Evaluation of medication administration timing variance using information from a large health system’s clinical data warehouse

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Purpose. An analysis to determine the frequency of medication administration timing variances for specific therapeutic classes of high-risk medications using data extracted from a health-system clinical data warehouse (CDW) is presented.
**Methods.** This multicenter retrospective, observational analysis of 1 year of medication administration data from 14 hospitals was conducted using a large enterprise health-system CDW. The primary objective was to assess medication administration timing variance for focused therapeutic classes using medication orders and electronic medication administration records data extracted from the electronic health record (EHR). Administration timing variance patterns between standard hospital staffing shifts, within therapeutic drug classes, and for as-needed (PRN) medications were also studied. Calculated variables for delayed medication administration (ie, administration time variance) were created for documented administration time intervals of 30-59, 60-120, and more than 120 minutes before or after medication orders.

**Results.** A total of 5,690,770 medication administrations (3,418,275 scheduled and 2,272,495 PRN) were included in the normalized data set. Scheduled medications were frequently subject to delays of ≥60 minutes (15% of administrations, n = 275,257) when scheduled for administration between 9-10 AM and between 9-10 PM. By therapeutic drug class, scheduled administrations of insulins, heparin products, and platelet aggregation inhibitors (most commonly heparin flushes and line-management preparations) were the most commonly delayed. For PRN medications, medications in the anticoagulant and antiplatelet agent class were most likely to be administered early (<60 minutes from the scheduled time of first administration).

**Conclusion.** The findings of this study assist in understanding patterns of delayed medication administration. Medication class, time of day of scheduled administration, and frequency were factors that influenced medication administration timing variance.

**Keywords:** dashboard, data warehouse, informatics, medication administration delay, pharmacy informatics
One of the benefits of adopting an electronic health record (EHR) is the opportunity to collect and aggregate large data sets of patient information. This big data can be applied to clinical questions and promotes quality improvement that expands beyond the capabilities of directly observable care. Because the EHR often contains a rich audit trail of events, patterns of behavior can be observed at unit, facility, multihospital health system, and enterprise health system scales. EHR data can be aggregated and analyzed to identify clinical opportunities and best practices.

Background

Medications are generally expected to be administered within a 30- to 60-minute window of scheduled time to ensure timely administration of drug therapy. Published literature has estimated that medications are administered at times outside the expected window in up to 73% of cases, primarily due to late administration.\(^1\) Delayed medication administration has the potential to significantly impact patient outcomes for high-risk medications such as antibiotics, anticoagulants, insulin, and opioids.\(^2,3\) In addition, the Centers for Medicare and Medicaid Service requires hospitals to develop policies that direct timing of medication schedules based on the medication indication, clinical condition of administration, and urgency of patient care.\(^4\) These forces drive the need to ensure the timely administration of drug therapy.

To assess the medication administration process, direct observation has been historically used, but limitations such as the observer effect, single unit observation, and nurse staffing can confound the findings of these studies.\(^5-9\) The use of data captured
through barcode medication administration (BCMA) in the EHR can be used to assess trends in medication administration and identify areas for improvement. Years of EHR data can be drawn from many hospitals within the health system and aggregated into a clinical data warehouse (CDW) to form a more robust sample population. Currently, there is limited literature on use of CDW data to assess trends in medication administration.\textsuperscript{10} The ability of an organization to use its data can drive clinical practice and improve the quality and accuracy of medical care. The goal of this analysis was to determine the frequency of medication administration timing variances for specific therapeutic classes of high-risk medications using data extracted from the CDW.

\textbf{Methods}

The study objectives for this analysis were to identify administration timing variance patterns for medications within the targeted therapeutic drug classes studied (anticoagulants, insulin, opioids, and antimicrobials), compare rates of medication administration delays based on standard hospital staffing shifts, and identify when as-needed (PRN) medications were administered earlier than their ordered schedule. Patient demographics, medication order information, and patient electronic medication administration record (eMAR) data were collected from the CDW of a large healthcare system.

