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Effect Of Therapeutic Interchange On Medication Errors At Hospital Admission And Discharge

Jessica S. Wang
Yale School of Medicine, jessica.wang@yale.edu

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Jessica S. Wang

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Abstract

Since the landmark Institute of Medicine report brought patient safety to the forefront of public concern, there has been intense effort to reduce medication errors in the hospital setting. One such method, medication reconciliation during transitions in care, is now standard practice. While many studies have explored contributory factors and consequences of medication reconciliation errors at hospital admission and hospital discharge, the role of therapeutic interchange, or the substitution of a chemically different but therapeutically equivalent drug for the one originally prescribed, on patients' medication regimens has not been adequately investigated. In fact, no study has examined the extent to which therapeutic interchange is employed in the hospital and the impact it has on unintentional medication reconciliation errors.

We analyzed data from a prospective, observational cohort study of patients 65 years or older admitted to a tertiary care hospital for acute coronary syndrome, heart failure, or pneumonia between May 2009 and April 2010 who were discharged home. We examined patients' medications from six commonly interchanged drug classes (ACE inhibitors, ARBs, H2 blockers, inhaled corticosteroids, PPIs, and statins) and measured the frequency of therapeutic interchange at hospital admission, the rate of suspected errors associated with therapeutic interchange at admission and at discharge, and the role of therapeutic interchange on drug changes at discharge.

We analyzed 555 admission medications taken by 303 patients that were within the six drug classes of interest. Of these, 244 (44.0%) were therapeutically interchanged during hospitalization while the remaining medications were continued or held. We identified 78 (32.0%) therapeutically interchanged medications with suspected errors made at time of interchange. At discharge, a total of 41 (7.4%) of the 555 medications of interest had a suspected medication reconciliation error at discharge. 28 of these were medications that were therapeutically interchanged at admission, giving a relative risk of suspected error of 2.75 (95% CI 1.45-5.19) compared to medications that were not interchanged. 28 of the 244 therapeutically interchanged medications (11.5%), as compared to 8 of the 311 non-therapeutically interchanged drugs (2.6%), were switched at discharge to a different medication within the same drug class as the patient's original home medication (RR 4.46, 95% CI 2.07-9.61).

Therapeutic interchange during hospitalization is a common practice associated with a significant number of potential errors at admission and at discharge, creating a risk for patient misunderstanding and adverse drug events. In light of these findings, methods for safely practicing therapeutic interchange should be developed to improve patient safety.

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Introduction

Transitions in Care

Since the Institute of Medicine's 1999 landmark report, "To Err is Human: Building a Safer Health System" brought patient safety and medical errors to the forefront of public concern, much research has focused on quality improvement in the inpatient and outpatient health care settings (1). Concurrently, patient safety advocates have increasingly identified transitions in care between these settings as an important source of medical error (2). Transitional care has been defined as "a set of actions designed to ensure the coordination and continuity of health care as patients transfer between different locations or different levels of care within the same location" (3). Ideally, transitions occur in a coordinated, transparent fashion based on comprehensive plans of care. However, due to the often urgent and unpredictable nature of care transfers, the medical complexity of patients being transferred, and the necessity of clear, timely, and accurate communication, transitions in care are periods of heightened vulnerability for patients (4). The increasing specialization of physicians as well as the restriction of their practices to specific phases of care (e.g. only hospital-based or ambulatory-based) can further fragment care (4). In fact, in only one such care transition, discharge following hospitalization, nearly half of patients may suffer from a medical error or adverse event (5).

Breakdown in care transitions may occur for many different reasons. These include poor communication of essential information between healthcare professionals, failure to complete follow-up care, too much time between follow-up care, lack of transportation, and incomplete preparation and education of the patient and/or family. One of the most

significant contributors to transitional care-related adverse events is medication errors (3).

Medication Reconciliation

Medication errors are one of the most common types of error affecting patient safety and broadly include any failure in treatment by medications that leads to real or potential harm to the patient (6). Preventable adverse drug events are associated with up to one in five healthcare-related injuries or deaths (7). Significantly, nearly half of these errors occur during transitions in care (8). Medication errors during these transfers are typically due to incomplete or incorrect transmission of information. The process of obtaining an accurate patient medication list and transmitting it to the next phase of care is complicated by the fact that there is often no consistent location for keeping this information, no integration of medication history across settings, and no standardized method for collecting the data (8). As such, medication reconciliation, a formal process of identifying the most accurate, current patient medication list and correcting unintended discrepancies, is a current patient safety focus aimed at reducing medication errors during transitions of care. International organizations such as the World Health Organization and Institute for Healthcare Improvement have widely endorsed medication reconciliation in the past decade, and the accrediting bodies The Joint Commission and Accreditation Canada mandate this process (9). Medication reconciliation is now standard practice during hospital admission and discharge as well as at other points of transfer. For the purposes of this thesis, the discussion of medication reconciliation will center on transitions related to hospital-based care, namely hospital admission and hospital discharge.

