JAMIA Open, 4(2), 2021, 1–10 doi: 10.1093/jamiaopen/ooab039 Brief Communications



OXFORD

# **Brief Communications**

# Design, development, and deployment of an indicationand kidney function-based decision support tool to optimize treatment and reduce medication dosing errors

Jamie S. Hirsch (),<sup>1,2,3</sup> Rajdeep Brar,<sup>1</sup> Christopher Forrer,<sup>1</sup> Christine Sung,<sup>1</sup> Richard Roycroft,<sup>1</sup> Pradeep Seelamneni,<sup>1</sup> Hemala Dabir,<sup>1</sup> Ambareen Naseer,<sup>1</sup> Pranisha Gautam-Goyal (),<sup>4</sup> Kevin R. Bock,<sup>1,5,#</sup> and Michael I. Oppenheim<sup>1,4,#</sup>

<sup>1</sup>Department of Information Services, Northwell Health, New Hyde Park, New York, USA, <sup>2</sup>Division of Kidney Diseases and Hypertension, Department of Medicine, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Great Neck, New York, USA, <sup>3</sup>Center for Health Innovations and Outcomes Research, Institute of Health System Science, Feinstein Institutes for Medical Research, Manhasset, New York, USA, <sup>4</sup>Division of Infectious Diseases, Department of Medicine, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Manhasset, New York, USA, and <sup>5</sup>Department of Pediatrics, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, USA

<sup>#</sup>Co-senior authors with equal contribution.

Corresponding Author: Jamie S. Hirsch, MD, MA, MSB, Department of Information Services, Northwell Health, 100 Community Drive, 2nd floor, Great Neck, NY 11021, USA; jhirsch8@northwell.edu

Received 20 January 2021; Revised 13 April 2021; Editorial Decision 23 April 2021; Accepted 26 April 2021

#### ABSTRACT

Delivering clinical decision support (CDS) at the point of care has long been considered a major advantage of computerized physician order entry (CPOE). Despite the widespread implementation of CPOE, medication ordering errors and associated adverse events still occur at an unacceptable level. Previous attempts at indicationand kidney function-based dosing have mostly employed intrusive CDS, including interruptive alerts with poor usability. This descriptive work describes the design, development, and deployment of the Adult Dosing Methodology (ADM) module, a novel CDS tool that provides indication- and kidney-based dosing at the time of order entry. Inclusion of several antimicrobials in the initial set of medications allowed for the additional goal of optimizing therapy duration for appropriate antimicrobial stewardship. The CDS aims to decrease order entry errors and burden on providers by offering automatic dose and frequency recommendations, integration within the native electronic health record, and reasonable knowledge maintenance requirements. Following implementation, early utilization demonstrated high acceptance of automated recommendations, with up to 96% of provided automated recommendations accepted by users.

Key words: clinical decision support medication drug dosing medical error kidney antimicrobial stewardship

© The Author(s) 2021. Published by Oxford University Press on behalf of the American Medical Informatics Association.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

#### LAY SUMMARY

Delivering clinical decision support at the point of care has long been considered a major advantage of computerized physician order entry, yet despite widespread implementation, medication ordering errors, and associated adverse events still occur at an unacceptable level. Previous attempts with decision support that have included intrusive interruptive alerts have been marred by poor usability and acceptance. This descriptive work describes the design, development, and deployment of the Adult Dosing Methodology module, a novel decision support tool that provides indication- and kidney-based dosing at the time of order entry. The module aims to decrease order entry errors and burden on providers by offering automatic dose and frequency recommendations, integration within the native electronic health record, and reasonable knowledge maintenance requirements. Following implementation, early utilization demonstrated high acceptance of automated recommendations, with 96% of automated recommendations accepted by users.

#### INTRODUCTION

Clinical decision support (CDS) has positively impacted patient care processes such as timeliness of preventive services, <sup>1–3</sup> adherence to appropriate care pathways,<sup>4–8</sup> and medication safety.<sup>9–12</sup> However, while CDS can decrease medication error rates,<sup>13–16</sup> they can also facilitate them<sup>17</sup> when not designed and implemented carefully.

Approximately 19% of adverse events in hospitalized patients are related to medications<sup>18</sup> and are associated with excess morbidity, mortality, costs, and length of stay.<sup>19</sup> Studies have shown that 28%–52% of adverse drug events (ADEs) are preventable and 56%–77% are rooted in the stage of medication ordering.<sup>20–22</sup> Drugs cleared by the kidneys are particularly problematic, with ADEs occurring at an unacceptable rate of 10% in 1 study, with 91% being preventable.<sup>23</sup>

Patients with underlying acute or chronic kidney disease are at high risk of medication errors and ADEs,<sup>24</sup> with antimicrobials a particular risk area.<sup>25–27</sup> Providers are often unaware of necessary adjustments, 28,29 and while pharmacist interventions are helpful, they are resource intensive.<sup>30,31</sup> CDS alerts for appropriate kidneybased adjustments have shown marginal improvements and a low level of user acceptance,<sup>32–35</sup> with less than 20% medication adjustment in 1 study<sup>36</sup> and only about 50% in another.<sup>24</sup> The lack of significant impact may be due to the interruptive alert strategy, which directs the user's action while still requiring additional steps.<sup>37</sup> Although many forms of CDS exist, including alerts, visual reminders, order sets, and smart forms, interruptive alerts have been studied most commonly, and the well-cited development of alert fatigue can habituate users to ignore alerts,<sup>38</sup> despite the alerts largely providing clinically appropriate recommendations.35,39 Early attempts at guided dosing for kidney disease built into homegrown electronic health record (EHR) systems proved effective at reducing inappropriate orders, although half of orders were still deemed inappropriate. This system also did not incorporate indication-based dosing; has not been translated into modern vendor-based EHRs; and presented only 3 categories of kidney dysfunction, neglecting the nuances of medication-specific ranges or cutoffs.<sup>40</sup>

