Impact of a Process Change on Prevalence of Prescribed Unmeasurable Liquid Doses in a Neonatal Intensive Care Unit

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OBJECTIVES Most prescribing through the electronic health record (EHR) in the NICU at St. Vincent Women's Hospital use a weight-based dosing calculator. Prescribers receive no alert if the resulting volume is unmeasurable. Study definition of measurable was a dose volume with a visible hash mark on an appropriately sized oral syringe. The primary objective was to compare the rate of unmeasurable oral liquid doses prescribed at discharge before and after implementation of educational process changes. Secondary objectives assessed patient and discharge medication characteristics in relation to the unmeasurable doses prescribed.

METHODS This study was a 2-phase retrospective analysis of patients discharged from the NICU between January 1 and June 30, 2016 (phase I), and between October 1, 2017, and March 31, 2018 (phase II). Patients were included in the analysis if they were discharged on at least 1 oral liquid medication, excluding vitamins. Demographic and discharge medication information was collected.

RESULTS There were 58 patients discharged on a total of 118 oral liquid medications in phase I and 63 patients discharged on a total of 111 oral liquid medications in phase II. Following implementation of the process change, the percentage of unmeasurable discharge prescriptions decreased from 27 (23%) to 5 (4.5%) ($p < 0.001$).

CONCLUSIONS The educational process change implemented in the NICU effectively reduced the rate of unmeasurable doses prescribed at discharge from 1 in 4 to 1 in 25. Additional system-level changes may result in further reductions.

ABBREVIATIONS CPOE, computerized prescriber order entry; EHR, electronic health record; eMAR, electronic medication administration record; H2 blocker, histamine 2 blocker; NICU, neonatal intensive care unit; PPI, proton pump inhibitor

KEYWORDS electronic prescribing; infant; medication error; medication safety; neonatal intensive care unit; patient safety

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Introduction

A significant number of errors occur with dosing of liquid medications in pediatric patients.^{1–6} This can result from caregivers misunderstanding the appropriately prescribed dosage or confusion with the appropriate way to measure the dose.^{1–6} Errors can also occur as a result of the device used by caregivers to provide the dose, such as dosing spoons, dosing cups, syringes, and kitchen spoons.^{1,3,6} If a patient's label states teaspoon or tablespoon, caregivers may be under the impression that they should use a kitchen utensil; however, this is an inaccurate measuring device for medications.¹ Additionally, devices such as a dosing cup may display more than one type of unit, such as milliliter (mL), teaspoon (tsp) and dram, which adds confusion for

the caregiver.¹ In 2016, poison control centers reported more than 14,000 cases of therapeutic mistakes that resulted from “confused units of measure” or “dispensing cup errors.”⁷ A recent study conducted by Yin et al² stratified 2110 children 8 years or younger who were randomly assigned to 1 of 5 study arms, where they were given labels and dosing tools that varied in unit pairings. Each caregiver measured 9 doses (3 amounts [2.5, 5, and 7.5 mL] with 3 tools [1 cup; 2 syringes, with 0.2- and 0.5-mL increments, respectively]), in random order.² A total of 84.4% of parents made 1 or more dosing errors, defined as greater than 20% deviation, and 21% made at least 1 large dosing error, defined as greater than 2 times the dose.²

St. Vincent Women's Hospital considers doses to be unmeasurable if they are not dosed within an incre-

Table 1. Defined Measurable Doses

Dose, mL	Smallest Syringe Increment, mL	Unmeasurable Example, mL	Measurable Example, mL
≤1	0.01	0.976	0.98
1–3	0.1	1.87	1.9
>3 to 10	0.2	3.7	3.8

ment where a hash mark would be visible on an appropriately sized oral syringe (Table 1). When patients are discharged home on unmeasurable doses such as these, there is an additional threat for confusion beyond the tool and units of measurement. This will inevitably result in a higher risk of dosing errors.

