INPLASY

A Systematic Review and Meta-Analysis of Prognostic Factors for All-Cause Mortality and Functional Dependence Following Hip Fracture Surgery in Older Adults: a study protocol

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ADMINISTRATIVE INFORMATION

Support - No.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2025120068

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 December 2025 and was last updated on 18 December 2025.

INTRODUCTION

Review question / Objective The primary objective of this systematic review is to identify and synthesize evidence on prognostic factors associated with adverse health outcomes in older adults following surgical treatment for a hip fracture. The review question is structured using the PICOS framework:
Population: Patients aged 60 years or older who have undergone surgery (internal fixation or arthroplasty) for a low-trauma hip fracture (femoral neck or intertrochanteric).
Prognostic Factors (Exposure): Any potential prognostic factor, including but not limited to: patient demographics (e.g., age, sex), comorbidities (e.g., cardiovascular disease, dementia), functional and nutritional status, fracture characteristics, surgical details (e.g., time to surgery, type), and post-operative course variables.
Comparison: Comparisons between groups with different levels or presence/absence of the prognostic factors of interest.
Outcomes: The primary outcomes are: 1) All-cause mortality at a specified time point (e.g., 30-day, 6-month, or 1-year postoperatively); 2) Functional dependence in basic activities of daily living (BADL), assessed using standardized scales (e.g., Barthel Index) at approximately 6 months postoperatively.
Study Designs: Observational studies designed to investigate prognosis, specifically prospective or retrospective cohort studies and nested case-control studies.

Rationale Hip fracture is a devastating injury in older adults, associated with exceptionally high rates of mortality, functional decline, and loss of independence. These adverse outcomes impose a tremendous burden on patients, their families, and healthcare systems globally. Identifying which patients are at greatest risk is crucial for implementing targeted interventions to improve prognosis.
While numerous individual studies have explored various prognostic factors, the existing evidence remains fragmented and sometimes contradictory. To our knowledge, there is a lack of a

comprehensive, up-to-date systematic review that synthesizes evidence across the full spectrum of potential prognostic factors—spanning patient characteristics, clinical parameters, and care processes—using rigorous methodology. Previous reviews may have focused on a limited set of factors, excluded important observational designs, or are now outdated due to new evidence.

This systematic review aims to fill this critical knowledge gap. By comprehensively identifying and synthesizing the best available evidence on prognostic factors for adverse outcomes, this review will provide a clearer understanding of where modifiable risks lie. The findings are expected to directly inform clinical practice by aiding in the early identification of high-risk patients, guiding the development of personalized care pathways, and highlighting priority areas for future intervention research. Ultimately, this work seeks to contribute to improved patient outcomes and more efficient resource utilization in the management of geriatric hip fracture.

Condition being studied

Hip Fracture in Older Adults

The condition under study is hip fracture (including femoral neck and intertrochanteric fractures) occurring in adults typically aged 60 years and older. These fractures are predominantly caused by low-energy trauma, such as a fall from standing height, and are strongly associated with underlying osteoporosis and age-related decline in bone strength, balance, and muscle mass.

A hip fracture is a catastrophic health event for an older person. It almost universally requires surgical intervention (internal fixation or arthroplasty) and marks a dramatic turning point in the individual's health trajectory. The injury and subsequent recovery period are associated with exceptionally high risks of severe complications, including a significant rise in mortality (approximately 20-30% within one year), profound functional decline, loss of independence in basic activities of daily living, and a high likelihood of requiring long-term institutional care.

Due to global population aging, the incidence of hip fractures is rising, making it a major public health concern that places a substantial burden on healthcare systems, caregivers, and society due to high direct medical costs and indirect social costs.

METHODS

Search strategy

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(
(
"Aged"[Mesh] OR elder*[Title/Abstract] OR geriatric[Title/Abstract] OR "older adults"[Title/Abstract]
)
AND
(
"Hip Fractures"[Mesh] OR "hip fracture*"[Title/Abstract] OR "proximal femoral fracture*"[Title/Abstract] OR
"Femoral Neck Fractures"[Mesh] OR "femoral neck fracture*"[Title/Abstract] OR "intracapsular fracture*"[Title/Abstract] OR
intertrochanteric fracture*[Title/Abstract] OR trochanteric fracture*[Title/Abstract] OR pertrochanteric fracture*[Title/Abstract] OR
subtrochanteric fracture*[Title/Abstract] OR extracapsular fracture*[Title/Abstract] OR "extracapsular hip fracture*"[Title/Abstract]
)
AND
(
"Surgical Procedures, Operative"[Mesh] OR "Arthroplasty, Replacement, Hip"[Mesh] OR "Fracture Fixation, Internal"[Mesh] OR
surgery[tiab] OR surgical[tiab] OR operative[tiab] OR postoperat*[tiab] OR
arthroplasty[tiab] OR hemiarthroplasty[tiab] OR "joint replacement"[tiab] OR
"internal fixation"[tiab] OR osteosynthesis[tiab] OR "intramedullary nail*"[tiab]
)
)

