

Xiyanping injection as adjunctive therapy for viral diarrhea in children under 5 years of age: a systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

Introduction Diarrhea is a common and consequential gastrointestinal disorder in children aged <5 years and remains a major global public health concern. Viral pathogens account for most cases of pediatric diarrhea; however, no specific antiviral treatment is available. Xiyanping injection, a traditional Chinese medicine with antiviral and anti-inflammatory properties, has been increasingly adopted in clinical practice. This study aimed to systematically evaluate the efficacy and safety of Xiyanping injection as an adjunct to conventional treatment for viral diarrhea in children aged <5 years. **Methods** A comprehensive search of PubMed, the Cochrane Library, Web of Science, China National Knowledge Infrastructure, Wanfang, Chinese Scientific Journals Database, and SinoMed was conducted from database inception to October 1, 2025 (updated to July 15, 2026), to identify randomized controlled trials (RCTs). Methodological quality was assessed using the Cochrane Risk of Bias tool. Meta-analyses were conducted using R software, and certainty of evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation approach. **Results** Twenty-seven RCTs involving 3721 children were included. Compared with control interventions, adjunctive Xiyanping injection significantly improved the 3-day cure rate (relative risk [RR] = 1.52, 95% confidence interval [CI]: 1.32, 1.75) and 3-day efficacy rate (RR = 1.16, 95% CI: 1.13, 1.19). It also shortened diarrhea duration (mean difference [MD] = -1.54 days, 95% CI: -1.87, -1.20) and hospital stay (MD = -1.60 days, 95% CI: -2.35, -0.844), although substantial heterogeneity was observed. No statistically significant difference in adverse reactions was found between the groups. Sensitivity analyses supported the robustness of the results, with evidence certainty ranging from low to very low. **Conclusion** Xiyanping injection may improve short-term clinical outcomes in children with viral diarrhea. However, overall certainty of evidence is limited, and the available safety evidence remains insufficient. Further high-quality RCTs are needed to confirm its efficacy and safety.

Registration: This study was registered with the International Prospective Register of Systematic Reviews (<https://www.crd.york.ac.uk/prospero/>, CRD420251238691).

KEYWORDS

systematic review, Xiyanping injection, meta-analysis, diarrhea, children, traditional Chinese medicine

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1. Introduction

Diarrhea is a common gastrointestinal disorder in children and is associated with high incidence, transmissibility, and substantial morbidity. It remains a major global public health challenge. Data from the World Health Organization and United Nations International Children's Emergency Fund identify diarrhea as the second leading cause of mortality among children aged <5 years.¹⁻⁴ The etiology of childhood diarrhea is complex and multifactorial, involving noninfectious and infectious factors. Noninfectious diarrhea is often associated with dietary indiscretion, allergies, or adverse drug reactions. Infectious diarrhea is primarily caused by viruses, bacteria, and parasites, with viral pathogens accounting for approximately 75% of cases.⁵ Current management of pediatric diarrhea focuses on symptomatic and supportive care, including oral rehydration salts to prevent dehydration, zinc supplementation to shorten disease duration, and probiotics to modulate the gut microbiota.^{6,7} No specific antiviral therapy is currently available for children with viral diarrhea. Xiyanping injection is widely used in clinical practice

because of its anti-inflammatory, antiviral, and immunomodulatory effects and has been used for conditions such as bronchitis, tonsillitis, and bacterial dysentery.⁸⁻¹⁰ Its primary active component, andrographolide sulfonate, has heat-clearing, detoxifying, anti-inflammatory, and analgesic properties.¹¹ Xiyanping injection exerts antiviral activity through multiple mechanisms, including inhibition of inflammatory mediator release, modulation of immune function, and direct suppression of pathogen replication.¹²⁻¹⁴ Although viral diarrhea is not an approved indication in its labeling, numerous clinical studies have investigated Xiyanping injection for pediatric viral diarrhea, particularly in children aged <5 years, who are disproportionately affected. Therefore, this study aimed to comprehensively evaluate the efficacy and safety of Xiyanping injection for viral diarrhea in children aged <5 years to inform rational clinical use and guide future high-quality research.

2. Methods

We conducted and reported this review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 guidelines.¹⁵

2.1. Literature search

We searched PubMed, the Cochrane Library, Web of Science, China

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National Knowledge Infrastructure, Wanfang, Chinese Scientific Journals Database, and SinoMed for studies evaluating Xiyanping injection for viral diarrhea in children. The search covered all records from database inception to October 1, 2025. An updated literature search was subsequently conducted on July 15, 2026, covering the period from the initial search to June 30, 2026. The Chinese search terms were “Xiyanping,” “andrographolide sulfonate,” and “diarrhea.” The corresponding English free-text terms were “Xiyanping,” “andrographolide sulfonate,” and “diarrhea.” We also used the Medical Subject Headings term “diarrhea” (Appendix 1).

2.2. Inclusion and exclusion criteria

We included randomized controlled trials (RCTs) published in English or Chinese to assess Xiyanping injection for pediatric diarrhea. Studies were included if they met the following criteria:

Participants: Children aged <5 years with a diagnosis of viral diarrhea, as defined in the original trials.

Interventions: Intravenous Xiyanping injection administered alongside conventional treatment, typically including rehydration, nutritional support, and symptomatic management.

Comparators: The control group received conventional treatment alone or conventional treatment combined with a different medication for comparison.

Outcomes: Primary outcomes: Three-day cure rate (complete resolution of diarrhea-related symptoms within 72 h) and 3-day efficacy rate (partial symptom remission within the same period); secondary outcomes: Changes in stool consistency and frequency, duration of diarrhea, hospital stay, and incidence of adverse reactions.

Studies were excluded if complete outcome data were unavailable.

2.3. Literature screening and data extraction

Two researchers (XL and XTW) independently screened the literature and extracted the data. Disagreements were resolved through discussion or, when necessary, adjudication by a third reviewer (JPL). All records were managed using Zotero (version 9.0.6; Corporation for Digital Scholarship, Vienna, VA). After titles and abstracts were screened, irrelevant studies were excluded. The full texts of potentially eligible studies were then assessed against the inclusion criteria, and eligible studies were included. Data from the included studies were extracted and organized in Excel spreadsheets (version 16.109, Microsoft Corporation, Redmond, WA). Extracted study characteristics included the title, first author, publication year, sample size, age, disease duration, inclusion and exclusion criteria, intervention and control measures, outcome measures, and corresponding measurement data.

