International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Clinical Outcomes of TCF3-PBX1-Positive Childhood Acute Lymphoblastic Leukemia: A Systematic Review and Meta-Analysis

INPLASY202680033
doi: 10.37766/inplasy2026.8.0033
Received: 7 August 2026
Published: 7 August 2026

Tao, ML; Bin, Q.

Corresponding author:
Meiling Tao

taomeiling1232021@163.com

Author Affiliation:
Guangzhou Women and Children's Medical Center Liuzhou Hospital.

ADMINISTRATIVE INFORMATION

Support - No external funding was received for this systematic review.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202680033

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 August 2026 and was last updated on 7 August 2026.

INTRODUCTION

Review question / Objective The aim of this systematic review is to comprehensively evaluate the clinical outcomes of children with TCF3-PBX1-positive acute lymphoblastic leukemia under contemporary treatment strategies, including 5-year overall survival, 5-year event-free survival, and relapse rates. This review intends to provide updated evidence for risk-stratified treatment decisions.

The proposed systematic review will address the following main question: In children diagnosed with TCF3-PBX1-positive acute lymphoblastic leukemia, what are the pooled estimates of 5-year overall survival, 5-year event-free survival, and overall relapse rate? Given that this is a single-arm meta-analysis, no comparator group is included.

Condition being studied Pediatric acute lymphoblastic leukemia (ALL).

METHODS

Participant or population Children (age ≤ 18 years) diagnosed with acute lymphoblastic leukemia (ALL) carrying the TCF3::PBX1 (E2A-PBX1) fusion gene.

Intervention Not applicable. This is a single-arm meta-analysis of retrospective cohort studies. We aim to describe clinical outcomes in children with TCF3-PBX1-positive ALL, without comparison to a separate intervention group.

Comparator Not applicable.

Study designs to be included Retrospective cohort studies of children (age ≤ 18 years) diagnosed with TCF3-PBX1-positive acute lymphoblastic leukemia. Both single-center and multi-center studies with a minimum follow-up of 24 months will be included. No restrictions on geographic region or sample size will be applied. As this is a single-arm meta-analysis, no comparator group is required.

Tao et al. INPLASY protocol 202680033. doi:10.37766/inplasy2026.8.0033 Downloaded from https://inplasy.com/inplasy-2026-8-0033/

Eligibility criteria Studies will be included if they meet all of the following criteria: (1) Population: Children (age ≤ 18 years) diagnosed with acute lymphoblastic leukemia (ALL) carrying the TCF3::PBX1 (E2A-PBX1) fusion gene; (2) Study design: Retrospective cohort studies (both single-center and multi-center), reporting at least one of the outcomes of interest; (3) Outcomes: The study must report extractable data (number of events and total sample size) on at least one of the following outcomes: 5-year overall survival, 5-year event-free survival, overall relapse rate, median time to relapse, central nervous system relapse rate, testicular relapse rate, central nervous system leukemia at diagnosis, or minimal residual disease positivity after induction therapy; (4) Follow-up: Median follow-up time of at least 24 months.

Studies will be excluded if they: (1) are case reports, reviews, conference abstracts, animal experiments, or basic research; (2) have a sample size of <10 patients; (3) contain duplicate or overlapping data; (4) are not available in Chinese or English; or (5) lack sufficient data to calculate the effect size.

Information sources PubMed, CNKI (China National Knowledge Infrastructure), Wanfang Data, and VIP (Chinese Science and Technology Periodical Database). All databases will be searched from inception to May 2026. No language restrictions will be applied to the search, but only studies published in English or Chinese will be included for full-text review. Additionally, the reference lists of relevant articles and included studies will be manually screened to identify additional eligible studies.

Main outcome(s) 1.5-year overall survival (OS) rate
2.5-year event-free survival (EFS) rate.

