

# Systematic Review of Chinese Medicine for the Treatment of Dysfunctional Uterine Bleeding

**Liping Ma, Haiyong Chen, Yanbo Zhang and Wei Meng\***

Hong Kong Branch of Zhu's School of Gynecology of Chinese Medicine from Shanghai  
Workstation of Zhu Nansun, National Master of Chinese Medicine, Hong Kong  
School of Chinese Medicine, The University of Hong Kong

**\*Corresponding author:** Wei Meng, School of Chinese Medicine, The University of  
Hong Kong, Pokfulam, Hong Kong, Tel: +852 39170483; Email: bmeng@hku.hk

## Research Article

Volume 2 Issue 4

**Received Date:** September 03, 2018

**Published Date:** October 29, 2018

**DOI:** 10.23880/ipcm-16000146

## Abstract

**Objectives:** To evaluate the effectiveness of Chinese medicine in treating dysfunctional uterine bleeding via a systematic review and meta-analysis.

**Methods:** Clinical trials of Chinese medicine treating dysfunctional uterine bleeding were retrieved with specific search strategy in the following databases: CNKI (from 1994 to December 2016), Wan Fang (from 1980 to December 2016), Pro Quest Medical Database (from 1980 to December 2016), MEDLINE (from 1950 to December 2016) and PUBMED (from 1980 to December 2016). Eligible randomized controlled trials (RCTs) were selected with the inclusion and exclusion criteria. The quality of trials was assessed by the risk of bias assessment tool. Data was extracted into Excel and analyzed by Software Rev Man 5.3.

**Result:** A total of 21 RCTs were included with 2167 patients. The meta-analysis showed that the Chinese medicine group had higher recovery rate than that of the Western medicine group [OR=2.26, 95% CI (1.86, 2.74), P<0.00001]. The effectiveness of Chinese medicine was superior to the Western medicine [OR=3.93, 95% CI (2.99, 5.169), P<0.00001]. There were no significant difference in bleeding arrest in 3 days [OR=0.90, 95% CI (0.49, 1.63), P=0.73] and in 10 days [OR=1.40, 95% CI (0.80, 2.44), P=0.24] between Chinese medicine group and Western medicine group. Few side effects were observed in the Chinese medicine group [OR=0.04, 95% CI (0.01, 0.11), P<0.0001]. The Chinese medicine group also had a lower recurrence rate than that of Western medicine group [OR=0.16, 95% CI (0.06, 0.47), P=0.0008].

**Conclusion:** Chinese medicine appears to have better overall clinical effect in treating dysfunctional uterine bleeding with less side effects and lower chance of recurrence. However, the quality of the included studies needs to be improved; the findings should be interpreted with caution. Further large-scale, rigorously designed trials are warranted to confirm the findings.

**Keywords:** Hemostatic; Chinese Medicine; Uterine Bleeding

## Background

Metrorrhagia in Chinese medicine is equivalent to the anovulatory dysfunctional uterine bleeding in Western medicine. The incidence of dysfunctional uterine bleeding is 22%, of which 85% involved anovulatory dysfunctional uterine bleeding [1]. In China, about 10% of gynecological outpatients are suffering from dysfunctional uterine bleeding. Among them, 50% are menopause women over 40 years of age, 20% are unmarried adolescents (less than 19 years old) and 30% are 19 -40 years old women [2]. The principles of treatment are: (1). Stop bleeding at acute stage; (2). Adjust the menstrual cycle and (3). Promote ovulation. Medications and surgery are the commonest therapies for the dysfunctional uterine bleeding. Medications are mainly hormonal drugs which usually causes gastrointestinal discomfort. High relapse rate after discontinuation and risk of bleeding after drug withdrawal are also disadvantages of hormonal drugs [3].

Many clinical trials were conducted to evaluate the effect of Chinese medicine in the treatment of dysfunctional uterine bleeding. But study methods in these

trials were inconsistent and the definitions of effectiveness in outcome measures were different, causing the low comparability of the studies. This study assessed the effectiveness of Chinese and Western medicines in the treatment of dysfunctional uterine bleeding by a systematic review and Meta-analysis, which aimed to provide evidence for the clinical practice, identify the gaps that exist in Chinese medicine treating dysfunctional uterine bleeding, and figure out future research directions.

## Search Strategy for Identification of Studies and Source of Literatures

Following databases were searched for relevant studies: Chinese literatures were obtained from CNKI (from 1994 to December 2016) and Medicine and Health Journal of Wan Fang Data (from 1980 to December 2016), English literatures were obtained from Pro Quest Medical Database (from 1980 to December 2016), MEDLINE (from 1950 to December 2016) and PUBMED (from 1980 to December 2016). Every database was searched from its starting date to December 2016 in Chinese and English. The search strategies are illustrated in Table 1.

