Evidence-Based Quality Improvement: A recipe for improving medication safety and handover of care

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CHAPTER 6

The Trigger Tool as a Method to Measure Harmful Medication Errors in Children

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Abstract

Objectives
To improve the medication safety for children, it is important to quantify the occurrence of medication errors (MEs). A trigger tool may be an effective and time-saving strategy, but its measurement performance is unclear. Therefore, we aimed to estimate the diagnostic accuracy of a pediatric medication-focused trigger tool in detecting harmful MEs.

Methods
The study was designed according to the STARD recommendations. Firstly, we established the reference standard. Secondly, we compared the pediatric medication-focused trigger tool with the reference standard in a new cohort of patients. All patients admitted in February and March 2013 were screened using the trigger tool and the reference standard to obtain full verification. Data collection was performed in separate teams to guarantee blinding of the test results.

Results
Review of the clinical records and the voluntary incident reports were most effective in detecting harmful MEs, so this approach was chosen as reference standard. In the second part of the study 369 patients were included. The reference standard identified 33 harmful MEs. In contrast, the trigger tool did not identify any harm. When the two symptoms "pain" and "nausea/vomiting" were added to the trigger tool, 19 harmful MEs were identified. This extended trigger tool resulted in a sensitivity of 21.2 and a positive predictive value of 36.8.

Conclusions
The original pediatric medication-focused trigger tool yielded only false positive scores and left unsafe situations undiscovered. We conclude that the review of clinical records plus voluntary incident reports remains the "gold standard" to detect harmful MEs.

Keywords: sensitivity, specificity, trigger tool, medication errors, harm, pediatric
INTRODUCTION

Medication-related adverse events are one of the most common types of adverse events that endanger hospitalized patients. A substantial part of these adverse events that is preventable and must be considered is medication errors (MEs). Children are especially at high risk for harm because MEs are potentially more hazardous to them than to adults. To move forward toward preventive interventions, it is necessary to be able to quantify medication safety. However, measuring MEs accurately is difficult, and the results of the various measurement methods vary widely. Therefore, to obtain reliable data, a multifaceted approach is recommended. However, such an approach is time consuming, thus hampering both routine monitoring and clinical research.

To overcome this problem, the trigger tool methodology has been developed. A trigger tool is a collection of “alerts” that serve as indicators of potential adverse events. In recent decades, several trigger tools have been developed, including trigger tools to measure specific adverse events (such as adverse drug events) and trigger tools to be used in specific patient populations (e.g., children).

Research on trigger tools designed specifically to detect adverse drug events in children is limited. To the best of our knowledge, only one pediatric medication-focused trigger tool has been developed, and the measurement performance of this trigger tool is not yet studied in depth. Moreover, most studies have focused on all adverse drug events and have not specifically investigated preventable drug events defined as MEs. This knowledge is essential to develop risk reduction programs and therewith medication safety for children.

Therefore, in this study, our aims were to (a) estimate the performance of a pediatric medication-focused trigger tool in detecting harmful MEs, using a multifaceted method as a reference comparison, and (b) calculate the time investments needed for the use of the trigger tool and the multifaceted method. Patients of interest were hospitalized children from birth up to 18 years old.
METHODS
Setting and study population
The study took place at the Emma Children’s Hospital in the Netherlands, which is part of the Academic Medical Center and is affiliated with the University of Amsterdam. We conducted our study on 3 general pediatric wards and a pediatric oncology ward. All patients who were admitted to one of these wards with at least 1 medication prescription during the study period were eligible. Patients with a hospital admission shorter than 24 hours and patients participating in other medication trials were excluded.

Study design
We conducted a cross-sectional study consisting of 2 parts. In the first part, we established a multifaceted method to identify harm due to MEs to obtain a reference comparison. In the second part, we compared this multifaceted method with the pediatric medication-focused trigger tool in a new cohort of patients. The primary outcome was patient harm due to MEs. The secondary outcome was the difference in time investment between the 2 methods. We used the definitions and categories for error and harm as described by the National Coordinating Council for Medication Error Reporting and Prevention. The institutional review board of the Academic Medical Center determined that the protocol did not require medical ethical approval according to the Dutch Medical Ethics Law. All data were analyzed and reported anonymously.

Part 1
Establishing the multifaceted method
In the first part of this study, we established the most effective combination of methods to identify harmful MEs. To do this, we reanalyzed the clinical data from a previous study, in which we used 4 methods: review of the clinical records, analysis of incident reports, direct observations, and analysis of pharmacy logs.

