Active Surveillance and Clinical Analysis of anaphylaxis Based on China Hospital Pharmacovigilance System

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Abstract

Objective This study aimed to construct active surveillance programs for anaphylaxis based on China Hospital Pharmacovigilance System(CHPS) and analyze the characteristics, allergens, and management for anaphylaxis in a tertiary hospital in China. **Methods** The anaphylaxis cases reported to the National Adverse Drug Reaction Monitoring System in our hospital from 2014 to 2021 were retrospectively analyzed. Characteristic medical orders, progress notes, and diagnoses in these cases were recorded to obtain initial anaphylaxis trigger entries. According to the initial entries, the questionnaire was designed, and the Delphi method was used to develop consensus entries for anaphylaxis triggers. The CHPS was used to program these trigger entries and construct active surveillance programs. The programs were then ran on the 238,194 discharged patients to evaluate their performance and analyze the relevant clinical data. **Results** A total of 10 anaphylaxis triggers and 3 active surveillance programs were finally identified. 309 cases were obtained by the active surveillance program, and 94 cases were identified as anaphylaxis after the manual screening. After removing duplicates,76 patients with 79 times of anaphylaxis were finally obtained. The positive rate of triggers and the positive predictive value (PPV) of the programs were 0.13% and 30.42%, respectively. The incidence of anaphylaxis in our study was 0.03%, and the number of anaphylaxis cases detected by the active surveillance programs was 5.64 times higher than that by the spontaneous reporting system. Anaphylaxis was more common in female patients. Antibacterial drugs, antineoplastic drugs, and contrast media were the most common allergens in clinical practice, and the proportion of anaphylaxis to antineoplastic drugs was highest (0.6%) when compared with patients admitted during the same period. Significant underuse of epinephrine and overuse of second-line therapy (glucocorticoids and antihistamines) existed in the management of anaphylaxis, and the usage and dosage of epinephrine were irrational. **Conclusion** CHPS can effectively use both structured and unstructured data to construct anaphylaxis active surveillance programs, and this could compensate for the under-reporting by spontaneous reporting system, which was the primary adverse reaction monitoring method in China. The treatment and management of anaphylaxis are inappropriate and needed to be improved to reduce the risk of death.

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Keywords: Active surveillance, Anaphylaxis, China Hospital Pharmacovigilance system (CHPS), Epinephrine, Delphi method

Abstract

Objective This study aimed to construct active surveillance programs for anaphylaxis based on China Hospital Pharmacovigilance System(CHPS) and analyze the characteristics, allergens, and management for anaphylaxis in a tertiary hospital in China. **Methods** The anaphylaxis cases reported to the National Adverse Drug Reaction Monitoring System in our hospital from 2014 to 2021 were retrospectively analyzed. Characteristic medical orders, progress notes, and diagnoses in these cases were recorded to obtain initial anaphylaxis trigger entries. According to the initial entries, the questionnaire was designed, and the Delphi method was used to develop consensus entries for anaphylaxis triggers. The CHPS was used to program these trigger entries and construct active surveillance programs. The programs were then ran on the 238,194 discharged patients to evaluate their performance and analyze the relevant clinical data. **Results** A total of 10 anaphylaxis triggers and 3 active surveillance programs were finally identified. 309 cases were obtained by the active surveillance program, and 94 cases were identified as anaphylaxis after the manual screening. After removing duplicates,76 patients with 79 times of anaphylaxis were finally obtained. The positive rate of triggers and the positive predictive value (PPV) of the programs were 0.13% and 30.42%, respectively. The incidence of anaphylaxis in our study was 0.03%, and the number of anaphylaxis cases detected by the active surveillance programs was 5.64 times higher than that by the spontaneous reporting system. Anaphylaxis was more common in female patients. Antibacterial drugs, antineoplastic drugs, and contrast media were the most common allergens in clinical practice, and the proportion of anaphylaxis to antineoplastic drugs was highest (0.6%) when compared with patients admitted during the same period. Significant underuse of epinephrine and overuse of second-line therapy (glucocorticoids and antihistamines) existed in the management of anaphylaxis, and the usage and dosage of epinephrine were irrational. **Conclusion** CHPS can effectively use both structured and unstructured data to construct anaphylaxis active surveillance programs, and this could compensate for the under-reporting by spontaneous reporting system, which was the primary adverse reaction monitoring method in China. The treatment and management of anaphylaxis are inappropriate and needed to be improved to reduce the risk of death.

