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Assessing the reliability of an automated dose-rounding algorithm

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ABSTRACT

Objective: Pediatric dose rounding is a unique and complex process whose complexity is rarely supported by e-prescribing systems, though amenable to automation and deployment from a central service provider. The goal of this project was to validate an automated dose-rounding algorithm for pediatric dose rounding.
Methods: We developed a dose-rounding algorithm, STEPSTools, based on expert consensus about the rounding process and knowledge about the therapeutic/toxic window for each medication. We then used a 60% subsample of electronically-generated prescriptions from one academic medical center to further refine the web services. Once all issues were resolved, we used the remaining 40% of the prescriptions as a test sample and assessed the degree of concordance between automatically calculated optimal doses and the doses in the test sample. Cases with discrepant doses were compiled in a survey and assessed by pediatricians from two academic centers. The response rate for the survey was 25%.
Results: Seventy-nine test cases were tested for concordance. For 20 cases, STEPSTools was unable to provide a recommended dose. The dose recommendation provided by STEPSTools was identical to that of the test prescription for 31 cases. For 14 out of the 24 discrepant cases included in the survey, respondents significantly preferred STEPSTools recommendations ($p < 0.05$, binomial test). Overall, when combined with the data from all test cases, STEPSTools either matched or exceeded the performance of the test cases in 45/59 (76%) of the cases. The majority of other cases were challenged by the need to provide an extremely small dose. We estimated that with the addition of two dose-selection rules, STEPSTools would achieve an overall performance of 82% or higher.
Conclusions: Results of this pilot study suggest that automated dose rounding is a feasible mechanism for providing guidance to e-prescribing systems. These results also demonstrate the need for validating decision-support systems to support targeted and iterative improvement in performance.

1. Introduction

E-prescribing has emerged as a core component of an assumed safe national healthcare system [1–6]. Federal initiatives such as the HITECH (Health Information Technology for Economic and Clinical Health) Act specifically require the use of e-prescribing by all medical specialties [7].

However, despite this widespread enthusiasm for e-prescribing, not all e-prescribing systems support the needs of all specialties. A recent AHRQ report [8] noted issues of usability with these systems. There is less data to support the use of e-prescribing in the ambulatory pediatric community [9], despite the challenges associated with pediatric patient medication management [10]. A study by Kaushal noted the potential for e-prescribing to prevent up to 21% of adverse drug events in outpatient settings, including those related to drug frequency and weight/dose checks [11].

Pediatric prescribing is a complex process that requires the prescriber to calculate a medication dose that is appropriate for the treatment goals and for the child's weight or body surface area [6]. While some medications are relatively tolerant of inaccurate dosing, others with narrow therapeutic indices (e.g., Digoxin) have a great potential for adverse consequences if dosed improperly [12–14]. This process is sufficiently complicated that most pediatricians rely on prescribing guides in print or electronic form to practice safely [15,16]. Recent advances in medications available to treat severe conditions also impact children with these conditions [15,17].

One particular area of concern is the lack of sophistication used when e-prescribing systems automatically calculate doses. Should a 4.7 kg child receiving 5 mcg/kg/dose of digoxin, totaling 23.5 mcg, receive 0.5 ml (25 mcg, or 10.6 mcg/kg/day) or 0.4 ml (20 mcg, or 8.51 mcg/kg/day)? Or should the child receive the

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exact dose of 0.47 ml, which would likely be complicated to administer at home or require asking for a custom formulation, which can be expensive?

In the spirit of "a rising tide lifts all boats," one method to systematically improve dose-rounding decision support in pediatric e-prescribing is through the use of cloud-based tools that may be developed and maintained by knowledge experts and adopted by all e-prescribing systems with a minimum of effort. This approach goes by many names, including "Software as a Service," or web services. The goal of this project was to design, develop and evaluate an algorithm for use in this manner.

2. Methods

2.1. Rounding algorithm

We used a combination of data sources to develop the dosing algorithm. First, as a part of a previous study, we used literature about the pharmacokinetic and potential adverse drug event to develop rounding tolerances for each medication [18]. These rounding tolerances were combined with the following knowledge sources to develop a range of allowable doses for each prescription:

- Medication knowledge (STEPSTools knowledgebase): frequencies of administration, rounding tolerances, minimum and maximum daily and per-dose amounts.
- RxNorm, developed by the National Library of Medicine, to provide a mapping between any string representation of a generic or brand medication and all dosage forms of that medication.

Finally, we convened a number of expert panels as described in [18]. Using example prescribing cases to create discussion, pediatricians and pharmacists in these panels provided a number of heuristics they use to create a safe and administrable prescription. These heuristics became the foundation for selecting an easily administered dose.