Optimizing antimicrobial therapy duration is a key component of antimicrobial stewardship programs.<sup>41</sup> Avoiding excessive durations of antimicrobial use<sup>42</sup> has been shown to decrease the incidence of colonization or invasive infection with resistant organisms<sup>43–46</sup> and decrease the incidence of *Clostridioides difficile* infection.<sup>43,46,47</sup> Studies examining CDS for appropriate stewardship are limited, but have shown successes in specific uses cases, including intravenous immunoglobulins.<sup>48</sup>

When considering appropriate medication dosing, CDS that recommends appropriate antibiotics<sup>49,50</sup> and related orders<sup>51</sup> have been described. There have been fewer efforts describing automated, indication- and kidney function-based dosing recommendations in the health informatics literature.<sup>24,52</sup>

We describe the planning, design, development, and deployment of an innovative CDS tool, the Adult Dosing Methodology (ADM) module, embedded within the medication ordering process of the EHR. The primary goal was to improve EHR usability while reducing the incidence of medication errors with automated dose, frequency, and duration calculation, accounting for age, weight, indication, kidney function, and clinical conditions. By optimizing ordering in an intuitive manner, we believe that this form of CDS will be more widely accepted and prove to be far more effective than traditional forms of decision support such as traditional burdensome interruptive alerts, informational boxes, or notifications outside of the EHR.

# MOTIVATION AND DEVELOPMENT GOVERNANCE

The ADM module was developed at Northwell Health in New York, and deployed into the enterprise acute care EHR, Sunrise Clinical Manager (Allscripts, Chicago, IL, USA), which is used at 13 acute care hospitals, covering approximately 700 000 emergency department visits and 280 000 inpatient discharges annually. Smaller, community hospitals that were recently integrated into the health system but not yet on the enterprise EHR were not included in the rollout.

Prior to ADM implementation, medication orders followed a standard workflow. Some medications had a limited form of CDS, including dose checking with informational interruptive alerts for significantly out-of-range values, although this was not widely implemented. A clinical pharmacist verified all medication orders but had no form of CDS to ensure appropriate dose, frequency, or duration.

Given significant override rates with traditional interruptive alerts<sup>53–55</sup> and ensuing alert fatigue,<sup>56</sup> leadership teams from quality, medicine, pharmacy, and informatics embarked on the development of the ADM module. Planning began in December 2017, with full deployment by June 2019. The 1.5-year development included preparatory planning; stakeholder alignment; medication clinical guideline finalization; conversion of guidelines to database format; kidney dose adjustment logic design, build, and testing; module coding and development; system testing; end-user testing; end-user education; and system-wide deployment. Despite the lengthy initial development, the system was designed for efficient management of

medication dosing updates or addition of new medications, with simple database table updates.

Clinical governance and oversight were provided by health system leadership in collaboration with internal multidisciplinary thrombosis and antimicrobial stewardship committees, as well as leadership from the fields of infectious diseases and kidney diseases. Clinical guidelines with recommendations and content were translated into a reference table, computable by the EHR, which included the following attributes: medication name; indication; age range cutoffs; weight adjustments; dialysis status; and kidney function ranges [using serum creatinine and estimated glomerular filtration rate (eGFR)]. For each unique combination of attributes, the appropriate dose, dose ranges, dose unit of measure, frequency, and duration are specified in the Supplementary Table S1. The initial list of medications included the therapeutic classes of antithrombotics (anticoagulants and antiplatelets) and antimicrobials (Table 1), as they represent high volume and/or impact medications with significant risk for adverse events.

Prior to implementation, the module underwent hundreds of hours of rigorous testing, including evaluation of each row in the reference table, as well as clinical scenario-based end-user testing. Approximately 860 rows and dozens of clinical scenarios were exhaustively reviewed and tested (see Supplementary Table S2, eg, scenario used in testing and a detailed explanation of the testing process). Three different education and marketing mediums were prepared in parallel: prerecorded, on-demand video instruction; presentations and announcements in numerous clinical forums and meetings; and individual hospital representative education. The ADM module went live across all hospitals on the enterprise EHR simultaneously with concurrent elimination of all prior ordering methods for the impacted medications for all patients, thus obviating workarounds and CDS avoidance.

#### **ADM MODULE**

By retaining the native EHR look and feel, and integrating directly into the medication ordering workflow, the ADM module was designed to be intuitive and user-friendly, without need for significant end-user training. Upon medication selection from the order entry screen, a simple action window appears requiring the ordering provider to select an indication for the given medication (Figure 1A). Once chosen, the module accesses the reference table and uses the patient's height, weight, body mass index (BMI), kidney function and stability, dialysis status, and presence of contraindications to select the appropriate medication dose, frequency, and duration. This process occurs for all patients for the medications included in the ADM module, including those with normal kidney function (as these patients also benefit from dose, frequency, and duration CDS optimization). If no satisfactory indication is listed, the provider has the option to select "Other," manually enter a free-text indication, and complete the medication order form without any decision support of automated dose, frequency, or duration (see Figure 1A).

The medication order form is automatically completed, allowing the ordering provider to simply review the information and submit without additional data entry (Figure 1B). To maintain flexibility, the ordering provider can override the module-calculated dose or frequency, although a justification is mandatory. Upon order submission, standard pharmacist verification and dispensing processes are followed.

