

# Computerized Indicators of Potential Drug-related Emergency Department and Hospital Admissions

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**H**ealthcare quality is a serious public health concern. The prevalence of drug-related admissions in the United States has been reported to be 3% to 12% of hospital admissions.<sup>1</sup> Annual costs of drug-related problems in the United States are estimated to be more than \$150 billion, and hospital admissions account for most of these costs.<sup>2</sup> The Institute of Medicine<sup>3</sup> has proposed a 50% reduction in medical errors. To achieve this in medications use, the following are needed: an efficient measurement technique to gather baseline information about drug-related morbidity (DRM), an assessment of system-related causes and rational interventions that target system failures, and follow-up measurements to gauge the effects of the interventions.

The use of computerized indicators to search electronic databases for DRM has been proposed as a method that healthcare organizations can use to obtain efficient baseline and follow-up measurements.<sup>4-12</sup> Mackinnon and Hepler<sup>8</sup> used a Delphi approach to develop and validate a set of indicators of potential DRMs among older persons, and they used a combination of manual and computerized search criteria to identify potential DRMs through administrative data and information from the Personal Welfare Profile Senior Assessment Survey.<sup>9</sup> In another study,<sup>11</sup> the indicators were revalidated and coded to computerize the search method for use in administrative databases.

Reducing DRM would significantly improve the safety and quality of medical care provided by a managed care organization and at the same time potentially reduce the mean per-patient costs.<sup>9</sup> The indicators used in this study were designed to link possible suboptimal patterns of care with their subsequent adverse outcomes. The objectives of this study were to computerize indicators of potential drug-related emergency department (ED) and hospital admissions and to report the incidence of these potential DRMs in a managed care organization.

## METHODS

This study used a historical open cohort design and was based on a retrospective review of a healthcare purchasing coalition's claims data.

Enrollees had to have at least 1 pharmacy or outpatient claim to be included in the analysis. Person-time was calculated for each individual based on his or her enrollment start and end dates during the study period from July 1999 to June 2001.

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Appendices A and B

**Objectives:** To computerize indicators of potential drug-related emergency department and hospital admissions and to report the incidence of these potential drug-related morbidities for a managed care organization.

**Study Design:** Retrospective review of healthcare organizations' pharmacy and administrative claims databases.

**Methods:** Thirty-nine indicators were coded and were used in an automated search of claims data. The indicators of potential drug-related morbidities comprised a pattern of care and an associated adverse outcome. Poisson distribution regression analysis was performed to assess the association of patient factors with indicator positives.

**Results:** The incidence densities for indicator positives were 1.96 (95% confidence interval, 1.60-2.40) per 1000 patient-years in the general population and 13.6 (95% confidence interval, 8.8-20.2) per 1000 patient-years among older persons. Age, male sex, number of medical conditions, and number of medications from different classes were associated with an increased rate of indicator positives.

**Conclusions:** Indicators of potential drug-related morbidities can be fully automated and used to search through medical and pharmacy claims. The indicators investigated in this study show promise as a quality improvement tool and should be further developed and evaluated.

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**For author information and disclosures, see end of text.**

Ethics approval for the study was obtained from the University of Florida Health Science Center Institutional Review Board.

### Study Database

The database contained administrative data about enrollees in a preferred provider organization. The preferred provider organization administered coverage to families of employees of corporate members of the healthcare coalition. The population included patients of all ages. The data consisted of all claims made by professionals and facilities for outpatient and inpatient care, as well as data on all ambulatory prescriptions for the plan enrollees provided by the pharmacy benefit manager. A unique patient identifier was used to link the 3 data sets; patients were deidentified to protect patient confidentiality.

