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Brief Communication

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Calculating maximum morphine equivalent daily dose from prescription directions for use in the electronic health record: a case report

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ABSTRACT

To demonstrate a process of calculating the maximum potential morphine milligram equivalent daily dose (MEDD) based on the prescription Sig for use in quality improvement initiatives. To calculate an opioid prescription's maximum potential Sig-MEDD, we developed SQL code to determine a prescription's maximum units/day using discrete field data and text-parsing in the prescription instructions. We validated the derived units/day calculation using 3000 Sigs, then compared the Sig-MEDD calculation against the Epic-MEDD calculator. Of the 101 782 outpatient opioid prescriptions ordered over 1 year, 80% used discrete-field Sigs, 7% used free-text Sigs, and 3% used both types. We determined units/day and calculated a Sig-MEDD for 98.3% of all the prescriptions, 99.99% of discrete-Sig prescriptions, and 81.5% of free-text-Sig prescriptions. Analyzing opioid prescription Sigs to determine a maximum potential Sig-MEDD provides greater insight into a patient's risk for opioid exposure.

Key words: opioid, pain, population health, morphine, prescription

INTRODUCTION

In response to the opioid crisis, health systems have increased efforts to analyze opioid prescriptions. In this paper, we describe a method for determining maximum units per day from prescription instructions (Sigs) within the electronic health record (EHR) to calculate a maximum potential morphine equivalency (Sig-morphine milligram equivalent daily dose [MEDD]). Our aim was to develop a metric that would aid in quantifying the daily opioid exposure a patient might experience based on the Sig. Studying patient populations using this metric could allow us to identify the influence of patient instructions on opioid overdose, addiction, and potential misuse.

Most pharmacoepidemiology studies utilize Defined Daily Dose (DDD) or Morphine Milligram Equivalents (MME). DDD tries to estimate the expected daily dose; however, we were interested in determining the maximum daily dose exposure based on Sig instructions.[1] MME provides us with the total morphine equivalency exposure on a total prescription level. This method, however, does not help us understand the daily exposure risk. Determining daily exposure is often dependent on knowing the days' supply, which is often omitted, and may underestimate potential exposure compared to the Sig, especially for "as needed" medications.[1,2]

There have been several efforts to parse out discrete variables from free-text Sigs or clinician encounter notes using methods, programs, or manual abstraction—the latter which is neither feasible nor preferred for real-time health system data needs.[3,4] Several research groups have developed Natural Language Processing

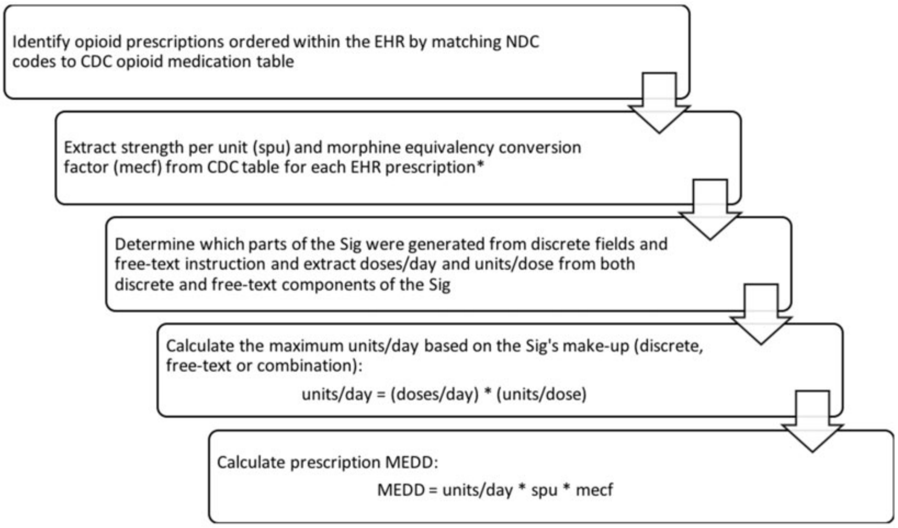

Figure 1. Calculating an opioid prescription's Sig-MEDD using EHR prescription data. **NOTE:* Exceptions exists for certain medications, such as buprenorphine and methadone. EHR: electronic health record; MEDD: morphine milligram equivalent daily dose; spu: strength per unit.

applications (PredMED, MedEx, and MedXN) that extract prescription information from the Sig, clinical notes, medication reconciliation notes.[5–8] We chose the SQL free-text abstraction method as a single system to extract data, convert Sigs, and make calculations.

