substitutions. Of 71 bidirectional transfers that were reviewed by 2 physician investigators, ADEs attributable to medication changes occurred during 14 (20%). The overall risk of ADE per drug alteration ($n=320$) was 4.4% (95% confidence interval, 2.5%-7.4%). Although most medication changes (8/14) implicated in causing ADEs occurred in the hospital, most ADEs (12/14) occurred in the nursing home after nursing home readmission.

Conclusions: Medication changes are common during transfer between hospital and nursing home and are a cause of ADEs. Research is needed on interinstitutional patient care and systems interventions designed to prevent ADEs.

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In the past 2 decades, care transitions and relocations have become commonplace for older adults with acute and chronic illness. Unfortunately, clinicians have observed that patient relocation, even appropriately performed, can have adverse effects on health and function in vulnerable individuals. These adverse effects include a risk of iatrogenic harm from failure of the process of relocation itself, which involves patient transportation between sites, communication between practitioners, and initiation of a care plan at the destination site.

Of classes of iatrogenic harm, older adults’ use of multiple medications confers significant risk of experiencing adverse drug events (ADEs) in the community, hospital, and long-term care settings. Harm can occur from drugs at the time of initiation, when drug dosage is changed, when a drug is substituted for another in the same class, or as an effect of discontinuation in drug use. Drug dosage changes and discontinuations are common at the time of hospital admission of older adults and after discharge. Despite the frequency at which medications are altered on patient relocation, no studies to our knowledge have investigated the incidence of ADEs as a result of medication changes at the time of patient transfer.

The objectives of this study were to measure the frequency of changes and discontinuations in medication use that occur at the time of transfer of older adults between hospital and nursing home in both directions of transfer and to identify adverse events related to these changes. We hypothesized that we would be able to use existing methods for identifying ADEs to identify and measure the incidence of ADEs caused by medication changes that occur on interinstitutional transfer. Such ADEs have not been measured quantitatively in...
work that has been performed within individual institutions.\textsuperscript{4,5} We chose to study nursing home residents because of their high rate of transfer to and from the hospital,\textsuperscript{13} their high medication use,\textsuperscript{14} and the accuracy of determining medication regimens at each site by review of nursing home and hospital medical records.

METHODS

SETTING AND PARTICIPANTS

Participants were residents of 4 nursing homes in the New York City metropolitan area who were admitted to 1 of 2 tertiary care academic medical centers. The participating facilities were part of a collaborative consortium that endeavored to improve continuity of nursing care for nursing home residents who were hospitalized. Each hospital had a transfer agreement with 2 of the 4 nursing homes. However, each hospital’s medical staff, nursing staff, medical records, and medication ordering systems were separate from those of any of the nursing homes. When patients were transferred between facilities, handwritten transfer documents were used to communicate patient information in each direction of transfer. Hospital and nursing home practitioners could also communicate by telephone. Eligible participants were individuals transferred from nursing home to hospital and admitted and who remained in the hospital for at least 24 hours. Individuals who were seen in the emergency department alone were excluded. Individuals were included whether they survived until hospital discharge and whether they returned to the nursing home from which they originated. Patients or legal surrogates gave informed consent to participate. Institutional review boards of each study institution approved the study.

MEASUREMENTS

Participants were followed from hospital admission until death or discharge and, for participants transferred back to one of the study nursing homes (whether it was to the one from which they originated), for 2 months after nursing home admission. All data were collected by medical record review. Trained research personnel reviewed nursing home and hospital medical records to identify changes in medication regimens between sites. Sources of medication data that were reviewed were as follows: (1) prehospitalization nursing home physician orders, (2) nursing home–to–hospital transfer documents, (3) hospital physician admission orders, (4) hospital physician discharge orders, (5) hospital–to–nursing home transfer documents, and (6) nursing home physician readmission orders. Nursing medication administration information was also reviewed whenever physician orders were unclear.

Medications from sequential sources (items 1-6) were matched and compared regarding dosage, route, and frequency of administration. Codes were assigned for (1) no change, (2) increase in daily dose, (3) decrease in daily dose, (4) route change, (5) change from routine to as-needed administration, (6) change from as-needed to routine administration, (7) substitution for a medication with the same indication (excluding substitutions between generic and brand-name versions of the same drug), and (8) discontinuation. Daily dosage changes were identified separately from changes in frequency of administration. Any of codes 2 through 8 was considered an alteration in a previously prescribed medication. Newly prescribed medications were also recorded. Medications were divided into major therapeutic classes that included cardiovascular, gastrointestinal, neuropsychiatric, and antibiotic agents. Topical agents, vitamins, minerals, and nonpsychiatric as-needed medications were not recorded.

