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Accuracy of extracted data, cohort overlap and robustness of conclusions in published meta-analyses of pathological prognostic factors in primary IgA nephropathy: protocol for a methodological study with de-duplicated reanalysis

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ADMINISTRATIVE INFORMATION

Support - 2024C03212.

Review stage at the time of initial registration - Preliminary searches

Conflicts of interest - he authors declare no financial or non-financial conflicts of interest. None of the authors is an author of any systematic review or meta-analysis eligible for inclusion in this audit, and none has received support from any party with an interest in the reviews to be examined. If an eligible review is found during screening to have been authored by a member of this team, that review will be verified independently by the two team members who are not among its authors, the affected person will take no part in any judgement concerning it, and the arrangement will be reported in the final article. The declaration of funding in the preceding field does not replace this declaration.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 November 2026 and was last updated on 26 November 2026.

INTRODUCTION

Study aim Primary aim. Among published systematic reviews and meta-analyses of pathological or immunopathological lesions and hard kidney outcomes in primary IgA nephropathy, to quantify the proportion of reported item-level effect estimates that can be traced back to the primary study from which they are said to come, and to classify the specific reasons when they cannot. An item is one effect estimate in a review attributable to one named primary study.
Secondary aims. First, to describe the extent to which these reviews draw on the same primary studies, using a review-by-study matrix and the corrected covered area, computed separately for the whole set and for same-topic subsets. Second, where populations, exposure definitions, outcomes, follow-up and effect measures are comparable, to re-analyse the research-level estimates after removing duplicated cohorts and correcting confirmed extraction errors, and to present the result alongside the originally published pooled value. Third, to compare traceability and the three problem proportions across prespecified strata: review topic, publication year, whether a registration number is reported, appraisal result, and accessibility of the primary article.
Boundaries. This study will not produce an updated pooled estimate of any prognostic association. Re-analysis will be confined to the studies already included in each audited review; no additional search for primary studies will be

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performed, which is the operational line between an audit reanalysis and an updated meta-analysis. The study reports measurements, not verdicts on individual reviews: it will not assess the reproducibility of pathological scoring itself, and will make no judgement about the intentions of review authors. A finding of few errors, or of no material change after de-duplication, will be reported as fully as a finding of many errors, and the research question will not be revised after preliminary results are seen.

Background Pathological indices measured on kidney biopsy are central to prognostication in IgA nephropathy. The Oxford MEST-C lesions, the proportion of crescents, and immunopathological findings such as glomerular C4d and
complement deposition are all used to estimate the risk of progression, and the number of systematic reviews and meta-analyses synthesising these associations continues to grow. Their pooled estimates are cited in subsequent guidance-oriented literature and in clinical discussion.
Two structural risks attach to this particular literature, and neither is visible when reading a single review. First, primary studies in this field usually report prognostic associations inside multivariable regression tables that carry many adjacent rows, several competing models, and variable names that differ by one or two words. Taking the coefficient of the wrong variable, taking an estimate from a different model, or carrying an odds ratio across as a hazard ratio is therefore more likely here than in a typical intervention review, where effect estimates are usually reported in a single clearly labelled table. Second, the primary cohorts in this field are concentrated in a small number of large centres and registries. The same patients may consequently be counted in several reviews, yet reviews seldom report how far their included studies overlap with those of neighbouring reviews. When several reviews report concordant pooled estimates for the same lesion, a reader naturally reads this as independent replication; if those reviews rest on the same cohorts, that reading does not hold.
Detecting either problem requires returning to the primary studies item by item and registering, for every review, the complete list of studies it included. Definitions used throughout this protocol are as follows. An item is one effect estimate in a review attributable to one named primary study; where a review reports five lesions for the same primary study, that counts as five items. A traceable item is one whose primary article can be obtained, so that the value the review reports can be checked against it. The corrected covered area is the established index of overlap between reviews, calculated from the review-by-study matrix. These terms are used consistently in the eligibility criteria, outcome definitions and analysis plan below.

