



## Original Article

# Chinese patent herbal medicine (Shufeng Jiedu capsule) for acute upper respiratory tract infections: A systematic review and meta-analysis

Ying-ying Zhang<sup>a,1</sup>, Ru-yu Xia<sup>a,1</sup>, Shi-bing Liang<sup>a</sup>, Xiao-yang Hu<sup>b</sup>, Meng-yuan Dai<sup>c</sup>, Yi-lin Li<sup>d</sup>, Le-yi Zhao<sup>d</sup>, Michael Moore<sup>b</sup>, Yu-tong Fei<sup>a</sup>, Jian-ping Liu<sup>a,\*</sup>

<sup>a</sup> Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, Beijing, China

<sup>b</sup> School of Primary Care, Population Sciences, and Medical Education, University of Southampton, Southampton, United Kingdom

<sup>c</sup> Department of Respiratory and Critical Care Medicine, First Affiliated Hospital of Anhui Medical University, Hefei, China

<sup>d</sup> Beijing University of Chinese Medicine, Beijing, China



## ARTICLE INFO

## Article history:

Received 17 August 2020

Revised 22 March 2021

Accepted 23 March 2021

Available online 2 April 2021

## Keywords:

Chinese herbal medicine

Shufeng Jiedu

Respiratory tract infections

Randomized controlled trials

Systematic review

## ABSTRACT

**Background:** Shufeng Jiedu capsule has been widely used in China for acute upper respiratory tract infections (AURTIs). The aim of this study was to evaluate its effectiveness and safety for AURTIs.

**Methods:** Randomized controlled trials comparing SFJD with conventional drug for patients with AURTIs were included. Eight databases were searched from their inception to February 2021. Data was synthesized using risk ratio (RR) or mean difference (MD) with their 95% confidence interval (CI). The primary outcome was resolution time of typical symptoms.

**Results:** Twenty-five RCTs involving 3410 patients were included. SFJD in combination with conventional drug was associated with; in common cold shortening the duration of fever (MD −1.54 days, 95% CI [−2.15, −0.92],  $I^2 = 80\%$ ,  $n = 385$ , 3 trials) and cough (MD −1.22 days, 95% CI [−1.52, −0.93]); in herpangina, shortening the duration of fever (MD −0.68 days, 95% CI [−1.15, −0.21],  $I^2 = 68\%$ ,  $n = 140$ , 2 trials) and blistering (MD −0.99 days, 95% CI [−1.23, −0.76],  $n = 386$ , 3 trials); in acute tonsillitis and acute pharyngitis shortening the duration of fever (MD −1.13 days, 95% CI [−1.36, −0.90],  $I^2 = 33\%$ ,  $n = 688$ , 7 trials) and sore throat (MD −1.13 days, 95% CI [−1.40, −0.86],  $I^2 = 84.1\%$ ,  $n = 1194$ , 10 trials). SFJD also improving their cure rate with a range (1–5 days). No serious adverse events were reported.

**Conclusion:** Low certainty evidence suggests that SFJD appears to shorten the duration of symptoms in AURTIs, improve cure rate and seems safe for application. However, high quality placebo controlled trials are warranted to confirm its benefit.

© 2021 Published by Elsevier B.V. on behalf of Korea Institute of Oriental Medicine.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

## 1. Introduction

Upper respiratory tract infections (URTIs) are one of the most commonly occurring diseases. In 2017, the global incidence of URTIs was 17.1 billion worldwide<sup>1</sup>, which posed substantial socio-economic burden to public health. The global 6090,503 disability-adjusted life years due to URTIs were lost in 2016<sup>2</sup>. Acute upper respiratory tract infections (AURTIs) are the most common type of URTIs. According to the International Statistical Classification of

Diseases (ICD-10), AURTIs include common cold, acute sinusitis, acute pharyngitis, acute tonsillitis, acute laryngitis and tracheitis, acute epiglottitis, and acute upper respiratory infections of multiple and unspecified sites<sup>3</sup>. AURTIs are predominantly viral, and most AURTIs are mild and self-limited within 7 days<sup>4</sup>. Antibiotics are recommended only for specific URTIs and validated clinical indications (such as acute pharyngitis and acute tonsillitis caused by streptococcus) in existing guidelines, for other AURTIs, symptomatic treatment were recommended<sup>5,6</sup>. It was reported that the majority of antibiotic prescriptions for AURTIs were unnecessary and ineffective<sup>7–9</sup>. Additionally, inappropriate use of antibiotics may lead to bacterial resistance, and as many as 35,000 people die each year as a result in US<sup>10</sup>.

\* Corresponding author.

E-mail address: [liujp@bucm.edu.cn](mailto:liujp@bucm.edu.cn) (J.-p. Liu).

<sup>1</sup> Ying-Ying Zhang and Ru-Yu Xia are co-first authors.

Shufeng Jiedu (SFJD) capsule as an oral Chinese patent herbal medicine has been widely used in China for the treatment of AURTIs for 30 years<sup>11</sup>. The ingredients of SFJD were presented in (Supplementary material). SFJD has been recommended in several Chinese national guidelines for the treatment of AURTIs<sup>12–14</sup>. There are many clinical trials comparing the effect of SFJD with conventional drug for the treatment of AURTIs. Additionally, an *in vitro* study of antibacterial testing suggested that SFJD capsule had a broad-spectrum antibacterial effect<sup>15</sup>, moreover, SFJD combined with oseltamivir had synergistic antiviral effects on respiratory infection<sup>16</sup>. However, there is no systematic review to evaluate the effectiveness of SFJD on AURTIs. Therefore, this systematic review aims to collect all relevant randomized controlled trials (RCTs) on SFJD capsule for patients with AURTIs and to evaluate its therapeutic effect and safety.

## 2. Methods

This systematic review was reported following PRISMA<sup>17</sup> statement, and the protocol has been registered on INPLASY (INPLASY202050083)<sup>18</sup>.

### 2.1. Inclusion and exclusion criteria

#### 2.1.1. Inclusion criteria

Parallel group RCTs regardless of blinding were included. The study population (P) was patients diagnosed with AURTIs or one of the classification of AURTIs regardless of gender, age or ethnicity from primary care or outpatient department of hospitals. AURTIs might include common cold, acute rhinitis, herpangina, acute pharyngitis or acute tonsillitis. The interventions (I) were SFJD capsule used alone or in combination with conventional drug. Conventional drug referred to symptomatic treatment (e.g., antipyretic and decongestant, etc.), symptomatic treatment plus antivirals or antibiotics. The controls (C) were placebo or conventional drug. The primary outcome (O) was the duration of typical symptoms in AURTIs (time to fever, cough, blisters or sore throat resolution). The secondary outcomes were cure rate and adverse events. Follow up of outcome measurements were all limited to within 5 days of treatment.

#### 2.1.2. Exclusion criteria

Studies with a course of treatment over 7 days, and studies with other Chinese patent medicine controlled or studies failed to report the minimal required outcomes were excluded.

### 2.2. Search strategy

PubMed, the Cochrane Library, EMBASE, Web of Science, China National Knowledge Infrastructure (CNKI), Chinese Scientific Journal Database (VIP), SinoMed and Wanfang databases were searched from their inception to February 2021. A systematic search was also conducted in Clinical Trials.gov ([www.clinicaltrials.gov](http://www.clinicaltrials.gov)) and Chinese Clinical Trial Registry (<http://www.chictr.org.cn/index.aspx>). Search strategy for PubMed: Shufengjiedu[Title/Abstract] OR Shu Feng Jie Du [Title/Abstract] OR Shu-Feng-Jie-Du [Title/Abstract] OR Shufeng Jiedu [Title/Abstract] OR Shufeng-Jiedu [Title/Abstract]. There was no limitation of language.

