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Association between prospective and retrospective protocol registration and reporting quality and methodological rigor of systematic reviews: a protocol for a meta-research study

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ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 April 2026 and was last updated on 29 July 2026.

INTRODUCTION

Study aim To evaluate whether the timing of protocol registration (prospective versus retrospective) is associated with the reporting quality and methodological rigor of systematic reviews with meta-analysis of healthcare interventions including randomized controlled trials. Additionally, among retrospectively registered reviews, we will evaluate the transparency of retrospective registration practices and examine whether these practices are associated with reporting quality and methodological rigor.

Background Prospective protocol registration is widely recommended as a core methodological standard for systematic reviews because it promotes transparency, reduces the risk of selective reporting, and supports the prespecification of review methods before study conduct. Despite these well-recognized benefits, a substantial proportion of systematic reviews continue to be registered retrospectively.
Although retrospective registration may improve transparency compared with the absence of protocol registration, its ability to preserve methodological rigor and reduce the risk of bias remains uncertain, particularly when registration occurs after key stages of the review process have already been completed. Consequently, it is unclear whether the timing of protocol registration is associated with differences in the reporting quality and methodological rigor of published systematic reviews.

Rationale Previous meta-epidemiological studies have suggested that protocol registration is associated with improved reporting quality and methodological rigor in systematic reviews. However, the interpretation of these findings remains challenging because widely used reporting and methodological assessment tools often include protocol registration as one of their evaluation domains. Consequently, comparisons between registered and non-registered reviews may be affected by methodological circularity, potentially inflating the observed association between registration and study quality.
Furthermore, the distinction between prospectively and retrospectively registered reviews has received limited empirical attention. Although prospective

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registration is intended to promote transparency and reduce bias through the prespecification of review methods, retrospective registration may occur after key stages of the review process have already been completed. Consequently, retrospective registration cannot provide the same assurance that methodological decisions were established before review conduct.

Recent conceptual work has proposed that retrospectively registered protocols should not be interpreted solely according to the timing of registration but also according to the transparency with which retrospective registration is reported, including clear disclosure of its retrospective nature, justification for delayed registration, and transparent reporting of methodological changes. Although this transparency-oriented framework provides a conceptual basis for interpreting retrospectively registered protocols, it has not yet been empirically evaluated.

Existing meta-epidemiological studies have rarely compared prospectively and retrospectively registered systematic reviews while simultaneously minimizing methodological circularity and evaluating transparency practices among retrospectively registered reviews. Consequently, it remains unclear whether differences in reporting quality and methodological rigor are primarily associated with the timing of registration itself or with the extent to which retrospective registration is transparently reported.

To address these gaps, this study will compare prospectively and retrospectively registered systematic reviews using assessment instruments specifically designed to avoid circularity. In addition, among retrospectively registered reviews, we will evaluate the transparency of retrospective registration practices and examine whether greater transparency is associated with higher reporting quality and methodological rigor. By empirically testing this recently proposed transparency-oriented framework, this study aims to provide evidence to inform the interpretation of retrospectively registered protocols in evidence synthesis.

METHODS

Search strategy A comprehensive dataset will be constructed from systematic reviews registered in the INPLASY registry and subsequently published in peer-reviewed journals. The analytical sample will be restricted to systematic reviews with meta-analysis evaluating healthcare interventions and including randomized controlled trials (RCTs).

INPLASY was selected as the data source because it permits both prospective and retrospective protocol registration and systematically records information on the stage of the review at the time of registration. In addition, the registry includes optional fields describing the reasons for retrospective registration, allowing the evaluation of transparency-related practices that are central to the objectives of this study.

The registry also maintains an active follow-up process to identify completed reviews and link registered protocols to their corresponding peer-reviewed publications, including cases in which authors do not subsequently update the registry. This process improves the completeness of protocol–publication linkage and facilitates the construction of a comprehensive analytical dataset.

These registry characteristics enable the identification of prospectively and retrospectively registered reviews using standardized registry information and provide the data required to evaluate transparency practices associated with retrospective registration.

Eligible studies will be identified through a structured process consisting of: (1) extraction of records from the INPLASY registry that are classified as completed and linked to a peer-reviewed publication; and (2) linkage of registered protocols to their corresponding publications using Digital Object Identifiers (DOIs) and registry identification numbers.

For the analytical sample, eligibility will be restricted to systematic reviews with meta-analysis evaluating healthcare interventions that exclusively include randomized controlled trials (RCTs).