Part 2
Estimating the performance of the pediatric medication-focused trigger tool
To establish the performance of the pediatric medication-related trigger tool, we used a new consecutive cohort of patients admitted in the period between February 1, 2013, and March 31, 2013. All included patients were screened for harmful MEs using the pediatric medication-focused trigger tool and the multifaceted method to obtain full verification. We created 2
teams, each consisting of a pediatrician, a pediatric nurse, and a research assistant, who were responsible for the data collection with the trigger tool and the multifaceted method. To guarantee blinding of the test results, the 2 teams worked independently and were each unaware of the results of the other team. The pediatricians and the pediatric nurses all had at least 5 years of postgraduate experience and were members of the ward safety teams. The teams were assisted by a qualified pharmacy assistant and a registered nurse, who were supervised on a daily basis by the last author. Before the start of data collection, the protocol was discussed with the teams to ensure a clear understanding of definitions and methods. The research assistants were trained with the help of the Pediatric Trigger Toolkit24 and an instruction sheet based on the local situation, followed by a pilot to test their understanding. Data were collected on digital case record forms. We adapted the pediatric medication-focused trigger tool developed by Takata et al.18 Some triggers were slightly changed to reflect the Dutch situation. In addition, 2 triggers on pain and nausea/vomiting, which were established as symptoms associated with harmful MEs in our previous research, were added to the trigger tool. The performance of both the original and the extended version of the trigger tool was studied separately.23 The clinical records of all included patients were reviewed manually using the trigger tool. When a trigger was found, a full review of the clinical records was performed to determine whether a harmful ME was associated with the trigger. Medication errors that were found “spontaneously” and were not associated with a trigger were ignored.

The clinical records of all included patients were reviewed and analyzed for harmful MEs. Data were extracted from the medication overviews, medication administration records, medical progress summaries, medical daily notes, medical order sheets, nursing daily notes, nursing order sheets, symptom registrations, and anesthetist postoperative notes. In addition, the incident reports that involved MEs were analyzed. This method created 10 locations per patient where an ME could be identified.

**Time investment**

The time investment needed to establish harmful MEs was recorded in real time in 100 patients, equally divided over the study period. For the trigger tool, the data collector recorded the time needed to identify a trigger and to determine whether that trigger was associated with an ME. For the multifaceted method, the data collector recorded the time needed to perform a
full review of a clinical record and an incident report.

Reliability
To study interobserver reliability, data from 100 included patients were collected using the trigger tool method by 2 reviewers (A.B. and M.S.) independently. We calculated the reliability of Interobserver reliability of the multifaceted approach had already been established in our previous study.23

Statistical analysis
Descriptive statistics were used to summarize patient demographics and MEs. If normally distributed, continuous values were expressed as mean and SD; otherwise, median and interquartile range (IQR) were used. The performance of the pediatric medication-focused trigger tool was described using sensitivity, specificity, positive and negative predictive values, as well as positive and negative likelihoods. The 95% confidence interval (CI) was used to quantify statistical uncertainty. Measures of inter-observer reliability were calculated using percentages of absolute agreement and κ statistics. All analyses were performed using SPSS software (version 20.0, IBM, Armonk, NY) and MedCalc software (version 12.7.5, Ostend, Belgium).

Table 1. Patient characteristics (N = 369)

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>208 (56)</td>
</tr>
<tr>
<td>Age, median (IQR), y</td>
<td>8 (2-14)</td>
</tr>
<tr>
<td>Specialty, n (%)</td>
<td></td>
</tr>
<tr>
<td>Oncology</td>
<td>83 (22)</td>
</tr>
<tr>
<td>Pediatrics</td>
<td>58 (16)</td>
</tr>
<tr>
<td>Surgery</td>
<td>86 (23)</td>
</tr>
<tr>
<td>Orthopedics</td>
<td>26 (7)</td>
</tr>
<tr>
<td>Ear, nose, and throat</td>
<td>36 (10)</td>
</tr>
<tr>
<td>Other</td>
<td>80 (22)</td>
</tr>
<tr>
<td>Surgery, n (%)</td>
<td>218 (59)</td>
</tr>
<tr>
<td>Planned admission, n (%)</td>
<td>292 (79)</td>
</tr>
<tr>
<td>Length of stay, median (IQR), d</td>
<td>3 (2-5)</td>
</tr>
<tr>
<td>Medication orders, median (IQR)</td>
<td>6 (3-11)</td>
</tr>
<tr>
<td>Medication administrations, median (IQR)</td>
<td>18 (7-42)</td>
</tr>
</tbody>
</table>
RESULTS

Part 1

Establishing the multifaceted method

We reanalyzed the data from a previous study that had a population of 426 patients. In these patients, a total of 327 MEs were identified, 39 of which had caused patient harm (9%). In total, 32 harmful MEs were found in clinical records (82%). The incident reports yielded 7 additional MEs that were considered harmful (18%). The observations yielded no harmful MEs, and the pharmacy logs identified only 1 harmful ME (3%), which was also found in the clinical records. In conclusion, all MEs were found by review of the clinical records and analysis of the incident reports. This multifaceted method was used as the reference comparison for the second part of the study.