### Indicator Coding Concepts and Analysis

Thirty-nine of 49 potential DRM indicators by Faris<sup>11</sup> were used in this study; the 10 not used were deemed outdated or impractical to automate. These indicators are believed to represent potentially preventable cases of DRM because a Delphi panel of reviewers agreed that the indicators fit the criteria for preventability.<sup>8</sup> For a DRM to be considered preventable, the following 4 elements are required: (1) the drug-therapy problem has to be recognizable, (2) the potential adverse outcome associated with the drug therapy problem (DTP) has to be foreseeable, (3) the immediate cause has to be identifiable, and (4) the immediate cause must be controllable.<sup>8</sup> Faris<sup>11</sup> translated the potential DRM scenarios into the medical event codes used to construct the computerized indicators and verified them with expert review. The list of 39 indicators used in this study is available in online [Appendix A](#) (available at [www.ajmc.com](http://www.ajmc.com)).

### Search Algorithms

Each indicator had the following format: a pattern of care and an associated adverse outcome (eg, the use of warfarin sodium *and* prothrombin time or international normalized ratio [for anticoagulant monitoring] not evaluated every month *and* ED visit *or* hospital admission for hemorrhagic event). The pattern of care is the process component of the indicator, and it represents a possible DTP.<sup>13</sup> An ED visit or hospitalization was required to represent an adverse outcome of care. Outcome identification was restricted to the primary diagnosis because it is intended to represent the cause of an ED visit or hospital admission.<sup>14</sup> A potential DRM required the process and the outcome components of the indicator to be present (positive) in a patient.

The indicators fit into the following 3 general categories: disease–drug interaction, drug monitoring, and drug–drug interaction. Each required different programming algorithms, which are described herein.

**Disease–Drug Interaction.** The disease–drug algorithms required the presence of specific diagnosis codes and pharmacy claims before a claim for the associated outcome. A process positive was recorded when a diagnosis claim was present before or during the inferred use of the medication from pharmacy claims. A period of medications use was considered to have lasted up to 100 days after the last prescription refill date, to recognize that many patients received 90-day prescription quantities. A potential DRM required the outcome, the disease diagnosis codes, and a pharmacy claim for the medication within 100 days before the outcome.

**Drug Monitoring.** Drug monitoring algorithms required the presence of specific pharmacy claims and procedural codes. *Current Procedural Terminology* codes were used to indicate whether specified laboratory tests were conducted. Two search algorithms were required for monitoring indicators, one for the process component and another for the process and outcome simultaneously. Once the process was initiated by specific pharmacy claims, lags were calculated to represent the interval from first drug claim date to first laboratory test, from laboratory test to laboratory test, and from last drug claim date to last laboratory test. Patients were considered at risk and were included in the analysis if they were taking the medication for at least as long as the monitoring interval defined in the indicator. If any lag exceeded the defined monitoring interval, the member was recorded as having a process positive or potential DTP.

A potential DRM for a monitoring-related indicator was recorded (1) when a patient had a pharmacy claim for the specified medication and the outcome and (2) the lag between the outcome and the laboratory test closest to the outcome exceeded the indicator-specific monitoring interval. If the lag was less than 4 days, the lag between the outcome date and the second-to-last laboratory test date was used to avoid false-negative results. The assumption is that monitoring within 4 days of hospitalization identified the impending injury and the need for emergency or hospital care.

**Drug–Drug Interaction.** The third search algorithm considered multiple drugs. This included drug–drug interactions, drug–no drug situations (eg, the use of  $\beta$ -agonist without a disease-modifying medication in patients with asthma), and overuse of one drug and underuse of another. The process component is indicator specific. In the case of a simple drug–drug interaction in which drug A is a chronic medication and drug B is an acute medication, the process positives

were recorded when a claim for drug B occurred between the first and last claims for drug A. A potential DRM was recorded when the ED or hospital claim occurred within the specified number of days for each lag.

