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Evidence and Potential Mechanisms of Traditional Chinese Medicine for the Treatment of Atopic Dermatitis: A Systematic Review and Meta-Analysis

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Keywords: Atopic Dermatitis, Traditional Chinese Medicine, Randomized Controlled Trials, Meta-Analysis, Pharmacological Mechanism.

Abstract: Atopic dermatitis (AD) is a common chronic inflammatory skin disease with complex clinical mechanisms. This article searched for randomized controlled trials published over the past two decades, and ultimately screened 16 high-quality articles. The results showed that TCM treatment could reduce the SCORAD score. We also analyzed the safety of traditional Chinese medicine in the treatment of AD. However, more rigorous and larger sample evidence is needed to further prove in the future.

1. Introduction

Atopic dermatitis (AD) is a common chronic inflammatory skin disease[1], Traditional Chinese medicine has a long history in the treatment of AD. Compared with traditional western medicine,According to the principle of dialectical treatment, different traditional Chinese medicine schools will adopt different methods for the treatment of atopic dermatitis. Its efficacy has been confirmed in a large number of clinical trials. The treatment of traditional Chinese medicine can relieve the symptoms of atopic dermatitis.

2. Materials and Methods

2.1. Databases Search

This review was stated according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. Computer Search:PubMed Cochrane Library, Embase, CNKI, WanFang, VIP, CBM database, the search time limit is set from January 1, 2000 to February 3, 2021. Search terms include: ("Atopic dermatitis" or "Constitutional prurigo" or "atopic eczema") and ("RCT" or "randomized controlled trial" or "random" or "randomized" or "randomly" or "controlled clinical trial") and ("TCM" or "traditional Chinese medicine" or "formula" or "decoction" or "prescription" or "Chinese herbal compound prescription" or "Chinese herbal medicine" or "Chinese patent medicine" or "Chinese patent drug").

2.2. Inclusion and Exclusion Criteria

(1) Requirements for literature research: Randomized controlled trials involving both the treatment group and the control group have obtained clear evaluation results, and the Jadad score should not be lower than 4. (2) Intervention measures: The experimental group was treated with traditional Chinese medicine or integrated traditional Chinese and western medicine, and the control group was treated with conventional western medicine or traditional Chinese medicine placebo. (3) Subjects: Patients with a clear diagnosis of atopic dermatitis.

2.3. Data Extraction

According to the inclusion and exclusion criteria previously formulated, the extracted contents: first author's name, publication time, sample size of experimental group/control group, course of treatment, control method, intervention measures, course of treatment, evaluation indicators (mainly based on SCORAD score), adverse effects events etc.

2.4. Statistical Methods

Using RevMan5.3 software, select random effect model or fixed effect model according to whether there is heterogeneity in the collected data. When the forest plot results show that $I2>50\%$, $P<0.1$ means that the heterogeneity is large, when $I2<50\ \%$, $P>0.1$, the heterogeneity is considered to be small, and RR (95% CI) is used as the statistic of binary variables, and MD (95%CI) is the statistic of continuous variables. And through the funnel chart analysis to determine whether the research is biased.

3. Results

3.1. Literature Search

A total of 343 papers were retrieved (59 PubMed, 45 Embase and 2 Cochrane Libraries); 111 articles from CNKI, 47 articles from Wanfang, 76 articles from Sinomed, and 3 articles from VIP). The flow chart is presented in appendix figure 1. A total of 1168 patients with atopic dermatitis from 16 clinical trials were included in the study[2-17], 588 in the treatment group and 580 in the control group. All basic characteristics of selected RCTs are presented in Table 1.

