Supplementary Material A

1 Diagnostic criteria for Chronic Hepatitis B

This section summarizes the operational diagnostic framework used to map trial populations to chronic hepatitis B (CHB) and related CHB with fibrosis/cirrhosis phenotypes during study selection. The review accepted the diagnostic criteria reported by eligible randomized trials and mapped them to contemporary guideline terminology where possible.

The level of evidence for diagnostic tests and general screening is not specified, as recommendations are primarily based on clinical experience, observational studies, epidemiological data, and expert consensus.

The initial screening for HBV should include HBsAg (hepatitis B surface antigen) and anti-HBc (hepatitis B core antibody) assessments. HBsAg positivity is the most important screening parameter. When the HBV infects hepatocytes, large amounts of HBsAg are secreted. This excess antigen is released into the bloodstream, making it relatively easy to detect even in the early stages of infection HBsAg testing is well-established and standardised worldwide, making it reliable and easy to interpret in different clinical and epidemiological settings. HBsAg is typically measured using highly sensitive enzyme immunoassays with a limit of detection (LOD) of <0.05 IU/ml. However, during the early stages of acute HBV infection.

HBsAg levels may fall below the detection threshold, potentially leading to false-negative results. This pre-HBsAg window where HBV DNA is positive but HBsAg is not detectable may last weeks. Low HBsAg levels can also occur in persistent or reactivated HBV infection under immunosuppression.11 More sensitive HBsAg assays (LOD <0.005 IU/ml) can be useful when nucleic acid testing (NAT) is not available. False-negative and -positive HBsAg results can complicate the diagnosis. False-negative HBsAg results may occur due to variations in HBsAg epitopes not recognised by all assays. Additionally, different HBsAg tests use various antibodies and have different capabilities to dissociate HBsAg from immune complexes, potentially leading to conflicting results. Anti-HBc and HBV DNA testing are reliable methods to resolve these discrepancies.

False-positive HBsAg results, which can occur in patients on haemodialysis, post-mortem organ donors, individuals with heterophilic antibodies, or those receiving G-CSF, can generally be ruled out by performing neutralisation with anti-HBs, the manufacturer-recommended confirmatory test. Sequential HBsAg measurements, combined with other virological markers, can further enhance diagnostic accuracy and provide a more comprehensive understanding of the infection status.

Anti-HBc antibodies may arise after any encounter with HBV and indicate a past or current infection. Although historically there were many versions of anti-HBc tests, nowadays most countries and laboratories are using state-of-the-art FDA approved or CE-marked assays, which are more than 99.8% specific and are considered the most sensitive for donor screening and assessment of past HBV exposure. These are total anti-HBc assays, since they detect both immunoglobulinM (IgM) and immunoglobulin G (IgG) antibodies to HBcAg; no test for IgG anti-HBc alone is commercially available. Importantly, detection of anti-HBc IgG alone does not indicate whether the infection is

ongoing or resolved. These individuals may be HBsAg-negative but anti-HBc-positive, necessitating monitoring and/or preventive measures (see section "Prophylaxis of HBV reactivation"). Thus, anti-HBc screening enhances the understanding of an individual's HBV history and informs appropriate clinical actions to manage reactivation risks.

Anti-HBs can provide valuable insights into vaccination status, particularly when both HBsAg and anti-HBc are negative, and can aid in risk stratification for HBVr in patients undergoing immunosuppressive treatment. However, routine anti-HBs testing is not essential for determining HBV infection status. While including anti-HBs testing in initial screening may offer additional information, it is likely not cost-effective. Screening for HBV in diverse populations is crucial for early detection, transmission prevention, and effective infection management, ultimately alleviating the disease burden on individuals and society. Given the global prevalence of chronic HBV infection (HBsAg-positive) at approximately 3.2%, a proactive approach to HBV diagnosis is warranted.

HBV infections are widespread, with highly endemic regions, such as parts of Asia, the South Pacific, sub-Saharan Africa, South America, and the Middle East, showing anti-HBc positivity rates exceeding 50%. Intermediate-prevalence regions, including the Mediterranean and Eastern Europe, have antiHBc positivity rates of 10-50%. Individuals born in these regions, or whose mothers are from these areas, are at an elevated risk of being HBsAg-positive. Screening migrants from these regions enables early diagnosis, helps to slow the progression of liver disease, and has been proven to be cost-effective. To protect public health and prevent transmission, household members, sexual partners, and close contacts of individuals with HBV infection should be screened for HBV. Those who test negative for both HBsAg and anti-HBc should be offered vaccination.

HBV DNA serves as a key marker for HBV viraemia, commonly assessed using sensitive NAT in clinical settings. Numerous commercial NAT assays, predominantly using realtime PCR, are available to quantify HBV DNA in clinical samples. The prognostic significance of HBV viraemia is substantial, establishing quantitative HBV DNA detection (standardised in IU/ml) as the gold standard.

HBeAg, a marker for the replication of the wild-type virus, is essential for classifying the phase of HBV infection (Table 1). ELISA (enzyme-linked immunosorbent assay) and enzyme-linked fluorescence assays are commonly used to detect HBeAg.

In resource-limited areas where HBV DNA is not available, HBeAg (in combination with alanine aminotransferase [ALT]) can be used to establish the indication for therapy and predict the risk of vertical transmission. Due to their low cost and ease of use, rapid diagnostic tests (RDTs) are widely used in resource-limited countries. However, the diagnostic performance of the currently commercialised HBeAg RDTs is insufficient to recommend their use as an alternative to standard ELISA.

Anti-HBe serostatus is used to define the disease phase and to assess the evolution of the disease, as well as a patient's response to therapy, since spontaneous or treatment-

induced HBeAg/anti-HBe seroconversion is associated with a decline in viral replication, lower rates of disease progression and improved survival rates.

Quantitative HBsAg cannot replace HBV DNA measurement but can provide additional value, such as helping to differentiate the phases of chronic HBV infection (see Table 1) and guiding treatment. Quantitative HBsAg testing is valuable in distinguishing between low viraemic phases of HBeAgnegative chronic HBV infection and HBeAg-negative chronic hepatitis. Individuals with HBeAg-negative infection (formerly “inactive carriers”) can be identified by HBV DNA levels <2,000 IU/ml and HBsAg <1,000 IU/ml, achieving a diagnostic accuracy of 85-94% in Asian and European cohorts. In a multicentre cohort across Asia, Europe, and Australia, HBsAg <100 IU/ml combined with HBV DNA <2,000 IU/ml offered greater specificity and the highest positive predictive value for identifying HBeAg-negative infection across all HBV genotypes. A higher risk of reactivation, i.e. progression from HBeAg-negative infection to HBeAg-negative hepatitis, exists with HBV DNA <2,000 IU/ml and HBsAg >1,000 IU/ml. In addition, Asian cohort studies showed that, in HBeAgnegative individuals with HBV DNA <2,000 IU/ml, the risk of HCC is significantly higher in those with HBsAg levels ≥ 1,000 IU/ml than in those with HBsAg <1,000 IU/ml. In HBeAgpositive individuals, HBsAg levels help to classify the phase of infection, with patients showing exceptionally high HBsAg (>25,000 IU/ml) being less likely to have significant fibrosis, representing a population at lower risk for HCC during HBeAg-positive infection. Monitoring HBsAg dynamics in untreated HBeAg-positive individuals can provide valuable insights into disease progression, HCC risk, a possible phase transition, the durability of spontaneous seroconversion, and the potential for subsequent HBsAg seroclearance.

HBsAg quantification is important for managing pegylated interferon-alfa (PEG-IFNa) treatment and stratification of patients eligible for stopping therapy with nucleos(t)ide analogues (NAs). Quantitative HBsAg testing is increasingly important for defining treatment endpoints. While the ultimate goal of treatment and the primary endpoint for phase II/III trials of finite treatments for chronic HBV infection is a "functional" cure, defined as sustained HBsAg loss (at least 24 weeks off therapy) with HBV DNA below the limit of quantification (LOQ), a sustained HBsAg level <100 IU/ml with HBV DNA <LOQ at 24 weeks off therapy is now being proposed as an alternative intermediate endpoint, or "partial cure".

Anti-HBc IgM is typically present in high concentrations during acute hepatitis B and usually declines to undetectable levels within 6 months. However, lower concentrations can also be detected in chronic HBV infection and during exacerbations of chronic hepatitis B. Consequently, anti-HBc IgM alone has limited diagnostic value, as it may be present in both acute and chronic stages of infection. However, quantifying anti-HBc IgM can help differentiate acute hepatitis B from chronic hepatitis B with acute exacerbation, as higher concentrations are more indicative of acute infection.

Anti-HBs antibodies indicate natural or post-vaccination immunity. Testing anti-HBs level is not necessary for screening (see above). Measurement of anti-HBs antibodies can be considered to document anti-HBs seroconversion following HBsAg

loss. Additionally, it may help assess the risk of HBVr in patients undergoing immunosuppressive therapy.

Table A1. Phase of chronic HBV infection

	Phase 1 HBeAg-positive chronic infection	**Phase 2 HBeAg-positive chronic hepatitis**	**Phase 3 HBeAg-negative chronic infection**	**Phase 4 HBeAg-negative chronic hepatitis**
HBsAg	High	Intermediate to high	Low, usually <1,000 IU/ml	Intermediate, usually >1,000 IU/ml
HBV DNA	High, usually ≥10^7 IU/ml	Moderate to high, usually 10^4–10^7 IU/ml	Usually <2,000 IU/ml	Usually >2,000 IU/ml
ALT	Normal	Elevated	Normal	Elevated*
Liver disease progression (if untreated)	None/minimal	Moderate to severe	None	Mild to severe

ALT, alanine aminotransferase; HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus.

*Either persistently or intermittently.

Table A2. Recommended serological and virological diagnostics for HBsAg-positive/anti-HBc-positive individuals

Diagnostic test	**Recommendation**	**Grade**
HBV DNA quantitative	HBV DNA should be tested, as it serves as the most important prognostic marker and is critical for treatment indication and treatment monitoring.	Strong
HBsAg quantitative	HBsAg quantification should be tested to characterize disease phase, define prognosis and guide treatment.	Strong
Anti-HBs	Anti-HBs is not necessary for diagnosis of HBV infection; anti-HBs is useful to determine immunisation status if HBsAg is negative and to evaluate seroconversion after	Weak

	HBsAg loss.	
HBeAg	HBeAg should be tested to define the disease phase.	Strong
Anti-HBe	Anti-HBe can be tested to define the disease phase (especially if HBeAg is negative).	Weak
Anti-HBc IgM	If acute hepatitis B is suspected, anti-HBc IgM can be tested (ideally quantitative).	Weak
HBV genotype	Genotype can be tested to optimise stratification for interferon-based treatment and estimate risk of HCC.	Weak
HDV screening	Anti-HDV should be tested.	Strong
HCV screening	Anti-HCV should be tested.	Strong
HIV screening	Anti-HIV1/2 should be tested.	Strong

HBeAg, hepatitis B e antigen; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HDV, hepatitis D virus; HEV, hepatitis E virus; HIV, human immunodeficiency virus.

The following are the criteria for evaluating total clinical efficacy:

Significantly effective: HBsAg loss or seroconversion with HBV DNA undetectable by a sensitive assay and ALT normalization. If baseline HBeAg-positive, HBeAg negativity was considered supportive of this status.

Effective: Virological suppression (HBV DNA undetectable) together with ALT normalization; for HBeAg-positive cases, HBeAg negativity further supported effectiveness. No clinical worsening was observed during the reported observation period.

Ineffective: Failure to meet the above targets or occurrence of virological breakthrough (a ≥1 log10 IU/mL increase from nadir or rebound to detectability after suppression), persistent or worsening ALT elevation, lack of meaningful HBV DNA decline, or clinical deterioration.

Total clinical efficacy rate = (Significantly effective + Effective) / total cases × 100%.

2 Detailed information for Xiaochaihu decoction

Xiaochaihu decoction (XCHD) is a classical Chinese herbal formula composed of Radix Bupleuri, Radix Scutellariae, Rhizoma Pinelliae, Rhizoma Zingiberis Recens, Fructus Jujubae, Radix Ginseng, and Radix Glycyrrhizae. Trials were considered eligible when the intervention retained this core prescription and was explicitly described as XCHD or a modified XCHD-based formula.

Analytic handling of intervention heterogeneity: studies were eligible only when XCHD was added to the same background western medicine within each trial. Across-

trial variation in background western medicine and syndrome-based modifications of XCHD was judged acceptable for a review of adjunctive therapy, but pooled effects were interpreted as average add-on effects across heterogeneous clinical settings rather than as proof of a single standardized co-intervention.

Dose form was usually a decoction taken orally; however, reporting of dose, preparation details, and permitted modifications was inconsistent across trials, which precluded meaningful quantitative subgrouping by formulation or dosage. These sources of intervention heterogeneity were therefore considered narratively in the interpretation of results. The details are shown in Table A.3.

Table A3. Intervention Details of Included Studies

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
Dong 2002	XCHD + conventional treatment	Chaihu (Bupleurum chinense DC), Huangqin (Scutellaria baicalensis Georgi), Gancao (Glycyrrhiza uralensis Fisch), Banxia (Pinellia ternata （Thunb.）Breit), Shengjiang (Zingiber officinale Rosc), Renshen (Panax ginseng C. A. Mey), Dazao (Ziziphus jujuba Mill).	Decoction + oral bifendate	Energy mixture, Ganbifu, Yiganning granules, Vidarabine
Yuan 2002	XCHD + lamivudine	Chaihu (Bupleurum chinense DC), Huangqin (Scutellaria baicalensis Georgi), Gancao (Glycyrrhiza uralensis Fisch), Banxia (Pinellia ternata （Thunb.）Breit), Shengjiang (Zingiber officinale Rosc), Renshen (Panax ginseng C. A. Mey), Dazao (Ziziphus jujuba Mill).	Decoction	Yinzhihuang injection, Ganlixin, Ganyanling, Yiganning granules
Sun 2005	XCHD + IFN-α-2b	Chaihu (Bupleurum chinense DC), Huangqin (Scutellaria baicalensis Georgi), Gancao (Glycyrrhiza uralensis Fisch), Banxia (Pinellia ternata （Thunb.）Breit),	Decoction	Potassium magnesium aspartate injection

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
		Shengjiang (Zingiber officinale Rosc), Renshen (Panax ginseng C. A. Mey), Dazao (Ziziphus jujuba Mill).		
Zhang 2008	XCHD + IFN-α-2b	Chaihu (Bupleurum chinense DC) 12 g, Huangqin (Scutellaria baicalensis Georgi) 9 g, Renshen (Panax ginseng C. A. Mey) 6 g, Banxia (Pinellia ternata （Thunb.）Breit) 9 g, Danshen (Salvia miltiorrhiza Bge) 25 g, Huangqi (Astragalus membranaceus) 20 g, Gancao (Glycyrrhiza uralensis Fisch) 5 g, Shengjiang (Zingiber officinale Rosc) 9 g, Dazao (Ziziphus jujuba Mill) 4 pieces.	Decoction	IFN-α-2b + conventional liver protection
Wu 2009	Modified XCHD	Chaihu (Bupleurum chinense DC) 10 g, Dangshen (Codonopsis pilosula) 10 g (or Pseudostellaria root 15 g), Banxia (Pinellia ternata （Thunb.）Breit) 6 g, Huangqin (Scutellaria baicalensis Georgi) 6 g, Gancao (Glycyrrhiza uralensis Fisch) 5 g, Curcuma root tuber 12 g, Baizhi (Angelica dahurica) 15 g.	Decoction	Conventional western liver protection, enzyme reduction, anti-liver fibrosis
Yang 2009	XCHD + conventional liver protection	Chaihu (Bupleurum chinense DC) 15g, Huangqin (Scutellaria baicalensis Georgi) 15g, Gancao	Decoction	Conventional liver protection drugs