Eligibility criteria Initially, all evidence syntheses registered in the INPLASY registry and subsequently published in peer-reviewed journals, with full-text availability, will be identified to characterize the overall study sample.

The analytical sample will be restricted to systematic reviews with meta-analysis evaluating healthcare interventions that exclusively include randomized controlled trials (RCTs). This restriction is intended to enhance methodological comparability across studies and reduce heterogeneity arising from differences in review design, methodological approaches, and underlying evidence.

Protocol-only publications, narrative reviews, scoping reviews, umbrella reviews, diagnostic test accuracy reviews, qualitative evidence syntheses, and other forms of evidence synthesis that do not meet the eligibility criteria will be excluded.

Studies will not be excluded based on reporting quality or methodological rigor. Information that is not reported will be coded as "not reported" according to predefined operational definitions.

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Studies will only be excluded if insufficient information is available to determine eligibility.

Data extraction Data extraction will be conducted using a structured and standardized data collection form. Reviews that have not resulted in a full-text peer-reviewed publication will be excluded, as assessment of reporting quality, methodological rigor, and transparency requires access to the complete published manuscript.
Data will be primarily extracted from INPLASY registry records and supplemented with information from corresponding published articles. The extraction process will be performed by one reviewer, with independent verification conducted in a random subset (10–20%) by a second reviewer with experience in evidence synthesis. Discrepancies will be resolved through discussion.
For all included studies, the following variables will be extracted:
1. Registration characteristics
1.1 Registration type (prospective or retrospective)
1.2 Review stage at the time of submission
1.3 Number of protocol versions
1.4 Registration ID
1.5 Protocol status in the registry
1.6 Registration date
1.7 Presence of a hyperlink to the full registration record
1.8 Type of hyperlink (if applicable)

2. Publication characteristics
2.1 DOI
2.2 Title of the manuscript
2.3 Journal name
2.4 Open access status
2.5 Year of publication
2.6 Time from protocol registration to publication (in days)

3. Journal and bibliometric characteristics
3.1 Journal Citation Reports (JCR) year
3.2 Journal Impact Factor
3.3 Journal category
3.4 Publisher
4. Study characteristics
4.1 Type of evidence synthesis (e.g., systematic review, systematic review with meta-analysis)
4.2 Country of the corresponding author
4.3 Source of funding

5. Protocol-related characteristics
5.1 Presence of a published peer-reviewed protocol
5.2 If applicable, journal of protocol publication

In cases where discrepancies exist between registry records and published articles, registry data will be considered the primary source, and publication data will be used to complement missing or unclear information. Missing data will not lead to study exclusion and will be coded as "not reported" when applicable.
Derived variables, such as time intervals (e.g., time from registration to publication), will be calculated based on extracted dates. All variables will be coded according to predefined operational definitions to ensure consistency across reviewers.
Data extraction for the analytical subset will be conducted using a structured and standardized form specifically designed to capture reporting quality, methodological rigor, and integrity of prospectively and retrospectively registered systematic reviews.

Reporting quality
Reporting quality will be assessed using a modified version of the PRISMA checklist, (mPRISMA, Protocol-related Reporting Transparency Score), excluding items directly related to protocol registration.
Given the focus on systematic reviews with meta-analysis of healthcare interventions, a predefined subset of PRISMA items will be evaluated to ensure applicability and consistency across studies. The selected items reflect key domains of reporting quality, including search strategy, study selection, risk of bias, synthesis methods, and transparency.
The following items will be assessed:
Title identifying the report as a systematic review and/or meta-analysis
Structured abstract reporting key elements of the review
Clear statement of objectives, including research question and eligibility criteria
Explicit eligibility criteria (PICO elements)
Information sources (databases and search dates)
Reproducible search strategy
Description of study selection process
Use of duplicate study selection
Description of data extraction process
Use of duplicate data extraction
Description of risk of bias assessment methods
Reporting of risk of bias results
Description of methods for data synthesis (including meta-analysis)
Assessment of heterogeneity
Assessment of publication bias (when applicable)
Presentation of study selection results (e.g., PRISMA flow diagram)
Summary of main findings
Consideration of risk of bias in interpretation of results
Reporting of funding sources
Each item will be coded as:

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adequately reported (1 point)
partially reported (0.5 points)
not reported (0 points)
The total mPRISMA score for each study will be calculated as the sum of the item-level scores across all included items. Because the analytical sample is restricted to systematic reviews with meta-analysis, all selected items are expected to be applicable; therefore, no adjustment for non-applicable items will be performed.
Higher scores will indicate better reporting quality.
All items will be assessed according to predefined operational definitions to ensure consistency across reviewers.