This study was approved for expedited review by the University of Tennessee institutional review board. The data set excluded patient identifiers to maintain confidentiality. A sample of the health system, composed of 1 hospital from each of the 14 geographically distributed divisions of the health system (located primarily across the West Coast, Midwest, Southwest, and Southeast of the United States), was selected for inclusion.
While data were available for all hospitals within the health system for the time period studied, a geographically distributed sample composed of urban and suburban community hospitals was selected due to the large volume of resulting medication administration data. The median number of licensed beds was 488 beds (range, 318-981 beds). Pediatric (0-18 years) and adult (>18 years) patients on all inpatient units (both intensive care and non-intensive care units) with at least 1 medication administration documented in the eMAR were included in the study. Patients were excluded if their date of admission or discharge was outside the study period or they had not received a medication within the targeted therapeutic classes. Exclusion criteria are outlined in Figure 1.

A retrospective review of medication administration data for the period August 1, 2017, to July 31, 2018, was conducted using data collected from the CDW using Structured Query Language (SQL) queries. Patient demographics, hospital identification, medication administration time documented using BCMA timestamps, and medication order time were collected. To focus on high-risk medications, data were abstracted for therapeutic classes of interest (anticoagulants, insulin, opioids, and antimicrobials).

During this research, a significant amount of data normalization was required to operationalize existing medication administration data. First, data analysts familiar with our CDW identified accurate data sources from which to draw medication administration information. Upon identification of these sources, joining SQL queries were written to connect medication administration data with medication ordering information. As expected, a substantial amount of information was drawn from this query. In order to limit the data extract to a manageable volume, 1 hospital from each of the 14 geographically distributed divisions in the enterprise were selected for inclusion. Value sets are numerical codes that correspond to standard medication definitions and are used to focus the data set to the
information of interest. Value sets were created based on therapeutic class codes
developed by proprietary drug information software (First DataBank Inc., San Bruno, CA).
Data were curated to value sets of medications of interest: antimicrobials, opioids,
benzodiazepines, anticoagulants/antiplatelets, nonopioid combination analgesics, and
insulins. To limit the size of the data extraction, our final data set included only medication
administrations and patients who had received a drug from one of these therapeutic
classes, as defined by value set. The research team reviewed therapeutic class codes for
value set inclusion. RxNorm is a standard nomenclature developed by the US National
Library of Medicine (NLM) and can be used to normalize variations in medication build in
the EHR. To develop these focused therapeutic classes, initially the research team sought to
use RxNorm concept unique identifiers (RxCUIs), but due to limitations in the medical
record, this approach was not feasible. Instead, a proprietary therapeutic class convention
developed by a commercial drug information vendor was reviewed by the research team
and used to develop the focused therapeutic classes. After reviewing the data extracted
from the SQL query results and removing any clinically irrelevant data (including entries for
billing purposes), the final data set was loaded and prepared for analysis. These steps in the
data normalization process were crucial in the development of a clinically useful final data
set and represent a repeatable extract, transform, load (ETL) methodology for future
analyses.

Calculated variables for delayed medication administration (ie, administration time
variance) were created for 3 documented administration timeframes (30-59, 60-120, and
>120 minutes after a medication order). Because delayed administration time was assessed
for scheduled medications and early administration for as-needed (PRN) administrations,
the aggregated data were split for these groups. Early administration of PRN medication
orders was analyzed, as these orders cannot be considered “late” due to the inherent nature of PRN administration. In addition, PRN medications without a frequency (eg, every 4 hours, every 6 hours) were excluded from the PRN data set. Early administration was identified by comparing the timing of the second dose to the dosing frequency for the PRN medication order. Subsequent administrations were not analyzed. For PRN orders, the same timing parameters (30-59, 60-120, and >120 minutes after ordering) were used to assess frequency of early administration. Administrations with nonstandard routes, such as those used for billing or documentation, were excluded. Standard hospital shift conventions (day shift defined as 7 AM-7 PM and night shift defined as 7 PM-7 AM) were used for the analysis. Descriptive statistics, including a Pearson chi-square analysis, were used to evaluate the data set. Tableau (version 2018.2.7; Tableau Software, Mountain View, CA) was used to create graphs and descriptive tables for the scheduled administration data set.

