Author's response to reviews

Title: Using a computerized provider order entry system to meet the unique prescribing needs of children: description of an advanced dosing model

Authors:

Jeffrey M. Ferranti (ferra007@mc.duke.edu)
Monica M. Horvath (monica.horvath@duke.edu)
Jeanette Jansen (jeanette.jansen@duke.edu)
Patricia Schellenberger (tricia.schellenberger@duke.edu)
Tres Brown (brown109@mc.duke.edu)
Christopher M. DeRienzo (chris.derienzo@duke.edu)
Asif Ahmad (asif.ahmad@duke.edu)

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Author's response to reviews: see over
Melissa Norton, MD  
Editor-in-Chief, BMC Pediatrics  

Diana Marshall, PhD  
Senior Scientific Editor, BioMed Central  

Dear Dr. Norton and Dr. Marshall:

Thank you for considering our manuscript. Our goal is to describe the formulation of our model for pediatric dosing at Duke Children’s Hospital and the lessons learned in deploying this model as part of pediatric computerized provider order entry (CPOE). We wish for our work to be considered as a Technical Advance, and understand if the editorial team makes an internal transfer to BMC Medical Informatics and Decision Making. We do note, however, that we are not able to systematically address why our system is methodologically “better” than other CPOE products as we have only deployed one product. There is a lack of information in the literature regarding the conceptual design of pediatric medication dosing for academic CPOE products, and the “gray” literature that describes commercial products is even sparser. As a result, we feel our work is extensible to other organizations looking for a dosing model that goes beyond only weight-based considerations. Although we appreciate the referees’ thoughts, we will keep this manuscript as a description of our model and not further evaluate patient outcomes at this time.

We feel that it’s important to note that Referee #2 is one of the developers of the original WizOrder CPOE system that was later sold to McKesson. At the time of sale, there was no pediatric advanced dosing functionality in WizOrder. Since the time of sale, Vanderbilt has independently added pediatric functionality to their WizOrder product. While the WizOrder product is a fantastic system, it is functionally and programmatically different than the McKesson product developed at Duke. To our knowledge there are no peer-reviewed publications that systematically describe the methodology, thought process, and design principles used in developing pediatric WizOrder. We feel that Referee #2 may have inadvertently allowed his personal knowledge of WizOrder to cause him to underestimate the interest of your general readership. We also sense there is some misperception regarding the feature set Vanderbilt sold to McKesson as well as the timeline of that process.

All authors have reviewed and approved the revised manuscript. Thank you for your continued interest in this work, and we look forward to your review.

Sincerely,

Jeffrey M. Ferranti, MD  
DUKE HEALTH TECHNOLOGY SOLUTIONS
REFEREE 1

Major compulsory

1) As a technical advance, the submission does not focus on enhancing adult-focused CPOE but is more about meeting the prescribing needs of pediatrics via CPOE using an advanced dosing model.

Upon reflection, we agree with the reviewer’s assessment. Our notion of enhancing adult-focused CPOE hinges more upon the historical nature of the project than what was actually performed for pediatric medication dosing. We are altering the title and several areas of the document that overstate that we are adapting adult CPOE versus devising a new model of medication dosing for pediatrics.

2) Authors should state more clearly the problems associated with pediatric prescribing in general and at Duke, and with which medications? There does not appear to be data from Duke regarding its own vulnerabilities pre-implementation (which speak to outcomes). As a tertiary pediatric center, are there variations in clinical areas or specific medication processes which have their own error rates that vary from the average?

In the background section, we speak toward the challenges of pediatric prescribing noted in the literature, and these challenges persist at Duke Children’s Hospital. Because this was a topic of a previous publication from our group, we did not originally go into these details. We have added a brief summary regarding pre-implementation vulnerabilities in the needs assessment section, as well as a discussion of how these issues map to specific care areas.

3) The dosing region definition is unclear.

The definition is stated under “Development of pediatric clinical content.” We feel the definition is as clear as possible, and the other reviewers did not have an issue with this term.

4) The broad clinical parameters suggest that the authors may have been thinking of some sort of logistical regression and begs the question as to how they impact on errors before and after implementation/deployment.