### 2.3. Study selection and data extraction

After removing duplicates, two authors (YY Zhang and RY Xia) independently screened studies by titles and abstracts. In the full text screening process, uncertainty and insufficient information was determined for eligibility through obtaining full texts, and discrepancies were resolved by discussion or determined by a third-party adjudication. Reasons for excluding studies were recorded at

this stage. A predefined data extraction form was used by paired reviewers (YY Zhang and SB Liang; YL Li and LY Zhao) to extract data independently, including study ID, population, interventions, comparisons, outcomes, and design characteristics (sample size, setting and funding).

### 2.4. Quality assessments

The quality assessment of individual trial was performed using Cochrane Risk of Bias tool 2.0<sup>19</sup>. This revised tool includes five items as following: randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome and selection of the reported result. The included trials were assessed as low risk of bias, some concerns or high risk of bias in each domain<sup>19,20</sup>. The method of GRADE<sup>21</sup> (Grading of Recommendations Assessment, Development and Evaluation) was employed to rate the certainty of evidence in five domains (risk of bias, directness, precision, consistency, and the possibility of publication bias).

### 2.5. Data synthesis

For dichotomous data, we calculated risk ratio (RR) with 95% confidence interval (CI); for continuous data, we calculated mean difference (MD) with 95% CI. Cochrane Review Manager 5.4 software was employed for data analyses. In meta-analysis, Cochrane Q test and  $I^2$  statistic were employed to assess statistical heterogeneity<sup>20</sup>. A fixed-effects model was considered when  $I^2 < 30\%$ , otherwise, a random-effects model was used. According to the classification of AURTIs in ICD-10<sup>3</sup>, there is no substantial pathophysiologic difference between common cold and acute rhinitis, and therefore we combined them together. Additionally, conventional drug refers to symptomatic treatment used alone or in combination with antibiotics or antivirals, they were considered as a whole. We lumped them together to demonstrate the overall differences of therapeutic effect between SFJD and conventional drug, as well as to make the results more clearly. Funnel plots were performed through Review Manager 5.4 software to detect the possibility of publication bias, if ten or more studies were included in a meta-analysis. To explain heterogeneity, we predefined subgroup analysis in terms of the severity of AURTIs and different ages of patients (adults, children aged between 2 and 14 years old). When the primary outcomes showed clinically meaningful differences between groups, sensitivity analysis was employed to test the robustness of the results in following methodological domains: comparison between clear and unclear randomization concealment; comparison between placebo used and not used; comparison between reported loss- to-follow-up and not reported.

## 3. Results

### 3.1. Screening

Initially 1524 records were retrieved. Among which 908 duplicates were removed. 550 records were excluded after title and abstract screening, remaining 66 records. Full-text screening identified 25 RCTs involving 3410 participants, of which 1069 were children. One placebo controlled trial on common cold<sup>29</sup> was narratively described and hence could not be included in the quantitative synthesis (Fig. 1).

### 3.2. Study characteristics

There were ten trials<sup>22–31</sup> focused on common cold, three<sup>33–35</sup> on herpangina, four<sup>36–39</sup> on acute pharyngitis, seven<sup>40–46</sup> on

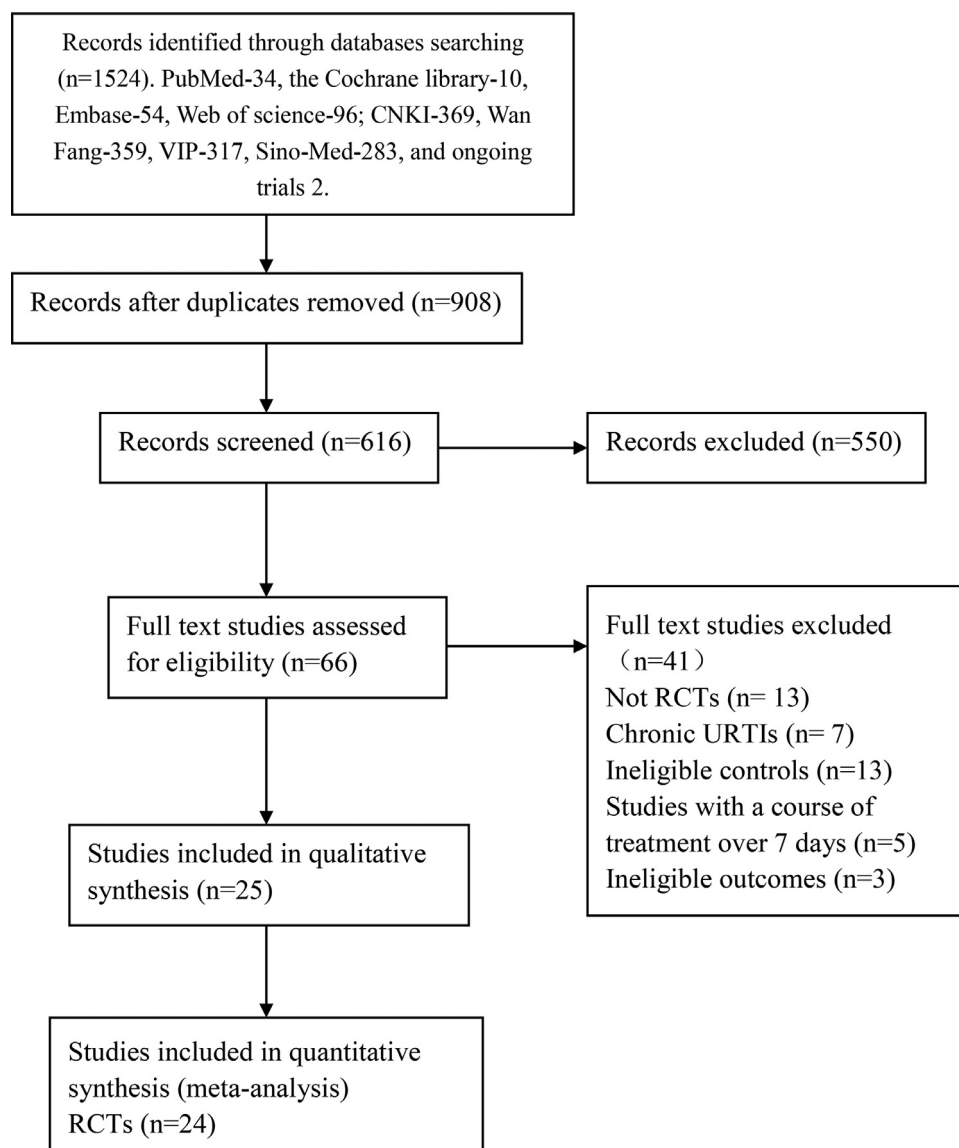


Fig. 1. Flow chart of study selection. RCT: randomized controlled trials; URTIs: upper respiratory tract infections.

acute tonsillitis and one <sup>32</sup> on acute rhinitis. All trials were conducted in China and there was only one <sup>29</sup> multi-center trial, the rest were single center trials. None of the trials reported the funding or conflicts of interest. Sample size varied from 60 to 246 and the mean age varied from 2.4 to 70.9 years. Baseline major symptoms reported were fever, cough and stuffy nose in common cold; fever and blisters in herpangina; fever and sore throat in acute pharyngitis and acute tonsillitis. The duration of treatment varied from 3 to 7 days, and the outcomes were all measured within 5 days from starting treatment. The baseline body temperature in trials were presented in (Table 1). The criteria details of cure rate in individual studies were presented in (Supplementary material). The dose reported in these trials was three times daily administration of SFJD, for adults and children over 10 years old was 4 capsules per time, 3 capsules for 6 to 10 years old, 2 capsules for 3 to 6 years old, and 1 capsule for 2 to 3 years old. Conventional drug referred to symptomatic treatment used alone or in combination with antibiotics or antivirals. Symptomatic treatment included antipyretic <sup>22,24,33,45</sup>, decongestant <sup>26,36</sup>, antitussive <sup>22-24</sup>, expectorants <sup>25, 28</sup> and saline nasal spray <sup>32</sup>; antiviral drugs included ribavirin <sup>22-23,34-35</sup> and interferon <sup>33</sup>; antibiotics included amoxi-

cillin <sup>41,45</sup>, cefaclor <sup>40,46</sup> and cefuroxime <sup>42,44</sup>. Only one included trial was placebo controlled <sup>29</sup>. The characteristics of included trials were shown in Table 1.