The primary outcome was ADEs attributed to transfer-related medication changes. An ADE was defined as any noxious, unintended, and undesired effect of change in administration of a previously prescribed medication.\textsuperscript{13} Two physician investigators (K.B., A.M.) reviewed nursing home and hospital medical records of participants for medical incidents that were possible ADEs. They rated whether each incident was related to a change in a previously prescribed medication according to criteria adapted from Naranjo et al.\textsuperscript{16} using structured implicit review.\textsuperscript{17} Review criteria included the following: (1) whether there was a note in the medical record that suggested that a medication change caused the incident, (2) whether the timing of medication change and incident suggested that the incident was related to the medication change, (3) whether the patient could have been caused by something other than a medication change, (4) whether the incident was a known possible reaction to this medication change, and (5) whether the patient’s condition improved after correction of the medication change. Physician reviewers then assigned a score indicating the overall certainty that the incident was caused by a medication change, using a 3-point Likert scale adapted from Brennan et al,\textsuperscript{18} with 1 indicating extreme doubt and 5 indicating extreme certainty. An ADE was defined as any incident for which the certainty score recorded by both physician reviewers was at least 3 (indicating moderate certainty), with 1 physician reviewer recording at least a 4 (indicating greater than moderate certainty). Severe ADEs were defined as those that resulted in death, increased hospital length of stay, or readmission to the hospital, as determined by consensus between the 2 physician reviewers.

Information was also collected on participant characteristics that could be associated with study outcomes, including resident age, sex, race, and duration of nursing home stay. A score for burden of chronic disease, adapted from Charlson et al,\textsuperscript{19} was calculated from chronic medical problems listed in the nursing home medical record. Physical and cognitive functions were measured using information from the nursing home Minimum Data Set (MDS). The MDS is a federally mandated assessment instrument with which nurses document observations of resident function and clinical status. Physical function was graded from 0 to 6 (0 indicating complete independence and 6 indicating total dependence), using the Activities of Daily Living Self Performance Hierarchy,\textsuperscript{20} a scale that uses MDS items for personal hygiene, toileting, locomotion, and eating. Cognitive function was graded from 0 to 6 (0 indicating no impairment and 6 indicating very severe impairment) using the MDS Cognitive Performance Scale,\textsuperscript{21} a scale that uses MDS items for short-term memory, cognitive skills for daily decision making, making self understood, eating, and coma. Information on inpatient diagnoses, medical events, and length of stay was obtained from the hospital medical record.

STATISTICAL ANALYSIS

More than one hospital admission was allowed per participant. The unit of analysis was hospital admission. Frequency and types of changes in previously prescribed medications were calculated at each step in each direction of transfer. In a pilot test of the data collection instruments, interrater reliability for determining number and types of medication changes was high, with a weighted $k$ statistic of 0.89.\textsuperscript{22} The ADEs were classified by where they occurred (hospital or nursing home) and by which step in the transfer the medication change to which they were attributed occurred. The overall incidence of ADEs was estimated. Multivariate regression was performed to determine participant characteristics that were associated with the occurrence of medication changes and ADEs. Both 95% confidence intervals (CIs) and $P$ values were calculated using standard for-
Eighty-seven residents participated. Sixty-four (73%) residents were admitted to the hospital once and 23 (27%) more than once, for a total of 122 admissions. Participant characteristics are given in Table 1. The most common hospital diagnoses were pneumonia, urinary tract infection, sepsis, and dehydration. Median hospital length of stay was 6 days (range, 1-55 days). Nine participants (7% of admissions) died in the hospital. Of those who survived to hospital discharge, 111 admissions (98%) were discharged to one of the study nursing homes.

The mean number of medications prescribed before nursing home–to–hospital transfer was 6.1 (SD, 2.7; median, 6; range, 0-14). For 96 episodes of hospitalization for which the required documents could be examined, the mean number of medications altered between nursing home–to–hospital transfer documents and hospital admission orders was 3.1 (SD, 2.3; median, 3; range, 0-11) not including newly prescribed medications. For 86% of these transfers, at least 1 medication was altered. Sixty-five percent of drug use changes were discontinuations, 19% were dose changes, and 10% were substitutions for medications with the same indication. The most common classes of medications altered at the time of nursing home–to–hospital transfer were cardiovascular medications, followed by gastrointestinal agents, neuropsychiatric medications, and antibiotics.