Part 2

Estimating the performance of the pediatric medication-focused trigger tool

Study population

During the 2-month study period, 384 patients met our inclusion criteria. The clinical data of 369 of these patients were collected; we could not evaluate 15 patients as a result of insufficient documentation. Our study population represented 1864 admission days, during which 3237 prescriptions were written and 18,476 medication doses were administered. The patients’ characteristics are summarized in Table 1.

Prevalence of harmful MEs and severity of harm

On the basis of the multifaceted method, we found at least 1 ME in 168 patients (46%). A total of 242 MEs were identified, of which 33 had caused patient harm. In total, 31 patients were affected by these harmful MEs, and 2 patients experienced 2 harmful events. Of the 33 harmful MEs, 27 were described in the clinical records, 5 were derived from incident reports, and 1 was recorded in both. The observed harm was classified as minor (category E) in 91% (30/33) and significant (category F) in 9% (3/33). None of the observed MEs were categorized as permanently harmful, life threatening, or fatal. The results are summarized in Tables 2 and 3.

Performance of the pediatric medication-focused trigger tool

With the use of the pediatric medication-focused trigger tool, a total of 392 positive triggers were identified in 204 patients. The trigger tool did not identify any MEs or harm, that is, no relation was found between the positive triggers, MEs, or harm. When 2 symptoms pain and nausea/vomiting were added
to the trigger tool, the number of positive triggers increased to 688 in 270 patients. This extended trigger tool yielded 19 harmful events in 18 patients. Of the 3690 possible harmful MEs that could be identified (10 locations to identify error multiplied by 369 patients), the multifaceted method identified 33 harmful MEs and the trigger tool (plus the symptoms pain and nausea/vomiting) successfully identified 19 harmful MEs. In total, 7 harmful MEs were detected by both methods. This extended trigger tool resulted in a sensitivity of 21.2 and a positive predictive value of 36.8, when compared with the multifaceted method. The performance of the extended trigger tool is summarized in Table 4, and an overview of the individual triggers is presented in Table 5.

### Table 2. Prevalence of harmful MEs

<table>
<thead>
<tr>
<th>Per 100</th>
<th>Harmful MEs identified by the multifaceted method (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>N = 369</td>
</tr>
<tr>
<td>Admission days</td>
<td>N = 1864</td>
</tr>
<tr>
<td>Prescriptions</td>
<td>N = 3237</td>
</tr>
<tr>
<td>Doses administered</td>
<td>N = 18,476</td>
</tr>
</tbody>
</table>

### Table 3. Severity of the MEs

<table>
<thead>
<tr>
<th>Category*</th>
<th>Prevalence</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>30</td>
<td>Wrong rate of the infusion pump with morphine resulted in postoperative pain; the child needed an extra bolus of analgesics. Unintended discontinuation of antiepileptic home medication resulted in a convulsion.</td>
</tr>
<tr>
<td>F</td>
<td>3</td>
<td>Omission in prescribing antiemetics during chemotherapy resulted in severe vomiting and delay of discharge.</td>
</tr>
</tbody>
</table>

*According to the National Coordinating Council for Medication Error Reporting and Prevention
### Table 4. Performance of the pediatric medication-focused trigger tool

<table>
<thead>
<tr>
<th></th>
<th>Multifaceted method: harmful ME present</th>
<th>Multifaceted method: harmful ME absent</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trigger tool</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>harmful ME Present</td>
<td>7</td>
<td>12</td>
<td>19</td>
</tr>
<tr>
<td>harmful ME Absent</td>
<td>26</td>
<td>3645</td>
<td>3671</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>33</td>
<td>3657</td>
<td>3690</td>
</tr>
</tbody>
</table>

95% CI 

- Sensitivity: 212 (9.0–38.9)
- Specificity: 99.7 (99.4–99.8)
- Positive predictive value: 36.8 (16.3–61.6)
- Negative predictive value: 99.3 (99.0–99.5)
- Positive likelihood ratio: 64.6 (272–153.8)
- Negative likelihood ratio: 0.8 (0.7–0.9)