### 3.3. Risk of bias assessment

In terms of randomization process, the baseline data were comparable in all the included trials.

Clear random allocation sequence and allocation concealment were reported in only one trial<sup>29</sup>, and which was assessed as low risk of bias. Besides, the remaining 24 trials <sup>22-28,30-46</sup> only mentioned random without describing detailed randomization methods. In terms of deviations from intended interventions, participants and personnel were blinded in only two trials<sup>28-29</sup>. Apart from that, deviations from interventions were not mentioned in other 23 trials <sup>22-27,30-46</sup>, and therefore the majority of the included trials were assessed as some concerns in this domain. All trials were considered as low risk of bias in missing outcome data domain due to complete outcome data or there was evidence that the result was not biased by the missing data. In terms of measurement of outcomes, nineteen trials <sup>22-24, 26,32-46</sup> were assessed as

**Table 1**

Characteristics of included randomized trials on SFJD capsules for AURTIs.

Study ID	Population	Sample size	Average age (year)	Male (%)	Time from symptom onset when included (Hours)	TCM syndrome differentiation	Baseline major symptoms	Intervention	Comparison	Treatment duration (days)	Measurement time of outcomes (days)	Outcomes reported <sup>a</sup>
<b>Common cold</b>												
Chen H 2016 [22]	Children	78/78	6.3/6.5	44.9/52.6	NR	NR	<b>Fever, cough</b> >37.3°C	SFJD+ST+ +ribavirin	ST+ ribavirin	7d	5d	2,3,6
Zhou XF 2016[23]	Children	70/70	5.1/4.8	48.6/44.348	48hr	Wind-heat syndrome	37.3–41.6°C	SFJD +ST+ ribavirin	ST+ ribavirin	5d	5d	2,3,6
Wang Q 2018[24]	Children	45/44	7.15/7.2	53.3/52.27	NR	NR	>37.3°C	SFJD +ST+ antivirals	ST+ antivirals	5d	5d	2,3,6
Zhang YP 2014[25]	Adults	110/110	40.2/39.81	54.5/59.0	NR	NR	>37.3°C	SFJD+ST	ST	7d	1d	1
Ye XQ 2013[26]	Adults	100/100	38.55/37.85	52/49	48hr	Wind-heat syndrome	37.3–39.0°C	SFJD+ST	ST	3d	3d	1,2,6
Zhao JL 2018[27]	Adults	61/62	45.69/45.21	49.1/53.2	NR	NR	>37.3°C	SFJD+ST	ST	3d	3d	1,6
Zhang B 2020[28]	Adults	119/118	31.94/35.94	56.8/54.6	NR	NR	37.3–39.0°C	SFJD+ST	ST	3d	3d	1,6
Xu YL 2015[29]	Adults	120/120	49.24/47.77	60/57.9	36hr	Wind-heat syndrome	37.3–39.0°C	SFJD	placebo	7d	3d	1,2,6
Wu XJ 2015[30]	Adults	112/119	70.9/70.8	59.8/59.8	NR	NR	>37.3°C	SFJD+ST+ antibiotics	ST+ antibiotics	7d	3d	1
Zhao LB 2020 [31]	Adults	78/78	37.3/36.8	52.3/51.3	36h	Wind-heat syndrome	37.1–39.1°C	SFJD +ST+ antivirals	ST+ antivirals	5d	5d	6
<b>Acute rhinitis</b>												
Li Y 2015[32]	Adults	30/30	49.2/50.3	43.3/46.7	72hr	Wind-heat syndrome	<b>Fever, stuffy nose</b> >37.3°C	SFJD+ST	ST	7d	5d	6
<b>Herpangina</b>												
Yang Y 2019[33]	Children	35/35	4.55/4.2	51.4/42.9	48hr	NR	<b>Fever, blisters</b> >37.3°C	SFJD +ST+ interferon	ST+ interferon	5d	5d	2,5,6
Yang ML 2016[34]	Children	123/123	4.2/4.1	49.6/47.9	48hr	NR	>37.3°C	SFJD+ST+ ribavirin	ST+ ribavirin	5d	5d	2,5,6
Liu CX 2015[35]	Children	37/33	2.4/2.5	NR	48hr	NR	37.3–41.0°C	SFJD +ST+ ribavirin	ST+ ribavirin	5d	5d	2,5,6
<b>Acute pharyngitis</b>												
Zhu SM 2019[36]	Adults	38/38	41.34/41.25	57.9/52.6	48hr	Wind-heat syndrome	<b>Fever, sore throat</b> 37.3–38.5°C	SFJD+ ST	ST	5d	5d	4,6
Jiang JQ 2018[37]	Adults	48/48	37/39.81	47.9/43.8	48hr	NR	>37.3°C	SFJD+ST	ST	7d	5d	4,6
Dong W 2020[38]	Adults	45/45	30.1/32.1	48.89/53.33	36h	NR	>37.3°C	SFJD+ST	ST	6s	5d	2,4
Zhou QQ 2020[39]	Adults	106/106	32.75/30.63	69.8/74.53	48h	NR	NR	SFJD+ST	ST	7d	5d	4

(continued on next page)

Table 1 (continued)

Study ID	Population	Sample size	Average age (year)	Male (%)	Time from symptom onset when included (Hours)	TCM syndrome differentiation	Baseline major symptoms	Intervention	Comparison	Treatment duration (days)	Measurement time of outcomes (days)	Outcomes reported <sup>a</sup>
<b>Acute tonsillitis</b>							<b>Fever, sore throat</b>					
Zhang JY 2015[40]	Adults	45/45	22.94/24.17	68.9/60	48hr	NR	37.3–39.1 °C	SFJD +ST+ cefaclor	ST+ cefaclor	7d	5d	2,4,6
Wang ZB 2018[41]	Adults	55/55	16.39/20.73	56.4/49.1	72hr	NR	>37.3 °C	SFJD +ST+ amoxicillin	ST+ amoxicillin	7d	5d	2,4,6
Li G 2017[42]	Adults	50/50	27.1/27.3	56/52	NR	NR	≥38.0 °C	SFJD +ST+ cefuroxime	ST+ cefuroxime	5d	5d	2,4,6
Li BR 2020[43]	Adults	50/50	22/21	52/42	NR	NR	>37.3 °C	SFJD+ST+ penicillin	ST+ penicillin	7d	5d	2,4,6
Zhao ZY 2015[44]	Children	58/50	5.9/6.1	53.4/54	72hr	NR	≥38.0 °C	SFJD +ST+ cefuroxime	ST+ cefuroxime	5d	5d	2,4,6
Yang X2017 [45]	Children	35/35	3.52/3.53	48.6/51.4	48hr	NR	38.4–39.8 °C	SFJD +ST+ amoxicillin	ST+ amoxicillin	5d	5d	2,4,6
Huang PL 2016[46]	Children	60/60	7.12/6.74	51.7/53.3	72h	Wind-heat syndrome	>37.3 °C	SFJD +ST+ cefaclor	ST+ cefaclor	6d	5d	2,4,6

**Notes:** AURTIs, acute upper respiratory tract infections; d, days; hr, hours; NR, not reported; SFJD, Shufeng Jiedu; ST, symptomatic treatment.