Database	Published Date	Keywords
CNKI	1994 to Dec 2016	"中藥" 與 "崩漏" 與 "隨機" 與 "對照"
Medicin and health Journal of WangFang Data	1980 to Dec 2016	"中醫" 與 "崩漏" 與 "隨機" 與 "對照" "中藥" 與 "功血" 與 "隨機" 與 "對照" "中醫" 與 "功血" 與 "隨機" 與 "對照" "chinese medicine" AND "'metrorrhagia'/"dysfunctional uterine bleeding" AND "random" AND "Control"
Medline	1950 to Dec 2016	"Chinese Medicine" AND "Dysfunctional uterine bleeding"
ProQuest Medical Dtabase	1980 to Dec 2016	
Pubmed	1980 to Dec 2016	

Table 1: Search strategy and source of literature.

## Systematic Review

### Inclusion criteria:

- Types of Studies: All RCTs reporting the applications of Chinese Medicine to anovulatory dysfunctional uterine bleeding. Chinese medicine must be used in treatment groups and Western medicine used in control groups.
- Participants: Anovulatory dysfunctional uterine bleeding patients diagnosed under the diagnostic criteria by Chinese or Western medicine. While clinical effects were assessed using the "TCM Standard of Diagnostic Effectiveness".
- Interventions: All types of Chinese medicines of oral administration in either standard or combined formulas

in the treatment group were included. All types of Western medicines in the control group were included.

- Outcome Measures: The effective rate, recurrence rate, pregnancy rate and also the safety of the intervention were studied.

### Exclusion criteria:

- Participants: Uterine bleeding caused by pregnancy, genital tumors, infections, etc.
- Combined Therapies: The study using the combined therapy (Chinese medicines plus Western medicines) was excluded.
- Treatments before experiment: Excluded studies involving the treatment by Western medicine (including

hemostasis drug or blood transfusion) prior to the start of the experiment

- Other Type of Studies: Case reports, commentary studies, animal experiments and review articles were excluded.

### Selection of Literatures

A preliminary screening by reading the titles and abstracts of the literature was performed according to the inclusion and exclusion criteria. The literatures were secondarily screened by assessing the full text. Any discrepancy was resolved by the independent reviewer.

### Quality Assessment

The risk of bias assessment tool developed in Cochrane collaboration was employed to evaluate the quality of the included literatures, including (1) whether randomized allocation was applied; (2) whether there were hidden allocations; (3) whether blinding was applied on participants and personnel; (4) whether blinding was applied on outcome assessment; (5) whether there was incomplete data; (6) was there selective bias; (7) was there any other bias.

### Data Extraction

The following information from the literatures was extracted into Excel: (1) general data including title, author, publication date and source, etc.; (2) study characteristics including general conditions of the study subjects (including age and treatment duration) and

interventions (drugs used); (3) outcome measures; (4) side effects, follow-up, and incompleteness of treatment and cases.

### Outcome

The clinical efficacy assessed by “TCM standard of diagnostic effectiveness”. The following information was extracted for meta-analysis: (1) cure rate; (2) effective rate; (3) hemostatic effectiveness; (4) side effects occurrence; (5) recurrence rate.

### Statistical Analysis

Rev Man 5.3 statistical software developed by the Cochrane Collaboration was used for meta-analysis. Quantitative data was analyzed by standard mean differences (SMD), while categorical variables were analyzed with using odds ratio (OR). If substantial statistical heterogeneity ( $P < 0.05$ ) were detected, a random effects model (RE) was applied, otherwise, fixed model (FE) was used. Results were presented in forest plot with its 95% confidence interval. The funnel plot was used for the potential publication bias in the studies if necessary.

## Results

### Literatures Searching Result

1041 studies were retrieving according to designed search strategy. After the preliminary screen, 155 studies were identified. Following the full text assessment, 21 eligible studies were included as shown in Figure 1.