At the time of hospital discharge, the mean number of medications prescribed was 3.9 (SD, 2.3; median, 4; range, 0-11). For 99 episodes of hospitalization for which the required documents could be examined, the mean number of medications altered between hospital–to–nursing home transfer documents and nursing home readmission orders was 1.4 (SD, 1.7; median, 1; range, 0-9) not including newly prescribed medications. For 64% of these transfers, at least 1 medication was altered. Fifty-seven percent of changes were discontinuations, 21% were dose changes, and 22% were substitutions for medications in the same class. Fewer medications were altered on hospital–to–nursing home transfer than on nursing home–to–hospital transfer (P<.001). Overall, 21% of medication changes at the time of nursing home readmission were reversions to medications and dosages prescribed before hospital admission (of medications that were altered in the hospital).

Of 71 bidirectional transfers that were reviewed by 2 physician investigators (K.B., A.M.), ADEs attributable to medication changes occurred during 14 (20%) (Table 2). Two ADEs were considered severe in that they caused increased hospital length of stay or readmission to the hospital. No ADE resulted in death. Seven (50%) of the ADEs were caused by discontinuations in drug use, representing a 3.5% risk of ADE per discontinuation in drug use (7 of 198 total discontinuations in drug use). Five (36%) of the ADEs were caused by drug dosage changes, including 3 dosage increases and 2 dosage decreases, representing a 7.9% risk of ADE per drug dosage change (5 of 63 total drug dosage changes).

No ADE was attributed to a drug substitution. The overall risk of ADE per drug alteration was 4.4% (95% CI, 2.5%-7.4%) (14 of 320 drug alterations of any type). Four ADEs (29%) were related to alterations in neuropsychiatric medications and 2 each (14%) to alterations in cardiovascular medications, insulin, or colchicine (Table 2).

The mean time interval from medication change to ADE was 14 days (median, 13.5 days; range, 1-34 days). Six medication changes implicated in causing an ADE occurred on nursing home readmission, and 5 occurred on hospital admission. Three occurred during the hospital stay. Although most medication changes (8/14) implicated in causing an ADE occurred on hospital admission or during the hospital stay, most ADEs (12/14) occurred in the nursing home after nursing home readmission, because the time interval from medication change to ADE was greater than the duration of hospital stay. No interinstitutional transfer was implicated in more than 1 ADE.

In multivariate linear regression, a greater number of medication changes at the time of nursing home–to–hospital transfer was associated with a greater number of medications prescribed before transfer (P<.001) but no other participant characteristic (including sex, age, race, length of nursing home stay, chronic comorbid illness, cognitive function, and physical function). After controlling for number of medications prescribed before transfer, a greater number of medication changes at the time of hospital–to–nursing home transfer was associated with Latino or Asian American race (P= .045) but no other participant characteristic. In a multivariate logistic regression model, a higher likelihood of experiencing an ADE from a transfer-related medication change was associ-
have incurred injury due to omission of a medication, change in medication dosing, or prescription of a medication to which the patient had a past adverse reaction.23 Our study suggests that alterations in medication prescribing are common during transfer between institutions and are a cause of ADEs. Clinicians may alter or discontinue medication use at the time of hospital or nursing home admission as a result of changes in a patient’s clinical condition or to adhere to institutional formulary requirements. Clinicians may also temporarily discontinue medication use at the time of hospital admission if they believe it is contraindicated or inessential to acute care. In this study, it is not surprising that the frequency of medication change observed on hospital admission was greater than that observed on return to the nursing home, because the time of hospital admission is typically a time of greater change in patient clinical status and a time of in-detail assessment of medication use.

A proportion of transfer-related medication changes and ADEs may occur because of inaccurate or incomplete communication of medication regimens between facilities.23,24 Because most nursing homes and hospitals

[Table 2. Adverse Events From Medication Changes in Nursing Home Residents Transferred to and From the Hospital*]