2.4. Risk of bias assessment

Two independent reviewers (XL and XTW) assessed the risk of bias in all included RCTs using the Cochrane Risk of Bias Tool (RoB 1.0), as described in the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0).¹⁶ The following domains were evaluated: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, completeness of outcome data, selective outcome reporting, and other sources of bias. Each domain was rated as “high risk,” “unclear risk,” or “low risk.” Disagreements between reviewers were resolved through discussion or consultation with a third reviewer (JPL). A risk-of-bias summary plot was generated using R software (version 4.4.2, R Foundation for Statistical Computing, Vienna, Austria) to visualize the results.

2.5. Statistical analysis

Statistical analyses were performed using R software (R Foundation for Statistical Computing), and data from individual studies were pooled. Relative risk (RR) was used as the effect measure for dichotomous variables, and mean difference (MD) was used for continuous variables; both were reported with 95% confidence intervals (CIs).

Heterogeneity among the included studies was evaluated using Cochran’s

Q test and quantified using the I^2 statistic (R Foundation for Statistical Computing). A fixed-effect model was applied when I^2 was $\leq 50\%$, indicating low heterogeneity; otherwise, a random-effects model was used. When substantial heterogeneity was present and sufficient data were available, subgroup analyses based on treatment duration, age, and disease course were conducted to identify potential sources of heterogeneity. Publication bias was assessed using funnel plots for meta-analyses that included >10 studies.

2.6. Sensitivity analysis

To assess the robustness and stability of the pooled estimates, leave-one-out sensitivity analyses were conducted by sequentially removing each study and recalculating the effect sizes. When substantial heterogeneity was observed, alternative effect models (fixed-effect and random-effects) were compared. Consistency across these analyses was examined to determine whether any individual study or analytical decision disproportionately influenced the overall findings.

2.7. Certainty of evidence assessment

The certainty of evidence for each major outcome was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, including evaluation of risk of bias, inconsistency, indirectness, imprecision, and publication bias. In accordance with GRADE guidance, the certainty of evidence was rated as “high,” “moderate,” “low,” or “very low.” A Summary of Findings table was generated to present the effect estimates and certainty ratings for the primary and secondary outcomes.

3. Results

3.1. Literature search results and characteristics of included studies

Overall, 1921 records were initially retrieved from Chinese- and English-language databases. After duplicates were removed, 688 records remained. Screening of titles and abstracts excluded 599 records, and subsequent full-text review excluded another 62 records. Ultimately, 27 RCTs were included, all of which were published in Chinese. The study-selection process is shown in Figure 1.

The 27 included studies involved 3721 children aged 0–5 years with viral diarrhea. All intervention groups received Xiyanping injection in addition to routine care for 3–7 days. Thirteen studies used routine care alone as the control intervention, whereas 14 studies used routine care plus ribavirin injection as the control intervention. Additional details are provided in Table 1.

3.2. Quality assessment of included studies

Seven studies^{19–21,28,29,41,43} used appropriate random number tables for sequence generation, whereas the remaining 20 did not specify the method used. Allocation concealment was unclear in all 27 studies. Only one study²⁶ reported double-blinding; the other 26 provided no information on blinding of participants and personnel. The risk of bias for blinding of outcome assessment was unclear in all studies. Incomplete outcome data were judged to be at low risk of bias in 25 studies and at high risk of bias in two studies.^{25,34} None of the studies provided a sample size justification, although baseline characteristics were comparable between groups. All studies met the predefined inclusion and exclusion criteria, and selective reporting was judged to be at low risk in 24 studies and at high risk in three studies.^{21,26,32} The risk of bias from other sources was judged to be low in 19 studies and high in eight studies.^{19,22,26,28,32,33,35,36} A detailed risk-of-bias assessment is presented in Figure 2 and Appendix 2.

3.3. Therapeutic effect analysis results

3.3.1. Three-day cure rate

A total of 23 studies reported the 3-day cure rate. Of these, 11

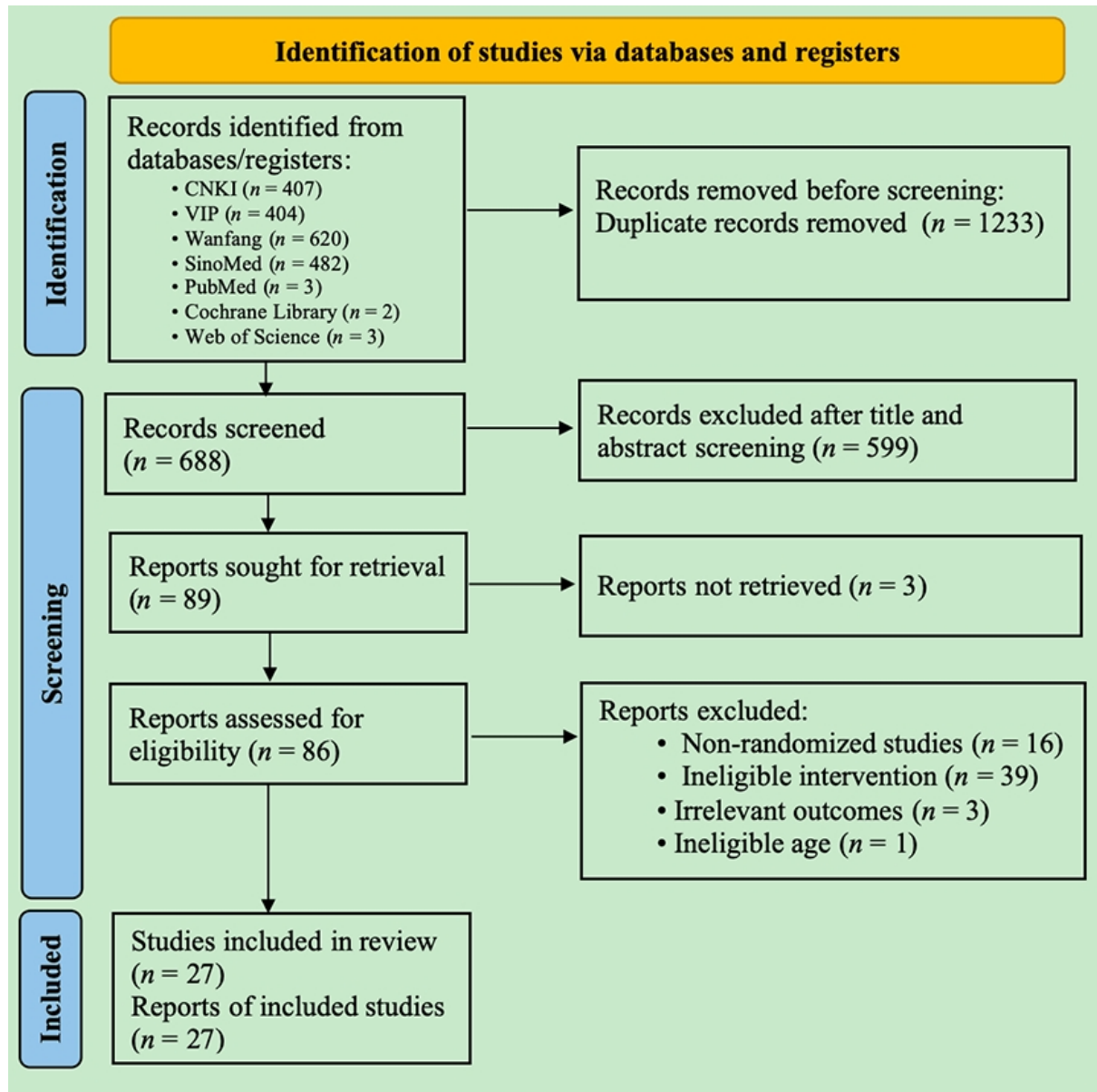


Figure 1 PRISMA flow diagram of study selection

Notes: CNKI: China National Knowledge Infrastructure; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses; VIP: Chinese Scientific Journals Database.