Medication reconciliation has been consistently shown to reduce errors and adverse drug events (ADEs). For example, Pronovost and colleagues employed a medication reconciliation tool in the intensive care unit setting of an academic medical center, which required nurses to reconcile prehospital, ICU-admission, and ICU-discharge medications. They found that prior to implementation, 94% of ICU patients had at least one medication error; 24 weeks afterward, none did (7). At another academic center, use of an electronic documentation tool led to a reduction in discharge medication errors from 90% to 47% on a surgical unit and from 57% to 33% on a medical unit (10). Vira and colleagues showed that pharmacist-led reconciliation in a community hospital was able to detect and prevent 75% of clinically important errors (11). One systematic review found that 7 of 8 studies demonstrated statistically significant decreases in potential ADEs or ADEs (12).

However, while nearly all medication reconciliation interventions show reductions in medication discrepancies and adverse drug events, the effect of these studies on health care utilization is less clear. Mueller *et al.* (2012) identified decreases in post-discharge health care utilization in only 2 of 8 studies, and the two that showed improvement required intensive pharmacy participation during and after hospitalization (12). Similarly, in another systematic review, Kwan *et al.* (2013) found that medication reconciliation is unlikely to affect 30-day readmission rates or emergency department visits unless coupled with additional care coordination interventions (9). Thus, while medication reconciliation is able to detect many errors and may avoid ADEs and potential poor outcomes, it may not be sufficient to decrease health care utilization.

Of note, despite the national implementation of medication reconciliation processes around transitions in care, there is no single standardized method of performing medication reconciliation, and many different approaches have been shown to be helpful in improving accuracy. Hospital-based medication reconciliation practices can occur at multiple times and be completed by various healthcare professionals in many formats (12). Medication reconciliation typically occurs at admission and discharge but also may be performed in the emergency department, during hospitalization, and after discharge. Doctors, nurses, pharmacists, technicians, and/or students can perform reconciliation. Information gathering comes from sources such as the patient, caregivers, previous or outside hospital records, outpatient physician records, outpatient pharmacies, and inpatient progress notes and care teams. Many studies have developed paper and electronic tools and protocols to assist in medication documentation, and it is unclear which of these methods is superior (12).

Because of the complex nature of hospital-based medication reconciliation, even effective medication reconciliation practices are prone to errors. The following is a discussion of the types, reasons, and frequency of medication reconciliation errors at hospital admission and hospital discharge.

Medication Reconciliation Errors at Admission

Obtaining an accurate medication history at the time of hospital admission is an integral part of patient assessment. First, a thorough medication reconciliation may uncover the reason for hospitalization, such as an adverse drug event or exacerbation of disease due to nonadherence to drug therapy (13). Furthermore, errors in acquiring the outpatient medication regimen may lead to interrupted or inappropriate drug therapy during

hospitalization and possibly after discharge, which may then cause adverse outcomes (13). Though the importance of performing a comprehensive medication reconciliation at admission is well understood, many barriers exist to obtaining complete and accurate information.

As noted above, transitions in care are often abrupt and unexpected events in which patients and healthcare providers may be unprepared for the change in level of care. One important source of information for gathering medication history is the patient. However, patient knowledge of his/her medications at transitions in care is frequently unreliable and incomplete. In one study, only half of patients presenting to the emergency department were able to give a list of all of their medications, and only 17% brought a written list or their prescription bottles with them. Fewer than one fourth of patients were aware of the dosages of their medications (14). In another study, even among patients asked to keep a written medication list, 56% of patients had information missing (medication, dose, and/or frequency) from the list, and 94% of the lists had at least one discrepancy with clinical medical records (15). Because healthcare providers cannot rely solely on patient accounts of medication use, they must turn to other sources for data gathering and verification.

Other common sources include family and caregivers, primary care providers, outpatient pharmacies, and previous hospital records. Collecting this information is time- and labor-intensive, and even the most thorough review of data cannot guarantee complete accuracy of the patient's outpatient medication regimen. Instead, the goal of medication reconciliation at hospital admission is to obtain the best possible medication history

(BPMH) (16). This BPMH list then becomes the gold standard that is used throughout hospitalization.

The difficulties involved in acquiring the outpatient medication regimen and then translating them into inpatient medication orders commonly leads to medication errors. In fact, errors at admission are among the most common type of hospital-based medication errors, accounting for up to 27% of all inpatient prescribing errors (17-19). In one well-recognized systematic review of studies describing medication reconciliation errors at hospital admission, Tam and colleagues summarized that up to 67% of patients experience at least one medication reconciliation error at admission, with a range of 10-67% (17).

Studies classifying errors made in medication reconciliation at admission consistently show that omission of a home medication is the most common type of error, comprising approximately half of admission errors (13,17-19). Other errors include commission, or the inpatient prescription of a drug that was not being taken prior to admission (13-22% of errors), as well as discrepancies in dose and/or frequency of drug (30-42% of errors) (17).

Consequences of Medication Reconciliation Errors at Admission

Fortunately, while admission medication reconciliation errors are very common, most of these discrepancies have no potential for patient harm. Analyses of the clinical importance of these errors show that between 60-73% of admission discrepancies are unlikely to cause adverse events (13,18,20). Still, the remainder of medication reconciliation errors at admission either does cause harm or has the potential to cause

patient discomfort or clinical deterioration, as judged by the authors of the studies. Examples of potential adverse drug events caused by admission medication reconciliation errors include continuation of an NSAID after gastrointestinal hemorrhage or unintentionally prescribing an increased dose of a sulfonylurea during hospitalization (13,20).