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
		(Glycyrrhiza uralensis Fisch) 5g, Banxia (Pinellia ternata （Thunb.）Breit) 10g, Shengjiang (Zingiber officinale Rosc) 10g, Renshen (Panax ginseng C. A. Mey) 15g, Dazao (Ziziphus jujuba Mill) 10 pieces.		
Qiu 2010	XCHD + conventional liver protection	Chaihu (Bupleurum chinense DC) 20g, Huangqin (Scutellaria baicalensis Georgi) 12g, Gancao (Glycyrrhiza uralensis Fisch) 5g, Banxia (Pinellia ternata （Thunb.）Breit) 12g, Shengjiang (Zingiber officinale Rosc) 9g, Renshen (Panax ginseng C. A. Mey) 9g, Dazao (Ziziphus jujuba Mill) 12g.	Decoction	Conventional liver protection drugs
Tian 2010	XCHD + interferon	Chaihu (Bupleurum chinense DC) 10 g, Huangqin (Scutellaria baicalensis Georgi) 15 g, Banxia (Pinellia ternata（Thunb.） Breit) 10 g, Dangshen (Codonopsis pilosula) 10 g, Gancao (Glycyrrhiza uralensis Fisch) 5 g, Shengjiang (Zingiber officinale Rosc) 5 g, Dazao (Ziziphus jujuba Mill) 10 g.	Decoction	Interferon
Hu 2011	XCHD + adefovir dipivoxil	Chaihu (Bupleurum chinense DC) 15 g, Huangqin (Scutellaria baicalensis Georgi) 10 g, Gancao (Glycyrrhiza uralensis Fisch)	Decoction	Adefovir dipivoxil

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
		6 g, Dangshen (Codonopsis pilosula) 30 g, Banxia (Pinellia ternata（Thunb.）Breit) 10 g, Chishao (Paeonia lactiflora Pall) 15 g, Baizhi (Angelica dahurica) 12 g, Danshen (Salvia miltiorrhiza Bge) 15 g, Cangzhu (Atractylodes lancea) 15 g, Yinchen (Artemisia capillaris Thunb) 10 g, Fuling (Poria cocos) 30 g.		
Shi 2012	XCHD + entecavir	Chaihu (Bupleurum chinense DC), Huangqin (Scutellaria baicalensis Georgi), Gancao (Glycyrrhiza uralensis Fisch), Banxia (Pinellia ternata（Thunb.）Breit), Shengjiang (Zingiber officinale Rosc), Renshen (Panax ginseng C. A. Mey), Dazao (Ziziphus jujuba Mill).	Decoction	Entecavir
Chen 2013	XCHD + lamivudine	Specific ingredients and doses were not clearly reported; the article only stated that Xiaochaihu decoction was additionally administered (100 mL each time, twice daily).	Decoction	Lamivudine
Wang 2013	XCHD + conventional liver protection	Chaihu (Bupleurum chinense DC) 15 g, Huangqin (Scutellaria baicalensis Georgi) 9 g, Gancao (Glycyrrhiza uralensis Fisch) 9 g, Banxia (Pinellia ternata（Thunb.）Breit) 9 g, Shengjiang (Zingiber	Decoction	Conventional liver protection treatment

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
		officinale Rosc) 9 g, Renshen (Panax ginseng C. A. Mey) 9 g, Dazao (Ziziphus jujuba Mill) 9 g.		
Wang 2013	XCHD + adefovir dipivoxil	Chaihu (Bupleurum chinense DC) 15 g, Danshen (Salvia miltiorrhiza Bge) 10 g, Huangqin (Scutellaria baicalensis Georgi) 10 g, Banxia (Pinellia ternata （Thunb.）Breit) 6 g, Renshen (Panax ginseng C. A. Mey) 6 g, Gancao (Glycyrrhiza uralensis Fisch) 3 g, Shengjiang (Zingiber officinale Rosc) 6 g, Dazao (Ziziphus jujuba Mill) 12 g, Baizhi (Angelica dahurica) 12 g, Cangzhu (Atractylodes lancea) 15 g, Yinchen (Artemisia capillaris Thunb) 10 g, Fuling (Poria cocos) 30 g.	Decoction	Adefovir dipivoxil
Chen 2013	XCHD + routine anti-TB + lamivudine	Chaihu (Bupleurum chinense DC), Huangqin (Scutellaria baicalensis Georgi), Gancao (Glycyrrhiza uralensis Fisch), Banxia (Pinellia ternata （Thunb.）Breit), Shengjiang (Zingiber officinale Rosc), Renshen (Panax ginseng C. A. Mey), Dazao (Ziziphus jujuba Mill).	Decoction	Routine anti-tuberculosis + lamivudine
Wang 2014	XCHD + adefovir dipivoxil	Chaihu (Bupleurum chinense DC) 12 g, Xuejie (Daemonorops draco Bl) 15 g, Fuling (Poria cocos) 15 g,	Decoction	Adefovir dipivoxil

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
		Huangqi (Astragalus membranaceus) 30 g, Huangqin (Scutellaria baicalensis Georgi) 12 g, Banxia (Pinellia ternata （Thunb.）Breit) 12 g, Chenpi (Citrus reticulata Blanco) 12 g, Dangshen (Codonopsis pilosula) 9 g, Baizhi (Angelica dahurica) 9 g, Zhuru (Bambusa tuldoides Munro) 9 g, Gancao (Glycyrrhiza uralensis Fisch) 6 g, Dazao (Ziziphus jujuba Mill) 3 pieces, Shengjiang (Zingiber officinale Rosc) 3 slices.		
Zhao 2014	Modified XCHD + adefovir dipivoxil	Chaihu (Bupleurum chinense DC) 6 g, Huangqin (Scutellaria baicalensis Georgi) 10 g, Dangshen (Codonopsis pilosula) 10 g, Huangqi (Astragalus membranaceus) 24 g, Fuling (Poria cocos) 15 g, Yinchen (Artemisia capillaris Thunb) 15 g, Xuejie (Daemonorops draco Bl) 15 g, Gancao (Glycyrrhiza uralensis Fisch) 6 g.	Granules	Adefovir dipivoxil
Zeng 2015	XCHD + conventional treatment	Chaihu (Bupleurum chinense DC) 15g, Huangqin (Scutellaria baicalensis Georgi) 12g, Banxia (Pinellia ternata（Thunb.）Breit) 9g, Shengjiang (Zingiber officinale Rosc) 9g, Shaoyao (Radix Paeoniae)12g, Danggui (Radix Angelicae	Decoction	Conventional western treatment

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
		Sinensis) 12g, Danshen (Radix Salviae Miltiorrhizae) 15g, Yujin (Radix Curcumae) 10g, Baizhu (Rhizoma Atractylodis Macrocephalae) 10g, Fuling (Poria Cocos) 20g.		
Dong 2015	XCHD + conventional treatment	Chaihu (Bupleurum chinense DC) 15g, Huangqin (Scutellaria baicalensis Georgi) 9g, Gancao (Glycyrrhiza uralensis Fisch) 9g, Banxia (Pinellia ternata （Thunb.）Breit) 9g, Shengjiang (Zingiber officinale Rosc) 9g, Renshen (Panax ginseng C. A. Mey) 9g, Dazao (Ziziphus jujuba Mill) 9g.	Decoction	Conventional western treatment
Li 2015	XCHD + adefovir dipivoxil	Chaihu (Bupleurum chinense DC), Huangqin (Scutellaria baicalensis Georgi), Gancao (Glycyrrhiza uralensis Fisch), Banxia (Pinellia ternata （Thunb.）Breit), Shengjiang (Zingiber officinale Rosc), Renshen (Panax ginseng C. A. Mey), Dazao (Ziziphus jujuba Mill).	Decoction	Adefovir dipivoxil
Wang 2015	XCHD + dexamethasone	Chaihu (Bupleurum chinense DC) 15 g, Danshen (Salvia miltiorrhiza Bge) 15 g, Huangqin (Scutellaria baicalensis Georgi) 9 g, Shengjiang (Zingiber officinale Rosc) 9 g, Banxia (Pinellia ternata（Thunb.）	Decoction	Dexamethasone

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
		Breit) 6 g, Gancao (Glycyrrhiza uralensis Fisch) 3 g, Dazao (Ziziphus jujuba Mill) 5 pieces.		
Wu 2015	XCHD + lamivudine	Chaihu (Bupleurum chinense DC) 12g, Huangqin (Scutellaria baicalensis Georgi) 6g, Gancao (Glycyrrhiza uralensis Fisch) 9g, Banxia (Pinellia ternata （Thunb.）Breit) 9g, Shengjiang (Zingiber officinale Rosc) 9g, Renshen (Panax ginseng C. A. Mey) 9g, Dazao (Ziziphus jujuba Mill) 9g.	Decoction	Lamivudine
Xue 2015	XCHD + basic liver protection	Chaihu (Bupleurum chinense DC) 12g, Huangqin (Scutellaria baicalensis Georgi) 9g, Gancao (Glycyrrhiza uralensis Fisch) 9g, Banxia (Pinellia ternata （Thunb.）Breit) 9g, Shengjiang (Zingiber officinale Rosc) 9g, Renshen (Panax ginseng C. A. Mey) 6g, Dazao (Ziziphus jujuba Mill) 3 pieces.	Decoction	Conventional liver protection treatment
Zhou 2015	XCHD + entecavir	Chaihu (Bupleurum chinense DC) 9g, Huangqin (Scutellaria baicalensis Georgi) 9g, Gancao (Glycyrrhiza uralensis Fisch) 5g, Banxia (Pinellia ternata （Thunb.）Breit) 9g, Shengjiang (Zingiber officinale Rosc) 6g, Renshen (Panax ginseng C. A. Mey)	Decoction	Entecavir

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
		9g, Dazao (Ziziphus jujuba Mill) 4 pieces.		
Kang 2016	XCHD + entecavir	Chaihu (Bupleurum chinense DC), Huangqin (Scutellaria baicalensis Georgi), Gancao (Glycyrrhiza uralensis Fisch), Banxia (Pinellia ternata （Thunb.）Breit), Shengjiang (Zingiber officinale Rosc), Renshen (Panax ginseng C. A. Mey), Dazao (Ziziphus jujuba Mill).	Decoction	Entecavir
Wang 2016	Modified XCHD + entecavir	Dangshen (Codonopsis pilosula) 30 g, Fuling (Poria cocos) 30 g, Chishao (Paeonia lactiflora Pall) 15 g, Danshen (Salvia miltiorrhiza Bge) 15 g, Chaihu (Bupleurum chinense DC) 15 g, Cangzhu (Atractylodes lancea) 15 g, Baizhi (Angelica dahurica) 12 g, Huangqin (Scutellaria baicalensis Georgi) 10 g, Banxia (Pinellia ternata （Thunb.）Breit) 10 g, Yinchen (Artemisia capillaris Thunb) 10 g, Gancao (Glycyrrhiza uralensis Fisch) 6 g.	Decoction	Entecavir + diammonium glycyrrhizinate
Zou 2016	Modified XCHD + entecavir	Chaihu (Bupleurum chinense DC), Huangqin (Scutellaria baicalensis Georgi), Banxia (Pinellia ternata（Thunb.） Breit), Gancao (Glycyrrhiza uralensis Fisch), Shengjiang (Zingiber officinale Rosc),	Decoction	Entecavir

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
		and Dazao (Ziziphus jujuba Mill). Note: the original article did not report the dose of each herb in the main formula.		
Chen 2017	Modified XCHD + conventional treatment	Huangqi (Radix Astragali), Danshen (Radix Salviae Miltiorrhizae), Nvzhenzi (Fructus Ligustri Lucidi), Mohanlian (Herba Ecliptae), Yinchenhao (Herba Artemisiae Scopariae)	Decoction	Conventional western treatment
Fang 2017	Modified XCHD + silymarin	Chaihu (Bupleurum chinense DC) 15 g, Huangqin (Scutellaria baicalensis Georgi) 10 g, Banxia (Pinellia ternata（Thunb.）Breit) 10 g.	Decoction	Silymarin
Hu 2017	Modified XCHD + entecavir	Chaihu (Bupleurum chinense DC) 30 g, Huangqin (Scutellaria baicalensis Georgi) 18 g, Huangqi (Astragalus membranaceus) 20 g, Renshen (Panax ginseng C. A. Mey) 18 g, Banxia (Pinellia ternata（Thunb.）Breit) 18 g, Gancao (Glycyrrhiza uralensis Fisch) 18 g, Shengjiang (Zingiber officinale Rosc) 18 g, Dazao (Ziziphus jujuba Mill) 12 pieces.	Decoction	Entecavir + insulin
Lin 2017	XCHD + entecavir	Chaihu (Bupleurum chinense DC) 9g, Huangqin (Scutellaria baicalensis Georgi) 9g, Gancao	Decoction	Entecavir

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
		(Glycyrrhiza uralensis Fisch) 5g, Banxia (Pinellia ternata （Thunb.）Breit) 9g, Shengjiang (Zingiber officinale Rosc) 6g, Renshen (Panax ginseng C. A. Mey) 9g, Dazao (Ziziphus jujuba Mill) 4 pieces.		
Liu 2017	XCHD + adefovir + entecavir	Shengjiang (Zingiber officinale Rosc) 3 g, Gancao (Glycyrrhiza uralensis Fisch) 6 g, Huangqin (Scutellaria baicalensis Georgi) 6 g, Dangshen (Codonopsis pilosula) 6 g, Banxia (Pinellia ternata（Thunb.） Breit) 6 g, Chaihu (Bupleurum chinense DC) 10 g, Dazao (Ziziphus jujuba Mill) 10 pieces.	Decoction	Adefovir + entecavir
Lu 2017	XCHD + entecavir	Chaihu (Bupleurum chinense DC) 20 g, Renshen (Panax ginseng C. A. Mey) 6 g, Dazao (Ziziphus jujuba Mill) 20 g, Gancao (Glycyrrhiza uralensis Fisch) 8 g, Huangqin (Scutellaria baicalensis Georgi) 10 g, Banxia (Pinellia ternata （Thunb.）Breit) 10 g, Shengjiang (Zingiber officinale Rosc) 5 g.	Decoction	Entecavir
Chen 2018	XCHD + entecavir	Chaihu (Bupleurum chinense DC), Huangqin (Scutellaria baicalensis Georgi), Gancao (Glycyrrhiza uralensis Fisch), Banxia (Pinellia ternata （Thunb.）Breit),	Decoction	Entecavir

