Annals of Pharmacotherapy
47(11) 1414–1419

DOI: 10.1177/1060028013500939
aop.sagepub.com
SAGE

Performance of the Adverse Drug Event Trigger Tool and the Global Trigger Tool for Identifying Adverse Drug Events: Experience in a Belgian Hospital

Lise Carnevali, MSc[1,*], Bruno Krug, PhD[1,*], Fabienne Amant, RN[1], Dominique Van Pee, PhD[1], Véronique Gérard, MD[1], Xavier de Béthune, MD[2], and Anne Spinewine, PhD[1,3]

Abstract

Background: Medication-related harm can be detected using the adverse drug event (ADE) trigger tool and the medication module of the Global Trigger Tool (GTT) developed by the Institute for Healthcare Improvement (IHI). In recent years, there has been some controversy on the performance of this method. In addition, there are limited data on the performance of the medication module of the GTT as compared with the ADE trigger tool. **Objectives:** To evaluate the performance of the ADE trigger tool and of the medication module of the GTT for identifying ADEs. **Methods:** The methodology of the IHI was used. A random sample of 20 adult admissions per month was selected over a 12-month period in a teaching hospital in Belgium. The ADE trigger tool was adapted to the Belgian setting and included 20 triggers. The positive predictive value (PPV) of each trigger was calculated, as well as the proportion of ADEs that would have been identified with the medication module of the GTT as compared with the ADE trigger tool. **Results:** A total of 200 triggers and 62 ADEs were found, representing 26 ADEs/100 admissions. Nineteen ADEs (31%) were found spontaneously without the presence of a trigger. Three triggers never occurred. The PPVs of other triggers varied from 0 to 0.67, with half of them having PPVs less than 0.20. If we had used the medication triggers included in the GTT (n = 11), we would have identified 77% of total ADEs and 67% of preventable ADEs. **Conclusions:** Applying the trigger tool method proposed by the IHI to a Belgian hospital led to the identification of one ADE out of 4 admissions. To increase performance, refining the list of triggers in the ADE trigger tool and in the medication module of the GTT would be needed. Recording nontriggered events should be encouraged.

Keywords

trigger tool, medication errors, adverse drug reactions reporting systems, safety management, Belgium

Received May 30, 2013

Introduction

The trigger tool methodology is a retrospective review of a random sample of patient records using triggers to identify possible adverse events associated with patient care. Medication-related harm can be detected using adverse drug event (ADE) triggers. The generic ADE trigger tool was developed in 2004 by the Institute for Healthcare Improvement (IHI) to specifically identify ADEs. It has 19 triggers.[1] This IHI ADE trigger tool provided the basis for development of subsequent trigger tools. Among these, the IHI Global Trigger Tool (GTT), developed in 2009, goes beyond medications to include any noxious or unintended event occurring in association with medical care.[2] Triggers in the GTT are grouped into six modules. The medication module is one of them, and includes 12 of the 19 triggers of

[1]Université catholique de Louvain, CHU Mont-Godinne Dinant, Yvoir, Belgium
[2]Alliance Nationale des Mutualités Chrétiennes, Brussels, Belgium
[3]Université catholique de Louvain, Louvain Drug Research Institute, Brussels, Belgium
[*]These authors contributed equally to the study

Corresponding Author:
Anne Spinewine, PhD, Université catholique de Louvain, Louvain Drug Research Institute, Clinical Pharmacy Research Group, Av E Mounier, 73 B1.72.02, 1200 Brussels, Belgium.
Email: anne.spinewine@uclouvain.be

Table 1. ADE Triggers and Medication Module Triggers From the GTT.