For patients receiving any form of kidney replacement therapy, a dropdown list is available in the initial indication window to designate that status (Supplementary Figure S1). In the current ADM module version, automated ascertainment of dialysis status was not possible given inter-hospital variability in the documentation.

If any automatic adjustments are made to the medication dose or frequency beyond standard regimens, various notifications are presented to the ordering provider (Table 2). Simple adjustments based upon kidney function or dialysis status are indicated as such on the order form (Supplementary Figure S2 and Table 2). If automated dosing recommendations are unavailable due to missing data (eg, relevant necessary labs), similar notifications are present. If necessary, the ordering provider does have the opportunity to change the patient's recorded height and weight values to recalculate the BMI at the time of order entry. For circumstances where a medication is contraindicated; the kidney function is unstable; or medication dosing is complex, order form notifications and interruptive alert messages appear (Supplementary Figure S3 and Table 2), and the provider must determine proper dosing.

# **ADM LOGIC**

The ADM module follows a series of logical steps (Figure 2), beginning with evaluation of kidney replacement (ie, dialysis) status, kidney function, and kidney function stability. If the patient is receiving dialysis therapy, then the appropriate dose/frequency is provided, if available. For patients not on dialysis but with unstable kidney function (and concern for acute kidney injury), automated calculations are unavailable given the complexity of medication dosing<sup>26</sup> and the infeasibility of automated calculations.<sup>57</sup> Unstable kidney function was defined as either a rising serum creatinine, defined as  $\geq$ 50% increase from nadir in a 96-h period, or a falling serum creatinine, defined as a  $\geq$ 25% decrease from peak in a similar timeframe. These values represent significant changes in kidney function whereupon automated calculations would be unreliable.

If the patient's kidney function is stable, the module checks for contraindications. Many medications are contraindicated with reduced kidney function given the risk for ADEs. In this scenario, no automated recommendation is made, and an interruptive alert is shown instead (see Table 2). Upon kidney function stability and lack of contraindication determination, the system reviews the patient's body metrics (eg, height, weight, BMI, etc.) in situations where these parameters impact the calculations.

To account for variations in assessment of kidney function in the extremes of body habitus (obesity or severe malnutrition), age, or illness,<sup>58,59</sup> the module evaluates 2 different estimating equations: the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) eGFR<sup>60</sup> and the Cockcroft-Gault creatinine clearance.<sup>61</sup> If both the absolute difference between the 2 values is >30% and a discrepant dose recommendation exists, the automated system does not provide a recommendation. The module otherwise follows the result of the CKD-EPI eGFR results for all medications, based upon health system clinical guidance (Supplementary Table S3). The value of 30% was selected based upon an analysis of 416 574 serum creatinine values (the primary variable in both equations), which found that the 2 equations are within 30% of each other 93% of the time. Instances where the 2 estimating values are highly discrepant leading to a difference in dose recommendations, an alert fires notifying the provider that "Renal function estimating equations may be inaccurate" (see Table 2).

At the conclusion of the logical sequence, the system identifies the correct row in the reference table from which to gather the relevant dosing/frequency/duration information, which is then automat-

Table 1. Initial medications included in the ADM module and post-implementation usage

		Pre-implemen- tation of ADM module				Post-imple	mentation of ADM	module		
Medication M class	Aedication name	Orders placed in 2018, $n$	Orders placed within 90 days of ADM implemen- tation, <i>n</i>	Orders with avail- able dosing rec- ommendation, $n$ $(\%)^a$	Orders where recommendation was accepted by provider, $n (\%)^{b}$	Orders where recommendation was rejected by provider, $n$ (%) <sup>b</sup>	Orders without available dosing recommendation, $n (\%)^a$	Orders with missing data precluding dos- ing recommendation, $n (\%)^{c}$	Orders with clinical situation precluding dosing recommendation, $n$ (%) <sup>c</sup>	Orders where provider en- tered "Other" indication pre- cluding dosing recommendation, $n$ (%) <sup>c</sup>
Anticoagulant Alt	teplase	1612	412	345 (84)	320 (93)	25 (7)	67 (16)	39 (58)	0 (0)	28 (42)
Ap	vixaban	18601	6604	3279 (50)	3165 (97)	114(3)	3325 (50)	1048(32)	612 (18)	1665(50)
$\mathrm{D}^{\hat{a}}$	abigatran	1287	228	153 (67)	141 (92)	12 (8)	75 (33)	19 (25)	22 (30)	34 (45)
Ri	varoxaban	9830	2557	1523(60)	1426(94)	97 (6)	1034 (40)	343 (33)	259 (25)	432 (42)
Antiplatelets Cl.	opidogrel	32088	8184	5664 (69)	5542 (98)	122 (2)	2520 (31)	0 (0)	0 (0)	2520(100)
Pri	asugrel	747	177	89 (50)	85 (96)	4 (4)	88 (50)	30 (34)	0 (0)	58 (66)
Tic	cagrelor	5031	1426	1177(83)	1147(98)	30 (2)	249 (17)	0 (0)	0 (0)	249 (100)
AntimicrobialsCe	ftriaxone	77273	18915	11898~(63)	11 546 (97)	352 (3)	7017 (37)	0 (0)	0 (0)	7017 (100)
$\mathrm{D}^{\hat{a}}$	aptomycin	2050	526	200 (38)	151 (76)	49 (24)	326 (62)	27 (8)	76 (23)	223 (69)
En	tapenem	6831	1624	918 (57)	889 (97)	29 (3)	706 (43)	164(23)	194(28)	348 (49)
Im	iipenem/	806	44	35 (80)	22 (63)	12 (37)	9 (20)	4 (44)	5 (56)	0 (0)
-	cilastatin									
W	eropenem	17961	4722	2338 (49)	2135 (91)	203 (9)	2384 (51)	235 (10)	1050(44)	1099 (46)
Pi	peracillin/	60148	17959	16648~(93)	16101(97)	547 (3)	1311 (7)	290 (22)	1021 (78)	0 (0)
	tazobactam									
Totals		234 265	63378	44 267 (70)	42 670 (96)	1596 (4)	19111 (30)	2199 (12)	3239 (17)	13673(71)
Note: The list in	ncluded medic	cations from the	classes of antithrom	botics (anticoagulan	ts and antiplatelets) a	nd antimicrobials. The	e table demonstrates	the general utilization in	the year preceding AD.	M implementation and in the 90