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
		Shengjiang (Zingiber officinale Rosc), Renshen (Panax ginseng C. A. Mey), Dazao (Ziziphus jujuba Mill).		
Ma 2018	XCHD + entecavir	Chaihu (Bupleurum chinense DC) 10g, Huangqin (Scutellaria baicalensis Georgi) 10g, Gancao (Glycyrrhiza uralensis Fisch) 6g, Banxia (Pinellia ternata （Thunb.）Breit) 9g, Shengjiang (Zingiber officinale Rosc) 6g, Renshen (Panax ginseng C. A. Mey) 6g, Dazao (Ziziphus jujuba Mill) 5g.	Decoction	Entecavir
Sheng 2018	XCHD + IFN-α-2b	Chaihu (Bupleurum chinense DC) 12 g, Huangqin (Scutellaria baicalensis Georgi) 9 g, Renshen (Panax ginseng C. A. Mey) 6 g, Banxia (Pinellia ternata （Thunb.）Breit) 9 g, Gancao (Glycyrrhiza uralensis Fisch) 5 g, Shengjiang (Zingiber officinale Rosc) 9 g, Dazao (Ziziphus jujuba Mill) 4 pieces.	Decoction	IFN-α-2b
Wang 2018	Modified XCHD + entecavir	Chaihu (Bupleurum chinense DC) 15 g, Cangzhu (Atractylodes lancea) 15 g, Dazao (Ziziphus jujuba Mill) 12 g, Baizhi (Angelica dahurica) 12 g, Huangqin (Scutellaria baicalensis Georgi) 10 g, Yinchen	Decoction	Entecavir

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
		(Artemisia capillaris Thunb) 10 g, Renshen (Panax ginseng C. A. Mey) 6 g, Banxia (Pinellia ternata （Thunb.）Breit) 6 g, Shengjiang (Zingiber officinale Rosc) 6 g, Gancao (Glycyrrhiza uralensis Fisch) 3 g.		
Wu 2018	Modified XCHD + entecavir	Chaihu (Bupleurum chinense DC) 15 g, Huangqin (Scutellaria baicalensis Georgi) 10 g, Banxia (Pinellia ternata（Thunb.） Breit) 10 g, Shengjiang (Zingiber officinale Rosc) 10 g, Dazao (Ziziphus jujuba Mill) 10 g, Dangshen (Codonopsis pilosula) 10 g, Gancao (Glycyrrhiza uralensis Fisch) 10 g, Yinchen (Artemisia capillaris Thunb) 15 g, Fuling (Poria cocos) 10 g.	Decoction	Entecavir
Zhang 2018	Modified XCHD + entecavir	Chaihu (Bupleurum chinense DC) 15 g, Huangqin (Scutellaria baicalensis Georgi) 10 g, Banxia (Pinellia ternata（Thunb.） Breit) 10 g, Shengjiang (Zingiber officinale Rosc) 10 g, Dangshen (Codonopsis pilosula) 15 g, Dazao (Ziziphus jujuba Mill) 15 g, Gancao (Glycyrrhiza uralensis Fisch) 10 g.	Decoction	Entecavir + magnesium isoglycyrrhizinate + reduced glutathione
Zong 2018	XCHD + entecavir		Decoction	Entecavir

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
Yan 2019	Modified XCHD + adefovir dipivoxil	Fuling (Poria cocos) 30 g, Chaihu (Bupleurum chinense DC) 15 g, Cangzhu (Atractylodes lancea) 15 g, Baizhi (Angelica dahurica) 12 g, Dazao (Ziziphus jujuba Mill) 12 g, Danshen (Salvia miltiorrhiza Bge) 10 g, Yinchen (Artemisia capillaris Thunb) 10 g, Huangqin (Scutellaria baicalensis Georgi) 10 g, Shengjiang (Zingiber officinale Rosc) 6 g, Banxia (Pinellia ternata （Thunb.）Breit) 6 g, Renshen (Panax ginseng C. A. Mey) 6 g, Gancao (Glycyrrhiza uralensis Fisch) 3 g.	Decoction	Adefovir dipivoxil
Zhou 2021	Modified XCHD + entecavir	Huangqin (Scutellaria baicalensis Georgi) 9 g, Shengjiang (Zingiber officinale Rosc) 9 g, Gancao (Glycyrrhiza uralensis Fisch) 9 g, Renshen (Panax ginseng C. A. Mey) 9 g, Banxia (Pinellia ternata（Thunb.） Breit) 9 g, Chaihu (Bupleurum chinense DC) 24 g, Dazao (Ziziphus jujuba Mill) 2 pieces.	Decoction	Entecavir
Hu 2022	Modified XCHD + tenofovir disoproxil fumarate	Chaihu (Bupleurum chinense DC) 25 g, Huangqin (Scutellaria baicalensis Georgi) 15 g, Banxia (Pinellia ternata（Thunb.） Breit) 15 g, Renshen (Panax ginseng C. A. Mey) 15 g, Shengjiang (Zingiber	Decoction	Tenofovir disoproxil fumarate

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
		officinale Rosc) 10 g, Dazao (Ziziphus jujuba Mill) 10 g, Gancao (Glycyrrhiza uralensis Fisch) 10 g		
Huang 2022	Modified XCHD + entecavir	Chaihu (Bupleurum chinense DC) 24 g, Huangqin (Scutellaria baicalensis Georgi) 9 g, Renshen (Panax ginseng C. A. Mey) 9 g, Gancao (Glycyrrhiza uralensis Fisch) 9 g, Banxia (Pinellia ternata（Thunb.） Breit) 9 g, Shengjiang (Zingiber officinale Rosc) 9 g, Dazao (Ziziphus jujuba Mill) 2 pieces.	Decoction	Entecavir
Li 2022	XCHD + tenofovir + entecavir	Chaihu (Bupleurum chinense DC) 12g, Huangqin (Scutellaria baicalensis Georgi) 9g, Gancao (Glycyrrhiza uralensis Fisch) 6g, Banxia (Pinellia ternata （Thunb.）Breit) 9g, Shengjiang (Zingiber officinale Rosc) 6g, Renshen (Panax ginseng C. A. Mey) 6g, Dazao (Ziziphus jujuba Mill) 3 pieces.	Decoction	Tenofovir + entecavir
Shi 2022	XCHD + entecavir	None	Decoction	Entecavir
Wang 2023	XCHD + entecavir	Chaihu (Bupleurum chinense DC) 9g, Huangqin (Scutellaria baicalensis Georgi) 9g, Gancao (Glycyrrhiza uralensis Fisch) 5g, Banxia (Pinellia ternata （Thunb.）Breit) 6g,	Decoction	Entecavir

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
Wu 2023	Modified XCHD + entecavir	Shengjiang (Zingiber officinale Rosc) 6g, Renshen (Panax ginseng C. A. Mey) 6g, Dazao (Ziziphus jujuba Mill) 4 pieces. Dazao (Ziziphus jujuba Mill) 12 g, Shengjiang (Zingiber officinale Rosc) 15 g, Banxia (Pinellia ternata（Thunb.）Breit) 15 g, Gancao (Glycyrrhiza uralensis Fisch) 15 g, Dangshen (Codonopsis pilosula) 15 g, Huangqin (Scutellaria baicalensis Georgi) 15 g, Chaihu (Bupleurum chinense DC) 20 g.	Decoction	Entecavir
Zhou 2023	Modified XCHD + tenofovir disoproxil fumarate	Fuling (Poria cocos) 30 g, Chaihu (Bupleurum chinense DC) 15 g, Cangzhu (Atractylodes lancea) 15 g, Baizhi (Angelica dahurica) 12 g, Dazao (Ziziphus jujuba Mill) 12 g, Yinchen (Artemisia capillaris Thunb) 10 g, Huangqi (Astragalus membranaceus) 10 g, Danshen (Salvia miltiorrhiza Bge) 10 g, Renshen (Panax ginseng C. A. Mey) 6 g, Banxia (Pinellia ternata（Thunb.）Breit) 6 g, Gancao (Glycyrrhiza uralensis Fisch) 3 g, Shengjiang (Zingiber officinale Rosc) 3 g.	Decoction	Tenofovir disoproxil fumarate
Li 2025	XCHD + diammonium	Renshen (Panax ginseng C. A. Mey) 20 g, Chaihu	Decoction	Diammonium glycyrrhizinate

Study	Intervention group	Added/modified herbs	Dosage form	Control intervention
	glycyrrhizinate capsules	(Bupleurum chinense DC) 10 g, Huangqin (Scutellaria baicalensis Georgi) 10 g, Banxia (Pinellia ternata （Thunb.）Breit) 10 g, Gancao (Glycyrrhiza uralensis Fisch) 10 g, Dazao (Ziziphus jujuba Mill) 10 g, Shengjiang (Zingiber officinale Rosc) 6 g.		

3 Full search strategies

The searches covered database inception to October 5, 2025, and were executed between October 3 and October 5, 2025. The full reproducible strings used for CNKI, VIP, Wanfang, SinoMed, Web of Science, PubMed, Embase, and the Cochrane Library are shown in Table A4. Search outputs were supplemented by manual screening of reference lists from eligible reports and relevant reviews.

Table A4. Full database search strategies

Database	Search query
CNKI	(SU = '慢性乙肝' OR SU = '慢性乙型肝炎' OR SU = '乙肝' OR SU = '乙型肝炎' OR SU = 'HBV 感染' OR SU = '慢性 HBV 感染' OR SU = '乙型肝炎病毒' OR SU = '乙肝病毒' OR SU = 'HBsAg 阳性') AND (SU = '小柴胡汤' OR SU = '小柴胡湯' OR SU = '加味小柴胡汤' OR SU = '小柴胡汤加减') AND FT = '随机'
VIP	M = (慢性乙肝 OR 慢性乙型肝炎 OR 乙肝 OR 乙型肝炎 OR HBV 感染 OR 慢性 HBV 感染 OR 乙型肝炎病毒 OR 乙肝病毒 OR HBsAg 阳性) AND M = (小柴胡汤 OR 小柴胡湯 OR 加味小柴胡汤 OR 小柴胡汤加减) AND U = 随机
Wanfang	主题:(慢性乙肝 OR 慢性乙型肝炎 OR 乙肝 OR 乙型肝炎 OR HBV 感染 OR 慢性 HBV 感染 OR 乙型肝炎病毒 OR 乙肝病毒 OR HBsAg 阳性) AND 主题:(小柴胡汤 OR 小柴胡湯 OR 加味小柴胡汤 OR 小柴胡汤加减) AND 全部:(随机)
SinoMed	("随机"[全部字段:智能]) AND ("小柴胡汤"[常用字段:智能] OR "小柴胡湯"[常用字段:智能] OR "加味小柴胡汤"[常用字段:智能] OR "小柴胡汤加减"[常用字段:智能]) AND ("慢性乙肝"[常用字段:智能] OR "慢性乙型肝炎"[常用字段:智能] OR "乙肝"[常用字段:智能] OR "乙型肝炎"[常用字段:智能] OR "HBV 感染"[常用字段:智能] OR "慢性 HBV 感染"[常用字段:智能] OR "乙型肝炎病毒"[常用字段:智能] OR "乙肝病毒"[常用字段:智能] OR "HBsAg 阳性"[常用字段:智能])

Web of Science	#1 TS=("xiaochaihu" OR "shosaiko-to" OR "sho-saiko-to" OR "shosaiko-toh" OR "TJ-9" OR "TJ9" OR "xiaochaihutang" OR "xiao-chai-hu-tang" OR "xiaochaihu-tang" OR "xiao chai hu" OR "minor bupleurum" OR "small bupleurum" OR "radix bupleuri" OR "Chaihu (Bupleurum chinense DC)") #2 TS=("Hepatitis B, Chronic" OR "Hepatitis B Virus Infection, Chronic" OR "Chronic Hepatitis B Virus Infection" OR "Chronic Hepatitis B") #3 TS=("randomized controlled trial" OR "randomized clinical trial" OR "randomized trial" OR "clinical trial" OR randomized) #4 #1 AND #2 AND #3
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 "Chaihu (Bupleurum chinense DC)"[Title/Abstract] #3 "randomized controlled trial"[Publication Type] OR "randomized clinical trial"[Publication Type] OR "randomized trial"[Title/Abstract] OR "clinical trial"[Title/Abstract] OR randomized[Title/Abstract] #4 #1 AND #2 AND #3
Embase	#1 'xiaochaihu':ti,ab,kw OR 'shosaiko-to':ti,ab,kw OR 'sho-saiko-to':ti,ab,kw OR 'shosaiko-toh':ti,ab,kw OR 'TJ-9':ti,ab,kw OR 'TJ9':ti,ab,kw OR 'xiaochaihutang':ti,ab,kw OR 'xiao-chai-hu-tang':ti,ab,kw OR 'xiaochaihu-tang':ti,ab,kw OR 'xiao chai hu':ti,ab,kw OR 'minor bupleurum':ti,ab,kw OR 'small bupleurum':ti,ab,kw OR 'radix bupleuri':ti,ab,kw OR 'Chaihu (Bupleurum chinense DC)':ti,ab,kw #2 'hepatitis B, chronic':ti,ab,kw OR 'hepatitis B virus infection, chronic':ti,ab,kw OR 'chronic hepatitis B virus infection':ti,ab,kw OR 'chronic hepatitis B':ti,ab,kw #3 'randomized controlled trial'/exp OR 'randomized controlled trial':ti,ab,kw OR 'randomized clinical trial':ti,ab,kw OR 'randomized trial':ti,ab,kw OR 'clinical trial':ti,ab,kw #4 #1 AND #2 AND #3
The Cochrane Library	#1 MeSH descriptor: [Hepatitis B, Chronic] explode all trees #2 (Hepatitis B Virus Infection, Chronic OR Chronic Hepatitis B Virus Infection OR Chronic Hepatitis B):ti,ab,kw #3 #1 OR #2 #4 (xiaochaihu OR shosaiko-to OR sho-saiko-to OR shosaiko-toh OR TJ-9 OR TJ9 OR xiaochaihutang OR xiao-chai-hu-tang OR xiaochaihu-tang OR xiao chai hu OR minor bupleurum OR small bupleurum OR radix bupleuri OR Chaihu

(Bupleurum chinense DC)):ti,ab,kw
#5 (randomized controlled trial OR randomized clinical trial OR randomized trial OR clinical trial OR randomized):ti,ab,kw
#6 #3 AND #4 AND #5

Abbreviations: CNKI, China National Knowledge Infrastructure Database; VIP, VIP Database for Chinese Technical Periodicals; Wanfang, Wanfang Database; SinoMed, Chinese Biomedical Literature Database.

3.1 Study selection, data extraction, and decision rules

Two reviewers independently screened titles/abstracts and then full texts against the predefined eligibility criteria. Disagreements were resolved by discussion and, when necessary, third-reviewer adjudication.

A standardized extraction form captured study design, participant characteristics, diagnostic criteria, background western medicine, XCHD formulation or modification, treatment duration, follow-up, outcome definitions, and numerical outcome data required for meta-analysis.

Prespecified decision rules were as follows: duplicate publications were collated and the most complete report was retained; end-of-treatment data were preferred when multiple time points were available; change scores were calculated when baseline and post-treatment values were both reported; and adverse events were extracted exactly as reported by trial authors. Trials with insufficient quantitative data after clarification attempts were excluded from quantitative synthesis.