Outcomes: 1, Resolution rate of fever at day 3 of treatment; 2, Time to fever resolution; 3, Time to cough resolution; 4, Time to sore throat resolution; 5, Time to blister resolution; 6, Cure rate.

<sup>a</sup> 1–5 were primary outcomes, 6 was secondary outcome.



high risk of bias due to the outcomes were patients self-reported and likely influenced, other 6 trials<sup>25,27–31</sup> were of low risk of bias since the outcomes were objective or outcome assessors were not aware of the interventions received by participants. In terms of selection of the reported result, twenty-one trials<sup>22–24,29–46</sup> were assessed as some concerns due to lack of pre-specified analysis plan, four trials<sup>25–28</sup> were assessed as high risk of bias due to lack of pre-specified analysis plan and multiple time points outcome measurements. The overall bias was assessed as low for only one trial<sup>29</sup> and high for the remaining 24 trials<sup>22–28,30–46</sup>. The methodological quality of the included trials were shown in Fig. 2.

### 3.4. Effect estimates

#### 3.4.1. Common cold/acute rhinitis

There were 10 trials<sup>22–31</sup> focused on common cold, of these, three trials<sup>22–24</sup> reported the time to fever and cough resolution, as well as the cure rate, the other 7 trials<sup>25–31</sup> reported the cure rate. Only one trial<sup>32</sup> on acute rhinitis and reported the cure rate.

**3.4.1.1. Time to fever and cough resolution.** Three trials<sup>22–24</sup> compared SFJD plus conventional drug (symptomatic treatment and antivirals) with conventional drug for common cold in children, and reported the time to fever and cough resolution. The pooled results showed that SFJD was superior to control group in shortening the time to fever resolution (MD −1.54 days, 95% CI [−2.15, −0.92],  $I^2 = 80\%$ ,  $n = 385$ , 3 trials, very low certainty) and cough resolution (MD −1.22 days, 95% CI [−1.52, −0.93],  $n = 385$ , 3 trials, low certainty) (Table 2, Supplementary material).

**3.4.1.2. Clinical cure.** SFJD combined with conventional drug (symptomatic treatment alone<sup>25–28,32</sup>, symptomatic treatment plus antivirals<sup>22–24,31</sup> or symptomatic treatment plus antibiotics<sup>30</sup>) were also found more effective than conventional drug in improving the cure rate in common cold with a range (1–5 days) of treatment (RR 1.26, 95% CI [1.17, 1.35],  $n = 1593$ , 10 trials<sup>22–28,30–32</sup>, low certainty) (Fig. 3, Table 2). Subgroup analysis by age suggested that SFJD in combination with conventional drug was still superior to conventional drug in improving the cure rate in adults (RR 1.27, 95%CI [1.18, 1.36],  $n = 1208$ , 7 trials<sup>25–28, 30–32</sup>, moderate certainty). But this effect was not significant in children (RR 1.22, 95%CI [0.97, 1.54],  $n = 385$ , 3 trials<sup>22–24</sup> low certainty) (Fig. 3, Table 2). There was only one double blinded, placebo-controlled trial<sup>29</sup> which comparing the effect of SFJD with placebo on common cold, the result was narratively described. The cure rate was 44.2% in SFJD group and 9.3% in placebo group (RR 4.74, 95%CI [2.61, 8.61],  $n = 238$ , 1 trial, moderate certainty) (Supplementary material).

#### 3.4.2. Herpangina

**3.4.2.1. Time to fever and blisters resolution.** Three trials<sup>33–35</sup> compared SFJD in combination with conventional drug (symptomatic treatment plus antivirals) with conventional drug on herpangina. Which showed that SFJD plus conventional drug was superior to conventional drug in shortening the duration of fever (MD −0.68 days, 95% CI [−1.15, −0.21],  $I^2 = 68\%$ ,  $n = 140$ , 2 trials, very low certainty) and blisters (MD −0.99 days, 95% CI [−1.23, −0.76],  $n = 386$ , 3 trials, low certainty) (Supplementary material).

**3.4.2.2. Clinical cure.** The cure rate was defined as resolution of fever and blisters with a range (1–5 days) of treatment. SFJD plus conventional drug was superior to conventional drug for cure rate (RR 1.30, 95% CI [1.12, 1.51],  $n = 386$ , 3 trials, low certainty) (Supplementary material).

#### 3.4.3. Acute tonsillitis and acute pharyngitis

**3.4.3.1. Time to fever and sore throat resolution.** SFJD plus conventional drug (symptomatic treatment and antibiotics) compared with conventional drug for acute tonsillitis and acute pharyngitis. Seven trials<sup>40–46</sup> indicated that the duration of fever was shorter in SFJD group than conventional drug group (MD −1.13 days, 95% CI [−1.36, −0.90],  $I^2 = 33\%$ ,  $n = 688$ , 7 trials, moderate certainty) (Fig. 4, Table 3). This effect was still observed regardless of adults (MD −1.24 days, 95% CI [−1.46, −1.01],  $n = 390$ , 4 trials, low certainty) or children (MD −0.93 days, 95% CI [−1.30, −0.55],  $n = 298$ , 3 trials, low certainty).

SFJD was also more effective than conventional drug (symptomatic treatment alone or symptomatic treatment plus antibiotics) in shortening the time to sore throat resolution in acute tonsillitis and acute pharyngitis (MD −1.13 days, 95% CI [−1.40, −0.86],  $I^2 = 84.1\%$ ,  $n = 1194$ , 10 trials, low certainty). This effect was still observed regardless of adults (MD −1.29 days, 95% CI [−1.60, −0.97],  $I^2 = 70\%$ ,  $n = 896$ , 7 trials, low certainty) or children (MD −0.73 days, 95% CI [−1.03, −0.43],  $n = 298$ , 3 trials, low certainty) (Table 3, Supplementary material).

**3.4.3.2. Clinical cure.** The criteria for cure rate was resolution of sore throat and fever with a range (1–5 days). SFJD was superior to conventional drug (symptomatic treatment alone or symptomatic treatment plus antibiotics) for cure rate (RR 1.26, 95% CI [1.13, 1.41],  $I^2 = 29.4\%$ ,  $n = 1082$ , 10 trials, low certainty) (Table 3, Supplementary material). This effect was still observed regardless of the age of patients.

#### 3.4.4. Adverse events

There were 7 trials<sup>25,26,31,36,38,40,46</sup> reported transient and minor gastrointestinal adverse events both in SFJD group (nausea in 6 cases, diarrhea in 4 cases) and in conventional drug group (nausea in 9 cases, diarrhea in 3 cases). SFJD was not judged as directly related to nausea and diarrhea in these trials, and no serious adverse events were reported in the included trials.