studies^{18,21,24,25,28,29,32,33,35,39,40} compared Xiyanping injection added to conventional treatment with conventional treatment alone. The pooled analysis showed that adjunctive Xiyanping injection increased the 3-day cure rate by 79% (RR = 1.79, 95% CI: 1.40, 2.28, 1467 participants). The remaining 12 studies^{17,19,22,23,27,31,34,36,38,41–43} compared Xiyanping injection plus conventional treatment with conventional treatment plus antiviral therapy. The pooled results indicated that adjunctive Xiyanping injection was associated with a 36% higher 3-day cure rate (RR = 1.36, 95% CI: 1.17, 1.57, 1925 participants). Overall, the random-effects meta-analysis showed that Xiyanping injection as an adjunct to conventional treatment significantly improved the 3-day cure rate by 52% relative to the control interventions (RR = 1.52, 95% CI: 1.32, 1.75). A statistically significant difference was observed between the two comparator subgroups ($P = 0.03$). The corresponding forest plot is presented in Figure 3.

3.3.2. Three-day efficacy rate

A total of 22 studies reported the 3-day efficacy rate. Among these, 10

studies^{18,21,24,25,28,29,32,33,35,40} compared Xiyanping injection combined with conventional treatment with conventional treatment alone. The pooled analysis indicated that adding Xiyanping injection to conventional treatment increased the 3-day efficacy rate by 19% (RR = 1.19, 95% CI: 1.13, 1.25, 1163 participants). In the remaining 12 studies^{17,19,22,23,27,31,34,36,38,41–43}, Xiyanping injection plus conventional treatment was compared with conventional treatment plus antiviral therapy. The pooled estimate showed a 15% improvement in the 3-day efficacy rate (RR = 1.15, 95% CI: 1.11, 1.19, 1925 participants). Overall, adding Xiyanping injection to conventional treatment significantly improved the 3-day efficacy rate by 16% relative to the control interventions (RR = 1.16, 95% CI: 1.13, 1.19). No statistically significant difference was observed between the two comparator subgroups ($P = 0.28$). The corresponding forest plot is presented in Figure 4.

3.3.3. Duration of diarrhea

Seventeen studies reported data on diarrhea duration. Of these, nine studies^{20,21,24,25,30,33,34,36,40} compared Xiyanping injection plus conventional treatment

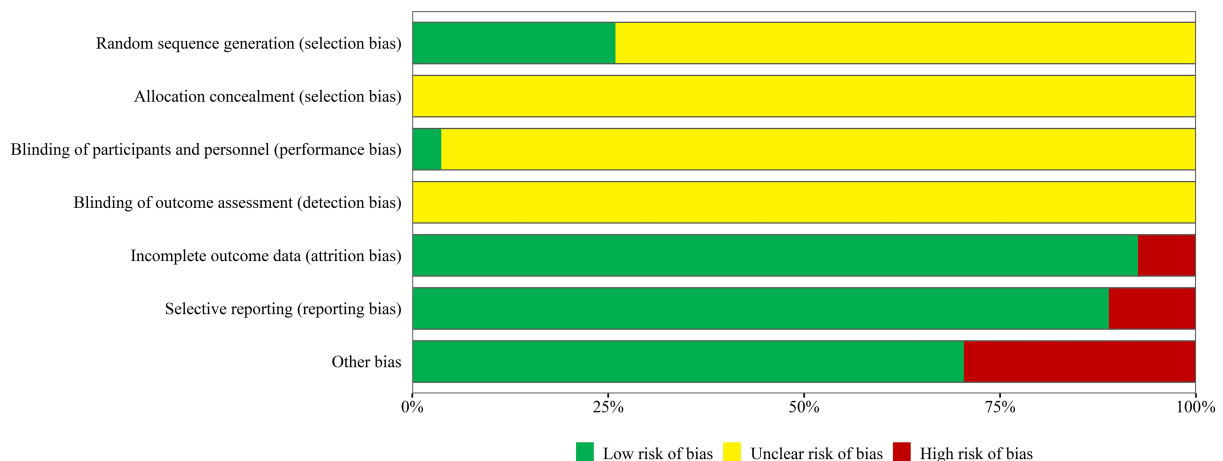
Table 1 Baseline characteristics and interventions of included studies