Table A5. PRISMA-aligned details

PRISMA item	Reporting element	Operational detail	Location
Item 6	Information sources	Databases: CNKI, VIP, Wanfang, SinoMed, Web of Science, PubMed, Embase, Cochrane Library; inception to Oct 5, 2025; plus manual reference screening.	Supplementary A Section 3; Table A4
Item 7	Full search strategies	Full reproducible search strings provided for all databases; executed Oct 3–5, 2025.	Supplementary A Section 3; Table A4
Item 8	Selection process	Two-stage screening; two reviewers independently screened; disagreements resolved by	Methods 2.4; Supplementary A 3.1

		discussion or third reviewer.	
Item 9	Data collection	Independent extraction using standardized form; authors contacted for missing data.	Methods 2.4; Supplementary A 3.1
Item 10a	Outcomes	Outcome definitions and numerical data extracted; end-of-treatment prioritized.	Methods 2.4; Supplementary A 3.1
Item 10b	Other variables	Study design, participants, diagnostic criteria, WM, XCHD details, duration, follow-up.	Methods 2.4
Item 13a	Duplicates	Duplicates collated; most informative report retained.	Methods 2.4; Supplementary A 3.1
Item 13b	Time points	End-of-treatment data preferred.	Methods 2.4
Item 13b	Change scores	Change scores derived when baseline and post-treatment available.	Methods 2.4
Item 27	Reproducibility	Full materials provided in Supplementary Material A.	Supplementary A

4 Rules for assessment of the certainty of evidence

The certainty of evidence was judged across risk of bias, inconsistency, indirectness, imprecision, and publication bias, with the downgrade rules summarized in Table A6. Because many review outcomes were surrogate or short-term, these rules were applied conservatively and interpreted together with the broader clinical context.

Table A6. Rules used to rate certainty of evidence

Element	Criteria for downgrade
Study design	If the majority of the information based on the revised Cochrane Risk of Bias tool assessment was rated as moderate, the evidence was downgraded by one level. If the majority was rated as high, the evidence was downgraded by two levels.

Inconsistency	If heterogeneity tests showed I^2 exceeding 75%, the evidence was downgraded by two levels. If I^2 was exceeding 50% and less than 75%, the evidence was downgraded by one level.
Indirectness	Assessment included several components: Population differences, Intervention differences, Outcome measurement differences, and Indirect comparisons. If there was a serious suspicion regarding the directness of the evidence, the evidence was downgraded by one level. If there was a very serious suspicion regarding the directness of the evidence, the evidence was downgraded by two levels.
Imprecision	If the 95% confidence interval crossed the null line, the evidence was downgraded by one level. With a total sample size of less than 300 for categorical variables and less than 400 for continuous variables included in all studies, the evidence was downgraded by one level.
Publication bias	If there was publication bias, the evidence was downgraded by one level.

5 Publication bias

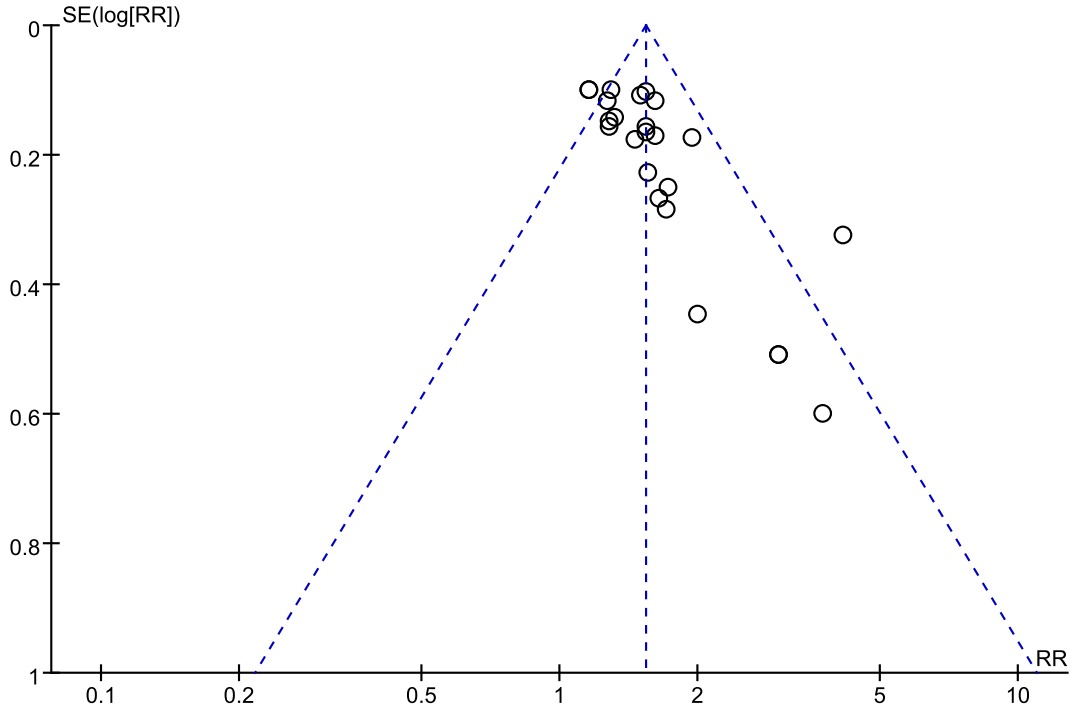

Figure A1. HBV-DNA negativity rate.

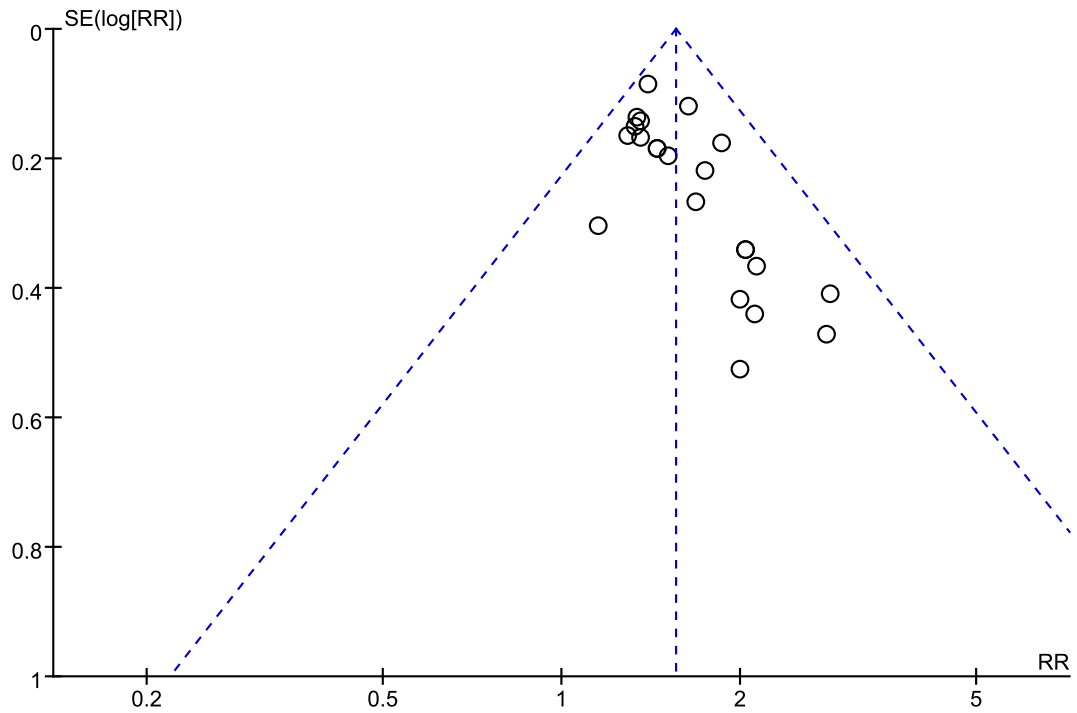

Figure A2. HBeAg negativity rate.

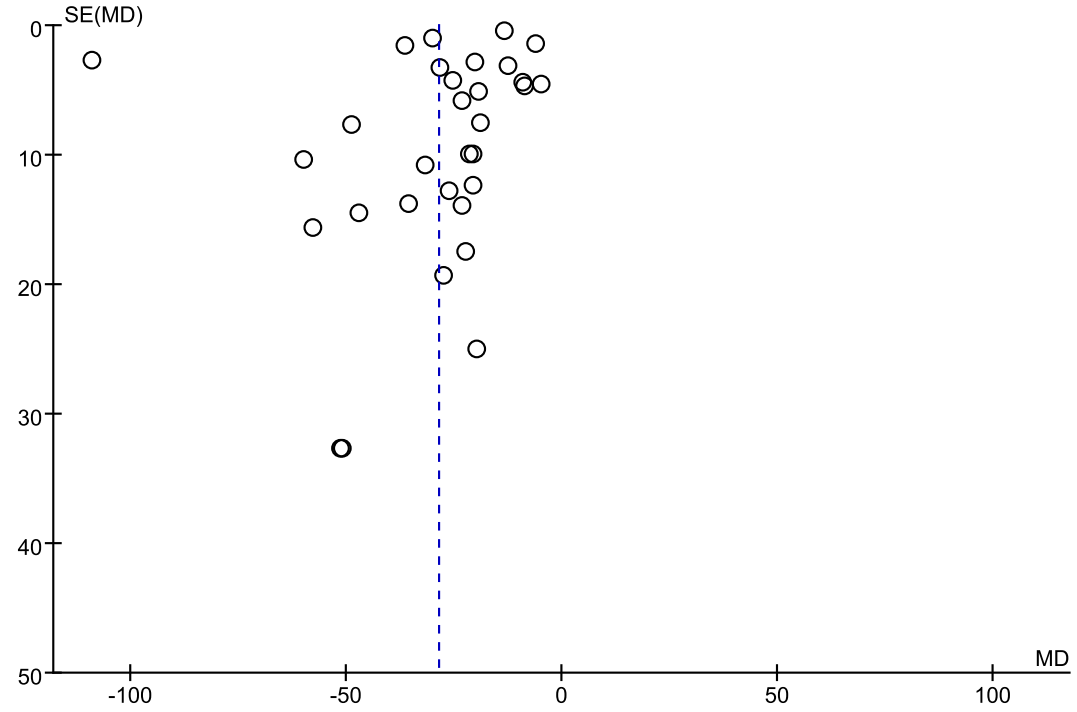

Figure A3. ALT.

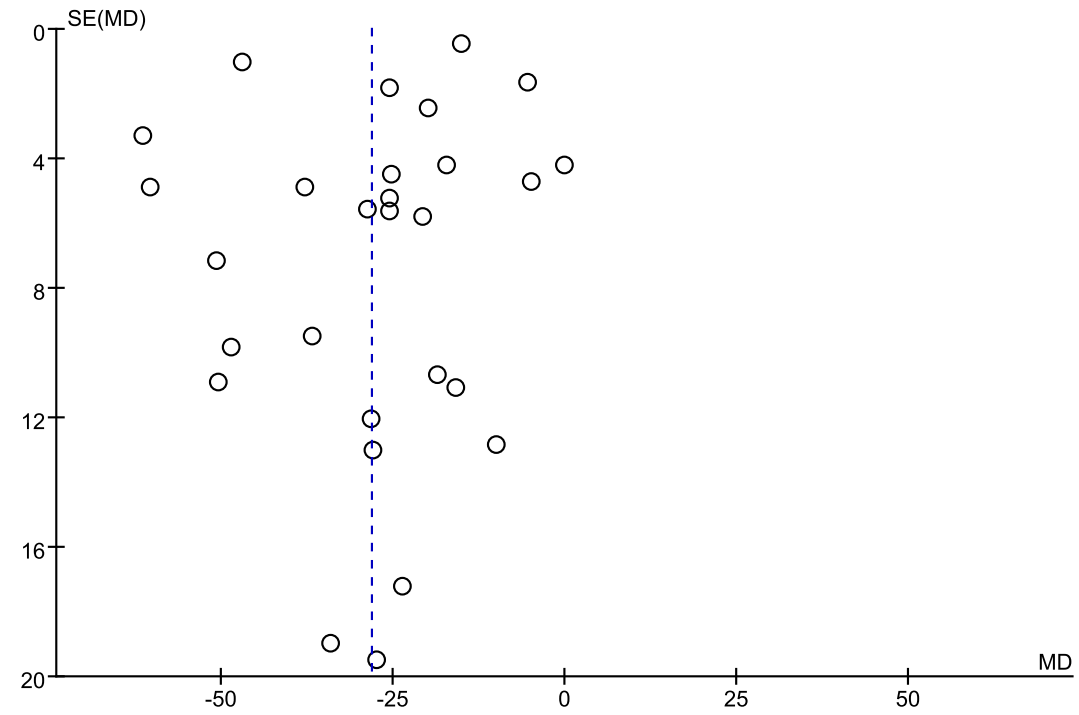

Figure A4. AST.

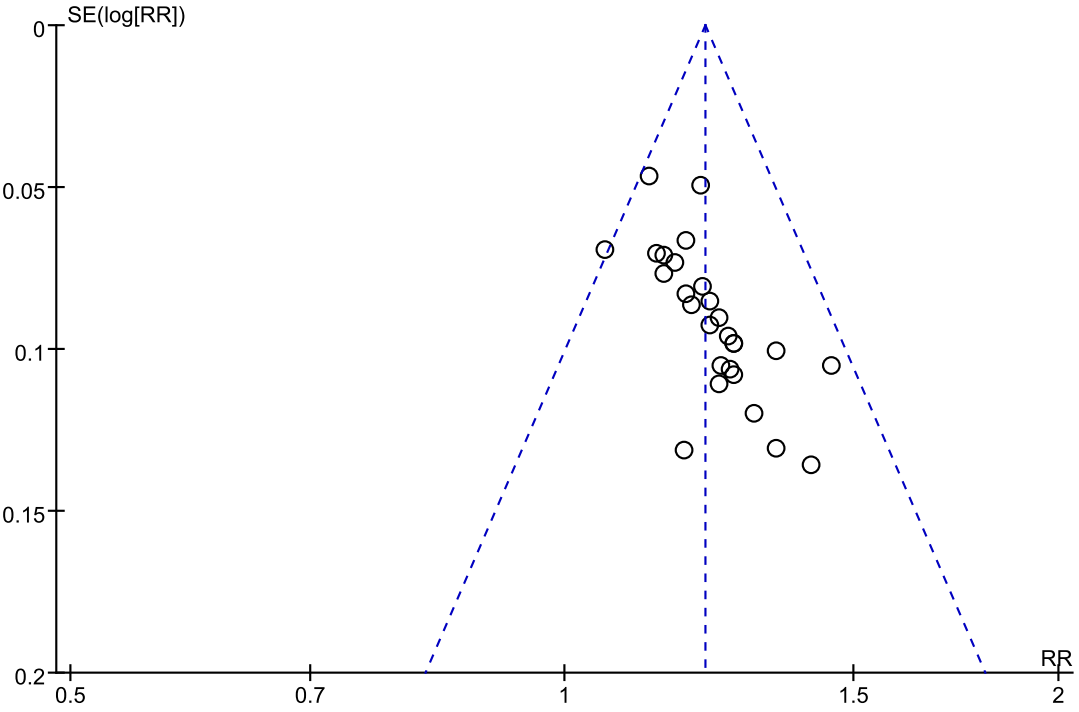

Figure A5. Total clinical efficacy.