Methodological rigor
Methodological rigor will be assessed in a predefined subsample using a modified version of the AMSTAR-2 tool (mAMSTAR-2), focusing on key domains considered critical for the validity of systematic reviews.
Item 2 (protocol registration) will be excluded to avoid circularity with the exposure of interest.
The following core domains will be assessed:
Adequacy of the literature search strategy
Study selection performed in duplicate
Data extraction performed in duplicate
Adequacy of risk of bias assessment methods
Consideration of risk of bias in the interpretation of results
Appropriateness of meta-analytical methods
Assessment of publication bias (when applicable)
Reporting of sources of funding for included studies
Each domain will be coded as:
adequately fulfilled (1 point)
partially fulfilled (0.5 points)
not fulfilled (0 points)
A total mAMSTAR-2 score will be calculated by summing the domain-level scores, resulting in a continuous measure of methodological rigor.
Higher scores will indicate greater methodological rigor.
All domains will be evaluated according to predefined operational criteria to ensure consistency across reviewers.

Transparency-oriented interpretation
For retrospectively registered reviews, additional variables will be extracted to enable the analytical assessment of retrospective registration practices in relation to study quality.
Three primary domains will be operationalized based on predefined criteria:

Transparency of timing
Data will be extracted on whether retrospective registration is explicitly stated in the final manuscript and whether information on the timing of registration relative to key stages of the review process is reported. When available, dates will be recorded to allow classification of registration timing (e.g., before or after literature search, study selection, or data analysis).

Justification for delayed registration
Information will be collected on whether authors provide a justification for retrospective registration and, if so, the type of justification (e.g., editorial requirement, lack of awareness, administrative delay, or other). This variable will be used to distinguish between the presence and absence of justification, with additional categorization applied where appropriate.

Transparency regarding methodological changes
Data will be extracted on whether authors explicitly report whether methodological changes occurred during the conduct of the review. When such statements are present, it will be recorded whether changes are described and whether they are justified.

Derived exposure variables
Based on the extracted information, categorical variables representing each domain will be created (e.g., presence vs absence of transparency or justification). When applicable, additional levels (e.g., absent, partial, complete) will be defined according to predefined operational criteria.
An additional variable representing the number of domains fulfilled (range: 0–3) will be derived by summing the presence of the three primary domains, namely transparency of timing, justification for delayed registration, and transparency regarding methodological changes. This variable will serve as an indicator of the overall level of transparency in retrospective registration practices. For interpretative purposes, values will be categorized as follows: 0 indicating no transparency practices reported, 1 indicating low transparency, 2 indicating moderate transparency, and 3 indicating high transparency. This approach enables the assessment of potential dose–response relationships between the level of transparency and study outcomes.

Study Outcomes The primary outcomes of this study are reporting quality and methodological rigor of systematic reviews with meta-analysis.
Reporting quality will be defined as the completeness and transparency with which essential methodological aspects of a systematic review are reported. It will be assessed using the mPRISMA, an adapted reporting assessment instrument based on the PRISMA 2020 Statement.

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The mPRISMA evaluates twelve reporting domains covering key aspects of review reporting. Domain scores will be summed to generate a continuous overall score, with higher values indicating greater reporting transparency.

Methodological rigor will be defined as the extent to which fundamental methodological standards for the conduct of systematic reviews are fulfilled. It will be assessed using an adapted version of the AMSTAR-2 instrument, focusing on four core methodological domains: comprehensive literature search, duplicate study selection, duplicate data extraction, and appropriate risk of bias assessment. Domain scores will be summed to generate a continuous overall score, with higher values indicating greater methodological rigor.

The secondary outcomes concern transparency practices among retrospectively registered reviews. These will be assessed using the Retrospective Registration Transparency Index (RRTI), which evaluates three domains: (1) transparency of registration timing, (2) justification for delayed registration, and (3) transparency regarding methodological changes during review conduct.

Initially, the frequency of each transparency domain will be described. Subsequently, each domain and the overall RRTI score will be analyzed as explanatory variables to investigate their association with reporting quality and methodological rigor.

Strategy of data synthesis / Statistical analysis

Descriptive analyses will be conducted to summarize the characteristics of the included studies overall and according to protocol registration timing (prospective versus retrospective). Categorical variables will be presented as frequencies and percentages, whereas continuous variables will be summarized as means and standard deviations or medians and interquartile ranges, as appropriate. The distribution of continuous variables will be assessed using graphical methods and the Shapiro–Wilk test.

