International Journal of Clinical Pharmacy (2019) 41:1174–1183
https://doi.org/10.1007/s11096-019-00871-x

RESEARCH ARTICLE

# Development of a trigger tool for the detection of adverse drug events in Chinese geriatric inpatients using the Delphi method

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Received: 15 August 2018 / Accepted: 20 June 2019 / Published online: 28 June 2019


## Abstract

*Background* The global trigger tool is a method of retrospective medical record review that identifies possible harm in hospitalized patients using "triggers". Elderly patients with multiple co-morbid illnesses are especially vulnerable to adverse drug events (ADEs) that have high prevalence rates. *Objective* The purpose of this study was to develop an appropriate trigger tool to detect ADEs in Chinese geriatric inpatients by combining a literature review with the Delphi method. *Setting* Chinese geriatric inpatients. *Methods* Two steps were used to develop the trigger tool. First, we conducted a comprehensive literature review for existing ADE triggers (adult or elderly) to form the initial triggers for the Delphi process. Second, a group of clinical experts, including physicians, clinical pharmacists and nurses, was established to score candidate triggers for utility according to the usefulness and feasibility of implementing triggers in clinical practice. *Main outcome measures* The frequency of the full mark, arithmetic mean and coefficient of variation of each trigger. *Results* An initial set of 51 triggers was selected by literature review for evaluation. The group of experts was composed of 18 clinical experts: 13 physicians, 4 clinical pharmacists, and 1 nurse. Based on the two-phase Delphi process, 42 triggers in five categories (laboratory index, plasma concentration, antidotes, clinical symptoms and intervention) were retained. *Conclusion* The 42-trigger tool was developed to identify ADEs in Chinese geriatric inpatients. A pilot study that tests the list of triggers to identify ADEs in Chinese geriatric inpatients is the next step for establishing a specific trigger tool for Chinese geriatric inpatients.

**Keywords** Adverse drug events · China · Delphi method · Geriatric patients · Global trigger tool

## Impacts on practice

- Adverse drug events (ADEs) are common in Chinese geriatric patients.
- The global trigger tool can be used as a quality improvement tool in clinical practice to estimate and track ADE rates.
- It is desirable that the specific trigger tool for Chinese geriatric inpatients is further developed and studied.

## Introduction

Adverse drug events (ADEs) are defined as "the injuries resulting from a medical intervention related to a drug and can manifest as signs, symptoms or laboratory abnormalities" by the Institute of Medicine [1]. In the Harvard Medical Practice Study, injuries due to drugs were the most frequent cause of adverse events and correlated with about 1% of all hospitalized patients suffering a disabling injury [2]. Other studies have also suggested that medication-related harms not only account for prolonging hospital stay, but also cause 100,000 deaths per year and as much as $10 to $150 billion in United States health care costs annually [3, 4]. It should be noted that according to a meta-analysis, approximately half of ADEs are preventable among both inpatients and outpatients [5]. Therefore, proper steps should be taken to establish appropriate methods to detect and characterize ADEs, especially those classified as preventable, with the aim of preventing their occurrence and improving patient safety [6].

**Electronic supplementary material** The online version of this article (https://doi.org/10.1007/s11096-019-00871-x) contains supplementary material, which is available to authorized users.

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Several methods have been used to identify and measure ADEs to provide health care teams with an adequate picture of potential ADEs, including screening voluntary reports, mining administrative databases, and reviewing patient claims and medical records [7, 8]. For example, the National Center for Adverse Drug Reactions Monitoring has established the National Adverse Drug Reaction Monitoring System, a spontaneous reporting system, to report each adverse drug reaction or adverse drug event (ADR/ADE) in China and to improve the data quality management of ADR/ADE reports, a normative grading criterion based on the World Health Organization criteria.

However, public health researchers have established that only 10–20% of errors are ever reported [9]. A 10-year study of adult inpatients in North Carolina, United States showed that the vast majority of ADEs go undetected by traditional methods, and common detection techniques have not produced consistent approaches to measure harm [10]. Thus, alternative surveillance strategies are needed to supplement existing detection strategies.