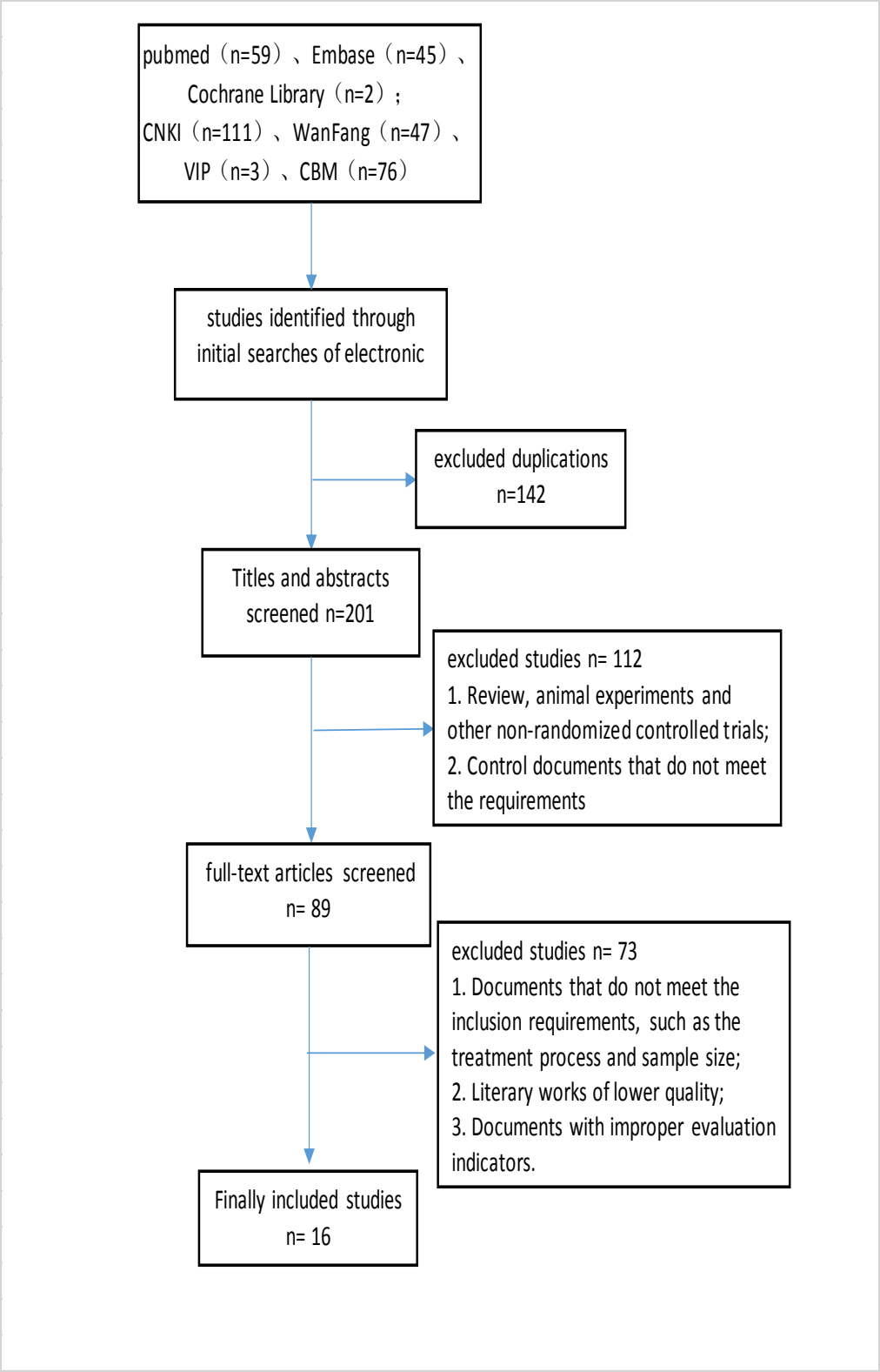

Figure 1. Flow chart

Table 1. Summary of the included studies

Study	Subjects (T/C)	Duration	Intervention	TCM Outcome (SCORAD)	Control	Control Outcome (SCORAD)
Wang 2020	44/44	4w	Jianpi Huashi Decoction+basic treatment	24.83±12.84	Basic treatment	35.16±12.67
Jiang 2019	68/68	4w	Jianpi Jiedu Decoction+basic treatment	19.06±2.85	Basic treatment	26.64±3.86
Tian 2019	22/22	8w	Jianpi Zhuyun Decoction	16.88±11.17	Placebo	31.08±10.54
Yang 2018	30/30	4w	Jianpi Yangxuequfeng Decoction	19.25±5.84	Basic treatment	28.46±8.48
Yao 2018	20/20	12w	Jianpi Qingxin Decoction+basic treatment	15.96±5.54	Basic treatment	21.58±2.82
Dong 2015	47/48	8w	Self-made Jianpi Huashi decoction+basic treatment	33.2±7.4	Basic treatment	39.1±8.6
Zhou 2015	30/30	4w	YuPingFeng particles+basic treatment	21.52±5.89	Basic treatment	26.45±6.28
Yang 2015	45/45	12w	Xiaoyi Zhiyang decoction+ basic treatment	27.2±8.5	Basic treatment	38.5±10.4
Zhang 2014	30/30	4w	Ziyin Chushi decoction	22.93±19.65	Basic treatment	34.87±18.29
Zhou 2014	30/30	4w	Self-made Jianpi Huashi decoction	31.68±13.92	Basic treatment	39.92±13.22
Qin 2012	30/30	8w	Flavored purslane decoction	35.85±11.56	Basic treatment	44.58±10.66
Lang 2012	32/32	8w	Long Mu Soup	19.23±10.22	Basic treatment	19.39±12.40
Mo 2012	58/52	12w	Peitu Qingxin Particles	28.79±17.61	Placebo	23.85±13.78
Zhang 2011	30/26	8w	Self-made Ziyin Qingre Decoction	30.24±9.52	basic treatment	45.67±9.26
Xiao 2010	30/30	4w	Huailian decoction	32.627±9.416	basic treatment	47.581±11.140
K.L.E. 2007	42/43	12w	Self-made Decoction	49.7±15.6	Placebo	46.9±18.1

3.2. Risk of Bias