Results

A total of 5,690,770 medication administrations (3,418,275 scheduled and 2,272,495 PRN) were included in the final data set. Demographic information, collected during the admission when the patient received the drug administration, is displayed in Table 1.

For scheduled medications, 20,250 licensed practitioners administered 3,418,275 medications (168.8 medications administered per licensed practitioner) over the study period. For PRN medications, 18,549 licensed practitioners administered 2,272,495 medications (122.5 administrations per licensed practitioner) over the study period.

Timing of medication administration by hour of day was assessed. Between the hours of 7 AM to 7 PM, 63% (n = 213,8690) of the high-risk medication classes studied in this analysis were administered. Of these medications, 21% (n = 458,415) were administered 60
or more minutes after the scheduled time. Scheduled medications were frequently subject to delays of ≥60 minutes (15% of administrations, \( n = 275,257 \)) when scheduled during the hours of 9 and 10 AM or 9 to 10 PM. Medications administered at exactly 60 minutes after the scheduled due time were included as delayed but did not make up a significant proportion of the total data set (0.5%, \( n = 17,598 \)). Of the scheduled medications, 54.9% (\( n = 1,876,112 \)) were administered between 9 and 10 AM or 9 and 10 PM (Figure 2). The time periods 9-10 AM and 9-10 PM accounted for 44.9% (\( n = 275,257 \)) of administration delays of ≥60 minutes; in comparison, medications administered during the remaining 22 hours of the day accounted for 55.1% of delays. There was a statistically significant difference in the numbers of administrations delayed at least 60 minutes between the 2 time slots (Pearson \( \chi^2 = 30,301.28; P < 0.0001 \)).

Antimicrobials were the focused therapeutic class with the highest number of administrations (Table 2), accounting for 38% (\( n = 1,299,744 \)) of the total number of administrations. Topical antibiotics, including mupirocin and povidone-iodine, comprised the highest proportion of medications included in this class. The most common medications included in our therapeutic groups were insulin lispro, heparin porcine, and mupirocin, accounting for 27.5% (\( n = 941,111 \)) of all scheduled medication administrations (Table 3).

The therapeutic class that accounted for the highest number of PRN administrations was opioid medications, primarily morphine, hydrocodone/acetaminophen, and oxycodone (Table 4). PRN antimicrobials included nystatin, miconazole, and bacitracin. Heparin flushes and line-management preparations were the primary medications included in the anticoagulant medication class.

**Discussion**
Of all delayed administrations for the day, 44.9% \((n = 275,257)\) occurred during the time periods of 9-10 AM and 9-10 PM, likely because medication administration burden for the high-risk medication classes studied were greatest during these time periods. This analysis provides the framework and guidance for assessing trends in medication administration timing variance. Modifications in medication schedules to reduce medication administration burden on staff may be a method to reduce medication administration delays.

The use of medication administration data gathered from the CDW has the potential to shift quality measures from adverse patient events to metrics focused on reducing administration timing deviations. For example, in addition to reporting frequency of venous thromboembolism in the unit, anticoagulant administration delays can be a targeted standard. This data also has the potential to shift standard hospital medication administration times (traditionally, 9 AM-10 AM and 9 PM-10 PM) to mitigate medication burden. As the availability of clinical data improves, future studies can seek to identify reasons why medications are administered outside the expected time range, such as delayed delivery to bedside or delays due to patient logistics.

One consideration when evaluating this data set is the possibility of appropriate medication administration outside of the scheduled medication administration time. Insulins were the medication class for which the percentage of administrations delayed 60 minutes or more was highest. While information on reasons for medication delays was not available due to limitations of the data set, variance in insulin administration may reflect an appropriate delay due to meal timing. In addition, patient preference or individualized schedules may be a contributing factor in appropriately delayed medication administration. For example, patients are often instructed to take their oral anticoagulants, such as...
warfarin, at the same time every day. Hospital policies for medication administration often do not consider these factors when directing care. A final reason for appropriate medication administration variance may be pending laboratory test results. Vancomycin may be administered later than ordered while clinicians await trough concentration determination. These factors should be considered when assessing medication administration delays, and future studies can consider strategies for differentiating appropriate delays from those due to modifiable factors.