days post go-live, including the frequency of provided recommendations and how often they were followed or overridden.

Abbreviation: ADM: Adult Dosing Methodology.

aPercent is calculated as total number of orders in cell divided by number of orders placed within 90 days. bPercent is calculated as total number of orders in cell divided by number of orders with available dosing recommendation. cPercent is calculated as total number of orders in cell divided by number of orders without available dosing recommendation.



daptomycin		_
Order Cost Rating	Solutions	
DAPTOmycin IVPB .		
*This is a Northwell Health Restricted Medication* This is a Look-alike/Sound-alike Medication	DAPTOmycin IVPB	
	Indications:	
	Complicated skin and skin structure infections (cSSSI)	
	Empiric dosing	
	Osteomyelitis	
	Septic joint infection	
	Staphylococcus aureus bloodstream intection	
	Vancomycin-resistant Enterococcus pacteremia	
	Vancomycin-resistant Enterococcus infections (UTL without bacteremia)	
	Other	
	-	
	Stat and then	
	Base solution: codium chloride 0.0%	
	Sodium chionae 0.976	
	Diaborie Stature	
	Patient is not on dialysis	
	Submit	
DL8Drawin NBE	Drider ID	
ted Bp	Template Name DAPROmycin IVPB .	
"This is a Northwell Health Restricted Medication"     This is a Look-alike/Sound-alike Medication		
Name Equivalent		
Metros Crestinine Gearance (Estimated (Cockord Gasti))	Relevant Results	
74.8         74.8         1.12         27.4         1.10         67.9         Estimated           12.Jan-2021 12:13         12.Jan-2021 12:13         12.Jan-2021 06:36         67.9         Estimated	a	
g Alert	Prescribing Information Duration of therapy: 4 - 6 weeks	
ation Adult Calc Info	System Calc Info Dose Override Dose	Override Reason
myetts Calculator : (6 mG AG) Calculator 20 mG		
& Then	Frequency Override Freq	Override Reason
	Tanàna amin'ny fisiana	
Units Route	Preparacy internative approximation (Constraint)	
Uots Paule P	rregionery international and a second secon	Time

Figure 1. Screenshot of Adult Dosing Methodology (ADM) module. Embedded in workflow of medication ordering process within electronic health record. (A) Example indication window of ADM and (B) example of completed order form. The indication window provides the medication-specific recommended indications, along with default options for fluid diluent (where applicable) and dialysis status, with ability for direct override. After selecting the indication, the order form is automatically completed (including dose, frequency, and duration) and available for provider review, prior to submission.

ically populated into the medication order form for the provider to review and submit.

The coding of the module with Medical Logic Modules in Arden syntax,<sup>62</sup> stored procedures, and relational database tables, follows best practices per the EHR vendor guidelines. It leverages the cache of patient data loaded as part of normal processes to avoid repeated database queries. The technical teams created modular code for quick turnaround of future enhancements. The reference table was designed specifically to facilitate timely updates without requiring module coding updates.<sup>63</sup> This design also facilitates straightforward incorporation of new knowledge or data into the logic and reference table that may impact dosing recommendations, including pharmaco-genetic or other information (which can be done by inserting an additional logic statement into the code and a new column into the table).

For any updates to ADM logic, the degree of regression testing required is determined by the level of impact. More extensive changes require full execution of all functional testing scenarios, though full execution of rows in the reference table are only necessary if changes are made to the row content. Instead, execution of separate detailed logic functional test scripts, which capture all the logic scenarios and include approximately 5% of the dosing table scenarios, are performed to validate any logic changes. As part of testing, analysts detected no noticeable system performance impact with module implementation.

The ADM module was designed to store all the data points that lead to a specific recommendation in an easily retrievable part of the EHR database as well as on the order form directly, in order to facilitate retrospective analysis for research and quality assurance pur-

Table 2. Adult Dosing Me	thodoloav orderina sc	enarios that result in n	otification or interruptive alert

