Drug Therapy Problems Identified by Pharmacists Through Comprehensive Medication Management Following Hospital Discharge

Journal of Pharmacy Technology
2017, Vol. 33(3) 96–107
© The Author(s) 2017
Reprints and permissions:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/8755122517698975
journals.sagepub.com/home/pmt

Sarah M. Westberg, PharmD¹, Sarah K. Derr, PharmD²,
Eric D. Weinhandl, PhD, MS¹, Terrence J. Adam, BSPharm, PhD, MD¹,
Amanda R. Brummel, PharmD³, Joseph Lahti, PharmD³,
Shannon L. Reidt, PharmD, MPH¹, Brian T. Sick, MD¹,
Kyle F. Skiermont, PharmD², and Wendy L. St. Peter, PharmD¹

Abstract

Background: Pharmacists influence health care outcomes through the identification and resolution of drug therapy problems (DTPs). **Objective:** The objectives of this study were to describe number, type, and severity of DTPs based on clinical significance and likelihood of harm in patients transitioning from hospital to home as assessed during a comprehensive medication management (CMM) visit with a pharmacist. Secondary objectives were to assess intrarater reliability in severity ratings and assess likelihood of harm for adverse drug reactions (ADR) by drug classes. **Methods:** Retrospective review of 408 patients having a face-to-face, telephonic, or virtual CMM visit within the Fairview Health System. Teams of 3 investigators reviewed each DTP from the electronic medical record for each of the 408 patients and assigned a severity score (0-10) for clinical significance and likelihood of harm. **Main Results:** The highest severity DTP classes were adherence and ADR. The lowest severity DTP class was unnecessary drug therapy. An average of 2.5 DTPs was found per patient at the index CMM visit following hospital discharge. The most common DTP classes were needs additional therapy and dose too low. There were statistically significant differences in DTP severity scoring between reviewer types, though differences were <5%. Drug classes with the highest severity ADR included diabetes, cardiovascular, and anticoagulant/antiplatelet agents. **Conclusions:** The DTP severity ratings indicated that reviewers found ADR and adherence DTPs were potentially the most severe. There were differences in DTP ratings between reviewer types, though clinical significance of these differences is unclear.

Keywords

drug-related problem, medication therapy management, drug safety, adverse drug reactions, pharmaceutical care

Introduction

Pharmacists' impact on patient health care outcomes is based on the ability to identify and resolve drug therapy problems (DTPs), a skill for which pharmacists are specifically trained.¹⁻³ DTPs are defined as any undesirable event experienced by a patient involving drug therapy and potentially interfering with the patient reaching his or her drug-related goals of therapy.⁴ Approximately 20% of patients experience a DTP after discharge from the hospital.⁵ DTPs are typically classified based on the cause of the problem and not on the clinical impact of the problem.^{4,6-8} However, the precise classification of DTPs varies across practices and research studies.^{7,9} Several researchers have worked to develop an aggregated system of DTP classification to assist in the ability to compare and aggregate data.⁶⁻⁸ Despite

this work, DTPs are not typically classified with a severity score. Previous studies have evaluated predictors for total number of DTPs,^{10,11} with one considering the severity of the DTPs as low, moderate, or severe.¹⁰ Quintana-Bárcena developed a validated process to rate severity of DTPs in chronic kidney disease patients in community pharmacies based on interventions required to manage DTPs, but is not

¹University of Minnesota, Minneapolis, MN, USA

²Iowa Pharmacy Association, Urbandale, IA, USA

³Fairview Pharmacy Services, Minneapolis, MN, USA

Corresponding Author:

Sarah M. Westberg, University of Minnesota College of Pharmacy, 308 Harvard St SE, 7-178 Weaver-Densford Hall, Minneapolis, MN 55455, USA.

Email: swestber@umn.edu

generalizable due to limitations of contextual design and population.¹² Dean and Barber created a validated tool to assess severity of medication errors using a 1 to 10 scale, as assessed by various health care professionals, but it is not clear if this can be applied more broadly to DTP severity.¹³

The primary objective of this study was to describe the number, classification, and severity of DTPs in patients transitioning from hospital to home. Secondary objectives included assessment of intrarater reliability between investigator severity ratings and assessment of the likelihood of harm for adverse drug reactions by drug classes.

Methods

Study Design and Data Source

This is a retrospective observational study that utilized an electronic medical record (EMR) to assess DTPs and DTP severity. Investigators created and evaluated a tool for rating clinical significance and likelihood of harm for DTPs in patients. Investigators utilized the Fairview Health Services (FHS) EMR, EPIC (Epic 2014 IU1), to review hospital discharge notes and comprehensive medication management (CMM) notes to evaluate DTPs.