The clinical parameters described are in place solely to facilitate pediatric prescribing. The purpose of this report is to describe our dosing model, and the discussion of the voluntarily reported ADEs is not meant to be a full evaluation. Logistic regression is a technique properly applied to consistently collected data, such as medical errors revealed under chart review, and does not apply to voluntarily reported data as described in the article.

5) It is unclear whether the reported limitations refer to the CPOE evaluation of ADEs or the CPOE implementation.

We respectfully disagree as each of the described limitations refers to the CPOE implementation of the advanced dosing model. The limitations of the ADE data are discussed when the results are presented as this information is an imperfect secondary outcome that does not represent the focus of the paper. However, given the large concern in the literature regarding pediatric dosing and
harmful errors, we feel it timely and important to share what limited safety data we do have that had been collected and analyzed as part of regular quality improvement operations.

6) Clarify how ADEs were chosen in the analysis with regard to impact, such as mortality.

We have updated our Methods with a reference for ADE severity.

7) There is previous work on pediatric CPOE and CDS for the "problem areas" of medication prescribing: infusions, chemotherapy, etc. How were these handled and resolved at Duke? State how these problems were navigated via the ADM.

We state in the manuscript under “Development of pediatric clinical content” that dosing regions were not built for medications that already had robust clinical decision support through elaborate advisor interfaces (e.g., insulin or intravenous fluids). These web-based advisors guide the user through the complex process of ordering drips, complex IV fluids, PCAs, and other “problem areas.” We have added to this statement that chemotherapy dosing at Duke Hospital remains paper-based and protocol-driven and is therefore not part of the ADM. Pediatric chemotherapy prescribing is extremely complicated and could be the focus of its own manuscript.

8) Authors should focus the paper either as a descriptive study or as an implementation evaluation.

This paper is intended as a descriptive study of the advanced dosing model, a framework that has not been published elsewhere. We include voluntarily reported safety incidents for the sake of due diligence given that this brief analysis had been performed for internal quality improvement review. We realize that this analysis is not a complete study design and has numerous limitations, which we detail in the Results section. Although we could remove this information from the manuscript, we believe it would be doing the pediatrics community a disservice to not share our findings given the broad national concerns regarding pediatric medication safety. We feel that, after revision, we have more solidly shaped our manuscript as a description of our model and have removed ADE results from the abstract so that there is no misunderstanding regarding the paper’s goal.

Minor

1) Reference the Longhurst paper.

Please note that we did include a reference for time series analysis of medication errors in the Background section, and the Longhurst paper was published after submission. We have updated our manuscript with the more recent reference as requested.

Discretionary

1) The Referee has shared the STARE-HI framework for evaluation reporting and notes that voluntary reporting is not a robust measurement.

We agree that voluntary reporting is not a perfect manner of evaluation and noted this in our manuscript. As such, this manuscript is not intended to be a formal evaluation of the CPOE system as indicated above. Thus, STARE-HI does not apply. We are describing our model formulation for advanced dosing and the lessons learned.
2) The discussion and conclusion sections need more structure to bring the narrative into focus.

We have revised these sections with this comment in mind and added additional subheadings to better orient the reader.

REFEREE 2

Referee #2 presents two levels of comments depending on the scope of the paper—as an evaluation of the CPOE implementation or as a technical advance. For all the reasons mentioned by the referee, as well as for issues we outlined in the manuscript, voluntarily reported data create weak outcome metrics and should not be used alone to wholly evaluate the safety of an HIT system. We emphasize that this is an implementation study and should be presented as a Technical Advance.

Major compulsory

1) The study design is weak for determining impact on ADEs.

We agree wholeheartedly, which is why the manuscript is a description of our advanced dosing model and not a formal evaluation of the CPOE system. The limitations of the ADE data are clearly outlined in our draft. As indicated in our response to other referees, limited ADE data from our internal quality and safety systems were included for the sake of due diligence given the national concerns surrounding pediatric medication prescribing and unintended harm. The manuscript can stand independent from this information, but we feel it adds important “food for thought.”

2) Many of the components of the advanced dosing model were present in the predecessor “WizOrder” system from Vanderbilt in 2003. The novelty of this work in light of the prior Vanderbilt system was in explicitly requiring indication and location.