<table>
<thead>
<tr>
<th>Medication</th>
<th>Adverse Event</th>
<th>Type of Medication Change</th>
<th>Timing of Change</th>
<th>Location When Adverse Event Occurred</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoprolol tartrate</td>
<td>Blood pressure, 94/58 mm Hg</td>
<td>Discontinuation</td>
<td>On hospital admission</td>
<td>During hospital stay</td>
<td>Resolved with restarting metoprolol, caused increased hospital length of stay; resolved with treatment</td>
</tr>
<tr>
<td>Colchicine</td>
<td>Crystal arthritis (elbow)</td>
<td>Discontinuation</td>
<td>On hospital admission</td>
<td>During hospital stay</td>
<td>Resolved with treatment</td>
</tr>
<tr>
<td>Metoclopride</td>
<td>Vomiting</td>
<td>Discontinuation</td>
<td>On hospital admission</td>
<td>After nursing home readmission</td>
<td>Resolved with treatment</td>
</tr>
<tr>
<td>Risperidone</td>
<td>Lethargy</td>
<td>Dose increase</td>
<td>On hospital admission</td>
<td>After nursing home readmission</td>
<td>Resolved with discontinuation of risperidone</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>Lethargy; fall</td>
<td>Dose increase</td>
<td>During hospital stay</td>
<td>After nursing home readmission</td>
<td>Clonazepam dose not corrected</td>
</tr>
<tr>
<td>Warfarin sodium</td>
<td>Clotted dialysis access</td>
<td>Dose decrease</td>
<td>During hospital stay</td>
<td>After nursing home readmission</td>
<td>Readmitted to hospital to establish dialysis access</td>
</tr>
<tr>
<td>Insulin human, isophane</td>
<td>Blood glucose, 517 mg/dL; vomiting</td>
<td>Discontinuation</td>
<td>During hospital stay</td>
<td>After nursing home readmission</td>
<td>Resolved with restarting insulin</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>Diarrhea (positive for Clostridium difficile)</td>
<td>Duration decrease</td>
<td>On nursing home readmission</td>
<td>After nursing home readmission</td>
<td>Resolved with restarting metronidazole</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Seizure</td>
<td>Dose decrease</td>
<td>On nursing home readmission</td>
<td>After nursing home readmission</td>
<td>Dose increased; no additional seizures</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Seizure</td>
<td>Discontinuation</td>
<td>On nursing home readmission</td>
<td>After nursing home readmission</td>
<td>Carbamazepine restarted; no additional seizures</td>
</tr>
<tr>
<td>Codeine sulfate</td>
<td>Severe pain</td>
<td>Discontinuation</td>
<td>On nursing home readmission</td>
<td>After nursing home readmission</td>
<td>Resolved with restarting codeine</td>
</tr>
<tr>
<td>Insulin human, isophane</td>
<td>Blood glucose, 68 mg/dL; lethargy</td>
<td>Dose increase</td>
<td>On nursing home readmission</td>
<td>After nursing home readmission</td>
<td>Resolved with decreasing insulin dose</td>
</tr>
<tr>
<td>Isosorbide dinitrate</td>
<td>Blood pressure, 94/58 mm Hg</td>
<td>Reversion to prehospitalization dose</td>
<td>On nursing home readmission</td>
<td>After nursing home readmission</td>
<td>Resolved with discontinuation of isosorbide</td>
</tr>
</tbody>
</table>

*During 71 hospitalization episodes that could be reviewed by 2 physician investigators.

**SI conversion factor: To convert blood glucose from milligrams per deciliter to millimoles per liter, multiply by 0.0555.

In the United States, where older adults are routinely transferred among multiple sites of care, little is known about how relocation affects patient health. In this sample of individuals transferred between nursing home and hospital, discontinuations of use and dose changes in existing medications on hospital admission, during the hospital stay, and on nursing home readmission were implicated in causing ADEs. The incidence of ADEs measured in this study (20%) exceeded that found in studies of ADEs occurring during episodes of care within acute or long-term care facilities, although the severity of ADEs seemed to be less.

Few previous studies have looked systematically at the relationship between transitions in care location and ADEs. Only case reports have been published of patients transferred from hospitals to nursing homes who incurred injury due to omission of a medication, change in medication dosing, or prescription of a medication to which the patient had a past adverse reaction.23 Our study suggests that alterations in medication prescribing are common during transfer between institutions and are a cause of ADEs. Clinicians may alter or discontinue medication use at the time of hospital or nursing home admission as a result of changes in a patient’s clinical condition or to adhere to institutional formulary requirements. Clinicians may also temporarily discontinue medication use at the time of hospital admission if they believe it is contraindicated or inessential to acute care. In this study, it is not surprising that the frequency of medication change observed on hospital admission was greater than that observed on return to the nursing home, because the time of hospital admission is typically a time of greater change in patient clinical status and a time of in-detail assessment of medication use.