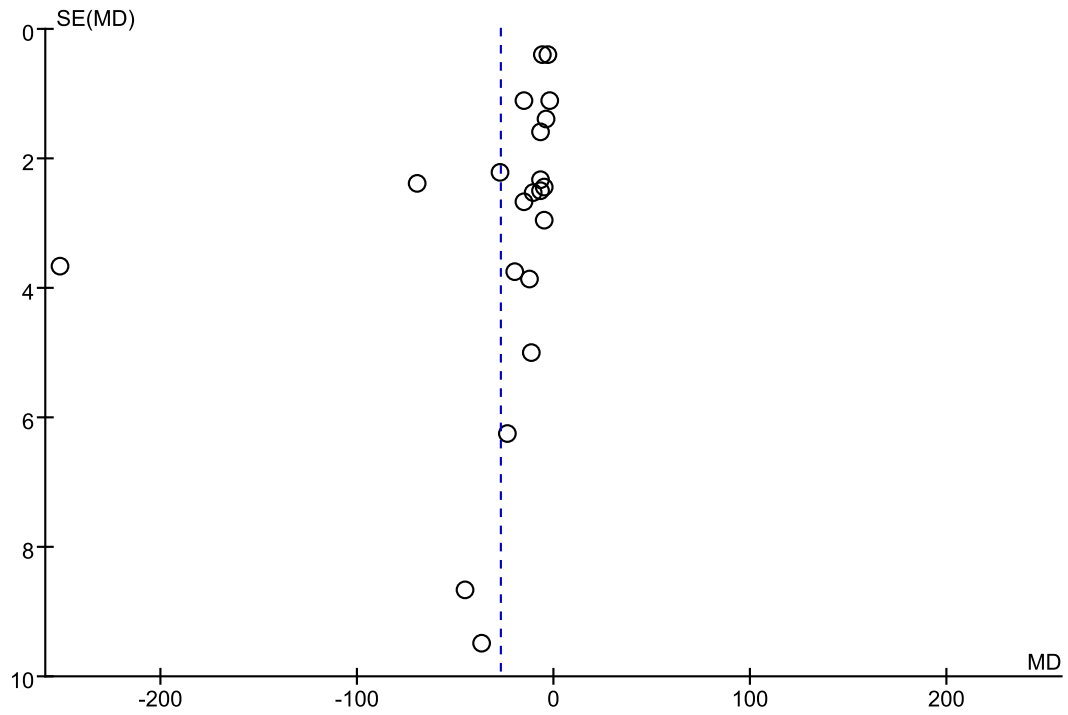

Figure A6. TBil.

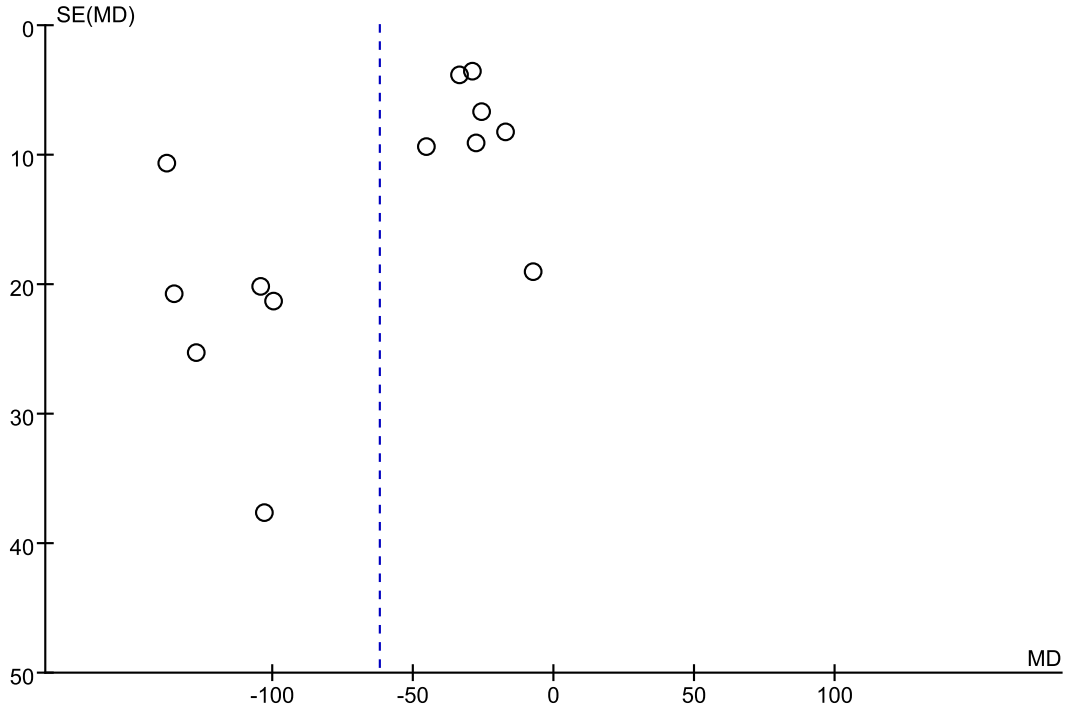

Figure A7. HA.

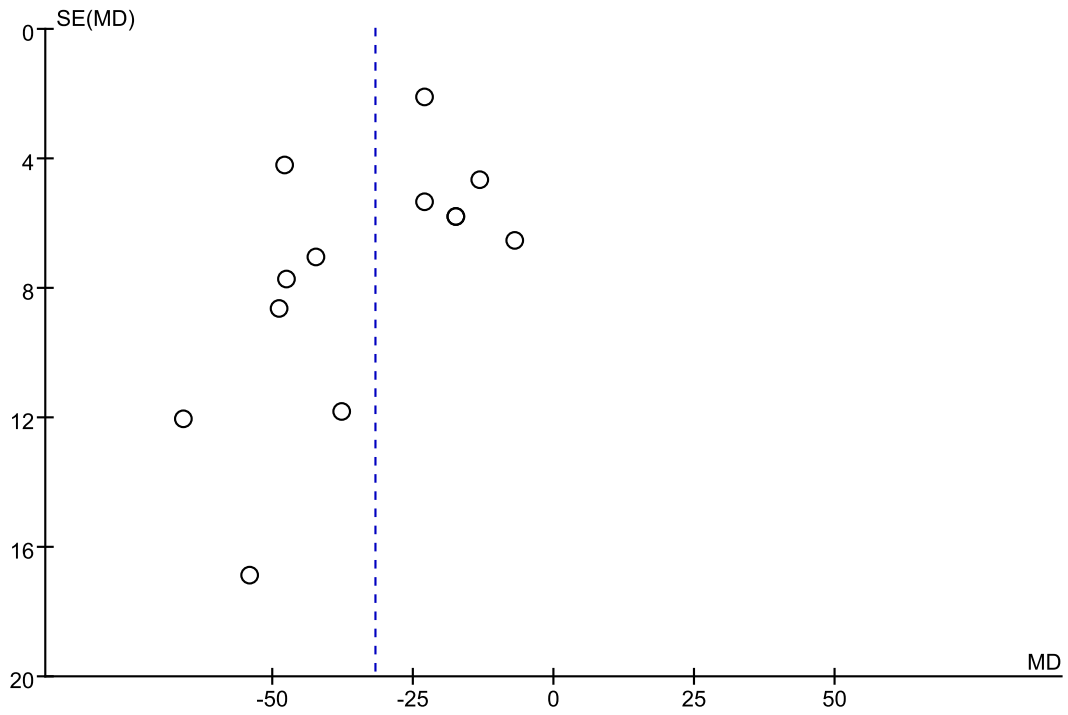

Figure A8. LN.

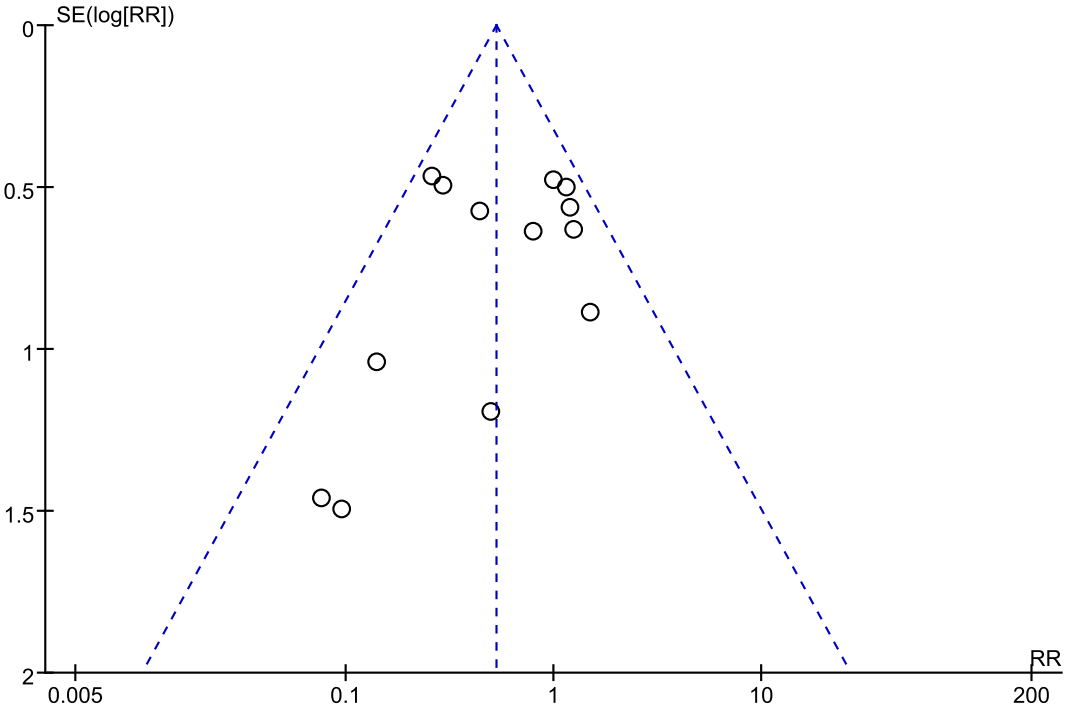

Figure A9. Adverse events.

6 Sensitivity analysis

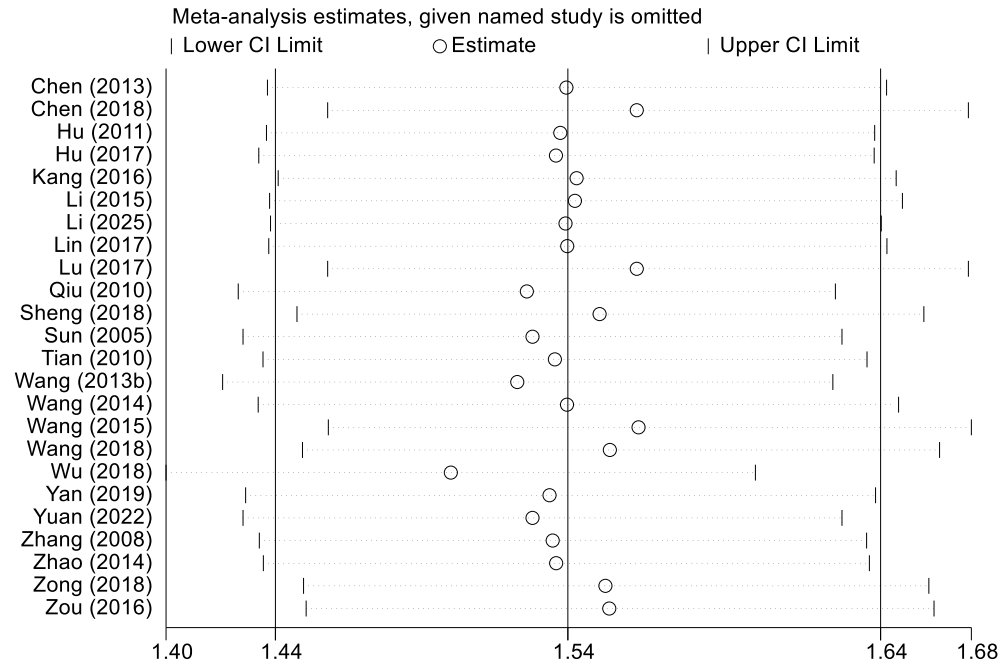

Figure A10. The results of the sensitivity analysis of Hepatitis B Virus Deoxyribonucleic Acid (HBV-DNA) clearance.

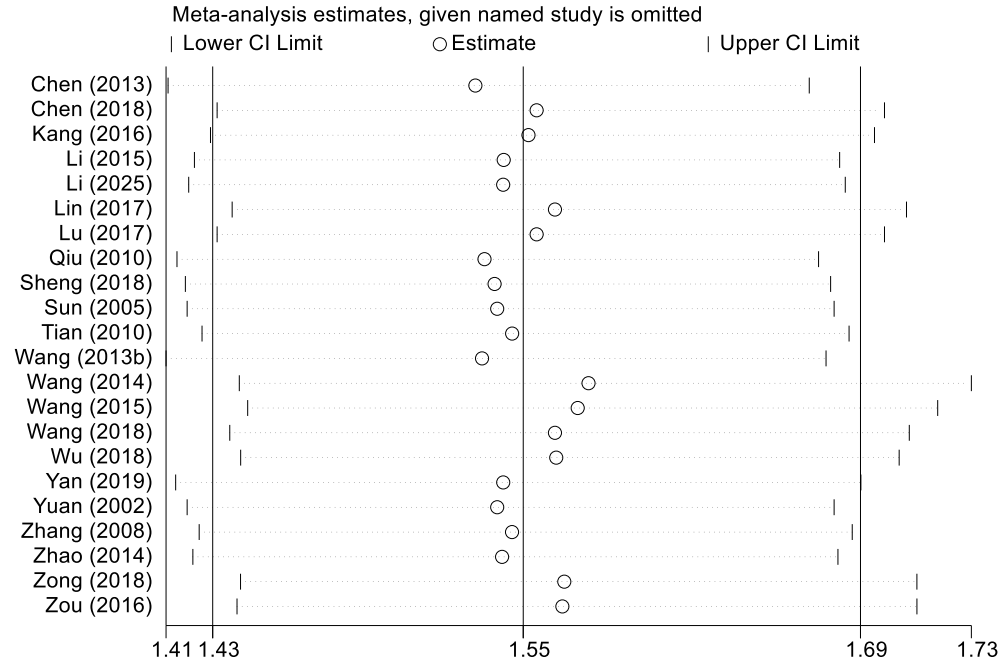

Figure A11. The results of the sensitivity analysis of Hepatitis B e Antigen (HBeAg) clearance.

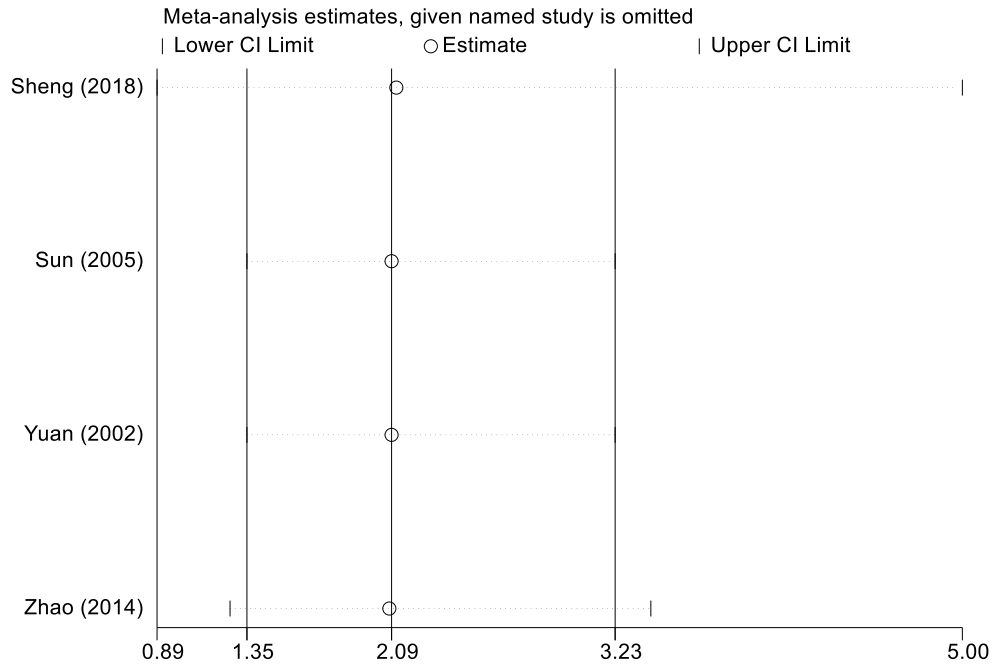

Figure A12. The results of the sensitivity analysis of Hepatitis B surface antigen (HBsAg) clearance.