Previous published MEDD calculations rely primarily on claims data, retail prescription data, or retrospective clinical data; to our knowledge, there are not published papers detailing the calculation of an efficient MEDD.[9–12] In these studies, the MEDD is calculated by summing the total daily amount of opioid prescription (the product of frequency, dose, and strength) and converting by a conversion factor.[13] However, recent studies using MEDD data for dashboards do not detail text-parsing methods for free-text Sigs, either relying on discrete field or making assumptions about the MEDD based on the days' supply.

Our objectives were as follows: (1) to demonstrate the feasibility of using a Sig to determine units/day for calculating Sig-MEDD and (2) to illustrate 2 validation methods. While we focused on opioid prescriptions, the Sig data extraction could be used for other medications.

METHODS

Setting

Our academic health system includes an 886-bed tertiary care hospital and a 133-bed community hospital. The system also includes various multispecialty, primary care, and urgent care clinics. From 2017 to 2018, the health system had 794 312 outpatient visits, 56 636 inpatient admissions, 123 161 emergency department (ED) admissions, and 277 023 inpatient days. In 2017, the net patient service revenue by payer source was Medicare (25%), Medicaid (5%), Health Maintenance Organization/Preferred Provider Organization (64%), and self-pay/other (6%).[14]

Data source

Data were extracted from our organization's Epic EHR's Clarity database using Oracle SQL. We used the Centers for Disease Control and Prevention (CDC) opioid data files which contain morphine equivalent conversion factors, strength per unit (spu), and a National Drug Code for the available nonintravenous opioid medication based on formulation.[13,15] For methadone, the CDC table provides a morphine equivalency for the lowest dose. However, methadone's morphine equivalency must be adjusted based on the total daily dose: the higher the daily dose and the higher the conversion factor. We developed logic to calculate the daily dose and applied the appropriate conversion factor. For buprenorphine films, we used a regular expression to extract the spu and assigned a morphine equivalency conversion factor (MECF) of 12.6 based on Centers for Medicare and Medicaid Services (CMS) conversion factors.[16]

The date range for prescriptions was limited to prescriptions ordered between July 1, 2017 and June 30, 2018. We included all outpatient opioid prescriptions, including discharge medications, ED visit discharge prescriptions, or ambulatory care prescriptions. We excluded intravenous medications from our analysis. We excluded medications discontinued within 3 days of ordering. The study was deemed exempt from Institutional Review Board review.

Method development

Calculating a MEDD requires 3 components: (1) the number of units per day; (2) the medication's spu; and the (3) MECF. The spu and conversion factor are based on the medication, administration route (eg, transdermal), and form prescribed.

The prescription's units per day can be derived from the units/dose and doses/day found in the prescription Sig. We demonstrate the equation for calculating an estimated MEDD below:

$$\text{EDD} = \text{Units per day} \times \text{Medication strength per unit} \times \text{MECF}.$$

We detail the process of calculating a Sig-MEDD in Figure 1.

Number of units per day

Through an iterative process, we identified the various ways opioid prescription Sigs were written by providers within our system. We first separated the Sig into both its discrete and free-text components. We developed logic to extract the doses per day and units per dose from the discrete fields. We used a combination of prescribing knowledge and a review of the data to identify common Sig patterns to develop string-matching case statements that translate the num-

Table 1. Sample Sig free-text instruction translation

Free-text phrase	Maximum potential units per dose	Maximum potential doses per day	Strength per unit	Conversion factor	Total maximum daily dose
Hydrocodone 5/325 "Take 1–2 tablets every 4–6 h"	2	6	5	1	60 MEDD
Hydrocodone 10/325 "Take 2 tables twice daily"	2	2	5	1	20 MEDD
Oxycodone 30 mg "Take 1–2 tablets bid"	2	2	30	1.5	180 MEDD

Abbreviation: MEDD: morphine milligram equivalent daily dose.