Setting

Fairview Health Services is a not-for-profit, large integrated health care system located in Minnesota. FHS includes 7 hospitals, 55 specialty clinics, and 44 primary care clinics.

This study only included patients admitted to 3 of the hospitals: University of Minnesota Medical Center (UMMC), Fairview Ridges Hospital (FRH), and Fairview Southdale Hospital (FSH). Within the clinics, FHS has 24 pharmacists providing CMM. CMM is “the standard of care that ensures each patient’s medications are individually assessed.”¹ The CMM practice model is completed through an assessment of indication, efficacy, safety, and adherence of each medication for the patient. The CMM pharmacist gathers information from the medical record and through the patient (or through a caregiver if requested by patient) interview to complete this assessment. This includes creation of an individual care plan and follow-up to evaluate outcomes.¹ Visits can be completed face-to-face, via phone call, or through secure video conferencing (referred to as “virtual” visits). The CMM practice model care process remains the same, regardless of the method for communication with the patient. To be included in this study, patients could have had an encounter with any of the CMM pharmacists in the system. All of the pharmacists are credentialed and privileged by the Fairview Health system. Medication therapy management pharmacists’ responsibilities include the following: (a) focus on the “whole” patient (ie, the pharmacist assesses all of the patient’s diseases and medications); (b) identification

of a patient’s drug-related needs; (c) promotion of appropriate indications, safety, and adherence for all drug therapies by identification, resolution, and prevention of drug-related problems; (d) achievement and documentation of therapy outcomes; and (e) collaboration with all members of a patient’s care team. Some sites do include pharmacy students and/or residents at their sites, but all learner visits are closely precepted and approved by the credentialed CMM pharmacist.

In order to improve patient outcomes and reduce readmission rates, Fairview created a process in 2012 to identify patients who may benefit from CMM after hospital discharge. These criteria and processes have evolved based on literature and clinical experience. Initially, patients at a moderate or high risk (based on internal risk scoring including multiple patient-specific factors) were all referred for CMM follow-up from FSH and FRH. After several months, additional criteria were implemented: patients had to be moderate to high risk based on internal scoring plus newly diagnosed diabetes, heart failure, chronic obstructive pulmonary disease (COPD), acute myocardial infarction (MI), ≥ 2 chronic medication changes during the transition, or nonadherent to medication regimen. When UMMC began referrals, they used slightly different criteria: diagnosis of heart failure, COPD, MI on ≥ 5 chronic medications; outpatient medication list containing rifaximin, lactulose, or oral chemotherapy; hospitalization or emergency department visit within the last 6 months on ≥ 10 chronic medications; or documented medication nonadherence. Patients are identified through these criteria in a best practice alert, triggered within the EMR, for inpatient pharmacists and care coordinators at UMMC to refer to a CMM pharmacist postdischarge. At FRH and FSH, the care coordination team refers patients to CMM directly.

Patient Population

Patients with a first-ever, face-to-face, telephonic, or virtual CMM visit in the FHS network between February 1, 2013, and July 31, 2015, and within 30 days of hospital discharge, were eligible for this study. Inclusion criteria were the following: ages 18 to 90 years; hospitalized at UMMC, FSH, or FRH; and established primary care within FHS network (defined as at least 2 primary care clinic visits during the 2 years before the index hospital admission). Exclusion criteria were the following: discharged to hospice or seen by palliative care during admission, discharged against medical advice, discharged or transferred to a post-acute facility, or neoplasm or pregnancy as primary discharge diagnosis. From these patients, we selected a stratified random sample of 400 patients, with strata defined by discharging hospitals and sampling fractions intended to maintain the same distribution of hospitals as in the entire study population. Nonsampled patients were

Figure 1. Flowchart of inclusion and exclusion criteria defining the study cohort. A *clinical consultation* is an encounter with a CMM pharmacist for a limited purpose (typically, for patient education only); such encounters are not comprehensive visits and therefore were excluded from this study. Each *qualifying hospital discharge* met 3 criteria: (1) admission that was either urgent or emergent; (2) discharge to home or home health agency; and (3) principal discharge diagnosis for condition other than neoplasm or pregnancy.

placed on a “wait-list.” Wait-list patients were chosen to replace patients that were found to have exclusions after visual inspection of the EMR by reviewers via stratified sampling to match the distribution of the 3 discharging hospitals (see Figure 1).

DTP Number and Type

Pharmacy practitioners at FHS enter the number of DTPs in the EMR for each CMM encounter. The templated form allows for a maximum of 8 DTPs per encounter, though additional DTPs can be added through a secondary process

if needed. DTP classifications are tracked in the EMR utilizing standard categories (see Appendix A).⁴

Data Collection Tool

Research Electronic Data Capture (REDCap), a secure, HIPAA compliant database, was utilized to create a standardized data form for reviewers. An online survey tool was built and reviewed by investigators. The REDCap form provided information on study patients to the investigators in order to utilize the EMR to review patient information, and rate DTPs according to clinical significance and likelihood

of harm on a continuous scale from 0 to 10, with 10 representing the highest severity.