Study ID	Sample size		Age [†]		Intervention		Course (days)	Outcomes
	Treatment	Control	Treatment	Control	Treatment	Control		
Cao LL 2018 ¹⁷	50	50	3.03 (0.11) y	3.05 (0.14) y	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	5	①②③
Chen DC 2015 ¹⁸	30	30	6–24 m	6–24 m	Routine therapy + Xiyanning injection	Routine therapy	3	①②⑤
Chen GL 2015 ¹⁹	60	60	2–60 m	2–60 m	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	3–5	①②③⑤
Chen YY 2021 ²⁰	53	52	2.25 (0.22) y	2.15 (0.63) y	Routine therapy + Xiyanning injection	Routine therapy	7	①③
Gan LM 2014 ²¹	44	44	21.43 (8.94) m	20.85 (9.06) m	Routine therapy + Xiyanning injection	Routine therapy	3	①②③④⑤
Gu YH 2011 ²²	90	90	4–24 m	4–24 m	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	3	①②
He JY 2012 ²³	116	116	6–36 m	6–36 m	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	6	①②③⑤
Huang C 2009 ²⁴	56	51	4–24 m	4–24 m	Routine therapy + Xiyanning injection	Routine therapy	5–7	①②③
Huang WY 2009 ²⁵	178	148	15.21 (6.89) m	15.64 (7.75) m	Routine therapy + Xiyanning injection	Routine therapy	3	①②③⑤
Jiang YX 2019 ²⁶	30	30	2.55 (0.38) y	2.55 (0.38) y	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	5	①③④⑤
Kang P 2020 ²⁷	45	45	12.0 (3.6) m	11.0 (3.5) m	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	5	①②⑤
Li D 2015 ²⁸	54	54	15.48 (2.11) m	15.65 (2.21) m	Routine therapy + Xiyanning injection	Routine therapy	3	①②
Li W 2018 ²⁹	34	34	2.2 (0.4) y	2.1 (0.6) y	Routine therapy + Xiyanning injection	Routine therapy	5	①②
Liu CX 2015 ³⁰	32	32	15.7 (4.3) m	15.7 (4.3) m	Routine therapy + Xiyanning injection	Routine therapy	5	①②③
Liu M 2016 ³¹	165	165	3.7 (1.1) y	3.5 (1.2) y	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	5	①②③④
Liu SW 2014 ³²	50	50	12.3 (3.6) m	12.3 (3.6) m	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	6	①②③⑤
Luo XL 2013 ³³	40	40	3–42 m	3–42 m	Routine therapy + Xiyanning injection	Routine therapy	3	①②③⑤
Ouyang XR 2018 ³⁴	90	90	1.86 (0.79) y	1.96 (0.75) y	Routine therapy + Xiyanning injection	Routine therapy	3–6	①②③④⑤
Tang FJ 2011 ³⁵	118	95	6–24 m	5–25 m	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	5	①②⑤
Wan YZ 2014 ³⁶	48	48	6–18 m	8–20 m	Routine therapy + Xiyanning injection	Routine therapy	3–5	①②③④⑤
Wang HX 2013 ³⁷	142	100	5–24 m	3–24 m	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	5	①②⑤
Yi JN 2021 ³⁸	29	29	19.24 (5.59) m	20.03 (5.33) m	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	5	①②③④⑤
Zhang B 2012 ³⁹	152	152	2.6 (0.5) y	2.6 (0.5) y	Routine therapy + Xiyanning injection	Routine therapy	5–7	①②⑤
Zhang JY 2016 ⁴⁰	25	25	10.3 (2.9) m	11.2 (1.4) m	Routine therapy + Xiyanning injection	Routine therapy	3	①②③④
Zhang LR 2010 ⁴¹	56	56	15.3 (1.4) m	16.5 (1.7) m	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	3	①②③④⑤
Zhao Q 2015 ⁴²	68	60	1.6 (0.4) y	1.4 (0.3) y	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	5	①②
Zhou YJ 2012 ⁴³	60	60	4–24 m	4–24 m	Routine therapy + Xiyanning injection	Routine therapy + ribavirin	3	①②

Notes: m: month; y: year. [†] Data are presented as mean (standard deviation), or as age range (minimum–maximum). ① efficacy rate; ② cure rate; ③ duration of diarrhea; ④ hospital stay; ⑤ adverse reaction.

with conventional treatment alone, and eight studies^{17,19,23,26,31,32,38,41} compared Xiyanning injection plus conventional treatment with conventional treatment plus antiviral therapy. Across all included studies, adding Xiyanning injection to conventional treatment was consistently associated with a shorter duration of diarrhea than the control interventions. Given the substantial

clinical and statistical heterogeneity, a random-effects model was used. The pooled analysis showed that Xiyanning injection significantly shortened diarrhea duration compared with control treatments (MD = −1.54 days, 95% CI: −1.87, −1.20). Subgroup analyses by comparator type (conventional treatment alone vs. conventional treatment plus antiviral therapy) yielded consis-

**Figure 2** Risk of bias assessment in included studies of Xiyanning injection for pediatric viral diarrhea

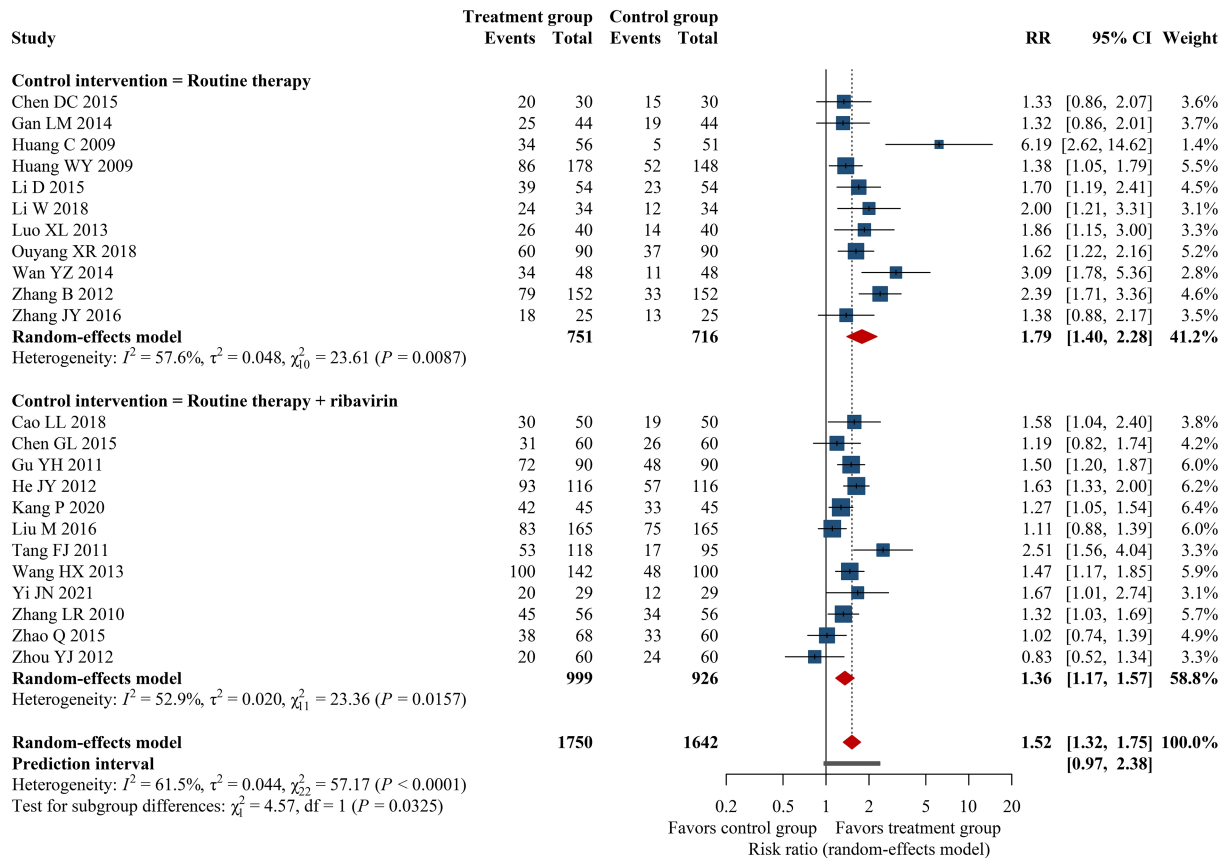


Figure 3 Forest plot of the 3-day cure rate in included studies of Xiyanping injection for pediatric viral diarrhea

Notes: CI: confidence interval; df: degrees of freedom; P: probability; RR: relative risk.

tent results, with no significant differences between subgroups ($P = 0.64$). Nevertheless, considerable heterogeneity persisted across studies ($I^2 = 98.9\%$), and stratification by treatment duration or age did not substantially reduce it. Detailed results are presented in Figure 5.

