Hepat Mon. Jan-Dec 2026; 26(1): e171178 https://doi.org/10.5812/hepatmon-171178

Published Online: 2026 June 22 **Systematic Review**

Efficacy and Safety of *Xiaochaihu decoction* in the Treatment of Chronic Hepatitis B: A Systematic Review and Meta-Analysis

Tongyang Jia [1], Kun Jiao [2], Zixuan Gao [1], Tao Zhang [1,*], Ling Xu [2,**]

[1] Tianjin University of Traditional Chinese Medicine, Tianjin, China
[2] Beijing University of Chinese Medicine Dongfang College, Cangzhou, China

[*] ***Corresponding Author:*** Tianjin University of Traditional Chinese Medicine, Tianjin, China. Email: zhangtaotcm@163.com
[**] ***Corresponding Author:*** Beijing University of Chinese Medicine Dongfang College, Cangzhou, China. Email: xiaoxing1998@126.com

Received: 1 April, 2026; **Revised:** 23 April, 2026; **Accepted:** 29 April, 2026

Abstract

Background: Chronic hepatitis B (CHB) remains a major cause of cirrhosis and hepatocellular carcinoma. *Xiaochaihu decoction* (XCHD) is frequently used in China as an adjunct to Western medicine (WM), but its incremental benefit remains uncertain. This review evaluated the efficacy and safety of XCHD added to WM in patients with CHB.

Methods: Eight databases were searched from inception to October 5, 2025, for randomized controlled trials comparing XCHD + WM with the same background WM alone. Full search strategies are provided in Supplementary Material A. Primary outcomes were virological response (HBV-DNA, HBeAg, and HBsAg negativity) and liver biochemical indices (ALT and AST). Secondary outcomes included total clinical efficacy, TBil, HA, LN, PCIII, IV-C, and adverse events. Risk of bias was assessed with RoB 2, certainty of evidence was assessed with GRADE, and trial sequential analysis (TSA) was used as a supplementary assessment of random error.

Results: Forty-nine trials (n = 4,768) were included. Compared with WM alone, XCHD + WM was associated with higher HBV-DNA, HBeAg, and HBsAg negativity rates and lower ALT, AST, TBil, HA, LN, PCIII, and IV-C values. Total clinical efficacy was higher, and the reported incidence of adverse events was not increased. However, most continuous outcomes showed substantial heterogeneity, several outcomes were affected by suspected publication bias, and certainty was low or very low for most biochemical and fibrosis-related outcomes.

Discussion: Current evidence suggests that XCHD may offer short-term adjunctive benefits for surrogate virological and biochemical outcomes when added to WM for CHB, without an apparent increase in reported adverse events. While these preliminary findings are promising, due to methodological limitations and heterogeneity, future large-scale and high-quality RCTs are warranted to confirm their long-term clinical benefits and establish definitive evidence.

Keywords: *Xiaochaihu decoction*, Chronic Hepatitis B, Systematic Review, Meta-Analysis, Randomized Controlled Trials

1. Introduction

Chronic hepatitis B (CHB) is a persistent hepatitis B virus infection characterized by the presence of hepatitis B surface antigen (HBsAg) for at least six months and encompasses a clinical spectrum ranging from inactive chronic infection and immune-active hepatitis to cirrhosis and hepatocellular carcinoma (1). Recent global modelling based on the 2022 WHO hepatitis report estimates that approximately 254 million people are living with HBV infection and CHB-related cirrhosis and hepatocellular carcinoma remain major causes of liver-related mortality despite expanded vaccination coverage and antiviral treatment programs (2). The burden is heaviest in the Western Pacific and African regions, where East and Southeast Asia contribute substantially to the global caseload due to historically high endemicity and predominant perinatal or early-childhood transmission. In China alone, tens of millions of adults remain chronically infected even as prevalence falls in younger cohorts (3). However, the global cascade of care remains weak: By 2022 only about 13% of people with chronic HBV had been diagnosed and fewer than 3% were receiving antiviral treatment —

How to Cite: Jia T, Jiao K, Gao Z, Zhang T, Xu L. Efficacy and Safety of Xiaochaihu decoction in the Treatment of Chronic Hepatitis B: A Systematic Review and Meta-Analysis. Hepat Mon. 2026;26(1):e171178. doi: https://doi.org/10.5812/hepatmon-171178

figures far below elimination targets and with particularly large gaps in Asia (4). Current CHB management still relies primarily on long-term nucleos(t)ide analogues, with or without pegylated interferon. These therapies effectively suppress HBV DNA replication and reduce the risks of decompensation and hepatocellular carcinoma, but they rarely achieve functional cure, often require lifelong administration, do not fully correct HBV-induced immune dysregulation, and leave a residual risk of progressive liver disease (5). These limitations underscore the need for adjunctive approaches that can act on complementary pathogenic pathways while remaining safe and practical in high-burden Asian settings.

Against this backdrop, traditional Chinese medicine has gained renewed attention as a potential adjunct to standard antiviral therapy for CHB. Recent reviews suggested that Chinese herbal formulas can exert multi-target anti-HBV, immunomodulatory, anti-inflammatory, and antifibrotic effects, and may enhance virological and biochemical responses when combined with nucleos(t)ide analogues, while generally maintaining acceptable safety (6). *Xiaochaihu decoction* (XCHD), a classic multi-herb formula originating from Shang Han Lun, is widely used across East Asia for chronic viral hepatitis, fatty liver disease and cirrhosis, and is traditionally regarded as a "pivot" prescription for disorders with fluctuating hepatic-biliary symptoms.

Modern pharmacology and network pharmacology analyses suggest that XCHD can attenuate hepatic inflammatory signalling, modulate bile acid and lipid metabolism, and interfere with hepatic stellate cell activation and extracellular matrix deposition, thereby alleviating fibrosis and improving hepatocellular function in experimental models (7). Clinically, contemporary evidence syntheses suggest that herbal formulas containing XCHD may improve alanine aminotransferase (ALT) normalization, reduce fibrosis-related biomarkers, and alleviate symptom burden when added to standard antivirals or hepatoprotective therapies, without a clear increase in adverse events (6). Combined with accumulating randomized trial data comparing XCHD plus Western medicine (WM) versus WM alone, these findings suggest that XCHD may serve as a valuable adjunct to existing CHB therapies, with potential benefits in improving liver biochemical profiles and patient-reported symptoms; therefore, it warrants rigorous quantitative evaluation. Moreover, numerous clinical trials of XCHD in CHB have been published. However, the methodological quality and combined effects of these clinical trials have not yet been systematically evaluated. Only a limited number of systematic reviews—mostly older and methodologically limited — have evaluated XCHD for CHB. Recently, the Rome consensus on good clinical trials for traditional medicine emphasized clear clinical questions, rigorous design, and clinically meaningful endpoints in traditional medicine research (8).

We performed an updated systematic review and meta-analysis of randomized trials evaluating XCHD as an adjunct to WM for CHB, aiming to estimate short-term adjunctive effects on virological, biochemical, fibrosis-related, and safety outcomes while explicitly appraising risk of bias, certainty of evidence, and the implications of between-trial heterogeneity.

2. Methods

The protocol for this systematic review was registered in PROSPERO (CRD420251147917) and the review was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement (9).

2.1. Ethical Statement

Ethics committee approval and written informed consent were not required for this study, as it included only previously published randomized clinical trials with prior ethics approval and informed consent.

2.2. Eligibility Criteria

Inclusion criteria were prespecified as follows: (1) Study design: Randomized controlled trials; quasi-randomized or non-randomized studies were excluded. (2) Participants: Patients diagnosed with chronic hepatitis B; trials enrolling CHB populations with fibrosis or cirrhosis remained eligible when CHB was the underlying disease of interest. Diagnostic terminology and operational criteria are summarized in Supplementary Material A1. (3) Intervention and control: Within each trial, both groups had to receive the same background WM, and the intervention arm additionally received XCHD. Background WM could include nucleos(t)ide analogues, interferon-based regimens, immunomodulators, and/or hepatoprotective therapies used in routine CHB care. Eligible XCHD interventions had to retain the core classical prescription; modified formulations were permitted only when they were explicitly described as XCHD-based formulas. Details of formulation consistency and outcome definitions are provided in Supplementary Material A2. (4) Outcomes: Primary outcomes: Hepatitis B virus DNA (HBV-DNA) negativity, hepatitis B e antigen (HBeAg) negativity,

HBsAg negativity, ALT and aspartate aminotransferase (AST). Secondary outcomes: Total clinical efficacy, total bilirubin (TBil), hyaluronic acid (HA), laminin (LN), type III procollagen (PCIII), and type IV collagen (IV-C). Safety outcome: Incidence of adverse events.

Exclusion criteria were: (1) Data insufficient for effect estimation after attempts to clarify the report; (2) concomitant traditional Chinese interventions other than herbal XCHD-based therapy, such as acupuncture or additional botanical formulas not shared across study arms; and (3) duplicate reports of the same trial, in which case the most complete dataset was retained.

2.3. Information Sources and Search Strategy

A comprehensive search of CNKI, VIP, Wanfang, SinoMed, PubMed, Embase, the Cochrane Library and Web of Science was conducted from database inception to October 5, 2025. Searches were run between October 3 and October 5, 2025. The PubMed search strategy is detailed below (Table 1). Full reproducible search strategies for all databases, including Boolean operators, field tags, and any limits used, are provided in Supplementary Material A3.

2.4. Study Screening and Data Extraction

Study selection was conducted in two stages: Title/abstract screening followed by full-text review. Two reviewers independently screened records against the eligibility criteria, with disagreements resolved by discussion or consultation with a third reviewer.

Data extraction and synthesis decisions: Data were extracted independently using a standardized form developed a priori and pilot-tested on three randomly selected studies. The form captured: (1) Study design and setting, (2) participant characteristics (age, sex, diagnostic criteria, disease duration, baseline severity), (3) background WM treatments permitted during the trial, (4) XCHD formulation details (herbal composition, dosage, preparation method, any modifications), (5) treatment duration and follow-up period, (6) outcome definitions and measurement instruments, and (7) numerical outcome data (mean, standard deviation, sample size at each time point).

Decision rules for data handling were established before analysis and applied consistently: (1) Duplicate reports of the same study were collated, and the report with the most complete outcome data was retained as the primary source; (2) when multiple post-treatment time points were reported, end-of-treatment data were prioritized for the primary synthesis, with sensitivity analyses using the longest follow-up data where available; (3) when both baseline and post-treatment values were reported, change-from-baseline scores were calculated and used in preference to final values, as prespecified; (4) when studies reported outcomes by subgroups without a combined total, the subgroups were combined according to Cochrane guidance; (5) standard deviations for change scores were calculated from available data using correlation coefficients derived from studies reporting all necessary components, or imputed as 0.5 when unavailable. Corresponding authors were contacted by email (up to two attempts, two weeks apart) when key information was unclear or missing. The full extraction form and a detailed calibration protocol are provided in Supplementary Material A Table A3.

2.5. Risk of Bias Assessment and Evidence Certainty

Risk of bias was assessed with the Cochrane Risk of Bias 2 (RoB 2) tool (10) across the five standard domains by two independent reviewers, with arbitration by a third reviewer when needed. Certainty of evidence was rated using GRADE as high, moderate, low, or very low by two independent reviewers, with disagreements resolved by discussion with a third reviewer (11). Because many outcomes were surrogate measures and several analyses were expected to show important clinical heterogeneity, certainty judgments were interpreted conservatively. Detailed decision rules are provided in Supplementary Material A4.

2.6. Statistical Analysis

Statistical analyses were performed using Review Manager (Cochrane Collaboration, version 5.4) and Stata 17.0. Dichotomous outcomes were pooled as relative risks (RR) with 95% confidence intervals (CI), and continuous outcomes were summarized as mean differences (MD) using change scores when available. Statistical heterogeneity was assessed using the chi-square test and the I^2 statistic. A fixed-effect model was used when heterogeneity was low ($I^2 \leq 50\%$) and clinical comparability was acceptable; otherwise, a random-effects model was used. Given the anticipated variation in background WM, disease stage, treatment duration, and XCHD modifications, pooled effects for highly heterogeneous outcomes were interpreted as exploratory average effects. Prespecified subgroup analyses explored treatment duration, age, and disease course. Sensitivity analyses were conducted by sequentially omitting individual studies. Publication bias was assessed by visual inspection of funnel plots and by Egger's regression test when more than 10 studies were available.

Table 1. PubMed Search Strategy [a]

No.	Search Query for PubMed
#1	"Hepatitis B, Chronic" [MeSH Terms] OR "Hepatitis B Virus Infection, Chronic" [Title/Abstract] OR "Chronic Hepatitis B Virus Infection" [Title/Abstract] OR "Chronic Hepatitis B" [Title/Abstract]
#2	"xiaochaihu" [Supplementary Concept] OR "shosaiko-to" [Title/Abstract] OR "sho-saiko-to" [Title/Abstract] OR "shosaiko-toh" [Title/Abstract] OR "TJ-9" [Title/Abstract] OR "TJ9" [Title/Abstract] OR "xiaochaihutang" [Title/Abstract] OR "xiao-chai-hu-tang" [Title/Abstract] OR "xiaochaihu-tang" [Title/Abstract] OR "XCHT herbal formula" [Title/Abstract] OR "xiao chai hu" [Title/Abstract] OR "bupleurum chinense DC formula" [Title/Abstract] OR "minor bupleurum" [Title/Abstract] OR "small bupleurum" [Title/Abstract] OR "radix bupleuri" [Title/Abstract] OR "bupleurum root" [Title/Abstract]
#3	"randomized controlled trial" [Publication type] OR "randomized clinical trial" [Publication type] OR "randomized trial" [Publication type] OR "clinical trial" [Publication type] OR "randomized controlled trial" [Title/Abstract] OR "randomized clinical trial" [Title/Abstract] OR "randomized trial" [Title/Abstract] OR "clinical trial" [Title/Abstract]
#4	#1 AND #2 AND #3

[a] Abbreviation: XCHD, *Xiaochaihu decoction*.

2.7. Trial Sequential Analysis

Trial sequential analysis (TSA) was performed using TSA software (version 0.9.5.10) as a supplementary assessment of the risk of random errors arising from repeated testing and sparse data. Crossing the conventional boundary but not the TSA monitoring boundary was interpreted as statistically suggestive but potentially premature evidence. Crossing both boundaries indicates that random error is less likely to explain the finding, but such results were not considered to override persistent concerns related to risk of bias, publication bias, indirectness, or substantial heterogeneity. Accordingly, TSA was used to complement, not replace, the RoB 2 and GRADE assessments (12).