### Statistical Analysis

The number of possible DTPs per indicator was limited to 1 per individual for incidence rates and for statistical analyses. However, patients could have DTPs from multiple indicators. No limits were placed on the number of potential DRMs. Available information from the database was used to explain the indicator findings. Variables were selected based on availability in the database and on previous studies.<sup>9,11</sup> Age, sex, and numbers of drug classes, office visits, pharmacies, and prescribers were used as independent variables, and they were treated as continuous variables whenever possible. Poisson distribution regression analysis was used to evaluate their association with potential DRMs. Significance was set at  $P = .05$ . The methods by Hennessy et al<sup>15</sup> were used to evaluate data quality and the overall integrity of the databases. Computerized search criteria and statistical analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC).

## RESULTS

### Population Demographics

During the study period from July 1999 to June 2001, 37 063 members with at least 1 medical or pharmacy claim had a total observation time of 51 892 years; the mean  $\pm$  standard deviation length of enrollment was  $511.04 \pm 201.73$  days. Population demographics are given in **Table 1**.

### Incidence Densities of Indicator Positives

There were 102 potential DRMs among 79 members. The incidence densities for potential DRMs were 1.96 (95% confidence interval [CI], 1.60-2.40) per 1000 patient-years in the general population and 13.6 (95% CI, 8.8-20.2) per 1000 patient-years among older persons. Twenty-one of 39 indicators had no DRM indicator positives. Of the remaining 18 indicators, the range of potential DRMs per indicator was 1 to 26. The indicator results are listed in **Table 2**.

### Variables Associated With Potential Drug-related Morbidities

In Poisson distribution regression analysis, age, male sex, number of medical conditions, and number of drug classes were significantly associated with an increased rate of potential DRMs. The number of outpatient clinic visits

showed a significant negative association with the rate of potential DRM. The rate for men was 2.05 (95% CI, 1.33-3.16) times the rate for women ( $P < .001$ ). The rate increased 3% (95% CI, 1.02%-1.05%) for each 1-year increase in age ( $P = .001$ ). Each additional medical condition increased the rate of potential DRMs by 15% (95% CI, 1.12%-1.19%) ( $P < .001$ ). Each additional drug class increased the rate by 14% (95% CI, 1.10%-1.17%) ( $P < .001$ ). Each additional outpatient physician visit decreased the rate of potential DRM by 5% (95% CI, 0.93-0.97). Although the numbers of different prescribers, and different pharmacies were significant in bivariate analysis, they were not independently associated with the rate of potential DRMs (**Table 3**).

## DISCUSSION

The incidence rate of potential DRMs from this study was lower than the incidence rates in previous studies<sup>9,11</sup> using indicators of potential DRMs and in studies<sup>1</sup> of preventable drug-related admissions. The lower rate found in our study population may be partially explained by variations in population demographics and by differences in search algorithms.

However, a subgroup analysis among older persons produced results that were somewhat similar to previous findings among a Medicare managed care population.<sup>9,11</sup> The subgroup analysis among older persons in the present study indicated an incidence rate of 13.6 per 1000 patient-years. Faris<sup>11</sup> found an incidence proportion of 62.5 per 1000 patients, and Mackinnon and Hepler<sup>9</sup> noted an incidence proportion of 28.8 per 1000 patients.

The rate of potential DRMs in the general population in our study was also lower (15 preventable drug-related ED visits and hospitalizations per 1000 persons [detailed in online **Appendix B**, available at [www.ajmc.com](http://www.ajmc.com)]) than the findings from a systematic review of preventable drug-related admissions would suggest. These articles<sup>16-20</sup> used a medical record review process to identify preventable drug-related admissions, while the present study used computer screening of administrative and pharmacy data. Explicit criteria for identifying potential DRMs may not identify as many cases as the less-specific medical record review. Different methods of case ascertainment yield different results. An inpatient study<sup>21</sup> compared yields of medical record review, automated computer screening, and stimulated voluntary report and found that each method identified different types of adverse drug events and that the computer screening method only identified about 45% of the total adverse drug events. The computer screening methods are believed to increase efficiency and reliability; however, the yield is limited to the explicit indicators used.