AND

(
(
"Mortality"[Mesh] OR
death[Title/Abstract] OR mortality[Title/Abstract] OR fatality[Title/Abstract] OR
deceased[Title/Abstract] OR survival[Title/Abstract] OR
"All-Cause Mortality"[Title/Abstract] OR "excess mortality"[Title/Abstract] OR
"post-fracture mortality"[Title/Abstract]
)
OR

(
"Activities of Daily Living"[Mesh] OR "Recovery of Function"[Mesh] OR
ADL[Title/Abstract] OR "activities of daily living"[Title/Abstract] OR
"functional status"[Title/Abstract] OR disability[Title/Abstract] OR dependency[Title/Abstract] OR
"Barthel Index"[Title/Abstract] OR "Katz Index"[Title/Abstract] OR "Lawton IADL"[Title/Abstract] OR
"functional decline"[Title/Abstract] OR "functional independence"[Title/Abstract] OR
"poor functional outcomes"[Title/Abstract]
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)
)

AND
(
"Risk Factors"[Mesh] OR
"Prognosis"[Mesh] OR
"Regression Analysis"[Mesh] OR
"Logistic Models"[Mesh] OR
"Proportional Hazards Models"[Mesh] OR
"risk factor*"[Title/Abstract] OR predictor*[Title/Abstract] OR prognos*[Title/Abstract] OR
"prediction model*"[Title/Abstract] OR "prognostic model*"[Title/Abstract] OR
"risk prediction"[Title/Abstract] OR "nomogram"[Title/Abstract] OR "risk score"[Title/Abstract]
).

Participant or population This systematic review will include studies whose participants meet the following criteria:
Age: Patients aged 60 years or older at the time of hip fracture.
Condition: Diagnosis of a low-trauma (fragility) hip fracture, primarily involving the femoral neck or intertrochanteric region.
Intervention: All patients must have undergone surgical management for the hip fracture, including but not limited to internal fixation (e.g., screws, intramedullary nails) or arthroplasty (hemiarthroplasty or total hip replacement).
Exclusion Concept: Studies focusing primarily on patients with pathological fractures (due to cancer), periprosthetic fractures, or fractures resulting from high-energy trauma (e.g., major vehicle accidents) will be excluded.

Intervention Not applicable as a traditional therapeutic intervention. This is a prognostic factor review. The "exposures" of interest are the potential prognostic factors themselves (e.g., patient demographics, comorbidities, surgical timing) as defined in the Population/Prognostic Factors section.

Comparator This is a prognostic factor review; therefore, the comparators are not therapeutic interventions but different levels or categories of the prognostic factors of interest. For example, comparisons will be made between older vs. younger age groups, presence vs. absence of specific comorbidities, early vs. delayed surgery, etc., as defined for each factor analyzed.

Study designs to be included This review will include prospective and retrospective cohort studies, as well as nested case-control studies. These designs are best suited for investigating prognostic factors as they establish a clear temporal sequence between exposure and outcome. Randomized trials will be considered only if they report observational (non-randomized) analyses of prognostic factors within their cohorts.

Eligibility criteria 1. Study Designs: Cohort studies (prospective or retrospective) will be included. Nested case-control studies within a defined cohort are eligible. Randomized controlled trials will be considered only if they report observational, multivariable analyses of baseline prognostic factors (not intervention effects).
2. Participants: Patients aged ≥60 years who sustained a primary, low-energy traumatic hip fracture (femoral neck or intertrochanteric) and subsequently underwent surgical management (internal fixation or arthroplasty).
3. Predictive/Prognostic Factors & Analysis: Studies must aim to explore the association between any potential prognostic factor (e.g., demographics, comorbidities, surgical details) and the outcome. The analysis must report a multivariable-adjusted effect estimate (adjusted Hazard Ratio, Odds Ratio, or Risk Difference) with its 95% Confidence Interval.
4. Outcome Measures: Studies must report predictors for at least one primary outcome: (1) All-cause mortality at a defined time point (e.g., 30-day, 1-year); or (2) Functional dependence in Basic ADL, assessed at 6 months (±1 month) using a standardized scale (e.g., Barthel Index).