According to the Jadad scoring table, the quality of the included 16 articles was evaluated from four aspects: Generation of Allocation sequence, Allocation concealment, Double Blinding Double Blinding, Withdrawals(see Table 2), and 3 reports with a final score of 7,one report with a final score of 6,one report with a final score of 5,The remaining studies are all 4 points, 16 studies all use the random number table allocation method, 4 of which are blinded.

Table 2. Jadad score of enrolled RCTs

Study	Generation of Allocation sequence	Allocation concealment	Double Blinding	Withdrawals	Total
Wang2020	2	1	0	1	4
Jiang 2019	2	1	0	1	4
Tian2019	2	2	2	1	7
yang2018	2	1	0	1	4
Yao2018	2	1	0	1	4
Dong 2015	2	1	0	1	4
Zhou2015	2	1	0	1	4
Yang 2015	2	1	0	1	4
Zhang2014	2	1	0	1	4
Zhou2014	2	1	0	1	4
Qin 2012	2	1	0	1	4
Lang2012	2	2	0	1	5
Mo2012	2	2	2	1	7
Zhang2011	2	1	0	1	4
Xiao2010	2	1	2	1	6
K.L.E.2007	2	2	2	1	7

3.3. Efficacy of Treatments

3.3.1. TCM Versus Western Medicine

Among the 16 included studies, a total of 7 literature studies are designed to compare traditional Chinese medicine treatment with western medicine treatment,The course of treatment of 7 randomized controlled trials ranged from 4-12 weeks, the sample size ranged from 60 to 90, and the Jadad scale score ranged from 4 to 6, The Jadad scores of the remaining 5 randomized controlled trials are all 4 points,The intervention measures of the 7 randomized controlled trial treatment groups were all experienced Chinese medicine decoctions. The other 5 RCTs are all in the control group with desloratadine citrate tablets or desloratadine citrate syrup as the main intervention measures.

After analyzing 7 randomized controlled trials, it was found that traditional Chinese medicine was more effective than Western medicine in reducing the SCORAD score (n = 420 RR-9.79; 95% confidence interval-13.71, -5.87; Figure 2).

