INPLASY

Reporting of component-level lesion response and biomarker-by-treatment interaction in randomised controlled trials of hidradenitis suppurativa: a methodological systematic review

INPLASY2026110045

doi: 10.37766/inplasy2026.11.0045

Received: 12 November 2026

Published: 12 November 2026

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ADMINISTRATIVE INFORMATION

Support - NSF-Xinjiang Youth 2024D01C304.

Review stage at the time of initial registration - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2026110045

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 November 2026 and was last updated on 12 November 2026.

INTRODUCTION

Study aim In randomised controlled trials of hidradenitis suppurativa published since 2010, what proportion report inflammatory and structural lesion components separately, prespecify a biomarker-by-treatment interaction test, and record baseline tunnel burden?

Background Hidradenitis suppurativa (HS) affects roughly 1% of adults and follows a chronic, relapsing course [1]. Three biologics, adalimumab, secukinumab and bimekizumab, now dominate the treatment of moderate-to-severe HS, and each has demonstrated efficacy in randomised trials, reducing inflammatory lesions and improving quality of life [2,3]. Yet in every one of those phase 3 programmes roughly half of randomised participants did not reach the primary response threshold, and a similar figure appears in real-world cohorts, where most patients still come to surgery [4,5].

Reviews usually explain this plateau by heterogeneity: HS is said to contain several molecular endotypes, trials have not stratified by them, and observed response rates therefore average across populations with different dominant pathways [6–8]. The explanation is plausible and widely repeated, but it has a rarely stated weakness: no study has yet shown that a molecular classification predicts a different response to two different drugs.

A second explanation receives less attention because it sits in the endpoint rather than in the patient. HiSCR, the instrument on which all three programmes were judged, counts abscesses, inflammatory nodules and draining tunnels together and requires that none of them increase [2]. The three components are not equivalent measurements. Abscess and nodule counts track inflammatory load and fall when cytokine signalling is blocked. Draining tunnels are epithelialised channels lined by keratinocytes and set in a remodelled dermis; once formed they persist for years, they account for much of the surgical workload, and adalimumab does not resolve them

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[4]. A composite that adds a slowly reversible structural component to a rapidly reversible inflammatory one has a response ceiling that depends on the baseline lesion mix: two patients with the same total lesion count can differ twofold or more in the structural fraction, and therefore in the response that any anti-inflammatory drug could produce. The trial records this difference as treatment failure.

Determining whether this endpoint arithmetic explains published response rates is not possible from primary publications alone, because the necessary analyses require component-level lesion counts by treatment arm and biomarker-by-treatment interaction data. These data are reported heterogeneously across trials, varying in which components are given, at which timepoints, and whether they appear in the main text or in supplementary appendices, and no systematic review has yet mapped how consistently they are reported or whether they are sufficient to test the endotype and endpoint explanations of non-response.

This review therefore takes a methodological (meta-research) approach. We will systematically identify randomised controlled trials of systemic therapy in HS and record how component-level lesion response and biomarker-by-treatment interaction are reported and analysed, including the completeness of component-level counts, their placement (main text versus supplementary appendix), and whether interaction analyses are pre-specified and interpretable. The results will show whether existing trial reporting already permits the stratified and component-level analyses that the endotype and endpoint hypotheses require, and will define reporting standards for the next generation of stratified HS trials.

Rationale O methodological review of outcome reporting in hidradenitis suppurativa trials was identified in a preliminary search. Reviews in HS have so far synthesised efficacy and safety, and methodological reviews in dermatology have examined outcome reporting in other inflammatory skin diseases, but none has addressed how HS randomised trials report outcomes at the level of individual lesion components, or whether they test biomarker-by-treatment interaction. It therefore remains unknown whether the component-level and interaction analyses needed to distinguish an endotype explanation from an endpoint explanation of non-response can be performed on already published trial data, or whether new primary studies will be required to generate them.

METHODS

Search strategy PubMed/MEDLINE, ClinicalTrials.gov, WHO ICTRP and ChiCTR will be searched from 1 January 2010 to [检索日期]. Embase and CENTRAL will not be searched because institutional access is unavailable; this will be reported as a limitation. Reference lists of included trials and of related systematic reviews will be hand-searched.

Eligibility criteria Eligibility criteria Types of participants. Adults and adolescents with hidradenitis suppurativa (HS) enrolled in randomised controlled trials. No restriction by sex, disease duration, Hurley stage, baseline lesion count or previous biologic exposure. Trials enrolling mixed populations are eligible where HS-specific outcome data are reported separately. Only reports published in English are eligible. Concept. Randomised controlled trials of any systemic or topical intervention for HS, including biologics (adalimumab, secukinumab, bimekizumab and other agents), Janus kinase inhibitors, antibiotics and other systemic or topical agents, compared with placebo or an active comparator. Because this is a methodological (meta-research) review, the concept of interest is not the effect of any individual drug but two reporting domains: first, outcome data reported at the level of individual lesion components (abscess, inflammatory nodule and draining tunnel counts), including whether these appear in the main text or only in supplementary appendices; second, biomarker-by-treatment interaction analyses, including whether they were pre-specified, reported and interpretable. Eligible designs are phase 3 randomised controlled trials; if fewer than eight phase 3 trials are identified, phase 2 trials with at least 100 participants will be added. Trials must report at least one HS-specific clinical outcome measure, such as HiSCR or component lesion counts. Context. Any clinical setting, including secondary and tertiary dermatology outpatient care and hospital-based or ambulatory services, in any country or health system. Trials with results reported from 1 January 2010 onwards are eligible. No restriction by funding source (industry-sponsored or investigator-initiated) or by trial registration status.

Data extraction Two reviewers will extract data independently using a piloted form of ten fields. Agreement will be assessed on three trials before full extraction and reported as Cohen's kappa. Disagreements will be resolved by a third reviewer.

Reporting completeness will be assessed against CONSORT 2010 items 6a, 6b, 12a, 12b, 17a, 17b

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and 18. Risk of bias in effect estimates will not be assessed because no effect estimates are pooled.Two reviewers will extract data independently using a piloted form of ten fields. Agreement will be assessed on three trials before full extraction and reported as Cohen's kappa. Disagreements will be resolved by a third reviewer.
Reporting completeness will be assessed against CONSORT 2010 items 6a, 6b, 12a, 12b, 17a, 17b and 18. Risk of bias in effect estimates will not be assessed because no effect estimates are pooled.

Outcome definitions Proportion of included trials that report abscess, inflammatory nodule and draining tunnel counts separately, with 95% confidence intervals
Proportion prespecifying a biomarker-by-treatment interaction test; proportion recording baseline tunnel count; change in these proportions over publication year; inter-rater agreement between reviewers.

Strategy of data synthesis / Statistical analysis Descriptive proportions with Wilson 95% confidence intervals; Cochran-Armitage test for trend by publication year; stratification by mechanism class. No meta-analysis of treatment effects will be performed.
Mechanism class (IL-17 or IL-23, TNF, JAK, other), publication year, and funding source.

Country(ies) involved China.

Keywords Hidradenitis suppurativa; randomised controlled trial; outcome reporting; meta-research.

Dissemination plans Peer-reviewed journal article, together with a recommendation for component-level outcome reporting in future trials.

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