A proportion of transfer-related medication changes and ADEs may occur because of inaccurate or incomplete communication of medication regimens between facilities.23,24 Because most nursing homes and hospitals...

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are loosely affiliated and do not share medical records, medication ordering systems, formularies, or pharmacies (as was the case for institutions that participated in this study), medication information may be inaccurately transcribed. Although we did not collect data regarding whether the changes that led to ADEs were purposeful or inadvertent (which is not feasible to do by medical record review), we collected data on the completeness of interinstitutional communication forms and found that on average 14 information items (in addition to medications) were recorded on each form. In addition, a subset of medication changes implicated in causing an ADE had a recognizable clinical rationale and would be considered reasonable even with advance knowledge that the ADE might occur. As such, this subset of ADEs might be classified separately in some definition schema.25

This study has several limitations. First, the participants were residents of nursing homes that were part of a nursing home and hospital research consortium, suggesting that the results may not be applicable to residents of facilities that lack such interinstitutional relations. However, the effect of consortium activities on physician medication prescribing habits during the study was likely to be small, if not zero, because the consortium worked to improve nursing procedures during patient relocation by standardizing nursing information communicated between settings and did not target physician medication prescribing.

Second, the sample was a small convenience sample. This gave us limited power to detect associations between participant characteristics and outcomes and may have introduced selection bias. Our sample limitations suggest a need to replicate the study in a larger sample of participants from a greater number of facilities. For example, the finding that the number of medication changes occurring on nursing home–to–hospital transfer varies by racial group needs to be replicated. Despite the small sample size, we obtained acceptable SDs for the number of medication changes per relocation and an acceptable 95% CI for the incidence of ADEs per medication change.

A third limitation is that it is unknown whether the medication changes identified in this study were purposeful or inadvertent and whether the prescribing changes that led to ADEs deviated significantly from standard of care (ie, would be considered negligent). Finally, the study did not ascertain ADEs in individuals seen in the emergency department only and not admitted to the hospital. These issues are important to examine in future studies, because they are needed to inform the design of any intervention directed at reducing harmful medication changes.

The results imply that optimizing management of previously prescribed medications has the potential to prevent ADEs associated with transfer of individuals between hospital and nursing home, in both directions of transfer. This study further suggests that clinicians should be alert to the possibility that patients can experience harm from discontinuation of medication use. Although polypharmacy is one of the most frequently cited hazards to older adults26 and there is evidence to suggest that in nursing home residents discontinuation of use of medications that are prescribed without appropriate indication is safe,27,28 other studies have identified harm from withdrawal of medications,9 and the abrupt discontinuation of use of a medication during hospitalization may be more risky than the tapered withdrawal of a medication in the outpatient setting.

Of note, although medication changes implicated in causing ADEs occurred in both directions of transfer and during the hospital stay, in most cases the ADE occurred after the study participant returned to the nursing home. This is in part because the interval from a hospital-based medication change to an ADE was greater than the duration of hospital stay. This result suggests that an intervention implemented at the time of nursing home readmission has the potential to prevent most ADEs. Such an intervention might identify and rectify medication changes that occur during hospitalization that have potential for harm, perhaps using the input of a clinical pharmacist.

In addition, a proportion of ADEs may be prevented by systems-level interventions. Improved transfer documentation or telephone communication at the time of transfer may prevent a proportion of inadvertent medication changes and ADEs. Institutions between which patients are frequently transferred might make efforts to minimize formulary-driven medication changes to reduce the number of medication changes that lack clinical rationale. Finally, Department of Veterans Affairs health facilities have an electronic medical record that is accessible to practitioners in inpatient, outpatient, and long-term care settings. Research is needed to determine if such a shared electronic medical record can improve the accuracy of interinstitutional communication of medication information, prevent errors that occur from handwritten transcribing, and prevent relocation-related ADEs.

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REFERENCES


Announcement

Effective January 2004, Philip Greenland, MD, succeeded James E. Dalen, MD, MPH, as Editor of the ARCHIVES. Editorial correspondence should be sent to the new address: Philip Greenland, MD, Editor, Archives of Internal Medicine, 680 N Lake Shore Dr, Suite 1102, Chicago, IL 60611; phone: 312-503-5387; fax: 312-503-5388; e-mail: archinternmed@jama-archives.org. Manuscript submissions should be sent to Dr Greenland’s attention via e-mail attachment to archinternmed@jama-archives.org.