3. Results

3.1. Study Screening

The search identified 353 studies. After 175 duplicates were removed, leaving 178 studies for title and abstract review; 94 of these did not meet eligibility criteria. 84 studies proceeded to full-text evaluation, where 35 were excluded: (1) Not RCTs (n = 5); (2) the outcome did not match the inclusion criteria (n = 7); (3) the intervention did not match the inclusion criteria (n = 13); (4) the study data were incomplete (n = 8); (5) repeated publications (n = 1); (6) abstract only (n = 1); Ultimately, 49 RCTs were included in the analysis. The study selection process is summarized in Figure 1.

3.2. Study Characteristics

Table 2 summarizes the included studies. All 49 RCTs were conducted in China and published in Chinese between 2002 and 2025, enrolling 4,768 participants (2,402 individuals assigned to the intervention group and 2,366 to the control group). All studies compared XCHD + WM with WM alone. In a subset of RCTs, the treatment regimen lasted between 28 and 365 days. Baseline characteristics were generally comparable between the intervention and control groups in all trials.

3.3. Risk of Bias Assessment

The 49 trials were evaluated using the five domains of RoB 2. In all trials, issues were identified with the randomization process; 27 of these trials referenced randomization but failed to specify the implementation method. Additionally, all trials failed to report allocation concealment. In 48 trials, concerns arose regarding deviations from the intended interventions, likely due to the absence of blinding. Missing outcome data: All trials reported complete outcome data for randomized participants. Measurement of the outcome: 32 studies lacked blinding of outcome assessors, which may have affected the objectivity of outcome measurement. Within the 32 trials, four trials were judged to be at high risk because knowledge of the intervention could plausibly influence outcome measurement. Selection of the reported result: All trials faced issues with selective reporting of results because none had a preregistered protocol, and three trials were high risk for selective outcome reporting. In total, 41 trials were assessed with some concerns, while 8 trials were deemed high risk. The assessment of bias risk for the included trials is presented in Figure 2.

3.4. Meta-Analysis Results

3.4.1. Primary Outcomes

Pooled estimates for dichotomous virological outcomes showed low heterogeneity, whereas several continuous biochemical and fibrosis-related outcomes

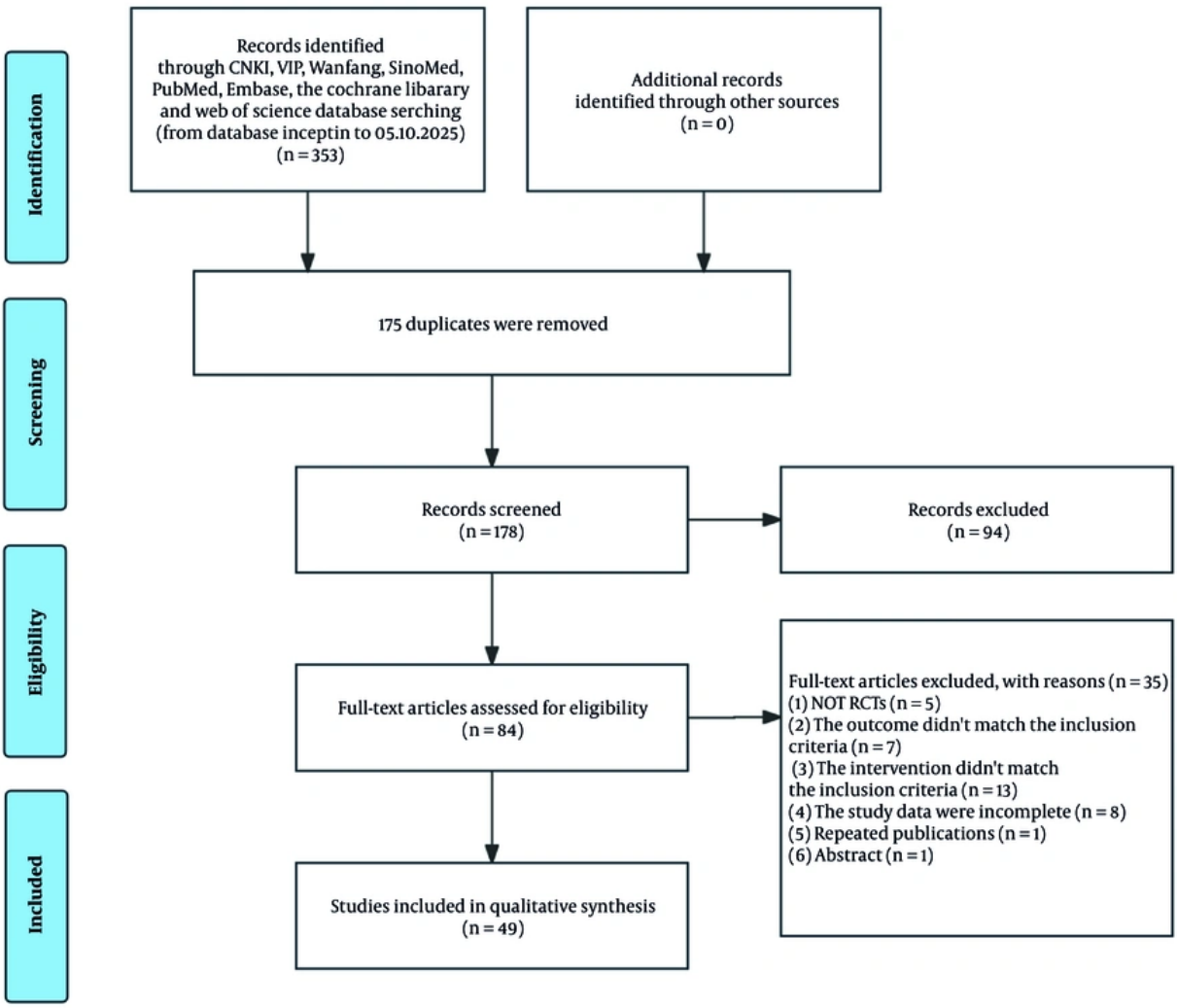

Figure 1. PRISMA flow diagram of study selection

showed substantial between-study heterogeneity. For the latter, pooled estimates should be read as exploratory signals of possible adjunctive benefit rather than as precise effect sizes.

3.4.1.1. HBV-DNA Negativity

HBV-DNA negativity was reported in 24 RCTs (n = 2,187; Figure 3). Heterogeneity was low (I^2 = 46%), and a fixed-effect model favored XCHD + WM [RR = 1.54, 95% CI 1.44 to 1.64, P < 0.00001].

3.4.1.2. HBeAg Negativity

HBeAg negativity was reported in 22 RCTs (n = 1,995; Figure 4). Heterogeneity was absent (I^2 = 0%), and a fixed-effect model favored XCHD + WM [RR = 1.55, 95% CI 1.43 to 1.69, P < 0.00001].

3.4.1.3. HBsAg Negativity

HBsAg negativity was reported in 4 RCTs (n = 289; Figure 5). Heterogeneity was absent (I^2 = 0%), and a fixed-effect model favored XCHD + WM [RR = 2.09, 95% CI 1.35

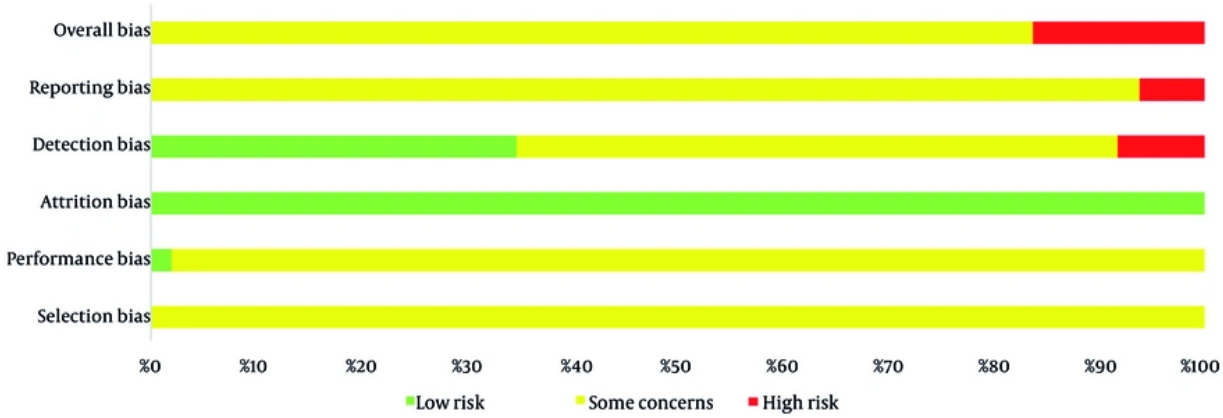

Figure 2. Risk of bias summary

to 3.23, P = 0.0009]. Because the evidence base was small, this result should be interpreted cautiously.

3.4.1.4. ALT

ALT was reported in 31 RCTs (n = 3,149; Figure 6). Heterogeneity was high (I^2 = 98%), and the random-effects model favored XCHD + WM [MD = -28.53, 95% CI -36.47 to -20.59, P < 0.00001]. This estimate should be interpreted cautiously because of marked heterogeneity.

3.4.1.5. AST

AST was reported in 29 RCTs; after leave-one-out exclusion of one study, 28 RCTs (n = 2,658) were included in the meta-analysis (Figure 7). Heterogeneity was high (I^2 = 98%), and the random-effects model favored XCHD + WM [MD = -28.10, 95% CI -35.26 to -20.93, P < 0.00001]. This estimate should be interpreted cautiously because of marked heterogeneity.

3.4.2. Secondary Outcomes

3.4.2.1. Total Clinical Efficacy

Total clinical efficacy was reported in 27 RCTs (n = 2,600; Figure 8). Heterogeneity was absent (I^2 = 0%), and a fixed-effect model favored XCHD + WM [RR = 1.22, 95% CI 1.18 to 1.26, P < 0.00001].

3.4.2.2. TBil

TBil was reported in 21 RCTs (n = 1,943; Figure 9). Heterogeneity was extremely high (I^2 = 100%), and the random-effects model favored XCHD + WM [MD = -27.16, 95% CI -36.67 to -17.65, P < 0.00001]. This estimate should be interpreted cautiously because of extreme heterogeneity.

3.4.2.3. HA

HA was reported in 13 RCTs (n = 1,471; Figure 10). Heterogeneity was substantial (I^2 = 93%), and the random-effects model favored XCHD + WM [MD = -61.95, 95% CI -80.16 to -43.73, P < 0.00001]. This estimate should be interpreted cautiously because of marked heterogeneity.

3.4.2.4. LN

LN was reported in 13 RCTs (n = 1,473; Figure 11). Heterogeneity was substantial (I^2 = 86%), and the random-effects model favored XCHD + WM [MD = -31.75, 95% CI -40.17 to -23.34, P < 0.00001]. This estimate should be interpreted cautiously because of marked heterogeneity.

3.4.2.5. PCIII

PCIII was reported in 12 RCTs; after exclusion of non-estimable studies, 9 RCTs (n = 725) were included in the meta-analysis (Figure 12). Heterogeneity was high (I^2 = 99%), and the random-effects model favored XCHD + WM [MD = -41.31, 95% CI -61.50 to -21.13, P < 0.0001]. This

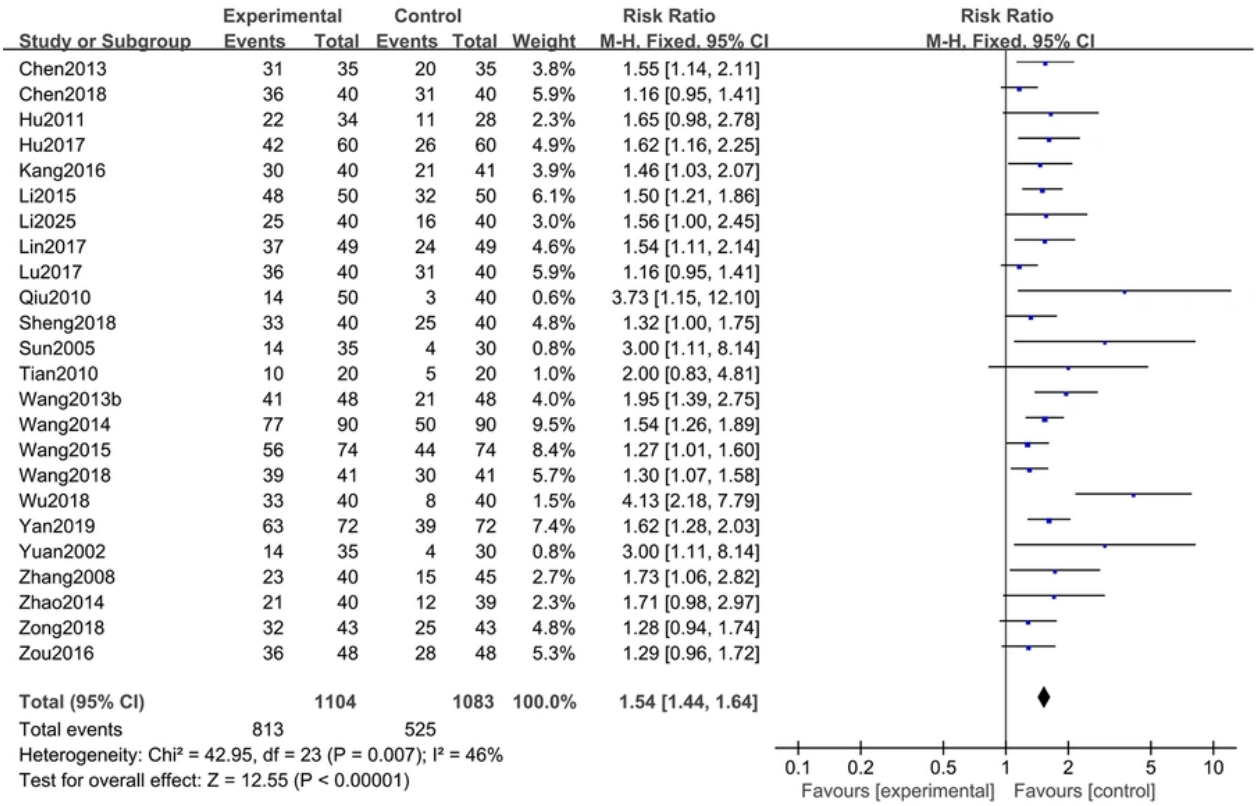

Figure 3. Meta-analysis results of HBV-DNA negativity (14, 16, 18, 19, 21, 24, 31, 37, 38, 43, 47-50, 54-60)

estimate should be interpreted cautiously because of marked heterogeneity.