An additional source of medication errors in pediatric patients may be from computerized physician order entry (CPOE). Overall, CPOE is a beneficial component of the electronic health record (EHR) that has been shown to reduce medication error rates.^{8–11} However, medication errors related to CPOE still occur.^{8–11} A recent study by Amato and colleagues⁸ reviewed patient safety medication reports from 6 sites participating in a US FDA-sponsored project examining CPOE safety. Of the 2522 medication error reports, 51.9% were related to CPOE. Of the CPOE-related events, 13.1% of the errors were facilitated by CPOE and 86.9% could have been prevented. Most of the errors resulted from orders not routing to the appropriate location, wrong doses, and duplicate orders.⁸ The potential for errors due to the EHR's rounding of weight-based doses has anecdotally been noted at St. Vincent Indianapolis. The NICU at St. Vincent Women's Hospital in Indianapolis, IN, was selected as the location for this study in order to target the neonatal population, which was previously identified in a retrospective study evaluating 395 patients younger than 18 years, as a population with the highest prevalence of unrounded doses.¹²

Many patients discharged home from the 85-bed NICU at St. Vincent Women's Hospital are prescribed at least 1 oral liquid medication. The frequency of prescribed unmeasurable doses, high-risk medications, compounded medications, and specific drug classes was previously unknown. Prior to this study, there were not any protocols or staff education regarding the dangers of prescribing unmeasurable doses. Most prescribing for pediatric patients in the current EHR is done using a weight-based dosing calculator, with no clinical decision support alert to the prescriber if the dose is unmeasurable. Depending on the patient's weight, medication dose, and available medication concentration, a patient may be prescribed dose volumes to the thousandth decimal place or smaller.

Discharge from the NICU can be overwhelming to families for many reasons. Not only are caregivers leaving with a new child, but that child may also have unexpected medical needs that require administration of medications. Caregivers are often discharged

with prescriptions for small medication doses that are challenging to administer or are unmeasurable. For example, a dose of 0.327 mL would be unmeasurable because 1-mL syringes only allow for measurement to the nearest hundredth milliliter (i.e., 0.33 mL). If caregivers are not educated upon discharge, they may not understand how to draw up the correct amount of medication. A lack of understanding may cause caregivers to be confused and could ultimately result in a risk to the patient's safety. Appropriate processes are necessary to prevent unmeasurable doses from being prescribed. Although there is a significant amount of data regarding dosing errors associated with pediatric liquid medications, to the authors' knowledge there are no studies that consider errors associated with unmeasurable doses prescribed at discharge.

The purpose of this study was to evaluate the frequency of dose-related prescribing errors within the neonatal patient population and, based on those results, investigate whether a process change implemented within the neonatal intensive care unit could reduce the rate of unmeasurable doses prescribed at discharge. The primary objectives of this study were to first describe the proportion of prescriptions for oral liquid medications that were written for an unmeasurable dose at discharge, then to compare the rate of unmeasurable oral liquid doses prescribed at discharge before and after implementation of a process change. Secondary objectives included a description of patient and discharge medication characteristics and assessment of these characteristics in relation to the unmeasurable doses prescribed. Table 2 describes the characteristics that were investigated for the secondary objectives.

Materials and Methods

This retrospective study consisted of 2 phases. The first phase included patients discharged from the NICU between January 1, 2016, and June 30, 2016. The second phase included patients discharged between October 1, 2017, and March 31, 2018. During the interim period between the 2 phases, a process change was initiated.

Patients discharged during the first phase were identified from a list generated by the billing department. An alternate data extraction method was used in phase II because of logistical difficulties in obtaining the needed reports from the original source. Patients discharged during the second phase were identified from a discharge patient report generated through

Table 2. Factors Considered When Describing Discharge Information

Discharge patient data
Age, days
Weight, kg
Month
Discharge medication data
Total number of discharge medications
Total number of discharge oral liquid medications
Prescriber status
Drug class
High alert
Documented education provided by nurse
Dose measurability
Last dose ordered on eMAR (phase II only)
Fill history at St. Vincent pharmacy (phase II only)

eMAR, electronic medication administration record

Neodata (Lisle, IL), a data system used for daily patient care in the NICU. All patients who were discharged on at least 1 oral liquid medication were included in a primary analysis during the first phase of the study, with a secondary analysis conducted that excluded vitamins as an oral liquid discharge medication. The primary analysis will be referred to as phase Ia and secondary analysis will be referred to as phase Ib. Vitamins were excluded in phase Ib because they are prescribed in standard dose volumes of 0.5 or 1 mL based on patient characteristics instead of a weight-based dose. It was found in phase Ia that the inclusion of vitamins would inaccurately skew the data because it would affect the proportion of prescriptions with an unmeasurable dose relative to the total number of prescriptions. Therefore, patients were only included in phase II if they were discharged on at least 1 oral non-vitamin liquid medication.