The global trigger tool (GTT), which was developed by the Institute for Healthcare Improvement in 2003, is a retrospective medical record review of a random sample of inpatient hospital records using "triggers" to identify possible adverse events [9]. These triggers are derived from clinical logic to flag medical records, which alerts reviewers to initiate further in-depth investigations regarding the patient's record to determine the presence or absence of an adverse event; for example, a trigger is a value of blood glucose lower than 28 mg/dL in a patient with oral antidiabetic or insulin, which may alert professionals to perform a more detailed record review for evidence that the patient has an associated hypoglycemia. This method can be used in practice to track and assess ADE rates [11] and to determine whether adverse events are reduced over time as a result of improvement efforts [9]. The GTT found at least ten times more confirmed events than traditional methods [8, 12]. Therefore, it has been widely used and improved worldwide, in countries such as Sweden [11], the United Sates [13], the United Kingdom [14] Australia [15], Korea [16], and Belgium [17]. Triggers are also being customized for use in perinatal inpatient, pediatric inpatient, outpatient, and ambulatory care settings [18].

Older adults have higher ADE prevalence rates compared with other age groups [19]. The high risks are often related to multiple co-morbid illnesses, polypharmacy, and difficulty monitoring prescribed medications [20, 21], as well as age-related changes in pharmacokinetics and pharmacodynamics that are linked mechanistically to altered drug handling, altered physiological reserve, and responses [22]. Statistical data from the United States have indicated that older adults account for 35% of all hospital stays, while at the same time accounting for 53.1% of hospital ADEs [23]. The reduction of ADEs in these vulnerable patients has become a major patient safety goal in various settings [24, 25]; however, few trigger tools have focused on geriatric inpatients.

## Aim of the review

The purpose of this study was to combine a literature review with the Delphi method to develop an appropriate trigger tool for Chinese geriatric inpatients to detect ADEs.

## Ethics approval

Ethics approval was obtained from the respective ethics committees at the West China Hospital of Sichuan University, China (2018-232). All of the panelists invited to participate in this study gave verbal consent before taking part in the study. To protect the participants from any consequences, data were made anonymous before analyses. The views and opinions of each panelist were considered equally.

## Methods

Two steps were conducted to develop the trigger tool for the detection of ADEs in Chinese geriatric inpatients, including a literature review and two-phase Delphi process.

### Literature review

A comprehensive search of multiple literature databases was conducted by two researchers (Hu and Zhan) to collect trigger tools already in use. The databases searched were PubMed (1978-2016.12), Embase (1974-2016.12), and the China National Knowledge Infrastructure (1979-2016.12) to obtain English or Chinese publications. A dual strategy employing a combination of Medical Subject Headings and 'free-text' terms was used where possible to ensure maximum coverage.

Studies that reported the development of an ADE trigger tool for adult and/or elderly patients, published in English or Chinese were included. The studies were excluded if they met any one of the following criteria: (1) only reported the surgical module triggers or care module triggers, instead of the medication module triggers; (2) the results of the study focused on perinatal inpatients or pediatric inpatients; (3) the purpose of the study was to establish a trigger tool for some special departments, such as stomatology or radiology; (4) the study just introduced the application of the trigger tool and did not try to develop a new trigger tool.

Two researchers (Hu and Zhan) independently abstracted the information from the original publications, including the

study characteristics, nation, study population, clinical setting, and triggers. One researcher (Wu) checked the information. Cases of divergence were resolved by discussion.

## Delphi method

### Expert panel

The criteria of the invited clinical experts were that: (1) the expert group would consist mainly of physicians and would also include clinical pharmacists and nurses; (2) the experts had been engaged in clinical and research work for more than 10 years in tertiary hospitals or universities; (3) the specialty of each clinical expert should involve the common diseases of the elderly.