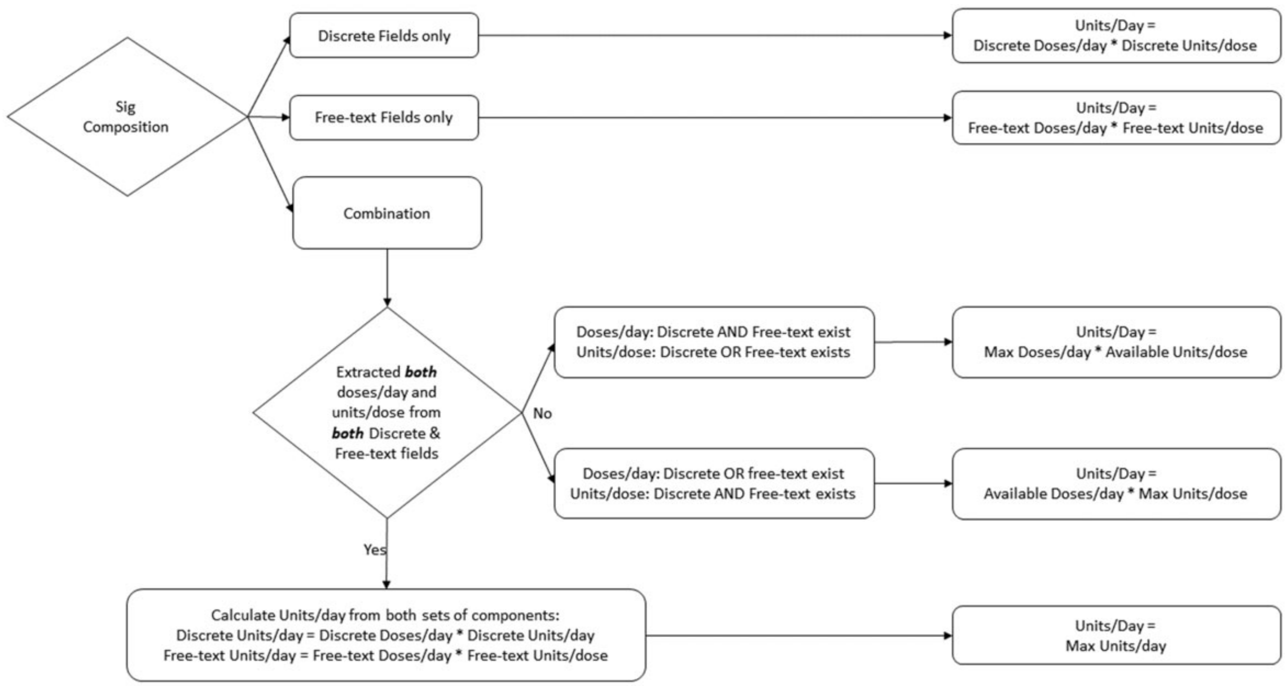

Figure 2. Determining a prescription's maximum units/day. *NOTE:* Doses/day or units/dose is null if it does not exist or the method could not determine a value.

ber of units per dose and the number of doses per day into discrete fields (see Table 1) (see Supplementary Appendix S1 for the SQL code).

When prescriptions had ranges of dosages or frequencies in either discrete or free-text form, we determined the maximum units per dose and maximum doses per day. When a Sig did not have a value for doses/day or units/day based on discrete or free-text components, the method entered a null value, which allowed us to flag those prescriptions for review and continue to improve our logic (see Figure 2).