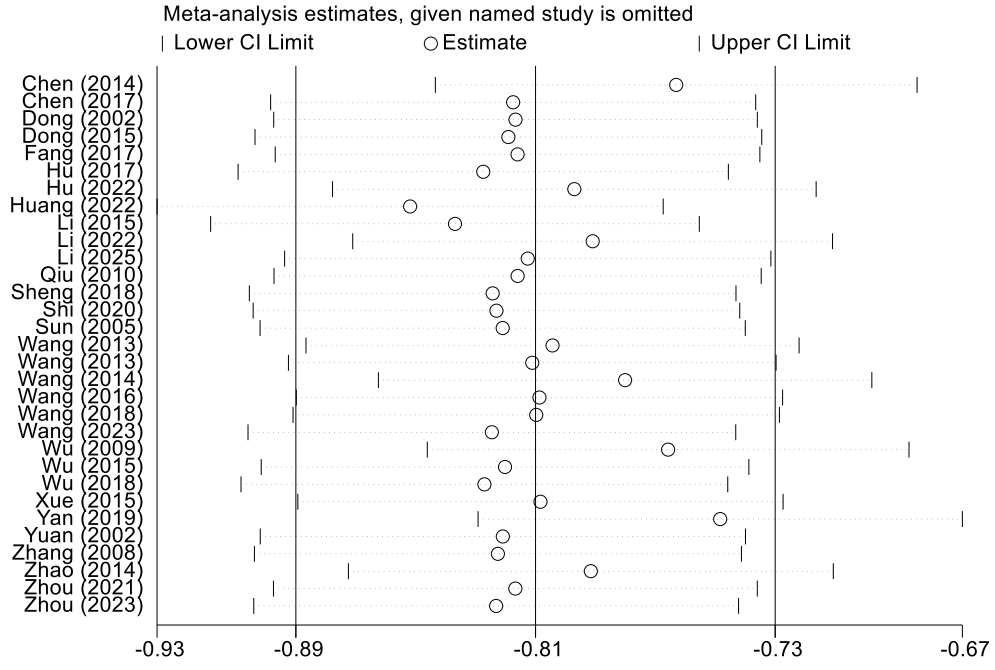

Figure A13. The results of the sensitivity analysis of Alanine aminotransferase (ALT).

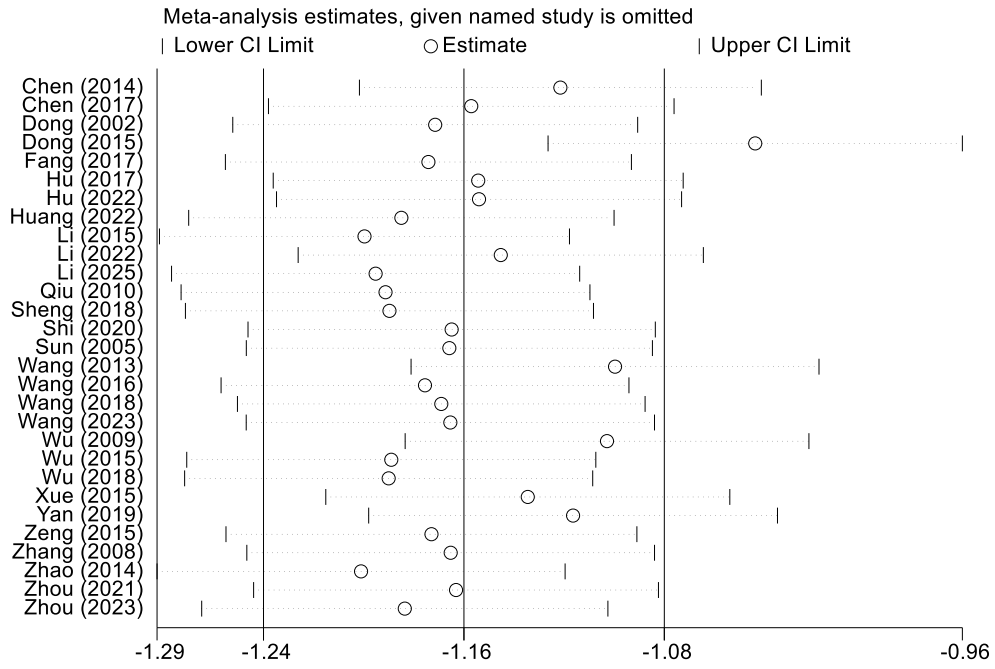

Figure A14. The results of the sensitivity analysis of Aspartate aminotransferase (AST).

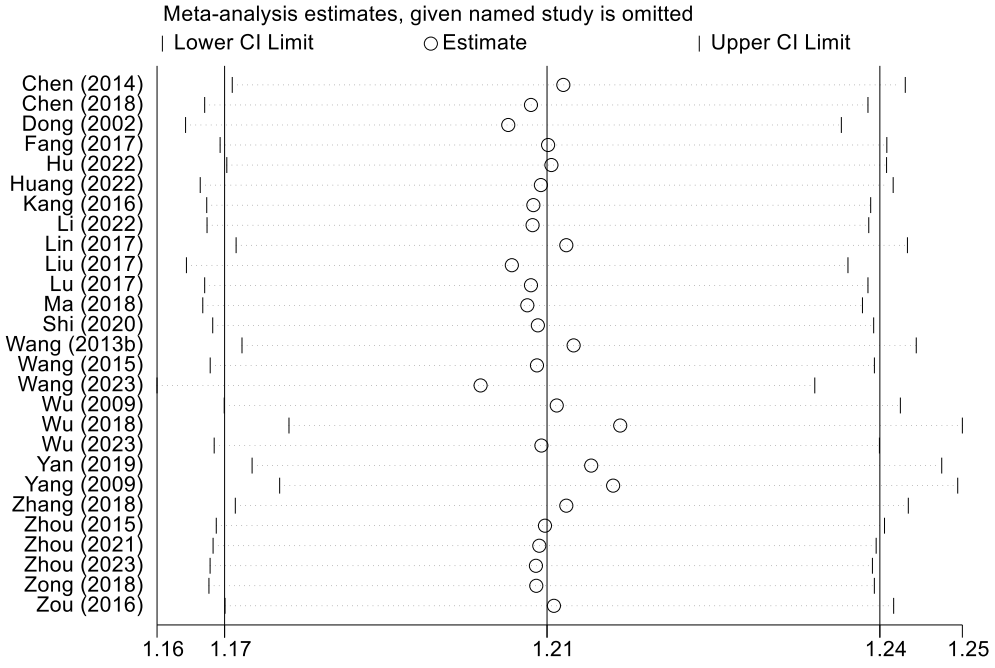

Figure A15. The results of the sensitivity analysis of total clinical efficacy.

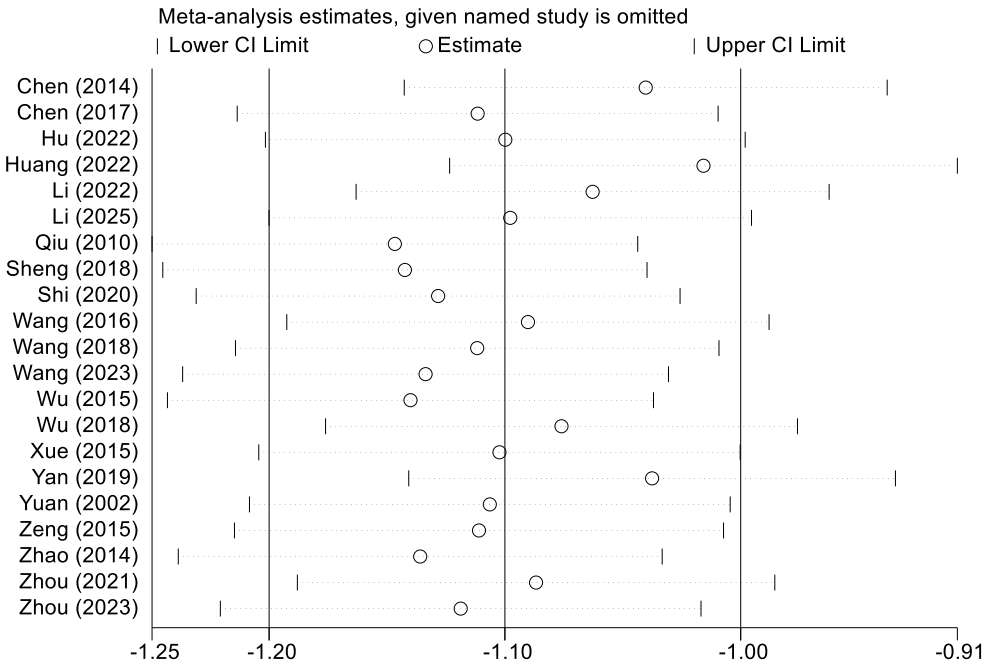

Figure A16. The results of the sensitivity analysis of Total bilirubin (TBiL).

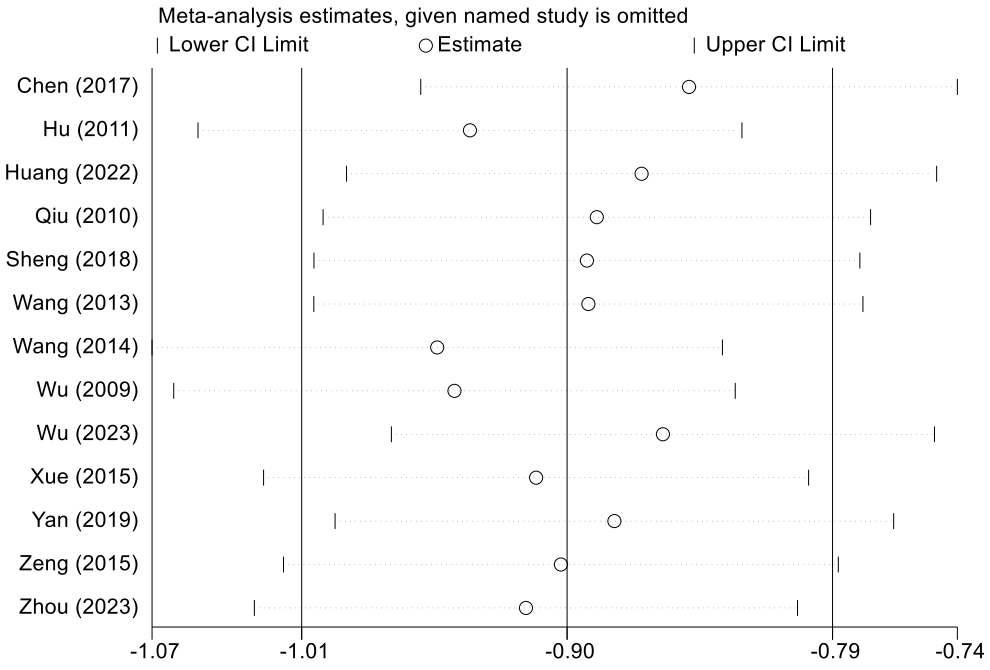

Figure A17. The results of the sensitivity analysis of Hyaluronic Acid (HA).

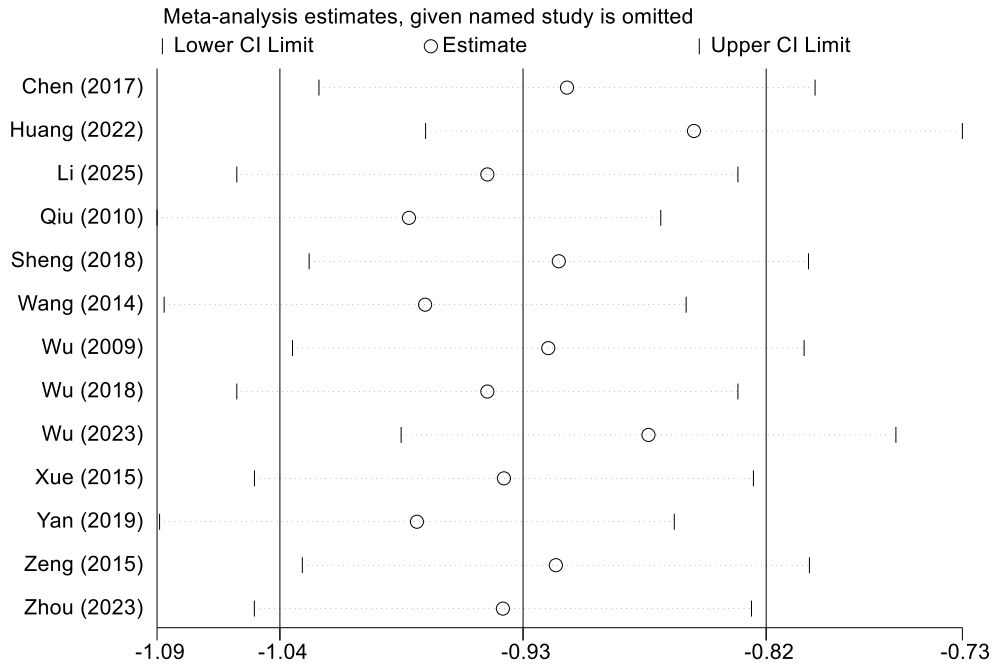

Figure A18. The results of the sensitivity analysis of Laminin (LN).

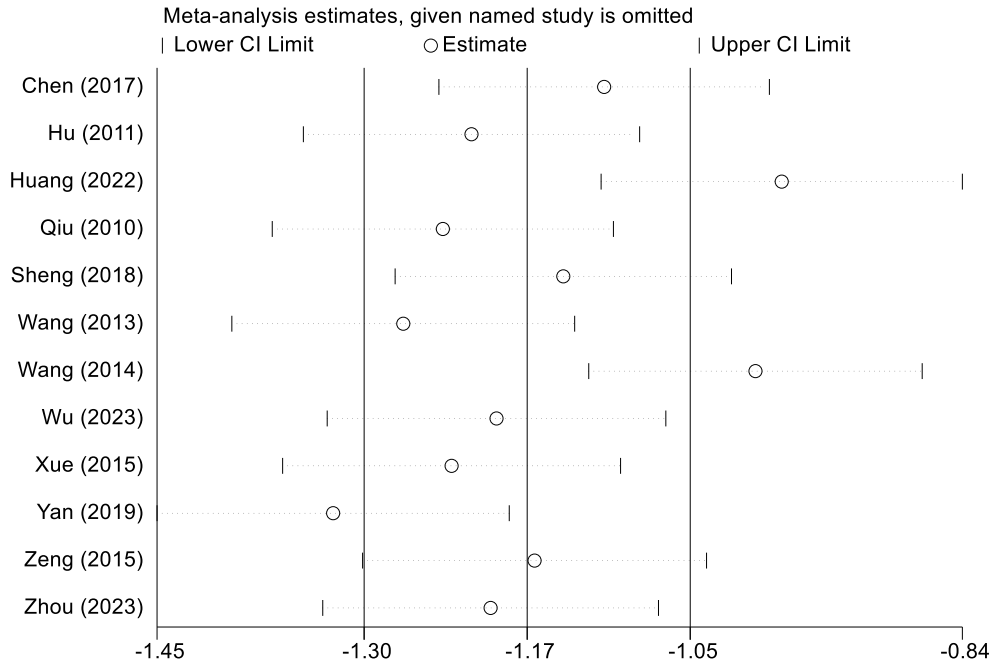

Figure A19. The results of the sensitivity analysis of Procollagen III (PCIII).