EMR Review Process

Clinician investigators, or “reviewers,” accessed the EMR and evaluated the discharge note from the index admission and the CMM note. Reviewers were instructed not to access any other data, in order to maintain consistency in the reviews. Specific information was collected and moved into REDCap for each patient with technology support (subject identifiers, name of reviewer, date of discharge, hospital discharged from, hospital discharge diagnosis, CMM date of service, and number of DTPs). For each DTP, the associated medication and DTP primary and secondary classification assigned by the CMM pharmacists during the encounter were included (Appendix A). Reviewers included 2 physicians, 2 CMM pharmacists, and 2 CMM resident pharmacists. The 400 patients were divided into eight 50-patient groups through block randomization by hospital, allocated by simple randomization within the block. Each group was reviewed by 3 reviewers, comprising a physician (one trained in internal medicine, and one in internal medicine/pediatrics), CMM pharmacist (ambulatory care residency trained pharmacists; one was from the study clinics and one was not), and CMM resident pharmacist (PGY1 pharmacy residents with emphasis in ambulatory in the health system studied). The 2 physicians and 2 pharmacists had 10 or more years of patient care experience post-licensure. Reviewers were trained on the appropriate use of the collection form and rating processes, including case examples to illustrate varying levels of severity ratings. Reviewers ranked each DTP with 2 separate scores ranging from 0 to 10, one for clinical significance and the other for likelihood of harm (see section “Definition and Assessment of Drug Therapy Problem Severity”) based on adaption of a validated scoring system devised by Dean and Barber for assessing severity of medication errors.¹³

Definition and Assessment of Drug Therapy Problem Severity

Clinical significance was defined in this study as the potential positive effect on patient’s health in 1 year if the DTP were resolved. This included the practical importance of a treatment effect (whether it would have a genuine, palpable, noticeable effect on daily life or prevents a poor health outcome). The likelihood of harm was defined as the potential negative health impact in 30 days if the DTP were unresolved. Both clinical significance and likelihood of harm were rated on a continuous 0 to 10 scale by reviewers, with 10 representing the highest severity and 0 representing very low severity.

Data Analysis

Once all reviewer scores were entered, each DTP score was evaluated for variation in reviewer ratings. Distance was assessed for each rating by plotting the rating of each of the 3 reviewers on a grid. If the 3 scores were more than a radius distance of 2.5 apart, the DTP was designated as an outlier and the 3 reviewers had a discussion to reach a consensus decision for each score (Appendix B). Reviewers also manually verified if patients met inclusion and exclusion criteria. Patients found to have exclusion criteria by reviewer consensus were excluded following the chart review process. Excluded patients were replaced from a wait-list, and these patients were reviewed following the same process. After completion, the total number of DTPs and DTP classifications were aggregated. In subanalysis, we calculated the mean and standard deviation of likelihood of harm scores, stratified by drug class for DTPs that were classified as an adverse drug reaction as most research in drug safety area focused on severity has revolved around adverse drug reactions or medication errors.

The mean and standard deviation of clinical significance and likelihood of harm scores were determined for each reviewer type. Box plots were constructed to describe score variability among reviewers. Intraclass correlation (ICC) was used to measure reviewer agreement for DTP ratings, with an ICC of near 50% representing moderate agreement. ICC was estimated by a mixed model, with a random intercept for each DTP. We used similarly structured mixed models, but with a fixed effect for reviewer type, to identify whether DTP scores were significantly different among physician, pharmacist, and resident pharmacist reviewers.

This study was approved by the University of Minnesota Institutional Review Board Code Number: 1509M77743. All analysis was conducted in SAS, version 9.4 (Cary, North Carolina).

Results

Patient Population

There were a total of 12 938 patients who received at least one CMM service at FHS from 2013 to 2015. After inclusion and exclusion criteria, there were 581 qualifying patients with postdischarge CMM encounters (Figure 1), with 217 (37%), 257 (44%), and 107 (18%) patients at FRH, FSH, and UMMC, respectively. The first sample included 400 patients; during EMR review, 25 patients were excluded for not meeting criteria. Thirty-four patients were subsequently sampled from the wait-list and one such patient was excluded during EMR review. The final analytical cohort comprised 408 patients.

Table 1. Mean, Standard Deviation, and Range of Clinical Significance and Likelihood of Harm Scores, by Drug Therapy Problem (DTP) Class^a.