**Table 1.** Population Demographics Among 47 953 Enrollees\*

Characteristic	Value
<b>No. of members with claims</b>	37 063
<b>Length of time enrolled, mean ± SD, d</b>	511.04 ± 201.73
<b>Age, y</b>	
Mean ± SD	33.97 ± 18.23
<45	23 141 (66.7)
45-64	10 743 (30.9)
≥65	835 (2.4)
<b>Sex</b>	
Female	22 861 (65.9)
Male	11 858 (34.2)
<b>No. of outpatient physician visits</b>	
Total	220 967
Mean ± SD per member	6.64 (7.05)
<b>No. of medical conditions</b>	
Total	34 938
Mean ± SD per member	5.8 ± 4.8
≤5	20 714 (59.3)
6-10	9161 (26.2)
≥11	5063 (14.5)
<b>No. of pharmacy claims</b>	
Total	33 891
Mean ± SD per member	13.93 ± 22.61
<b>No. of drug classes</b>	
Total	543 959
Mean ± SD per member	4.70 ± 5.31
≤5	25 135 (67.8)
6-10	7305 (19.7)
≥11	4623 (12.5)
<b>No. of different pharmacies</b>	
Mean ± SD per member	1.55 ± 1.45
1	17 981 (53.1)
2	8238 (24.3)
3	3919 (11.6)
≥4	3753 (11.1)
<b>No. of different prescribers</b>	
Mean ± SD per member	2.13 ± 2.07
1	12 482 (36.8)
2	8281 (24.4)
3	5302 (15.6)
4	3206 (9.5)
≥5	4620 (13.6)

\*Data are given as frequency (percentage) unless otherwise indicated. All analyses are for the 23-month time window. SD indicates standard deviation.

Implicit review methods allow for more flexibility and comprehensive assessments, but the limiting step is the knowledge and thoroughness of the reviewers and not the predefined search algorithms.

The present study required potential DRMs to have an ED visit or hospitalization for the outcome, and only the primary diagnosis was used for outcome identification; the primary diagnosis is intended to represent the cause of admission. The previous studies<sup>9,11</sup> of potential DRM indicators did not have the same requirements. Their search algorithms did not require ED visits or hospitalizations for more than half of the indicators, and the analyses were not limited to primary diagnosis codes to signify the reason for seeking medical treatment.<sup>9,11</sup>

The findings from our analysis of variables associated with the rate of potential DRM show important consistencies with previous inpatient<sup>22-24</sup> and outpatient<sup>9,11</sup> studies. Our Poisson distributed regression analysis showed that age, male sex, number of medical conditions and medications were also found to be independently associated with DRM. Moreover, MacKinnon and Helper<sup>9</sup> found that number of medical conditions and prescription medications, along with female sex, antihypertensive drug use, and number of prescribers had a positive association with the rate of potential DRM, and Faris<sup>11</sup> confirmed these findings. When considering the results from the present analysis in the context of previous research, the consistency of findings provides some evidence to support the use of the indicators to identify DRMs.

Our results are limited by the fact that the potential DRM indicators have not been criterion validated. Therefore, indicator positives represent possible DRMs. However, the indicators are based on accepted pharmacology and empirical studies.<sup>8</sup> They were content validated by independent expert panels using an accepted consensus-seeking procedure. The search algorithms took into account the proper sequence and the proximity of the potential DTP relative to the adverse outcome. Furthermore, Poisson distribution regression analysis supported findings from previous studies<sup>9,11,22-24</sup> of DRMs. Other work demonstrates that claims data are reasonably valid for identify-