3.4.2.6. IV-C

IV-C was reported in 10 RCTs (n = 849; Figure 13). Heterogeneity was substantial (I^2 = 84%), and the random-effects model favored XCHD + WM [MD = -20.43, 95% CI -30.88 to -9.98, P = 0.0001]. This estimate should be interpreted cautiously because of marked heterogeneity.

3.5. Adverse Events

Adverse events were reported in 16 RCTs (n = 1,890; Figure 14). Heterogeneity was low (I^2 = 34%), and a fixed-effect model showed fewer reported adverse events in the XCHD + WM group [RR = 0.53, 95% CI 0.38 to 0.73, P = 0.0001]. Because adverse-event reporting was available for only a subset of trials and follow-up was short, this result should be interpreted as evidence of no apparent short-term safety signal.

Table 3 summarizes the reported adverse events. Across trials reporting these data, 49/957 participants (5.1%) in the XCHD + WM group and 93/933 (10.0%) in the WM-alone group experienced at least one adverse event. Reported events were generally gastrointestinal symptoms, dizziness/fatigue, sleep disturbance, or laboratory hepatic dysfunction, but definitions and ascertainment were inconsistent across studies. Accordingly, the safety findings suggest that adding XCHD did not increase reported short-term adverse events.

3.6. Subgroup Analysis and Sensitivity Analysis

3.6.1. Treatment Duration

Subgroup analyses were performed by treatment duration, age, and disease course (Tables 4 -6). Most

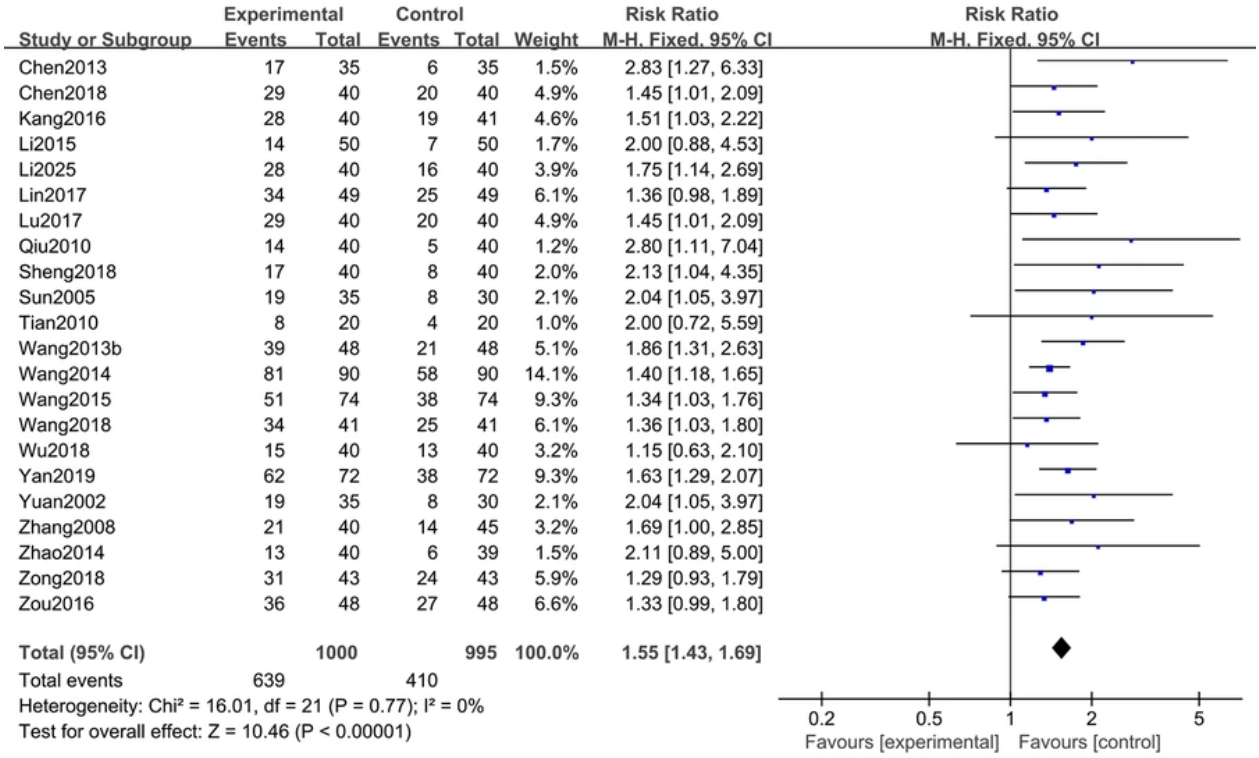

Figure 4. Meta-analysis results of HBeAg negativity (14, 16, 18, 19, 21, 24, 29, 31, 37, 38, 42, 43, 46, 48-50, 54-57, 59, 60)

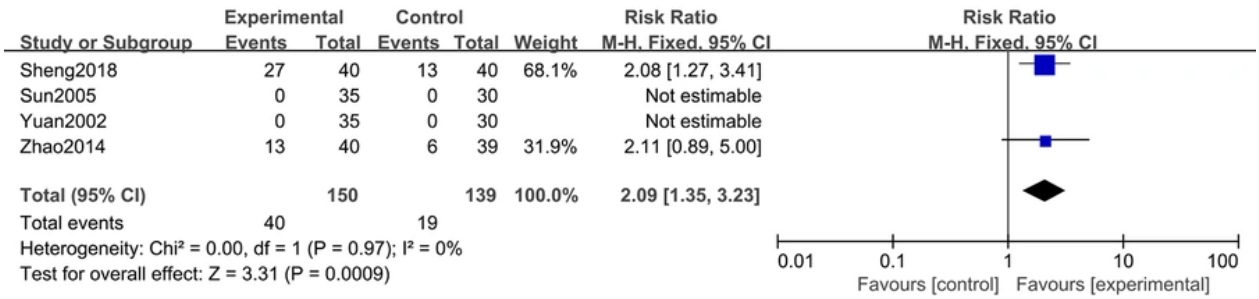

Figure 5. Meta-analysis results of HBsAg negativity (24, 29, 43, 49)

interaction tests were not statistically significant, suggesting no consistent effect modification across subgroups. Notable signals were a larger TBil reduction in studies with treatment duration ≤ 6 months (P for interaction = 0.002), a larger reduction in reported adverse events in participants aged ≤ 45 years (P for interaction = 0.003), a larger improvement in HBV-DNA negativity in the > 7 years disease-course subgroup (P = 0.002), and larger reductions in HA and LN in the ≤ 7 years subgroup (P < 0.05). Because subgroup sizes were

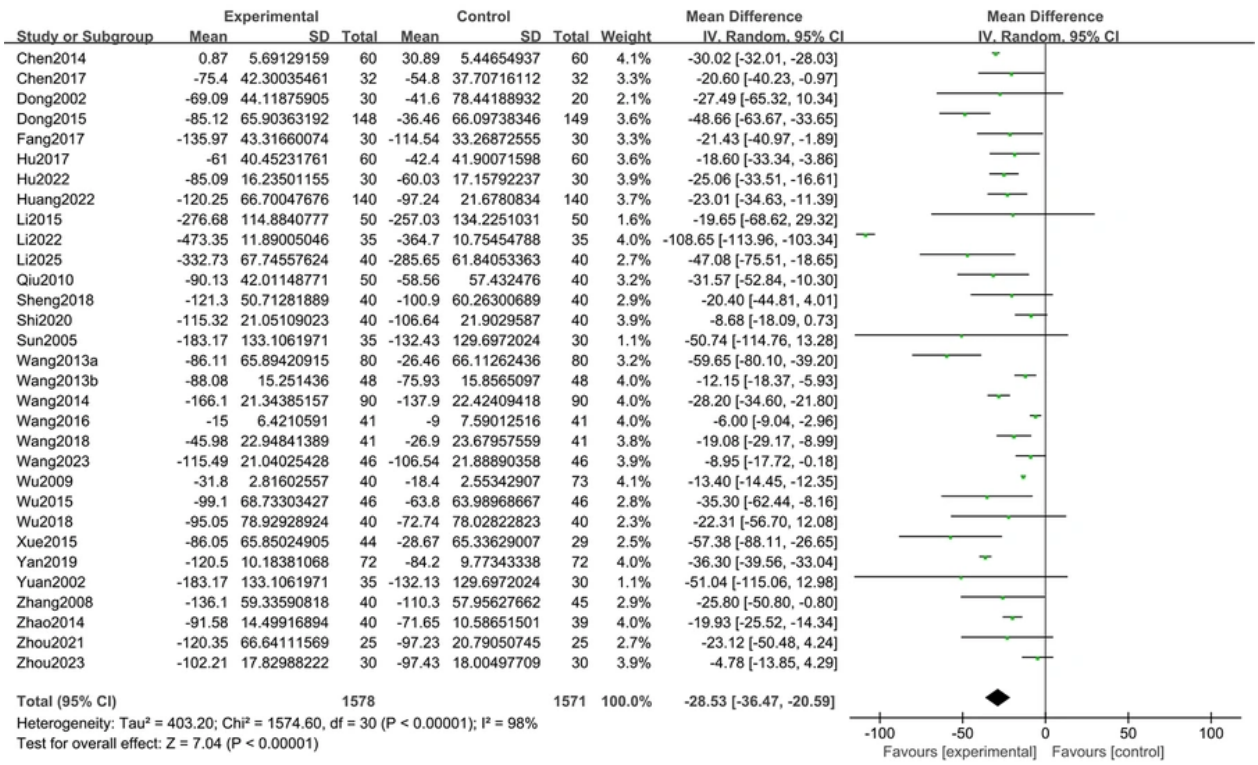

Figure 6. Meta-analysis results of ALT (13, 15, 17, 18, 21, 22, 24, 26, 27, 29, 33-39, 41-45, 48-51, 58-61)

uneven and multiple comparisons were performed, these findings should be considered exploratory.

Sensitivity analyses showed that removal of a small number of influential studies reduced heterogeneity for some outcomes but did not materially change the overall direction of effect. Detailed results are provided in Supplementary Material A6.

3.7. Publication Bias

Egger's tests suggested possible small-study effects or publication bias for HBV-DNA negativity ($P < 0.0001$), HBeAg negativity ($P = 0.001$), total clinical efficacy ($P < 0.0001$), and HA ($P = 0.033$). For ALT ($P = 0.195$), AST ($P = 0.171$), TBil ($P = 0.055$), LN ($P = 0.170$), and adverse events ($P = 0.301$), Egger's tests were not statistically significant, although visual inspection suggested mild asymmetry for some outcomes. Detailed plots are provided in Supplementary Material A5.

3.8. Certainty of Evidence

The certainty of evidence was evaluated using GRADE (Table 7). Evidence was moderate for HBeAg negativity, HBsAg negativity, and adverse events; low for HBV-DNA negativity and total clinical efficacy; and very low for ALT, AST, TBil, HA, LN, PCIII, and IV-C. Thus, moderate certainty was limited to only three outcomes, while most efficacy outcomes remained low or very low certainty. Downgrading was driven mainly by risk of bias, inconsistency, and suspected publication bias.

3.9. Trial Sequential Analysis

Supplementary Material A7 shows that the cumulative Z-curves for HBV-DNA negativity, HBeAg negativity, ALT, AST, LN, PCIII, IV-C, and total clinical efficacy crossed the conventional and TSA monitoring boundaries. Several of these outcomes crossed the TSA monitoring boundary before the required information size was reached. By contrast, HA, HBsAg negativity, and TBil did not cross the TSA monitoring boundary. For HA, the cumulative evidence crossed the conventional threshold but remained below the TSA boundary and

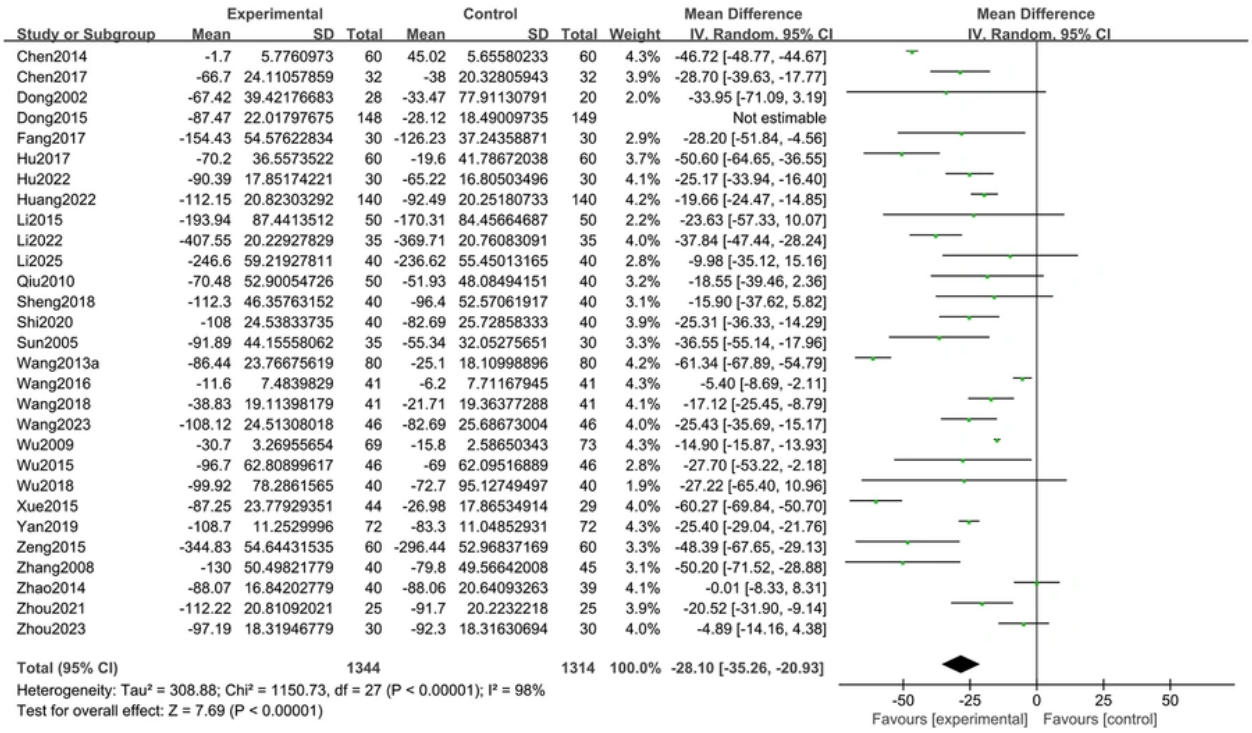

Figure 7. Meta-analysis results of AST (13, 15, 17, 18, 21, 22, 24-27, 32-36, 38, 39, 41-45, 48, 49, 51, 58-61)

required information size, while for HBsAg negativity the accrued sample size was far below the required information size.