We respectfully disagree with this statement. WizOrder, as sold to McKesson, had zero advanced therapeutic dosing functionality, and everything we reported was developed at Duke University Hospital. Our framework is separate and distinct from the effort for the Vanderbilt pediatric dosing model. We hold that dosing weight safety checks (against prior weight, actual weight, and normalized growth curves), indication, and location are the novel components.

3) Other academic institutions and commercial vendors of both clinical systems and drug content systems (such as Zynx, First Databank “FDB”, and Lexicon-Multum) provide advanced dosing decision support frameworks. The authors do not describe any of the prior literature in this area or review the available descriptions of commercial frameworks. This makes it difficult to understand which components of the described work are technical advances versus a description of the current art.

Our Discussion section now contains the section “Comparison to other dosing decision support methods.” However, we emphasize that a comprehensive comparison to other systems is severely hampered by the lack of design and deployment reports in the scholarly literature. For commercial products, it is even more difficult to make this assessment. The latter two systems the referee cites provide static dosing advice but not active dosing assistance, which is a critical difference that is now
emphasized in the manuscript. Zynx provides clinical content for the development of order sets, but not dosing assistance, so this is not a parallel comparison.

4) HEO uses First Databank as a source of medication decision support content. Authors should explain the deficiencies in the current FDB framework that necessitated the ADM approach. Since Horizon Expert Orders usually utilizes First Databank as a source of medication decision support content, as a starting point the authors might be in a position to strengthen their description of the technical advance by describing the deficiencies in the current FDB framework with a level of detail in concordance with the described approach. Such a comparison would be very informative to other organizations adopting systems that depend on such frameworks for their decision support.

We address this comment in concert with the previous request to describe other systems. However, we emphasize that McKesson Horizon Expert Orders does not use First Databank as a source of medication decision support for pediatrics.

Discretionary

1) Vanderbilt noted indication in the instructions in the dosing region and would provide a different menu option aligned with each indication. Vanderbilt also decided that they were able to use consistent dosing regions across all locations in the children’s hospital. That’s actually an interesting point for discussion as to why the author’s institution considered location AND indication a necessary mechanism for differentiating dosing decision support. One might assume that indication and patient characteristics should drive decision support and not necessarily the location performing care. This is an important topic for discussion because if decision support can be derived based on patient characteristics alone, the knowledge can be generalized and shared amongst other institutions; especially from academic centers to small community hospitals. If instead, decision support is dependent on knowledge of specific clinical locations, generalization is reduced and requires customization by local institutions which may lack such expertise.

Referee #3 made a similar comment on how location may not be a required parameter for pediatric dosing. We now clarify in our manuscript that we intend location to be an indication of care intensity fed to the ADM to identify a dosing region. On the other hand, indication is not necessarily synonymous with care intensity. Based on what is available in the published literature for Vanderbilt’s WizOrder system, we cannot conclude that Vanderbilt always uses a location-independent (i.e., care intensity-independent) dosing model for pediatrics. In the referenced 2003 AMIA proceeding describing CPOE rollout to the Vanderbilt NICU (AMIA Annu Symp Proc. 2003:1078), the authors state, “While other Vanderbilt general pediatric units have used WizOrder since 1997 and the Pediatric Critical Care Unit went live in December 2001, the NICU required new approaches to drug dosing and fluid management.” We feel the changes made to the manuscript clarifies that location is really meant to identify care intensity for dosing region selection by the ADM. As any organization can map physical locations to groups of care areas, this preserves our model’s generalizability.
REFEREE 3

Major

1) Table item ordering is confusing and should be harmonized across all tables.

   We have done our best to make the ordering appear as suggested. CPOE was deployed by care intensity as judged by collective clinical review, which explains the ordering in Table 1. Table 2 shows the criteria for model logic now in the same order as the column headers in Table 3. Within the location subcategories of Table 3, all dosing recommendations are presented in terms of increasing age. Figure 1 is a distinct idea, and we do not agree that the ordering of criteria must be matched to that in Table 2 in order to understand the diagram. Table 2 is a challenge to present as we want to show the most amount of information in the least space without excessive duplication of terms.

2) The discussion does not refer to other options for pediatric dosing guidance, such as alerting for over- and underdosing. This type of decision support would challenge providers to think themselves and make them less dependent. Furthermore, suppression and redirection logic would probably be superfluous and rounding methods could be simplified. Pediatric alerting logic can be based on the same criteria as mentioned in Table 2 to result in specific dosing alerts to prevent alert fatigue. This should be added to the discussion.