Patient information was collected from AllScripts Sun-

rise Clinical Manager (Chicago, IL), the EHR used by the institution. If the patient used the hospital's outpatient pharmacy for their discharge medications, prescription information was collected from McKesson EnterpriseRx (San Francisco, CA). Sunrise Clinical Manager was used to identify if each patient was discharged on 1 or more medications and the specific, active medications at discharge when applicable. Patient demographic information, including age and weight at discharge, were collected from the EHR. Discharge medication-specific information, including name, dose, route, frequency, drug class, risk classification, prescriber status, documented discharge education, measurability, discharge dose relative to last dose on the electronic medication administration record (eMAR), and use of St. Vincent's outpatient pharmacy were also collected. Medication risk classification was determined using the St. Vincent Hospital Indianapolis' high alert medication policy (Supplemental Table 1). Measurability is defined in Table 1.

After phase I of the study was complete, it was determined that a process change for oral liquid discharge prescriptions was necessary. Therefore, between July and September 2017 education was provided to the pharmacy and provider groups at departmental meetings. The pharmacy departmental meeting included both pharmacists and technician staff, and the provider departmental meeting included neonatologists, pediatric medical residents, neonatal nurse practitioners, and physician assistants. This education consisted of presentation of the phase I study results demonstrating the problem identified within the EHR as well as the definition of measurable and unmeasurable doses. Handouts were posted at pharmacist and prescriber workstations to assist in identifying medications commonly prescribed with unmeasurable doses in phase I and to outline how to approach ordering and verifying measurable liquid doses (Supplemental Tables 2 and 3). They were instructed to determine the nearest measurable volume, and then determine what the mg dosage of that volume would be based on the drug concentration. They should then convert that dosage to a mg/kg

Table 3. Age and Weight of Patients in Phases Ib and II

	Phase Ib, Median (25th, 75th percentile)		Phase II, Median (25th, 75th percentile)		p value
	Number		Number		
Discharged on ≥ 1 oral liquid medication*	58		63		
Weight, kg		3.26 (2.86, 3.87)		3.79 (3.17, 4.69)	0.004
Age, days		48.5 (14.75, 98.5)		55 (17, 120)	0.2
Discharged on ≥ 1 oral liquid medication who had ≥ 1 unmeasurable dosage*	24		5		
Weight, kg		3.63 (3.13, 4.42)		4.62 (3, 4.69)	0.3
Age, days		70.5 (15, 113.25)		43 (17.5, 83)	0.76

* Excluding vitamins.

Figure. Proportion of Unmeasurable Dosages Prescribed (Phase Ib vs Phase II)

dose based on the patient's weight. Ongoing education from pharmacists was also provided to prescribers on weekly multidisciplinary rounds. It is well known that 1 intervention does not likely prevent an error, so multiple risk reduction strategies were implemented. For the intended purpose of redundancy, an alert was built and implemented within our automated clinical decision support software, Senti7 (Madison, WI). This alert was designed by a clinical informatics pharmacist and identified patients who were prescribed any of the medications that had been identified during phase I of this study as commonly unmeasurable, triggering the pharmacists to review the patient's order for measurability and intervene if necessary.

The analysis of outcomes used a variety of descriptive statistics to summarize the outcomes listed above. Student *t* and Mann-Whitney *U* tests were used to compare age, weight, and number of oral medications prescribed, to the frequency of measurable versus unmeasurable doses, depending on whether the samples were normally distributed or not. Inappropriate dosing rates between the 2-phase time periods were compared using a z-test of 2 population proportions. Count and categorical data were compared between the 2 phases using Pearson χ^2 tests and Fisher exact tests as well. Analysis was completed with the use of a computer software called Statistical Package for Social Sciences (SPSS), version 24.¹³ The results of statistical tests were considered statistically significant if they had a *p* value <0.05.