The majority of investigations examining the clinical consequences of medication errors at admission are retrospective chart reviews that look for ADEs or potential ADEs that may occur during hospitalization. The studies almost never investigate events after hospital discharge. Instead, most discussions of post-discharge ADEs or potential ADEs focus on medication reconciliation errors made at discharge (see below). There thus may be utility in studying the effect of admission medication errors on patients after hospital discharge. For instance, Gleason and colleagues found that 22% of admission errors had the potential to cause harm during hospitalization but estimated that 59% of the admission errors could result in a potential ADE if the error was continued beyond discharge (20). Furthermore, in another study examining both admission and discharge medication reconciliation errors, one third of all unintentional medication discrepancies occurred at admission and were carried through discharge, so any potential ADEs associated with these inconsistencies could be attributed to the admission medication reconciliation process rather than at discharge (18). Thus, clarifying between post-discharge clinical consequences that originate upon admission versus at discharge may provide useful outcomes information.

Medication Reconciliation Errors at Discharge

The process of medication reconciliation is also essential at hospital discharge and involves merging the patient's best possible medication history obtained at admission with medication changes that occurred during the hospitalization. Hospitalization can significantly alter a patient's medication regimen. In response to acute illness, physicians may hold or discontinue medications, change dosages and frequency of drugs, or start new formulations. They may also substitute long-acting or oral medications with short-acting or intravenous drugs, respectively. Furthermore, hospital formularies may necessitate the use of drugs different from preadmission medications (therapeutic interchange; see below) (21). Then, at discharge, all of these modifications must be thoughtfully reconciled to create a new outpatient regimen that begins as soon as the patient leaves the hospital. Temporary inpatient medications must be stopped, outpatient medications may be restarted, and formulary substitutions should be switched back to home drugs; the new list should also reflect any additions or modifications made for clinical reasons (21). The many changes that occur between admission and discharge often lead to medication reconciliation errors at discharge. In fact, two studies have shown that half of discharge medication reconciliations contain unexplained discrepancies, involving up to 16% of all medications prescribed (22,23). Another study found a more conservative error rate of 24%, involving 5% of medications examined (24).

As with errors at admission, the most common type of medication reconciliation discrepancy at discharge is omission of a drug, which accounts for 30-45% of errors (11,25). Other contributors to discharge discrepancies include changes to dosage and/or

frequency, duplication of prescriptions, and incomplete prescriptions (11,25). (The continuation of therapeutic interchange has been cited as a potential source of error but has not been explicitly addressed; see below.)

Consequences of Medication Reconciliation Errors at Discharge

Overall, more medication reconciliation errors occur at hospital admission compared to at discharge, but more potential adverse drug events result with discharge. This reflects the differences between hospitalization, which is often brief and highly monitored, and the post-discharge outpatient setting, which has much less healthcare provider oversight so errors may continue for a prolonged period of time (18).

Adverse events related to medications are among the most common undesirable outcomes post-discharge. Adverse drug events may arise from various factors, including patient misunderstanding and inadequate discharge planning, but often can be traced back to medication reconciliation errors. Studies estimate that ADEs occur in 11-31% of patients within 30 days of hospital discharge (22,26-28). Many of these, up to 60%, are preventable or amendable (27,28).

These post-discharge ADEs can cause significant morbidity and potentially mortality. Patients who experience an ADE after discharge not only undergo additional symptoms or disabilities but also often require additional health care visits and laboratory testing (27). Approximately 16% of patients are readmitted to the hospital due to ADEs post-discharge (27).

The Rise of Therapeutic Interchange

The ever-increasing complexity and costs of various pharmacotherapies is a large contributing factor to our nation's continued rise in healthcare expenditures (29). Therapeutic interchange, or the substitution of a chemically different but therapeutically equivalent drug for the one originally prescribed, is a widely used option that theoretically allows healthcare systems to provide a safe yet cost-effective method to control pharmaceutical expenses and pharmacy size without compromising patient care (30). Therapeutic interchange is typically employed in the hospital setting in which there is an established formulary but also may occur in the ambulatory setting when patients are associated with pharmacy benefit programs (31). Hospitals that have implemented therapeutic interchange have reported savings ranging from less than $10,000 to greater than $1 million annually (32). Studies examining the economic effects of therapeutic interchange within individual drug classes in the outpatient environment have also shown the potential for significant cost savings among patients and healthcare systems (30,33-35).

A survey by Schachtner *et al*. that aimed to characterize the prevalence of inpatient therapeutic interchange identified the eleven most frequently interchanged medication classes in 2002: histamine H_2-receptor antagonists, proton pump inhibitors, antacids, quinolones, potassium supplements, first-, second-, and third-generation cephalosporins, hydroxymethylglutaryl CoA (HMG-CoA) reductase inhibitors, insulin, and laxatives/stool softeners (32). Over the past three decades, the percentage of hospitals using therapeutic interchange has increased dramatically from 31% in 1982 to 92% in 2010 (36,37).

Risks and Benefits of Therapeutic Interchange

Because the exchange of one medication for another may affect patient care and outcomes, the use of therapeutic interchange has caused significant debate. Critics of therapeutic interchange have highlighted several concerning factors related to patient care. Interchanged drugs are typically of the same pharmacologic class, but as they are chemically different, they may not be clinically equivalent. Differences in pharmacokinetics and pharmacodynamics such as absorption, therapeutic effect, and side effect profile may lead to a reduction in effectiveness or increase in side effects (31,38). The change in medication also opens the door to prescribing errors that may contribute to adverse drug events (21). Finally, pharmaceutical companies compete with each other and negotiate with hospital systems and pharmacy benefit programs to have their drugs included in these formularies, which can greatly affect prescribing practices (39). While hospitals may achieve cost-savings for their formularies, the medications used may not be cost-effective for patients when they transition to the outpatient setting. Therapeutic interchange may also limit patient choice in both the inpatient and outpatient settings.