Drug Therapy Problem Class ^b	N	Clinical Significance		Likelihood of Harm	
		Mean (SD)	Range	Mean (SD)	Range
Needs additional therapy	193	3.3 (1.4)	1.0-7.8	1.6 (1.3)	0.1-8.0
Unnecessary drug therapy	121	2.4* (1.0)	0.9-5.1	1.1* (0.6)	0.3-3.5
Different drug needed	54	3.3 (1.3)	1.0-8.5	1.7 (1.3)	0.2-8.0
Dose too low	204	3.1 (1.4)	0.8-7.0	1.6 (1.2)	0.2-8.0
Adverse drug reaction	141	3.5* (1.4)	1.0-9.0	1.9* (1.3)	0.3-8.0
Dose too high	131	3.3 (1.3)	1.2-7.3	1.7 (1.2)	0.3-5.8
Adherence	147	3.6* (1.4)	0.1-8.3	2.0* (1.4)	0.1-8.4

^aThis includes DTPs assigned 1 DTP classification, which was 991 of the 1033 total DTPs. This excluded DTPs coded incorrectly with 0 or 2 DTP classifications.

^bDrug therapy problem classification based on established Pharmaceutical Care Practice definitions (Cipolle Strand text).

* $P < .05$ for test of difference between drug therapy problem class mean and overall mean, by gamma regression.

Of the 408 patients, 282 CMM encounters were completed via telephone, 120 through face-to-face office visits, and 5 through virtual visits.

Mean patient age was 67.7 ± 13.8 years and white race was predominant (89.0%). Male and female sexes were balanced (49% male and 51% female). Most common comorbid conditions were hypertension (79%), diabetes (42%), cardiac arrhythmias (36%), chronic kidney disease (36%), and COPD (35%). More than half of patients had at least one hospital admission in the preceding 2 years. Appendix C displays additional patient characteristics.

Drug Therapy Problems

At least 1 DTP was identified in 365 (89.5%) patients. Cumulatively, there were 1033 DTPs, of which 1017 were evaluated by all 3 reviewers; 16 DTPs were only graded by only 2 reviewers, due to one reviewer having a conflict of interest (the reviewer had seen the patient at the CMM index visit). The mean number of DTPs per patient was 2.5 (standard deviation = 1.8).

Types of Drug Therapy Problems

The most common DTP classes in our cohort were “dose too low” and “needs additional therapy” (Table 1). The least common DTP class was “different drug needed.”

DTP clinical significance and likelihood of harm scores ranged from 0.1 to 9.0 and from 0.1 to 8.4, respectively; distributions of both scores were positively skewed. Mean DTP severity scores for each DTP class are displayed in Table 1. Mean scores for clinical significance ranged from 2.4 to 3.6 and for likelihood of harm from 1.1 to 2.0. Reviewers assigned the highest scores for both clinical significance and likelihood of harm to DTP problem class of “adherence” and

“adverse drug reaction” ($P < .05$). Reviewers assigned the lowest scores to DTP problem class “unnecessary drug therapy” ($P < .05$).

A few example case vignettes are included here for further description. A patient hospitalized with severe COPD was not adherent to tiotropium inhaler after discharge, because she did not understand the instructions; this DTP was assigned a likelihood of harm score of 8.4/10. Another example is a patient who was hospitalized for hypotension and was taking both terazosin and tamsulosin after discharge, a combination that could lead to hypotension (likelihood of harm score 7/10). In contrast, the DTP in a patient hospitalized for dyspnea who requested additional education on why glimepiride is dosed once daily was assigned a low likelihood of harm of 1/10.

Interrater Reliability in Scores

Box plots of clinical significance and likelihood of harm scores, stratified by reviewer, are displayed in Figure 2. Among 1017 DTPs with severity scoring by 3 reviewers, there were 945 (92.9%) DTPs with adequate agreement among reviewers after initial review and 72 outliers (7.1%). The ICC of clinical significance scores in DTPs was 47.2%, whereas the ICC of likelihood of harm scores in DTPs was 51.5%. This represents moderate agreement between reviewers. Scores varied by reviewer type (Appendix D). Relative to CMM resident pharmacists, the mean clinical significance score by CMM pharmacists was 0.2 points lower ($P < .001$) and the mean score by physicians was 0.4 points lower ($P < .001$). Regarding likelihood of harm and likewise relative to CMM resident pharmacists, the mean score by CMM pharmacists was 0.3 points lower ($P < .001$), but the mean score by physicians was 0.2 points higher ($P < .001$).

Figure 2. Box plots of clinical significance (A) and likelihood of harm (B) scores, by reviewer. Reviewers 1A and 1B were CMM resident pharmacists, reviewers 2A and 2B were CMM pharmacists, and reviewers 3A and 3B were physicians. Each plot displays the median (bold line); the first and third quartiles (box edges); the greater of the minimum or the first quartile minus 1.5 times the interquartile range (bottom whisker); the lesser of the maximum or the third quartile plus 1.5 times the interquartile range (top whisker); and outliers (open dots).