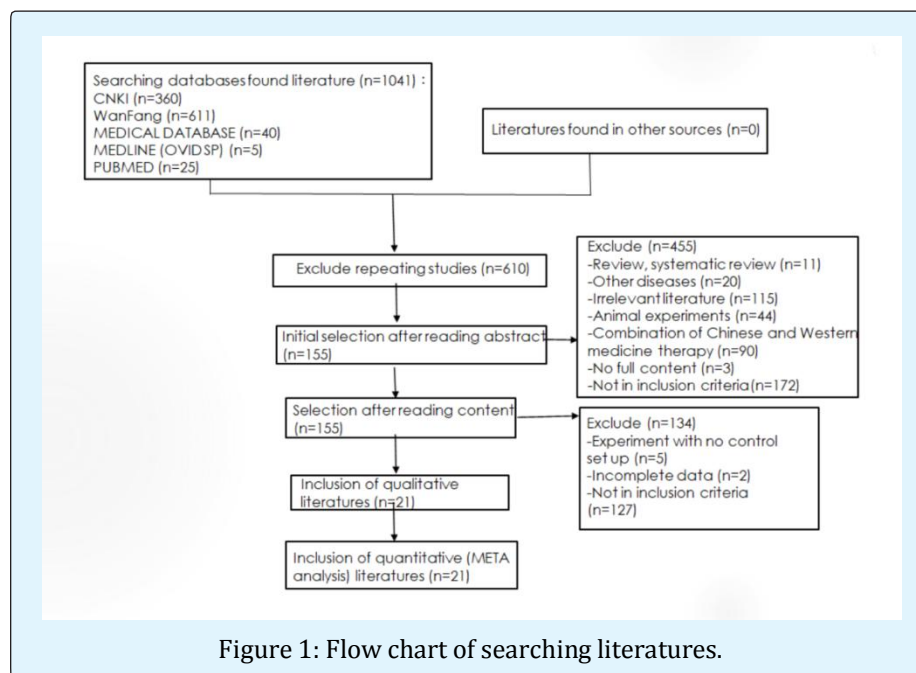


Figure 1: Flow chart of searching literatures.

### Characteristics of Included Studies

The characteristics of included studies were shown in Table 2.

Study	Case(T/C)	Chinese Medicine	Western Medicine	Outcome Measure
Chang [4]	49/48	Tradation Chinese Medicine	Conjugated Estrogens, Medroxyprogesterone	①
Cheng [5]	32/30	Gu Cheng Decoction	Norethisterone Tablets	①②
Chung, et al. [6]	58/34	Tradation Chinese Medicine	Stilboestrol, Medroxyprogesterone	①,③
Fan [7]	50/50	Gong Xue Yin	Tristeronum Compositum, Contraceptive pills, Ma FU Long, Conjugated Estrogens, Medroxyprogesterone	①②③④
Fan, et al. [8]	86/86	yi Qi Sheng Yang Zhi Beng Decoction	Norethisterone Tablets	①②
Hung, et al. [9]	70/65	Jiao Ai Decoction	Conjugated Estrogens, Medroxyprogesterone	①
Ip [10]	66/42	Bu Zhong Yi Qi Decoction	Norethisterone Tablets	①
Kung [11]	60/50	Ren Can Gui pi Decoction	Medroxyprogesterone	①
Li [12]	61/47	Tradation Chinese Medicine	Estrostilben, Medroxyprogesterone	①
Li [13]	86/86	Bu Zhong Yi Qi Decoction	Norethisterone Tablets	①
Pang [14]	30/30	Yi chun Jian	conjugated Estrogens, Medroxyprogesterone	①②
Sheh [15]	58/58	Traditional Chines Medicine	conjugated Estrogens, Medroxyprogesterone	①
Wang, et al. [16]	40/30	Traditional Chines Medicine	Estrogen, Medroxyprogesterone	①②③
Wang [17]	41/39	Traditional Chines Medicine	Stilboestrol, Medroxyprogesterone	①
Wang, et al. [18]	49/47	Traditional Chines Medicine	Desogetrel, Ethinylestradiol Tablets	①
Wang [19]	30/30	Traditional Chines Medicine	Ma Fu Long	①②
Yu [20]	82/40	Traditional Chines Medicine	Estrostilben,Adrenosin, Vitamin K, Vitamin C	①②③④
Zang [21]	32/30	Tradation Chinese Medicine	Ma Fu Long	①
Zang [22]	39/36	Tradation Chinese Medicine	Norethisterone Tablets	①②
Zhang, et al. [23]	75/75	Tradation Chinese Medicine	Norethisterone Tablets, Conjugated Estrogens, Medroxyprogesterone	①
Zhang, et al. [24]	70/50	Sheng Xian Decoction	Dydrogesterone	①②

Table 2: Basic features of studies (Outcome measures: ①cure rate and effective rate, ②hemostasis effect, ③side effects occurrence, ④recurrence rate).

### Quality Assessment of Included Studies

The quality of included studies was assessed by the Cochrane Handbook 5.3 Risk of Bias Assessment Tool (Figure 2 & 3).

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Chang 2013	●	?	●	?	?	?	?
Cheng et al. 2015	●	?	●	?	?	?	?
Chung et al. 2006	?	?	●	?	?	?	?
Fan 2007	?	?	●	?	?	?	?
Fan et al. 2009	?	?	●	?	?	?	?
Huang et al. 2011	●	?	●	?	?	?	?
Kung 2012	?	?	●	?	?	?	?
Li 2011	?	?	●	?	?	?	?
Li 2012	?	?	●	?	?	?	?
Pang 2008	?	?	●	?	?	?	?
Shih 2008	?	?	●	?	?	?	?
Wong 2009	?	?	●	?	?	?	?
Wong 2011	?	?	●	?	?	?	?
Wong 2015	?	?	●	?	?	?	?
Wong et al. 2013	●	?	●	?	?	?	?
Yip 2005	?	?	●	?	?	?	?
Yu 2005	?	?	●	?	?	?	?
Zhang 2010	?	?	●	?	?	?	?
Zhang 2013	?	?	●	?	?	?	?
Zhang et al. (2) 2013	?	?	●	?	?	?	?
Zhang et al. 2013	?	?	●	?	?	?	?

Figure 2: Literature bias risk summary table.