Rationale A duplication search was carried out on 26 November 2026. In PubMed, a search combining IgA nephropathy with systematic review or meta-analysis and with terms for audit, data extraction, error, reproducibility, accuracy, overlap or methodology returned 31 records; each title and abstract was read and none was an audit of data extraction in meta-analyses of pathological prognostic factors in this disease. PROSPERO was searched with the quoted phrase IgA nephropathy combined with Oxford and returned 45 records, none of which was identified as a methodological audit addressing the same question. INPLASY and OSF Registries were searched and returned no methodological audit in this field.
The closest related work is a systematic review of the Oxford classification itself, which identified 99 eligible papers and examined inter-observer reproducibility of scoring together with the results of 125 multivariable analyses in 92 papers. That study audits the primary studies: its units are papers and analyses, and its outcomes are observer agreement and the frequency with which each lesion is associated with outcomes. The present study audits the published reviews: its units are items within reviews, and its outcomes are traceability and overlap. The two are complementary and do not answer the same question, but the relationship will be stated explicitly in the discussion.
Audits of data-extraction accuracy in published meta-analyses exist in other fields, and the index of overlap between reviews is well established. The contribution expected here is therefore not the method but its application within one clinical domain where the two structural risks described above are plausible: item-level tracing back to the primary articles, explicit registration and handling of repeated cohorts, and an assessment of whether either materially changes the pooled values already in circulation. Feasibility has been checked rather than assumed: ten candidate reviews have already been identified, their bibliographic records verified and their expected disposition under the criteria below recorded in advance, and two pairs of same-topic reviews with probable cohort overlap have been located. Should the final sample prove smaller than expected, a small set of audited reviews is itself an informative finding, and the scope will not be widened in order to enlarge it.

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METHODS

Search strategy Sources. MEDLINE via PubMed; Embase via Embase.com; Web of Science Core Collection; Cochrane Library (CDSR and CENTRAL exported separately); CNKI; Wanfang; and Google Scholar (first 100 records of each of three term sets). Backward citation tracking of the reference lists of all included reviews and of the closest related review, and forward citation tracking of included reviews in Google Scholar and, where available, Web of Science or Scopus. No language and no publication-year limits. An updating search in PubMed and Google Scholar will be run in the seventh week of the project. Database and interface are recorded separately for each source, together with the date of searching, the full strategy line by line, the number of records retrieved per line, and the numbers before and after deduplication, following PRISMA-S.

Strategy validation. The strategy was validated against ten seed reviews known to be eligible or closely related; the final version retrieved all ten. An earlier version that additionally required a prognosis term block retrieved 94 records but missed one seed whose title and abstract contain no prognosis term, so that block was removed; the final version retrieved 130 records in PubMed on 26 November 2026 with no mapping warnings. The strategy will be peer reviewed by a second team member using the PRESS checklist before the searches are run.

PubMed strategy, final version, run 26 November 2026, 130 records:

#1 ("Glomerulonephritis, IGA"[Mesh] OR "IgA nephropathy"[tiab] OR IgAN[tiab])

#2 (patholog*[tiab] OR histolog*[tiab] OR biops*[tiab] OR Oxford[tiab] OR MEST[tiab] OR "MEST-C"[tiab] OR mesangial[tiab] OR crescent*[tiab] OR endocapillary[tiab] OR "tubular atrophy"[tiab] OR "interstitial fibrosis"[tiab] OR sclerosis[tiab] OR deposit*[tiab] OR immunofluorescence[tiab] OR C4d[tiab] OR complement[tiab] OR podocyt*[tiab])

#3 (meta-analy*[tiab] OR metaanaly*[tiab] OR "systematic review"[tiab] OR systematic[sb])

#4 #1 AND #2 AND #3

Embase strategy, to be run and calibrated within the database:

#1 'iga nephropathy'/exp OR 'iga nephropathy':ti,ab,kw

#2 ('kidney biopsy'/exp OR 'oxford classification':ti,ab,kw OR mest:ti,ab,kw OR mesangial:ti,ab,kw OR crescent*:ti,ab,kw OR endocapillary:ti,ab,kw OR 'tubular atrophy':ti,ab,kw OR 'interstitial fibrosis':ti,ab,kw OR sclerosis:ti,ab,kw OR deposit*:ti,ab,kw OR 'c4d':ti,ab,kw OR complement:ti,ab,kw OR podocyt*:ti,ab,kw OR patholog*:ti,ab,kw)

#3 ('systematic review'/exp OR 'meta analysis'/exp OR 'systematic review':ti,ab,kw OR 'meta-analysis':ti,ab,kw OR metaanaly*:ti,ab,kw)

#4 #1 AND #2 AND #3

Chinese-language strategies are retained in Chinese so that they remain reproducible in the source databases.

CNKI: SU=('IgA肾病'+'IgA肾炎') AND SU=('牛津分型'+'病理'+'新月体'+'系膜'+'C4d'+'补体'+'足突'+'硬化') AND SU=('Meta分析'+'荟萃分析'+'系统评价'+'系统综述').

Wanfang: 主题:(IgA肾病 OR IgA肾炎) AND 主题:(牛津分型 OR 病理 OR 新月体 OR 系膜 OR C4d OR 补体) AND 主题:(Meta分析 OR 荟萃分析 OR 系统评价).