### Table 5. Information on the individual triggers (N)

<table>
<thead>
<tr>
<th>Trigger</th>
<th>Positive triggers</th>
<th>Patient harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihistamine(^{1})</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Flumazenil</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Naloxone</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sodium polystyrene</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Antiemetic</td>
<td>120</td>
<td>0</td>
</tr>
<tr>
<td>Laxative or stool softener</td>
<td>89</td>
<td>0</td>
</tr>
<tr>
<td>Laboratory(^{1})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum glucose</td>
<td>78</td>
<td>0</td>
</tr>
<tr>
<td>Serum potassium</td>
<td>21</td>
<td>0</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Serum partial thromboplastin time</td>
<td>6</td>
<td>0</td>
</tr>
</tbody>
</table>
Table 5. Continued

<table>
<thead>
<tr>
<th>Trigger</th>
<th>Positive Triggers</th>
<th>Patient Harm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oversedation, lethargy, falls, hypotension</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>Rash</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Pain‡</td>
<td>155</td>
<td>13</td>
</tr>
<tr>
<td>Nausea, vomiting‡</td>
<td>141</td>
<td>6</td>
</tr>
<tr>
<td><strong>Clinical interventions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abrupt medication discontinuation</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Unplanned transfer to an intensive care unit, called codes§</td>
<td>7</td>
<td>0</td>
</tr>
</tbody>
</table>

*Antihistamines according to the hospital’s formulary: cetirizine, clemastine, or dimetinden. †All laboratory triggers were scored positive when outside the hospital’s range of reference values. ‡Not part of the original trigger tool. §Unplanned transfer to an intensive care unit was added to the trigger.

**Time investment**

Use of the original trigger tool required a mean of 4.43 (SD, 1.48) minutes, and the extended trigger tool required a mean of 100 patients. For the original trigger tool, we found a substantial reliability for the identification of positive triggers ($\kappa = 0.78$; 95% CI, 0.72–0.84). We found an overall agreement rate of 100% for ME identification and patient harm. For the extended trigger tool, a substantial reliability was also found for the identification of positive triggers ($\kappa = 0.76$; 95% CI, 0.72–0.81). The inter-observer reliability was fair for ME identification ($\kappa = 0.25$; 95% CI, 0.07–0.43) and patient harm ($\kappa = 0.28$; 95% CI, 0.08–0.48).

The inter-observer reliability of the multifaceted approach had already been established in our previous study, resulting in $\kappa$ values for ME identification of 0.56 (95% CI, 0.45–0.66) and patient harm of 0.64 (95% CI, 0.40–0.88).
DISCUSSION

We estimated the performance of a pediatric medication-focused trigger tool to detect harmful MEs, using a multifaceted method as the reference comparison. This multifaceted approach identified 33 harmful MEs, but none were identified by the trigger tool. The trigger tool revealed only false-positive scores and left harmful MEs undiscovered. Even after modification by adding the symptoms pain and nausea/vomiting, the measurement performance was poor.

The inability of the trigger tool to detect (harmful) MEs in our study deviates from the results of other studies. Takata et al\(^{18}\) identified 19 harmful MEs with the medication-focused trigger tool in a population of 960 pediatric patients. Furthermore, Burch\(^{25}\) discovered 5 harmful MEs in 59 patients with the same pediatric trigger tool in a rehabilitation hospital. Trigger tools developed for adult inpatients were also able to identify adverse drug events and MEs\(^{14,17,26}\). Conflicting results have been reported when comparing the trigger tool methodology with other detecting methods. Several studies reported that the trigger tool methodology is superior to the review of clinical records and voluntary incident reports\(^{14,18,25}\). However, other studies have reported limited efficiency gains in using a medication-focused trigger tool\(^{16,26,27}\). Our study supports this latter conclusion.