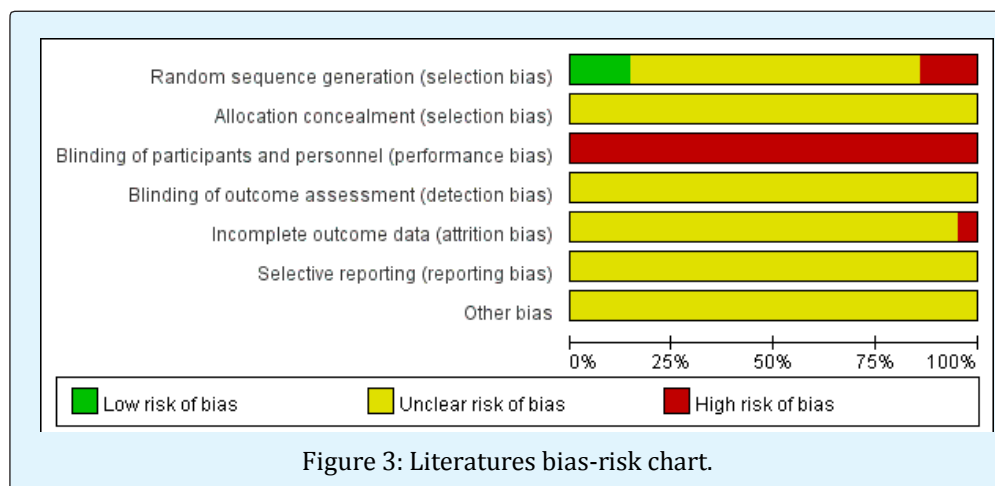


Figure 3: Literatures bias-risk chart.

## Outcomes

**Clinical Effectiveness - Cure Rate:** As shown in Figure 4, the heterogeneity test indicated there was no significant heterogeneity in the pooled studies ( $P=0.46$ ,  $I^2=0\%$ ). A fixed effect model was used for meta-analysis. The cure

rate in the treatment group (Chinese medicine) was significantly higher than that in the control group (Western medicine) [OR=2.26, 95% CI (1.86, 2.74),  $P<0.00001$ ] (Figure 4).

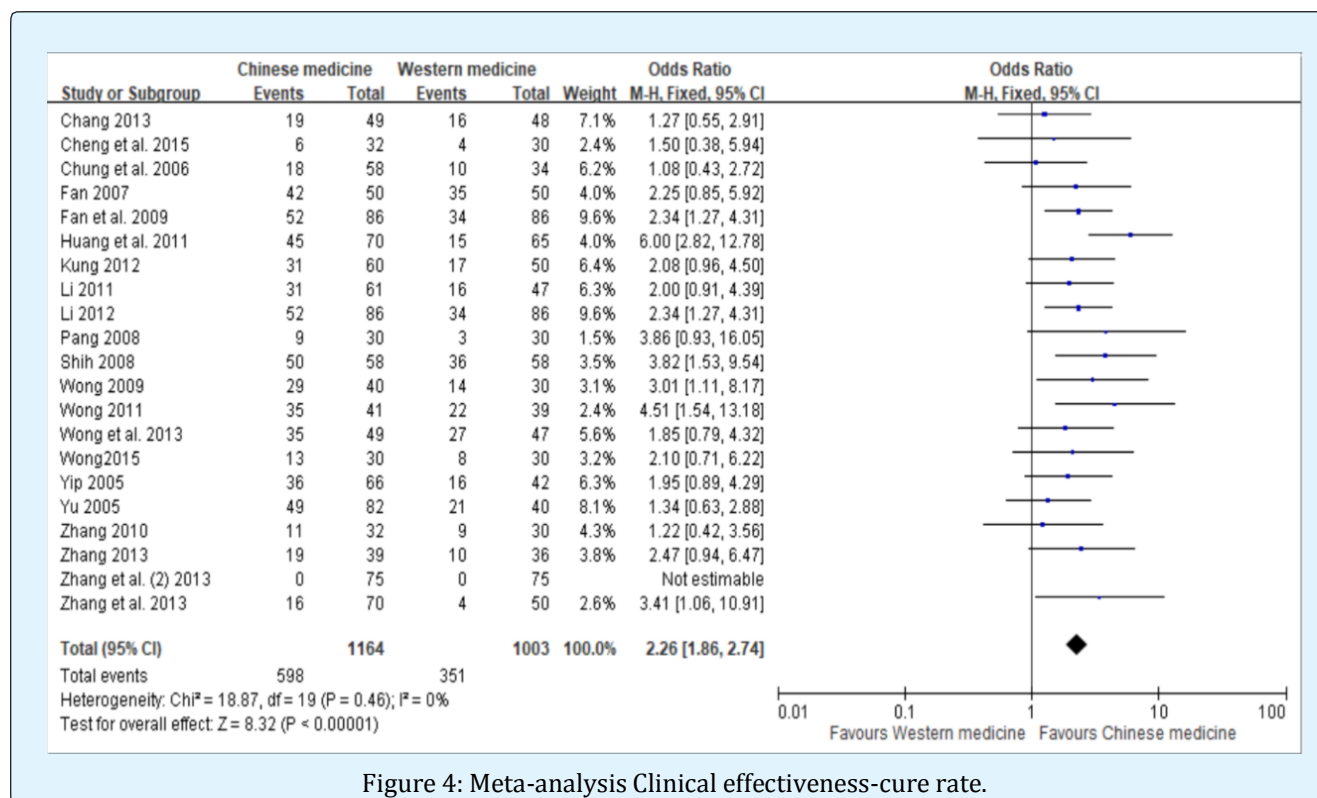


Figure 4: Meta-analysis Clinical effectiveness-cure rate.