Table 2. Occurrence of Classes and Mean Likelihood of Harm Score, in Drug Therapy Problems Classified as Adverse Drug Reactions.

Class	N	Mean
Analgesics	40	1.7
Nonsteroidal anti-inflammatory analgesics	24	1.7
Acetaminophen	13	1.6
Opioid analgesics	3	1.5
Psychotropic agents and hypnotics	32	1.5
Cardiovascular agents	29	2.4
Other agents	19	1.9
Antihistamines and cold/cough/allergy agents	15	1.8
Hematopoietic, anticoagulant, and antiplatelet agents	14	2.4
Gastrointestinal and genitourinary agents	12	1.9
Alternative medicinal agents	12	1.5
Antidiabetic agents	9	3.7
Vitamins, minerals, and nutrients	8	1.2
Anticonvulsants and muscle relaxants	6	1.4

Adverse Drug Reactions

Among DTPs classified as “adverse drug reaction,” analgesics were the most commonly cited class ($n = 40$), with a mean likelihood of harm score of 1.7 (Table 2). There were 24 DTPs related to nonsteroidal anti-inflammatory drugs,

13 related to acetaminophen, and 3 related to opioids; the mean likelihood of harm score were similar in each subgroup. Antidiabetic agents were associated with the highest mean likelihood of harm score (3.7), although the total number of DTPs was low ($n = 9$). Cardiovascular agents were associated with a higher mean likelihood of harm score (2.4) and high count ($n = 29$). Anticoagulants and antiplatelet agents were also associated with a higher mean likelihood of harm score (2.4); however, there were only 7 DTPs.

Discussion

We created and assessed a DTP rating scale using a patient population transitioning from hospital to home. We found that DTPs related to adverse effects and adherence had the highest potential of clinical significance and likelihood of harm. There were differences in DTP ratings between reviewer types, though the clinical significance of these differences is unclear.

In this study, patients who were discharged from the hospital and seen for CMM services within 30 days after discharge had an average of 2.5 DTPs. This number is similar to the average number of DTPs per patient found in other studies, with variability based on population studied.¹⁴⁻¹⁶ As other studies have shown, DTPs are often unresolved after a hospitalization, or new DTPs develop after discharge.¹⁷⁻²⁰

It is important for clinicians and researchers to better understand common types of DTPs found during transitions of care.

Consistent with other large evaluations of CMM practices, we found that common DTP classes included “needs additional therapy” and “dose too low.”^{6,14,15} In terms of severity (both clinical significance and likelihood of harm), the highest average rated DTP classes included “adherence” and “adverse drug reactions” and the lowest rated DTP class was “unnecessary drug therapy.” Challenges related to adherence, such as being able to access a medication and understand instructions, would not be evident until a patient becomes responsible for his or her own medication administration at home. Many adverse drug reactions may not appear immediately during a hospitalization or may not be a concern until the patient returns to his/her home environment. Therefore, the most severe DTPs were those that may not be apparent at discharge, but rather in the days following.

We found a significant difference between ratings between reviewer types. After outlier exclusion, both CMM resident pharmacists and physicians showed statistically significant differences in ratings when compared with CMM pharmacists for both clinical significance and likelihood of harm ratings. The subjective nature of rating clinical significance or likelihood of harm allowed past experiences and clinical knowledge to affect the scores each reviewer assigned to the DTPs. CMM resident pharmacists have up-to-date knowledge on clinical guidelines and DTPs; however, they have limited longitudinal patient care experience. Past clinical experience may have influenced higher average rating likelihood of harm seen in physician rankings and the lower average for clinical significance. We found smaller differences between reviewer scores after the first block of 50 patients (data not provided) indicating that practice with the scoring rubric may be helpful.

Although a statistically significant difference was shown between the mean score for clinical significance and likelihood of harm across reviewer types, the absolute differences in mean scores ranged from 0.2 to 0.4 out of 10 points. In a previous study using a 3-point categorical severity rating, there was unanimous agreement among external reviewers for the severity rating.¹⁰ By using a continuous scale for severity, the likelihood of discrepancy between reviewers is higher than if a categorical scale was used. The severity scale established in this study is a prelude to future research to study the associations between patient characteristics, conditions, and DTP type associated with highest severity risk. The small absolute difference in mean scores between reviewer types (<5%) is unlikely to affect the utility of the severity score in patient care decision making and research.