Key Points

China Hospital Pharmacovigilance System can effectively use both structured and unstructured data to construct anaphylaxis active surveillance programs, which compensate for the under-reporting by spontaneous reporting system.

The treatment and management of anaphylaxis are inappropriate and needed to be improved to reduce the risk of death.

Plain language summary

Anaphylaxis is a severe, potentially fatal adverse drug reaction(ADR), and drug induced anaphylaxis remains the leading cause of allergic death in adults. But there were few active surveillance studies and epidemiological data on anaphylaxis in China, and studies showed gaps in the initial treatment of anaphylaxis between China and international guidelines. This study aims to develop anaphylaxis triggers by the Delphi method and construct active surveillance programs based on China Hospital Pharmacovigilance System (CHPS). The programs were then ran on 238,194 discharged patients to evaluate their performances and analyze the characteristics, allergens, and management of anaphylaxis in the Chinese population. Results showed that the positive predictive value (PPV) of the program and the incidence of anaphylaxis were 30.42% and 0.03%, respectively. The number of anaphylaxis cases detected by the active surveillance programs was 5.64 times higher than that by the spontaneous reporting system. Significant underuse of epinephrine and overuse of second-line therapy (glucocorticoids and antihistamines) existed in the management of anaphylaxis, and the usage and dosage of epinephrine were irrational.

Introduction

Anaphylaxis is a severe, potentially fatal, systemic allergic reaction that occurs suddenly after contact with an allergy-causing substance[1], and it can lead to serious consequences if there exists delayed diagnosis and inappropriate treatments, drugs are generally considered to be the main cause of anaphylaxis[2]. Although anaphylaxis is a rare adverse drug reaction(ADR), drug induced anaphylaxis remains the leading cause of allergic death in adults [3; 4]. In addition, with the introduction of new medications such as biologics, small molecule drugs, and new chemotherapeutic drugs, the incidence of hospitalization caused by drug induced anaphylaxis continues to increase [5; 6]. During the past decade, there has been an advanced understanding of the diagnosis, pathogenesis, and treatment management of anaphylaxis [7; 8], but significant data and knowledge gaps remain in key clinical care and research domains, such as population science, validated clinical or biomarker-based models that predict disease outcome, acute management, etc. [7; 9], especially in China[10]. There were few active surveillance studies and epidemiological data on anaphylaxis in China, and studies showed gaps in the initial treatment of anaphylaxis between China and international guidelines[11].

China Hospital Pharmacovigilance System (CHPS) was developed and popularized by the China National Center for ADR Monitoring since 2016. The system can automatically collect and analyze information (such as diagnoses, medical orders, progress notes, test and examination results, and other information) extracted from the electronic hospital information systems (HIS) in sentinel hospitals (Figure 1)[12]. The connection to HIS makes it possible to simply, actively, and comprehensively obtain real-world drug safety data. At present, CHPS has covered more than 400 hospitals in China and can be used to carry out drug safety research with high operability and accessibility[12; 13].

This study aims to develop anaphylaxis triggers by the Delphi method and construct active surveillance programs based on CHPS. The programs were then ran on 238,194 discharged patients to evaluate their performances and analyze the characteristics, allergens, and management of anaphylaxis in the Chinese population.