## Computerized Indicators of Potential Drug-related Morbidity

■ **Table 2.** Indicator Results for Lithium Salts

Indicator	Indicator Description	At Risk	Potential Drug Therapy Problem	Potential Drug-related Morbidities
1	ACE inhibitor/ARB use and electrolytes not tested every 6 mo→hyperkalemia	2409	2209	2
2	ACE inhibitor/ARB use and BUN/serum Cr not tested every 6 mo→renal failure	2409	2282	5
3	Dx CHF and no ACE inhibitor or ARB→CHF	334	162	11
4	Dx CHF and use of an antiarrhythmic agent→CHF	334	10	2
5	Dx asthma and use of bronchodilator and no use of maintenance therapy→asthma	2153	190	26
6	Use of thyroid or antithyroid agent and thyroid tests not done every 12 mo→hypothyroidism	1510	915	5
7	Dx of depression and use of benzodiazepine→exacerbation depression	1898	321	9
8	Dx depression and barbiturate use→exacerbation depression	1898	51	0
9	Dx depression and sympatholytic antihypertensive use→exacerbation depression	1898	136	3
10	Dx depression and use of moderate-to-high lipophilic $\beta$ -adrenergic blocking agent→depression	1898	36	0
11	Use of theophylline sodium and drug level not tested every 6 mo→theophylline toxicity	79	75	0
12	Allopurinol and BUN/serum Cr not tested at least every 6 mo→renal failure	120	108	2
13	Use of warfarin sodium and INR not tested every month→hemorrhage	343	256	9
14	Dx MI and no aspirin or $\beta$ -blocker→secondary MI	181	89	5
15	Dx bipolar and lithium and drug levels not tested every 3 mo→bipolar exacerbation	9	9	0
16	Lithium and drug levels not checked every 3 mo→lithium toxicity	23	21	0
17	Lithium use and thyroid tests not done every 6 mo→hypothyroidism	23	16	0
18	Lithium use and BUN/serum Cr not tested every 3 mo→renal failure	23	21	0
19	Dx ulcer/GI bleed and NSAID use→disturbance	2526	316	0
20	Dx ulcers/GI bleeding and use of oral corticosteroid for $\geq 3$ mo→GI disturbance	2526	272	1
21	Anticonvulsant requiring monitoring and tests not done every 6 mo→seizure	159		2
22	Anticonvulsant requiring monitoring and tests not done every 6 mo→toxicity	159	145	0
23	Warfarin and NSAID simultaneously used and INR not tested within 10 d→hemorrhage	192	34	0
24	Ticlopidine hydrochloride use and CBC count/platelets not tested every 2 mo→blood dyscrasias	4	1	0
25	Dx bladder atony due to diabetes mellitus and imipramine hydrochloride use→acute urinary retention	105	0	0
26	Dx BPH and anticholinergic use→acute urinary retention	678	28	0
27	Dx high blood pressure or CHF and NSAID use $>3$ mo→CHF, fluid overload	6001	1427	3
28	Use of potassium-depleting diuretic and no potassium supplement and electrolytes not checked every 2 mo→hypokalemia	814	643	0
29	Aminoglycoside use and serum Cr not tested within 7 d→aminoglycoside toxicity	41	39	0
30	Dx COPD and $\beta$ -blocker use→COPD exacerbation	560	71	0
31	Dx COPD and use of medium-to-long-acting benzodiazepines→COPD exacerbation	641	102	3
32	Dx hypertension and sympathomimetic decongestant→tachycardia	6036	0	0
33	Carbamazepine and electrolytes/CBC count not tested every 6 mo→blood dyscrasias/hyponatremia	40	33	0
34	Digoxin and BUN/serum Cr not tested at least every 6 mo→digoxin toxicity	309	136	0

*(continued)*

■ **Table 2.** Indicator Results for Lithium Salts (*Continued*)

Indicator	Indicator Description	At Risk	Potential Drug Therapy Problem	Potential Drug-related Morbidities
35	Warfarin use and antibiotic use and INR not tested within 5 d→hemorrhage	343	32	0
36	α-Blocker use and standing blood pressure not checked within 2 mo of initiating therapy→fall fracture	355	0	0
37	65 Years or older and use of long half-life hypnotic/anxiolytic→fall/fracture	2689	179	1
38	65 Years or older and use of tricyclic antidepressant→fall/fracture	836	51	1
39	Dx CHF with heart block or advanced bradycardia and digoxin use→CHF/heart block	645	79	12
<b>TOTAL</b>			<b>10 495</b>	<b>102</b>

ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BUN, blood urea nitrogen; Cr, creatinine; Dx, diagnosis; CHF, congestive heart failure; INR, international normalized ratio; MI, myocardial infarction; GI, gastrointestinal; NSAID, nonsteroidal anti-inflammatory drug; CBC, complete blood cell; BPH, benign prostatic hypertrophy; and COPD, chronic obstructive pulmonary disease.

ing patients with specific diseases, especially when pharmacy claims that would be consistent with the disease are included.<sup>25</sup>

The search algorithms were limited to severe outcomes (ie, ED visits or hospitalizations). Studies<sup>26,27</sup> show that many DRMs are considered significant but not severe. The incidence rates likely underestimate the true DRM rate, which would include less severe outcomes. In our study, clinic visits were not included in outcomes assessments because of ambiguities in determining the cause and severity of an ambulatory visit using claims data.

Claims-based surveillance for potential DRMs could be enhanced by searching problem lists and clinical notes from electronic medical records. However, many clinics still do not have a computerized patient medical record; therefore, this

approach is not universally feasible. Because some data in an electronic medical record are in free text rather than being coded, text-search algorithms or natural language processors would be needed to identify meaningful terms and concepts. Searching free text would support the identification of less severe DRMs (ie, adverse outcomes that were identified and resolved in the clinic), and it would provide a more comprehensive assessment of DRM.

Further work is needed to refine the technical aspects of the potential DRM indicators. This would involve continuously updating the indicators to include newer therapies and more recent treatment evidence, evaluating their criterion validity with chart review, and adapting the search algorithms to include clinical data (eg, laboratory test results and problem lists) along with claims data. Careful and meaning-

ful analysis of the recent literature is needed to add additional performance indicators and to remove indicators that do not represent current best practice. Institutions and investigators should conduct an internal review of available indicators, such as the potential DRM indicators presented herein, to determine the usefulness of each indicator and to develop indicators that fit the needs of their specific institutions.

■ **Table 3.** Variables Associated With Drug-related Morbidity Indicator Positive Rates

Variable	Bivariate Analysis (95% Confidence Interval)	Multivariate Analysis (95% Confidence Interval)
Age	1.07 (1.05-1.08)*	1.03 (1.02-1.05)*
Male sex	0.94 (0.62-1.42)	2.05 (1.33-3.16)*
No. of medical conditions	1.19 (1.17-1.20)*	1.15 (1.12-1.19)*
No. of drug classes	3.35 (2.92-3.84)*	1.14 (1.10-1.17)*
No. of different prescribers	1.48 (1.41-1.55)*	0.95 (0.87-1.04)
No. of different pharmacies	1.50 (1.38-1.63)*	1.05 (0.94-1.16)
No. of outpatient physician visits	1.05 (1.05-1.06)*	0.95 (0.93-0.97)*

\*Statistically significant ( $\alpha = .05$ ).

## CONCLUSIONS

Indicators of DRMs can be automated and used to search administrative databases for cases of potential DRMs. In our study, the incidence densities for potential DRMs were 1.96 (95% CI, 1.60-2.40) per 1000 patient-years in the general population and 13.6 (95% CI, 8.8-20.2) per 1000 patient-years among older persons. Age, male sex, number of medical conditions, and number of medications from different classes were associated with an increased rate of potential DRMs. The information generated from the potential DRM indicators is the first step in a multistep process. Ongoing steps include identifying system problems, implementing solutions, and evaluating the effects of interventions. These indicators show promise as a quality assessment and as an improvement tool and should be further developed and evaluated.

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### Take-away Points

- Healthcare quality and safety are serious public health concerns.
- Computerized indicators can be used to identify potential drug-related quality and safety concerns.
- Computerized indicators of potential drug-related emergency department and hospital admissions show promise as a quality improvement tool and should be further developed and evaluated.

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