3.3.2. TCM+ Western Medicine Versus Western Medicine

Among the 16 included studies, there are a total of 6 literature studies designed to compare traditional Chinese medicine combined with Western medicine treatment with pure Western

medicine treatment,The treatment course of the 6 randomized controlled trials was 4-12 weeks, and the sample size ranged from 60 to 136. The Jadad scores of the 6 randomized controlled trials were all 4 points. The intervention of the experimental group except for one of them was the combination of traditional Chinese medicine particles. Except for western medicine, the other 5 RCTs are all empirical Chinese medicine decoction combined with western medicine treatment. The intervention measures of the control group were mainly external hormone ointment or antihistamine treatment.

After analyzing 6 randomized controlled trials, it was found that traditional Chinese medicine combined with western medicine had a more significant effect on reducing the SCORAD score than the western medicine group (n = 509 RR-6.67; 95% confidence interval -8.36, -4.98; Figure 2).

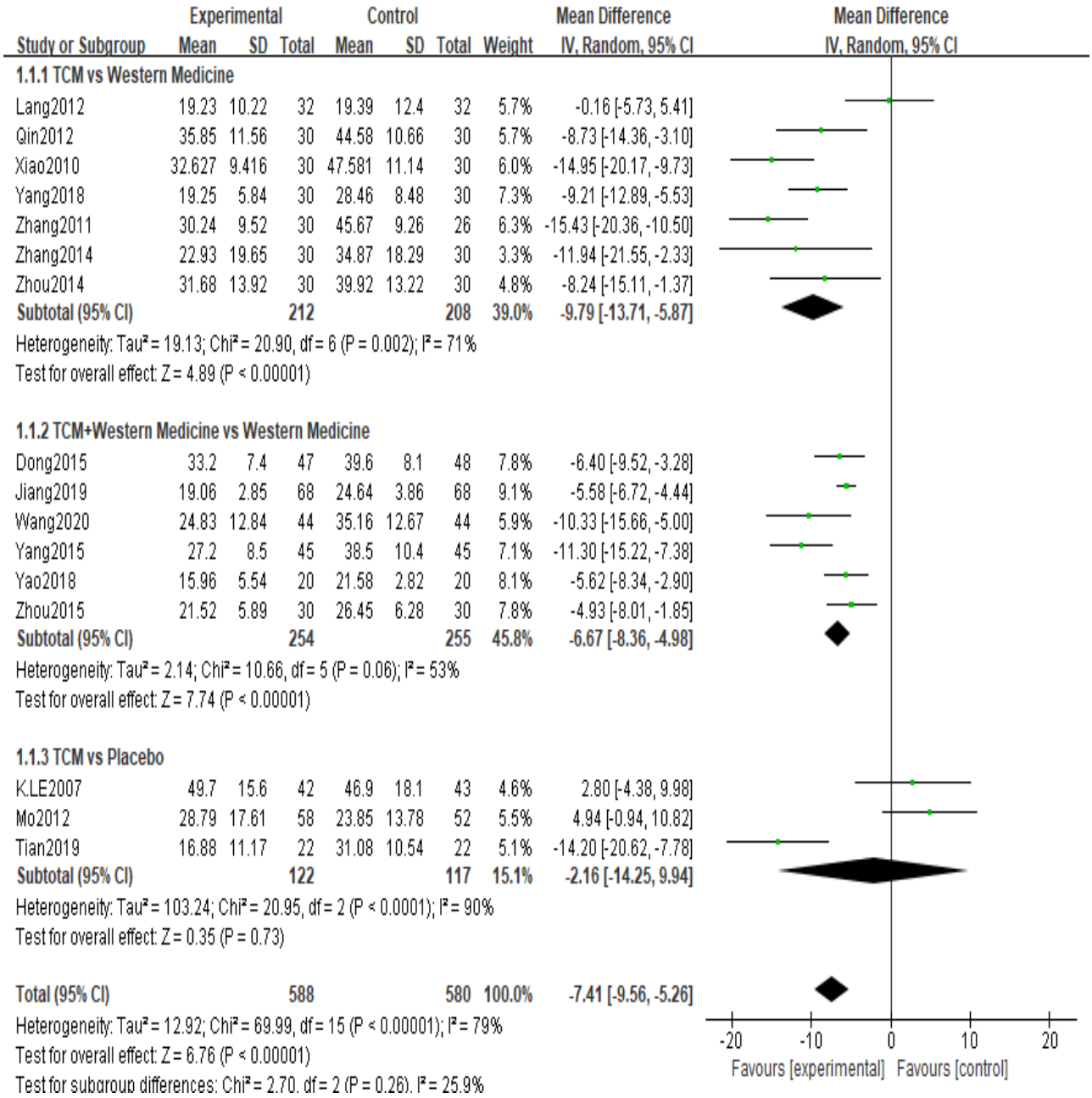

Figure 2. SCORAD score comparison

3.3.3. TCM Versus Placebo

Among the 16 included studies, a total of 3 literature studies are designed to compare traditional Chinese medicine treatment with placebo treatment,The treatment course of the 3 randomized controlled trials ranged from 8 to 12 weeks, the sample size was between 44 and 110, and the Jadad score of the 3 randomized controlled trials was 7 points. The intervention of the experimental group except for one of them was