The final algorithm for dose selection and rounding prefers as input the patient's age in months, the patient's weight in kilograms, the medication name, and desired mg/kg/day dosing formula. The service also accepts the number of doses per day, a code for the medication name, and a coding scheme as optional parameters. Once these data are received, the algorithm goes through three steps, each of which is discussed below.

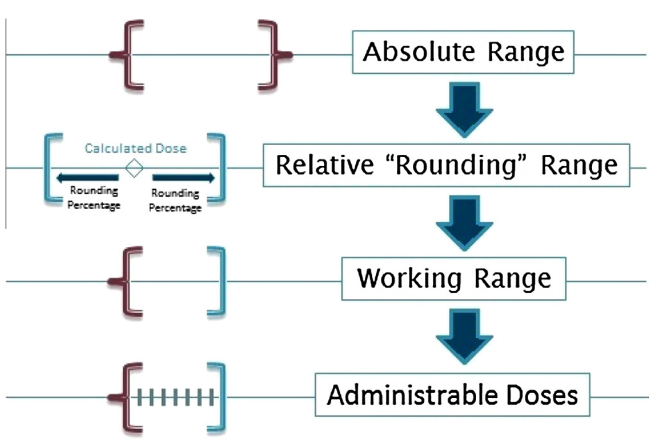

Fig. 1. STEPSTools dosing algorithm. The dosing process requires 4 steps: looking up the minimum and maximum allowable dose to create an absolute range; calculating a relative rounding range based on the weight-based dosing formula and rounding percentage; combining the two ranges to create a working range within calculated and allowable doses, and then using heuristics about administrable doses to select doses within the working range that are easily administered.

2.1.1. Data encoding

We use a version of RxNorm concepts distilled into a lookup table for all medications in the knowledgebase. This table matches up the inputted medication name with an RxCUI. If we are unsuccessful in matching the name to a CUI, we query RxNorm using the RxNorm API. We use this process to improve the performance of the web service. Once the RxCUI is found, the service retrieves the medication frequency, absolute minimum dose, maximum dose, and rounding tolerance.

2.1.2. Dose selecting

Fig. 1 summarizes the key steps in creating a set of safe and administrable doses. The rounding process requires 4 steps. First, STEPSTools retrieves information about the minimum and maximum therapeutic dose from its medication knowledgebase (based on data from the Harriet Lane Handbook, 18th Edition [19]) to set the absolute range of doses that can be calculated. Second, STEPSTools uses patient age and weight information, in addition to published formulae for weight-based dosing and the rounding tolerance for the medication's active ingredients to calculate a relative rounding range. Third, STEPSTools determines a working range, taking into account both the optimal and relative rounding ranges. In cases where the rounding range is completely within the absolute range, the relative rounding range is used as the working range; however, in other cases, STEPSTools defaults the lowest working dose to either the minimum rounded dose or the minimum absolute dose, whichever is higher. It performs a similar filter at the high end of the dosing range if necessary, selecting the lower dose of the two highest allowable doses. Finally, STEPSTools applies heuristics about home dosing capabilities to select doses within the working range that are easily administered. These doses are based on a review of common dosing implements available through pharmacies. For example, 1 ml syringes can typically be dosed in 0.1 mL increments, while 10 mL syringes are easily dosed in increments of 0.5 mL. Most capsules may not be split, but some pills may be. This list of possible doses and formulations within the working range is stored.

2.1.3. Dose recommendation

STEPSTools returns dose recommendations based on the list of possible doses and dosage forms previously described combined with heuristics derived from expert panels, which are weighted using cases from our test suite. The heuristics encompass information about the ideal ages for each formulation and the amounts that are best tolerated by children to score each dosing suggestion, as described below:

1. If the age of the patient is less than 7 years, and the dose is in liquid, suppository, or patch, boost the score by 8 points; if the form is chewable, boost the score by 4 points; if form is melt away, boost the score by 2 points.
2. If the form is

a. Liquid and

i. The dose is divisible by 0.5 ml, boost by 1 point for patients 7 or older, and 2 points for patients under age 7.

ii. The dose is divisible by 1 ml; add two points for patients 7 or older, and 4 points for patients under age 7.

iii. The volume is less than 10 mL, add one point for patients 7 and older, and 2 points for patients under age 7.

b. Tablet and

i. The dose is divisible by dosage form, add 2 points

1. If the dose quantity is less than 2 tablets, add 2 additional points.

ii. The dose is not divisible, half the current score (and exclude if a capsule)