Information sources To comprehensively identify relevant literature, the following electronic databases will be systematically searched from inception to 21 August 2025: Chinese databases, including China National Knowledge Infrastructure (CNKI), WanFang Data, VIP Database (VIP), and Chinese Biomedical Literature Database (CBM); and English databases, including PubMed/MEDLINE, Embase, Web of Science, CINAHL (via EBSCOhost), and The Cochrane Library (including CENTRAL).
The search strategy will utilize a combination of controlled vocabulary (e.g., MeSH, Emtree) and free-text terms related to the core concepts: older adults, hip fracture, postoperative period, prognostic factors, mortality, and functional dependence. Synonyms, near-synonyms, and variant spellings will be incorporated to maximize sensitivity. Boolean operators (AND, OR, NOT) will be applied.
Supplementary searches will include: (1) scanning reference lists of included studies and relevant reviews (citation chasing); (2) searching grey literature sources, such as conference proceedings

and dissertations (via ProQuest Dissertations & Theses Global); (3) searching trial registries (ClinicalTrials.gov, WHO ICTRP); and (4) forward citation tracking for key articles.
Initial searches will have no restrictions on language or study design to avoid missing relevant evidence (e.g., prognostic analyses embedded in RCTs). During screening, non-Chinese/English publications will be excluded if a reliable translation is unavailable, and studies will be rigorously assessed against the eligibility criteria (e.g., cohort or case-control designs). The full, detailed search strategies for all databases will be provided in an appendix, ensuring reproducibility per PRISMA-S guidelines.

Main outcome(s) This review will investigate prognostic factors for the following primary outcomes:
All-cause Mortality: Defined as death from any cause. The timing of measurement will be at specific postoperative time points, including 30-day, 6-month, and 1-year mortality, or as cumulative mortality within a defined follow-up period (e.g., within 2 years). The relevant effect measures are adjusted hazard ratios (aHR) or adjusted odds ratios (aOR) with 95% confidence intervals derived from multivariable survival or logistic regression models.
Functional Dependence in Basic Activities of Daily Living (BADL): Defined as a decline in or dependence on assistance for basic self-care tasks. It must be assessed using a standardized scale (e.g., Barthel Index, Katz Index) at a postoperative time point of 6 months (±1 month). The relevant effect measures are adjusted odds ratios (aOR) or adjusted risk ratios (aRR) with 95% confidence intervals from multivariable models.
Studies must report at least one of these outcomes in association with prognostic factors using multivariable-adjusted effect estimates to be eligible for inclusion.

Additional outcome(s)
Additional (Secondary) Outcomes
In-hospital Complications: Incidence of specific complications such as delirium, pneumonia, deep vein thrombosis/pulmonary embolism, and surgical site infection.
Instrumental Activities of Daily Living (IADL): Functional status assessed using standardized IADL scales (e.g., Lawton IADL scale) at 6 or 12 months postoperatively.
Health-Related Quality of Life (HRQoL): Measured using generic instruments (e.g., EQ-5D, SF-36) at 6 or 12 months postoperatively.
Place of Discharge: Discharge to a location other than home (e.g., rehabilitation facility, nursing home).
For these outcomes, relevant adjusted effect estimates (e.g., odds ratios, risk ratios, mean differences) from multivariable analyses will be extracted where reported.

Data management Data Management Plan
Record Management:
All records retrieved from database searches will be imported into EndNote (or similar reference management software).
Duplicate records will be removed first automatically using the software's function, followed by a manual check.
The unique records will then be imported into Rayyan for the screening process.
Study Selection Process:
The screening will be conducted in two stages (title/abstract, then full-text) by two independent reviewers.
All decisions (include/exclude) will be recorded within Rayyan. Any disagreements will be resolved through discussion or, if necessary, by consulting a third reviewer (senior researcher).
The reasons for exclusion at the full-text stage will be documented. The entire selection process will be presented in a PRISMA flow diagram.
Data Extraction and Management:
A standardized data extraction form will be pre-piloted and finalized in Microsoft Excel.
Data will be extracted by one reviewer and independently verified for accuracy by a second reviewer.Data extraction will be performed independently by two reviewers. The form will include fields for: study characteristics, population details, prognostic factors, outcome definitions and time points, adjusted effect estimates (with 95% CIs), and covariates adjusted for in the multivariable models.
The completed extraction files from both reviewers will be compared. Any discrepancies will be identified and resolved by consensus, referring back to the original publication.
Data Storage and Security:
All electronic files (search results, screening records, extracted data) will be stored on a password-protected shared drive with regular backups.
The final, verified dataset will be the basis for all subsequent analyses.