3.3.4. Changes in stool consistency and frequency

None of the studies reported changes in stool consistency or frequency.

3.3.5. Hospital stay

Eight studies reported hospital length of stay: four studies^{21,34,36,40} compared Xiyanping injection added to conventional treatment with conventional treatment alone, and four studies^{26,31,38,41} compared Xiyanping injection added to conventional treatment with conventional treatment plus antiviral therapy. Across all included studies, adding Xiyanping injection to conventional treatment was associated with a shorter hospital stay than the control interventions. Given the substantial heterogeneity, a random-effects model was used. The pooled analysis showed that Xiyanping injection significantly shortened the hospital stay (MD = -1.60 days, 95% CI: -2.35, -0.84). Subgroup analyses by comparator type yielded consistent findings, with no statistically significant difference between subgroups ($P = 0.37$). Nevertheless, considerable heterogeneity persisted across studies ($I^2 = 97.6\%$), and stratification by treatment duration or age did not meaningfully reduce it. Detailed results are presented in Figure 6.

3.3.6. Incidence of adverse reactions

Fourteen studies reported adverse reactions, accounting for approximately 52% of all included trials. Of these, seven studies^{18,23,34-37,41} reported no adverse reactions, whereas seven studies^{19,21,25,27,33,38,39} specified adverse reactions, including rash or allergic skin reactions, leukopenia, dry mouth,

headache, nausea, vomiting, and abdominal distension. Two studies^{21,39} did not report adverse reactions by group. A meta-analysis of five studies^{19,25,27,33,38} showed no statistically significant difference in the incidence of adverse reactions between the Xiyanping injection and control groups (Figure 7).

3.4. Sensitivity analysis

Sensitivity analyses for the primary outcomes were conducted by sequentially excluding each study (leave-one-out analysis) to assess the robustness of the pooled estimates. The direction and magnitude of the effect sizes remained largely unchanged after any single study was removed, suggesting that the meta-analytic findings were stable. Detailed sensitivity-analysis plots and corresponding numerical results are presented in Appendix 3.

3.5. Publication bias

Publication bias was assessed for the 3-day cure rate because >10 studies were available. Visual inspection of the funnel plot suggested asymmetry. Egger's regression test ($P = 0.036$) and Begg's rank correlation test ($P = 0.025$) showed significant evidence of funnel-plot asymmetry, suggesting possible small-study effects (Figure 8).

3.6. GRADE certainty of evidence assessment

The certainty of evidence for the 3-day efficacy rate was rated as low, mainly because of concerns regarding risk of bias and strongly suspected publication bias. Furthermore, the certainty of evidence for the 3-day cure rate, duration of diarrhea, hospital stay, and adverse events was rated as very low because of serious risk of bias, substantial heterogeneity, or publication bias across studies. A summary of the GRADE assessments for all outcomes is presented in Figure 9.

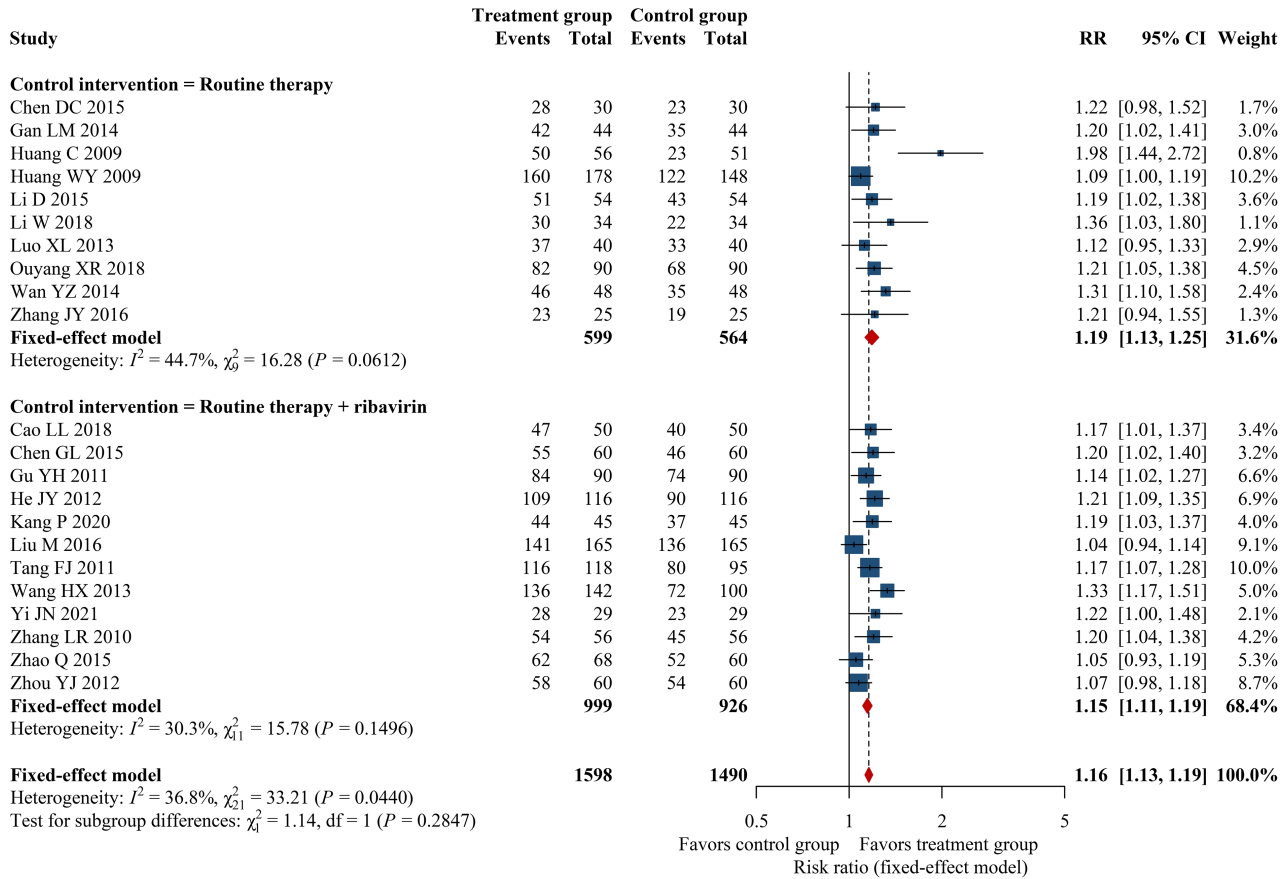


Figure 4 Forest plot of the 3-day efficacy rate in included studies of Xiyanning injection for pediatric viral diarrhea

Notes: CI: confidence interval; df: degrees of freedom; P: probability; RR: relative risk.