A secondary intent of this study was to demonstrate the feasibility of using medication administration data from a CDW. At this time, using clinical big data can be a labor-intensive process. Understanding the source of the CDW data, excluding incomplete records, and identifying the most accurate data sources to gather the clinical information were some of the most challenging steps in our analysis. In addition, use of a nonproprietary therapeutic class convention could assist with standardizing definitions, allowing replication of our analysis. Drug grouping conventions agnostic of drug information vendor, such as the Centers for Disease Control and Prevention’s RxNorm opioid value sets, have been developed in an effort to standardize drug concept definitions. Future studies should consider using standardized value sets for therapeutic class definitions. Another limitation observed during the research was the large volume of data that resulted for all hospitals within the health system for the study period. Due to the volume of data available for all hospitals within the health system for the time period, the study team narrowed hospitals for inclusion using number of beds, geographical location, and service line availability to determine a representative sample. Other limitations of this analysis include the descriptive nature of the study, insufficient nursing shift tracking data to identify number of medications administered per nursing shift, our ability to compare variance for only the first
and second PRN administrations, and lack of automated dispensing cabinet data inclusion. Future studies can consider these factors to improve or expand this analysis, such as through observations of the effect of targeted interventions on medication administration timing variance.

Leveraging medication administration data has the potential to change quality standards, reduce variability in care, and provide insight into the medication-use process at scale. The pharmacy department can take the lead in interprofessional collaboration to mitigate delays in medication administration and drive patient-centered care. Data warehouses containing clinical information provide the opportunity to reduce the burden of manual data extraction, but understanding the data sources and bedside workflows is key in improving patient care. Supporting and developing clinically relevant healthcare data warehouses will improve access to clinical big data and streamline future research opportunities.

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Additional Information

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Figure 1. Exclusions for analysis of scheduled and as-needed (PRN) administrations.

- Orders with “PRN” as their administration frequency were excluded, as the scheduled frequency could not be determined.
Figure 2: Delayed (≥60 Minute) Therapeutic Class Distribution by Due Time

Data represent percent of administrations given ≥60 minutes after scheduled due time for each hour of day.

^aData represent percent of administrations given ≥60 minutes after scheduled due time for each hour of day.
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Table 1. Summary Patient Demographics

| Data value |  |
|------------|--|
| **Age, mean (range), years** |  |
| Scheduled | 64 (0-117) |
| PRN | 56 (0-116) |
| **Length of inpatient admission, median (range), days**<sup>a</sup> |  |
| Scheduled | 4 (1-283) |
| PRN | 3 (1-283) |
| **Gender, No. (%)** |  |
| Female | 2,919,202 (51.3) |
| Male | 2,743,974 (48.3) |
| Unknown/missing<sup>b</sup> | 27,594 (0.4) |
| **Race/ethnicity, No. (%)**<sup>c</sup> |  |
| White | 3,724,842 (65.5) |
| Black | 930,574 (16.4) |
| Hispanic Other | 377,468 (6.6) |
| Hispanic White | 346,923 (6.1) |
| Unknown/other | 310,963 (5.5) |
| **ICU location** |  |
| ICU | 986,291 |
| Non-ICU | 4,704,479 |
| **Patient scanned during administration** |  |
| Yes | 5,665,592 |
| No | 25,178 |
| **Medication scanned during administration** |  |
| Yes | 5,570,233 |
| No | 120,537 |

<sup>a</sup>Due to duplicate patient counts in these areas, medication administrations are reported. To ensure accuracy in reporting, administration are categorized scheduled or PRN when necessary.

<sup>b</sup>Due to absence of patient demographic entry information from the medical record.