Validation

Validation of units per day

We selected 3000 unique Sigs for review and validation. Two analysts reviewed 1500 Sigs and 1 informaticist reviewed all 3000 Sigs. We used consensus to resolve differences between raters. The validation process consisted of manually reviewing prescriptions using the Sigs to derive the maximum units/day and compared against our SQL-derived units/day. Given the high skewness of the units/day, we log-transformed the units/day calculated by both methods. We plotted a Bland–Altman scatterplot (see Supplementary Appendix), which examines the quantification of the agreement between 2 continuous measurements by using the mean difference and constructing limits of agreement based on the difference.[17,18] We assessed agreement in units/day only when both methods reported results. We also conducted a 1-sample t-test to examine the mean difference and 95% confidence intervals (CIs) of units per day between the 2 methods.[17]

Validation of MEDD

The Epic-MEDD calculator went live within our health system on May 4, 2018 and back-dated past prescriptions with the Epic-MEDD. We compared the Sig-MEDD to the Epic-MEDD across both the discrete field and free-text prescriptions. Given the high skewness of MEDD distributions for both methods, we log-transformed the MEDDs calculated by both methods. We plotted a Bland–Altman scatterplot to look for systematic variation between the mean of the 2 differences.[18] We analyzed the mean difference in MEDDs only when both methods reported results. We conducted a 1-sample t-test to examine the mean difference and the 95% CIs of MEDDs between the 2 methods.[18]

RESULTS

Descriptive statistics

From July 1, 2017 to June 30, 2018, 101 782 opioid prescriptions were written within our organization using 7362 unique Sigs. Of these prescriptions, 81.5% were written as "prn" or "as needed"

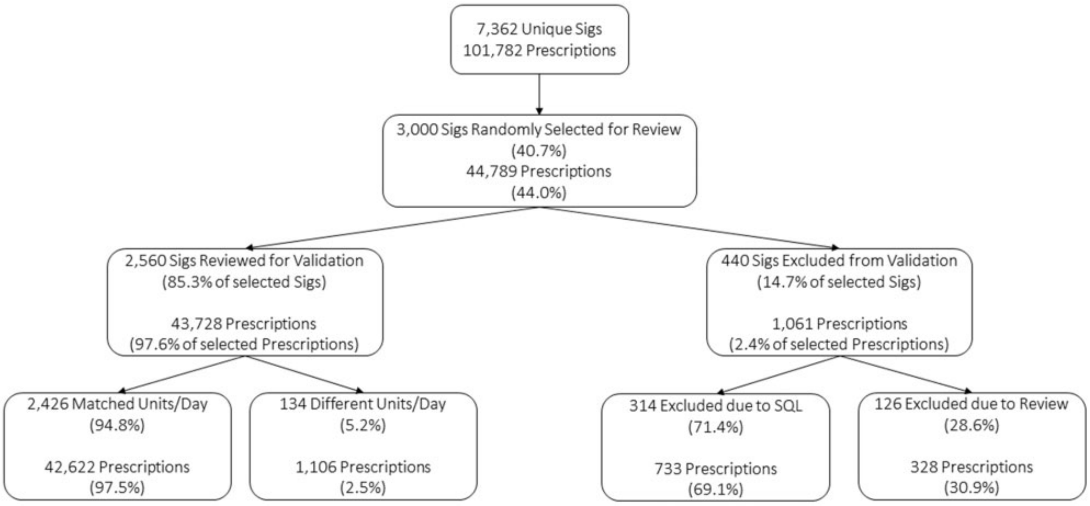

Figure 3. Manual review of prescriptions Sigs for unit/day validation.

Table 2. Examples of validated Sigs with different units/day

Example	SLQ method units/day	Manually reviewed units/day
"Take 1 tablet by mouth every 4 h as needed. Or 2 tabs every 6 h as needed for pain"	12	8
"Take 1 tablet by mouth daily. May take 1–2 extra"	1	3
"1 tablet 2 times daily and at nighttime as needed"	2	3

prescriptions, 9.2% were written as free-text Sigs and 13.6% of Sigs contained a range for either the units per dose or doses per day.

Our method calculated a Sig-MEDD for 98.3% of prescriptions, 99.99% of discrete Sigs, and 81.5% of free-text Sigs. We were unable to calculate a Sig-MEDD for 1765 prescriptions and 790 distinct Sigs. For these prescriptions, we found Sigs with time-based directions, non-English sigs, and missing information.

The majority of opioid prescriptions in the system were for short-acting opioids, including hydrocodone (45.63%), oxycodone (24.33%), and tramadol (15.42%). There were fewer recorded prescriptions of long-acting or sustained-released preparations of oxycodone (2.79%) and morphine (1.62%).