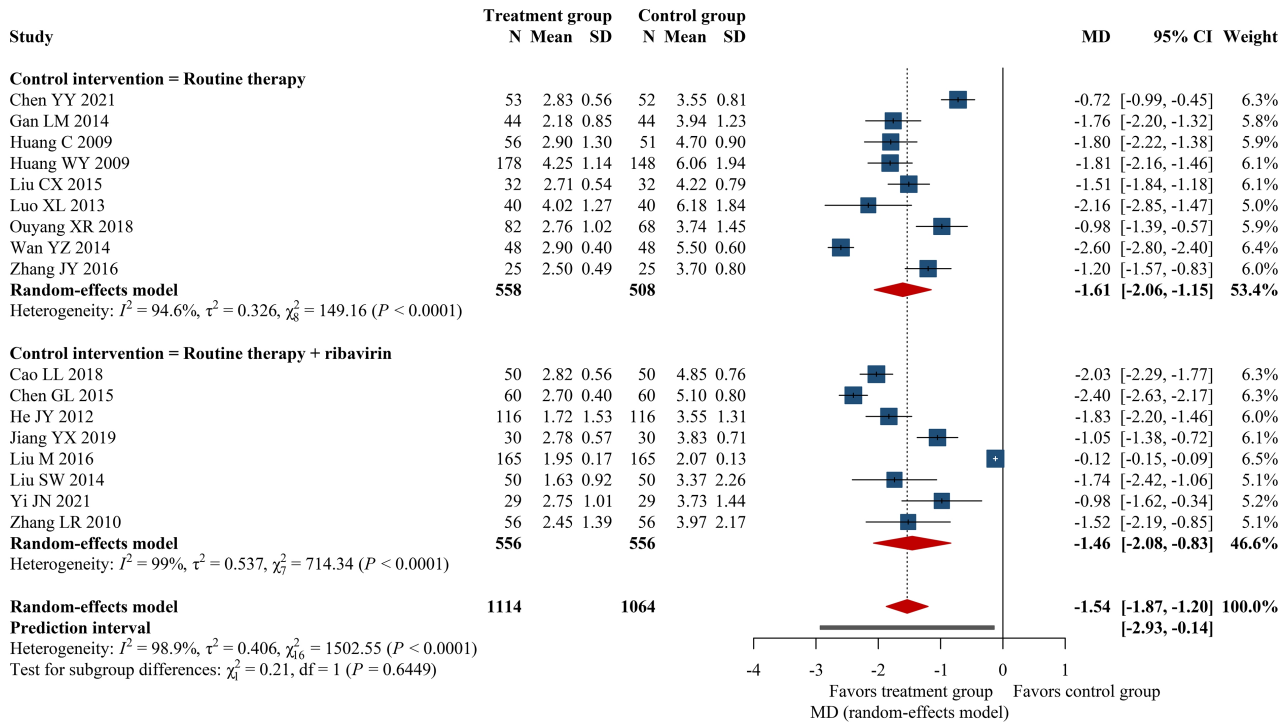


Figure 5 Forest plot of the duration of diarrhea in included studies of Xiyanning injection for pediatric viral diarrhea

Notes: CI: confidence interval; df: degrees of freedom; MD: mean difference; N: number; P: probability; SD: standard deviation.

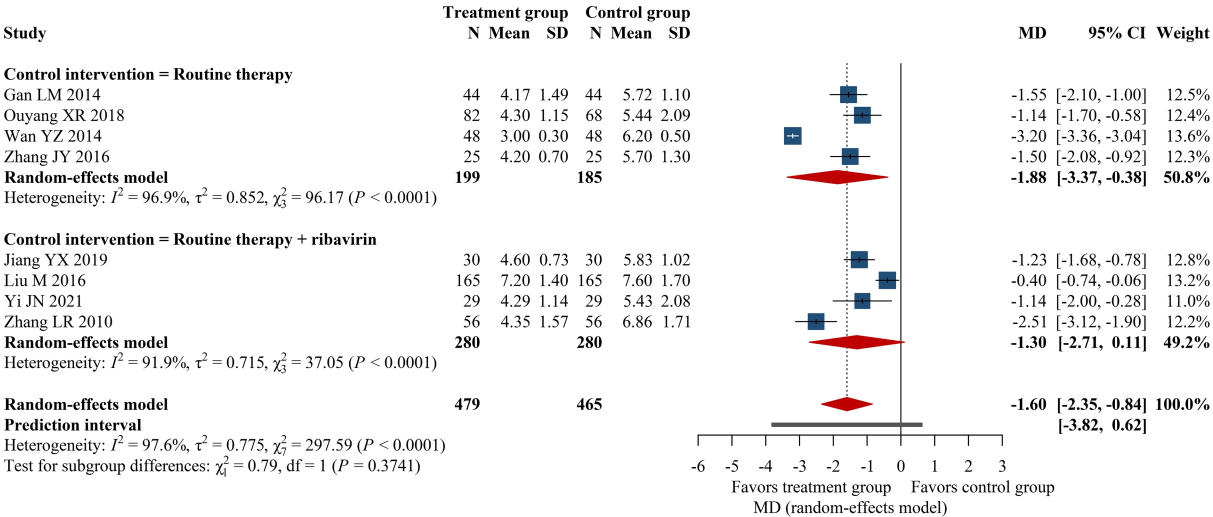


Figure 6 Forest plot of the hospital stay in included studies of Xiyanping injection for pediatric viral diarrhea

Notes: CI: confidence interval; df: degrees of freedom; MD: mean difference; N: number; P: probability; SD: standard deviation.