The funnel diagram indicated the studies were rather symmetrical (Figure 5). Low publication bias was found in the studies.



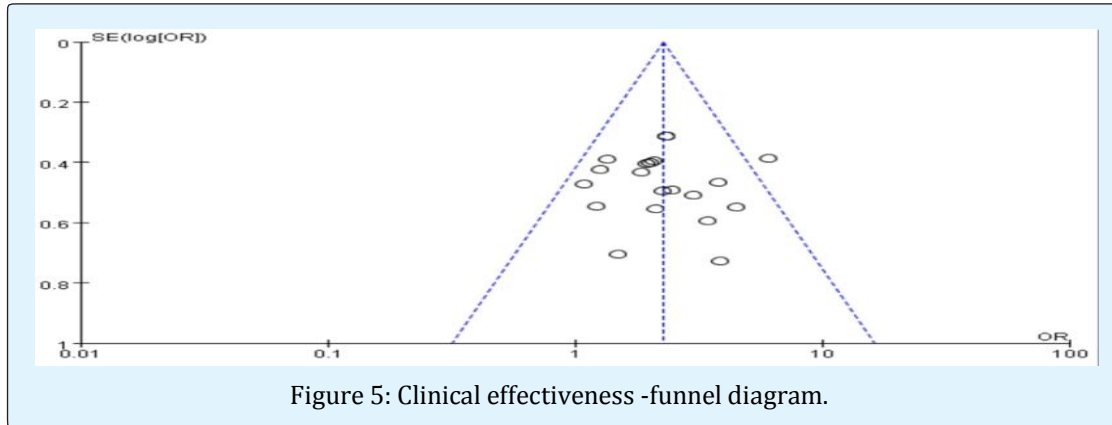


Figure 5: Clinical effectiveness -funnel diagram.

**Clinical Effectiveness –Effectiveness:** According to the “TCM standard of diagnostic effectiveness”, the clinical effectiveness of treating dysfunctional uterine bleeding was defined as the sum of the number of cases cured, markedly improved, and improved.

The heterogeneity test indicated there was no significant

heterogeneity in the pooled studies ( $P=0.86$ ,  $I^2=0\%$ ). A fixed effect model was used for meta-analysis. The effectiveness rate in the treatment group (Chinese medicine) was significantly higher than that in the control group (Western medicine) [OR=3.93, 95% CI (2.99, 5.16),  $P<0.00001$ ] (Figure 6).