#### 3.4.5. Publication bias

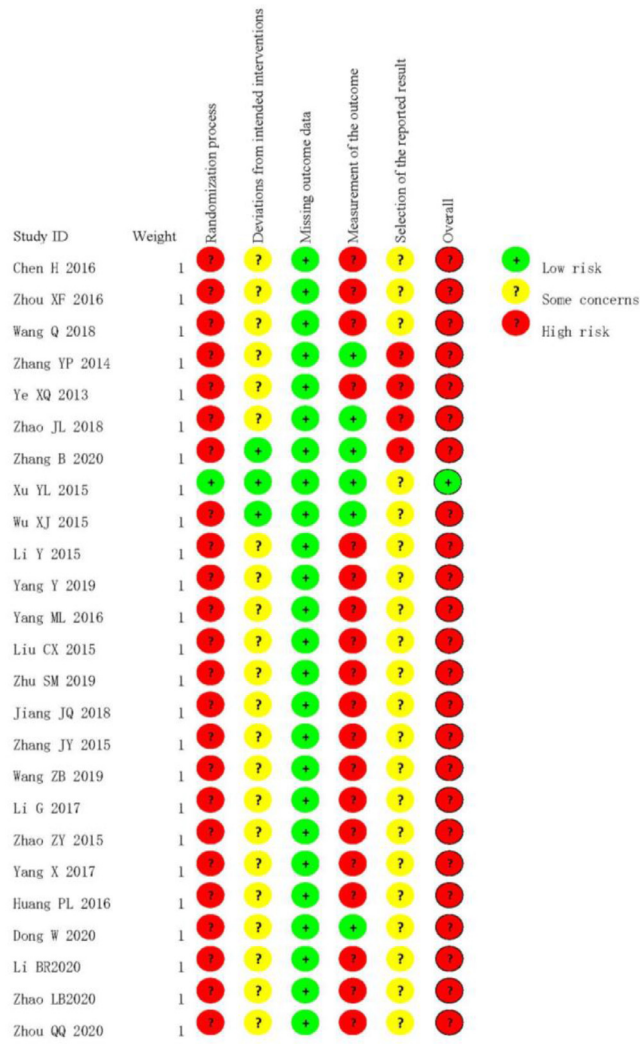
Funnel plots of cure rate in common cold seems to be symmetrical (Supplementary materials: Fig. 8), and funnel plots of time to sore throat resolution in acute tonsillitis and acute pharyngitis seems to be asymmetrical (Supplementary materials: Fig. 9). Suggesting that we cannot rule out the possibility of publication bias.

#### 3.4.6. Additional analysis

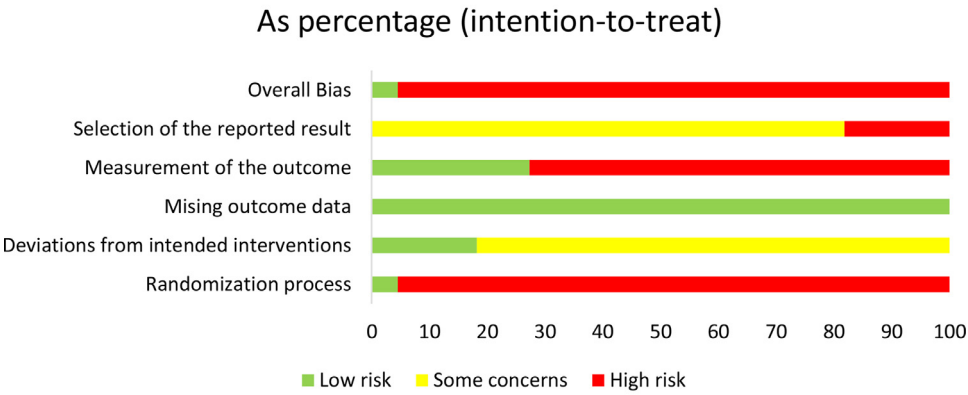
We were unable to conduct sensitivity analysis for placebo or allocation concealment in any meaningful primary outcomes, since the allocation concealment was clearly described in only one placebo-controlled trial<sup>29</sup> and the trial was narratively described. Two trials<sup>25,29</sup> reported drop outs but under different outcomes. Predefined subgroup analysis via the age of patients (adults and children) was conducted for 3 outcomes under common cold, acute tonsillitis and acute pharyngitis, we were unable to conduct other meaningful subgroup analysis due to limited trials.

#### 3.4.7. Certainty of evidence

GRADE approaches were employed to rate the certainty of evidence from all available outcomes. The quality of the evidence was downgraded to low or very low certainty due to lack of the blinding, imprecision (small number of events of less than 300 or number of patients included was less than 400), inconsistency ( $I$  square value was large) or indirectness of age (adults and children). The detailed evidence summary of outcomes were presented in (Table 2,3, Supplementary material).



(a) Risk of bias summary



(b) Risk of bias graph

Fig. 2. (a) Risk of bias summary.  
Fig. 2(b) Risk of bias graph.

**Table 2**

Evidence summary of common cold/ acute rhinitis: SFJD +conventional drug versus conventional drug.

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SFJD+ conventional drug	conventional drug	Relative (95% CI)	Absolute (95% CI)		
<b>Time to fever resolution</b> 3	randomized trials	serious <sup>a</sup>	serious <sup>b</sup>	not serious	serious <sup>c</sup>	undetected	193	192	-	MD <b>1.54 lower</b> (2.15 lower to 0.92 lower)	⊕○○○ VERY LOW	CRITICAL
<b>Time to cough resolution</b> 3	randomized trials	serious <sup>a</sup>	not serious	not serious	serious <sup>c</sup>	undetected	193	192	-	MD <b>1.22 lower</b> (1.52 lower to 0.93 lower)	⊕⊕○○ LOW	CRITICAL
<b>Cure rate</b> 10	randomized trials	serious <sup>a</sup>	not serious	serious <sup>d</sup>	not serious	undetected	554/792 (69.9%)	446/801 (57.7%)	<b>RR 1.26</b> (1.17 to 1.35)	<b>145 more per 1000</b> (from 95 more to 195 more)	⊕⊕○○ LOW	IMPORTANT
<b>Cure rate in adults</b> 7	randomized trials	serious <sup>a</sup>	not serious	not serious	not serious	undetected	463/599 (77.3%)	372/609 (61.1%)	<b>RR 1.27</b> (1.18 to 1.36)	<b>165 more per 1000</b> (from 110 more to 2more)	⊕⊕⊕○ MODERATE	IMPORTANT
<b>Cure rate in children</b> 3	randomized trials	serious <sup>a</sup>	not serious	not serious	serious <sup>e</sup>	undetected	91/193 (47.2%)	74/192 (38.5%)	<b>RR 1.22</b> (0.97 to 1.54)	<b>85 more per 1000</b> (from 12 fewer to 208 more)	⊕⊕○○ LOW	IMPORTANT

\*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

GRADE Working Group grades of evidence.

Moderate certainty (⊕⊕⊕○): We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty (⊕⊕○○○): Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.

Very low certainty (⊕○○○○): We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

**Notes:** CI, confidence interval; RR, risk ratio; SFJD, ShuFeng JieDu.<sup>a</sup> The blinding method was not used.<sup>b</sup> I square value was large.<sup>c</sup> Number of patients included was less than 400.<sup>d</sup> Indirectness of age (adults and children).<sup>e</sup> A small number of events of less than 300.