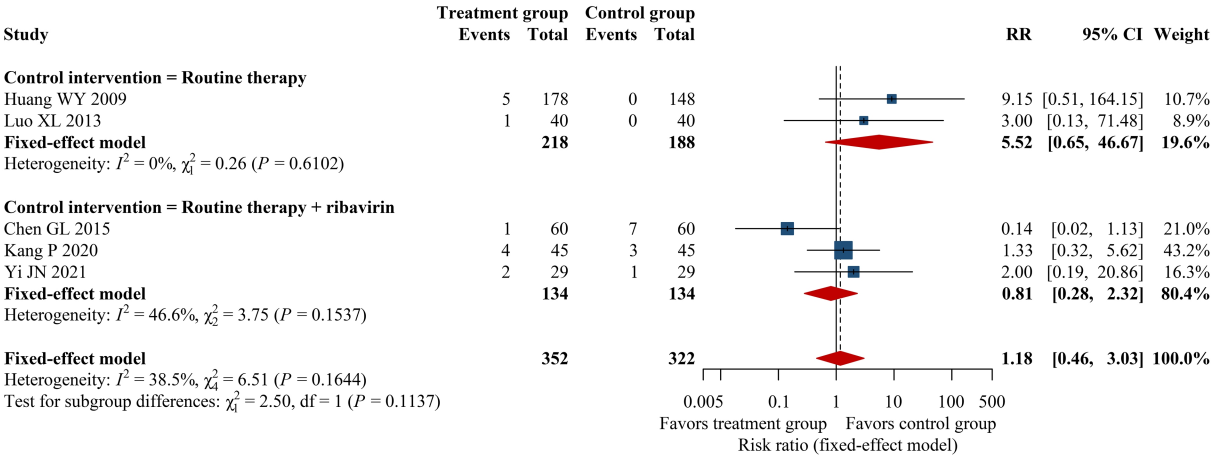


Figure 7 Forest plot of adverse events in included studies of Xiyanping injection for pediatric viral diarrhea

Notes: CI: confidence interval; df: degrees of freedom; P: probability; RR: relative risk.

4. Discussion

4.1. Summary of main findings

This systematic review and meta-analysis included 27 RCTs comparing Xiyanping injection added to conventional treatment with either conventional treatment alone or conventional treatment plus ribavirin in children with viral diarrhea. The 3-day cure and efficacy rates were selected as the primary outcomes for assessing short-term clinical effectiveness.

Compared with conventional treatment alone, Xiyanping injection significantly improved the 3-day cure and efficacy rates. Similar improvements were observed when Xiyanping injection was compared with conventional treatment plus ribavirin, indicating consistent short-term benefits across different comparator regimens. However, the magnitude of improvement in the 3-day cure rate differed significantly between the two comparator subgroups. For the secondary outcomes, Xiyanping injection was associated with a shorter diarrhea duration and shorter hospital stay, although substantial heterogeneity was observed across studies despite the use of random-effects models.

Regarding safety, the incidence of adverse reactions did not significantly differ between the Xiyanping injection and control groups. However, adverse events were reported in 14 studies, accounting for approximately 52% of the

included studies, and only five studies contributed to the quantitative synthesis. Therefore, the available evidence regarding the safety of Xiyanping injection remains limited, and the findings should be interpreted with caution.

Overall, although the pooled results suggest that adjunctive Xiyanping injection improves short-term clinical outcomes in children with viral diarrhea, the certainty of evidence ranged from low to very low according to the GRADE assessment. Significant funnel-plot asymmetry was also detected for the 3-day cure rate, suggesting possible small-study effects. Accordingly, the findings should be interpreted with caution and confirmed in high-quality, rigorously conducted RCTs.

4.2. Biological plausibility and pharmacological mechanisms

The mechanisms whereby Xiyanping injection exerts therapeutic benefits in pediatric viral diarrhea are multifactorial.⁴⁴ Xiyanping injection directly inactivates viruses and inhibits viral replication. It also enhances immune cell function, modulates immune homeostasis, and strengthens host immunity. Additionally, its anti-inflammatory effects reduce the release of inflammatory mediators and protect the intestinal mucosa. Furthermore, Xiyanping injection helps restore intestinal function and maintain gut microbiota home-

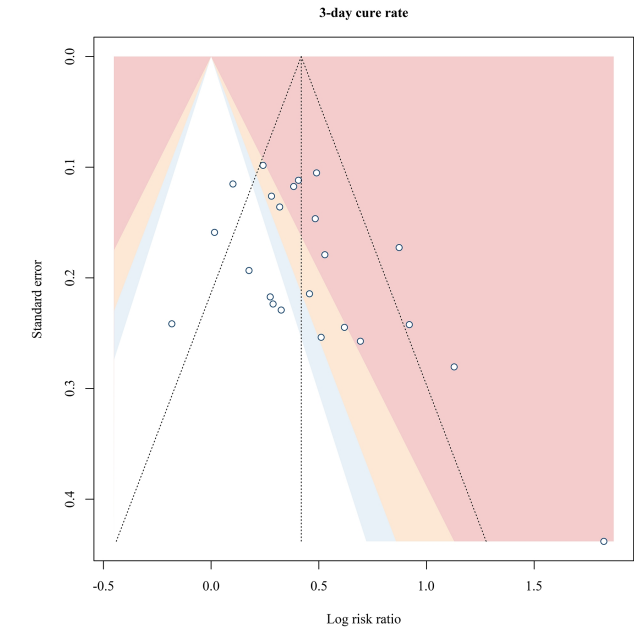


Figure 8 Funnel plot assessing publication bias for the 3-day cure rate in included studies of Xiyanping injection for pediatric viral diarrhea

ostasis, thereby alleviating symptoms of viral diarrhea.⁴⁵⁻⁴⁹

4.3. Comparison with previous research and added value

Previous systematic reviews and meta-analyses of Xiyanping injection and andrographolide derivatives have reported potential therapeutic benefits in infectious and inflammatory diseases, including gastrointestinal infections.^{12,50,51} However, these reviews were published several years ago and included a limited number of trials, whereas a more recent network meta-analysis evaluated Xiyanping injection alongside several other Chinese herbal injections rather than focusing exclusively on Xiyanping injection.⁵¹ Moreover, few previous reviews used a structured framework to assess the certainty of evidence.

This study advances the existing literature in several important respects. First, it focuses exclusively on pediatric viral diarrhea, a common but clinically distinct condition characterized by age-specific immune responses, rapid disease progression, and a strong need for timely symptom control. Second, by incorporating the largest number of RCTs to date in this population, this meta-analysis provides more precise pooled estimates for key clinical outcomes. Third, the use of the GRADE framework together with a Summary of Findings table enables transparent assessment of the certainty of evidence and allows clinicians and policymakers to interpret the findings more appropriately.

In addition, this study improves methodological consistency by standardizing the definitions and assessment time points of the primary outcomes, specifically the 3-day cure and efficacy rates, which have been inconsistently reported in previous trials. Beyond overall effectiveness, this review comprehensively synthesizes clinically relevant outcomes, including duration of diarrhea, hospital stay, and adverse reactions, providing a more balanced assessment of efficacy and safety.