Ordering scenario	Alert message	Alert location
Missing serum creatinine laboratory value	Automated dose adjustment is unavailable due to the lack of a recent creatinine mea- surement	Displayed on medication order form
Missing eGFR value	Automated dose adjustment is unavailable due to the lack of a recent CKD-EPI eGFR measurement	Displayed on medication order form
Unstable kidney function with rising serum creatinine	This patient's creatinine is unstable, which may represent acute kidney injury. As eGFR is inaccurate, use caution in dosing {insert MEDICATION}, and contact pharmacy and/or nephrology for further guidance	Interruptive alert and displayed on medica- tion order form
Unstable kidney function with falling serum creatinine	This patient's creatinine is unstable. As eGFR is inaccurate, use caution in dosing {insert MEDICATION}, and contact pharmacy and/or nephrology for further guidance	Interruptive alert and displayed on medica- tion order form
Unstable kidney function with both rising and falling serum creatinine	This patient's creatinine is unstable, which may represent acute kidney injury. As eGFR is inaccurate, use caution in dosing {insert MEDICATION}, and contact pharmacy and/or nephrology for further guidance	Interruptive alert and displayed on medica- tion order form
Automated dose adjustment made for re- duced kidney function	This medication has been dose-adjusted for reduced kidney function (CKD-EPI eGFR {insert GFR} mL/min/1.73 m <sup>2</sup> )	Displayed on medication order form
Automated dose adjustment made for hemo- dialysis	This medication has been dose-adjusted for hemodialysis dosing	Displayed on medication order form
Automated dose adjustment made for hemo- dialysis, with medication requiring thrice weekly administration	The recommended dose/frequency for {insert MEDICATION} is 3 times per week, dosed after hemodialysis. Order via Frequency <user schedule=""> &gt;&gt; Weekly &gt;&gt; select appropriate days</user>	Interruptive alert and displayed on medica- tion order form
Automated dose adjustment made for peri- toneal dialysis	This medication has been dose-adjusted for peritoneal dialysis dosing	Displayed on medication order form
Automated dose adjustment made for CRRT	Dose adjustment for {insert MEDI- CATION} is complex in patients receiv- ing CRRT. Contact pharmacy and/or nephrology for further guidance	Interruptive alert and displayed on medica- tion order form
Contraindicated medication ordered	Use caution in ordering {insert MEDI- CATION} in this patient with advanced kidney disease (CKD-EPI eGFR {insert GFR} mL/min/1.73 m <sup>2</sup> ). Consider alterna- tive medication or contact pharmacy and/ or nephrology for guidance	Interruptive alert and displayed on medica- tion order form
Discrepant kidney function estimating equa- tions	Renal function estimating equations may be inaccurate in this patient and automated dosing recommendations are unavailable. Use clinical judgment when ordering, or contact pharmacy and/or nephrology for further guidance	Interruptive alert and displayed on medica- tion order form
Unable to identify an appropriate single row from reference table	Automated dosing recommendations are unavailable for {insert MEDICATION}. Use clinical judgment when ordering, or contact pharmacy and/or nephrology for further guidance	Interruptive alert and displayed on medica- tion order form

Abbreviations: CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration; CRRT: continuous renal replacement therapy; eGFR: estimated glomerular filtration rate.



Figure 2. Flow diagram of Adult Dosing Methodology module logic. The decision support module follows a series of logical steps to identify the correct dose, frequency, and duration of an ordered medication. This includes checking for use of kidney replacement (dialysis), presence of required laboratory tests, kidney function stability, presence of contraindications, and additional checks of kidney function estimating equations and impact of body habitus on dosing. At the end of the sequence, the row in a reference table containing the correct information is identified, and the data are populated into the electronic health record medication order form. The ordering provider is then able to simply review the completed form and submit the desired order.



Figure 3. Distribution of decision support provision from Adult Dosing Methodology module during the first 90 days after implementation. A total of 63 378 orders were entered, of which 44 267 (70%) had an automated recommendation provided, with user acceptance of the recommendation in 42 670 (96%) orders and user override in 1596 (4%). Of the 19 111 (30%) orders without available recommendation, the cause was missing data in 2199 (12%), clinical conditions precluding accurate automated recommendation [eg, unstable kidney function; 3239 (17%)], and user selection of "Other" as indication in 13 673 (71%).

poses. Any updates to the underlying code or reference tables are stored as versions in a relational database.

lection of "Other" as indication in 13673 (71%). This latter scenario was designed to facilitate cases where an indication was not yet built. By forcing the user to free-text an indication, this field could be mined to inform future indication additions to the system.

# ADM UTILIZATION

During the first 90 days following ADM implementation, the system was used for a total of 63 378 orders, of which 44267 (70%) had an automated recommendation provided (see Table 1 and Figure 3). Users accepted the recommendation for 42 670 (96%) orders and overrode it in 1596 (4%). Of the 19 111 (30%) orders where a recommendation was unavailable, the cause was missing data in 2199 (12%), clinical conditions precluding accurate automated recommendation [eg, unstable kidney function; 3239 (17%)], and user se-

#### DISCUSSION

CDS that minimizes burden on clinicians and seamlessly fits into workflow has been challenging to achieve. Almost 20 years ago, Bates et al<sup>64</sup> described the "10 commandments" for CDS, including speed, avoidance of stopping mechanisms, improved usability, and fitting into the workflow. Combined with the 5 rights of decision

support,<sup>65</sup> a reliable framework for novel CDS—such as the ADM module—can be designed, implemented, and evaluated.

Medication ordering and dosing is a highly complex process, with significant possibility for error and adverse events.<sup>18–23</sup> For highly susceptible populations, including geriatrics and those with kidney disease, the risks are even higher.<sup>24,66</sup> CDS too often has marginal efficacy in this domain, often due to its interruptive and non-actionable design.<sup>8,24,36,38</sup> An early attempt within a home-grown EHR showed moderate effectiveness, although it lacked nuance for varying degrees of kidney function or dosing indication.<sup>40</sup>

By automatically calculating and inputting the correct dose, frequency, and duration, we designed the ADM module to avoid alert fatigue and make medication ordering easier while lowering patient risk, especially around highly complex and error-prone activities of medication ordering. The module was developed with stakeholder alignment and input from expert committees. Following systemwide implementation in the EHR, informal feedback has been positive with effectiveness evaluations ongoing. Utilization statistics demonstrate a high level of engagement and acceptance of the system, with 70% of included medication orders providing an automated recommendation, and 96% of provided recommendations accepted by users. The use of "Other" for an indication, which precludes automated calculation of dose, frequency, and duration, was seen in a substantial minority of orders (21.6% of orders), which may effectively represent another approach to circumvent the CDS. As the user must enter a free-text indication, this field can be mined to create subsequent indications that might have been missed in the initial rollout. Future work will also analyze this field to more precisely determine the extent to which users are inappropriately overriding the system, to help future design optimization.