Materials and Methods

2.1 Development of triggers for Anaphylaxis

ADR reports in our hospital from January 2014 to December 2021 were exported from the National Adverse Drug Reaction Monitoring System and retrospectively reviewed by a pharmacist and an allergist. Referring to the diagnostic criteria for anaphylaxis [1](Table 1) and the Technical Specifications and Evaluation Criteria for Common Serious Adverse Drug Reactions issued by the National Center for ADR, China, reviewers identified anaphylaxis cases and filled in the electronic case report forms, including diagnoses, department, characteristic medical orders, and progress notes,etal. Relevant data were analyzed and initial entries of triggers were formulated. An expert consultation questionnaire was designed according to the initial entries. The questionnaire comprises two parts, the first part was the basic information of experts, including major, education background, working years, professional title, etc. The second part was the evaluation of experts on the importance, familiarity, and judgment basis of trigger entries. We convened an 8-member multidisciplinary panel of experts involving one each of allergists, dermatologists, emergency specialists, cardiologists, intensivists, respiratory physicians, neurologists, and pharmacists, all members had rich experience in the diagnosis and treatment of anaphylaxis. All experts were asked to rate the importance and familiarity of each item on a 5-point Likert scale (with 1 meaning strongly disagree, 2 meaning agree, 3 meaning neutral, 4 meaning agree, and 5 indicating strongly agree). The judgment basis has 4 levels: theoretical analysis, practice, informed by domestic and foreign peers, and intuition. A score of 0.1-0.5 points was given according to the degree of influence on expert judgment. The highest score of 0.5 was obtained when the practice had a significant impact on expert judgment. Additionally, panel members were encouraged to submit free-text comments to clarify their responses to every question, suggest additional questions, or recommend modifications to exist questions. The indicators of the Delphi method include the positive coefficient of experts,

the degree of expert authority, the degree of expert opinion concentration, and the degree of expert opinion coordination[14]. The expert positivity coefficient was expressed as the questionnaire recovery rate. The authority coefficient of experts (Cr) was determined by the judgment basis of the entries (Ca) and familiarity with the consultation content (Cs), where Cr = (Ca + Cs)/2, and Cr [?] 0.7 was generally considered to be highly credible. The degree of expert opinion concentration was expressed by the mean value of importance score (Mj) and full score frequency (Kj) of trigger entries. The cut-off value of Mj and Kj = mean - standard deviation, and those with scores higher than the cut-off value were included. The degree of expert opinion coordination was expressed as the coefficient of variation (Vj). The cut-off value of Vj = mean + standard deviation and those with scores lower than the cut-off value were included. Entries that did not meet any of the three criteria were eliminated [15].

2.2 Construction and performance evaluation of active surveillance programs

The CHPS Drug Evaluation System (Figure 2) is one of the subsystems in the CHPS. It can obtain seven dimensions of clinical information from HIS, including patient retrieval (basic information of patients), test retrieval (test items, test values), medical order retrieval (drug ID), medical record retrieval (admission records, progress notes), diagnosis retrieval, physical sign retrieval, and examination retrieval, these seven dimensions can be easily connected with each other by Boolean logic operators. In this study, we used Boolean logic programming for triggers in medical orders, diagnoses, and progress notes to form retrieval rules. To improve the positive rate, the triggers in the progress notes and medical orders were connected by "AND". The rules were then run on the discharged patients to identify and analyze cases with positive triggers but not anaphylaxis, and exclusion rules were set accordingly to improve triggers performance. Finally, active surveillance programs were constructed by combining search rules and exclusion rules (Figure 3).

The positive predictive value (PPV) of the active surveillance programs was calculated as the number of anaphylaxis cases detected by active surveillance programs divided by the number of cases with positive triggers. The incidence of anaphylaxis was calculated as the number of anaphylaxis cases detected by active surveillance programs divided by the number of discharged patients. The performance of the active surveillance programs compared with the spontaneous reporting system was expressed as cases of anaphylaxis detected by active surveillance programs divided by reports of anaphylaxis in the spontaneous reporting system in the same period.

2.3 Statistic analysis

Categorical data were described by frequency counts and percentages. Continuous variables were presented as mean with standard deviation. Numerical differences between groups were assessed by the Chi-square test for categorical variables. The threshold for statistical significance was P=0.05. All statistical analyses were conducted using SPSS, Version 25.0 (SPSS Inc., Chicago, IL, USA)

Results

3.1 Trigger entries of anaphylaxis

A total of 1827 ADR cases were reported to the National Adverse Drug Reaction Monitoring System in our hospital from 2014 to 2021, and 22 cases were identified as anaphylaxis. Initial triggers were designed based on diagnoses, medical orders, and descriptions of progress notes. A 28-question online questionnaire was distributed to the experts, and all 8 questionnaires were effectively recovered, with a questionnaire recovery rate of 100%. Analysis of the questionnaire data showed that the expert authority coefficient was 0.92±0.10, indicating a high degree of expert authority. The Mj, Kj, and Vj of the triggered entries were shown in Table 2. Finally, 10 trigger entries were constructed by the Delphi method (Table 2).