Results

During phase Ia, prior to the process change implementation, there were 122 patients discharged on at least 1 weight-based oral liquid medication. A total of 218 oral liquid medications were prescribed during this phase of the study, 46% of which were vitamins. The

remainder of the results will focus on phases Ib and II, where vitamins were excluded. During phase Ib, there were 58 patients discharged on at least 1 weight-based oral liquid medication. These patients were prescribed a total of 118 oral liquid medications. During phase II, after implementation of the process change, there were a total of 63 patients who were discharged on at least 1 weight-based oral liquid medication. These patients were prescribed a total of 111 oral liquid medications (Figure).

Regarding the primary outcome, the proportion of oral liquid discharge prescriptions that were written for an unmeasurable dose were 27 of 118 (23%) and 5 of 111 (4.5%) before and after the process change, respectively ($z = 4.01$, $p < 0.001$; Figure). Given the retrospective nature of the study, a convenience sample was captured. A post hoc power analysis for the primary outcome demonstrated the study was powered at 0.98%. During phase Ib, 24 patients were prescribed at least 1 unmeasurable dosage for an oral liquid weight-based medication at discharge. Of these, 3 patients were prescribed 2 unmeasurable dosages, making a total of 27 unmeasurable dosages. During phase II, 5 patients were discharged on 1 unmeasurable dosage. A summary of the ages and weights of the patient populations is in Table 3.

In terms of secondary objectives, the drug classes involved in unmeasurable dosing in phase Ib included 9 pain/withdrawal medications (33%), 7 proton pump inhibitors/histamine 2 (PPI/H2) blockers (26%), 7 antibiotics (26%), 2 classified as other (7%), 1 supplement (4%), and 1 diuretic (4%). The "other" category included levocarnitine and cetirizine. The drug classes involved in unmeasurable doses in phase II included 2 pain/withdrawal medications (40%), 1 antibiotic (20%), 1 supplement (20%), and 1 other medication (20%), which was lactulose. The proportion of unmeasurable doses

Table 4. Unmeasurable Doses Relative to Drug Class

Drug Class	Phase Ib		Phase II	
	Total No. of Medications, N = 118	Unmeasurable, n = 27, No. (%)	Total No. of Medications, N = 111	Unmeasurable, n = 5, No. (%)
Pain/withdrawal	24	9 (38)	6	2 (33)
PPI/H2 blockers	24	7 (29)	24	0 (0)
Antibiotic	22	7 (32)	19	1 (5)
Other	16	2 (13)	18	1 (6)
Diuretic	13	1 (8)	26	0 (0)
Antiepileptic	6	0 (0)	13	0 (0)
Steroid	5	0 (0)	0	0 (0)
Benzodiazepine	5	0 (0)	0	0 (0)
Supplement	3	1 (33)	5	1 (20)

H2, histamine 2 receptor; PPI, proton pump inhibitor

relative to drug class was similar to the overall distribution of unmeasurable doses within the total (Table 4).

Among all phases there were 7 high alert medications, which accounted for 16 discharge prescriptions, all of which were measurable. This included 6 prescriptions for propranolol, 4 for phenobarbital, 2 for methadone, 1 for lorazepam, 1 for desmopressin, 1 for morphine, and 1 for oxcarbazepine. Nurse-provided discharge medication education was documented on 45 of the 118 oral, liquid, weight-based prescriptions in phase Ib (38%) and 97 of the 111 oral liquids in phase II (87%). This education was documented on 12 of the 27 (44%) and 2 of the 5 (40%) unmeasurable dosages prescribed in phases Ib and II, respectively ($z = 0.18$, $p = 0.86$; Table 5).

The percentage of unmeasurable prescriptions in relation to total number of prescribed discharge medications was similar for all prescriber statuses in both study phases (Table 6). The percentage of unmeasurable prescriptions decreased for each prescriber status before and after implementation of the process change. Neonatologist unmeasurable prescribing decreased from 24% to 4% ($z = 3.72$, $p < 0.001$), physician assistants/nurse practitioners from 19% to 6% ($z = 1.06$, $p = 0.29$), and pediatric residents from 25% to 0% ($z = 1.07$, $p = 0.28$).