Eligibility criteria Units of analysis. The sampling unit is the published review. The verification unit is the item, defined as one effect estimate reported in a review and attributable to one named primary study; where a review reports five lesions for the same primary study, that counts as five items. A third register, used only for the overlap analysis, records every primary study included in each review, whether or not an item-level estimate is reported for it.

Inclusion. (i) Systematic reviews or meta-analyses whose research question is the association between a
pathological or immunopathological lesion and a kidney outcome in primary IgA nephropathy, in adults, in all ages or in children. (ii) The outcome in the audited review must be a hard kidney outcome: kidney failure or end-stage kidney disease, a decline in estimated glomerular filtration rate of at least 40 per cent or at least 50 per cent,
doubling of serum creatinine, or a composite of these. (iii) The review must report item-level effect estimates
attributable to named primary studies, in a forest plot, a table or the text. No language and no publication-year limits apply.

Exclusion, with codes used in the flow diagram. X1 population: secondary IgA nephropathy, IgA vasculitis nephritis, or post-transplant IgA nephropathy as the subject of the review; or a review mixing glomerular diseases from which IgA nephropathy data cannot be separated. X2 topic: reviews evaluating only treatment response, only prevalence or distribution of lesions, or only the performance of imaging or artificial-intelligence tools. X3 outcome: reviews whose only outcome is proteinuria remission or a change in a laboratory measure. X4 no item-level data: reviews reporting only an overall pooled value without per-study

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estimates. X5 design: narrative reviews, commentaries, editorials, literature reviews without a systematic search, and evidence maps. X6 duplicate report: errata, reprints and conference versions of the same review, which are merged into one review unit and counted once. Each excluded record receives one code only, taking the first that applies in the order above.
Handling of particular cases. A review covering both prognostic association and treatment response is included, and only its prognostic items are verified; this is recorded in the table of review characteristics. Reviews restricted to children are included but reported separately, and are removed as a block in one sensitivity analysis. A review whose full text cannot be obtained by the end of the third week of the project is recorded in the flow diagram as a report whose full text was not retrieved, and is not counted as an exclusion. Where two reviews are plainly the same
project reported twice, the more complete report is retained. Eligibility decisions are made in duplicate and independently, after a calibration exercise; criteria will not be altered once verification has begun, and any change made before that point will be registered as an amendment with its date and reason.

Data extraction Records are deduplicated in a reference manager (EndNote or Zotero) and screened in Rayyan in blind mode. Two reviewers screen titles and abstracts independently after calibrating on 50 enriched records, the enrichment being necessary because the expected inclusion rate is near 5 per cent; the threshold is a Cohen kappa above 0.60, and raw agreement alone is not accepted as evidence of calibration at this prevalence. Full-text screening is also independent and in duplicate.
Two reviewers then verify every item independently on a piloted form with seven field modules: review identifiers, item location, the values as reported in the review, the corresponding values in the primary article, the status code, overlap registration, and process information. Verification is piloted on two reviews before the remainder, and the inter-rater kappa for the status code is computed after that pilot; if it falls below 0.60, the coding rules are restated and the pilot repeated. Every figure recorded carries its source: the figure or table number in the review, and the page and table number in the primary article.
Disagreements are discussed and, if unresolved, settled by a third reviewer; unresolved discrepancies in
the primary article are referred to its corresponding author.

Review quality is appraised independently in duplicate, with AMSTAR-PF for prognostic-factor reviews, AMSTAR 2 for reviews containing an intervention component, and ROBIS for all included reviews. The three are reported separately and are not combined into a single score. Analyses use R 4.2 or later. All screening, verification, appraisal and analysis decisions are made by human reviewers; no automated classifier or artificial-intelligence tool makes or ranks them.

Outcome definitions Every item is assigned exactly one of five mutually exclusive states, in a fixed order. V0, primary article not obtainable after library, interlibrary loan and author request. Otherwise V1, verified as consistent in measure, point estimate, interval, model and outcome definition. Otherwise, taking the first that applies: V2, confirmed extraction error, where the value in the review differs point by point from the corresponding value in the primary article; V3, source not reproducible, where the article is in hand but the value cannot be located or recomputed from it; V4, reporting problem in the primary article, where the value is copied correctly but the article reports it in a way that prevents its use on the scale the review assigns to it.
Primary outcome one, traceability rate: items in V1, V2, V3 or V4 divided by all items. The numerator includes V1. An item whose primary article cannot be obtained is not evidence that no error exists, and counting such items in the denominator of the problem proportions would make reviews drawing on less accessible primary literature appear more accurate.
Primary outcome two, problem proportions: V2, V3 and V4 each divided by the number of verifiable items, that is V1 plus V2 plus V3 plus V4. The three are reported separately with confidence intervals and are never summed into a single error rate.
Secondary outcomes: the review-by-study overlap matrix and the corrected covered area, for the whole set and for
same-topic subsets; and, where comparability permits, the change in the pooled estimate after de-duplication and
correction, shown beside the published value.