3.2 Active surveillance programs and performance

After using Boolean logic programming to integrate the trigger entries and optimizing the rules, the final surveillance programs were obtained (Table 3). The programs ran for about 3 minutes, 238,194 discharge medical records from 2018 to 2021 were automatically monitored, and 309 cases were positive for triggers, with a positive rate of 0.13%. After the manual screening, 94 cases of anaphylaxis were obtained, and the PPV was 30.42%. 76 patients with 79 cases of anaphylaxis were finally obtained after removing the duplicates, including 37 cases of anaphylactic shock and 42 none shock anaphylaxis. The incidence of anaphylaxis detected by the active surveillance programs was 0.03%. During the same period (2018-2021), 14 cases of anaphylaxis were reported to the National Adverse Drug Reaction Monitoring System in our hospital, and 7 cases could be detected by the active surveillance programs. The number of anaphylaxis detected by the active surveillance programs was 5.64 times higher than that by the spontaneous reporting system, and the under-reporting rate of the spontaneous reporting system was 83.72%.

3.3 Characteristics of anaphylaxis

Among the detected cases (Table 4), there were 25 (31.65%) males and 54 (68.35%) females, with a mean age of 55.78 years (ranging from 4 to 79 years). The incidence of anaphylaxis was highest in the emergency department, followed by the oncology and gynecology departments. It should be noted that all anaphylaxis in the gynecology department were caused by antineoplastic drugs.

3.4 Allergens of anaphylaxis

Among 79 cases of anaphylaxis, 66 were drug-induced (Table 5), 8 had unclear allergens, 3 were animal-induced (allergens were insects and shrimp), and 2 cases were caused by absolute alcohol and irritating odors.

3.5 Treatment regimen

Among all therapeutic drugs for patients with anaphylaxis, glucocorticoids were the most commonly used drugs, followed by promethazine and epinephrine. Other drugs, such as vitamin C injection and calcium gluconate were also used in the treatment of anaphylaxis (Table 6).

3.6 Dosage and administration of epinephrine

A total of 35 anaphylaxis cases treated with epinephrine were analyzed, and there was a statistically significant difference in the usage rate of epinephrine between patients with anaphylactic shock and those with non-anaphylactic shock ($P < 0.01$) (Table 7). The main route of administration of epinephrine was intramuscular injection (45.71%). Other routes of administration included subcutaneous injection (28.57%) and bolus (25.71%), but there was a wide variation in the dose of epinephrine (Table 8).

Discussion

Anaphylaxis is an acute, potentially life-threatening systemic allergic reaction. Measuring and evaluating epidemiological data related to anaphylaxis is an important way to identify disease burden trends and risk factors. Currently, epidemiological data resources for anaphylaxis included the purchase of epinephrine auto-injectors, national databases, primary care databases, surveys with representative samples of the general population, and hospitalization or emergency department admissions, [2; 16; 17], and hospital admissions datasets were deemed as the largest and most robust data available to understand trends in anaphylaxis[18]. Studies based on hospitalization usually used structured data such as the International Classification of Diseases (ICD)-9 and ICD-10 to identify anaphylaxis patients[19]. However, A weakness of such studies is misdiagnosis, and misclassification[16], which leads underestimate the incidence of anaphylaxis. For example, Klein and Yocum[20]conducted a retrospective analysis of patients records in the emergency department, and they identified 17 cases of anaphylaxis, only four of the 17 patients were diagnosed as anaphylaxis which could be identified by ICD-9.