In contrast, others argue that therapeutic interchange can be implemented safely while enhancing efficiency. Interchanged medications are similar in effect and mechanism of action, and their differences are often well-studied and well-known (31). Proponents argue that these changes can be made safely as long as physicians are aware of potential unintended consequences (31). A number of studies have shown that switching a medication to one within the same class leads to equivalent outcomes for patients without significant adverse or side effects (30,33,34,40,41). Furthermore, as the number of

available drugs continues to rapidly expand, hospitals utilize therapeutic interchange as a practical means of maintaining an efficient, high-quality formulary.

The debate regarding the relation of therapeutic interchange to patient care outcomes has led to mixed conclusions. Studies of clinical consequences of therapeutic interchange have been limited to the effect of single classes of medication on small numbers of patients rather than the use of therapeutic interchange as a whole. For example, a study looking at a policy change restricting the use of proton pump inhibitors to one preferred drug showed no change in clinical complications or noncompliance (30). Other reports have shown that exchanging statins or angiotensin receptor blockers leads to equivalent clinical outcomes or improvement in lab values without significant adverse events (33,40). In contrast, therapeutic interchange of proton pump inhibitors at another institution correlated with lack of treatment response and increased side effects (42). However, while therapeutic interchange may be controversial, its overall economic benefit will continue to drive its existence.

Role of Therapeutic Interchange in Medication Errors

Despite substantial research on the cost-effectiveness and equivalency of therapeutic interchange, the impact of this practice on patients' medication regimens and medication reconciliation errors has not been fully explored. Upon a patient's admission to a hospital, physicians often continue to prescribe the patient's outpatient medications with modifications as necessary, but hospital formularies frequently necessitate the interchange of home medications for others—formulary medications—that the hospital carries. These additional changes may increase the opportunity for medication errors. During hospitalization, the modifications may increase risk of drug-drug interactions,

side effects, or adverse effects. At discharge, when physicians perform medication reconciliation to determine the patient's new outpatient regimen, either the original or the interchanged drug (or both or neither) may be selected, possibly leading to unintended medication discrepancies (43). From the patient's perspective, the changes may cause confusion, and the patient may ultimately take both or neither medication after discharge. Continuing the interchanged medication upon discharge may allow cost savings for the patient with equivalent or better outcomes, or it may lead to increased prescription costs and serious adverse drug effects.

Medication reconciliation errors made at admission, throughout hospitalization, and at discharge have been well-investigated (18). However, though therapeutic interchange has been implicated as a possible cause of medication reconciliation errors during hospital stays (24), its contributory role has not been explicitly defined. Only one recent study by Glaholt *et al*. (2014) has calculated the frequency at which therapeutic interchange continues after discharge, but these were not further identified as intentional or unintentional modifications. Given the pervasiveness of therapeutic interchange in hospital settings and the many means in which it may negatively affect the patient, further characterization of its effect on medication regimens in hospitalized patients is warranted.

Statement of Purpose

Hypothesis

Therapeutic interchange occurs frequently at the time of hospital admission and contributes to prescriber error during hospitalization. The continuation of therapeutic interchange upon discharge is uncommon, as patients are typically placed back on their prior outpatient medications. However, the switching of medications via therapeutic interchange contributes to medication reconciliation discrepancies at discharge.

Specific Aims

1. To evaluate the frequency and accuracy at which therapeutic interchange occurs at hospital admission within a tertiary level healthcare system

2. To assess the extent to which therapeutic interchange continues at discharge into the outpatient setting

3. To determine whether therapeutic interchange contributes to medication reconciliation errors at discharge

Methods

We conducted a retrospective chart review of data collected from a previous study. The DIagnosing Systemic failures, Complexities and HARm in GEriatric discharges (DISCHARGE) study was a prospective, observational cohort study of patients 65 years or older admitted to Yale-New Haven Hospital for acute coronary syndrome, heart failure, or pneumonia between May 2009 and April 2010 who were subsequently discharged to home. Additional eligibility criteria included speaking English or Spanish, not being in hospice care, and participating in a telephone interview; caregivers could also take part on behalf of patients. Patients were excluded if they appeared delirious or failed a mental status exam. The DISCHARGE study included an examination of medication reconciliation accuracy and patient understanding of medication changes post-discharge (24). The initial study was approved by the Yale Human Investigation Committee.

During the time period of the study, the hospital used a combination of electronic health records (Sunrise Clinical Manager 5.8 (Eclipsys Corporation, Atlanta, GA)) and paper medical charts. The admitting physician recorded the admission medication list, or the medications being taken upon arrival to hospital, in a paper or electronic note. Medications prescribed during hospitalization were documented in handwritten or typed progress notes, medication orders were entered electronically, and medications dispensed were tracked by an electronic medication administration record (MAR). The discharging physician used a prescription writer module to create the discharge medication list, which automatically populated into the discharge instructions given to the patient. Clinicians performed the medication reconciliations; pharmacists did not systematically review the

final discharge list, and there was no active electronic medication reconciliation technology.