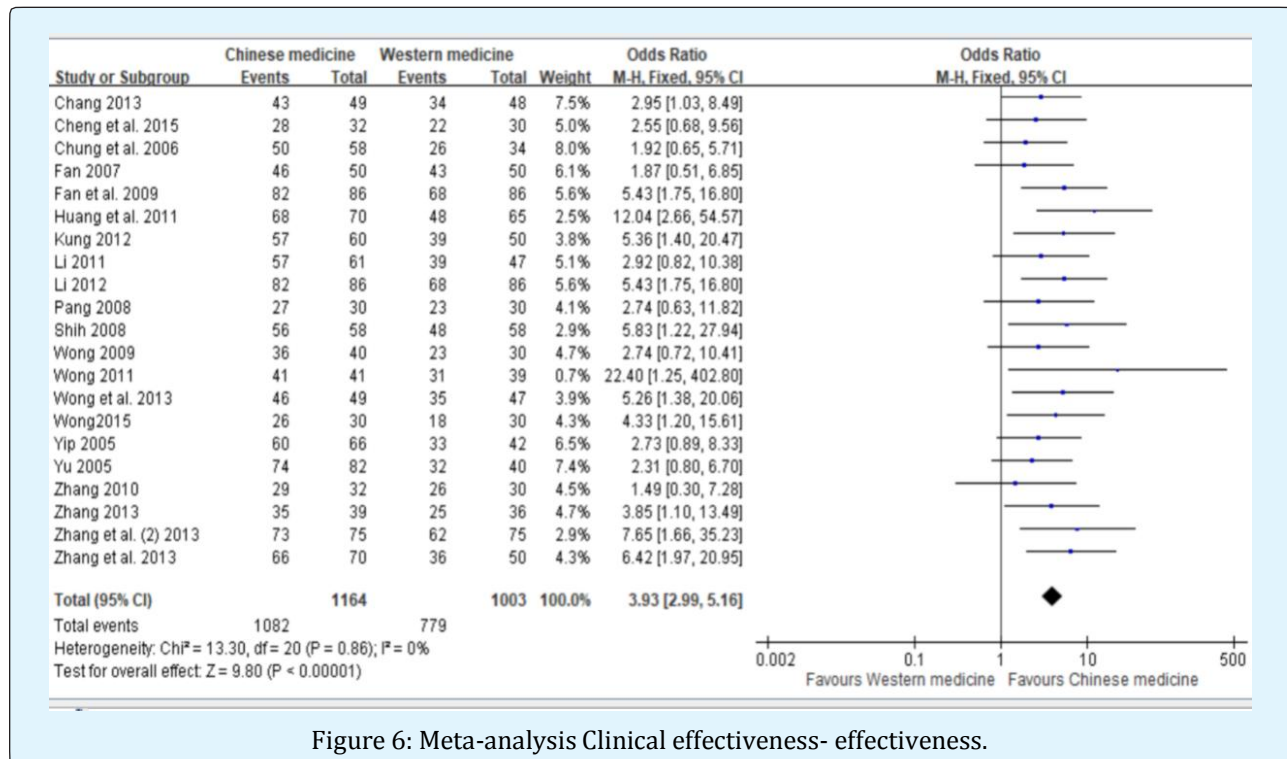


Figure 6: Meta-analysis Clinical effectiveness- effectiveness.

**Hemostasis Effect - Hemostasis Within 3 Days:** As shown in Figure 7, the heterogeneity test indicated there was no significant heterogeneity in the pooled studies ( $P=0.19$ ,  $I^2=37\%$ ). A fixed effect model was used for meta-

analysis. The hemostasis within 3 days in the treatment group (Chinese medicine) was not significantly different in comparison to the control group (Western medicine) [OR=0.90, 95% CI (0.49, 1.63),  $P=0.73$ ] (Figure 7).

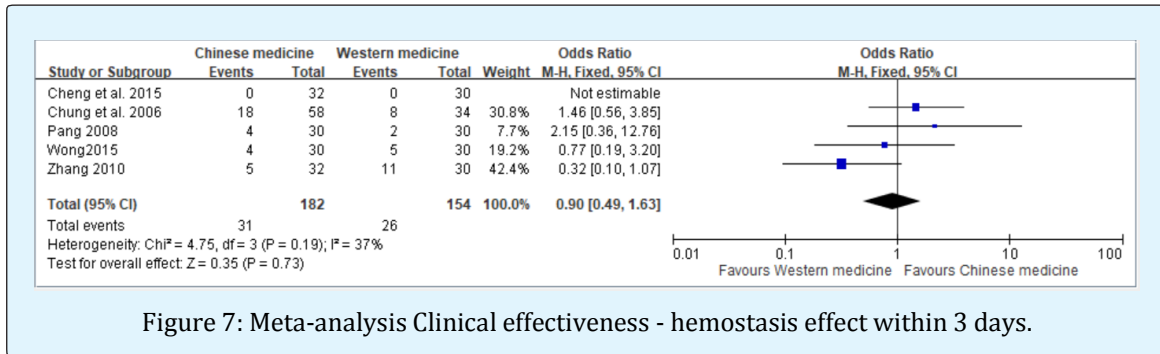


Figure 7: Meta-analysis Clinical effectiveness - hemostasis effect within 3 days.

**Hemostasis Effect- Hemostasis within 10 Days:** As shown in Figure 7, the heterogeneity test indicated there was no significant heterogeneity in the pooled studies ( $P=0.84, I^2=0\%$ ). A fixed effect model was used for meta-analysis. The hemostasis within 10 days in the treatment

group (Chinese medicine) was not significantly different in comparison to the control group (Western medicine) [OR=1.40, 95% CI (0.80, 2.44),  $P=0.24$ ] (Figure 8).

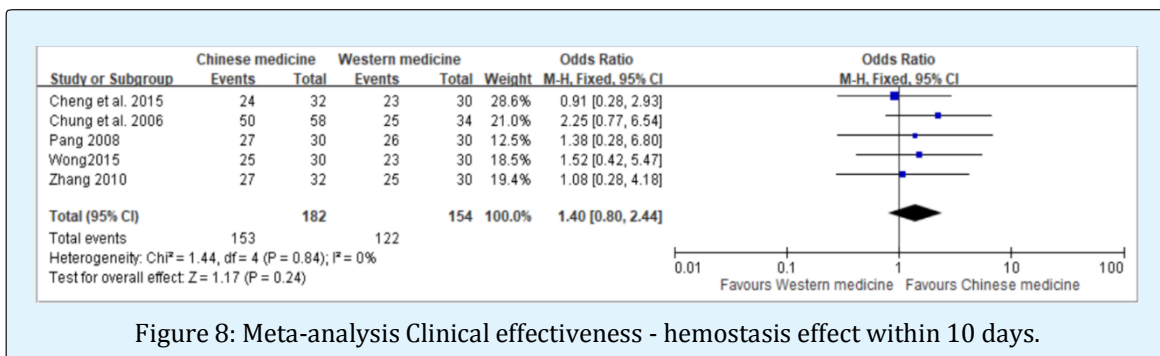


Figure 8: Meta-analysis Clinical effectiveness - hemostasis effect within 10 days.