4. Discussion

4.1. Interpretation of the Results

This review suggested that adding XCHD to WM may improve several short-term surrogate outcomes in CHB, including virological response measures and some biochemical indices. These were selected because they are common treatment targets in CHB trials and conform to EASL Clinical Practice Guidelines on the management of hepatitis B virus infection, although they remain surrogate outcomes for long-term clinical benefit (62). The outcomes are biologically plausible and directionally consistent across many analyses. However, these should be interpreted as exploratory estimates of average effect rather than established evidence of long-term clinical benefit, given that the available trials were generally small, methodologically limited, and most pooled endpoints were surrogate markers rather than patient-important outcomes such as progression to cirrhosis, hepatic decompensation, hepatocellular carcinoma, mortality, or quality of life. In addition, because variation in background WM, disease stage, treatment duration, and XCHD modifications was anticipated, pooled effects for highly heterogeneous outcomes were likewise considered exploratory average effects.

Within each trial, both groups received the same background WM, including nucleos(t)ide analogues, interferon-based regimens, immunomodulators, and/or hepatoprotective therapies, but WM varied across trials. Otherwise, since XCHD is a compound preparation, some studies have variations in the core herbal composition, dosage, and compatible interventions, which may also contribute to clinical heterogeneity. Therefore, these reasons may be the source of clinical heterogeneity after merging data from the experimental group and control group. The findings therefore represent XCHD-based therapy, not a single standardized product.

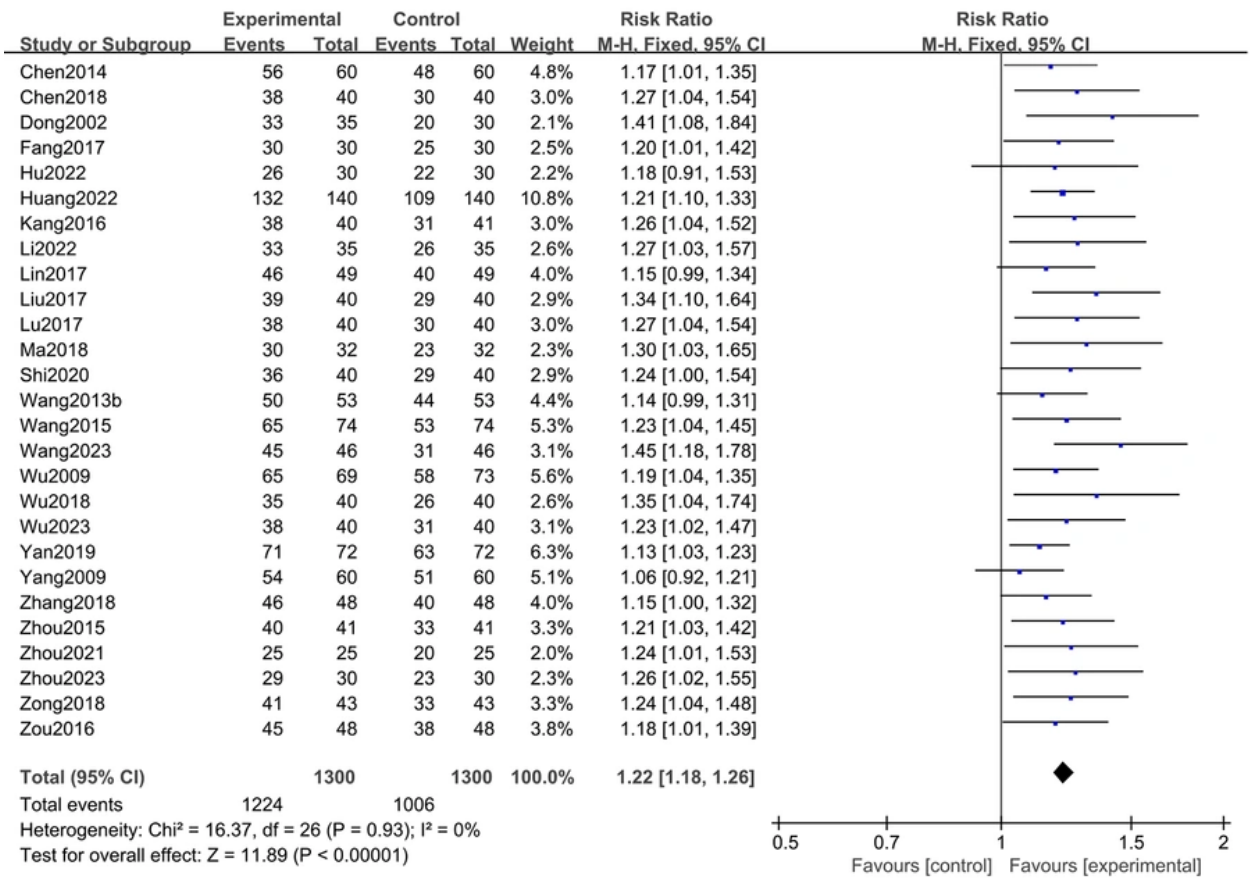

Figure 8. Meta-analysis results of total clinical efficacy (13, 14, 16, 17, 19, 20, 22, 25, 28, 30, 31, 34-36, 40-42, 44, 45, 50, 52-56, 59, 61)

Supplementary Material A7 showed that the cumulative Z-curves for HBV-DNA negativity, HBeAg negativity, ALT, AST, total clinical efficacy, LN, PCIII, and IV-C crossed both the conventional and TSA monitoring boundaries. In most of these analyses, however, boundary crossing occurred before the required information size was reached, suggesting a reduced risk of random error under the prespecified TSA assumptions rather than definitive or high-certainty evidence. By contrast, HA and TBil crossed the conventional threshold but not the TSA monitoring boundary and remained below the required information size, while for HBsAg negativity the accrued sample size was far below the required information size. These outcomes should therefore be considered inconclusive from a TSA perspective. TSA findings were interpreted together with RoB 2, GRADE, publication bias, and clinical heterogeneity.

The reported incidence of adverse events was not higher with XCHD + WM and was numerically lower in the pooled analysis. Even so, adverse events were reported in only 16 of 49 trials, and follow-up was short. Accordingly, the safety findings supported no clear short-term harm signal, but they did not establish long-term comparative safety.

4.2. Mechanistic Evidence

Consistent with prior preclinical research, XCHD appeared to modulate inflammatory and fibrogenic pathways, including NF-κB and TGF-β1, in a manner broadly consistent with the biochemical and fibrosis-marker improvements observed in this review (63, 64). In animal and cellular models of chronic liver injury, XCHD-based interventions were reported to alleviate oxidative stress, regulate bile-acid and lipid metabolism, and ameliorate steatosis and cholestasis (65, 66). In

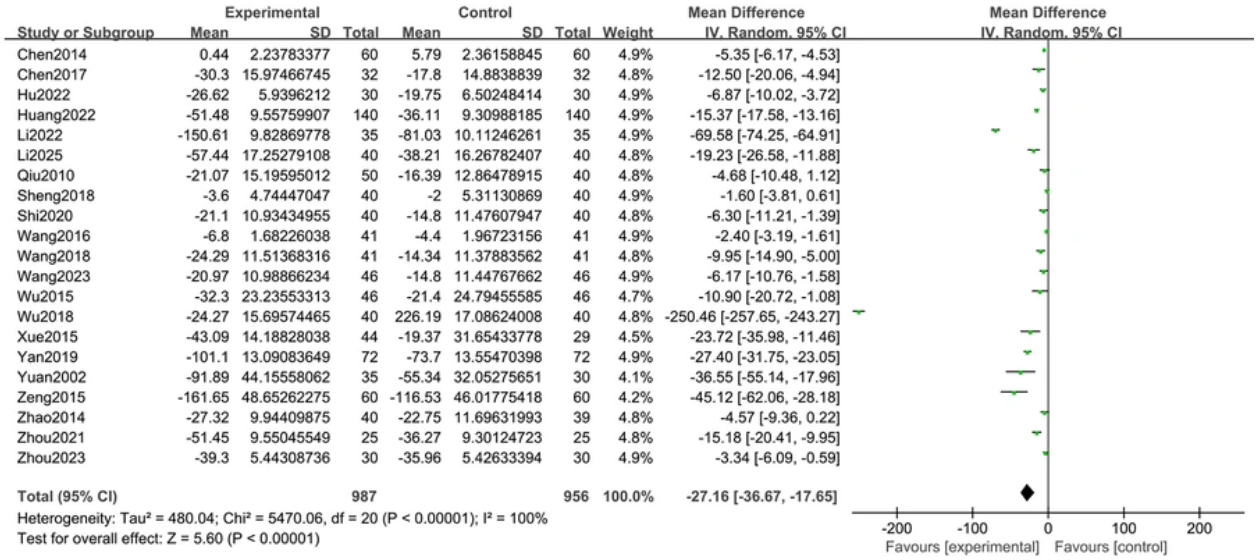

Figure 9. Meta-analysis results of TBil (13, 17, 21, 22, 25-27, 29, 32, 33, 35, 36, 38, 39, 42-45, 48, 49, 59)

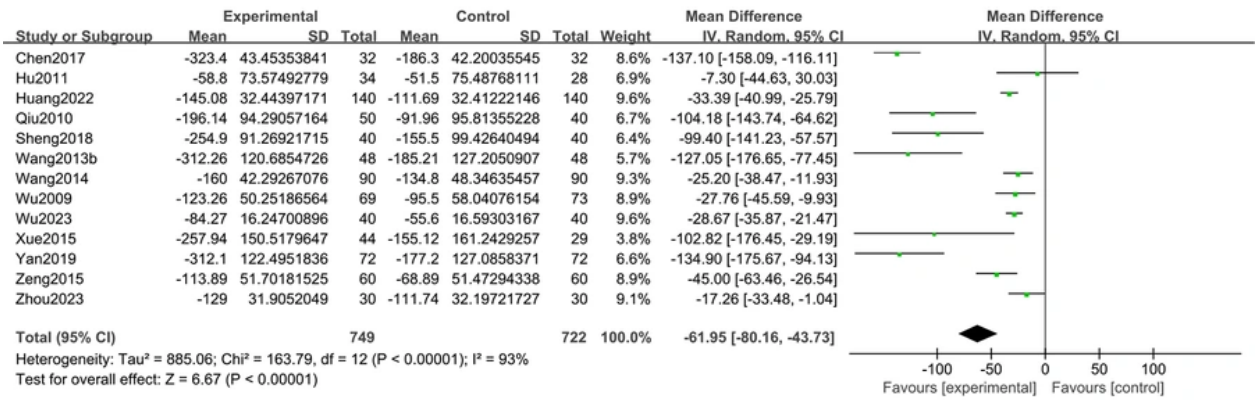

Figure 10. Meta-analysis results of HA (21, 27, 32, 33, 36, 37, 40-42, 45, 47, 49, 50)

addition, XCHD was shown to inhibit TGF-β1-driven hepatic stellate-cell activation, downregulate profibrotic mediators such as HSP47 and collagen I/III, and reduce extracellular-matrix deposition in experimental fibrosis models (7). Taken together, these mechanistic observations suggested that XCHD might mitigate hepatocellular injury, support antiviral and immune-regulatory activity, and help restore immune–metabolic balance in chronic hepatitis B, thereby providing only tentative mechanistic support for the clinical findings observed in this meta-analysis.

In addition to the primary outcomes, secondary outcomes — including total clinical efficacy, TBil, and fibrosis-related serum markers such as HA, LN, PCIII, and IV-C — were evaluated to provide a broader assessment of treatment benefit. In the included trials, adjunctive XCHD was associated with improvements in these outcomes. However, these findings were accompanied

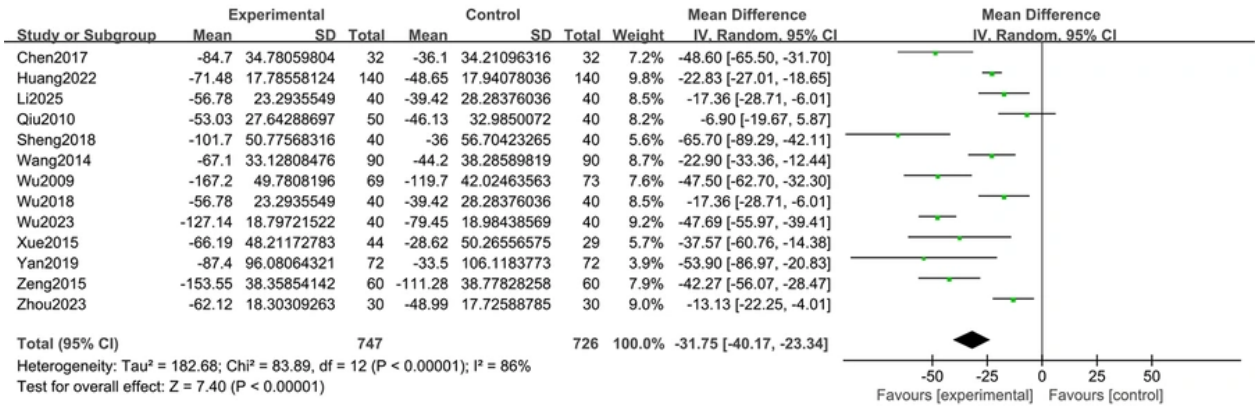

Figure 11. Meta-analysis results of LN (21, 27, 32, 33, 36, 37, 40-42, 45, 48, 49, 59)

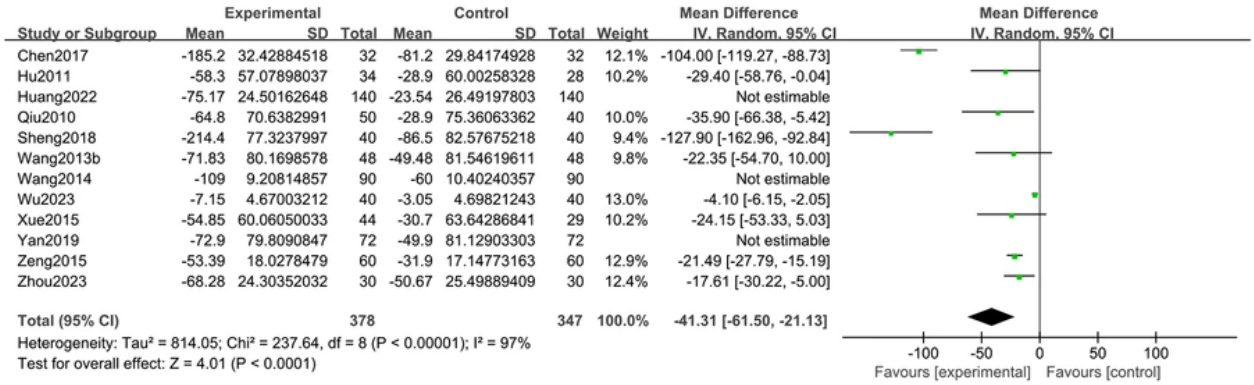

Figure 12. Meta-analysis results of PCIII (21, 27, 32, 33, 36, 40, 45, 47, 49, 50)

by substantial heterogeneity, and the certainty of evidence for most of these outcomes was low or very low. Moreover, several of these measures were indirect surrogate markers rather than hard clinical endpoints. These findings were therefore best interpreted as signals that warranted further confirmation rather than as definitive evidence of antifibrotic or cholestasis-modifying effects.