<sup>c</sup>Race/ethnicity information was sourced directly from the EHR. Standard race and ethnicity codes were not available in this data set.
Table 2. Total Administrations of Medication Classes and Percentage Delayed

| Medication Class             | Total\(^a\) | Patients | Delay of 60-120 min, % | Delay of >120 min, % |
|-----------------------------|-------------|----------|------------------------|----------------------|
| Insulins                    | 859,610     | 56,132   | 22.6                   | 6.2                  |
| Heparin and related preparations | 446,196     | 52,517   | 10.1                   | 4.1                  |
| Platelet aggregation inhibitors | 440,867     | 70,131   | 9.7                    | 5.4                  |
| Topical antibiotics         | 226,639     | 32,762   | 8.8                    | 4.2                  |
| Direct factor Xa inhibitors | 135,047     | 19,034   | 11.6                   | 3.8                  |
| Topical preparations, antibacterials | 114,613     | 19,708   | 6.6                    | 2.7                  |
| Opioid analgesics           | 103,470     | 9,977    | 8.8                    | 2.9                  |
| Topical antifungals         | 102,102     | 6,660    | 11.5                   | 5                    |
| Penicillin antibiotics      | 100,964     | 11,115   | 9.8                    | 3.9                  |
| Antivirals, general         | 81,610      | 7,893    | 9                      | 3.7                  |

\(^a\)Data represent total administrations for each class; patients included in the analysis may have received medications in more than one class.
Table 3. Scheduled Medication Distribution

| Medication                          | Medication Class               | Patient Count | Total Medication Administrations<sup>a</sup> | Delay of 60-120 min, % | Delay of >120 min, % |
|-------------------------------------|--------------------------------|---------------|----------------------------------------------|------------------------|----------------------|
| Insulin lispro 100 units/1 mL       | Insulins                       | 36,537        | 468,642                                      | 28.1                   | 7.3                  |
| Heparin 5,000 units/1 mL            | Heparin and related preparations | 25,301        | 280,456                                      | 9.7                    | 3.8                  |
| Mupirocin, 2% cream                 | Topical antibiotics            | 29,734        | 192,013                                      | 8.4                    | 3.9                  |
| Aspirin 81-mg chewable tablet        | Platelet aggregation inhibitors | 29,980        | 154,727                                      | 9.8                    | 5.7                  |
| Aspirin 81-mg enteric-coated tablet | Platelet aggregation inhibitors | 28,896        | 141,867                                      | 9.5                    | 5.0                  |
| Insulin regular, 100 units/1 mL     | Insulins                       | 9,498         | 111,556                                      | 17.1                   | 4.1                  |
| Clopidogrel 75-mg tablet            | Platelet aggregation inhibitors | 23,815        | 111,345                                      | 9.5                    | 5.7                  |
| Enoxaparin injection, 40 mg/0.4 mL  | Heparin and related preparations | 19,876        | 91,194                                       | 10.9                   | 5.4                  |
| Apixaban 5-mg tablet                | Direct factor Xa inhibitors    | 9,923         | 75,593                                       | 11.2                   | 3.4                  |
| Acyclovir 200-mg capsule            | Antivirals, general            | 1,925         | 30,937                                       | 7.0                    | 2.7                  |

<sup>a</sup>Data represent total administrations for each class; patients included in the analysis may have received medications in more than one class.
Table 4. As-Needed Drug Class Distribution

| Medication Class                                           | Total Medication Administrations | Delay of 60-120 min, % | Delay of >120 min, % |
|------------------------------------------------------------|----------------------------------|------------------------|----------------------|
| Anticoagulants and antiplatelet/platelet-reducing agents   | 115                              | 6.1                    | 27.8                 |
| Antimicrobials                                             | 374                              | 2.9                    | 11.8                 |
| Benzodiazepines                                            | 2,613                            | 3.8                    | 6.5                  |
| Insulins                                                   | 546                              | 3.5                    | 1.3                  |
| Nonopioid combination analgesic                           | 18                               | 0                      | 0                    |
| Opioids                                                    | 229,432                          | 0.8                    | 1                    |

aData represent total administrations for each class; patients included in the analysis may have received medications in more than one class.