#### Limitations

There are some limitations to the ADM module and current description. Although the user experience is simple, the design is complex and took 18 months of skilled programming, testing, and user validation to operationalize. The maintenance is straightforward but does require ongoing knowledge base updates to avoid recommending outdated information. At the time of go-live, only a small number of medications were included, indicative of the complexity of building clinical stakeholder alignment and creating standardized medication guidelines. Finally, although fully deployed, the ADM module's impact is currently unknown, with future studies assessing user acceptability and impact to dosing errors. We anticipate fewer errors, however, as the module is difficult to bypass and actually simplifies the ordering process. It will be crucial to monitor for unanticipated untoward effects, given the potential harm that can be induced by CDS.<sup>17,67</sup>

#### CONCLUSION

Through a process involving numerous stakeholders, the ADM CDS module was implemented, with the goal of facilitating medication ordering, improving patient safety, reducing medication errors, supporting antimicrobial stewardship, and improving provider satisfaction. With a particular focus on kidney-based dosing schedules, the ADM module involves complex logic yet is intuitive for end-users. By automatically calculating and inputting the correct dose, frequency, and duration, this module simplifies the highly complex and error-prone process of medication ordering, while lowering patient risk and optimizing duration of therapy, including for antimicrobials. Early user feedback has been positive, and initial utilization data indicate that ADM recommendations are accepted a majority of the time. We believe this module has the potential for significant positive clinical impact, with effectiveness studies ongoing.

# **AUTHOR CONTRIBUTIONS**

JSH, RB, CF, CS, KRB, and MIO contributed materially to study conception and design. RR, PS, HD, and AN contributed technical advice and coding expertise to design and build of application, as well as materially contributing technical expertise to study. JSH, CF, CS, PG-G, and MIO contributed clinical content to application and study design. JSH, RB, CF, and RR were responsible for data management. JSH and RB analyzed the data. JSH, RB, and CF wrote the article. All authors reviewed the manuscript and contributed to revisions. All authors reviewed and interpreted the results and read and approved the final version.

# SUPPLEMENTARY MATERIAL

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

# **CONFLICT OF INTEREST STATEMENT**

None declared.

#### DATA AVAILABILITY STATEMENT

The data, code, and logic that support the Adult Dosing Methodology module and analytic findings of this study are available upon reasonable request from the corresponding author, JSH.

#### REFERENCES

- Litzelman DK Dittus RS Miller ME Tierney WM. Requiring physicians to respond to computerized reminders improves their compliance with preventive care protocols. J Gen Intern Med 1993; 8 (6): 311–7.
- Demakis JG Beauchamp C Cull WL, *et al.* Improving residents' compliance with standards of ambulatory care: results from the VA cooperative study on computerized reminders. *JAMA* 2000; 284 (11): 1411–6.
- Kucher N Koo S Quiroz R, *et al.* Electronic alerts to prevent venous thromboembolism among hospitalized patients. *N Engl J Med* 2005; 352 (10): 969–77.
- Bilaver LA Martusiewicz MN Jiang J Gupta RS. Effectiveness of clinical decision support tools on pediatrician adherence to peanut allergy prevention guidelines. JAMA Pediatr 2019; 173 (12): 1198–9.
- Karlsson LO Nilsson S Bång M Nilsson L Charitakis E Janzon M. A clinical decision support tool for improving adherence to guidelines on anticoagulant therapy in patients with atrial fibrillation at risk of stroke: a cluster-randomized trial in a Swedish primary care setting (the CDS-AF study). *PLoS Med* 2018; 15 (3): e1002528.
- Bright TJ Wong A Dhurjati R, et al. Effect of clinical decision-support systems. Ann Intern Med 2012; 157 (1): 29–43.
- Kawamoto K Houlihan CA Balas EA Lobach DF. Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. *BMJ* 2005; 330 (7494): 765.
- Kwan JL Lo L Ferguson J, *et al.* Computerised clinical decision support systems and absolute improvements in care: meta-analysis of controlled clinical trials. *BMJ* 2020; 370: m3216.
- Marasinghe KM. Computerised clinical decision support systems to improve medication safety in long-term care homes: a systematic review. *BMJ Open* 2015; 5 (5): e006539.