### Questionnaire

Triggers from the literature were initially revised by our study group. These revisions included: adapting to local laboratory indices and merging of similar triggers. Our study group classified the initial triggers into five categories (laboratory index, plasma concentration, antidotes, clinical symptoms and intervention) and produced the initial questionnaire.

To measure the utility of geriatric trigger tools, panelists were required to rate the initial set of trigger tools on a scale from 0 to 10 (10: high; 0: low) according to the following criteria. The criteria included: usefulness of triggers in Chinese geriatric patients; and feasibility of implementing triggers' use in clinical practice. After the first round, panelists could suggest additional triggers and provide suggestions to improve the test characteristics of each trigger. In the second round, the modified set of triggers were rated again using the same selection criteria.

In addition, panelists were required to conduct a self-evaluation of judgment criterion (Ca) for the indicators and familiarity with the indicators (Cs) in two-round. The sum of the scores of four dimensions were used to calculate the Ca, including practical experiences, theoretical analysis, reference to the literature and intuition (Table 1). The Cs scores were 1.0, 0.8, 0.6, 0.2, and 0, respectively.

In the Delphi process, questionnaires were delivered to the experts individually by email. Each Delphi round was open for 2 weeks, and reminders were emailed at the beginning and end of each 2-week period. Each survey took approximately 30 min to complete. If the experts had any question about this study, they could contact to the researcher (Hu). The non-completion of the previous round did not rule out panelists from contributing to the following round.

**Table 1** The rating scale of judgment criterion for the indicators

| Judgment criterion | Strong | Good | Moderate | Weak |
|---|---|---|---|---|
| Practical experiences | 0.5 | 0.3 | 0.1 | 0 |
| Theoretical analysis | 0.3 | 0.2 | 0.1 | 0 |
| Reference literature | 0.1 | 0.1 | 0.1 | 0 |
| Intuition | 0.1 | 0.1 | 0.1 | 0 |

### Screening criteria of triggers

The proportion of getting full mark (Kj), arithmetic mean (Mj), and coefficient of variation (CV) of each trigger were calculated. Exclusion criteria included: Kj and Mj < mean value (MD) — standard deviation (SD), and CV > MD + SD. To avoid eliminating important trigger, the trigger which only met all of exclusion criteria was rejected [26].

### Authority coefficient and agreement coefficient

The experts' authority coefficient (Cr) is the degree of authority of experts on the evaluated indicators, which is defined as $Cr = (Ca + Cs)/2$. Cr ranges from 0 to 1. In general, $Cr \geq 0.7$ means a high expert authority degree [27].

The agreement among responders is measured using Kendall's coefficient of concordance (W). Using W, one can make a realistic determination of whether a consensus has been reached and whether the consensus strength is increasing, as well as a determination of the relative strength of the consensus. W ranges from 0 to 1. In general, the higher the W, the more consistent the analysis is. $W \leq 0.3$ means weak agreement, $0.3 < W < 0.7$ means moderate agreement, and $W \geq 0.7$ means high agreement. However, there is not the exact cut-offs to the W [28].

### Statistical analysis

The databases were established using Excel 2016, and statistical analyses were performed using SPSS 23.0. The test indicates the statistical significance ($P$) of the correlation coefficient. $P < 0.05$ was considered statistically significant.

## Results

### Studies characteristics

Of the 328 articles retrieved from the databases, 324 were in English and 4 were in Chinese. A total of 316 articles that were repetitive studies or did not meet the inclusion criteria were excluded, so ultimately 12 articles were included [9, 13, 18, 29–37] (Fig. 1). These articles were published between 2003 and 2015. Six of them were from the United States [9, 13, 18, 29, 31, 32], and the other were from France