In this study, we developed anaphylaxis trigger entries that contained both structured data (e.g., medical orders and diagnostic data) and unstructured data (e.g., progress notes). The use of unstructured data resulted in a 2-fold increase in the detection rate of anaphylaxis compared to diagnosis-based structured data, which definitely improved the performance of the programs. In addition, compared with the spontaneous reporting system of our hospital during the same period, 83.72% of cases of anaphylaxis were under-reported, suggesting that the active surveillance programs can significantly make up for the deficiency of the spontaneous reporting system, which was the primary adverse reaction monitoring method in China. Panesar[21] et al. showed that the incidence rates for anaphylaxis in Europe ranged from 1.5 to 7.9 per 100,000 person-years, In our study, the incidence of anaphylaxis in the Chinese population was 8.29 episodes per 100,000 person-years, which was higher than other studies[22; 23] based on electronic medical records, indicating that the active surveillance programs performed well. However, the sensitivity of our programs was still low; we analyzed 4874 medical records of discharged patients in our hospital from December 1st to 31st, 2020, recorded all suspected ADRs (according to the progress notes and diagnoses), 3 cases were identified as anaphylaxis, and only 1 case could be which definitely improved the performance of the programs monitored by the active surveillance programs. Analysis of undetected anaphylaxis in the above-discharged patients and the spontaneous reporting system revealed that 1 case did not receive drug treatment after anaphylaxis, 4 cases were treated with dexamethasone only, and 2 cases had no progress notes reflecting "allergy", this is why they could not be monitored by the active surveillance programs. Therefore, the management of anaphylaxis and medical record writing should be standardized to improve the sensitivity of the method.

Regarding demographic characteristics, our study showed that the incidence of anaphylaxis in females was significantly higher than in males. Combined with the gender composition of patients during the same period, the ratio of incidence of anaphylaxis in males to females was 1:2.1. Similar results of gender difference were reported by Banerji et al.[24] who analyzed 716 patients with anaphylaxis, and 71% were female. Studies showed that anaphylaxis in females was lower than in males before puberty but increased rapidly and exceeded with age, but the specific mechanism is unknown[25; 26].

Drug induced anaphylaxis has become more frequent with age, and death rates from drug induced anaphylaxis have risen 300% over the last decade[17]. Drugs involved in anaphylaxis vary according to different populations, time, geographic regions, drug usage habits, genetic factors, anaphylaxis definitions, registries of cases, and study designs.[27].In our study, the drug accounted for up to 83.54% of all anaphylaxis, and the top drug classes associated with anaphylaxis were antibacterial drugs, antineoplastic drugs, and contrast media. After comparing with the number of patients treated in our hospital during the same period, the proportion of anaphylaxis caused by antineoplastic drugs was the highest (0.06%), followed by antibacterial drugs (0.02%) and contrast media (0.02%). Oxaliplatin was the most common trigger in antineoplastic drugs, and similar results were found in the Korean population[28].In fact, Oxaliplatin induced hypersensitivity reaction had raised widespread attention [29; 30; 31], and the China National Medical Products Administration issued a revision of the package insert in August 2021[32], adding a black box warning, warning that oxaliplatin might cause allergic reactions, which could lead to death in severe cases. Antibacterial drugs, especially beta-lactams, were recognized as the major causes of anaphylaxis, previous studies showed that the incidence of anaphylaxis to cephalosporin was lower than penicillin[27; 28], and amoxicillin-containing drugs were the most frequently reported cause of anaphylaxis to the FDA[33]. However, in our study, cephalosporins were the drugs most frequently involved, probably because of prescription habits in China. As routine skin tests are not recommended before the use of cephalosporins, future research should focus on exploring the prediction method of allergic reactions with higher sensitivity and specificity.