Triggers of the ADE Trigger Tool		Triggers of the Medication Module of the GTT	
IHI Version (n = 19)[1]	Version Used in the Present Study (n = 20)[8]	IHI Version (n = 12)[2]	Version Used in the Present Study (n = 11)
T1 Diphenhydramine	Antihistamine	M7 Diphenhydramine	Diphenhydramine
T2 Vitamin K	Vitamin K	M6 Vitamin K	Vitamin K
T3 Flumazenil	Flumazenil	M8 Flumazenil	Flumazenil
T4 Antiemetics	Antiemetics	M10 Antiemetic	Antiemetic
T5 Naloxone	Naloxone	M9 Naloxone	Naloxone
T6 Antidiarrheals	Antidiarrheals	—	—
T7 Sodium polystyrene	Sodium polystyrene	—	—
T8 Glucose <50 mg/dl	Glucose <50 mg/dL	M4 Glucose <50 mg/dL	Glucose <50 mg/dL
T9 Clostridium difficile positive stool	Clostridium difficile positive stool	M1 Clostridium difficile positive stool	Clostridium difficile positive stool
T10 PTT >100 seconds	—	M2 PTT >100 seconds	—
T11 INR >6	INR >6	M3 INR >6	INR >6
T12 WBC <3000/mm^3	WBC <3000/mm^3	—	—
T13 Platelet count <50 000/mm^3	Platelet count <50 000/mm^3	—	—
T14 Digoxin level >2 ng/mL	Digoxin level >2 ng/mL	—	—
T15 Rising serum creatinine	Rising serum creatinine twice over baseline	M5 Rising BUN or serum creatining 2 times (2×) over baseline	Rising BUN or serum creatining 2 times (2×) over baseline
T16 Oversedation, lethargy, falls	Oversedation, lethargy	M11 Oversedation, hypotension	Oversedation, lethargy
—	Emergence of confused state		
—	Falls		
T17 Rash	Rash	—	—
T18 Abrupt medication stop	Abrupt medication stop	M12 Abrupt medication stop	Abrupt medication stop
T19 Transfer to a higher level of care	Transfer to a higher level of care	—	—

Abbreviations: ADE, adverse drug event; BUN, blood urea nitrogen; GTT, Global Trigger Tool; IHI, Institute for Healthcare Improvement; INR, international normalized ratio; PTT, partial thromboplastin time; WBC, white blood cells.

the ADE trigger tool (Table 1).[1] To the best of our knowledge, there are no explicit data on the performance of the restricted list of triggers in the medication module of the IHI GTT as compared with the IHI ADE trigger tool.[1]

Both tools are widely used in North America, mainly in the acute care setting, but relatively few published studies reported the use of trigger tools in countries outside North America.[3-5] Moreover, in recent years, there has been some controversy on the performance of this method, with poor sensitivity described in a UK study, and low positive predictive values (PPVs) for many triggers in others.[3,6,7] Even though sensitivity will vary between sites and between providers, and interpretation of results will depend on the objectives of the study, the evaluation of performance of trigger tools remains a relevant research question.

Our objectives were to evaluate, outside North America (*a*) the PPVs of the triggers of the ADE trigger tool and (*b*) the performance of the medication module of the GTT in comparison with the ADE trigger tool for identifying ADEs.

Method

The study was conducted in a 450-bed teaching hospital with approximately 15 000 admissions per year (CHU UCL Mont-Godinne, Belgium). A monthly sample of 20 admissions was selected according to the methodology of the IHI over a 12-month period (February 2010 to January 2011) and using a computer-generated randomization process.[1] Exclusion criteria were as follows: patient younger than 18 years, length of stay <48 hours, and incomplete record (no discharge letter, no nurse chart, or no treatment available). During the 12-month period, 259 patient records were analyzed among which 19 (7%) had to be excluded because of missing data.

The IHI list of ADE triggers (n = 19) was adapted to the Belgian setting. One trigger was removed (partial thromboplastin time >100 seconds) because it was considered as redundant with the international normalized ratio (INR) trigger, one was added (emergence of confused state) because in a preliminary study it had been identified as a

Table 2. Characteristics of ADEs (n = 62) and Examples.