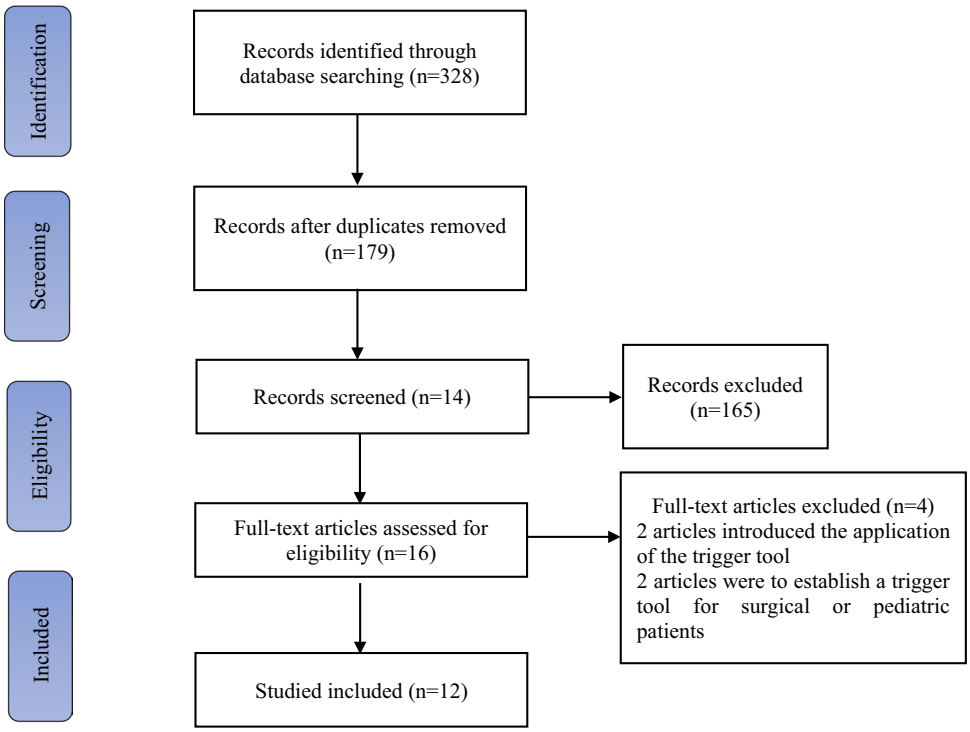


**Fig. 1** A flowchart of included studies

[30], the United Kingdom [33, 34], Belgium [35], Brazil [36], and the New Zealand [37] (Table 2).

## Expert panel

The expert panel comprised 18 experts (13 physicians, 4 clinical pharmacists and 1 nurse). The experts worked in different comprehensive tertiary hospitals or major universities in five provinces and cities of China. The physicians were from the departments of geriatric, oncology, respiration, gastroenterology, cardiology, endocrinology, nephrology, hematology, urology surgery, thoracic surgery, and general surgery. The clinical pharmacists worked in the departments of oncology, respiration, and general medicine. The nurse was from the departments of oncology. The response rate of the questionnaire was 94.44% (17/18) in round 1, and 61.711% (11/18) in round 2 (Table 3).

**Table 2** Characteristics of the included studies

| Study | Nation | Study population | Clinical setting | No. of triggers | Trigger type |
|---|---|---|---|---|---|
| Griffin [9] | USA | Adult patients | GW | 13 | 1, 3, 4, 5 |
| Brenner [29] | USA | Adult patients | GW | 5 | 1 |
| Hebert [30] | FRA | Cancer patients | Oncology | 25 | 1, 3, 4 |
| Rozich [31] | USA | Adult patients | GW | 24 | 1, 2, 3, 4, 5 |
| Marcum [32] | USA | Veterans | NH | 27 | 1, 2 |
| Franklin [33] | UK | Adult patients | GW | 23 | 1, 2, 3, 4, 5 |
| Resar [18] | USA | Adult patients | GW | 11 | 1, 2, 3, 5 |
| Handler [13] | USA | Elderly patients | NH | 40 | 1, 2, 3, 4, 5 |
| Iris [34] | UK | Adult patients | GW | 21 | 1, 2, 3, 4, 5 |
| Seynaeve [35] | BEL | Adult patients | ICU | 14 | 1, 3 |
| Rozenfeld [36] | BRA | Adult patients | GW | 18 | 1, 2, 3, 4, 5 |
| Falconer [37] | NZ | Adult patients | GW | 19 | 1, 2, 3, 4, 5 |

