INPLASY

Association between prospective and retrospective registration and the quality of systematic reviews: a protocol for a meta-epidemiological study

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

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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 24 April 2026.

INTRODUCTION

Study aim To evaluate whether the timing of protocol registration (prospective versus retrospective) is associated with reporting quality and methodological rigor of systematic reviews. In addition, we will assess the presence of key transparency-related practices in retrospectively registered reviews and examine their association with these outcomes.

Background Prospective protocol registration is widely recommended as a core methodological standard in systematic reviews, as it promotes transparency, reduces the risk of selective reporting, and supports the prespecification of methods.
Despite these well-recognized benefits, a substantial proportion of systematic reviews continue to be registered retrospectively. Although retrospective registration may enhance transparency compared with no registration, its ability to preserve methodological rigor and mitigate bias remains uncertain, particularly when registration occurs after key stages of the review process.
This raises important questions about whether the timing of protocol registration is associated with differences in reporting quality and methodological rigor in 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. In particular, widely used assessment tools such as PRISMA and AMSTAR-2 include items directly related to protocol registration, which may introduce methodological circularity when comparing registered and non-registered studies.
Furthermore, the distinction between prospectively and retrospectively registered reviews has received limited empirical attention. While prospective registration is intended to promote transparency and reduce bias through prespecification of methods, retrospective registration may occur after

key stages of the review process or even after results are known. This raises concerns that retrospective registration may overestimate agreement between protocols and final publications, thereby limiting its ability to function as a safeguard against selective reporting and post hoc decision-making.

Importantly, existing studies have rarely directly compared prospectively and retrospectively registered systematic reviews using approaches that minimize circularity and focus on core aspects of reporting quality and methodological rigor. As a result, it remains unclear whether the observed advantages associated with registration are primarily attributable to the timing of registration or to broader differences in study conduct and reporting practices.

In addition, retrospectively registered reviews are often treated as a homogeneous group, without consideration of variability in how transparently the registration process is reported. However, retrospective registration likely encompasses a spectrum of practices that differ in their interpretability and potential to mitigate bias.

To address these gaps, this study combines a comparative analysis of prospectively versus retrospectively registered systematic reviews with an evaluation of key transparency-related practices within retrospectively registered studies. This approach allows for a more nuanced understanding of the role of protocol registration timing and reporting practices in shaping the quality and methodological rigor of evidence synthesis.

METHODS

Search strategy A comprehensive dataset will be constructed from systematic reviews registered in the INPLASY platform and subsequently published in peer-reviewed journals, restricted to intervention reviews including randomized controlled trials (RCTs).

INPLASY was selected as the data source because, similar to other protocol registration platforms such as OSF, Research Registry, and protocols.io, it allows both prospective and retrospective registration. However, INPLASY provides a large and structured dataset of registered protocols and includes specific fields capturing the stage of the review at the time of registration, as well as optional reporting of justifications for retrospective registration.

In addition, the platform maintains an active system for updating the status of registered protocols, including identification of completed and published studies, even when authors do not update the registry after publication. This feature enhances the completeness of follow-up and enables the identification of a larger number of finalized systematic reviews, thereby supporting the construction of a more comprehensive analytical dataset.

Together, these features enable a more detailed and consistent assessment of registration timing and transparency-related practices, which are central to the objectives of this study.

The search for eligible studies will be identified through a structured process:

(1) extraction of records from the INPLASY registry updated as completed and published;

(2) linkage of registered protocols to corresponding publications using Digital Object Identifiers (DOIs) and unique identification number matching;

Only systematic reviews with meta-analysis evaluating healthcare interventions and explicitly including randomized controlled trials will be eligible. Reviews including mixed study designs will be retained only if RCTs constitute the primary source of evidence and are clearly identifiable within the synthesis.

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

For analyses of reporting quality and methodological rigor, inclusion will be restricted to systematic reviews with meta-analysis assessing healthcare interventions and including randomized controlled trials (RCTs). This restriction is intended to enhance methodological comparability across studies and to reduce heterogeneity arising from differences in review design and underlying evidence.