Validation of units per day

Three thousand Sigs were randomly selected for manual review and units per day calculations. Four hundred and forty were excluded because either our method or reviewers were not able to determine units/day. The remaining 2560 Sigs account for 35% of all Sigs and 43 728 (43%) of the prescriptions.

The manual review matched the SQL-derived units/day for 2426 (94.8%) Sigs, which accounted for 42 622 of the prescriptions (97.5%). The units/day differed for 134 Sigs (5.2%), which accounted for 1106 of the prescriptions (2.5%) (see Figure 3). We found a mean difference of 0.003 between the log-transformed units/day from both methods (95% CI: −0.0003 to 0.0055), which was not statistically significant ($P = .08$) (see Supplementary Appendix S3 for the Bland–Altman plot).

The manually derived units/day differed from the text-mined units/day for a several reasons. We found a small number of non-translatable Sigs. Second, our method examines the prescription Sig including the discrete and free-text fields. We aimed to maximize both the units/dose and doses/day across the entire Sig, which may overestimate the units/day because each component could potentially be derived from either the discrete portion of the Sig or the free-text portion of the Sig. In Table 2, we present examples of Sigs with different units/day from our validation process.

Validation of MEDDs

Our method calculated a Sig-MEDD for 98.3% of prescriptions, 99.99% of discrete Sigs, and 81.5% of free-text Sigs. Epic calculated a MEDD for 89.2% of all prescriptions, 98.2% of discrete Sigs, and 0% of free-text Sigs. Comparing the same prescription across both methods revealed that they were within 2 MEDDS of each other 96.07% of the time.

Of the 101 915 prescriptions, we calculated MEDDs by both methods for 90 427 prescriptions, or 88.7%. Of these 90 427 prescriptions, our algorithm resulted in an average MEDD of 45 with a standard deviation (SD) of 48. The Epic-MEDD calculation had an average MEDD of 45 with an SD of 61. The correlation between the MEDDs calculated by both methods was 0.98 (see Supplementary Appendix S2). The mean difference of the log-transformed MEDDs calculated by both methods was −0.01 (95% CI: −0.0113 to −0.0105). Although the t-test was statistically significant given the large sample size ($P < .001$), the mean difference was small and not clinically significant. The Bland–Altman scatterplot showed no systematic variation between the mean of the 2 differences (see Supplementary Appendix S4).

DISCUSSION

We were able to calculate a Sig-MEDD for nearly 90% of free-text Sigs, which allows for population health analytics of more prescriptions. A Bland–Altman analysis between the Sig-MEDD and the

Epic-MEDD reveals that the methods are comparable. Our method estimates a Sig-MEDD for a larger portion of prescriptions because we incorporate free-text instructions. Our method calculated a Sig-MEDD for 98.3% of prescriptions, 99.99% of discrete Sigs, and 81.5% of free-text Sigs. Our Sig-MEDD method performed equally well or better than other published text-parsing methods such as PredMED, MedEx, and MedXN on prescription extraction,[5] with similar levels of precision.

We envision several uses of the Sig-MEDD, including: (1) understanding prescribing behavior at the Sig level, which help design interventions to modify prescribing behavior, (2) identifying a more accurate picture of an individual's potential daily exposure, therefore helping identify risk for dependence or accidental overdose, and (3) using the Sig-MEDD to examine the role of different levels of daily opioid exposure on dose escalation.[2]

Limitations

We only used data from our EHR system, which does not include pharmacy fill data, claims data, or prescriptions documented within provider notes. Although the SQL code may not be generalizable to institutions that do not use Epic, the approach may be useful after a site analyzes their Sigs.

CONCLUSION

Using Sig-MEDD to determine a maximum potential MEDD provides greater insight into a patient's risk for opioid exposure. Our Sig-MEDD approach is generalizable to other institutions in that we parsed the majority of free-text Sigs (81.5%); clinicians at other institutions are likely to use similar free-text Sigs.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *Journal of the American Medical Informatics Association* online.

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Conflict of interest statement. None declared.

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