*USA* United States of America, *FRA* France, *UK* the United Kingdom, *BEL* Belgium, *BRA* Brazil, *NZ* New Zealand, *GW* general ward, *ICU* intensive care unit, *NH* nursing home, 1-laboratory index, 2-plasma concentration, 3-antidotes, 4-clinical symptoms, 5-intervention

**Table 3** Characteristics of the expert panel

| Characteristic | Round 1, n (%) | Round 2, n (%) |
|---|---|---|
| Number of panelists | 17 | 11 |
| Ages | | |
| 30–39 years | 1 (5.88) | 1 (9.09) |
| 40–49 years | 11 (64.71) | 8 (72.72) |
| 50–59 years | 5 (29.41) | 2 (18.18) |
| Professional field | | |
| Clinical medicine | 12 (70.58) | 7 (63.63) |
| Clinical pharmacy | 4 (23.53) | 4 (36.36) |
| Nursing | 1 (5.88) | 0 (0.00) |
| Title | | |
| Professor | 13 (76.47) | 8 (72.72) |
| Associate professor | 4 (23.53) | 3 (27.27) |
| Experience | | |
| More than 30 years | 5 (29.41) | 3 (27.27) |
| Between 20 and 30 years | 8 (47.06) | 7 (63.63 |
| Less than 20 years | 4 (23.53) | 1 (9.09) |

### Authority coefficient and agreement coefficient

In the two-phase Delphi process, the experts' authority coefficients were more than 0.7, which were 0.773 in round 1 and 0.778 in round 2. The experts' agreement coefficient (W) was 0.174 ($\chi^2 = 147.82$, $P = 0.000$) for the first-round triggers and 0.308 ($\chi^2 = 149.22$, $P = 0.000$) for the second-round triggers.

### Delphi process

According to the result of literature review, the initial set of trigger tool was established which included 51 triggers (Table 4). The two Delphi rounds were conducted consecutively. In the first-round, the critical values of Kj, Mj and CV were 14.32, 5.80, and 0.60, respectively. According to the screening criteria, the initial set of 51 triggers was pared to 45. 10 of 51 triggers were excluded, including one laboratory index trigger (creatine phosphokinase) and nine plasma concentration triggers (phenytoin, valproic acid, phenobarbital, carbamazepine, amikacin, lidocaine, lithium, procainamide, and quinidine). Four new triggers were added by expert panel (voriconazole > 5.5 mg/L, insulin used in non-diabetics, heart rates < 60 times/min, and respiratory rates < 12 times/min). In addition, five triggers were modified (international normalized ratio, liver function index, platelets, sodium polystyrene, and hemoglobin) (Supplement Table 1). In the second-round, the 45 triggers were measured, the critical values of Kj, Mj and CV were 6.04, 6.30 and 0.26, respectively. Three triggers were excluded (vancomycin, admission to the intensive care unit, and readmission within 30 days) (Supplement Table 2). Therefore, 42 triggers remained in the group after two Delphi rounds (Table 5).

## Discussion

In China, ADE monitoring still relies on a voluntary ADE reporting system. However, this traditional method overlooks as many as 95–99% of ADEs that are detectable by other methods [39, 40]. Hence, the development of a specific list of triggers to aid in the identification of ADEs should be more aligned with current strategies. In this study, a two-step process was conducted to design a trigger tool for the detection of ADEs in Chinese geriatric inpatients who are at high risk of ADEs. To the best of our knowledge, this is the first study to develop a trigger tool for Chinese geriatric inpatients [41, 42].

In our research, the literature review was an essential step to comprehend and build on the clinical logic involved in existing trigger tools. The literature review results were initially revised by our study group and presented to the Delphi panel to be revised and rated. The Delphi survey is a structured and reliable method to collate the opinions of an expert group to formulate a consensus decision [43]. As a classical research method, the Delphi method has been widely used to assess the extent of agreement and for resolving disagreements in various medical fields.