The last dose ordered on the eMAR in relation to what the patient was discharged on was only investigated during phase II of the study. In this phase, the discharge medication matched the last dose ordered on the eMAR for 88 prescriptions (79%), did not match the eMAR for 21 (19%), and was not on the eMAR at all for 2 prescriptions (2%). Of the 5 unmeasurable doses, 4 (80%) did not match the last prescribed order on the eMAR and 1 (20%) was not on the eMAR at all. Of the 4 that did not match the last prescribed order on the eMAR, 2 of these were measurable on the eMAR and 2 were unmeasurable. There were a total of 17 prescriptions that were measurable upon discharge but did

not match the last order prescribed on the eMAR. Of these 17 prescriptions, the last order on the eMAR was unmeasurable in 11 instances and measurable (with a different dose than at discharge) in 8 instances. The St. Vincent pharmacy was used for 8 of 111 discharge prescriptions (7%), and all of the medications that were filled there were measurable ($p = 1.00$).

Discussion

Although the EHR can positively influence medication safety, the EHR's inability to round oral liquid doses can cause a significant safety issue. This was confirmed during phase I of this study where specific areas for focused process improvement were identified. Approximately one-quarter of all weight-based oral liquid prescriptions, excluding vitamins, were unmeasurable prior to the implementation of a process change. It is clinically significant and concerning that 1 in 4 parents left the NICU with an unmeasurable dose for their child. Studies have shown that even when parents are provided with measurable doses for their children, administration errors are made.¹⁻³ By sending patients home with unmeasurable doses, an additional barrier to appropriate drug administration is introduced. Patients are at risk of a dosing error if their caregiver is unable to accurately measure their medication. When faced with an unmeasurable dose, parents who are unfamiliar with the appropriate way to round a dose might round outside of what would normally be considered a negligible range (i.e., 10%).

Based on the Institute of Safe Medication Practices' error reduction strategy hierarchy, system-based changes are the highest-level risk reduction strategy.¹⁴ Unfortunately, because of logistical and system-based challenges, a change within the EHR was not possible in this study. A lower-level risk reduction strategy that involved automated clinical decision support and education was implemented. Although the process change did not involve the highest-level risk reduction strate-

Table 5. Documented Discharge Education Provided by Nurse

	Education Documented, n (%)		Total No. of Prescriptions
	No	Yes	
Phase Ib			
Measurable prescription	58 (64)	33 (36)	91
Unmeasurable prescription	15 (56)	12 (44)	27
Total prescriptions	73 (62)	45 (38)	118
Phase II			
Measurable prescription	11 (10)	95 (90)	106
Unmeasurable prescription	3 (60)	2 (40)	5
Total prescription	14 (13)	97 (87)	111

gies, it did lead to a positive and statistically significant improvement in unmeasurable doses prescribed at discharge. The process change effectively produced a 4-fold reduction in the rate of unmeasurable doses prescribed at discharge.

The trend in the age of patients included in the study was similar in both phases. Although the weight between the 2 phases was statistically and potentially clinically different, this difference would not likely impact the dose measurability for one group versus the other because any weight used has the potential to result in an unmeasurable volume. For example, a prescription for 15 mg/kg acetaminophen 160 mg/5 mL would result in an unmeasurable dose if not rounded regardless of whether the patient weighed 2.8 kg vs 3.4 kg. In phase Ib, the most common drug classes associated with unmeasurable dosing included pain/sedation medications, PPI/H2 blockers, and antibiotics. Pain/sedation and antibiotics were seen as unmeasurable in phase II as well. Of all pain/withdrawal medications prescribed, 38% (9 of 24) were unmeasurable in phase I and 33% (2 of 6) were unmeasurable in phase II. The most common pain/sedation medication that was unmeasurable in both phases was acetaminophen. Although it is well known that if dosed incorrectly acetaminophen can have dangerous consequences, it is possible that because it is an over-the-counter product, health care professionals may take fewer precautions with this medication. Of all of the PPI/H2 blockers prescribed, 29% (7 of 24) were unmeasurable in phase I and none were unmeasurable in phase II.

High alert medications accounted for a small percentage of discharge prescriptions. All of these prescriptions were measurable in both phases. This was not unexpected, because high alert medications are often treated with extra caution; however, only 16 high alert prescriptions were identified, so the ability to draw generalizable conclusions is limited.