There are several possible explanations for the differences between our results and those presented in other studies. First, the ability of a trigger tool to detect (harmful) MEs is very much dependent on the choice of the triggers. In a systematic review, Handler et al\(^{28}\) stated that the number and combination of triggers vary considerably in different studies. In addition, more recent publications show variability in the number of triggers used\(^{15-21,25,29-43}\). We adapted an existing trigger tool developed in the United States. Hospital and patient characteristics could have affected the types of harmful MEs, requiring specific triggers to unravel hazardous situations. In our study, the trigger tool plus the symptoms pain and nausea/vomiting successfully identified 19 harmful MEs, of which 12 were identified by the extended trigger tool only. These results suggest that the additional benefit of the trigger tool is very much dependent on the triggers chosen. Second, the heterogeneity in results may also be explained by differences in definitions and reference values used. In the present study, we focused on harmful MEs, defined as adverse events that we decided were preventable and caused harm to the patient. We included all types of MEs, also omissions and deviations in administering time. This resulted in a prevalence of harmful MEs in our present study that is at the higher range of
results reported in other studies. This is particularly important because the prevalence has an impact on the predictive values. Third, the original medication-focused trigger tool did not identify any harmful ME, but this might be the result of the relatively small sample size in our study. Fourth, our deviating results might be explained by the main outcome of the study. The trigger tool methodology was designed for detecting a broad range of adverse events, taking time limitations into account. In our study, we chose a more narrow scope; for example, we defined preventable drug events associated with patient harm as the main outcome of interest. We believe that this information is most relevant because it presents situations that can be improved by risk reduction programs. The scope influences the results, and comparisons with other studies must be made with caution. Finally, experiences with the Global Trigger Tool show that up to 30% of adverse events are found without specific triggers. These adverse events are identified “spontaneously” while reviewing patient notes after a positive trigger. In this present study, we included only MEs associated with triggers and ignored MEs requiring specific triggers to unravel hazardous situations. In our study, the trigger tool plus the symptoms pain and nausea/vomiting successfully identified 19 harmful MEs, of which 12 were identified by the extended trigger tool only. These results that were not associated with the triggers. This might have influenced our results to be unfavorable for the trigger tool, but we considered this method necessary to establish the performance of the pediatric trigger tool accurately.

The mean time to perform a full review of clinical records was still consistent with recommendations from the Institute for Healthcare Improvement to spend no longer than 20 minutes reviewing each chart because this does not usually yield additional information. However, the trigger tool seemed more efficient as reflected in the time investment that was far less than the time needed to review the clinical records. This is an important advantage for both routine monitoring of medication safety and research projects.

Limitations

Although using 4 event detection methods to establish the reference comparison for the trigger tool method is a serious attempt to identify all MEs, it is likely, yet unknown, that MEs occurred that were not captured by this multifaceted method. Therefore, the reported sensitivity and specificity attribute to the growing knowledge of the trigger tool methodology but are limited by the absence of a criterion standard. Second, we collected our data retrospectively, which may have introduced documentation bias.
because the quality of the data relies entirely on the information recorded in the clinical records and incident reports.47 Third, the reliability of both the multifaceted method and the trigger tool methodology is a concern. The reliability of the extended version of the trigger tool especially is surprisingly low, suggesting the subjectivity of the triggers pain and nausea/vomiting. Experienced and trained teams that are familiar with the local situation, and have a structured strategy to reach consensus in identification and classification of MEs, seem essential to obtain reliable data.26,29,48,49 In our study, the experience with the trigger tool methodology was still growing, and we did not discuss all harmful MEs in the teams. More attention for these aspects might have increased the interobserver reliability.

**Future Directions**

At present, the limited ability of the trigger tool to detect MEs in children does not make it an attractive alternative to a multifaceted method. However, with medical records becoming more and more electronic, new possibilities and challenges arise. Integrating triggers in the electronic medical records allows real-time detection of adverse drug events and moves patient safety from a retrospective focus on errors to real-time detection of adverse drug events. Future research should focus on the use of triggers as part of the electronic patient records to identify patients at risk for adverse drug events, by combining patient information, for example, medication use and laboratory results. This real-time detection has the ability to capture the preventable adverse drug events but might also play an important role in amelioration and recovery of events that until now are thought to be unpreventable. In future research, the concept of preventability might be replaced by amelioration and mitigatibility.

Second, in the present research, most triggers are defined as biomedical signals and are less focused on organizational alerts. The evidence is growing that competencies of health care professionals50 and safety culture51,52 are also associated with adverse events. We recommend more research on these issues in relation to medication safety for children.
CONCLUSIONS
For the detection and reporting of MEs, a multifaceted approach is recommended. We used the combination of a review of clinical records and voluntary incident reports. This multifaceted approach was established as the most effective in the first part of our study. Therefore, we are confident that this approach establishes a high level of certainty for the presence or absence of harmful MEs.

The trigger tool methodology has been developed for the purpose of monitoring adverse events using a technique that would be applicable throughout the health care system. However, the results of our study suggest that exchange of trigger tools between organizations may be limited. The high number of false-negative scores represents unsafe situations that are not discovered and might result in a feeling of false security. This might delay the development and implementation of effective interventions and thus continue to threaten patient safety. We conclude that a multifaceted method remains the preferred method to detect harmful MEs. The additional value of the trigger tool stays unclear.

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Authors’ contributions
HV, study design and supervision; JM, DB, AB, PR, MS, data collection; JM, data analyses; JM, MS, HV, interpretation of data; JM drafting the manuscript; all authors, revising the manuscript for intellectual content and final approval.

Competing interest
The authors declare that they have no competing interests.

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