Clinically, several trials in CHB patients with liver fibrosis or cirrhosis reported that adding XCHD to conventional therapy reduced serum fibrosis markers, such as HA, LN, and procollagen peptides, and improved liver-function tests and imaging-based fibrosis scores; these findings were broadly consistent with the pattern of TBil and fibrosis-marker improvement observed in our meta-analysis (67). In animal models of chronic liver injury and parasite-induced fibrosis, XCHD was also reported to reduce serum ALT, bilirubin, and HA, decrease granuloma burden and collagen-rich areas on histology, and ameliorate architectural distortion of the liver, thus suggesting a possible protective effect on fibrogenic remodeling and cholestatic injury (7). Additional mechanistic studies indicated that key XCHD-related formulations and constituents might modulate extracellular-matrix turnover and hepatic stellate-cell behavior. For example, baicalin and baicalein derived from Scutellaria baicalensis were reported to inhibit PDGF-BB-induced stellate-cell activation and collagen synthesis, whereas XCHD-

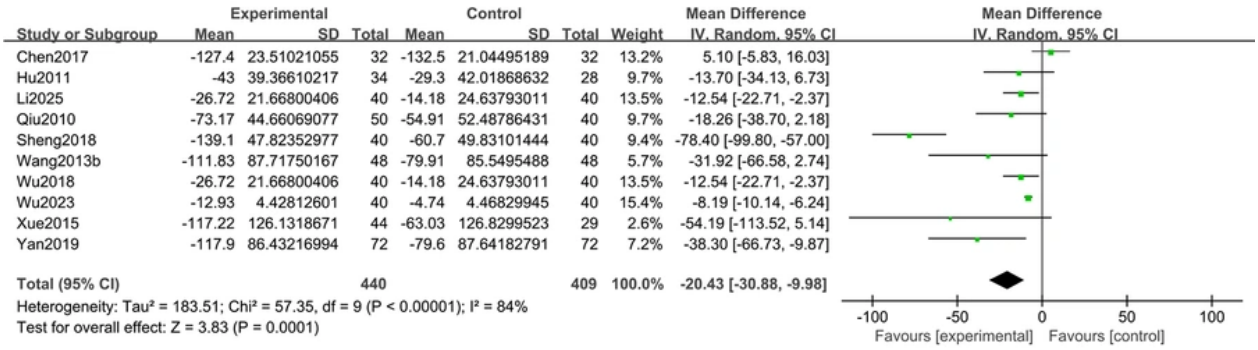

Figure 13. Meta-analysis results of IV-C (21, 27, 33, 40, 42, 47-50, 59)

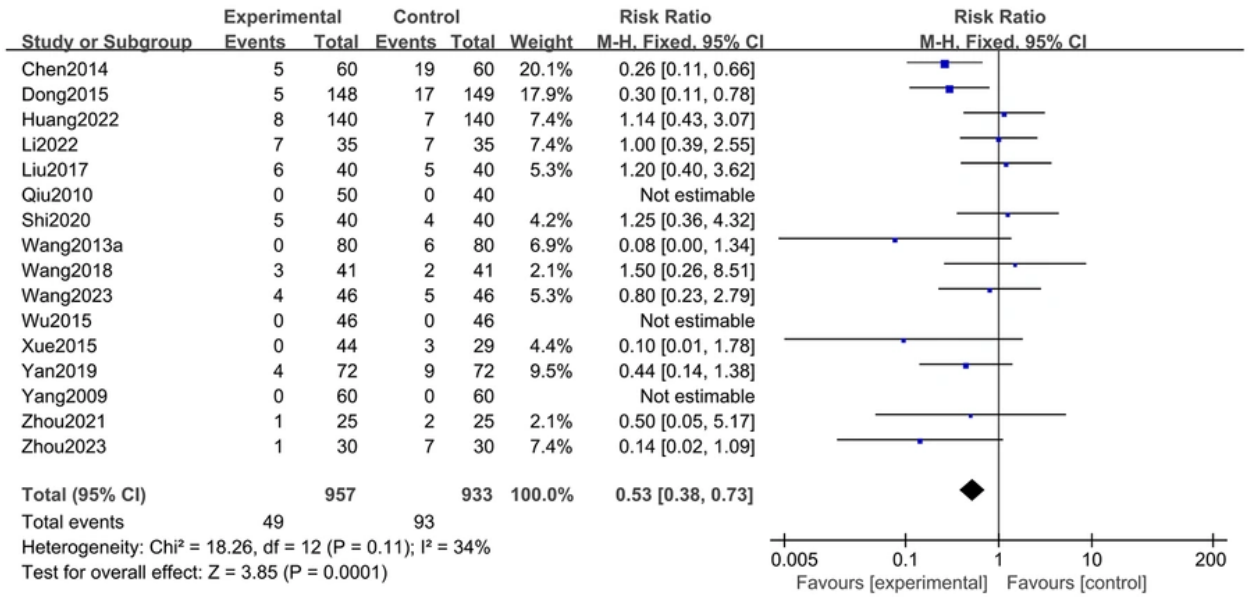

Figure 14. Meta-analysis results for adverse events (13, 15, 17, 21, 22, 25, 27, 36, 38, 42, 44, 45, 51, 53)

related formulations were reported to enhance matrix metalloproteinase (MMP-2 and MMP-13) expression and downregulate tissue inhibitors of metalloproteinases (TIMP-1/2), thereby potentially promoting collagen degradation in fibrotic livers (59). Overall, the mechanistic evidence was broadly compatible with a potential adjunctive role for XCHD.

4.3. Clinical Implications

Subgroup analyses suggested that the adjunctive effects of XCHD plus WM were broadly consistent across most subgroups, and statistically significant subgroup differences were limited to a few outcomes. By treatment duration, studies with treatment courses of ≤ 6 months showed a larger reduction in TBil than those with treatment courses > 6 months (P for interaction = 0.002). This may suggest that bilirubin improvement can be observed within the earlier treatment period. By

Table 3. Reported Adverse Events [a]

Study	Sample Size		Adverse Events	
	T	C	T	C
Chen and Zhou (2014), (13)	60	60	5 (hepatic dysfunction)	19 (hepatic dysfunction)
Dong, (2015), (15)	148	149	5 (nausea, dizziness, sleep disturbances)	17 (nausea, dizziness, sleep disturbances)
Huang and Xie, (2022), (36)	140	140	8 (3 nausea, 2 emesis, 3 diarrhea)	7 (2 nausea, 2 emesis, 3 diarrhea)
Li and Yu, (2022), (17)	35	35	7 (1 dry mouth and bitter taste, 1 dizziness and fatigue, 2 nausea and vomiting, 1 abdominal distension, 1 fever, 1 decreased appetite)	7 (1 dry mouth and bitter taste, 1 dizziness and fatigue, 2 nausea and vomiting, 1 abdominal distension (bloating), 1 fever, 1 decreased appetite)
Liu, (2017), (53)	40	40	6 (1 dry mouth and bitter taste, 1 dizziness and fatigue, 2 nausea and vomiting, 1 abdominal distension and belching, 1 poor appetite)	5 (1 dry mouth and bitter taste, 1 dizziness and fatigue, 1 nausea and vomiting, 1 abdominal distension and belching, 1 poor appetite)
Qiu et al., (2010), (21)	50	40	0	0
Shi, (2020), (22)	40	40	5 (2 dizziness, 2 nausea, 1 diarrhea)	4 (2 dizziness, 1 nausea, 1 diarrhea)
Wang, (2013), (50)	80	80	0	6 (2 nausea, 4 dizziness with sleep disturbances)
Wang, (2023), (25)	46	46	4 (1 diarrhea, 2 dizziness, 1 nausea)	5 (2 diarrhea, 2 dizziness, 1 nausea)
Wang, (2018), (38)	41	41	3 (1 nausea and vomiting, 2 dry mouth)	2 (1 nausea and vomiting, 1 dry mouth)
Wu, (2015), (26)	46	46	0	0
Xue, 2015 (27)	44	29	0	3 (1 sleep disturbance, 1 nausea, 1 dizziness)
Yan et al., (2019), (42)	72	72	4	9
Yang, (2009), (28)	60	60	0	0
Zhou, (2021), (44)	25	25	1 (nausea)	2 (diarrhea)
Zhou, (2023), (45)	30	30	1 (nausea)	7 (3 nausea, 2 vomiting, 2 diarrhea)

[a] Abbreviations: T, treatment group; C, control group.

age, studies with a mean age ≤ 45 years showed a larger relative reduction in adverse events than those with a mean age > 45 years (P for interaction = 0.003). This finding may indicate that any short-term tolerability advantage was more apparent in younger study populations, but it should not be interpreted as evidence of excess harm in older patients. By disease course, studies with a mean disease duration >7 years showed a larger improvement in HBV-DNA negativity (P = 0.002), whereas studies with a mean disease duration ≤ 7 years showed larger reductions in HA (P = 0.04) and LN (P = 0.03). These patterns may reflect differential study-level responses in virological and fibrosis-related surrogate outcomes, but they remain exploratory and are insufficient to support patient-level treatment stratification. Given the multiple comparisons, the substantial heterogeneity of several continuous outcomes, and the low or very low certainty of evidence for many biochemical and fibrosis-related endpoints, these subgroup findings should be regarded as exploratory. Clinically, XCHD may provide short-term improvements in surrogate virological and biochemical endpoints when added to guideline-based WM, but it should not be considered a replacement for established antiviral therapy, and treatment decisions should not be based solely on treatment duration, age, or disease course.

4.4. Strengths

This study integrates a comprehensive meta-analysis with rigorous evidence appraisal to clarify the potential role of XCHD as an adjunct to WM for CHB. Using large-scale aggregated data from randomized trials, the analysis evaluated virological responses, liver biochemistry, fibrosis-related markers, and adverse events, providing an integrated view of both benefits and harms. Prespecified subgroup and sensitivity analyses were applied to probe the robustness of findings across treatment duration, age, and disease course, while RoB 2 and GRADE were used to characterize methodological limitations and certainty.

Table 4. Subgroup Analyses by Treatment Duration [a]

Outcome	Subgroup (mo)	Number of Studies	Sample Size (T/C)	Measures	Effect Estimate (95% CI)	Heterogeneity (%) (I^2)	P Interaction
HBV-DNA negativity	≤ 6	12	475/460	RR	1.67 [1.33 to 2.08]	72	0.39
HBV-DNA negativity	> 6	10	507/501	RR	1.50 [1.37 to 1.63]	0	0.39
HBeAg negativity	≤ 6	10	370/365	RR	1.70 [1.43 to 2.01]	0	0.32
HBeAg negativity	> 6	8	424/424	RR	1.53 [1.37 to 1.70]	0	0.32
HBsAg negativity	≤ 6	3	110/100	RR	2.08 [1.27 to 3.41]	-	0.97
HBsAg negativity	> 6	1	40/39	RR	2.11 [0.89 to 5.00]	-	0.97
ALT	≤ 6	12	1121/1115	MD	-32.91 [-43.86 to -21.97]	99	0.11
ALT	> 6	8	411/410	MD	-21.60 [-29.91 to -13.29]	91	0.11
AST	≤ 6	21	965/936	MD	-30.17 [-39.51 to -20.83]	98	0.10
AST	> 6	7	319/318	MD	-19.85 [-27.59 to -12.12]	82	0.10
Total clinical efficacy	≤ 6	16	773/772	RR	1.20 [1.15 to 1.25]	0	0.71
Total clinical efficacy	> 6	9	405/406	RR	1.21 [1.15 to 1.29]	0	0.71
TBil	≤ 6	14	695/670	MD	-32.82 [-45.15 to -20.49]	100	0.002
TBil	> 6	6	269/268	MD	-10.22 [-17.11 to -3.33]	93	0.002
HA	≤ 6	8	445/424	MD	-62.53 [-86.04 to -39.02]	94	0.79
HA	> 6	4	244/238	MD	-71.26 [-130.81 to -11.72]	94	0.79
LN	≤ 6	10	525/504	MD	-30.72 [-40.64 to -20.80]	88	0.82
LN	> 6	2	162/162	MD	-34.27 [-63.55 to -4.99]	67	0.82
PCIII	≤ 6	7	236/211	MD	-51.13 [-88.90 to -13.37]	98	0.26
PCIII	> 6	4	82/76	MD	-26.22 [-47.96 to -4.47]	0	0.26
IV-C	≤ 6	7	286/261	MD	-18.93 [-31.09 to -6.76]	88	0.60
IV-C	> 6	3	154/148	MD	-24.26 [-39.94 to -8.58]	7	0.60
Adverse events	≤ 6	12	758/734	RR	0.45 [0.31 to 0.67]	47	0.13
Adverse events	> 6	4	199/199	RR	0.80 [0.43 to 1.50]	0	0.13

[a] Abbreviations: C, control group; T, treatment group; CI, confidence interval; MD, mean difference; RR, relative risk; P for interaction, P value for subgroup interaction; HBV-DNA, hepatitis B virus DNA; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBil, total bilirubin; HA, hyaluronic acid; LN, laminin; PCIII, type III procollagen; IV-C, type IV collagen.

In addition, trial sequential analysis was conducted to assess information size adequacy and confirm the stability of key findings under sparse-data conditions, thereby strengthening inference and highlighting outcomes that remain underpowered.