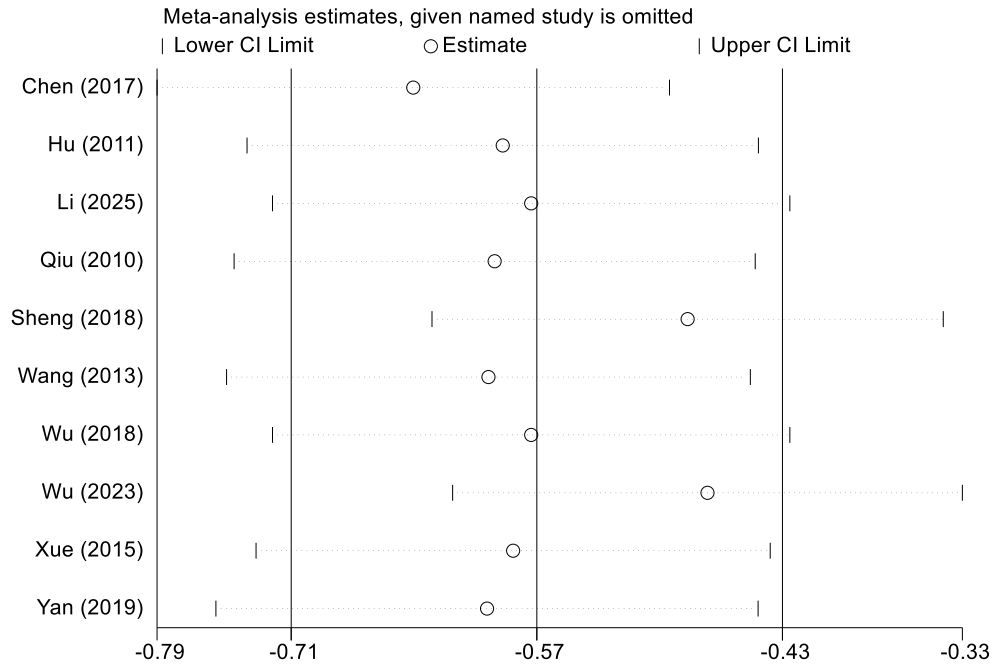

Figure A20. The results of the sensitivity analysis of Type IV Collagen (IV-C).

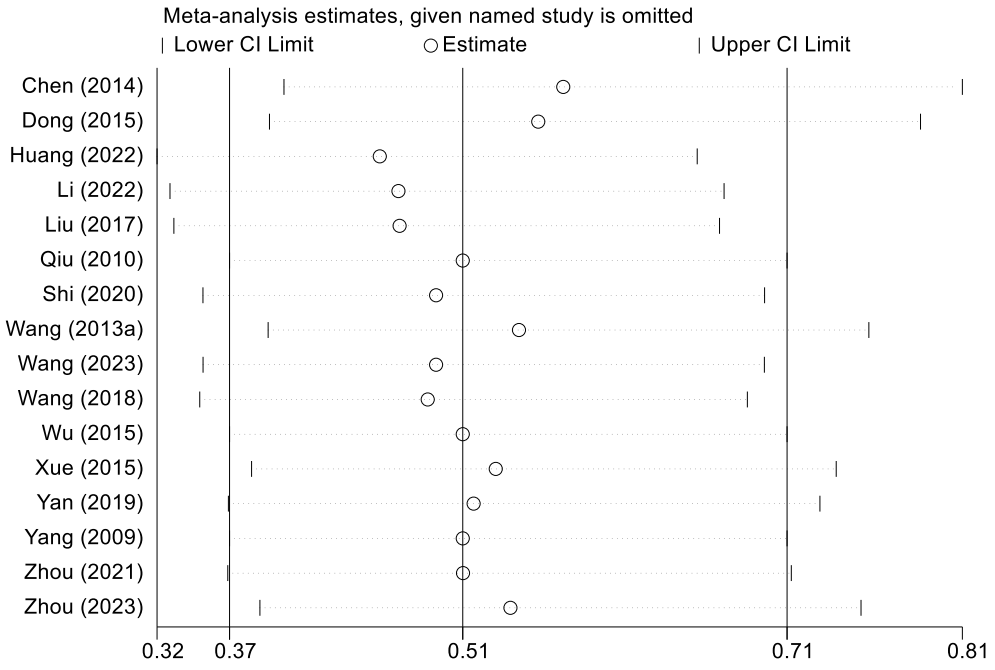

Figure A21. The results of the sensitivity analysis of adverse events.

7 Trial sequential analysis

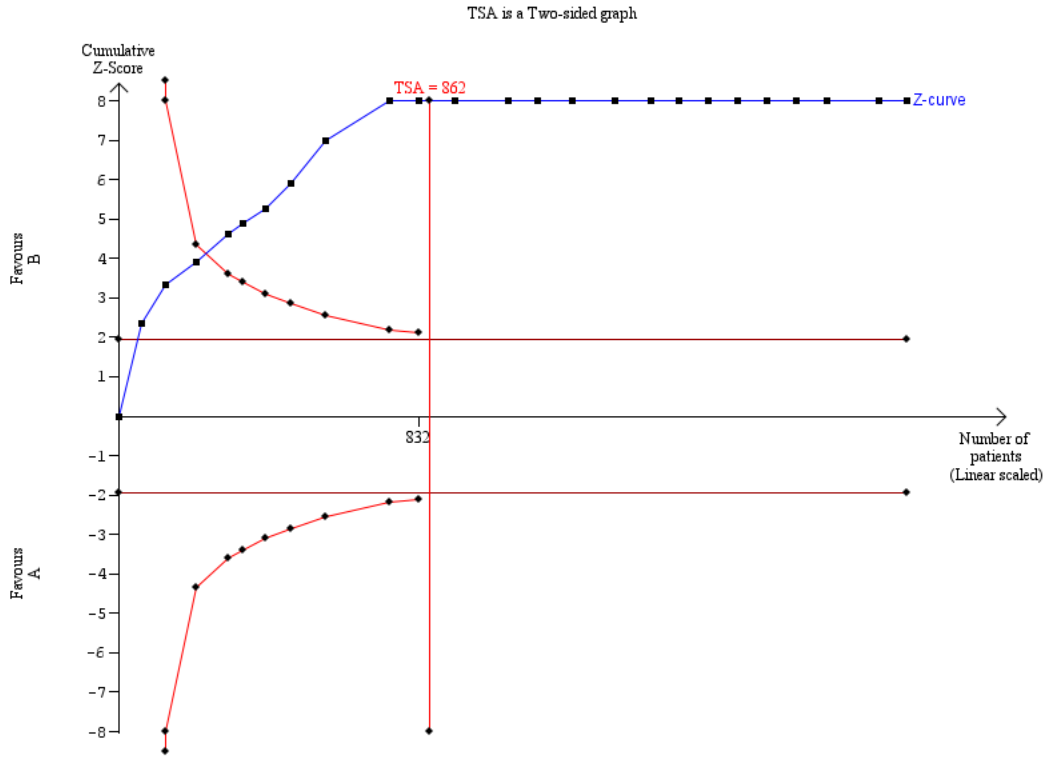

Figure A22. HBV-DNA.

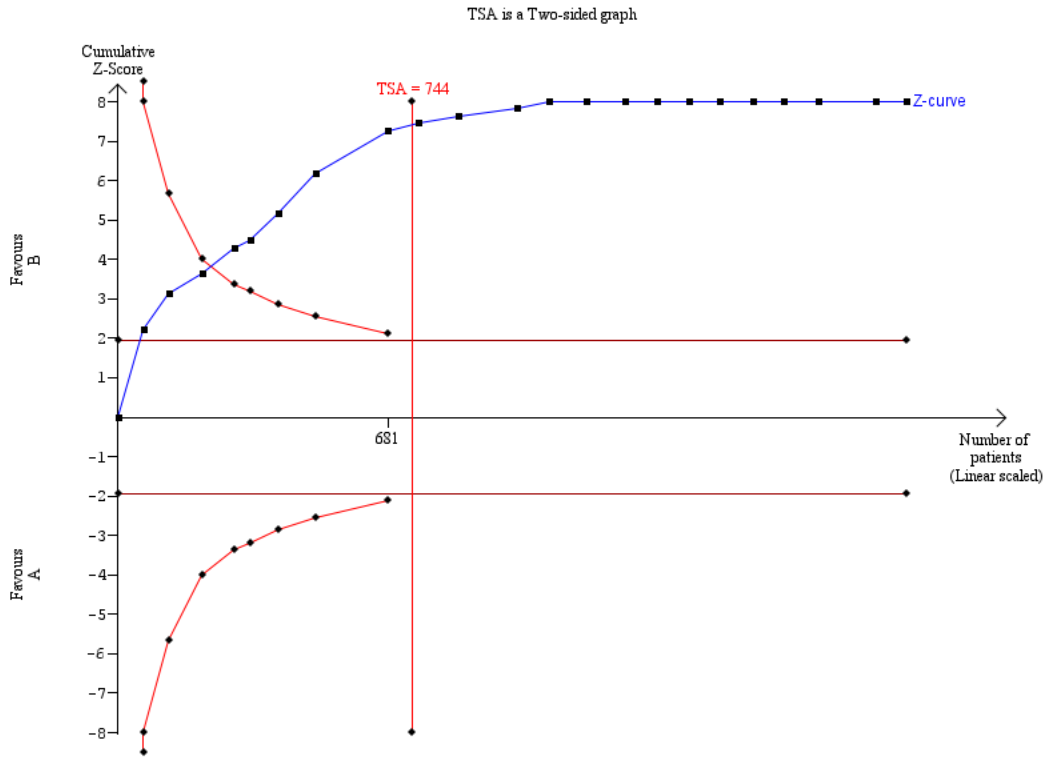

Figure A23. HBeAg.

Figure A24. HBsAg.

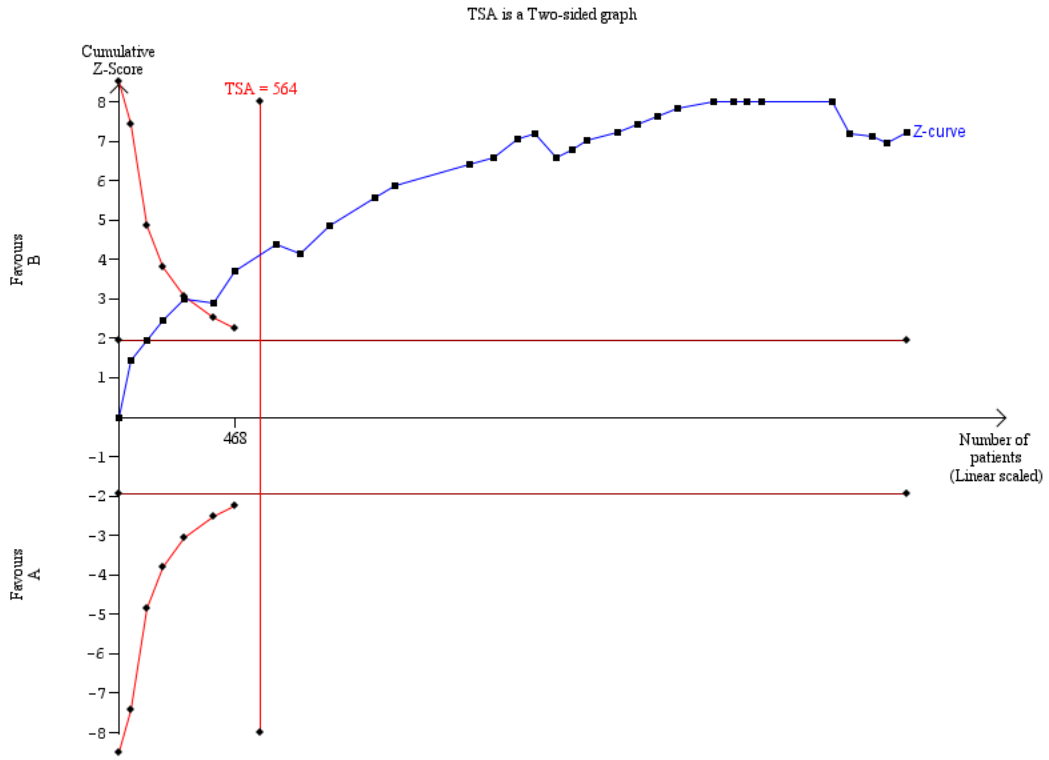

Figure A25. ALT.

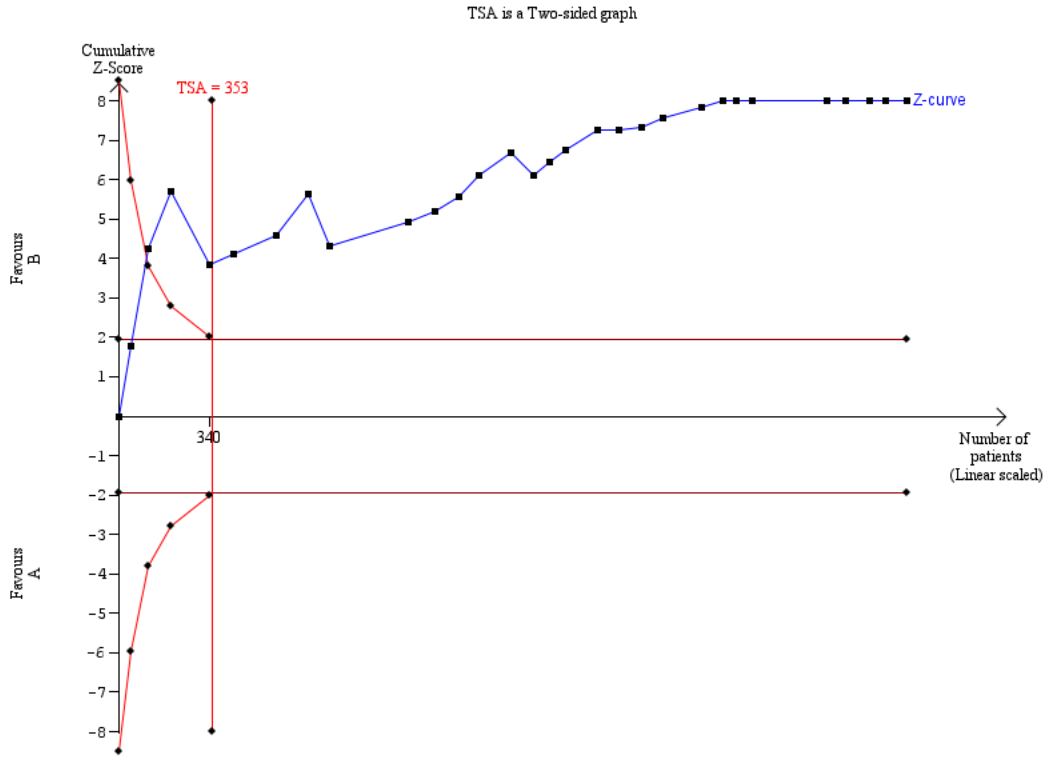

Figure A26. AST.