Many studies and initiatives in medication safety related to transitions of care have focused on high-risk drug classes, specifically opioids, hypoglycemics, and anticoagulants/antiplatelets.²¹⁻²⁴ We specifically looked at the rates of the DTP classification of adverse drug reactions by drug class. In this study, a high likelihood of harm was found with adverse drug reactions from antidiabetic agents, anticoagulants/antiplatelets, and cardiovascular agents. Only 3 adverse drug reactions from opioids were found, with a lower likelihood of harm score. In interpreting these data, it is important to note that classification of DTPs through the CMM practice model is done following an assessment of indication, efficacy, safety, and adherence of each medication.¹ Assessment occurs in that order; therefore, if a DTP is discovered and classified as not indicated or ineffective, there would not be a duplicate DTP under safety as an adverse drug reaction. These data help validate the importance of evaluating high-risk medications such as hypoglycemics and anticoagulants/antiplatelets, as the likelihood of harm from an adverse drug reaction with these classes was rated highly in this study. The lower number of adverse drug reaction DTPs from opioids and the higher likelihood of harm scores from cardiovascular drugs may be specific to this population.

Strengths of this study include a large patient population with diversity in health status using a well-established CMM program within FHS. There was a consistent, trained, interprofessional team for all chart reviews and DTP scoring, using consistent information during reviews.

Limitations of this study include the subjective nature of the DTP severity rating process. There was limited examples and time for reviewers to practice reviewing charts and ranking DTPs prior to starting study reviews. The templated DTP reporting form for the CMM pharmacist is built for 8 DTPs; it is possible that there could have been underreporting of DTPs due to this limitation in documentation.

Conclusions

Our study found the average number of DTPs in patients seen for CMM after hospital discharge was 2.5. DTPs with the highest severity ratings (both clinical significance and likelihood of harm) postdischarge being “adherence” and “adverse drug reactions.” Adverse drug reactions from antidiabetic agents, anticoagulants/antiplatelets, and cardiovascular agents were associated with a high likelihood of harm in this study. There was a statistically significant, but low absolute mean difference between ratings of physicians, CMM pharmacists, and CMM resident pharmacists in the DTP severity assessment. In the future, this DTP severity rating scale can be used to investigate patient factors associated with DTP severity and determine if these risk factors are associated with future hospitalizations and emergency visits.

Appendix A

Drug Therapy Problem Classification.

Primary Drug Therapy Problem Classification

Needs additional therapy

Unnecessary drug therapy

Different drug needed

Dose too low

Adverse drug reaction

Dose too high

Adherence

Secondary Drug Therapy Problem Classification

Preventative therapy
 Untreated condition
 Synergistic therapy
 Monitoring for screening needed
 Duplicate therapy
 No medical indication
 Nondrug therapy more appropriate
 Addiction/recreational drug use
 Treating avoidable adverse reaction
 More cost-effective drug available
 More effective drug available
 Condition refractory to drug
 Dosage form inappropriate
 Dose too low
 Monitoring needed to determine if dose is appropriate
 Duration or frequency inappropriate
 Incorrect administration
 Drug interaction
 Unsafe drug for patient
 Allergic reaction
 Contraindication present
 Incorrect administration
 Clinically relevant drug interaction
 Undesirable effect
 Dose too high
 Duration or frequency inappropriate
 Drug interaction
 Monitoring needed to determine safety
 Drug product not available
 Cannot afford drug product
 Cannot administer drug
 Does not understand instructions
 Patient prefers not to take
 Patient forgets to take
 Drug expired

Appendix B

Example of DTP severity scoring agreement

Examples of the DTP severity score distribution among 3 reviewers, including an example of reviewers with severity scores in adequate agreement (panel A) and an example of reviewers with severity scores that required additional discussion to reach consensus (panel B). Adequate agreement was defined by distance between each reviewer score and the mean score less than 2.5 units.

Appendix C

Patient Characteristics.

Characteristic	N or Statistic	Percentage
Age (years)		
Mean (standard deviation)	67.7 (13.8)	
Race		
White	363	89.0
Black	24	5.9
Other	21	5.2
Sex		
Female	210	51.5
Male	198	48.5
Payers ^a		
Medicare	236	57.8
Medicaid	34	8.3
Managed care organization	202	49.5
Indemnity insurer	162	39.7
Other payer	27	6.6
Comorbid conditions		
Cardiovascular disease and related conditions		
Hypertension	323	79.2
Cardiac arrhythmias	147	36.0
Congestive heart failure	93	22.8
Valvular disease	82	20.1
Peripheral vascular disorders	74	18.1
Pulmonary circulation disorders	42	10.3
Other conditions		
Diabetes	171	41.9
Chronic kidney disease	145	35.5
Chronic pulmonary disease	142	34.8
Depression	122	29.9
Fluid and electrolyte disorders	122	29.9
Hypothyroidism	96	23.5
Obesity	84	20.6
Deficiency anemia	52	12.8
Other neurological disorders	43	10.5
Coagulopathy	42	10.3
Liver disease	41	10.1
Solid tumor without metastasis	39	9.6
Alcohol abuse	26	6.4
Collagen vascular diseases	23	5.6
Drug abuse	20	4.9
Psychoses	19	4.7
Weight loss	19	4.7
Personal history of noncompliance	16	3.9
Peptic ulcer disease, excluding bleeding	13	3.2
Metastatic cancer	11	2.7
Blood loss anemia	7	1.7
Lymphoma	5	1.2
Paralysis	5	1.2
Estimated GFR (mL/min/1.73 m ²)		
Mean (standard deviation)	67.3 (25.8)	
Tobacco history exposure		
None	153	37.5
Prior user	208	51.0
Current user	47	11.5