Primary analysis

The primary objective is to evaluate the association between protocol registration timing (prospective versus retrospective) and reporting quality and methodological rigor.

Initially, unadjusted comparisons between prospectively and retrospectively registered reviews will be performed using appropriate parametric or non-parametric statistical tests according to the distribution of the outcome variables. However, the primary inference will be based on multivariable regression models.

Reporting quality, measured using the mPRISMA, and methodological rigor, measured using the adapted AMSTAR-2 score, will be analyzed as continuous outcomes using multivariable linear regression models. Generalized linear models will be considered if assumptions for ordinary least-squares regression are not satisfied.

Covariates will be selected a priori based on methodological relevance rather than statistical significance. All multivariable models will be adjusted for potential confounding factors, including publication year, journal impact factor (or an equivalent bibliometric indicator when unavailable), journal category, publisher, country of the corresponding author, source of funding, and the presence of a peer-reviewed protocol publication.

Given the potential non-independence of observations arising from multiple reviews conducted by the same research groups or published in the same journals, mixed-effects regression models will be fitted when supported by the data structure. Random intercepts for journal and corresponding author will be considered to account for clustering. As a sensitivity analysis, regression models with cluster-robust standard errors will also be evaluated.

Model assumptions, including linearity, homoscedasticity, and normality of residuals, will be examined using graphical diagnostics and formal statistical procedures where appropriate. Influential observations will be assessed using leverage statistics and Cook's distance. Robust standard errors or alternative modeling approaches will be considered when necessary.

Because reporting standards and protocol registration practices have evolved over time, publication year will be included in all multivariable models. Potential effect modification by publication year will be explored by incorporating interaction terms between registration timing and publication year.

Methodological rigor analyses will be conducted in the predefined subsample described above.

Secondary analyses: transparency practices in retrospectively registered reviews

Among retrospectively registered reviews, descriptive analyses will summarize the frequency and distribution of the three transparency domains evaluated by the Retrospective Registration Transparency Index (RRTI): transparency of registration timing, justification for delayed registration, and transparency regarding methodological changes during review conduct.

Each transparency domain will first be evaluated individually as an explanatory variable in relation to reporting quality and methodological rigor using univariable and multivariable regression models.

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Subsequently, the overall RRTI score (range 0–3, with 0.5-point increments) will be analyzed as a continuous explanatory variable to investigate whether increasing levels of transparency are associated with improved reporting quality and methodological rigor. These analyses will be considered exploratory and interpreted as hypothesis-generating.

Sensitivity analyses

Prespecified sensitivity analyses will be performed to evaluate the robustness of the findings. These analyses may include adjustment for the presence of a peer-reviewed protocol publication, exclusion of influential observations, alternative approaches for handling clustered data, and restriction of the analytical sample according to publication period when appropriate.

Handling of missing data

Missing data will not result in study exclusion. Primary analyses will be based on complete-case analysis. The extent and pattern of missing data will be summarized for all variables. If missing data exceed a prespecified threshold (e.g., 5%) for variables included in multivariable analyses, sensitivity analyses will be conducted to evaluate the robustness of the findings under alternative assumptions regarding missingness.

Statistical significance

All statistical tests will be two-sided, and a P value <0.05 will be considered statistically significant. Effect estimates will be reported with corresponding 95% confidence intervals. Standardized regression coefficients will also be presented, where appropriate, to facilitate comparison of effect sizes across models.

All statistical analyses will be performed using R (R Foundation for Statistical Computing, Vienna, Austria), using the most recent version available at the time of analysis. The R version and all packages used will be reported in the final manuscript to ensure full reproducibility.

Results will be interpreted primarily based on the magnitude and precision of effect estimates, considering confidence intervals and clinical or methodological relevance, rather than statistical significance alone.

Country(ies) involved Brazil and United States.

Keywords Systematic review; protocol registration; prospective registration; retrospective registration; meta-research; reporting quality; methodological rigor; research transparency.

Dissemination plans The findings of this study will be submitted for publication in a peer-reviewed, high-impact journal and presented at national and international scientific conferences. Reporting will follow relevant methodological reporting guidelines to ensure transparency and reproducibility. Where appropriate, supplementary materials, including data extraction forms and analytical code, will be made publicly available to facilitate reproducibility and future meta-research.

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