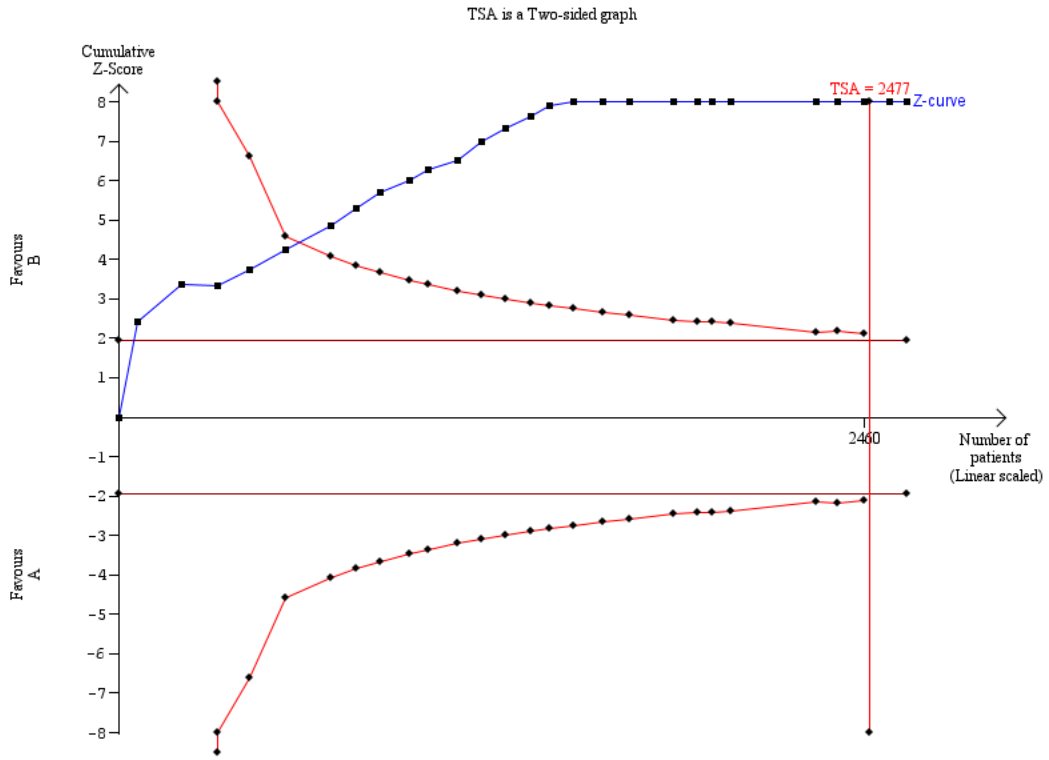

Figure A27. Total clinical efficacy.

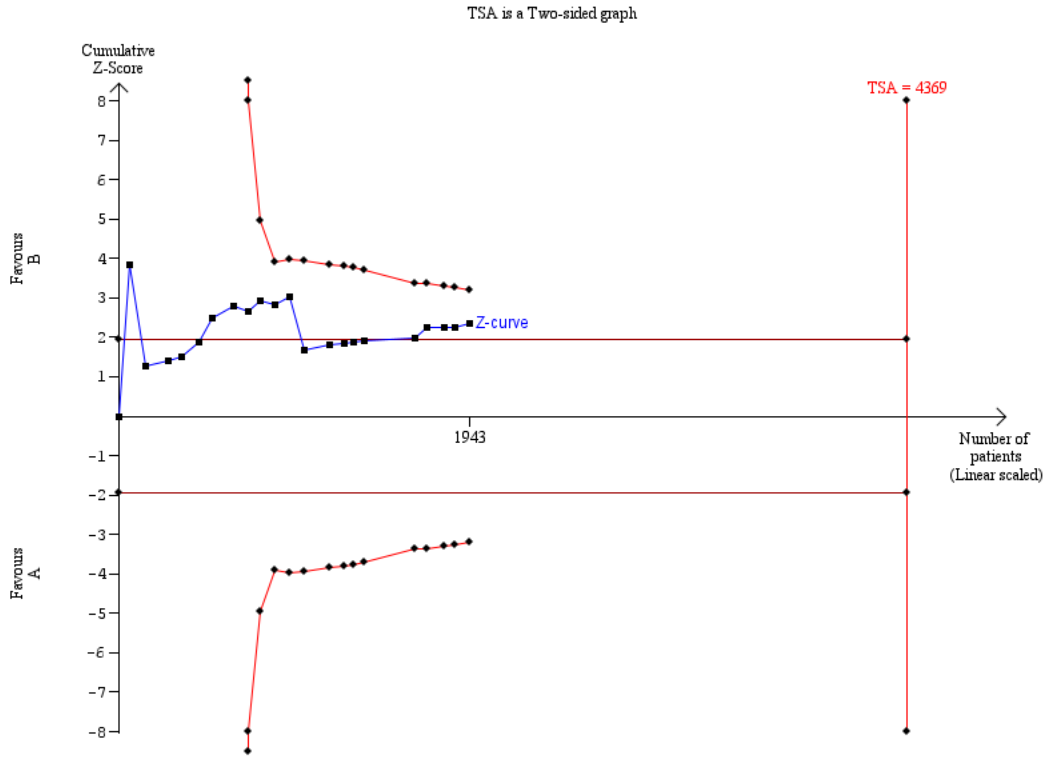

Figure A28. TBil.

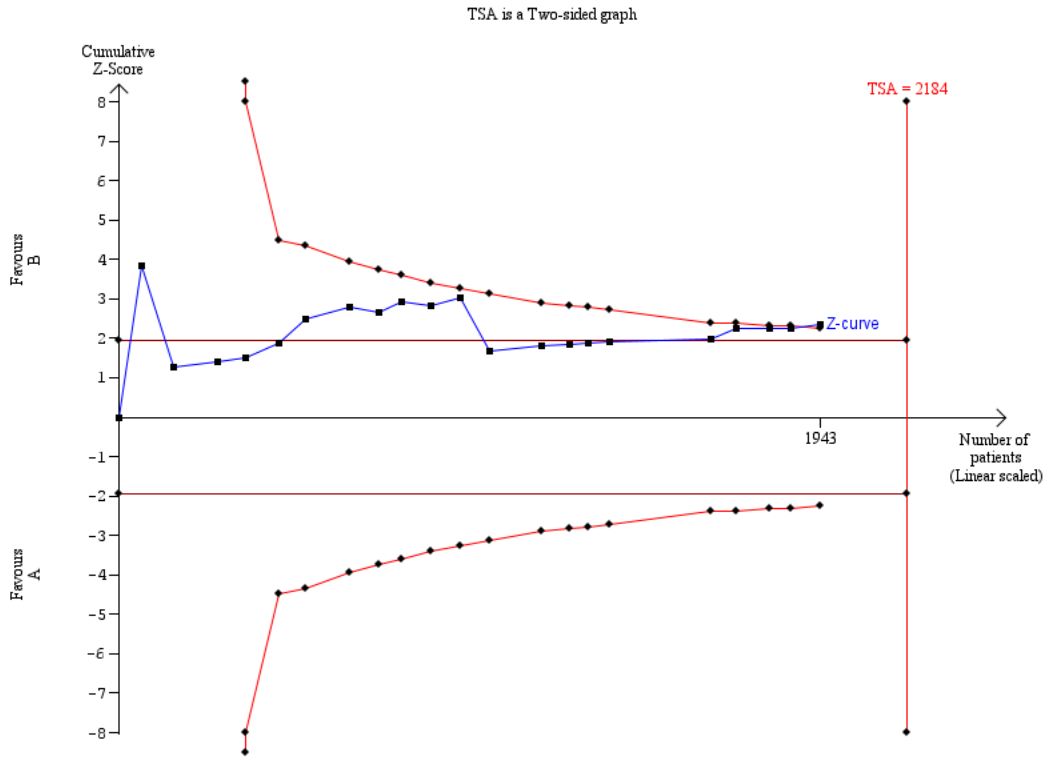

Figure A29. HA.

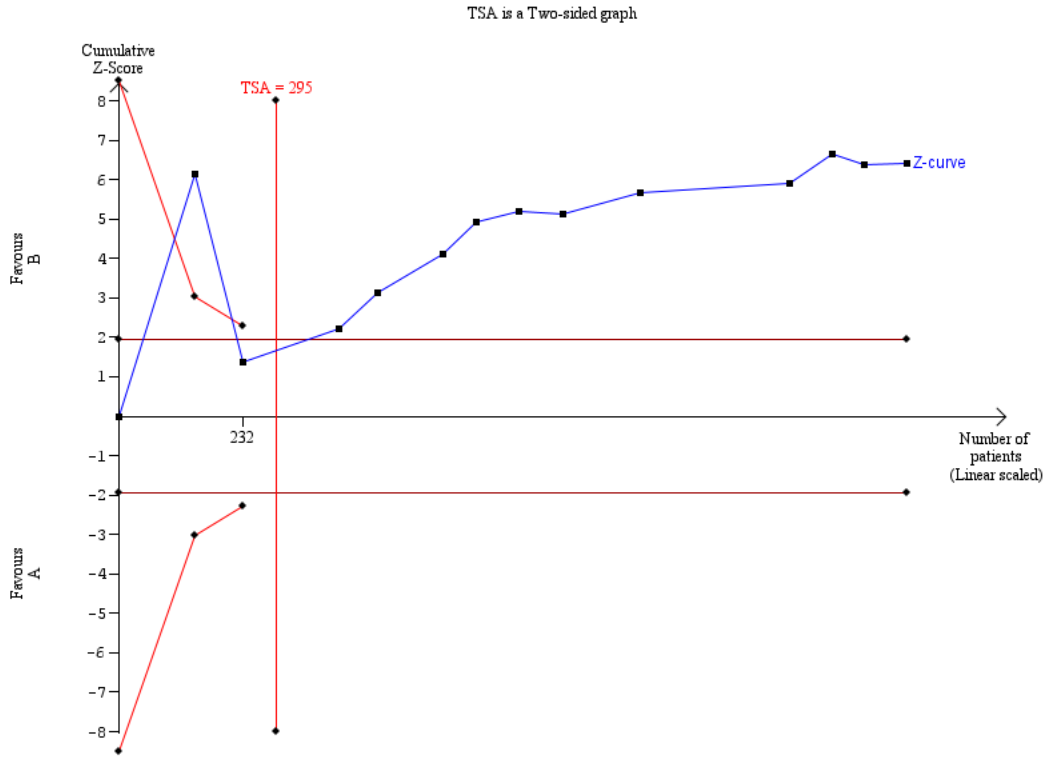

Figure A30. LN.

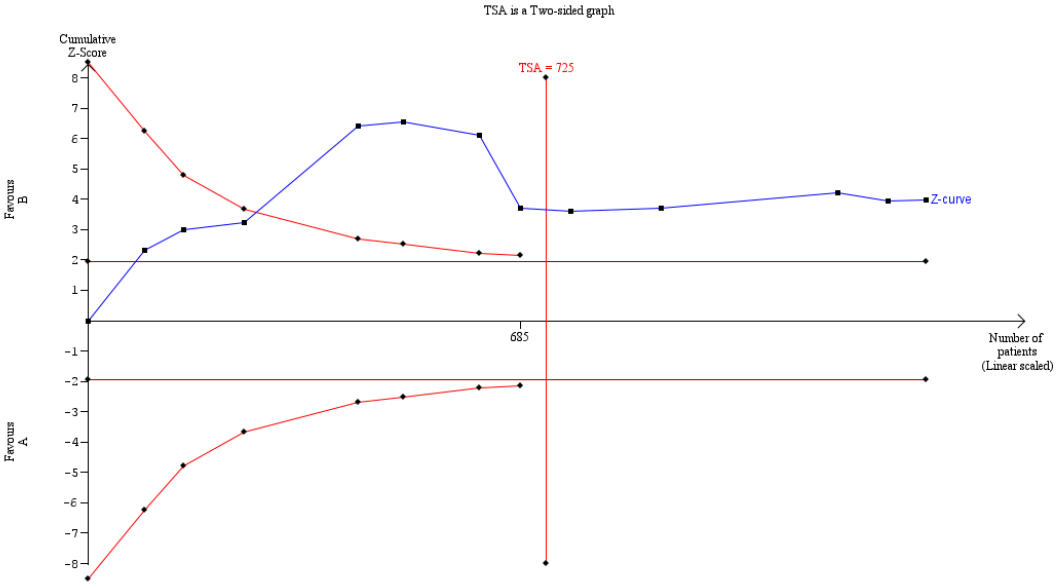

Figure A31. PCIII.

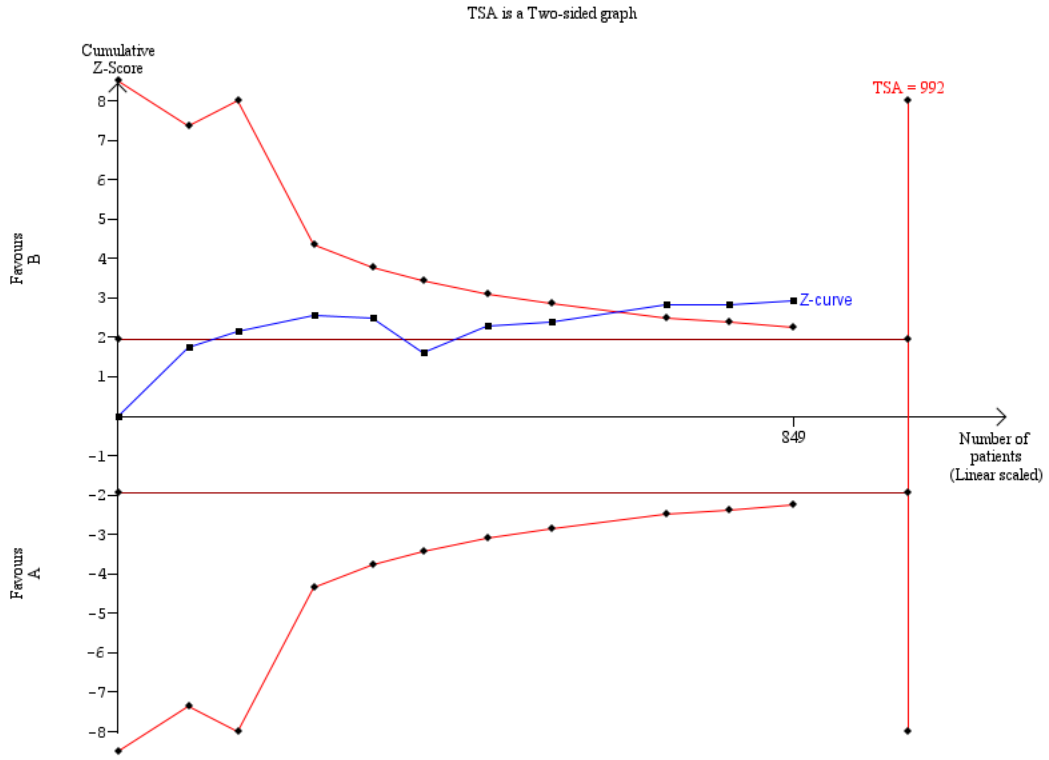

Figure A32. IV-C