(continued)

Appendix C (continued)

Characteristic	N or Statistic	Percentage
Number of prior hospital admissions ^b		
Mean (standard deviation)	1.2 (1.8)	
Number of prior hospital admissions ^b		
0	194	47.6
1	93	22.8
2	56	13.7
3	28	6.9
4	14	3.4
5	7	1.7
6	6	1.5
>6	10	2.5
ICU admission during hospitalization	17	4.2
Length of stay (days)		
Mean (standard deviation)	4.1 (3.2)	
Discharging hospital		
Fairview Ridges	152	37.3
Fairview Southdale	179	43.9
UMMC	77	18.9
Principal discharge diagnosis		
Myocardial infarction and heart failure	108	26.5
Other cardiovascular morbidity	87	21.3
Infection	68	16.7
Respiratory and gastrointestinal	63	15.4
Endocrine, metabolic, and renal	29	7.1
Other	53	13.0
Number of discharge medications		
Mean (standard deviation)	4.2 (2.7)	
Number of DTPs		
Mean (standard deviation)	2.5 (1.8)	
Number of DTPs		
0	43	10.5
1	88	21.6
2	92	22.6
3	74	18.1
4	52	12.8
5	38	9.3
6	11	2.7
7	5	1.2
8	5	1.2

Abbreviations: GFR, glomerular filtration rate; ICU, intensive care unit; UMMC, University of Minnesota Medical Center; DTP, drug therapy problem.

^aEither primary or secondary (categories are not mutually exclusive).

^bDuring 2 years preceding index hospital admission.

Appendix D

Mean (Standard Deviation) Clinical Significance and Likelihood of Harm Scores, by Reviewer Type, in 945 DTPs With Adequate Agreement After Initial Review by 3 Reviewers.

Reviewer Type	Clinical Significance	Likelihood of Harm
CMM resident pharmacist	3.3 (1.7)	1.6 (1.2)
CMM pharmacist	3.1 (1.4)	1.3 (1.2)
Physician	2.9 (1.5)	1.8 (1.5)

Abbreviations: DTP, drug therapy problem; CMM, comprehensive medication management.

Authors' Note

At the time of this research, Drs Derr and Lahti were pharmacy residents with University of Minnesota Pharmacy Residency Program at Fairview Health Services.

Acknowledgments

We would like to gratefully acknowledge Luke Bicknese, CTSI Informatics Consulting Service, and Sonya Grillo, University of Minnesota, Institute for Health Informatics, for their assistance in securing data for our project.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Dr Brummel was a part of an advisory board for Johnson & Johnson regarding transitions of care. Dr St. Peter is currently working with Astra Zeneca on a research project related to prevalence and treatment of anemia, but this research is not related to the subject matter of this paper. Dr Weinhandl is an employee of NxStage Medical, Inc (Lawrence, Massachusetts), a manufacturer of home hemodialysis equipment. Dr Skiermont has participated in advisory boards for Amgen and is a member of Amgen's speaker's bureau.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was supported by the University of Minnesota College of Pharmacy Kam/Chen Research Advancement Grant for Clinical Practice Faculty.