**Incidence of Side Effects:** Four of 21 studies documented the side effects of treatment. Only 2 studies included liver and kidney function tests before and after treatment. Both of the treatment group and control group did not show abnormal liver and kidney function after treatment.

of side effects in Western medicine group was higher than that in Chinese Medicine group [OR=0.04, 95% CI (0.01, 0.11),  $P<0.0001$ ] (Figure 9). Western medicine treatment was more likely to cause side effects such as gastrointestinal reactions (nausea, vomiting, loose stools), dizziness, allergic reactions and weight gain.

In terms of the incidence of side effects, the heterogeneity test  $P=1.00$  ( $P>0.05$ ),  $I^2=0\%$ . The incidence

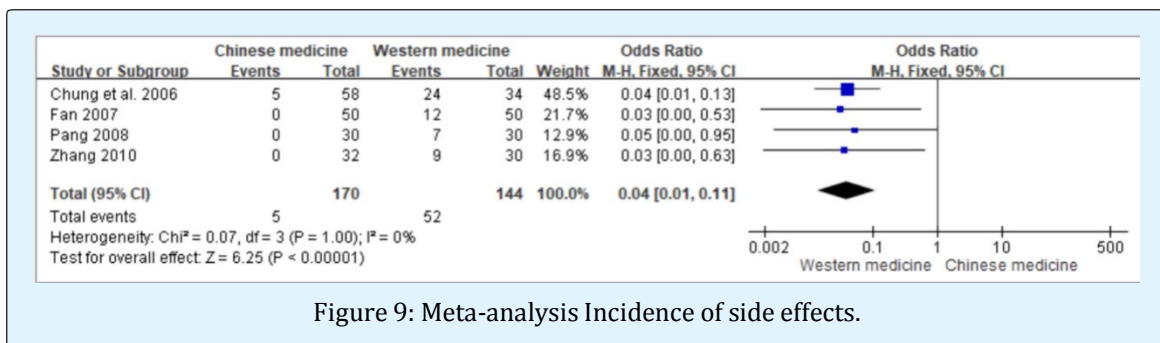


Figure 9: Meta-analysis Incidence of side effects.

**Recurrence Rate:** Two studies documented the recurrence of the patient and re-evaluated the effectiveness 6 months after discontinuation of treatment.]

In terms of recurrence rate, the heterogeneity was not

significant in the pooled studies ( $P=0.90$ ,  $I^2=0\%$ ). Western medicine treatment was more likely to cause recurrence than Chinese medicine treatment [OR=0.16, 95% CI (0.06, 0.47),  $P=0.0008$ ] (Figure 10).

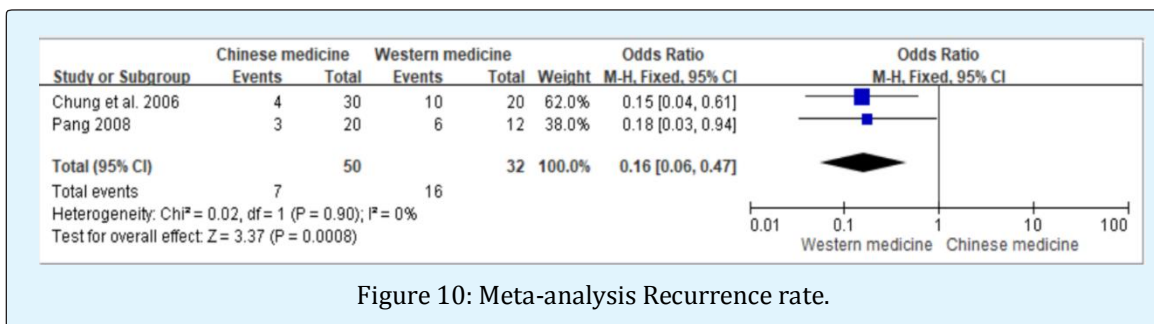


Figure 10: Meta-analysis Recurrence rate.

## Discussion and Conclusion

In this review, there is no significant difference in the effectiveness of hemostasis between traditional Chinese medicine and Western medicine. In terms of correcting the patient's constitutional bias, Chinese medicine has a better overall effect than Western medicine. Chinese medicine also has less side effects than Western medicine. Western medicine caused more gastrointestinal discomfort, dizziness, etc., while the side effects of Chinese medicine are relatively mild and can be easily eased. Moreover, Chinese medicine treatment caused less recurrence than Western medicine.

Chinese medicine appears to have better overall clinical effect in treating dysfunctional uterine bleeding with less side effects and lower chance of recurrence. However, due to low quality of the included studies, the findings should be interpreted with caution. Further large-scale, rigorously designed trials are warranted to confirm the findings.