After the two steps, 42 of 51 triggers achieving consensus agreement were retained. The reliability of this Delphi process was measured by the expert's authority coefficient and agreement coefficient. The value of the experts' authority coefficient suggested that the experts involved in the survey had a wealth of theoretical knowledge and clinical experience. More than half of the experts had more than 20 years of work experience, and the authority coefficients of the two rounds of Delphi process were greater than 0.75, indicating that the authority of the experts was high. Furthermore, agreement coefficient (W) increased to 0.308 ($P < 0.05$) in the second round, which means that the degree of expert coordination was acceptable [28]. Based on the objective and systematic Delphi method, we believe that we succeeded in gathering a panel of panelists representing distinct areas of medication experience and trigger tool expertise.

A total of 13 triggers were deleted from the initial list, including 10 plasma concentration triggers (e.g., phenytoin, valproic acid, phenobarbital, carbamazepine). Therapeutic drug monitoring (TDM) is required to optimize therapy of critical dose drugs with a narrow therapeutic range where there is a good chance of either over dosage or underdosage [44]. Since age-related changes in the pharmacokinetic parameters can influence drug elimination and response [45], TDM is a positive preventive measure to minimize the drug side effects, especially in elderly patients [46]. However,

**Table 4** The initial set of trigger tool

| No. | Triggers |
|---|---|
| Laboratory index | |
| 1 | PTT > 100 s |
| 2 | INR > 6[a] |
| 3 | Glucose < 2.8 mmol/L |
| 4 | Rising BUN or serum creatinine greater than 2 times baseline |
| 5 | ALT > 84U/L or AST > 80U/L (or ALP > 121U/L and T-BIL > 2UNL)[a] |
| 6 | CPK > 269 U/L |
| 7 | PLT < $50 \times 10^9$/L[a] |
| 8 | WBC < $3.0 \times 10^9$/L |
| 9 | HGB > 120 g/L[a] |
| 10 | Decrease of greater than 25% in hemoglobin or hematocrit |
| 11 | $K^+$ < 3.5 mmol/L |
| 12 | $K^+$ > 5.5 mmol/L |
| 13 | $Ca^{2+}$ > 2.62 mmol/L |
| 14 | TSH < 0.27 mU/L or FT4 > 22.40 pmol/L |
| 15 | TSH > 4.2 mU/L or FT4 < 12.0 pmol/L |
| 16 | Clostridium difficile positive |
| Plasma concentration | |
| 17 | Vancomycin peak > 40 mg/L, trough > 20 mg/L |
| 18 | Phenytoin > 20 μg/mL |
| 19 | Valproic acid > 100 μg/mL |
| 20 | Phenobarbital > 40 μg/mL |
| 21 | Carbamazepine > 15 μg/mL |
| 22 | Digoxin > 2 ng/mL |
| 23 | Amikacin levels peak > 30 μg/mL, trough > 10 μg/mL |
| 24 | Lidocaine > 5 μg/mL |
| 25 | Lithium > 1.5 mmol/mL |
| 26 | Theophylline > 20 mg/L |
| 27 | Procainamide > 4 mg/L |
| 28 | Quinidine > 5 mg/L |
| 29 | Gentamicin or Tobramycin levels peak > 10 mg/L, trough > 2 mg/L |
| 30 | Cyclosporine > 300 μg/mL |
| 31 | Tacrolimus > 20 ng/mL |
| Antidotes | |
| 32 | Vitamin K |
| 33 | Antiallergic |
| 34 | Romazicon (Flumazenil) |
| 35 | Naloxone (Narcan) |
| 36 | Anti-emetic |
| 37 | Antidiarrheal |
| 38 | Laxative |
| 39 | 50% glucose |
| 40 | Protamine |
| 41 | Epinephrine |
| 42 | Sodium polystyrene[a] |
| 43 | Transfusion or use of blood products |
| Clinical symptoms | |
| 44 | Over-sedation/hypotension |
| 45 | Rash |
| 46 | Dehydration |
| 47 | Alienation |