In the current study, we examined the therapeutic interchange of six drug classes: proton pump inhibitors (PPIs), histamine H_2-receptor antagonists (H2 blockers), hydroxymethylglutaryl CoA reductase inhibitors (statins), angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), and inhaled corticosteroids (ICS). We selected these drug classes based on their frequency of therapeutic interchange, frequency of use, potential health impact in the event of medication error, and large variances in cost within each drug class. The formulary medications and their appropriate conversion dosages for the study institution during the study period are listed in Table 1.

For the current study, the patient sample includes patients who were taking at least one medication on admission that fell within the six drug classes listed above (referred to henceforth as “medications of interest”). Admission and discharge medication lists were previously abstracted but this work was repeated to check for accuracy; inpatient medication lists were also abstracted. For each patient, we tracked medications of interest from admission to hospital stay to discharge. Using the admission medication list as the gold standard, we identified any therapeutic interchanges, change in dose or frequency, suspension or discontinuation of medication, and addition of new medication that occurred between admission and discharge.

The occurrence of therapeutic interchange was determined by comparing the admission medication list to inpatient lists and the MAR. If a patient was placed on a formulary

medication during hospitalization that was different from the home medication, but of the same drug class, we considered that medication to be therapeutically interchanged. In contrast, a home medication that was held or continued as the same medication throughout hospitalization was not therapeutically interchanged.

Suspected medication errors include any medication discrepancies at admission or discharge that did not appear intentional based on review of the medical record. The scope of this study does not include the characterization of all medication reconciliation errors at admission but rather focuses on suspected errors related to therapeutic interchange. A correct therapeutic interchange requires that the physician accurately converts the home medication—name, dose, and frequency—to the equivalent formulary medication's name, dose, and frequency. Using Table 1, we noted any inconsistencies in the therapeutic interchange as suspected medication conversion errors at admission.

To identify discrepancies in medication reconciliation at discharge, we compared discharge medication lists to their corresponding admission medication lists. Any differences to the medications of interest between admission and discharge that did not appear intentional were classified as suspected medication reconciliation errors at discharge. We then examined whether therapeutic interchange at admission was associated with these suspected errors at discharge.

We further characterized the medications of interest by whether they were changed to a different drug (within the same drug class) or not at discharge and examined whether therapeutic interchange at admission may be associated with these changes at discharge. A drug change at discharge indicates that a patient admitted to the hospital on one

medication was discharged to home on a different drug. A drug change may be intentional, meaning it was clinically indicated or the result of modifications made during hospitalization, or unintentional, meaning there was no apparent clinical indication and thus was a suspected error.

The primary outcomes of this study included the percentage of medications of interest that were therapeutically interchanged at admission and the frequency of suspected conversion errors made during the interchange, as well as the percentage of medications in which drug changes occurred at discharge and the rate of suspected medication reconciliation errors associated with therapeutic interchange.

Table 1: Formulary Conversions for Drug Classes of Interest

Table 1a: Formulary Conversions for ACE Inhibitors

FOR THE FOLLOWING ORDERS								**INTERCHANGE USING**	
benazepril	**enalapril**	**fosinopril**	**moexipril**	**perindopril**	**ramipril**	**trandolapril**	**quinapril**	**captopril**	**lisinopril**
5mg QD	----	5mg QD	3.75mg QD	4mg QD	1.25mg QD	0.5mg QD	5mg QD	25mg QD	**5mg QD**
10mg QD	5mg BID	10mg QD	7.5mg QD	8mg QD 4mg BID	2.5mg QD	1mg QD	10mg QD	25mg BID	**10mg QD**
20mg QD 10mg BID	10mg BID*	20mg QD	15mg QD	----	5 mg QD	2mg QD	20mg QD (HTN) 20mg BID (CHF)	----	**20mg QD (HTN)** **20mg BID (CHF)** ***20mg QD (HTN and CHF)**
40mg QD 20mg BID	20mg BID	40mg QD	30mg QD	----	10mg QD	4mg QD	40mg QD	----	**40mg QD**
80mg QD 40mg BID	----	80mg QD	----	----	20mg QD	----	80mg QD	----	**80mg QD**

QD = daily, BID = twice daily, HTN = hypertension, CHF = congestive heart failure

Table 1b: Formulary Conversions for ARBs

FOR THE FOLLOWING ORDERS					**INTERCHANGE USING**	
candesartan	**eprosartan**	**irbesartan**	**olmesartan**	**telmisartan**	**losartan**	**valsartan**
4mg QD	400mg QD	75mg QD	5mg QD	----	**25mg QD**	**40mg QD**
8mg QD	600mg QD	150mg QD	20mg QD	20mg QD	**50mg QD**	**80mg QD**
16mg QD 32mg QD	800mg QD	300mg QD	40mg QD	40mg QD 80mg QD	**100mg QD**	**160mg QD** **320mg QD**

QD = daily, BID = twice daily

Table 1c: Formulary Conversions for H2 Blockers

	FOR THE FOLLOWING ORDERS			**INTERCHANGE USING**
CRCL (ml/min)	**cimetidine**	**nizatidine**	**ranitidine**	**famotidine**
<50	<30 ml/min: 300mg BID <10ml/min: 300mg QD	150mg QD 150mg QOD	150mg QD	**20mg QD**
>50	300mg Q8H 400mg BID 800mg QD	150mg BID 300mg QD	150mg BID	**20mg BID**