References

1. Patient Centered Primary Care Collaborative. The patient-centered medical home: integrating comprehensive medication management to optimize patient outcomes. Resource guide. Second edition. <https://www.pcpc.org/sites/default/files/media/medmanagement.pdf>. Published June 2012. Accessed March 22, 2015.
2. Kilcup M, Schultz D, Carlson J, Wilson B. Post discharge pharmacist medication reconciliation: Impact on readmission rates and financial savings. *J Am Pharm Assoc (2003)*. 2013;53:78-84.
3. Joint Commission of Pharmacy Practitioners. Pharmacists' patient care process. <https://www.pharmacist.com/sites/default/files/files/PatientCareProcess.pdf>. Published May 29, 2014. Accessed November 2, 2016.
4. Cipolle RJ, Strand L, Morley P. *Pharmaceutical Care Practice: The Patient Centered Approach to Medication Management*. 3rd ed. New York, NY: McGraw-Hill; 2012.
5. American Pharmacists Association and American Society of Health-System Pharmacists. Improving care transitions: optimizing medication reconciliation. https://www.pharmacist.com/sites/default/files/files/2012_improving_care_transitions.pdf. Published March 2012. Accessed October 12, 2016.
6. Basger BJ, Moles RJ, Chen TF. Development of an aggregated system for classifying causes of drug-related problems. *Ann Pharmacother*. 2015;49:405-418.
7. Crisp GD, Burkhart JJ, Esserman DA, Weinberger M, Roth MT. Development and testing of a tool for assessing and resolving medication-related problems in older adults in an ambulatory care setting: the individualized medication assessment and planning (iMAP) tool. *Am J Geriatr Pharmacother*. 2011;9:451-460.
8. Hohmann C, Eickhoff C, Klotz JM, Schulz M, Radziwill R. Development of a classification system for drug-related problems in the hospital setting (APS-Doc) and assessment of inter-rater reliability. *J Clin Pharm Ther*. 2012;37:276-281.
9. Basger BJ, Moles RJ, Chen TF. Application of drug-related problem (DRP) classification systems: a review of the literature. *Eur J Clin Pharmacol*. 2014;70:799-815.
10. Pammett RT, Blackburn D, Taylor J, et al. Evaluation of a community pharmacy-based screening questionnaire to identify patients at risk for drug therapy problems. *Pharmacotherapy*. 2015;35:881-886.
11. Snyder ME, Frail CK, Jaynes H, Pater KS, Zillich AJ. Predictors of medication-related problems among Medicaid patients participating in a pharmacist-provided telephonic medication therapy management program. *Pharmacotherapy*. 2014;34:1022-1032.
12. Quintana-Bárcena P, Lord A, Lizotte A, Berbiche D, Jouini G, Lalonde L. Development and validation of criteria for classifying severity of drug-related problems in chronic kidney disease: a community pharmacy perspective. *Am J Health Syst Pharm*. 2015;72:1876-1884.
13. Dean BS, Barber ND. A validated, reliable method of scoring the severity of medication errors. *Am J Health Syst Pharm*. 1999;56:57-62.
14. Isetts BJ, Schondelmeyer SW, Artz MB, et al. Clinical and economic outcomes of medication therapy management services: the Minnesota experience. *J Am Pharm Assoc (2003)*. 2008;48:203-211.
15. Ramalho de Oliveira D, Brummel AR, Miller DB. Medication therapy management: 10 years of experience in a large integrated health care system. *J Manag Care Pharm*. 2010;16:185-195.
16. Isetts BJ, Brown LM, Schondelmeyer SW, Lenarz LA. Quality assessment of a collaborative approach for decreasing drug-related morbidity and achieving therapeutic goals. *Arch Intern Med*. 2003;163:1813-1820.
17. Westberg SM, Swanoski MT, Renier CM, Gessert CE. Evaluation of the impact of comprehensive medication management services delivered posthospitalization on readmissions and emergency department visits. *J Manag Care Pharm*. 2014;20:886-893.
18. Forster AJ, Murff HJ, Peterson JF, Gandhi TK, Bates DW. The incidence and severity of adverse events affecting

- patients after discharge from the hospital. *Ann Intern Med.* 2003;138:161-167.
19. Forster AJ, Murff HJ, Peterson JF, Gandhi TK, Bates DW. Adverse drug events occurring following hospital discharge. *J Gen Intern Med.* 2005;20:317-323.
 20. Bellone JM, Barner JC, Lopez DA. Postdischarge interventions by pharmacists and impact on hospital readmission rates. *J Am Pharm Assoc (2003).* 2012;52:358-362.
 21. Minnesota Hospital Association. Road map to a medication safety program. <https://www.mnhospitals.org/Portals/0/Documents/ptsafety/ade/Medication-Safety-Roadmap.pdf>. Published 2012. Accessed October 12, 2016.
 22. Dunn AS, Shetreat-Klein A, Berman J, et al. Improving transitions of care for patients on warfarin: the safe transitions anticoagulation report. *J Hosp Med.* 2015;10:615-618.
 23. Stafford L, Staffor A, Hughes J, Anglely M, Bereznicki L, Peterson G. Drug-related problems identified in post-discharge medication reviews for patients taking warfarin. *Int J Clin Pharm.* 2011;33:621-626.
 24. US Department of Health and Human Services, Office of Disease Prevention and Health Promotion. National action plan for adverse drug event prevention. <https://health.gov/hcq/pdfs/ade-action-plan-508c.pdf>. Published 2014. Accessed October 12, 2016.