## References

- Luo (2002) 40 cases of dysfunctional uterine bleeding treated by Xue Jie capsule. *J North China Coal Medical College* 4(5): 613.
- Luo (2014) Necessity of gynecology and gynecology in Traditional Chinese Medicine. Beijing: People's Military Surgeon Publishing House.
- Zhang (2015) Current situation of Chinese Medicine for reinforcing kidney in treating dysfunctional uterine bleeding. *Journal of Hebei TCM and Pharmacology* 30(4): 58-64.
- Chang (2013) Therapeutic effect of QingRe BuQi Fang on 49 cases of dysfunctional uterine bleeding in adolescence. *Asia-Pacific Traditional Medicine* 9(8): 161-162.
- Cheng (2015) Clinical observation on 32 cases of menopausal transitional metrorrhagia treated by Gu Chong Decoction. *Fujian Journal of TCM* 46(3): 4-5.
- Chung (2006) Treatment of 58 cases of adolescent dysfunctional uterine bleeding with Chinese Herbal Medicine. *Liaoning Journal of Traditional Chinese Medicine* 33(3): 327-28.
- Fan (2007) Clinical observation on 50 cases of treatment of metrorrhagia by Gongxue Decoction. *Hunan Journal of Traditional Chinese Medicine* 23(4): 31-33.
- Fan (2009) Clinical observation on treatment of 86 cases of spleen deficiency metrorrhagia with Yiqi Shengyang Zhibeng Decoction. *Journal of Sichuan of Traditional Chinese Medicine* 27(4): 90-91.
- Huang (2011) Clinical observation on treating 70 cases of adolescent dysfunctional uterine bleeding with the Jiaoai decoction. *Clinical Journal of Chinese Medicine* 3(10): 37-38.
- Ip (2005) Treatment of 66 cases of spleen deficiency metrorrhagia with Buzhong Yiqi Decoction. *Journal of New Chinese Medicine* 37(8): 76-77.
- Kung (2012) Therapeutic effect of Ginseng Guipi Decoction on 60 cases of menopausal metrorrhagia. *China Health Care & Nutrition* 10(18): 4127-4128.



12. Li (2011) Clinical observation on 61 cases of adolescent metrorrhagia treated with Tongbu Qijing Method. *Journal of New Chinese Medicine* 43(11): 45-46.
13. Li (2012) Clinical observation on treatment of 86 cases of spleen and kidney deficiency metrorrhagia with Buzhong Yiqi Decoction. *Guangming Journal of Chinese Medicine* 27(12): 2437-2439.
14. Pang (2008) Clinical research of Yichun Decoction in the treatment of spleen and kidney yang deficiency metrorrhagia. Thesis for Hubei University of Chinese Medicine.
15. Sheh (2008) Treatment of 58 cases of adolescent metrorrhagia with Bushen Gu Chong Method. *Modern Journal of Integrated Traditional Chinese and Western Medicine* 17(26): 4117-4118.
16. Wang (2009) Treatment of 40 cases of adolescent metrorrhagia by hemostasis and regulating menstruation cycles. *Journal of Shandong University of Traditional Chinese Medicine* 33(3): 229-230.
17. Wang (2011) Nourishing liver and kidney method for treatment of 41 cases of adolescent anovulatory dysfunctional uterine bleeding. *Chinese Medicine Modern Distance Education of China* 9(13): 137-138.
18. Wang (2013) Clinical observation on treatment of adolescent dysfunctional uterine bleeding with Qingyi Zhibeng Decoction. *Journal of Emergency in Traditional Chinese Medicine* 22(12): 2138.
19. Wang (2015) Clinical observation on the treatment of perimenopausal dysfunctional uterine bleeding by Professor Jin Jiling. *Proceeding of the 15th Academic annual meeting of China National TCM Gynecology Association*. Suzhou, pp: 239-241.
20. Yu (2005) Treating 82 Cases of metrorrhagia with Zhibeng Sailing Decoction. *Journal of Emergency in Traditional Chinese Medicine* 14(3): 273-274.
21. Zhang (2010) Clinical observation of Tiaojing Zhibeng Decoction in treating adolescent dysfunctional uterine bleeding (spleen and kidney yang deficiency type). Thesis for Hubei University of Chinese Medicine.
22. Zhang (2013) Treatment for 39 cases of metrorrhagia and metrostaxis during peri-menopausal period with the method of invigorating spleen, eliminating stasis and strengthening thoroughfare vessels. *Western Journal of Traditional Chinese Medicine* 26(3): 86-87.
23. Zhang (2013) Clinical study on 150 cases of anovulatory dysfunctional uterine bleeding treated by Wenjing Decoction. *China Health Care & Nutrition* 11(23): 6949.
24. Zhang (2013) Clinical observation on 70 cases of qi deficiency treated by Shengxian Decoction. *Hunan Journal of Traditional Chinese Medicine* 29(3): 50-51.