Promptly intramuscular injection of epinephrine into the mid-thigh area is the first-line management of anaphylaxis, with or without shock, in various guidelines[5; 6]. The recommended dose in adults is 0.01 mg/kg body weight, with a maximum total dose of 0.5 mg. Besides, subcutaneous injection is not recommended for emergency treatment because of its lower onset of action [10]. Glucocorticosteroids and antihistamines are commonly used in anaphylaxis, However, guidelines recommended them as the second-line medications for anaphylaxis, and there is increasing evidence that their routine use is controversial. Glucocorticosteroids may be of no benefit or even harmful in the acute management of anaphylaxis[5]. In this study, we found

that the proportion of glucocorticoids and antihistamines in the treatment of anaphylaxis was significantly higher than that of epinephrine (83.54% vs. 44.30%, 58.23% vs. 44.30%, $P < 0.01$), and the proportion of epinephrine used in non-anaphylactic shock was significantly lower than that of shock. In addition, the usage and dosage of epinephrine were irrational, such as the considerable proportion of subcutaneous injections of epinephrine and the huge dosage varies. Jiang et al.[11] also showed the significant underuse, as well as the inappropriate usage and dosage of epinephrine and the unreasonable high use of glucocorticoid in China. Therefore, it is urgent to improve the management and treatment of anaphylaxis by medical staff to reduce the death caused by anaphylaxis.

Our study has some limitations. First, this was a single-center study,the formulation of medical orders triggers was based on the prescribing habits of doctors in our hospital, which had low external validity. When applied to other hospitals, some items of the trigger need to be modified. In addition, there was a certain missed detection rate in our active surveillance programs due to the low sensitivity, and this might lead to the missed detection of anaphylaxis, which had a certain impact on the results.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

Chengcheng Wang, Zejing Li, and Anchang Liu contributed to conception and design of the study. Chengcheng Wang, Zejing Li, and Maoyan Feng reviewed the ADR reports and formulated the initial triggers. Chengcheng Wang, Yingying Yu performed the statistical analysis. Chengcheng Wang wrote the first draft of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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FIGURES AND TABLES

Table 1. Diagnostic criteria for anaphylaxis

Anaphylaxis is highly likely when any one of the following 3 criteria are fulfilled:
1. Acute onset of illness (minutes to several hours), with involvement of the skin, mucosal tissue, or both (eg, generalized hi

Table 2. Trigger entries and scores for anaphylaxis

Trigger entries	Mj (Cut-off=3.90)	Kj (Cut-off=0.36)	Vj (Cut-off=0.37)
Diagnosis contains "anaphylactic shock"	5.00	1.00	0.00
Medical orders contain "epinephrine"	4.88	0.88	0.07
Medical orders contain "glucocorticoids (dexamethasone or methylprednisolone) combined with promethazine"	4.13	0.50	0.31
Progress notes contain "anaphylactic shock"	4.88	0.88	0.07
Progress notes contain "allergy"	4.38	0.63	0.17
Progress notes contain "cutaneous adverse reactions" (e.g., rash, flushing, pruritus)	4.38	0.63	0.20
Progress notes contain "respiratory system adverse reactions" (e.g., chest tightness, dyspnea, suffocation)	4.88	0.88	0.07
Progress notes contain "nervous system adverse reactions" (e.g., dizziness, irritability, unconsciousness, confusion)	3.80	0.50	0.63
Progress notes contain "digestive system adverse reactions" (e.g., nausea, vomiting, diarrhea)	3.50	0.13	0.22
Progress notes contain "circulatory system adverse reactions " (e.g., reduced BP, palpitation, precordial discomfort)	4.25	0.38	0.13

Table 3. Active surveillance programs for anaphylaxis and its performance

Items in surveillance programs
Diagnosis contains "anaphylactic shock"
Progress notes contain "anaphylactic shock"and medical orders contain "epinephrine or glucocorticoids combined with prom
Progress notes contain "allergy"and "adverse skin or respiratory or nervous system or digestive or circulatory system reactio
Total

Table 4. Demographic characteristics of anaphylaxis

Demographic characteristics	**Numbers**
Age	55.78±17.56
Gender	
Male	25(31.65%)
Female	54(68.35%)
Department(n[?]2)	
Emergency department	19(24.05%)
Oncology department	12(15.19%)
Gynecology department	8(10.13%)
Cardiology department	5(6.33%)
Neurology department	4(5.06%)
Hepatology department	4(5.06%)
Critical care medicine	3(3.80%)
Neurosurgery department	3(3.80%)
Respiratory department	3(3.80%)
Hematology department	2(2.53%)
Gastroenterology department	2(2.53%)
Bone tumor department	2(2.53%)
Pediatrics department	2(2.53%)
Obstetrics department	2(2.53%)
Anorectal department	2(2.53%)