- Bates DW Leape LL Cullen DJ, *et al.* Effect of computerized physician order entry and a team intervention on prevention of serious medication errors. *JAMA* 1998; 280 (15): 1311–6.
- Bates DW Teich JM Lee J, *et al.* The impact of computerized physician order entry on medication error prevention. *J Am Med Inform Assoc* 1999; 6 (4): 313–21.
- 12. Kwok R Dinh M Dinh D Chu M. Improving adherence to asthma clinical guidelines and discharge documentation from emergency departments: implementation of a dynamic and integrated electronic decision support system. *Emerg Med Australas* 2009; 21 (1): 31–7.
- Kaushal R Shojania KG Bates DW. Effects of computerized physician order entry and clinical decision support systems on medication safety: a systematic review. Arch Intern Med 2003; 163 (12): 1409–16.
- Prgomet M Li L Niazkhani Z Georgiou A Westbrook JI. Impact of commercial computerized provider order entry (CPOE) and clinical decision support systems (CDSSs) on medication errors, length of stay, and mortality in intensive care units: a systematic review and meta-analysis. J Am Med Inform Assoc 2017; 24 (2): 413–22.
- Kuperman GJ Teich JM Gandhi TK Bates DW. Patient safety and computerized medication ordering at Brigham and Women's Hospital. *Jt Comm J Qual Improv* 2001; 27 (10): 509–21.
- Radley DC Wasserman MR Olsho LE Shoemaker SJ Spranca MD Bradshaw B. Reduction in medication errors in hospitals due to adoption of computerized provider order entry systems. J Am Med Inform Assoc 2013; 20 (3): 470–6.
- Koppel R Metlay JP Cohen A, *et al.* Role of computerized physician order entry systems in facilitating medication errors. *JAMA* 2005; 293 (10): 1197–203.
- Leape LL Brennan TA Laird N, et al. The nature of adverse events in hospitalized patients. N Engl J Med 1991; 324: 377–84.
- Classen DC Pestotnik SL Evans RS Lloyd JF Burke JP. Adverse drug events in hospitalized patients: excess length of stay, extra costs, and attributable mortality. JAMA 1997; 277 (4): 301–6.
- Bates DW Cullen DJ Laird N, *et al.* Incidence of adverse drug events and potential adverse drug events: implications for prevention. *JAMA* 1995; 274 (1): 29–34.
- 21. Kaushal R Bates DW Landrigan C, et al. Medication errors and adverse drug events in pediatric inpatients. JAMA 2001; 285 (16): 2114–20.
- 22. Kopp BJ Erstad BL Allen ME Theodorou AA Priestley G. Medication errors and adverse drug events in an intensive care unit: direct observation approach for detection. *Crit Care Med* 2006; 34 (2): 415–25.
- Hug BL Witkowski DJ Sox CM, et al. Occurrence of adverse, often preventable, events in community hospitals involving nephrotoxic drugs or those excreted by the kidney. *Kidney Int* 2009; 76 (11): 1192–8.
- Oppenheim MI Vidal C Velasco FT, *et al.* Impact of a computerized alert during physician order entry on medication dosing in patients with renal impairment. *Proc AMIA Symp* 2002: 577–81.
- 25. Prajapati A Ganguly B. Appropriateness of drug dose and frequency in patients with renal dysfunction in a tertiary care hospital: a cross-sectional study. J Pharm Bioallied Sci 2013; 5 (2): 136–40.
- Cox ZL McCoy AB Matheny ME, et al. Adverse drug events during AKI and its recovery. Clin J Am Soc Nephrol 2013; 8 (7): 1070–8.
- Eslami S Abu-Hanna A de Keizer NF de Jonge E. Errors associated with applying decision support by suggesting default doses for aminoglycosides. *Drug Saf* 2006; 29 (9): 803–9.
- Saad R Hallit S Chahine B. Evaluation of renal drug dosing adjustment in chronic kidney disease patients at two university hospitals in Lebanon. *Pharm Pract (Granada)* 2019; 17 (1): 1304.
- 29. Surana S Kumar N Vasudeva A, et al. Awareness and knowledge among internal medicine house-staff for dose adjustment of commonly used medications in patients with CKD. BMC Nephrol 2017; 18 (1): 26.
- Hassan Y Al-Ramahi RJ Aziz NA Ghazali R. Adverse drug events in hospitalized patients with chronic kidney disease. *Int J Clin Pharmacol Ther* 2010; 48 (9): 571–6.
- Tesfaye WH Castelino RL Wimmer BC Zaidi STR. Inappropriate prescribing in chronic kidney disease: a systematic review of prevalence, asso-