Characteristics	n (%)	Examples
Source of identification	62 (100)	
Triggered ADE	43 (69)	C difficile diarrhea secondary to piperacillin-tazobactam for pneumonia
Nontriggered ADEs	19 (31)	Esophageal candidiasis secondary to the administration of inhaled steroids
Setting where the ADE developed	62 (100)	
ADEs developing during hospital stay	43 (69)	Confusion secondary to hyponatremia caused by high amounts of intravenous glucose administration
ADEs developing prior to admission, and present on admission	19 (31)	Intracranial hemorrhage in a patient taking acenocoumarol and with an INR at 6.5 on admission
Severity score (NCC-MERP)	62 (100)	
E: Temporary harm to the patient and required intervention	42 (68)	Chemotherapy-induced anemia treated with erythropoietin
F: Temporary harm to the patient and required initial or prolonged hospitalization	17 (27)	Patient admitted for syncope with severe bradycardia secondary to a too high dose of bisoprolol
G: Permanent patient harm	2 (3)	Intracranial hemorrhage in a patient taking acenocoumarol, with subsequent hemiparesis
H: Intervention required to sustain life	1 (2)	Hyperkalemia associated with severe cardiac arrhythmia in a patient with renal failure and receiving spironolactone and candesartan
I: Patient death	0 (0)	
Preventability of hospital-acquired ADEs	43 (100)	
Nonpreventable	28 (65)	Morphine-induced pruritis
Preventable	15 (35)	Potassium supplementation administered during too long a period, leading to hyperkalemia requiring administration of sodium polystyrene

Abbreviations: ADE, adverse drug event; INR, international normalized ratio; NCC-MERP, National Coordinating Council–Medical Error Reporting and Prevention.

potentially valuable trigger, and the trigger "oversedation, lethargy, and falls" was divided in 2 separate triggers (oversedation, lethargy as one trigger and fall as another) because fall is a specific recorded trigger for quality of care in Belgium.[8] Our list therefore included 20 triggers (Table 1).

We used the method recommended by the IHI to identify ADEs, as explained in the 4 points described below. First, researchers were trained to detecting ADEs using the trigger tool. Second, 1 clinical pharmacist and 1 nurse (ie, members of the research team) identified triggers and ADEs in the electronic health records. They sequentially looked for triggers in the following documents: discharge summary, laboratory data, medical and medication orders, nursing flow sheets, and nursing or medical progress notes. When a trigger was found, patient record was investigated in depth to determine whether an ADE occurred. If an ADE was discovered incidentally when going through the patient charts, without the presence of a specific trigger, this ADE was also taken into account and recorded as a "nontriggered" or "spontaneous" ADE, in accordance with the IHI methodology. Third, the 2 reviewers spent a maximum of 20 minutes per patient record. Fourth, ADEs were validated each month by 3 physicians during a multidisciplinary meeting. Severity of the ADEs was evaluated using the National Coordinating Council–Medical Error Reporting and Prevention (NCC-MERP) Index.[9]

Researchers also determined if hospital-acquired ADEs could have been prevented, using Schumock and Thornton's[10] preventability criteria. The latter consist of 7 criteria, ranging from drug appropriateness to compliance. Participants addressed each of these criteria and based on their answers reached a consensus on preventability.

We calculated the PPV of each trigger (number of ADEs identified with the trigger/number of triggers found in the patient charts). We also calculated the proportion of ADEs that would have been identified with the medication module of the GTT as compared with the ADE trigger tool (number of ADEs identified with the medication module of the GTT/number of ADEs identified with the ADE trigger tool). We considered that spontaneous ADEs would have been identified whichever tool was used, and these ADEs were then included in both the numerator and denominator.

The work was conducted in compliance with the requirements of the local institutional review board.