CRCL = creatinine clearance, QD = daily, QOD = every other day, BID = twice daily

Table 1d: Formulary Conversions for ICS

FOR THE FOLLOWING ORDERS		**INTERCHANGE USING**	
budesonide	**fluticasone**	**beclomethasone**	**mometasone**
90mcg 1 puff BID 180mcg 1 puff BID	44mcg 1 puff BID 50mcg 1 puff BID 100mcg 1 puff BID	**40mcg 1 puff BID** **80mcg 1 puff BID**	**220mcg 1 puff QD**
180mcg 2 puffs BID	110mcg 2 puffs BID 220mcg 1 puff BID	**80mcg 2 puffs BID**	**220mcg 1 puff BID**
	110mcg 4 puffs BID 220mcg 2 puffs BID 250mcg 2 puffs BID		**220mcg 2 puffs BID**

QD = daily, BID = twice daily

Table 1e: Formulary Conversions for PPIs

FOR THE FOLLOWING ORDERS					**INTERCHANGE USING**
esomeprazole	**dexlansoprazole**	**lansoprazole**	**omeprazole**	**rabeprazole**	**pantoprazole**
20mg QD 40mg QD	30mg QD 60mg QD	15mg QD 30mg QD	20mg QD 40mg QD	20mg QD	**40mg QD**
40mg BID 60mg QD 60mg BID	----	30mg BID 60mg QD 60mg BID	20mg BID 40mg BID 60mg QD 60mg BID	20mg BID 40mg BID 60mg QD 60mg BID 100mg QD	**40mg BID**

QD = daily, BID = twice daily

Table 1f: Formulary Conversions for Statins

FOR THE FOLLOWING ORDERS			**INTERCHANGE USING***		
fluvastatin	**lovastatin**	**simvastatin**	**atorvastatin**	**rosuvastatin**	**pravastatin**
20mg QD	10mg QD	5mg QD	**----**	**----**	**10mg QD**
40mg QD	20mg QD	10mg QD	**----**	**----**	**20mg QD**
80mg QD	40mg QD	20mg QD	**10mg QD**	**----**	**40mg QD**
----	80mg QD	40mg QD	**20mg QD**	**5mg QD**	**80mg QD**
----	----	80mg QD	**40mg QD**	**10mg QD**	**----**
----	----	----	**80mg QD**	**20mg QD** **40mg QD**	**----**

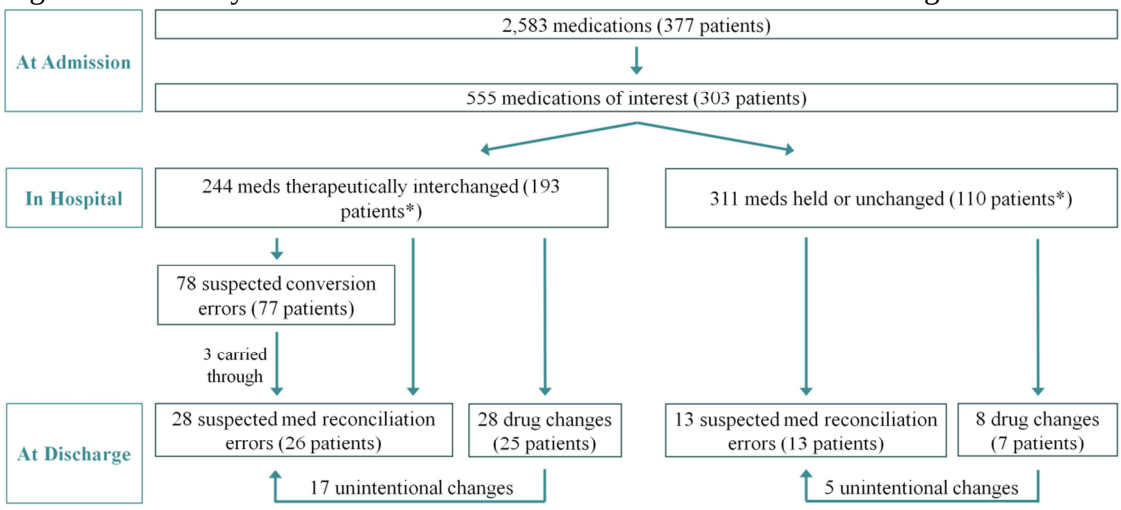
QD = daily. *Pravastatin was on formulary throughout study period (May 2009 – Apr 2010). Atorvastatin was on formulary from May 2009 – Oct 2009. Rosuvastatin was on formulary from Aug 2009 – Apr 2010

Results

Study Sample

A total of 377 patients were enrolled in the DISCHARGE study, collectively taking 2,583 oral medications on admission. Of these, 303 (80.4%) patients were taking 555 (21.5%) medications at admission that fell within the six drug classes of interest and were included in this analysis (see Figure 1). The largest class of medications was statins, which accounted for 41% of the medications of interest. On average, 49% of these admission medications were non-formulary, or not carried by the formulary of the hospital to which they were admitted; rates for individual classes ranged from 20% for ACE inhibitors to 75% for PPIs (see Table 2).