**Table 4** (continued)

| No. | Triggers |
|---|---|
| Intervention | |
| 48 | Abrupt medication stops |
| 49 | Admission to the intensive care unit |
| 50 | Readmission within 30 days |
| 48 | Abrupt medication stops |
| Other | |
| 51 | Others ADEs (ADEs not related to one of the triggers listed above) |

*PTT* partial thromboplastin time, *INR* international normalized ratio, *BUN* blood urea nitrogen, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *ALP* alkaline phosphatase, *T-BIL* total bilirubin, *CPK* creatine phosphokinase, *PLT* platelets, *WBC* white blood cells, *HGB* hemoglobin, $K^+$ potassium, $Ca^{2+}$ calcium, *TSH* thyroid stimulating hormone, *FT4* free thyroxine, *UNL* upper limit of normal

[a]According to the results of Delphi process, the trigger was modified in Table 5

TDM has not yet become widespread in China. Plasma concentration monitoring has not served as routine monitoring content in most Chinese elderly inpatient. Therefore, many of the plasma concentration triggers were deleted and six plasma concentration triggers, which were considered to be common medicines with a narrow therapeutic range for Chinese elderly inpatients, were retained. In addition, "admission to the intensive care unit" and "readmission within 30 days" were removed by the Delphi process. Repeated admission and transferred to a higher level of care are common in elderly patients [47] and are usually the results of advanced-age, co-morbid illnesses and some adverse events, such as falls, functional decline and nosocomial infections [48, 49]. ADEs might not be considered the major risk of "readmission within 30 days" or "admission to the intensive care unit" for Chinese elderly patients by consensus among the clinical advisory panel. The results were similar to our preliminary research, which was conducted in 480 elderly patients [50]. In this study of 480 elderly patients, the positive predictive value, representing the sensitivity of trigger, of readmission within 30 days was only 9.88% which was far below average (38.78%) [50].

Furthermore, based on expertise or guidelines, some triggers were modified, such as "INR > 5", "PLT < $75 \times 10^9$/L" and "ALT (or AST) ≥ 3ULN and/or ALP ≥ 2ULN and T-BIL > 2UNL (can have abnormal INR) [38]". We believe that these changes were made to make the trigger entries more suitable for Chinese elderly patients in ADE monitoring.

Comparing ours and other existing trigger tools for elderly patients, the primary difference existed in the number, composition and detail for certain trigger. In Marcum's and Handler's studies, they developed 27 triggers and 40 triggers, respectively [13, 32]. In Marcum's study, the 27 triggers comprised 2 categories (laboratory index, plasma concentration) [32]. Although similar to our study, the 40 triggers were divided into 5 categories in Handler's study, and the number of each category was different [13]. In these studies, the triggers of plasma concentration often covered more medications [13, 32], while most of them had poor feasibility in Chinese elderly patients by expert consensus. Furthermore, for the triggers of laboratory index, although they were similar in the number of triggers between our tool (15 triggers) and other existing tools (14 and 15 triggers), they varied in many details, such as INR above upper limit of normal range or > 6 in these tools [13, 32]. These distinctions did not represent which trigger tool had advantages over others, but rather, they just illustrated the fact that trigger tools with diversity can be customized to different populations.

## Limitations

There are several limitations to consider. First, in the Delphi method, the number and representativeness of panelists are the important factors affecting the generalizability of results. The expert panels comprised only a small number of panelists from five provinces in this study; thus, the generalizability of results may be affected. Second, the experts did not meet in face-to-face meetings, which would have allowed individual respondents to share opinions about the triggers. However, the possibility of having face-to-face meetings was limited by the broad geographic representation on the panel. Thirdly, although, the specialty of clinical expert involved the common diseases of the elderly, there was only one expert had background in geriatric medicine, which may make the potential impact on the results. Furthermore, the 42-trigger tool was not the final edition used for the detection of ADEs in Chinese geriatric patients. The tool we developed consisted of a high number of triggers that simply represent a consensus among experts in defining a specific trigger tool. Therefore, it is necessary to conduct a subsequent validation study, applying the list to elderly patients with multimorbidity, to obtain a more effective tool.