4.5. Limitations

Several limitations materially restrict confidence in the pooled estimates. First, many included trials inadequately reported random sequence generation, allocation concealment, blinding, and protocol registration, creating a substantial risk of exaggerated treatment effects. Many trials were relatively small with short treatment and follow-up durations, which constrains inference on longer-term clinical outcomes and late adverse events. Given that all trials were conducted in one country and were mostly small Chinese-language studies, publication bias and selective dissemination may have inflated some pooled benefits, so generalizability to other settings may be limited, and publication bias cannot be fully excluded. Although heterogeneity remained substantial for several continuous outcomes, the direction of effect was generally consistent across studies. We further explored sources of heterogeneity, but due to insufficient data in the included literature, we could only identify these as potential contributing factors of heterogeneity. Sensitivity analyses excluding a small number of influential trials reduced heterogeneity without materially changing the overall direction of the pooled estimates, which supported cautious interpretation of the findings. Additionally, most measures were surrogate markers rather than patient-important endpoints, and GRADE ratings were moderate for some outcomes but low for several key efficacy results.

4.6. Future Perspectives

Given the limited methodological quality and predominance of surrogate endpoints in the current evidence, the next generation of trials on XCHD for CHB should prioritize fewer but higher-quality studies rather than sheer numbers. Large, multicenter RCTs with

Table 5. Subgroup Analyses by Age [a]

Outcome	Subgroup (y)	Number of studies	Sample Size (T/C)	Measures	Effect estimate (95% CI)	Heterogeneity (I^2)	P interaction
HBV-DNA negativity	≤ 45	18	851/845	RR	1.52 [1.42 to 1.64]	51	0.63
HBV-DNA negativity	> 45	6	253/238	RR	1.60 [1.34 to 1.91]	35	0.63
HBeAg negativity	≤ 45	17	817/817	RR	1.52 [1.40 to 1.66]	0	0.30
HBeAg negativity	> 45	5	183/178	RR	1.76 [1.36 to 2.27]	17	0.30
HBsAg negativity	≤ 45	2	75/69	RR	2.11 [0.89 to 5.00]	-	0.97
HBsAg negativity	> 45	2	75/70	RR	2.08 [1.27 to 3.41]	-	0.97
ALT	≤ 45	19	993/983	MD	-25.85 [-32.93 to -18.77]	94	0.65
ALT	> 45	12	585/588	MD	-31.84 [-56.65 to -7.03]	99	0.65
AST	≤ 45	16	670/666	MD	-25.77 [-37.94 to -13.61]	98	0.52
AST	> 45	13	674/648	MD	-30.48 [-38.43 to -22.54]	92	0.52
Total clinical efficacy	≤ 45	17	787/783	RR	1.18 [1.14 to 1.23]	0	0.15
Total clinical efficacy	> 45	10	513/517	RR	1.24 [1.18 to 1.31]	0	0.15
TBil	≤ 45	11	477/471	MD	-34.57 [-49.21 to -19.92]	100	0.10
TBil	> 45	10	510/485	MD	-18.93 [-30.28 to -7.59]	99	0.10
HA	≤ 45	6	306/300	MD	-73.18 [-120.96 to -25.40]	96	0.29
HA	> 45	7	443/422	MD	-46.50 [-60.53 to -32.46]	79	0.29
LN	≤ 45	6	304/304	MD	-24.60 [-34.60 to -14.60]	72	0.13
LN	> 45	7	443/422	MD	-37.35 [-50.63 to -24.08]	90	0.13
PCIII	≤ 45	6	144/138	MD	-43.93 [-93.89 to 6.03]	96	0.74
PCIII	> 45	6	234/209	MD	-35.00 [-54.64 to -15.35]	95	0.74
IV-C	≤ 45	6	266/260	MD	-12.37 [-22.66 to -2.08]	62	0.19
IV-C	> 45	4	174/149	MD	-37.29 [-72.97 to -1.61]	93	0.19
Adverse events	≤ 45	8	537/538	RR	0.31 [0.19 to 0.51]	3	0.003
Adverse events	> 45	8	420/395	RR	0.86 [0.55 to 1.36]	0	0.003

[a] Abbreviations: C, control group; T, treatment group; CI, confidence interval; MD, mean difference; RR, relative risk; P for interaction, P value for subgroup interaction; HBV-DNA, hepatitis B virus DNA; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBil, total bilirubin; HA, hyaluronic acid; LN, laminin; PCIII, type III procollagen; IV-C, type IV collagen.

prospective registration, transparent statistical plans, robust randomization and allocation concealment, blinded outcome assessment, and intention-to-treat analyses are needed to provide more credible effect estimates. Treatment protocols should clearly standardize the core XCHD composition, permitted modifications, dosage form, course length, and background antiviral regimens so that results are comparable across centers and reproducible in clinical practice.

Future research should move beyond short-term virological and biochemical endpoints and instead prioritize long-term, patient-centred outcomes, such as progression to cirrhosis, hepatic decompensation, hepatocellular carcinoma, liver-related and all-cause mortality, together with validated quality-of-life measures. Non-invasive fibrosis indices, elastography findings, and quantitative HBsAg/HBV-DNA trajectories can still be incorporated, but mainly as intermediate surrogates prospectively anchored to these hard clinical events. In parallel, mechanistic and translational studies that integrate pharmacokinetic profiling, focused biomarker panels, and omics-based analyses are needed to elucidate how XCHD influences antiviral immunity, bile-acid and lipid homeostasis, and fibrogenic signalling, and to define the biological or clinical phenotypes of CHB patients most likely to benefit from XCHD as an adjunct to guideline-directed therapy.

4.7. Conclusions

The current evidence suggests that XCHD may have adjunctive short-term benefits for surrogate virological and biochemical outcomes in CHB, without an apparent increase in reported short-term adverse events. However, the evidence base remains limited by high bias risk and heterogeneity. Further large-scale, high-quality RCTs are warranted to validate these findings and assess their long-term clinical benefits.

Acknowledgements

Table 6. Subgroup Analyses by Disease Course [a]

Outcome	Subgroup	Number of studies	Sample Size (T/C)	Measures	Effect estimate (95% CI)	Heterogeneity (I^2)	P Interaction
HBV-DNA negativity	≤7	10	548/549	RR	1.40 [1.29 to 1.52]	22%	0.002
HBV-DNA negativity	>7	14	556/534	RR	1.74 [1.56 to 1.95]	51%	0.002
HBeAg negativity	≤7	9	488/489	RR	1.45 [1.31 to 1.60]	0%	0.06
HBeAg negativity	>7	13	512/506	RR	1.71 [1.49 to 1.98]	0%	0.06
HBsAg negativity	≤7	3	110/100	RR	2.08 [1.27 to 3.41]	-	0.97
HBsAg negativity	>7	1	40/39	RR	2.11 [0.89 to 5.00]	-	0.97
ALT	≤7	9	474/459	MD	-36.25 [-55.26 to -17.23]	99%	0.13
ALT	>7	22	1104/1112	MD	-21.17 [-25.81 to -16.53]	73%	0.13
AST	≤7	11	519/499	MD	-34.58 [-47.35 to -21.81]	98%	0.14
AST	>7	18	825/815	MD	-23.21 [-31.16 to -15.26]	93%	0.14
Total clinical efficacy	≤7	12	586/587	RR	1.20 [1.14 to 1.25]	0%	0.65
Total clinical efficacy	>7	15	714/713	RR	1.21 [1.16 to 1.27]	6%	0.65
TBil	≤7	8	384/369	MD	-22.18 [-30.17 to -14.18]	99%	0.54
TBil	>7	13	603/587	MD	-29.89 [-53.02 to -6.75]	100%	0.54
HA	≤7	6	338/323	MD	-88.80 [-134.46 to -43.15]	95%	0.04
HA	>7	7	411/399	MD	-37.79 [-52.02 to -23.56]	82%	0.04
LN	≤7	6	338/323	MD	-42.88 [-56.08 to -29.69]	69%	0.03
LN	>7	7	409/403	MD	-24.54 [-35.07 to -14.02]	89%	0.03
PCIII	≤7	6	176/161	MD	-68.57 [-123.09 to -14.06]	98%	0.07
PCIII	>7	6	202/186	MD	-16.87 [-29.75 to -3.99]	67%	0.07
IV-C	≤7	4	188/173	MD	-40.10 [-88.59 to 8.38]	94%	0.20
IV-C	>7	6	252/236	MD	-8.68 [-10.54 to -6.82]	0%	0.20
Adverse events	≤7	5	271/256	RR	0.42 [0.25 to 0.71]	43%	0.35
Adverse events	>7	11	686/677	RR	0.58 [0.38 to 0.87]	26%	0.35

[a] Abbreviations: C, control group; T, treatment group; CI, confidence interval; MD, mean difference; RR, relative risk; P for interaction, P value for subgroup interaction; HBV-DNA, hepatitis B virus DNA; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBil, total bilirubin; HA, hyaluronic acid; LN, laminin; PCIII, type III procollagen; IV-C, type IV collagen.

The authors thank all colleagues and collaborators who contributed to the completion of this study.

Supplementary Material

Supplementary material(s) is available here [To read supplementary materials, please refer to the journal website and open PDF/HTML].

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: Study concept and design: T. J., K. J., Z. G., T. Z., and L. X.; acquisition of data: T. J., K. J., and Z. G.; Analysis and interpretation of data: T. J., K. J., Z. G., T. Z., and L. X.; Drafting of the manuscript: T. J., K. J., and Z. G.; Critical revision of the manuscript for important intellectual content: T. Z. and L. X.; Statistical analysis: T. J., K. J., and Z. G.; Administrative, technical, and material support: T. Z. and L. X.; Study supervision: T. Z. and L. X. All authors read and approved the final manuscript. Equal contribution: T. J., K. J., and Z. G. contributed equally to this work.

Conflict of Interests Statement: The authors do not declare any conflicts of interests for this study.

Data Availability: The dataset presented in this study is available on request from the corresponding author during submission or after publication. The data are not publicly available as they are derived from previously published studies.

Funding/Support: This research was supported by Traditional Chinese Medicine Innovation Team and Talent Support Program - National Traditional Chinese Medicine Multidisciplinary Cross-Innovation Team Project (ZYYCXTD-D-202401); The 10th Youth Talent Support Project of the China Association for Science and Technology (CACM-2024)-(2024-QNRC1-02).

Table 7. GRADE Certainty of Evidence [a]

Outcome	Quality assessment							No. of Patients		Effect		Certainty
	No. of trials	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	T	C	Relative (95% CI)	Absolute (95% CI)	
HBV-DNA negativity	24	RCT	Serious	No serious	No serious	No serious	Strongly suspected	813/1104 (73.6%)	525/1083 (48.5%)	RR 1.54 (1.44 to 1.64)	262 more per 1000 (from 213 more to 310 more)	Low
HBeAg negativity	22	RCT	Serious	No serious	No serious	No serious	None	639/1000 (63.9%)	410/995 (41.2%)	RR 1.55 (1.43 to 1.69)	227 more per 1000 (from 117 more to 284 more)	Moderate
HBsAg negativity	4	RCT	Serious	No serious	No serious	No serious	None	40/150 (26.7%)	19/139 (13.7%)	RR 2.09 (1.35 to 3.23)	149 more per 1000 (from 48 more to 305 more)	Moderate
ALT	31	RCT	Serious	Very serious	No serious	No serious	None	1578	1571	-	MD 28.53 lower (36.47 to 20.59 lower)	Very low
AST	28	RCT	Serious	Very serious	No serious	No serious	Strongly suspected	1344	1314	-	MD 28.1 lower (35.26 to 20.93 lower)	Very low
Total clinical efficacy	27	RCT	Serious	No serious	No serious	No serious	Strongly suspected	1224/1300 (94.2%)	1006/1300 (77.4%)	RR 1.22 (1.18 to 1.26)	170 more per 1000 (from 139 more to 201 more)	Low
TBil	21	RCT	Serious	Very serious	No serious	No serious	Strongly suspected	987	956	-	MD 27.16 lower (36.67 to 17.65 lower)	Very low
HA	13	RCT	Serious	Very serious	No serious	No serious	Strongly suspected	749	722	-	MD 61.95 lower (80.16 to 43.73 lower)	Very low
LN	13	RCT	Serious	Very serious	No serious	No serious	Strongly suspected	747	726	-	MD 31.75 lower (40.17 to 23.34 lower)	Very low
PCIII	9	RCT	Serious	Very serious	No serious	No serious	Strongly suspected	378	347	-	MD 41.31 lower (61.5 to 21.13 lower)	Very low
IV-C	10	RCT	Serious	Very serious	No serious	No serious	None	440	409	-	MD 20.43 lower (30.88 to 9.98 lower)	Very low
Adverse events	16	RCT	Serious	No serious	No serious	No serious	None	49/957 (5.1%)	93/933 (10.2%)	RR 0.53 (0.38 to 0.73)	47 fewer per 1000 (from 27 fewer to 62 fewer)	Moderate

[a] Abbreviations: C, control group; T, treatment group; CI, confidence interval; MD, mean difference; RR, relative risk; HBV-DNA, hepatitis B virus DNA; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBil, total bilirubin; HA, hyaluronic acid; LN, laminin; PCIII, type III procollagen; IV-C, type IV collagen; RCT, randomized controlled trial.

References

1. Marrapu S, Kumar R. Chronic hepatitis B: Prevent, diagnose, and treat before the point of no return. *World J Hepatol*. 2024;**16**(10):1151-7. [PubMed ID: 39474571]. [PubMed Central ID: PMC11514616]. https://doi.org/10.4254/wjh.v16.i10.1151.
2. Ma L, Xing HC. Elimination of hepatitis B as a public health threat: Addressing the challenge and taking action. *World J Hepatol*. 2024;**16**(11):1361-4. [PubMed ID: 39606174]. [PubMed Central ID: PMC11586746]. https://doi.org/10.4254/wjh.v16.i11.1361.
3. Qi X, Hu Y, Jiang W. Epidemiological trends and projections to 2035 of hepatitis B burden in China, 1990-2021. *PLoS One*. 2025;**20**(9). e0330633. [PubMed ID: 40892756]. [PubMed Central ID: PMC12404462]. https://doi.org/10.1371/journal.pone.0330633.
4. Zhang S, Cui F. Global progress, challenges and strategies in eliminating public threat of viral hepatitis. *Infect Dis Poverty*. 2025;**14**(1):9. [PubMed ID: 39923069]. [PubMed Central ID: PMC11806526]. https://doi.org/10.1186/s40249-025-01275-y.
5. Peters MG, Yuen MF, Terrault N, Fry J, Lampertico P, Gane E, et al. Chronic Hepatitis B Finite Treatment: Similar and Different Concerns With New Drug Classes. *Clin Infect Dis*. 2024;**78**(4):983-90. [PubMed ID: 37633256]. [PubMed Central ID: PMC11006103]. https://doi.org/10.1093/cid/ciad506.
6. Zheng S, Qi W, Xue T, Zao X, Xie J, Zhang P, et al. Chinese medicine in the treatment of chronic hepatitis B: The mechanisms of signal pathway regulation. *Heliyon*. 2024;**10**(20). e39176. [PubMed ID: 39640799]. [PubMed Central ID: PMC11620126]. https://doi.org/10.1016/j.heliyon.2024.e39176.
7. Huang Y, Lu J, Xu Y, Xiong C, Tong D, Hu N, et al. Xiaochaihu decorction relieves liver fibrosis caused by Schistosoma japonicum infection via the HSP47/TGF-beta pathway. *Parasit Vectors*.