- Sellier E Colombet I Sabatier B, et al. Effect of alerts for drug dosage adjustment in inpatients with renal insufficiency. J Am Med Inform Assoc 2009; 16 (2): 203–10.
- Field TS Rochon P Lee M Gavendo L Baril JL Gurwitz JH. Computerized clinical decision support during medication ordering for long-term care residents with renal insufficiency. J Am Med Inform Assoc 2009; 16 (4): 480–5.
- Desmedt S Spinewine A Jadoul M Henrard S Wouters D Dalleur O. Impact of a clinical decision support system for drug dosage in patients with renal failure. *Int J Clin Pharm* 2018; 40 (5): 1225–33.
- 35. Galanter WL Didomenico RJ Polikaitis A. A trial of automated decision support alerts for contraindicated medications using computerized physician order entry. J Am Med Inform Assoc 2005; 12 (3): 269–74.
- 36. Awdishu L Coates CR Lyddane A, *et al.* The impact of real-time alerting on appropriate prescribing in kidney disease: a cluster randomized controlled trial. *J Am Med Inform Assoc* 2016; 23 (3): 609–16.
- Martin M Wilson FP. Utility of electronic medical record alerts to prevent drug nephrotoxicity. Clin J Am Soc Nephrol 2019; 14 (1): 115–23.
- Baysari MT Tariq A Day RO Westbrook JI. Alert override as a habitual behavior—a new perspective on a persistent problem. J Am Med Inform Assoc 2017; 24 (2): 409–12.
- Cho I Slight SP Nanji KC Seger DL Dykes P Bates DW. Understanding responses to a renal dosing decision support system in primary care. *Stud Health Technol Inform* 2013; 192: 931.
- Chertow GM Lee J Kuperman GJ, et al. Guided medication dosing for inpatients with renal insufficiency. JAMA 2001; 286 (22): 2839–44.
- 41. Barlam TF Cosgrove SE Abbo LM, *et al*. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis* 2016; 62 (10): e51–77.
- 42. Yi SH Hatfield KM Baggs J, et al. Duration of antibiotic use among adults with uncomplicated community-acquired pneumonia requiring hospitalization in the United States. *Clin Infect Dis* 2018; 66 (9): 1333–41.
- 43. Elligsen M Walker SAN Pinto R, et al. Audit and feedback to reduce broad-spectrum antibiotic use among intensive care unit patients: a controlled interrupted time series analysis. *Infect Control Hosp Epidemiol* 2012; 33 (4): 354–61.
- 44. Nathwani D Varghese D Stephens J Ansari W Martin S Charbonneau C. Value of hospital antimicrobial stewardship programs [ASPs]: a systematic review. *Antimicrob Resist Infect Control* 2019; 8 (1): 35.
- 45. García-Rodríguez JF Bardán-García B Peña-Rodríguez MF Álvarez-Díaz H Mariño-Callejo A. Meropenem antimicrobial stewardship program: clinical, economic, and antibiotic resistance impact. *Eur J Clin Microbiol Infect Dis* 2019; 38 (1): 161–70.
- 46. Baur D Gladstone BP Burkert F, et al. Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and Clostridium difficile infection: a systematic review and meta-analysis. Lancet Infect Dis 2017; 17 (9): 990–1001.
- 47. Nuila F Cadle RM Logan N Musher DM; Members of the Infectious Disease Section of the Michael E DeBakey VA Medical Center. Antibiotic stewardship and Clostridium difficile-associated disease. *Infect Control Hosp Epidemiol* 2008; 29 (11): 1096–7.
- 48. Tsapepas D Der-Nigoghossian C Patel K Berger K Vawdrey DK Salmasian H. Medication stewardship using computerized clinical decision support: a case study on intravenous immunoglobulins. *Pharmacol Res Perspect* 2019; 7 (5): e00508.
- Evans RS Classen DC Pestotnik SL Lundsgaarde HP Burke JP. Improving empiric antibiotic selection using computer decision support. *Arch Intern Med* 1994; 154 (8): 878–84.
- Holstiege J Mathes T Pieper D. Effects of computer-aided clinical decision support systems in improving antibiotic prescribing by primary care providers: a systematic review. J Am Med Inform Assoc 2015; 22 (1): 236–42.

- Pereboom M Mulder IJ Verweij SL van der Hoeven RTM Becker ML. A clinical decision support system to improve adequate dosing of gentamicin and vancomycin. *Int J Med Inform* 2019; 124: 1–5.
- 52. Goss FR Bookman K Barron M, et al. Improved antibiotic prescribing using indication-based clinical decision support in the emergency department. J Am Coll Emerg Physicians Open 2020; 1 (3): 214–21.
- Isaac T Weissman JS Davis RB, et al. Overrides of medication alerts in ambulatory care. Arch Intern Med 2009; 169 (3): 305–11.
- Nanji KC Seger DL Slight SP, et al. Medication-related clinical decision support alert overrides in inpatients. J Am Med Inform Assoc 2018; 25 (5): 476–81.
- 55. van der Sijs H Aarts J Vulto A Berg M. Overriding of drug safety alerts in computerized physician order entry. J Am Med Inform Assoc 2006; 13 (2): 138–47.
- 56. Ancker JS Edwards A Nosal S, et al.; with the HITEC Investigators. Effects of workload, work complexity, and repeated alerts on alert fatigue in a clinical decision support system. BMC Med Inform Decis Mak 2017; 17 (1): 36.
- 57. Chen S. Retooling the creatinine clearance equation to estimate kinetic GFR when the plasma creatinine is changing acutely. *J Am Soc Nephrol* 2013; 24 (6): 877–88.
- Hudson JQ Bean JR Burger CF Stephens AK McFarland MS. Estimated glomerular filtration rate leads to higher drug dose recommendations in the elderly compared with creatinine clearance. *Int J Clin Pract* 2015; 69 (3): 313–20.

- Flamant M Haymann J-P Vidal-Petiot E, *et al.* GFR estimation using the Cockcroft-Gault, MDRD study, and CKD-EPI equations in the elderly. *Am J Kidney Dis* 2012; 60 (5): 847–9.
- Levey AS Stevens LA Schmid CH, *et al.*; for the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009; 150 (9): 604–12.
- Cockcroft DW Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; 16 (1): 31–41.
- Pryor TA Hripcsak G. The Arden syntax for medical logic modules. J Clin Monit Comput 1993; 10 (4): 215–24.
- Oppenheim MI Mintz RJ Boyer AG Frayer WW. Design of a clinical alert system to facilitate development, testing, maintenance, and user-specific notification. *Proc AMIA Symp* 2000: 630–4.
- Bates DW Kuperman GJ Wang S, *et al.* Ten commandments for effective clinical decision support: making the practice of evidence-based medicine a reality. *J Am Med Inform Assoc* 2003; 10 (6): 523–30.
- Osheroff J Teich J Levick D, et al. Improving Outcomes with Clinical Decision Support: An Implementer's Guide. 2nd ed. Boca Raton, FL: HIMSS; 2012.
- 66. Jennings ELM Murphy KD Gallagher P O'Mahony D. In-hospital adverse drug reactions in older adults; prevalence, presentation and associated drugs a systematic review and meta-analysis. *Age Ageing* 2020; 49 (6): 948–58.
- Wilson FP Martin M Yamamoto Y, *et al.* Electronic health record alerts for acute kidney injury: multicenter, randomized clinical trial. *BMJ* 2021; 372: m4786.