Strategy of data synthesis / Statistical analysis
Frame. Eligible reviews are enumerated in full, not sampled; items are nested within reviews and not independent.
Proportions. Traceability and the three problem proportions are single-sample binomial proportions with Wilson and Clopper-Pearson 95% confidence intervals. No random-effects pooling, I-squared or prediction interval is reported. Item-level estimates use cluster-robust variance clustered on the

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review, with review-level estimates as a robustness check.
Overlap. The matrix and corrected covered area use each review's complete included-study register, not the item table.
Strata, each needing at least two reviews: topic, publication year, registration reported or not, appraisal result, and accessibility of the primary article. Comparisons use exact tests or item-level logistic regression; no meta-regression is performed.
Branching, decided once the audit set is final and before verification starts, on items counted rather than verified. The review count and the item count are banded separately (high: 8 or more and 100 or more; middle: 3 to 7 and 50 to 99; low: 2 or fewer and fewer than 50), and where the two fall in different bands the lower band governs. High band: the full plan with de-duplicated reanalysis, provided at least one pair of comparable same-topic reviews exists. Without such a pair, or in the middle band, the reanalysis is dropped and the study becomes a traceability and overlap survey. Low band: results are described without proportion inference. Thresholds are not relaxed after results are seen. Reanalysis stays within each review's included studies; within an overlapping set one study is kept by a prespecified order of preference, the displaced one being substituted in a sensitivity analysis.

Country(ies) involved China.

Other relevant information Review stage. The searches for competing studies in PubMed, PROSPERO, INPLASY and OSF Registries and the validation of the PubMed search strategy were repeated on 26 November 2026. At submission, neither formal screening nor formal data verification had begun.
Pilot. The feasibility pilot described in the research team's report covered the items of one forest plot in one review to confirm that item-level tracing was practicable. Those items will be re-assessed under the present protocol and the pilot result will not be carried over.
Choice of registry. This protocol is not registered in PROSPERO. PROSPERO registers systematic reviews with outcomes of direct relevance to health within humans and does not accept systematic critical appraisals; the primary outcomes here are reporting-level indices rather than health outcomes. PROSPERO was searched again for competing registrations on 26 November 2026.
Materials. A time-stamped backup record will be deposited in OSF Registries and cross-referenced with this registration. The search log, the item-level verification form, the included-study register used for the overlap analysis, and the analysis code will be deposited in a public repository at the time of submission.
Reporting follows PRISMA 2020 and PRISMA-S as far as they apply to a methodological study, with departures explained.
Keywords meta-research; data extraction accuracy; cohort overlap; corrected covered area; IgA nephropathy; pathological prognostic factors; research on research.

Dissemination plans Findings will be submitted to a peer-reviewed journal. The INPLASY registration number, the registration date and the digital object identifier will be reported in the abstract and in the methods section of the resulting article, and the backup record in OSF Registries will be cited alongside. At the time of submission the complete item-level verification table, the included-study register used for the overlap analysis, the search log with dates and per-line record counts, and the analysis code will be deposited in a public repository, so that any reader can repeat the verification and the calculations. Any departure from this protocol will be submitted as an amendment before the revised method is applied wherever that is possible, and every departure will also be reported in the final article with its date, the stage of the project at which it was decided, and the reason. Results will be reported in full whether or not errors are found and whether or not de-duplication changes any pooled value.

Contributions of each author
Author 1 - Chaofan Zhang - Designed the protocol and developed and validated the search strategy. Will independently screen records, verify each item-level effect estimate against the primary article, and appraise included reviews. Will lead the statistical analysis and draft and revise the full manuscript.
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Author 2 - Yining Chen - Will independently screen titles, abstracts and full texts, verify each item-level effect estimate against the primary article, and appraise included reviews. Will record decisions before discussing discrepancies with the first reviewer and will critically revise the manuscript.
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Author 3 - Xinyi Zhou - Will independently review the search strategy using the PRESS checklist, run the database searches, record search dates and result counts, remove duplicate records, and retrieve primary articles and supplementary materials for verification.
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Author 4 - De Jin - Will compile the list of primary studies included in each review, document potential cohort overlap, and construct the overlap matrix. Will assist with statistical analyses by calculating the corrected covered area and checking the analysis code.
Email: tcmjinde@126.com
Author 5 - Hongyu Chen - Will serve as corresponding author, review and approve the final protocol, and act as the third reviewer to adjudicate disagreements that the two independent reviewers cannot resolve through discussion.

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