A disconnect continues to be evident between discharge counseling and dose measurability at discharge, because in both phases almost half of the unmeasurable medications had documentation of discharge

counseling provided by a nurse. This demonstrates that discharge medication education was provided on a medication with an unmeasurable dose that was either not recognized or not corrected. These results illustrate the need to educate staff on the importance of double-checking measurability prior to discharge counseling. Caregivers need to not only be educated on the indication and adverse effects of a medication, but also on how to appropriately measure and administer medications to the patient, including over-the-counter medications. The first step in this process is for the health care professional providing the education to assess the dose and determine if that dose is measurable. If unmeasurable, the prescriber should be contacted to adjust the dose to a measurable amount. If the dose is measurable, it is vital that the caregiver understand how to appropriately measure and administer the dose.

There was no association between prescriber status and unmeasurable doses in either phase of the study. Medical residents did not prescribe any unmeasurable doses in phase II, but given the low overall number of unmeasurable doses seen in this phase, it is difficult to generalize this finding. This indicates that with respect to unmeasurable dosing, experience and training level did not affect the results of this study. Errors do not appear to be knowledge-based, but instead system-based. Therefore, all prescriber statuses need continued education on the challenges with weight-based dosing and the EHR. There was a statistically significant decrease in unmeasurable prescribing by neonatologists in phase II compared with phase Ib. Although the physician assistants/nurse practitioners and pediatric residents did not have a statistically significant decrease, it can be argued that because they have a lower prescription volume, the decrease in unmeasurable doses is still clinically significant.

For approximately 1 in 10 prescriptions in phase II, the last ordered dose on the eMAR was unmeasurable, yet the discharge prescription was measurable. This implies that prior to discharging the patient, an intervention was made, suggesting success of the process change implemented in the NICU prior to

Table 6. Discharge Prescriptions by Prescriber Status

	Medication Provided by Prescriber Status, n (%)		Total No. of Prescriptions
	Measurable	Unmeasurable	
Phase Ib			
Neonatologist	65 (76)	20 (24)	85
Physician assistant/nurse practitioner	17 (81)	4 (19)	21
Resident (PGY 2/3)	3 (75)	1 (25)	4
Unknown*	6 (75)	2 (25)	8
Total prescriptions	91 (77)	27 (23)	118
Phase II			
Neonatologist	88 (96)	4 (4)	92
Physician assistant/nurse practitioner	14 (93)	1 (7)	15
Resident (PGY 2/3)	4 (100)	0 (0)	4
Unknown*	0 (0)	0 (0)	0
Total prescriptions	106 (95.5)	5 (4.5)	111

PGY 2/3, postgraduate medical resident years 2 or 3

*Provider who wrote prescription was not specified in the discharge reconciliation or discharge summary

phase II. The prescriber may have corrected the dose prior to discharge or a pharmacist may have made an intervention on multidisciplinary rounds.

Additionally, it was anecdotally noted that there were instances where at some point during the patient's hospitalization, there was an unmeasurable dose on the eMAR even though the last dose ordered on the eMAR and the discharge prescription were measurable. This demonstrates there are still changes that need to be implemented to further reduce and prevent unmeasurable doses from being ordered while the patient is hospitalized. A pharmacist dose-rounding policy, for example, would allow pharmacists to round orders entered by prescribers to measurable doses within a reasonable amount without requiring a call to a prescriber. An EHR system that automatically rounds to measurable dosing would be an ideal solution, although this might not be feasible with all EHR systems.

There were several limitations to this study. Discharge patients were identified through 2 different processes from phase I to phase II because of logistical difficulties in obtaining the needed reports from the original source in a timely manner. However, once patients were identified, the data collections were completed the same way. The number of patients discharged during the study period was lower than expected and resulted in a small sample size. Because this was a retrospective chart review, it was not possible to determine what instruction caregivers were given about medication administration prior to discharge. Although other institutions may see a similar problem and this study may highlight opportunities for change when using EHRs and weight-based dosing, the results are specific to this institution and EHR, which limits

generalizability.

The implementation of a process change involving use of automated clinical decision support software and education effectively reduced the rate of prescription of unmeasurable doses at discharge in the NICU at St. Vincent Women's Hospital. This reduction was both statistically and clinically significant, when considering that prior to the intervention almost 1 in 4 patients left the NICU with an unmeasurable dose and this was reduced to 1 in 25. The importance of this change is heightened because of the vulnerability of this population.

Additional system-level changes may result in further reductions, with an end goal of eliminating prescribing of unmeasurable doses. Given the overall success of the educational and automated decision support intervention, consideration will be given to expanding to pediatric units across the statewide health system.

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Supplemental Material

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