**Table 3**

Evidence summary of acute tonsillitis and acute pharyngitis: SFJD + conventional drug versus conventional drug.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	SFJD +conventional drug	conventional drug	Relative (95% CI)	Absolute (95% CI)		
<b>Time to fever resolution</b>												
7	RCTs	serious <sup>a</sup>	not serious	serious <sup>b</sup>	not serious	undetected	348	340	-	MD <b>1.13 d lower</b> (1.36 lower to 0.90 lower)	⊕⊕⊕○ MODERATE	CRITICAL
<b>Time to fever resolution- adults</b>												
4	RCTs	serious <sup>a</sup>	not serious	not serious	serious <sup>c</sup>	undetected	195	195	-	MD <b>1.24 d lower</b> (1.46 lower to 1.01 lower)	⊕⊕○○ LOW	CRITICAL
<b>Time to fever resolution - children</b>												
3	RCTs	serious <sup>a</sup>	not serious	not serious	serious <sup>c</sup>	undetected	153	145	-	MD <b>0.93 d lower</b> (1.30 lower to 0.55 lower)	⊕⊕○○ LOW	CRITICAL
<b>Time to sore throat resolution</b>												
10	RCTs	serious <sup>a</sup>	not serious	serious <sup>b</sup>	not serious	undetected	601	593	-	MD <b>1.13 d lower</b> (1.40 lower to 0.86 lower)	⊕⊕○○ LOW	CRITICAL
<b>Time to sore throat resolution - adults</b>												
7	RCTs	serious <sup>a</sup>	serious <sup>d</sup>	not serious	not serious	undetected	448	448	-	MD <b>1.29 d lower</b> (1.60 lower to 0.97 lower)	⊕⊕○○ LOW	CRITICAL
<b>Time to sore throat resolution – children</b>												
3	RCTs	serious <sup>a</sup>	not serious	not serious	serious <sup>c</sup>	undetected	153	145	-	MD <b>0.73 d lower</b> (1.03 lower to 0.43 lower)	⊕⊕○○ LOW	CRITICAL

(continued on next page)

Table 3 (continued)

Certainty assessment							No of patients		Effect		Certainty	Importance
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	SFJD +conventional drug	conventional drug	Relative (95% CI)	Absolute (95% CI)		
<b>Cure rate</b> 10	RCTs	serious <sup>a</sup>	not serious	serious <sup>b</sup>	serious	undetected	289/545 (53.0%)	228/537 (42.5%)	RR 1.26 (1.13 to 1.41)	110more per 1000 (from 55 more to 174 more)	⊕⊕○○ LOW	IMPORTANT
<b>cure rate - adults</b> 7	RCTs	serious <sup>a</sup>	not serious	not serious	serious	undetected	239/392 (61.0%)	197/392 (50.3%)	RR 1.21 (1.09 to 1.35)	106 more per 1000 (from 45 fewer to 176 more)	⊕⊕⊕○ MODERATE	IMPORTANT
<b>cure rate - children</b> 3	RCTs	serious <sup>a</sup>	not serious	not serious	serious <sup>c</sup>	undetected	50/153 (32.7%)	31/145 (21.4%)	RR 1.54 (1.05 to 2.26)	115 more per 1000 (from 11 more to 269 more)	⊕⊕○○ LOW	IMPORTANT

\*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

GRADE Working Group grades of evidence.

Low certainty (⊕⊕○○): Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect;

Very low certainty (⊕○○○): We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect;

**Notes:** CI, Confidence interval; MD, Mean difference; RCTs, Randomized controlled trial; RR, Risk ratio; SFJD, ShuFeng JieDu.

<sup>a</sup> The blinding method was not used.

<sup>b</sup> Indirectness of age (adults and children).

<sup>c</sup> Number of patients included was less than 400.

<sup>d</sup> I square value was large.

<sup>e</sup> A small number of events of less than 300.

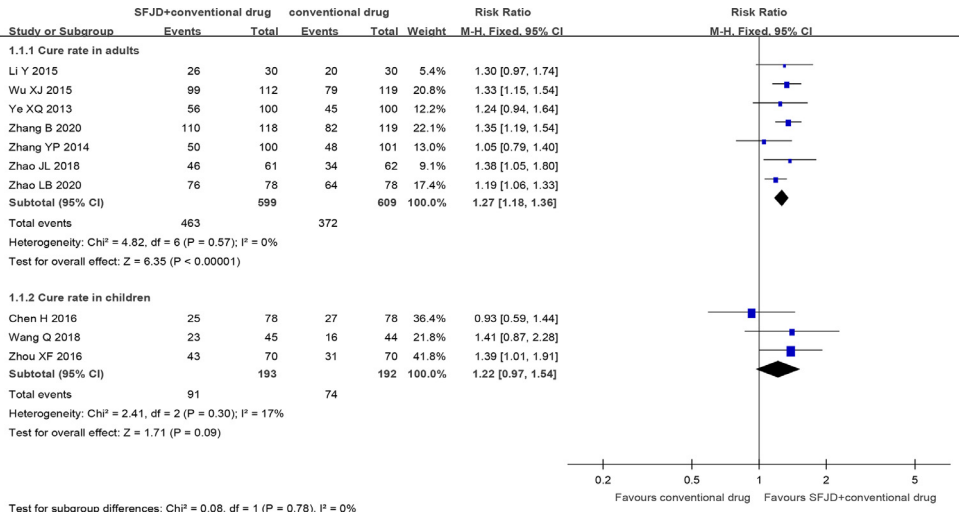


Fig. 3. Cure rate with a range (1–5days) of treatment in common cold. SFJD, Shufeng Jiedu.

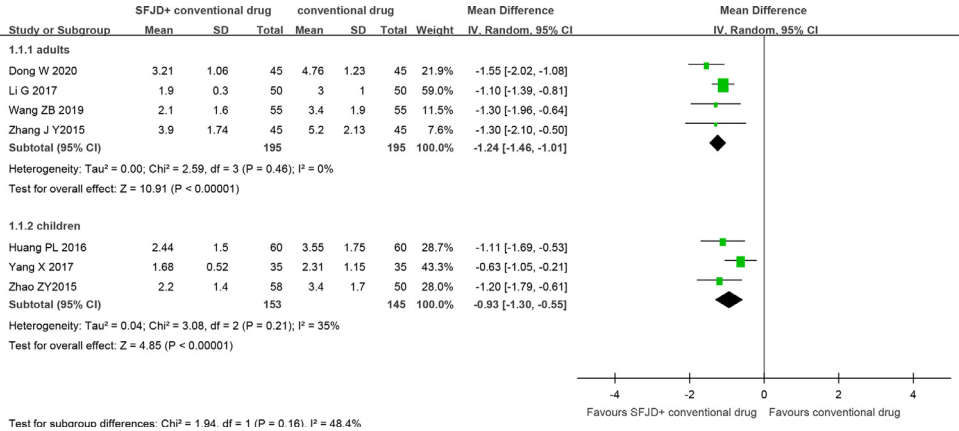


Fig. 4. Time to fever resolution (d) in acute tonsillitis and acute pharyngitis.SFJD, Shufeng Jiedu.

4. Discussion

4.1. Main findings

Low certainty evidence suggested that SFJD capsule as an adjunctive treatment to conventional drug was more beneficial than conventional drug alone to shorten the duration of symptoms in AURTIs, as well as improve cure rate with a range (1–5 days) of treatment. In common cold we found that SFJD was superior to conventional drug alone in shortening the duration of cough (–1.22 days) and fever (–1.54 days), as well as improving cure rate by 14.1%. In herpangina, SFJD plus conventional drug was more effective in shortening the duration of fever (–0.68 days), blisters (–0.99 days) and improving the cure rate by 15.8%. In acute tonsillitis and acute pharyngitis, SFJD combined with conventional drug was superior to conventional drug in shortening the duration of fever (–1.13 days), sore throat (–1.13 days) and increasing cure rate by 11%. These effects were still observed regardless of age. However, due to high risk of bias and small sample size, we downgraded these outcomes from high to low or very low certainty. In addition, there was no serious adverse events reported in the included trials.