Results

On reviewing the medical records of 240 patients, 200 triggers and 62 ADEs were found. Of these 62 ADEs, 19 (31%) were found spontaneously without the presence of a trigger (Appendix A). Prevalence of ADEs was as follows: 26

Table 3. Prevalence of Triggers and ADEs and PPVs of Triggers.

Triggers[a]	No. of Triggers Found in the Charts	All ADEs[b]		Preventable ADEs	
		n	PPV	n	PPV
C difficile positive stool[a]	3	2	0.67	1	0.33
Sodium polystyrene	10	5	0.5	1	0.10
INR >6[a]	4	2	0.5	0	0
Abrupt medication stop[a]	30	13	0.43	3	0.10
Rash	10	4	0.4	0	0
WBC <3000/mm^3	9	3	0.33	0	0
Platelet count <50 000/mm^3	6	2	0.33	0	0
Rising serum creatinine (twice baseline value)[a]	11	3	0.27	0	0
Antihistamine[a]	8	2	0.25	0	0
Falls	16	3	0.19	2	0.13
Vitamin[a]	6	1	0.17	0	0
Serum glucose <50 mg/dL[a]	8	1	0.13	0	0
Oversedation, lethargy[a]	21	2	0.10	0	0
Emergence of confused state	22	2	0.09	2	0.09
Antiemetic[a]	28	2	0.07	0	0
Antidiarrheals	1	0	0	0	0
Transfer to higher level of care	7	0	0	0	0
Flumazenil[a]	0	0	NA	0	NA
Digoxine level >2.6 nmol/L	0	0	NA	0	NA
Naloxone[a]	0	0	NA	0	NA

Abbreviations: ADE, adverse drug event; INR, international normalized ratio; NA, not applicable; PPV, positive predictive value (number of ADEs identified with the trigger/number of triggers found); WBC, white blood cells.
[a]Triggers included in the medication module of the Global Trigger Tool.
[b]In some cases, one ADE is identified with more than one trigger.

ADEs per 100 admissions, or 23 ADEs per 1000 patient days. The majority of ADEs were associated with a NCC-MERP harm score of E (68%) and F (27%). Of all ADEs, 69% were hospital-acquired (n = 43), and 35% of the hospital-acquired ADEs were considered to be preventable (n = 15). Forty percent of these preventable ADEs were nontriggered events (n = 6). Characteristics and examples of ADEs are presented in Table 2.

The PPV of the individual triggers ranged from 0 to 0.67 (Table 3). Three triggers had PPVs at 0.5 or higher (C difficile positive stool, sodium polystyrene, and INR >6), 6 triggers had PPVs ranging between 0.25 and 0.49, 8 triggers had PPVs less than 0.2, and 3 triggers never occurred. The trigger that was added as compared with the IHI ADE trigger tool (ie, emergence of confused state) predicted 2 ADEs and had a PPV at 0.09. If we had used the list of 11 ADE triggers included in the medication module of the GTT, we would have identified 77% (48/62) of the ADEs found with the 20 triggers of the ADE trigger tool. This means that almost 1 out of 4 ADEs detected by the ADE trigger tool remains undetected with the medication module of the GTT. When looking exclusively at preventable ADEs, using the medication module of the GTT would have led to the identification of 67% (10/15) of the preventable ADEs identified with the ADE trigger tool.

Discussion

Applying the trigger tool method to a Belgian teaching hospital led to the identification of 1 ADE out of 4 admissions. We followed the rigorous method described by the IHI for the ADE trigger tool and looked at all types of admissions in our hospital. However, the study was monocentric, and we observed high variability between wards in completeness of the charts, which might affect sensitivity. This variability is mainly related to the type of admission. In contrast to medical admissions, discharge summaries and daily notes from surgical admissions had scarce data on patient profiles and evolution during hospital stay. Despite these limitations, we believe that 3 points of interest emerge from the findings: low sensitivity of many triggers, suboptimal performance of the GTT, and added value of recording nontriggered events.