Additional outcome(s) 1.Overall relapse rate

2.Median time to relapse (months)

3.Central nervous system (CNS) relapse rate

4.Testicular relapse rate

5.Central nervous system leukemia (CNSL) at diagnosis rate

6.Minimal residual disease (MRD) positivity rate after induction therapy

Quality assessment / Risk of bias analysis The methodological quality of each included retrospective cohort study will be independently assessed by two reviewers using the Newcastle-Ottawa Scale (NOS) for cohort studies. The NOS evaluates studies across three domains: selection of study groups (4 items), comparability of groups (2 items), and ascertainment of outcomes (3 items), with a maximum total score of 9 points. Studies will be categorized as having low (7–9 points), moderate (4–6 points), or high (0–3 points) risk of bias. Any disagreements between reviewers will be resolved through discussion or consultation with a third reviewer if consensus cannot be reached. The results of the quality assessment will be presented in a summary table and will be considered in the interpretation of the meta-analysis results.We will not apply the GRADE system to rate the overall quality of evidence, as all included studies are retrospective cohort studies.

Strategy of data synthesis The meta-analysis of proportions will be conducted using Stata 17.0 . Given the expected clinical and methodological heterogeneity across the included retrospective cohort studies, all pooled estimates will be calculated using a random-effects model with the restricted maximum likelihood (REML) method . To stabilize the variance and normalize the distribution of proportions, the Freeman-Tukey double arcsine transformation will be applied before pooling . Pooled proportions with their corresponding 95% confidence intervals will be presented for all outcomes. Heterogeneity will be assessed using both the Cochran's Q test and the I^2 statistic . An I^2 value greater than 50% will be considered indicative of substantial heterogeneity . When substantial heterogeneity is present, subgroup analyses will be performed to explore its potential sources . Subgroup analyses will be conducted based on treatment intensity (contemporary/intensive regimens versus early/conventional chemotherapy regimens), study region (China versus other countries), study design (multi-center versus single-center studies), and sample size (≥50 versus <50 patients). Additionally, sensitivity analyses will be performed using the leave-one-out approach to evaluate the robustness of the pooled estimates and to identify influential studies . Publication bias will be assessed using Egger's test and Begg's test when at least 10 studies are included in the meta-analysis . Funnel plots will be generated for visual assessment. If asymmetry is detected and publication bias is suspected, the trim-and-fill method will be used to adjust the pooled estimates for potential missing studies. All statistical analyses will be performed using Stata version 17.0 (StataCorp, College Station, TX, USA). The results of the selection process will be summarized using a PRISMA flow diagram , and

Tao et al. INPLASY protocol 202680033. doi:10.37766/inplasy2026.8.0033 Downloaded from https://inplasy.com/inplasy-2026-8-0033/

the characteristics and results of included studies will be presented using tables and forest plots.

Subgroup analysis To explore potential sources of heterogeneity, subgroup analyses will be conducted based on the following factors: (1) treatment intensity: contemporary/intensive chemotherapy regimens versus early/conventional regimens; (2) study region: China versus other countries; (3) study design: multi-center versus single-center studies; (4) sample size: studies with ≥50 patients versus <50 patients; and (5) MRD assessment time point: Day 33 versus Day 46 versus other time points. Subgroup analyses will be performed only when at least two studies are available in each subgroup category.

Sensitivity analysis To assess the robustness of the pooled estimates and to identify potential influential studies, a leave-one-out sensitivity analysis will be performed. This will be done by sequentially excluding each included study one at a time and recalculating the pooled effect sizes for the remaining studies. If a particular study is found to have a substantial influence on the overall estimate or heterogeneity, the results with and without this study will be reported and discussed. Additionally, sensitivity analyses will be conducted by excluding studies with a high risk of bias, as determined by the Newcastle-Ottawa Scale.

Country(ies) involved China.

Keywords Acute Lymphoblastic Leukemia, TCF3-PBX1, Childhood,Overall Survival, Relapse.

Contributions of each author
Author 1 - Meiling Tao.
Author 2 - Qiong Bin.

Tao et al. INPLASY protocol 202680033. doi:10.37766/inplasy2026.8.0033 Downloaded from https://inplasy.com/inplasy-2026-8-0033/