4.2. Relation to previous research

Currently, there was one systematic review<sup>47</sup> on SFJD for chronic obstructive pulmonary disease (COPD) suggested that SFJD

may be beneficial to shorten the length of hospitalization and improve symptoms related to COPD. Another prior systematic review<sup>11</sup> narratively reviewed the clinical and experimental findings of Chinese herbal medicine for the treatment of AURTIs. Suggesting that SFJD capsule was effective in improving symptoms of AURTIs, such as fever and cough. Which was consistent with our study. However, only one RCT on SFJD for AURTIs was identified and meta-analysis was not performed in this previous review. We conducted a more comprehensive search and meta-analysis was performed for more available outcomes. In addition, the protocol of this systematic review was registered prospectively and GRADE approaches were employed to assess the certainty of evidence.

4.3. Strengths and limitations

This is the first systematic review and meta-analysis based on RCTs to assess therapeutic effect and safety of Chinese patent herbal medicine SFJD capsule for AURTIs. We comprehensively searched the Chinese and English databases and identified all available RCTs. The outcomes were all assessed within 5 days of treatment, since many types of AURTIs were self-limited in 7 days<sup>4</sup>. The protocol of this systematic review was registered on INPLASY, and subgroup analysis via the age of patients was conducted. The methodological quality of RCTs were evaluated comprehensively by the latest Cochrane Risk of Bias tool 2.0, and GRADE criteria was also employed to determine the certainty of evidence.

However, there are several limitations. Firstly, antibiotics are not recommended for most AURTIs in guidelines, but they were used in the included trials. Secondly, predefined outcomes of symptom improvement rate and the severity of AURTIs were not reported in included trials. Additionally, only one double-blinded, placebo-controlled trial was assessed as having low risk of bias, the remaining included trials were of high risk of bias.

#### 4.4. Implications for clinical practice

The diagnosis and treatment of AURTIs should strictly following guidelines. Antibiotics are recommended only for specific AURTIs (such as acute pharyngitis and acute tonsillitis caused by streptococcus) in existing guidelines, for other AURTIs, symptomatic treatment were recommended<sup>5,6</sup>. Standard care following guidelines are recommended, considering the potential effect of SFJD capsule, it might be a safe symptomatic treatment for AURTIs.

#### 4.5. Implications for research

SFJD may have a role to play for the relief of symptoms from common AURTIs, but there is uncertainty due to the high risk of bias in the current studies. High quality placebo controlled RCTs with SFJD used alone or in combination with standard care are needed. Outcome reporting needs to be improved, the time from symptoms onset when included and the time point for every outcome measured should be clearly reported, since most AURTIs resolve from 3 to 7 days<sup>4</sup>. In addition, cure rate was widely used in these trials as composite outcomes<sup>48</sup> (usually included a set of symptoms and signs), but the detailed measurement of individual symptoms or signs could not be determined.

#### 4.6. Conclusion

Currently, low certainty evidence suggests that SFJD may be effective in shortening the duration of typical symptoms in AURTIs, and improve cure rate with a range (1–5 days) of treatment. No serious adverse event was reported. However, high quality placebo-controlled trials are needed to confirm its benefits.

#### 4.7. Author contributions

Conceptualization: YY Zhang, JP Liu and RY Xia. Methodology: RY Xia and S B Liang. Software: YY Zhang and S B Liang; YL Li and LY Zhao. Formal Analysis: YY Zhang and RY Xia. Data Curation: YY Zhang and RY Xia. Writing – Original Draft: YY Zhang. Writing – Review & Editing: RY Xia, SB Liang, XY Hu, MY Dai, YL Li, LY Zhao, M Moore, YT Fei and JP Liu. Funding Acquisition: JP Liu. YY Zhang and RY Xia are co-first authors. All authors approved the final manuscript.

#### Conflict of interest

The authors declare that they have no conflicts of interest.

#### Funding

This work is supported by the National Key Research and Development Project: Adding Chinese herbal medicine to antibiotic treatment for acute exacerbation of chronic obstructive pulmonary disease (Grant no. 2018YFE0102300).

#### Ethical statement

This work did not require an ethical approval as it does not involve any human or animal experiment.

#### Data availability

The data will be made available upon request.

#### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.imr.2021.100726](https://doi.org/10.1016/j.imr.2021.100726).

#### References

- James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet North Am Ed.* 2018;392(10159):1789–1858.
- Geneva. *Disease Burden and Mortality Estimates*. WHO; 2020 website [http://www.who.int/gho/mortality\\_burden\\_disease/en/index.html](http://www.who.int/gho/mortality_burden_disease/en/index.html) Published 2018. Accessed June 20.
- International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). 23. WHO; 2021 website <http://www.bmj.com/content/346/bmj.f2914> Published 2019. Accessed February.
- King D, Mitchell B, Williams CP, Spurling G. Saline nasal irrigation for acute upper respiratory tract infections. *Cochrane Database Syst Rev.* 2015(4).
- Harris AM, Hicks LA, Qaseem A. Appropriate antibiotic use for acute respiratory tract infection in adults: advice for high-value care from the American college of physicians and the centers for disease control and prevention. *Ann Intern Med.* 2016;164(6):425–434.
- Hersh AL, Jackson MA, Hicks LADISEASES TCOL. Principles of judicious antibiotic prescribing for upper respiratory tract infections in pediatrics. *Pediatr Off Publ Am Acad Pediatr.* 2013;132(6):1146–1154.
- Shapiro DJ, Hicks LA, Pavia AT, Hersh AL. Antibiotic prescribing for adults in ambulatory care in the USA, 2007–09. *J Antimicrob Chemother.* 2014(1):234–240.
- Wang J, Wang P, Wang X, Zheng Y, Xiao Y. Use and prescription of antibiotics in primary health care settings in China. *JAMA Intern Med.* 2014;174(12):1914.
- Alves Galvão MG, Rocha Crispino Santos MA, Alves Da Cunha A. Antibiotics for preventing suppurative complications from undifferentiated acute respiratory infections in children under five years of age. *Cochrane Database Syst Rev.* 2016(2).
- CDC. 2019 AR Threats Report, CDC Newsroom. <https://www.cdc.gov/media/releases/2019/t1113-ar-threats.html>. Published 2019. Accessed June 25, 2020.
- Huang ZS, Pan XY, Zhou J, Leung WT, Li CT, Wang L. Chinese herbal medicine for acute upper respiratory tract infections and reproductive safety: a systematic review. *Biosci Trends.* 2019;13(2):117–129.
- Li J, Yu X. Guidelines for the diagnosis and treatment of common cold in traditional Chinese medicine. *J Tradit Chin Med.* 2016;57(08):716–720.
- China Association of Traditional Chinese Medicine. *Guidelines for Diagnosis and Treatment of Common Diseases of Otolaryngology in Traditional Chinese*. Beijing: China Press of Traditional Chinese Medicine; 2012.
- National Administration of Traditional Chinese Medicine (NATCM). *The Office of the NATCM Issued a Circular on TCM Clinical Pathways and TCM Diagnosis and Treatment Plans (2017 edition) for 92 Diseases Including Stroke (cerebral infarction)*. NATCM; 2021 website <http://www.satcm.gov.cn/yizhengsi/gongzuodongtai/2018-03-24/2651.html> Published in 2018. Accessed February 10.
- Bao YY, Gao YJ, Cui XL. Effect of Shufeng Jiedu capsules as a broad-spectrum antibacterial. *Biosci Trends.* 2016;10(1):74–78.
- Ji S, Bai Q, Wu X, Zhang DW, Wang S, Shen JL, et al. Unique synergistic antiviral effects of Shufeng Jiedu Capsule and oseltamivir in influenza A viral-induced acute exacerbation of chronic obstructive pulmonary disease. *Biomed Pharmacother.* 2020;121.
- Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred Reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Revista Espanola de Nutricion Humana y Dietetica.* 2014;18(3):172–181.
- Zhang Y.Y., Xia R.Y., Liang S.B., Dai M.Y., Hu X.Y., Willcox M., et al. Chinese Patent Medicine Shufengjiedu Capsule for Acute Upper Respiratory Tract Infections: A Protocol of a Systematic Review of Randomized Clinical Trials. *Inplasy protocol* 202050083. doi:10.37766/inplasy2020.5.0083.
- Higgins JPT, Savović J, Page MJ, Elbers RG, Sterne JAC. *Cochrane Handbook For Systematic Reviews of Interventions Version 6.0 (updated July 2019)*. Chapter 8: assessing risk of bias in a randomized trial. Cochrane; 2019 Available from [www.trainingcochrane.org/handbook](http://www.trainingcochrane.org/handbook) Accessed September 22, 2020.
- Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. *Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019)*. Cochrane; 2020; 2019 Available from [www.training.cochrane.org/handbook](http://www.training.cochrane.org/handbook) Accessed September 1.
- Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ.* 2008;336(7650):924–926.
- Chen H, Su YM, Luan JQ. Clinical observation of Shufeng Jiedu capsule in the treatment of acute upper respiratory tract infection in children. *Word J Integr Tradit West Med.* 2016;11(05):716–718.
- Zhou XF, Wang XJ. Clinical observation of Shufeng Jiedu capsule on wind-heat syndrome of children with acute viral upper respiratory tract infection. *Beijing J Tradit Chin Med.* 2016;25(01):84–86.