Three triggers never occurred (flumazenil, digoxine >2.6 nmol/L, and naloxone), and PPVs of other triggers were highly variable. Overall, half of triggers had PPVs less than 0.20. Although there is no cutoff value to dichotomize good

and bad PPVs, we believe that having so many triggers at this lower range questions the performance of the tool.

The 5 triggers with the highest PPVs in our study were the same as those found in another UK study: C difficile positive stool, sodium polystyrene, INR >6, abrupt medication stop, and rash.[3] Some other studies reported also high PPVs for the trigger INR >6 and sodium polystyrene, but overall the results for other triggers are generally inconsistent.[6,7,11] We therefore suggest that to optimize performance, refining the list of triggers would be needed before using this tool in routine. Furthermore, for an institution considering implementation of trigger tools, there should be at least a literature search for other institutions experiences with the use of various triggers, if not also a site-specific evaluation of effectiveness.

Special attention should be paid to the list of medication triggers in the GTT. To the best of our knowledge, this is the first study to report the performance of the medication module of the GTT as compared with the ADE trigger tool for identifying ADEs. Our results indicate that one fourth to one third of ADEs would not have been detected by the medication module of the GTT. For example, sodium polystyrene is not included in the GTT but was one of the most informative triggers in our study. In contrast, flumazenil and antiemetic had limited or no added value in our study but are included in the GTT. If the GTT trigger list was refined as suggested in Appendix B, we would have identified 89% (55/62) of the ADEs and 87% (13/15) of the preventable ones. Before using a modified list of triggers for detecting ADEs as part of the GTT in the acute care setting, our results should be complemented by similar analyses from multicenter studies.

Similarly to Szekendi et al,[11] we found that 40% of preventable ADEs were identified with nontriggered events. A detailed analysis of the nontriggered events identified in the present study revealed that these ADEs were variable (see Appendix B). Interpretation of these findings generates 2 interesting points for discussion. (*a*) As recommended by the IHI tools, the extension of medical record review to capture events beyond those related to triggers is therefore valuable. This could be better highlighted in the tools and should be systematically reported in studies using the trigger tool method, which was not the case in several recent publications.[7,12] (*b*) It is not possible to identify 1 or 2 new triggers that could capture most of them. However, our data suggest that hyperglycemia, hypokalemia, and hyponatremia could be further studied as possible triggers. Specificity would need to be evaluated, including for preventable ADEs, as the PPV might be low.

In conclusion, applying the trigger tool method proposed by the IHI to a Belgian hospital led to the identification of 1 ADE out of 4 admissions. However, to increase performance, refining the list of triggers in the ADE trigger tool and also in the medication module of the GTT would be needed. Special attention should be paid to preventable events in future studies. Recording nontriggered events should be encouraged.

Appendix A

List of ADEs found spontaneously (without the presence of a trigger).

1. Anemia secondary to chemotherapy, treated with red-blood cell transfusion and erythropoietin (detected twice)
2. Pancytopenia secondary to chemotherapy, leading to local bleeding
3. Diurnal hypercapnia secondary tramadol
4. Hyponatremia secondary to the administration of diuretic therapy and fluid therapy with glucose 5%
5. New onset diabetes secondary to high doses of methylprednisolone
6. Deterioration of diabetes control in a patient receiving steroids
7. Epistaxis secondary to steroids
8. Oral candidiasis secondary to the administration of inhaled steroids
9. Hypocorticism secondary to steroid therapy (high doses)
10. Sodium and water retention secondary to nonsteroidal anti-inflammatory drug (NSAID) therapy for which a diuretic was needed
11. Allergic reaction to anti-lymphocyte antibodies
12. Respiratory tract infection secondary to the administration of leflunomide
13. Nausea and vomiting secondary to opioids, leading to local bleeding (inguinal area)
14. Esophageal candidiasis secondary to the administration of inhaled steroids
15. Severe hypokalemia secondary to diuretic therapy
16. Severe constipation in a patient receiving strong opioids but no laxative (detected twice)
17. Inhalation pneumonia secondary to enteral nutrition

Appendix B

List of ADE Triggers in the Global Trigger Tool.