Table 5. Drugs that induced anaphylaxis

Drug classification	**Drug**
Antibacterial drugs	11 cephalosporins (4 unspecified cephalosporins, 3 cefoperazone-sulbactam, 3 cefo
Antineoplastic drugs	5 oxaliplatin, 4 carboplatin, 3 doxorubicin liposome, 2 cetuximab, 1 nedaplatin, 1
Contrast media	3 iodixanol, 3 iopromide, 1 iodine contrast agent with unknown details
Traditional Chinese medicine injections	2 Shenmai injections, 1 Xingnaojing injection
Glucocorticoid	2 dexamethasone, 1 methylprednisolone
Blood products	2 plasma,1 platelet
Other drugs	1 potassium sodium dehydroandroandrographolide succinate for injection, 1 extra
Unclear drugs	2
Total	

Table 6. Drugs for the treatment of anaphylaxis

Treatment Drugs	**Case Numbers (%)**
Glucocorticoids (dexamethasone, methylprednisolone, and betamethasone)	66 (83.54%)
Promethazine	46 (58.23%)
Epinephrine	35 (44.30%)
Vitamin C	18 (22.78%)
Calcium gluconate	16 (20.25%)
Others (e.g., dopamine, norepinephrine, etc.)	17 (21.52%)

Table 7. Epinephrine use in patients with anaphylaxis

Patient classification	With Epinephrine	Without epinephrine	P value
Anaphylactic shock	29	8	¡0.01
Non-anaphylactic shock	6	36	

Table 8. Dosage and administration of epinephrine

Dosage and administration of epinephrine	Dosage and administration of epinephrine	Number (%)
Intramuscular injection (16)	0.5mg	10(28.57%)
	0.3mg	3(8.57%)
	4mg	1(2.86%)
	1mg	1(2.86%)
	0.4mg	1(2.86%)
Subcutaneous injection(10)	0.5mg	4(11.43%)
	0.3mg	3(8.57%)
	1mg	2(5.71%)
	0.15mg	1(2.86%)
Bolus(10)	1mg	2(5.71%)
	0.02mg	2(5.71%)
	0.25 mg	1(2.86%)
	0.2mg	1(2.86%)
	0.1mg	1(2.86%)
	0.03mg	1(2.86%)
	unknown	1(2.86%)