2020;**13**(1):254. [PubMed ID: 32410640]. [PubMed Central ID: PMC7227055]. https://doi.org/10.1186/s13071-020-04121-2.

8. Zhang J, Zhang B, Fauci AJ, Lee MS, Wieland L, Majd I, et al. The Rome consensus: good clinical trials for traditional medicine. *Acupuncture Herbal Med*. 2025;**5**(3):271-2. https://doi.org/10.1097/hm9.0000000000000167.
9. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *Int J Surg*. 2021;**88**:105906. [PubMed ID: 33789826]. https://doi.org/10.1016/j.ijsu.2021.105906.
10. Balshem H, Helfand M, Schunemann HJ, Oxman AD, Kunz R, Brozek J, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol*. 2011;**64**(4):401-6. [PubMed ID: 21208779]. https://doi.org/10.1016/j.jclinepi.2010.07.015.
11. Sterne JAC, Savovic J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;**366**:l4898. [PubMed ID: 31462531]. https://doi.org/10.1136/bmj.l4898.
12. De Cassai A, Pasin L, Boscolo A, Salvagno M, Navalesi P. Trial sequential analysis: plain and simple. *Korean J Anesthesiol*. 2021;**74**(4):363-5. [PubMed ID: 33333708]. [PubMed Central ID: PMC8342843]. https://doi.org/10.4097/kja.20637.
13. Chen Y, Zhou X. [Xiao Chaihu decoction combined with lamivudine in the treatment of chronic hepatitis B complicated with pulmonary tuberculosis: a clinical study of 60 cases]. *Henan Tradit Chinese Med*. 2014;**34**(129):1-2. ZH. https://doi.org/10.16367/j.issn.1003-5028.2014.07.123.
14. Chen Y. [Clinical efficacy study of Xiaochaihu decoction combined with entecavir in the treatment of chronic hepatitis B]. *Diet Health*. 2018;(1-2). ZH. https://doi.org/10.3969/j.issn.2095-8439.2018.48.112.
15. Dong S. [Clinical observation on the efficacy of entecavir combined with Xiaochaihu decoction in the treatment of hepatitis B liver cirrhosis]. *J Med Inform*. 2015;**1**. ZH. https://doi.org/10.3969/j.issn.1006-1959.2015.09.321.
16. Kang Z. [Randomized controlled trial of Xiaochaihu decoction combined with entecavir in the treatment of chronic hepatitis B]. *Practical Clin J Integrated Tradit Chinese Western Med*. 2016;**16**:71-2. ZH. https://doi.org/10.13638/j.issn.1671-4040.2016.02.038.
17. Li J, Yu X. [Clinical efficacy of Xiao Chaihu decoction combined with antiviral agents in the treatment of hepatitis B]. *Chinese J Clin Rational Drug Use*. 2022;**15**:132-40. ZH. https://doi.org/10.15887/j.cnki.13-1389/r.2022.28.041.
18. Li J. [Clinical observation of Xiao Chaihu decoction combined with adefovir dipivoxil in the treatment of chronic hepatitis B]. *For All Health*. 2015;**1**. ZH. https://doi.org/10.3969/j.issn.1009-6019.2015.03.422.
19. Lin J, Zhang Y, Lin P. [Analysis of the clinical efficacy of Xiao Chaihu decoction combined with entecavir in the treatment of chronic hepatitis B]. *Guide China Med*. 2017;**15**:204-5. ZH. https://doi.org/10.15912/j.cnki.gocm.2017.20.165.
20. Ma G. [Clinical observation of the efficacy of Xiao Chaihu decoction combined with entecavir in patients with chronic hepatitis B and its effects on liver function]. *China Practical Med*. 2018;**13**:135-6. ZH. https://doi.org/10.14163/j.cnki.11-5547/r.2018.08.079.
21. Qiu B, Zhang P, Tang X, Li Q, Li D. [Efficacy analysis of Xiao Chai Hu decoction combined with silymarin in the treatment of hepatic fibrosis in chronic hepatitis B]. *Chinese J Primary Med Pharm*. 2010. ZH. https://doi.org/10.3760/cma.j.issn.1008-6706.2010.01.018.
22. Shi H. [Clinical efficacy of entecavir combined with Xiao Chai Hu decoction in the treatment of liver cirrhosis secondary to chronic hepatitis B]. *Shenzhen J Integrated Tradit Chinese Western Med*. 2020;**30**:40-2. ZH. https://doi.org/10.16458/j.cnki.1007-0893.2020.15.020.
23. Shi X. [Clinical efficacy analysis of Xiao Chai Hu decoction combined with entecavir in the treatment of chronic hepatitis B]. *Chinese Community Doctor*. 2012. ZH. https://doi.org/10.3969/j.issn.1007-614x.2012.24.180.
24. Sun W, Xun S, Liu S, Liu Z. *[Clinical observation of 35 cases of chronic hepatitis B treated with Xiao Chaihu decoction combined with interferon-α2b]*. 2005. ZH. Available from: https://med.wanfangdata.com.cn/Paper/Detail?id=PeriodicalPaper_zgzyykj200501047.
25. Wang C. [Clinical efficacy analysis of Xiao Chaihu decoction combined with entecavir in the treatment of chronic hepatitis B]. *Chinese Sci J Database Med Health*. 2023:101-3. ZH.
26. Wu H. [Clinical observation of the efficacy of Xiao Chai Hu decoction combined with lamivudine in the treatment of hepatitis B-related liver cirrhosis]. *World Clin Med*. 2015;**1**. ZH.
27. Xue J. [Clinical observation of Xiao Chaihu decoction in the treatment of hepatic fibrosis in chronic hepatitis B]. *Health Everyone*. 2015:1-2. ZH.
28. Yang Y. [Treatment of 60 cases of chronic hepatitis B with Xiao Chaihu decoction]. *Inner Mongolia J Traditional Chinese Med*. 2009. ZH. https://doi.org/10.3969/j.issn.1006-0979.2009.11.044.
29. Yuan Y, Liu S, Liu Z. [Treatment of 35 cases of chronic hepatitis B with Xiao Chaihu decoction combined with lamivudine]. *Chinese J Integrated Traditional Western Med Liver Dis*. 2002. ZH.
30. Zhou W. [Evaluation of the efficacy of Xiao Chaihu decoction as an adjunctive treatment for chronic hepatitis B]. *Inner Mongolia J Traditional Chinese Med*. 2015;**34**. ZH. https://doi.org/10.16040/j.cnki.cn15-1101.2015.08.041.
31. Zong X, Tan M. *[Clinical observation of the efficacy of Xiao Chaihu decoction combined with entecavir in the treatment of chronic hepatitis B]*. 2018. ZH. Available from: https://med.wanfangdata.com.cn/Paper/Detail?id=PeriodicalPaper_zwnxjkyj201804072.
32. Zeng B, Hu Y, Jiang H, Liu Z. [Treatment of 60 cases of HBV-related liver cirrhosis with modified Xiao Chaihu decoction]. *Henan Traditional Chinese Med*. 2015;**35**:1284-6. ZH. https://doi.org/10.16367/j.issn.1003-5028.2015.06.0538.
33. Chen X. [Treatment of 32 cases of hepatic fibrosis in chronic hepatitis B with modified Xiao Chaihu decoction]. *Hunan J Traditional Chinese Med*. 2017;**33**:57-8. ZH. https://doi.org/10.16808/j.cnki.issn1003-7705.2017.05.025.
34. Dong L, Zhao J. [Clinical observation of Xiao Chaihu decoction combined with bifendate in the treatment of chronic hepatitis B and alpha-fetoprotein-positive patients]. *Ningxia Med J*. 2002:1-2. ZH. https://doi.org/10.3969/j.issn.1001-5949.2002.08.014.
35. Hu F. [Clinical observation of modified Xiao Chaihu decoction in the treatment of chronic hepatitis B with liver-qi stagnation and spleen-deficiency pattern]. *China's Naturopathy*. 2022;**30**:66-9. ZH. https://doi.org/10.19621/j.cnki.11-3555/r.2022.0725.
36. Huang W, Xie L. [Clinical study on supplemented minor bupleurum decoction combined with entecavir tablets in the treatment of chronic hepatitis B]. *Henan Traditional Chinese Med*. 2022;**42**:1305-8. ZH. https://doi.org/10.16367/j.issn.1003-5028.2022.09.0278.
37. Wang M, Zheng D, Cheng Q. [Clinical study of modified Xiao Chaihu decoction combined with adefovir dipivoxil tablets in the treatment of chronic hepatitis B]. *J Commun Med*. 2014:1-2. ZH.
38. Wang R. [Clinical observation of the efficacy of Chaihu decoction combined with antiviral drugs in the treatment of hepatitis B]. *Chinese J Clin Rational Drug Use*. 2018;**11**:68-9. ZH. https://doi.org/10.15887/j.cnki.13-1389/r.2018.22.036.
39. Wang Y. [Effects of Xiao Chaihu decoction combined with Western medicine on liver function and HBV-DNA copy number in patients

with chronic hepatitis B]. *New Chinese Med*. 2016. ZH. https://doi.org/10.13457/j.cnki.jncm.2016.07.033.

40. Wu J, Yang L, Zhang L. [Clinical study on the effects of modified Xiao Chaihu decoction combined with entecavir on serum HA, PC-III, IV-C, LN and IL-17 levels in patients with hepatic fibrosis secondary to chronic hepatitis]. *Women's Health*. 2023:1-2. ZH.
41. Wu Q. [Clinical observation on modified Xiao Chaihu decoction in the treatment of 69 cases of hepatitis B-related liver cirrhosis]. *J Zhejiang Chinese Med Univ*. 2009;**33**(517). ZH. https://doi.org/10.16466/j.issn1005-5509.2009.04.015.
42. Yan K, Cui H, Liu H. [Study on the effects of modified Xiao Chaihu decoction on clinical efficacy and serum liver function-related indices in patients with hepatitis B]. *J Gansu Sci*. 2019:1-6. ZH. https://doi.org/10.16468/j.cnki.issn1004-0366.2019.01.013.
43. Zhao H, Hou T, Shao D. Clinical study on treatment of chronic viral cholestatic hepatitis with chishaodanpi decoction. *J Tradit Chin Med*. 2014;**34**(6):646-51. [PubMed ID: 25618967]. https://doi.org/10.1016/s0254-6272(15)30077-7.
44. Zhou D, Bian Y. [Clinical study on the efficacy of Xiao Chaihu decoction combined with entecavir in the treatment of chronic hepatitis B]. *Electronic J Clin Med Literature*. 2021:1-3. ZH.
45. Zhou L, Ni C. [Efficacy analysis of modified Xiao Chaihu decoction in the treatment of chronic hepatitis B]. *Gems Health*. 2023:1-2. ZH.
46. Tian G, Chi X, Wu L, Chen P, Xiao H. [Interventional effect of modified Xiao Chaihu decoction on common adverse reactions in chronic hepatitis B patients receiving interferon therapy]. *Mod Hospital J*. 2010. ZH. https://doi.org/10.3969/j.issn.1671-332X.2010.09.025.
47. Hu Y. [Clinical observation of 34 cases of chronic hepatitis B-related hepatic fibrosis treated with adefovir dipivoxil combined with modified Xiao Chaihu decoction]. *Hainan Med J*. 2011:1-2. ZH. https://doi.org/10.3969/j.issn.1003-6350.2011.06.014.
48. Li M. [Clinical observation of Xiao Chaihu decoction combined with modern therapy in the treatment of chronic hepatitis B]. *Chinese Sci J Database Med Health*. 2025:1-4. ZH.
49. Sheng X, Zou Z. [Efficacy of Xiao Chaihu decoction combined with interferon-α in the treatment of hepatic fibrosis in chronic hepatitis B and its effects on cellular immune status]. *Chinese Arch Tradit Chinese Med*. 2018;**36**:2016-8. ZH. https://doi.org/10.13193/j.issn.1673-7717.2018.08.060.
50. Wang M. [Clinical observation of Xiao Chaihu decoction in the treatment of hepatic fibrosis in chronic hepatitis B]. *J Frontiers Med*. 2013. ZH. https://doi.org/10.3969/j.issn.2095-1752.2013.33.443.
51. Wang C. [Exploratory study on the application of Xiao Chaihu decoction combined with antiviral drugs in the treatment of hepatitis B]. *Practical Clin J Integrated Traditional Chinese Western Med*. 2013:1-3. ZH.
52. Zhang J, Li Z, Kong C. [Clinical Study of Modified Xiao Chaihu Decoction in Chronic Hepatitis B]. *Shandong J Tradit Chin Med*. 2018:1-6. ZH.
53. Liu L. *[Exploration of the clinical efficacy of Xiao Chaihu decoction in the treatment of chronic hepatitis B]*. 2017. ZH. Available from: https://med.wanfangdata.com.cn/Paper/Detail?id=PeriodicalPaper_yiyqy201723308.
54. Lu L. [Clinical study on the efficacy of Xiao Chaihu decoction combined with entecavir in the treatment of chronic hepatitis B]. *Diet Health*. 2017;**1-2**. ZH. https://doi.org/10.3969/j.issn.2095-8439.2017.21.122.
55. Wang Q. [Clinical study of modified Xiao Chaihu decoction combined with glucocorticoids in the treatment of severe hepatitis B]. *Henan Traditional Chinese Med*. 2015. ZH. https://doi.org/10.16367/j.issn.1003-5028.2015.08.0738.
56. Zou Z. [Clinical observation of modified Xiao Chaihu decoction combined with entecavir in the treatment of chronic hepatitis B with liver-qi stagnation and spleen-deficiency pattern]. *Clin J Chinese Med*. 2016. ZH.
57. Chen L. [Clinical observation of 35 cases of chronic hepatitis B treated with Xiao Chaihu decoction combined with lamivudine]. *Chinese Med Mod Distance Educ China*. 2013;**1**. ZH.
58. Hu D, Wei Y. [Study on modified Xiao Chaihu decoction in the treatment of chronic hepatitis B and the mechanism of its formula composition]. *Inner Mongolia J Traditional Chinese Med*. 2017:1-2. ZH. https://doi.org/10.16040/j.cnki.cn15-1101.2017.20.069.
59. Wu X. [Treatment of 80 cases of chronic hepatitis B with modified Xiao Chaihu decoction combined with lamivudine]. *J Guizhou Univ Traditional Chinese Med*. 2018;**40**:66-9. ZH. https://doi.org/10.16588/j.cnki.issn1002-1108.2018.05.015.
60. Zhang Y, Liu Z. [Preliminary clinical observation of the efficacy of modified Xiao Chaihu decoction combined with interferon in the treatment of HBeAg-positive chronic hepatitis B]. *China Practical Med*. 2008:1-2. ZH. https://doi.org/10.14163/j.cnki.11-5547/r.2008.33.074.
61. Fang A. [Clinical observation of the efficacy of modified Xiao Chaihu decoction on abnormal liver function in patients with chronic hepatitis B]. *Inner Mongolia J Traditional Chinese Med*. 2017;**36**(48). ZH. https://doi.org/10.16040/j.cnki.cn15-1101.2017.14.049.
62. Qian Z, Hu M, Wu H, Chen H, Liao G, Kang Z, et al. The Efficacy of Antiviral Treatment for Chronic Hepatitis B Patients with Normal ALT Levels: A Systematic Review and Meta-analysis. *Hepat Mon*. 2022;**22**(1). https://doi.org/10.5812/hepatmon-129836.
63. Qiang R, Zhang Y, Wang Y. Mechanisms of Xiaochaihu Decoction on Treating Hepatic Fibrosis Explored by Network Pharmacology. *Dis Markers*. 2022;**2022**:8925637. [PubMed ID: 36246566]. [PubMed Central ID: PMC9553551]. https://doi.org/10.1155/2022/8925637.
64. Hu R, Jia WY, Xu SF, Zhu ZW, Xiao Z, Yu SY, et al. Xiaochaihutang Inhibits the Activation of Hepatic Stellate Cell Line T6 Through the Nrf2 Pathway. *Front Pharmacol*. 2018;**9**:1516. [PubMed ID: 30666206]. [PubMed Central ID: PMC6330344]. https://doi.org/10.3389/fphar.2018.01516.
65. Wang SJ, Ye W, Li WY, Tian W, Zhang M, Sun Y, et al. Effects and mechanisms of Xiaochaihu Tang against liver fibrosis: An integration of network pharmacology, molecular docking and experimental validation. *J Ethnopharmacol*. 2023;**303**:116053. [PubMed ID: 36529247]. https://doi.org/10.1016/j.jep.2022.116053.
66. Li J, Hu R, Xu S, Li Y, Qin Y, Wu Q, et al. Xiaochaihutang attenuates liver fibrosis by activation of Nrf2 pathway in rats. *Biomed Pharmacother*. 2017;**96**:847-53. [PubMed ID: 29078262]. https://doi.org/10.1016/j.biopha.2017.10.065.
67. Kong DZ, Liang N, Yang GL, Zhang Z, Liu Y, Li J, et al. Xiao Chai Hu Tang, a herbal medicine, for chronic hepatitis B. *Cochrane Database Syst Rev*. 2019;**2019**(11). https://doi.org/10.1002/14651858.CD013090.pub2.