Figure 1: Summary of Medications of Interest from Admission to Discharge



*193 patients had at least 1 medication therapeutically interchanged, 110 patients had no medications therapeutically interchanged

Table 2: Medications of Interest Characterized by Drug Class and Formulary Status

Admission Meds	Non-formulary	Formulary
ACE inhibitor	25 (20%)	97 (80%)
ARB	15 (25%)	44 (75%)
H2 blocker	14 (56%)	11 (44%)
ICS	6 (60%)	4 (40%)
PPI	84 (75%)	28 (25%)
statin	129 (57%)	98 (43%)
Total	**273 (49%)**	**282 (51%)**

Suspected Medication Conversion Errors at Admission

Of the 555 medications, 244 (44.0%) were therapeutically interchanged to an approved formulary drug at admission. This affected 64% (193 of 303) of the study patients who had at least one medication of interest interchanged at admission. The remaining medications which were not therapeutically interchanged were either continued unchanged as the same drug or were held for the duration of the hospital stay (Table 3).

Table 3: Classification of Medication Modifications During Hospitalization

Admission Meds	TI	Unchanged	Held
ACE inhibitor	11%	63%	25%
ARB	19%	54%	27%
H2 blocker	36%	48%	16%
ICS	50%	10%	10%
PPI	53%	23%	24%
statin	64%	30%	5%
Total	**44%**	**40%**	**16%**

TI = therapeutic interchange, unchanged = admission medication given during hospitalization, held = medication not given throughout hospitalization

Among the therapeutically interchanged drugs, we identified 78 (32.0%) suspected medication conversion errors, affecting 77 different patients, which resulted in the patient receiving incorrect treatment in hospital (Fig. 1). Most of the suspected conversion errors involved statins (79.2%). For example, one patient taking simvastatin 40mg daily prior to admission was placed on pravastatin 40mg daily while inpatient instead of the correct

interchange of pravastatin 80mg daily. Of the 78 suspected dose conversion errors made at admission, the same potential error was carried forward to the discharge medication list in 3 (3.8%) instances.

Suspected Medication Reconciliation Errors at Discharge

We identified potential medication reconciliation errors at discharge involving 41 (7.4%) of the 555 medications of interest (Fig 1). 28 of these were medications that had been therapeutically interchanged during admission. This corresponds to a suspected error rate of 11.5% (28 of 244) among therapeutically interchanged medications compared to 4.2% (13 of 311) among unaffected medications; suspected medication reconciliation errors were significantly more likely to occur among medications that had been therapeutically interchanged than those that had not been (RR 2.75, 95% CI 1.45-5.19).

The most common form of suspected medication reconciliation error at discharge involved unindicated changes to medication type, with or without additional errors in dosage or frequency (first two rows in Table 4). Omission of a medication was also frequent; other suspected errors included duplication, inadvertent continuation, or incorrect dosing changes.

Drug Changes at Discharge

36 (6.5%) of the 555 medications of interest were changed at discharge to a different medication within the same drug class as the patient's original admission medication (Fig 1). The regimen change occurred in 28 of the 244 therapeutically interchanged medications (11.5%) as compared to 8 of the 311 non-therapeutically interchanged drugs (2.6%), indicating a statistically significant difference (relative risk (RR) 4.46, 95%

confidence interval (CI) 2.07-9.61). In 39% of total cases, these drug changes appeared intentional as consequences of inpatient management; for example, a patient admitted on esomeprazole was switched to a therapeutically equivalent dose of the formulary drug pantoprazole, but because of GI symptoms, the frequency of pantoprazole administration was increased, and she was discharged on this new regimen. For the majority of drug changes, however, the replacement appeared unintended and was classified not only as a drug change but also as a suspected medication reconciliation error at discharge.

Table 4: Suspected Medication Reconciliation Errors at Discharge Characterized by Type

Type of Suspected Error at Discharge	**TI**	**No TI**
Different medication in same drug class as admission medication prescribed, equivalent in dose/frequency, without clear indication	10	2
Different medication in same drug class as admission medication prescribed, not equivalent in dose/frequency, without clear indication	5	3
Two medications in same drug class prescribed	3	1
Admission medication discontinued without clear indication; no equivalent medication prescribed	6	4
Dose of admission medication incorrect	2	2
Admission medication continued when intended to be stopped	1	0
Admission medication prescribed when intended to change to different medication	1	1
Total	**28**	**13**

TI = therapeutic interchange occurred at admission, No TI = therapeutic interchange did not occur—admission medication unchanged or held during hospitalization

Discussion

Our study found that, within six commonly used drug classes, close to half of medications were therapeutically interchanged at admission, and errors occurred in one-third of these conversions. Furthermore, therapeutic interchange led to 2.75 times more suspected medication reconciliation errors and 4.5 times as many changes in drug type at discharge. Together, these results indicate that therapeutic interchange is a common process that affects patients' medication regimens from admission to beyond discharge, and suggest that therapeutic interchange may be a key contributor to medication reconciliation errors.

This study was limited to six classes of medications; however, of all eligible patients included in the original DISCHARGE study, 80.4% of patients were taking at least one medication in these six classes, making our study highly generalizable. 64% of included patients experienced at least one therapeutic interchange during hospitalization, suggesting the importance of thorough evaluation of the effects that therapeutic interchange has on medication regimens and errors.