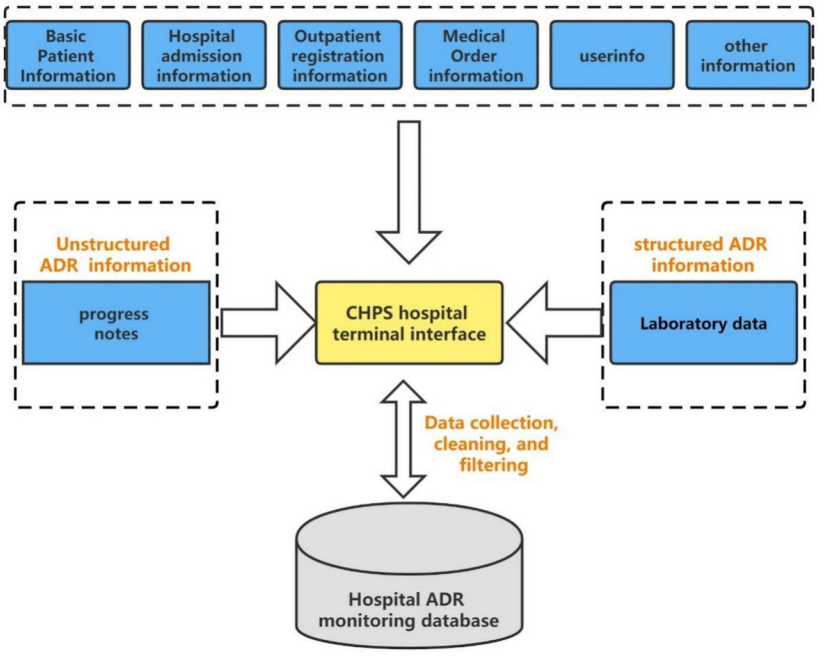

Figure 1 Data acquisition structure diagram of CHPS

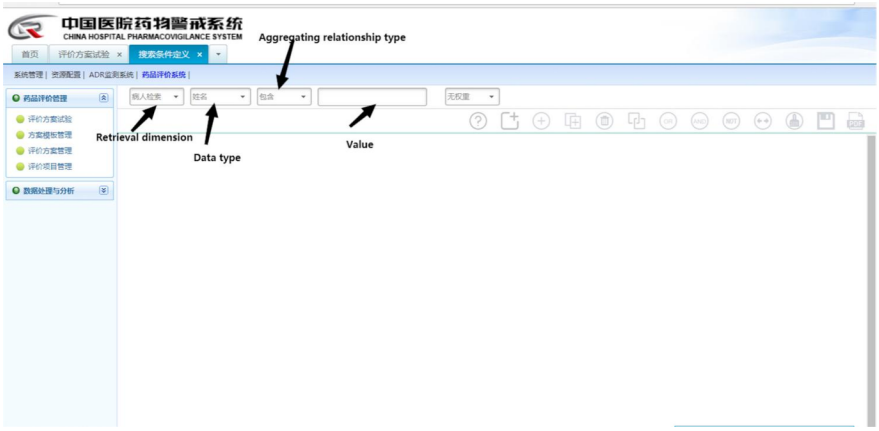

Figure 2 Website of CHPS Drug Evaluation System

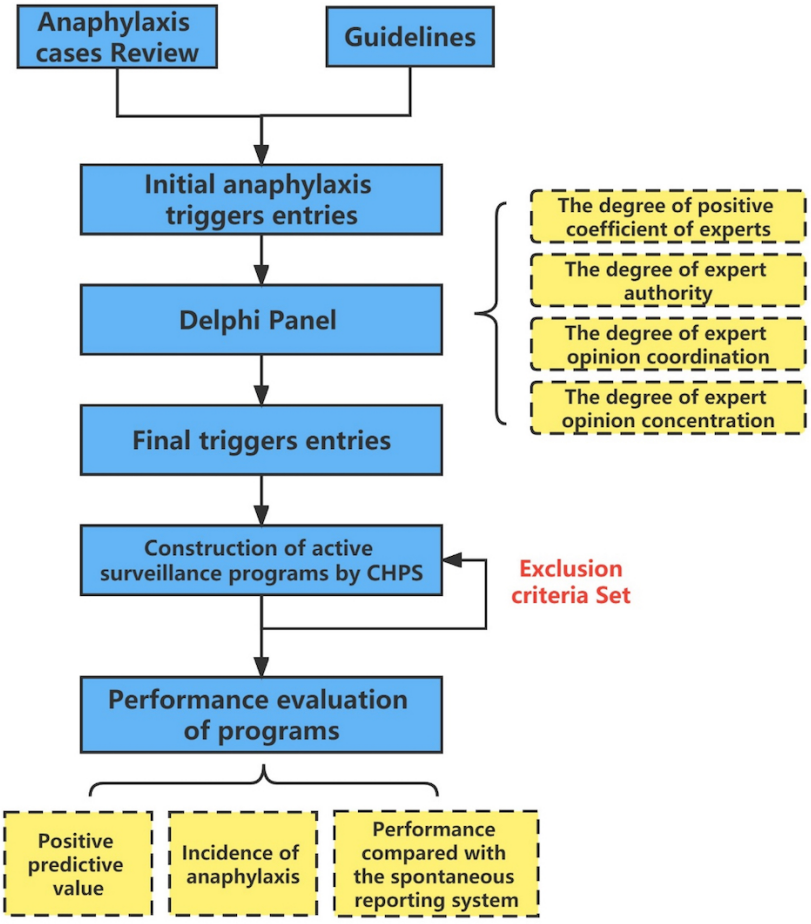

Figure 3 Flow chart of active surveillance for anaphylaxis