**Table 5** Modified trigger tool for measuring potential ADEs in Chinese geriatric inpatients

| No. | Triggers |
|---|---|
| Laboratory index | |
| 1 | PTT > 100 s |
| 2 | INR > 5 |
| 3 | Glucose < 2.8 mmol/L |
| 4 | Rising BUN or serum creatinine greater than 2 times baseline |
| 5 | ALT (or AST) ≥ 3 ULN and/or ALP ≥ 2 ULN and T-BIL > 2UNL (can have abnormal INR) [38] |
| 6 | PLT < $75 \times 10^9$/L |
| 7 | WBC < $3.0 \times 10^9$/L |
| 8 | HGB > 170 g/L (man), > 150 g/L (woman) |
| 9 | Decrease of greater than 25% in hemoglobin or hematocrit |
| 10 | $K^+$ < 3.5 mmol/L |
| 11 | $K^+$ > 5.5 mmol/L |
| 12 | $Ca^{2+}$ > 2.62 mmol/L |
| 13 | TSH < 0.27 mU/L or FT4 > 22.40 pmol/L |
| 14 | TSH > 4.2 mU/L or FT4 < 12.0 pmol/L |
| 15 | Clostridium difficile positive |
| Plasma concentration | |
| 16 | Digoxin > 2 ng/mL |
| 17 | Gentamicin or Tobramycin levels peak > 10 mg/L, trough > 2 mg/L |
| 18 | Cyclosporin > 300 μg/mL |
| 19 | Theophylline > 20 mg/L |
| 20 | Tacrolimus > 20 ng/mL |
| 21 | Voriconazole levels > 5.5 mg/L |
| Antidotes | |
| 22 | Vitamin K |
| 23 | Antiallergic |
| 24 | Romazicon (Flumazenil) |
| 25 | Naloxone (Narcan) |
| 26 | Anti-emetic |
| 27 | Antidiarrheal |
| 28 | Laxative |
| 29 | 50% glucose |
| 30 | Protamine |
| 31 | Epinephrine |
| 32 | Glucose injection and regular insulin[a] |
| 33 | Transfusion or use of blood products |
| 34 | Insulin (regular insulin or insulin analogue) used in non-diabetics |
| Clinical symptoms | |
| 35 | Over sedation/hypotension |
| 36 | Rash |
| 37 | Dehydration |
| 38 | Psychosis |
| 39 | Heart rates < 60/min |
| 40 | Respiratory rates < 12/min |
| Intervention | |
| 41 | Abrupt medication stops |
| Other | |
| 42 | Others ADEs (ADEs not related to one of the triggers listed above) |

[a]In China, sodium polystyrene is not widely used for treatment hyperkalemia in the inpatient department, but the most common treatments for hyperkalemia is glucose injection and regular insulin

## Conclusions

ADEs are common in elderly patients [19], which causes serious consequences in their health and quality of life. By integrating the findings of trigger tool studies with a Delphi process, we developed a specific trigger tool to detect ADEs in Chinese geriatric inpatients. Pilot-testing of this 42-trigger tool is the next phase of our work and will involve adjusting triggers and identifying positive predictive values for each trigger to establish a propagable trigger tool for Chinese geriatric inpatients.

**Acknowledgements** The authors thank all of the experts for their participation in the modified Delphi processes. The authors also thank the Preventive Medicine Association of Sichuan (2017KJFW01), which approved the planning, execution and analysis as proposed in the grant application.

**Funding** The Preventive Medicine Association of Sichuan supported this study.

**Conflicts of interest** The authors have no conflicts of interest to declare.

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