traditional Chinese medicine granules,The other 2 RCTs are all experienced Chinese medicine decoction treatments.The control group was mainly treated with traditional Chinese medicine placebo. After analyzing 3 randomized controlled trials, it was found that traditional Chinese medicine treatment had a more obvious effect on reducing SCORAD score than placebo treatment.

2.4. Safety of Treatments

Table 3. Adverse events

Study	Treatment	Control	Types of AEs (n)	Risk ratio (95% CI)
Jiang 2019	6/68	7/68	Experimental: Headache(2), Gastrointestinal discomfort(1), Elevated blood pressure(3); Control: Stomach discomfort(3), Irregular menstruation(1), Headache(1), Facial acne(2).	0.86 [0.30 2.42]
Tian 2019	0/22	0/22	No obvious adverse events	Not estimable
Yang 2018	0/30	0/30	No obvious adverse events	Not estimable
Yao 2018	0/20	0/20	No obvious adverse events	Not estimable
Dong 2015	0/47	0/48	No obvious adverse events	Not estimable
Zhou 2015	0/30	2/30	Control : Mild lethargy(2)	0.20 [0.01, 4.00]
Zhang 2014	1/30	2/30	Experimental: Diarrhea(1); Control: lethargy(2)	0.50 [0.05, 5.22]
Qin 2012	2/30	3/30	Experimental:Diarrhea(2); Control: lethargy(3)	0.67 [0.12, 3.71]
Lang 2012	0/32	1/32	Not described	0.33 [0.01, 7.89]
Mo 2012	3/58	0/52	Experimental: Diarrhea(3)	6.29 [0.33, 118.93]
Xiao 2010	0/30	3/30	Control: lethargy(3)	0.14 [0.01, 2.65]
K.L.E. 2007	29/42	19/43	Experimental: Upper respiratory tractinfection(8), Diarrhoea (3), Abdominal pain (4), Episodes of asthma(6), New rash(8); Control: Upper respiratory tractinfection(9), Diarrhoea (0), Abdominal pain (2), Episodes of asthma(3), New rash(5)	1.56 [1.06, 2.31]