   Per other referee requests, we have added a description of other dosing options in the literature. However, the referee seems to suggest that, instead of suggesting dosing based on a set of parameters, we should instead send alerts based on these same parameters after an inappropriate dose is entered. We feel this will add considerable time to the ordering process as providers receive numerous alerts from the ADM until they choose a dosage that fits the needs of all the parameters. We do recognize that over-dependence on technology is a risk of any electronic system, which was highlighted in the Limitations section. Given the flexibility of the ADM (and ultimately the ability to override the system), we believe providers are still called upon to “think for themselves,” as the referee recommends. Per another referee’s request, we have added descriptive subheadings to the Results and Discussion to clarify the paper’s organization, including “Guarding against over- and under-dosing.” We cannot envision how suppression and redirection logic could be removed if one application has access to clinical decision support for both adults and pediatrics, as highlighted under “Error prevention measures.”

3) It is not clear what is meant by ‘their immature renal and hepatic systems inconsistently clear drugs’. During many years of childhood hepatic function exceeds adult hepatic function; it should not be described as immature. Pediatric clearance of drugs is not inconsistent but deviating from clearance in adults.

   We are puzzled by this statement as we have heard pediatric renal and hepatic systems characterized in this exact manner in many other forums. However, we have altered our wording per this request.

4) Authors do not mention recent literature on the effect of CPOE on outcome measures (2009 JAMIA article is cited).
We cited several recent sources as well as a 2009 systematic review of CPOE and outcomes in terms of medication errors. Given this is highly active research area, we used our best judgment to decide which papers were most pertinent to our discussion. The JAMIA paper has similar results to a 2008 Pediatrics study (Effect of computer order entry on prevention of serious medication errors in hospitalized children. Pediatrics 2008, 121[3]:e421–427). This study also performed a time series analysis and noted that, while decision support reduced the incidence of medication errors, a direct effect on patient harm was not identified. Nevertheless, we have included the identified JAMIA reference as requested.

5) It would be interesting for the reader to know which expiry dates are configured by the development team.

We apologize, but we do not understand the request. If the question is how often do dosing regions get re-reviewed for relevance based on evolving data, the answer is once every two years (and this information is now present in the text).

6) The distinction between impaired and normal renal function misses the details required for correct dose recommendations (based on percentage renal function or calculated with help of the Schwartz formula). This should be mentioned.

As stated in the manuscript, renal impairment is based upon a qualitative assessment by the ordering provider. No calculations are involved. We are aware of four distinct ways to calculate creatinine clearance and are without consensus from our providers regarding which method should be used. Most methods depend on K-values, which lack granularity for pediatrics. In our opinion, renal function is best assessed by the expert physician and pharmacist by the bedside and thus it is a qualitative parameter.

7) The emphasis on location makes the pediatric ADM very context specific and not transferrable to other hospitals. Would it be possible to accommodate the criterion ‘location’ into care intensity (ICU/medium care), age, and indication? It is not clear whether location should be an independent criterion.

We understand that we have mischaracterized our intent. Per Table 1, we view location as synonymous with care intensity. In the ADM, dosing regions are designed with regard to care intensity, which then specifically maps to certain nursing stations. Given this, our design centers on care intensity (with location being the best indicator available) and not a specific pediatric floor such as “general pediatrics station 5100” versus “general pediatrics station 5300.” Other organizations can use this same approach, as the location groups represent different patient populations that have commonality when it comes to treatment regimens. We have updated our terminology throughout the paper to clarify this intent. We have also added a few sentences to describe how location is a critical dosing parameter for the bone marrow transplant unit.

Minor

1) Explain why the British National Formulary was not used as a pediatric dosing reference.

This simply is not a reference used frequently at Duke Hospital and thus was not used by the clinical review committee in the definition of dosing regions. Our approach does not hinge upon the specific
reference used, and other organizations following our model are free to use their own guiding material.

Discretionary

1) The paragraph defining the pediatric patient is long.

   We are unclear which paragraph is in question as the definition of “pediatric” is one sentence. We have adjusted this sentence for clarity.

2) A screenshot would be helpful.

   A screenshot (Figure 2) has been added per this request.