Protocol-only publications, narrative reviews, and other forms of non-systematic evidence synthesis will be excluded. Studies will not be excluded based on reporting quality; items that are not reported will be coded as “not reported” and handled accordingly in the analysis. Studies will only be excluded if insufficient information is available to confirm 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), 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:
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.
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.

Outcome definitions The primary outcomes of this study are reporting quality and methodological rigor of systematic reviews.
Reporting quality will be defined as the completeness and transparency of reporting, as assessed using a modified version of the PRISMA checklist (mPRISMA). A total score will be calculated based on item-level assessments, with higher scores indicating better reporting quality.
Methodological rigor will be defined as the extent to which key methodological standards are fulfilled, as assessed using a modified version of the AMSTAR-2 tool (mAMSTAR-2). A total score will be calculated by aggregating domain-level assessments, with higher values indicating greater methodological rigor.
As secondary analyses, we will first describe the presence of key transparency-related practices among retrospectively registered reviews. These practices include transparency of registration timing, justification for delayed registration, and transparency regarding methodological changes. Subsequently, these practices will be analyzed as explanatory variables to examine whether they are associated 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. Categorical variables will be presented as frequencies and percentages, and continuous variables 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 analysis will evaluate the association between the timing of protocol registration (prospective versus retrospective) and study outcomes.

Comparisons between prospectively and retrospectively registered reviews will be performed using appropriate statistical tests: independent t-tests or Mann–Whitney U tests for continuous outcomes (mPRISMA and mAMSTAR-2 scores), depending on data distribution, and chi-square tests for categorical variables, when applicable.

To further examine these associations, multivariable regression models will be applied, using linear regression for continuous outcomes (reporting quality and methodological rigor).

Given the potential non-independence of observations, as multiple reviews may be conducted by the same research groups or published within the same journals, mixed-effects regression models will be used when appropriate based on the data structure. Random intercepts at the journal and/or author level will be included to account for clustering effects. As a sensitivity approach, clustered standard errors may also be applied.

Given the known temporal improvements in reporting standards and protocol registration practices, year of publication will be treated as a key confounder and included in all multivariable models. All models will be adjusted for potential confounders, including journal impact factor (or proxy), journal category, publisher, country of the corresponding author, and source of funding.

Model assumptions, including linearity, homoscedasticity, and normality of residuals, will be assessed. Where appropriate, transformations or robust standard errors will be considered. Additionally, stratified analyses by publication period will be conducted to evaluate potential effect modification over time.

Analyses of methodological rigor (mAMSTAR-2) will be conducted in the predefined subsample described above.

Secondary analyses: transparency practices in retrospectively registered reviews
Among retrospectively registered reviews, descriptive analyses will first be conducted to assess the frequency and distribution of the three transparency-related domains: transparency of timing, justification for delayed registration, and transparency regarding methodological changes.

Subsequently, these variables will be analyzed as explanatory variables to examine their association with reporting quality and methodological rigor. Univariable and multivariable linear regression models will be used to assess these associations, with each domain modeled as a categorical variable.

In addition, an exploratory analysis will be conducted using a derived variable representing the number of domains fulfilled (range: 0–3) to assess potential trends between increasing levels of transparency and study outcomes. This analysis will be considered exploratory and will not be interpreted as a validated composite measure.

Handling of missing data
Missing data will not lead to study exclusion and will be handled using complete-case analysis. The extent and pattern of missing data will be described for all variables. Given the potential for missingness to be related to reporting quality, sensitivity analyses may be conducted to assess the robustness of the findings under different assumptions regarding missing data.

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.

All statistical analyses will be performed using R, using the most recent version available at the time of analysis. The R version and packages used will be reported in the final manuscript to ensure reproducibility.

Country(ies) involved Brazil.

Keywords Systematic review; INPLASY; retrospective registration; prospective registration;

meta-epidemiology; research integrity; PRISMA; AMSTAR-2.

Dissemination plans Results will be submitted to a high-impact journal and presented at international conferences.

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