Previous studies characterizing medication errors made at time of hospital admission do not include errors related to therapeutic interchange. Typically, such investigations focus on discrepancies made between the admission medication list and patients' actual outpatient regimen when constructing the best possible medication history, but do not explore therapeutic interchange as the next step of the transition process. Thus, the discovery of a 32% suspected error rate in the implementation of therapeutic interchange

is a novel finding. Given the high rate of the possible interchange errors, more attention should be placed on addressing this aspect of patient care around the time of admission.

These suspected conversion errors suggest that therapeutic equivalence was not achieved during hospitalization. This creates an opportunity for adverse drug events and complications in inpatient care to arise. Potential adverse events may be exacerbated by the fact that patients are likely to be unaware of the changes in medication and do not have the means to verify their inpatient regimen for dosing accuracy, as illustrated in a study which found that 36% of patients subject to PPI therapeutic interchange during hospitalization were unaware that a substitution had occurred (44). Prior studies demonstrate that 27-40% of admission medication discrepancies have the potential to cause harm during hospitalization, and as they do not include the role of therapeutic interchange, the potential for harm may be significantly higher (13,18,19).

Suspected conversion errors at admission may also have potential for harm beyond hospitalization if they are not remedied at discharge. In this study, 3 of the 78 (3.8%) suspected conversion errors were continued at discharge such that the patient may have continued the incorrect therapeutic interchange at home. This occurred far less frequently than the one-third of admission discrepancies observed by Pippins and colleagues, although that included all unintentional medication discrepancies rather than only ones related to therapeutic interchange (18).

At the time of discharge, suspected medication reconciliation errors were identified in 7.4% of medications analyzed, affecting 12.5% of the patients involved. This rate is comparable to other studies, although this study was far reaching than most by including

errors of omission, duplication, changes in dosage and frequency, inadvertent continuations and therapeutic interchange (24). Again, while other types of medication errors at discharge have been previously described, discrepancies related to therapeutic interchange have thus far not been specifically examined. Suspected errors were almost three times more likely to occur in medications that were interchanged during hospitalization; many of these suspected errors involved medications that were not reverted back to the home regimen, and were likely a direct consequence of therapeutic interchange. The potential for error after discharge is high, as patients may take the incorrect dosage of a medication, take two medications of the same class, or discontinue an essential treatment.

Furthermore, we found that in 6.5% of cases, a patient's admission medication changed to a different drug of the same class at discharge. Such changes in medication regimen, whether clinically indicated or not, affected 13% of patients who underwent at least one therapeutic interchange. This coincides with the 2014 findings of Glaholt *et al.* who observed that 15% of adult patients admitted to an academic medical center who experienced therapeutic interchange were not restarted on their original outpatient therapy. Medication switches were significantly more likely to occur to medications that were changed for formulary reasons than for medications that were unchanged or held during hospitalization.

Minimizing changes to drug regimens, especially in vulnerable populations such as the elderly in this study, is important in avoiding patient misunderstanding and potential adverse drug effects. Alterations are problematic because patients may have a previous home supply available but be required to obtain a new prescription for a therapeutically

equivalent drug following discharge. Subsequent confusion may increase the likelihood of medication duplication or omission, possibly putting the patient at risk for drug-drug interactions, side effects, and adverse reactions. For these reasons, physicians should make changes from one medication to another carefully and only when indicated, and be aware of potential unintentional consequences.

Our study shows that therapeutic interchange is a common practice that likely contributes to medication errors at admission and discharge. Given this, healthcare providers must give appropriate attention to therapeutic interchange during all aspects of hospitalization, and physicians must be careful when making medication modifications due to formulary restrictions rather than clinical indication. Aside from provider awareness, we may be able to reduce errors related to therapeutic interchange by instituting systems-level changes to hospitals. For example, just as standardized protocols can improve medication reconciliation, the use of formalized tools likely can make therapeutic interchange safer. Medication reconciliation protocols should indicate which medications undergo therapeutic interchange at admission and include a means of ensuring that this interchange is reversed at discharge. Formulary conversion charts such as Table 1 should be readily accessible to promote accurate changes. Another potential method of improvement is to include pharmacists in the medication reconciliation process. In comparison to physicians and other providers, pharmacists are especially suited to this responsibility because of their training, but they also are extremely familiar with their hospital's formulary, which may specifically reduce therapeutic interchange errors (17,20,45). The use of an active electronic medication reconciliation system that can flag therapeutic interchanges may also aid providers (46). Finally, further studies of the use of

therapeutic interchange, reasons for associated errors, and potential adverse events during and after hospitalization should be performed to better elucidate the impact of therapeutic interchange on patient care.

Limitations

There are several limitations to this study. First, as a retrospective chart review, the admission medication list documented in the patient charts was treated as the gold standard although, as discussed above, numerous studies have shown high rates of medication reconciliation errors at admission. Furthermore, we could not verify intentional changes or suspected errors to regimens at admission or discharge with the patients' actual providers. Third, the study is limited to patients from a single tertiary level hospital in an urban area and may not be generalizable to practices at other hospitals. Limiting the investigation to six drug classes rather than all medications may affect rates of therapeutic interchange and suspected errors.

Conclusion

Therapeutic interchange is highly prevalent in the hospital setting but markedly elevates the risk for potential medication errors during and after hospitalization. The benefits of therapeutic interchange should be carefully weighed against the potential for increased errors and adverse events.

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