24. Wang Q, Liu K, Chen F, Zhao L. Therapeutic effect of Shufeng Jiedu capsule on acute upper respiratory tract infection in children. *J Clin Pulm Med*. 2018;23(10):1842–1845.
25. Zhang YP, Lin Y, Min M, Xi PL, Tong CY. Effects of Shufengjiedu capsules on serum amyloid A in the treatment of patients with an acute viral upper respiratory tract infection. *J Pathogen Biol*. 2014;9(08):734–736.
26. Ye XQ, Zeng DZ, Luo SF. Clinical observation of Shufeng Jiedu capsule in the treatment of wind-heat syndrome of cold. *Anhui Med Pharm J*. 2013;17(04):664–666.
27. Zhao JL, Xu DF, Li CY. Effect of Shufeng Jiedu capsule on acute upper respiratory tract infection. *Chin Arch Tradit Chin Med*. 2018;36(05):1222–1225.
28. Zhang B, Zhang W. Clinical effect of Shufeng Jiedu Capsules for acute upper respiratory tract infection and its effect on inflammatory factors. *J New ChinMed*. 2020;52(04):50–53.
29. Wu XJ, Xue MM, Huang JL, Zhang YP, Wang CL, Song ZJ, et al. Effect of Shufeng Jiedu capsule combined with antibiotics on aged patients with bacterial acute upper respiratory tract infection. *Practical Journal of Cardiac Cerebral Pneumal and Vascular Disease*. 2015;23(03):97–99.
30. Xu YL, Xue YL, Zhang HH, Lv FY, Tian ZJ, Xing ZH, et al. Clinical observation on treatment of acute upper respiratory infection wind-heat syndrome with Shufeng Jiedu capsules randomize-controlled double-blind test. *J Tradit Chin Med*. 2015;56(08):676–679.
31. Zhao LB, Wang ZB. Clinical observation of Shufeng Jiedu capsule in treating acute upper respiratory tract infection (wind-heat syndrome). *J Emerg Tradit Chin Med*. 2020;29(07):1278–1279.
32. Li Y, Wang XJ. Clinical observation on the treatment of acute rhinitis (Wind Heat Syndrome) with Shufeng Jiedu capsule. *Guid J Tradit Chin Med Pharm*. 2015;21(21):49–51.
33. Yang Y, Li DY. Effect of Shufeng Jiedu capsule combined with recombinant alpha 1B interferon on children with herpetic pharyngitis. *J Emerg Tradit Chin Med*. 2019;28(05):899–900.
34. Yang ML. Effect of Shufeng Jiedu capsule on 123 children with herpetic pharyngitis. *J Emerg Tradit Chin Med*. 2016;25(12):2364–2365.
35. Liu CX. Treatment of 37 cases of infantile herpetic angina with Shufeng Jiedu Capsule. *Henan Tradit Chin Med*. 2015;35(07):1695–1697.
36. Zhu SM, Mao XP, Liu Q. Clinical observation on the treatment of acute pharyngitis (Wind Heat Syndrome) with Shufeng Jiedu capsule combined with budesonide atomization. *Chin Med Innov*. 2019;16(08):67–71.
37. Jiang JQ, Cheng LL, Li Q. Clinical observation on the treatment of acute pharyngitis with TCM combined with Western medicine. *J Emerg Tradit Chin Med*. 2018;27(08):1448–1450.
38. Dong W, Zheng RH. Effect of Shufeng Jiedu capsule combined with dexamethasone ultrasonic atomization inhalation on TNF- $\alpha$  and IL-6 in patients with acute pharyngitis. *Mod J Integr Tradit Chin West Med*. 2020;29(35):3936–3939.
39. Zhou QQ, Ji Zhu, Pu LC. Clinical study on Shufeng Jiedu capsules for acute laryngopharyngitis. *J New Chin Med*. 2020;52(10):96–98.
40. Zhang JY. Clinical observation on the treatment of acute attacks of chronic tonsillitis with Shufeng Jiedu capsule. *J Emerg Tradit Chin Med*. 2015;24(12):2230–2232.
41. Wang ZB, Zhao LB. Clinical observation on the treatment of Acute tonsillitis with Shufeng Jiedu capsule. *J Emerg Tradit Chin Med*. 2019;28(10):1827–1829.
42. Li G, Ding Y, Wang SS, Xie H, Xu DM. Clinical observation on the treatment of acute suppurative tonsillitis with Shufeng Jiedu capsule combined with cefuroxime sodium. *Anti-Infect Pharm*. 2017;14(02):475–476.
43. Li BR, Yang LL, Si JY. Clinical study of Shufeng Jiedu capsule for acute tonsillitis. *J Emerg Tradit Chin Med*. 2020;29(10):1849–1851.
44. Zhao ZY. Treatment of 58 cases of acute tonsillitis in children with Shufeng Jiedu Capsule. *Henan Tradit Chin Med*. 2015;35(07):1690–1692.
45. Yang X, Yang XW. Observation on efficacy of Shufengjiedu capsules in treatment of acute Suppurative Tonsillitis. *Eval Anal Drug-Use Hosp China*. 2017;17(01).
46. Huang PL, Pan YD. Clinical observation on the treatment of Tonsillitis in children (Wind Heat Syndrome) with Shufeng Jiedu capsule combined with Cefaclor for oral suspension. *J Emerg Tradit Chin Med*. 2016;25(10):1984–1986.
47. Xia RY, Hu XY, Fei YT, Willcox M, Wen LZ, Yu MK, et al. Shufeng Jiedu capsules for treating acute exacerbations of chronic obstructive pulmonary disease: a systematic review and meta-analysis. *BMC Complement Med Ther*. 2020;20(1):151.
48. Christopher MC. Understanding the use of composite endpoints in clinical trials. *West J Emerg Med*. 2018;19(4):631–634.