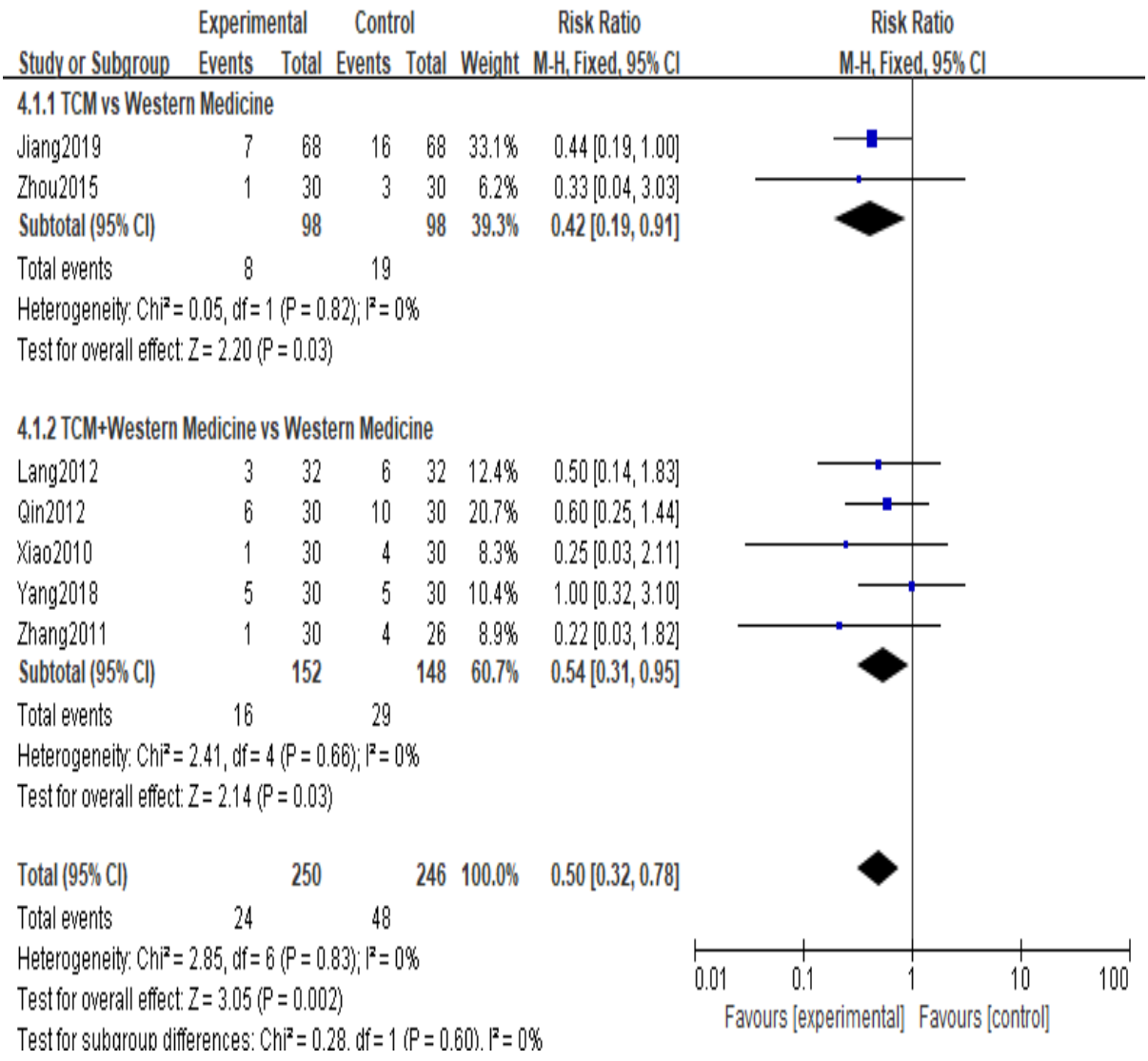

Figure 3. Recurrence rates comparison

A total of 12 of the 16 included randomized controlled trials reported adverse events(see Table 3), 4 of which described the absence of serious adverse events in either the treatment or control groups, and the remaining 8 studies reported specific numbers of adverse events in both groups. The adverse reactions in the treatment group were mainly gastrointestinal reactions, including abdominal pain, diarrhea, and loose stools. In the control group, adverse events were mainly caused by varying degrees of somnolence. The occurrence of adverse events in the two groups is shown in Appendix 3. The results showed that the recurrence rate of AD with traditional Chinese medicine or integrated traditional Chinese and western medicine was lower than that of western medicine, and the difference was statistically significant (p=0.002). See Figure 3.

4. Conclusion

The above analysis shows that traditional Chinese medicine can effectively reduce the SCORAD score and control the further development of the disease. They have a similar mechanism of action compared to Western medicine. However, according to our analysis, Chinese medicine treatment can significantly reduce the SCORAD score compared with Western medicine, and it is safer:

compared with pure Western medicine, Chinese medicine supplemented with Western medicine can also reduce the SCORAD score better, and has a higher safety. higher security. Compared with placebo, the effect of traditional Chinese medicine treatment was more obvious, and there was no significant difference in safety.

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Data Availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

Conflict of Interest

The author states that this article has no conflict of interest.

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