Current international evidence-based guidelines for pediatric acute viral gastroenteritis recommend supportive care, including oral rehydration therapy, continued feeding, and appropriate nutritional management, as the cornerstone of treatment; routine antiviral therapy is generally not recommended.⁶ In this context, our findings suggest that Xiyanping injection provides additional short-term clinical benefits when used as an adjunct to conventional treatment. However, because the certainty of evidence ranged from low to very low, these findings are insufficient to support changes to current guideline recommendations. Well-designed, multicenter RCTs are still needed before Xiyanping injection can be recommended for routine clinical practice.

Overall, by focusing on a clearly defined pediatric population, applying rigorous evidence-synthesis methods, and comprehensively evaluating efficacy and safety outcomes, this review provides an updated and more clinically informative summary of the available evidence and may help guide future research in this field.

4.4. Limitations

This study has several limitations that should be considered when interpreting the findings. First, substantial statistical heterogeneity was observed for several outcomes. Although subgroup analyses based on age and disease duration were performed, these analyses did not meaningfully reduce hetero-

Certainty assessment						No. of patients		Effect		Certainty
Outcome / No. of studies	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Treatment	Control	Relative effect (95% CI)	Absolute effect (95% CI)	
3-day cure rate										
23 RCTs	Serious ^a	Serious ^b	Not serious	Not serious	Strongly suspected ^d	1750	1642	RR 1.52 (1.32, 1.75)	209 more per 1000 (129 more, 300 more)	●○○○ Very low
3-day efficacy rate										
22 RCTs	Serious ^a	Not serious	Not serious	Not serious	Strongly suspected ^d	1598	1490	RR 1.16 (1.13, 1.19)	124 more per 1000 (99 more, 151 more)	●●○○ Low
Duration of diarrhea										
17 RCTs	Serious ^a	Very serious ^b	Not serious	Not serious	Strongly suspected ^d	1114	1064	MD −1.54 d (−1.87, −1.20)	1.54 d lower (1.87 lower, 1.20 lower)	●○○○ Very low
Hospital stay										
8 RCTs	Serious ^a	Very serious ^b	Not serious	Not serious	Undetected / not assessed ^e	479	465	MD −1.60 d (−2.35, −0.84)	1.60 d lower (2.35 lower, 0.84 lower)	●○○○ Very low
Adverse reactions										
5 RCTs	Serious ^a	Not serious	Not serious	Very serious ^c	Undetected / not assessed ^e	352	322	RR 1.18 (0.46, 3.03)	6 more per 1000 (19 fewer, 69 more)	●○○○ Very low

Figure 9 Summary of Findings for all outcomes based on the GRADE assessment in included studies of Xiyanping injection for pediatric viral diarrhea

Notes: CI: confidence interval; d: day; MD: mean difference; No.: number; RCTs: randomized controlled trials; RR: relative risk. ^a: Lack of reporting for blinding use on patients, health-care providers, data collectors, outcome assessors, and data analysts; inadequate reporting for allocation concealment. ^b: Larger I square. ^c: Wider CI, which may result in different clinical decisions. ^d: Funnel plot asymmetry was observed. ^e: Only a few number of studies were included.

geneity. The residual heterogeneity may be attributable to differences in conventional treatments, Xiyanping injection dosage and treatment duration, disease severity, and the viral pathogens responsible for gastroenteritis, all of which were inconsistently reported across the included studies and therefore could not be explored further. Second, the overall methodological quality of the included trials was generally low. Many studies provided insufficient information on random sequence generation, allocation concealment, and blinding, increasing the risk of selection and performance bias. According to the GRADE assessment, the certainty of evidence ranged from low to very low for all outcomes, indicating that further well-designed studies are likely to influence the current effect estimates. Third, although no statistically significant difference in adverse events was observed between groups, approximately half of the included studies reported safety-related information, and only five studies contributed to the meta-analysis of adverse events. Therefore, the current evidence remains insufficient to draw firm conclusions about the safety profile of Xiyanping injection. Finally, all included studies were conducted in China and published in Chinese, which limits the generalizability of the results to other healthcare settings and populations and may increase the potential for publication and language bias. Therefore, the present findings should be interpreted with caution.

4.5. Recommendations for future research

Based on the findings and methodological limitations of this study, several recommendations for future research emerge. First, future clinical trials should use guideline-recommended therapies as the standard comparator to ensure that control interventions reflect current best practice and strengthen external validity. Second, researchers should use standardized, clearly defined efficacy assessment criteria, including uniform outcome definitions and assessment time points, to reduce clinical heterogeneity and improve comparability across individual studies and future meta-analyses. Third, future studies should offer detailed information on viral etiology, disease severity, Xiyanping injection dosage, treatment duration, and concomitant therapies to facilitate more comprehensive subgroup analyses and exploration of potential sources of heterogeneity. Finally, future trials should be designed, conducted, and reported in adherence to internationally recognized methodological standards, such as the Standard Protocol Items: Recommendations for Interventional Trials and the Consolidated Standards of Reporting Trials, to improve methodological rigor, transparency, and reproducibility.

5. Conclusion

This systematic review and meta-analysis suggests that the addition of Xiyanping injection to conventional treatment improves short-term clinical outcomes in children with viral diarrhea. However, the certainty of evidence ranged from low to very low because of methodological limitations and clinical heterogeneity among the included studies. Although no significant difference in adverse events was observed, the available safety evidence remains limited because safety outcomes were infrequently reported. Therefore, the current evidence is insufficient to support the routine clinical use of Xiyanping injection, and further well-designed, adequately powered, multicenter RCTs are needed to confirm its efficacy and safety.

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Data Availability

Additional data related to this paper may be obtained from the corresponding author upon reasonable request.

Author Contribution Statement

Xia Li: Data curation, methodology, formal analysis, software, investigation, visualization, project administration, writing – original draft, and writing – review & editing. **Xiao-ti Wu:** Data curation, formal analysis, investigation, and writing – original draft. **Heng Yin:** Investigation, visualization, software, and writing – review & editing. **Jing-ling Zuo:** Formal analysis, investigation, and writing – review & editing. **Guo-yan Yang:** Methodology and writing – review & editing. **Jian-ping Liu:** Conceptualization, methodology, funding acquisition, supervision, validation, and writing – review & editing.

Use of AI Statement

None.

Declaration of Competing Interest

The authors declare that this research was conducted without any commercial or financial relationships that could be perceived as a potential conflict of interest. Prof. Jian-ping Liu, who serves as Co-Editor-in-Chief of *Evidence-Based Chinese Medicine and Technology Assessment*, was not involved in the review process or the final decision-making on this paper.

Electronic Supplementary Material

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