Table 2. Study Characteristics [a]

Study	Disease	Age (T/C)	Sample Size (T/C)	Course of the Disease (y) (T/C)	Intervention (T/C)		Course of Treatment (mon)	Outcome
Chen et al. (2014), (13)	CHB with pulmonary tuberculosis	34.32 ± 3.19	60/60	2.81 ± 0.3	XCHD + WM	WM	3	①④⑤⑥⑦⑫
Chen, (2018), (14)	CHB	40.72 ± 7.28/ 41.3 ± 8.44	40/40	5.02 ± 3.11/ 5.56 ± 2.7	XCHD + WM	WM	5	①②④⑥
Dong, (2015), (15)	CHB	42.5 ± 11.3	148/149	8.2 ± 4.1	XCHD + WM	WM	3	④⑤⑫
Kang, (2016), (16)	CHB	41.89 ± 8.34/ 42.33 ± 7.58	40/41	4.77 ± 2.87/ 4.46 ± 2.66	XCHD + WM	WM	7	①②④⑥
Li and Yu (2022), (17)	CHB	48.19 ± 4.21/ 48.51 ± 4.45	35/35	6.25 ± 0.17/ 6.56 ± 0.15	XCHD + WM	WM	3	④⑤⑥⑦⑫
Li, (2015), (18)	CHB	44.85 ± 12.42/ 45.10 ± 13.24	50/50	-	XCHD + WM	WM	10	①②④⑤
Lin et al., (2017), (19)	CHB	43.53 ± 10.31	49/49	6.78 ± 3.12	XCHD + WM	WM	7	①②④⑥
Ma, (2018), (20)	CHB	37.09 ± 7.64/ 36.83 ± 7.39	32/32	4.61 ± 1.8 /4.58 ± 2.14	XCHD + WM	WM	7	④⑥⑦
Qiu et al., (2010), (21)	CHB with HF	48.1 ± 6.9/ 46.2 ± 5.8	50/40	-	XCHD + WM	WM	6	①②④⑤⑦⑧⑨⑩⑪⑫
Shi, (2020), (22)	CHB	54.20 ± 5/ 53.09 ± 4.5	40/40	7.9 ± 2.5/ 7.2 ± 2	XCHD + WM	WM	8	④⑤⑥⑦⑫
Shi, (2012), (23)	CHB	41.4 ± 10.9/ 42.6 ± 11.2	46/46	5.3 ± 3.5/ 4.9 ± 3.1	XCHD + WM	WM	8	①②④
Sun et al., (2005), (24)	CHB	-	35/30	-	XCHD + WM	WM	6	①②③④⑤
Wang, (2023), (25)	CHB	52.23 ± 5.16/ 51.12 ± 4.36	46/46	8.01 ± 2.16/ 7.67 ± 2.35	XCHD + WM	WM	8	④⑤⑥⑦⑫
Wu, (2015), (26)	CHB cirrhosis	44.5 ± 7.6/ 44.1 ± 7.3	46/46	12.5 ± 4.7/ 12.1 ± 4.4	XCHD + WM	WM	5	④⑤⑦
Xue, 2015 (27)	CHB with HF	47.35 ± 4.36/ 48.67 ± 4.91	44/29	3.9 ± 0.7/ 4.0 ± 0.9	XCHD + WM	WM	4	④⑤⑦⑧⑨⑩⑪⑫
Yang, (2009), (28)	CHB	36.8/37	60/60	5.5/ 6.5	XCHD + WM	WM	2	①②⑥⑫
Yuan et al., (2002), (29)	CHB	29.7/32.3	35/30	31.5/28.2	XCHD + WM	WM	6	①②③④⑦
Zhou, (2015), (30)	CHB	43.81 ± 5.76/ 43.77 ± 5.82	41/41	4.73 ± 3.32/ 4.7 ± 3.28	XCHD + WM	WM	3	⑥
Zong, (2018), (31)	CHB	41.78 ± 10.85/ 42.11 ± 11.12	43/43	5.32 ± 1.54/ 5.58 ± 1.61	XCHD + WM	WM	8	①②④⑥
Zeng et al., (2015), (32)	CHB cirrhosis	64.42 ± 3.81/ 64.56 ± 3.9	60/60	4.53 ± 1.66/ 4.61 ± 1.72	XCHD + WM	WM	-	④⑤⑦⑧⑨⑩
Chen, (2017), (33)	CHB with HF	32.5 ± 10.2/ 35.2 ± 9.7	32/32	3.1 ± 1.6/ 3.8 ± 1.2	XCHD + WM	WM	3	④⑤⑦⑧⑨⑩⑪
Dong and Zhao, (2002), (34)	CHB	36/33	35/30	1-4.5/ 0.6-5	XCHD + WM	WM	1	④⑤⑥
Hu, (2022), (35)	CHB	47.33 ± 7.23/ 48.67 ± 8.22	30/30	7.23 ± 2.65/ 7.61 ± 2.98	XCHD + WM	WM	11	④⑤⑥⑦
Huang and Xie, (2022), (36)	CHB	48.51 ± 7.27/ 48.74 ± 7.31	140/140	7.68 ± 1.06/ 7.93 ± 1.18	XCHD + WM	WM	6	④⑤⑥⑦⑧⑨⑩⑫
Wang et al., (2014), (37)	CHB	40.2 ± 5.2	90/90	6.8 ± 1.8	XCHD + WM	WM	11	①②④⑧⑨⑩
Wang, (2018), (38)	CHB	41.78 ± 15.16/ 41.29 ± 15.42	41/41	-	XCHD + WM	WM	12	①②④⑤⑦⑫
Wang, (2016), (39)	CHB	35.1 ± 7.9/ 35.8 ± 8.1	41/41	2.5 ± 0.8/ 2.4 ± 0.9	XCHD + WM	WM	6	④⑤⑦
Wu et al., (2023), (40)	CHB with HF	46.83 ± 8.16/ 46.85 ± 8.14	40/40	8.29 ± 2.71/ 8.26 ± 2.73	XCHD + WM	WM	6	⑥⑧⑨⑩⑪
Wu, (2009), (41)	CHB	56/56	69/73	5/ 9.5	XCHD + WM	WM	6	④⑤⑥⑧⑨⑩
Yan et al., (2019), (42)	CHB	39.7 ± 7.5/ 39.3 ± 7.2	72/72	2.3 ± 0.9/ 2.1 ± 0.7	XCHD + WM	WM	12	①②④⑤⑥⑦⑧⑨⑩⑪⑫
Zhao et al., (2014), (43)	CHB	38.1 ± 3.1/ 40 ± 4.6	40/39	0.8-20/ 1-18	XCHD + WM	WM	12	①②④⑤⑦
Zhou and Bian,								

Study	Disease	Age (T/C)	Sample Size (T/C)	Course of the Disease (y) (T/C)	Intervention (T/C)		Course of Treatment (mon)	Outcome
(2021), (44)	CHB	48.49 ± 3.53/ 47.61 ± 3.22	25/25	8.12 ± 1.47/ 7.69 ± 1.23	XCHD + WM	WM	6	④⑤⑥⑦⑫
Zhou and Ni (2023), (45)	CHB	44.26 ± 2.17/ 44.85 ± 2.15	30/30	7.06 ± 1.34/ 7.15 ± 1.25	XCHD + WM	WM	4	④⑤⑥⑦⑧⑨⑩⑫
Tian et al., (2010), (46)	CHB	-	20/20	39	XCHD + WM	WM	6	①②④
Hu, (2011), (47)	CHB with HF	45	34/28	9	XCHD + WM	WM	11	①④⑧⑩⑪
Li, (2025), (48)	CHB	37.34 ± 6.24/ 38.82 ± 5.75	40/40	2.95 ± 0.64/ 3.27 ± 0.75	XCHD + WM	WM	6	①②④⑤⑦⑨⑪
Sheng and Zou (2018), (49)	CHB with HF	48.4 ± 8.9/ 49.1 ± 9.9	40/40	6.5 ± 1.8/ 6.1 ± 2.1	XCHD + WM	WM	5	①②③④⑤⑦⑧⑨⑩⑪
Wang, (2013), (50)	CHB with HF	40.2 ± 1.2/ 42.1 ± 1.5	80/80	0.75-10/ 0.6 - 9	XCHD + WM	WM	4	④⑤⑫
Wang, (2013), (51)	CHB	43.60/ 45.1	48/48	0.5 -6/ 0.5 - 5	XCHD + WM	WM	12	①②④⑧⑩⑪
Zhang et al., (2018), (52)	CHB	41.83 ± 3.5/ 40.91 ± 3.26	48/48	69.65 ± 5.37/ 68.54 ± 5.29	XCHD + WM	WM	1	①②③⑥
Liu, (2017), (53)	CHB	63.50 ± 4.7/ 63.6 ± 4.3	40/40	-	XCHD + WM	WM	3	⑥⑫
Lu, (2017), (54)	CHB	40.72 ± 7.28/ 41.3 ± 8.44	40/40	5.02 ± 3.11/ 5.56 ± 2.70	XCHD + WM	WM	5	①②④⑥
Wang, (2015), (55)	CHB	43.18 ± 8.62/ 44.05 ± 9.17	74/74	5.18 ± 3.26/ 5.36 ± 3.19	XCHD + WM	WM	-	①②④⑥⑦
Zou, (2016), (56)	CHB	58	48/48	-	XCHD + WM	WM	-	①②④⑥
Chen, (2013), (57)	CHB	39	35/35	-	XCHD + WM	WM	6	①②
Hu, (2017), (58)	CHB	55.5	60/60	2.7 ± 1.0	XCHD + WM	WM	3	①④⑤
Wu, (2018), (59)	CHB	38.88 ± 13.33/ 37.61 ± 12.78	40/40	10 ± 0.51/ 11 ± 0.52	XCHD + WM	WM	3	①②④⑤⑥⑦⑧⑨⑪
Zhang and Liu, (2008), (60)	CHB	41.25 ± 6.55/ 40.67 ± 6.48	40/45	7.55 ± 3.58/ 7.17 ± 3.45	XCHD + WM	WM	6	①②④⑤
Fang, (2017), (61)	CHB	36.6 ± 14.71/ 42.2 ± 12.13	30/30	-	XCHD + WM	WM	1	④⑤⑥

[a] Abbreviations: T, treatment group; C, control group; XCHD, *Xiaochaihu decoction*; WM, Western medicine; CHB, chronic hepatitis B; HF, Hepatic Fibrosis; ① HBV-DNA, hepatitis B virus DNA; ② HBeAg, hepatitis B e antigen; ③ HBsAg, hepatitis B surface antigen; ④ ALT, alanine aminotransferase; ⑤ AST, aspartate aminotransferase; ⑥ total clinical efficacy; ⑦ TBil, total bilirubin; ⑧ HA, hyaluronic acid; ⑨ LN, laminin; ⑩ PCIII, type III procollagen; ⑪ IV-C, type IV collagen; ⑫ adverse events.