Triggers in the Medication Module of the Global Trigger Tool[a]	Modified List With Improved Performance Based on the Results of the Present Study
1. C difficile positive stool	1. C difficile positive stool
2. INR >6	2. INR >6
3. Antihistamine	3. Antihistamine
4. Rising serum creatinine (twice baseline value)	4. Rising serum creatinine (twice baseline value)
5. Abrupt medication stop	5. Abrupt medication stop
6. Vitamin K	6. Sodium polystyrene
7. Serum glucose < 50 mg/dL	7. WBC <3000/mm^3
8. Oversedation	8. Platelet count <50 000/mm^3
9. Antiemetic	9. Falls
10. Flumazenil	10. Rash
11. Naloxone	

Abbreviations: ADE, adverse drug event; INR, international normalized ratio; PTT, partial thromboplastin time; WBC, white blood cells.
[a]PTT >100 seconds was not included in present study.

Authors' Note

This work was presented as a poster at the International Forum on Quality and Safety in Health Care, Paris, France in April 2012.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Institute for Healthcare Improvement. IHI trigger tool for measuring adverse events. http://www.ihi.org/knowledge/Pages/Tools/TriggerToolforMeasuringAdverseDrugEvents.aspx. Accessed January 1, 2004).
2. Klaeser B, Nitzsche E, Schuller JC, et al. Limited predictive value of FDG-PET for response assessment in the preoperative treatment of esophageal cancer: results of a prospective multi-center trial (SAKK 75/02). *Onkologie*. 2009;32:724-730.
3. Franklin BD, Birch S, Schachter M, Barber N. Testing a trigger tool as a method of detecting harm from medication errors in a UK hospital: a pilot study. *Int J Pharm Pract*. 2010;18:305-311.
4. Schildmeijer K, Nilsson L, Arestedt K, Perk J. Assessment of adverse events in medical care: lack of consistency between experienced teams using the global trigger tool. *BMJ Qual Saf*. 2012;21:307-314.
5. Lipczak H, Knudsen JL, Nissen A. Safety hazards in cancer care: findings using three different methods. *BMJ Qual Saf*. 2011;20:1052-1056.
6. Brenner S, Detz A, Lopez A, Horton C, Sarkar U. Signal and noise: applying a laboratory trigger tool to identify adverse drug events among primary care patients. *BMJ Qual Saf*. 2012;21:670-675.
7. Singh R, McLean-Plunckett EA, Kee R, et al. Experience with a trigger tool for identifying adverse drug events among older adults in ambulatory primary care. *Qual Saf Health Care*. 2009;18:199-204.
8. Staines A, de Bethune X. L'outil déclencheur pour la mesure des événements indésirables médicamenteux de l' "Institute for Healthcare Improvement": analyse exploratoire et adaptation au milieu francophone. *Risques et qualité*. 2010;7:145-154.
9. Schmidt M, Bollschweiler E, Holscher A. F-18-fluorodeoxiglucose positron emission tomography for the evaluation of neoadjuvant therapy response in esophageal cancer. *Ann Surg*. 2010;252:412-413.
10. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. *Hosp Pharm*. 1992;27:538.
11. Szekendi MK, Sullivan C, Bobb A, et al. Active surveillance using electronic triggers to detect adverse events in hospitalized patients. *Qual Saf Health Care*. 2006;15:184-190.
12. Good VS, Saldana M, Gilder R, Nicewander D, Kennerly DA. Large-scale deployment of the Global Trigger Tool across a large hospital system: refinements for the characterisation of adverse events to support patient safety learning opportunities. *BMJ Qual Saf*. 2011;20:25-30.