Quality assessment / Risk of bias analysis Risk of Bias Assessment in Primary Studies
The risk of bias in included prognostic studies will be assessed using the Quality In Prognosis Studies (QUIPS) tool. This tool is specifically designed for

prognostic factor studies and evaluates six domains: (1) Study Participation, (2) Study Attrition, (3) Prognostic Factor Measurement, (4) Outcome Measurement, (5) Study Confounding, and (6) Statistical Analysis and Reporting.
Two reviewers will independently assess each included study. Each domain will be judged as having "Low," "Moderate," or "High" risk of bias based on the tool's signaling questions and criteria. Any disagreements will be resolved through discussion or by consulting a third reviewer.The results of the assessment will be presented in a summary table and a graph. In the evidence synthesis, the overall confidence in the evidence for each prognostic factor will be explicitly considered in light of the risk of bias findings. Sensitivity analyses may be conducted by excluding studies rated as having a high risk of bias in key domains to explore their impact on the overall results.

Strategy of data synthesis The strategy for data synthesis will follow a structured, multi-stage approach:
1. Descriptive Synthesis and Categorization
Study and population characteristics will be summarized descriptively. Categorical variables will be reported as frequencies (n) and percentages (%), and continuous variables as mean ± standard deviation or median (interquartile range). All extracted prognostic factors and their adjusted effect estimates (e.g., aOR, aHR) will be tabulated. Crucially, identified factors will be qualitatively mapped by two independent reviewers onto the five tiers of a health-ecological model to conceptualize their levels of influence.
2. Quantitative Synthesis (Meta-Analysis)
Feasibility and Effect Measures: Meta-analysis will be considered if ≥2 studies report compatible adjusted estimates for the same factor-outcome pair. The primary effect measures are adjusted Hazard Ratios (aHR) or Odds Ratios (aOR). If only unadjusted estimates are available, authors will be contacted; if unavailable, their impact will be tested in sensitivity analysis. For continuous functional outcomes (e.g., Barthel Index), the Standardized Mean Difference (SMD) will be used.
Statistical Model: Given anticipated heterogeneity, the generic inverse-variance random-effects model will be the primary model. A fixed-effect model will only be considered if heterogeneity is negligible ($I^2 \leq 50\%$ and $P > 0.1$ for Cochran's Q test).
Heterogeneity Assessment: Statistical heterogeneity will be quantified using the I^2 statistic (interpreted as: ≤40% low, 30-60% moderate, 50-90% substantial, 75-100% considerable). Sources of heterogeneity will be explored via pre-specified subgroup analyses or meta-regression (e.g., by study design, mean age, risk of bias, follow-up time, geographic region).
3. Additional Analyses and Reporting
Sensitivity analyses will be conducted by excluding studies one by one and by excluding those with a high risk of bias.
If a meta-analysis includes ≥10 studies, potential publication bias will be assessed visually via a funnel plot and statistically using Egger's test.
All analyses will be performed using R software (version 4.4.4 or later). The threshold for statistical significance is set at $\alpha=0.05$.

Subgroup analysis Planned Subgroup Analyses
To explore potential sources of heterogeneity and assess the robustness of associations, the following subgroup analyses are planned for meta-analyses containing a sufficient number of studies (typically ≥ 3 per subgroup):
1. Study and Population Characteristics
Analyses will compare prospective versus retrospective cohort studies; studies with a mean patient age of < 80 years versus ≥ 80 years; femoral neck fractures versus intertrochanteric fractures; arthroplasty versus internal fixation procedures; and studies conducted in different geographic regions (e.g., East Asia, North America, Europe).
2. Methodological Characteristics
Analyses will compare studies rated as having an overall "Low/Moderate" versus "High" risk of bias based on the QUIPS assessment, and for mortality outcomes, studies reporting 30-day/in-hospital mortality versus 1-year mortality.
Methodologically, for continuous moderators, clinically relevant cut-points will be applied. Statistical tests for interaction (e.g., meta-regression) will be used where possible. All subgroup analyses are considered exploratory, and interpretation will focus on the consistency of effects across groups rather than on statistical significance alone.

Sensitivity analysis Planned Sensitivity Analyses
Sensitivity analyses will be conducted to assess the robustness and stability of the primary meta-analysis findings. The following approaches are planned:
1. One-study-removed analysis
Sequentially excluding each individual study from the meta-analysis to determine if any single study disproportionately influences the overall pooled effect estimate.
2. Analysis by risk of bias
Repeating the meta-analysis after excluding studies judged to have a "High" overall risk of bias according to the QUIPS tool, to examine their impact on the results.

3. Analysis by effect measure adjustment
If applicable, conducting an analysis to evaluate the impact of including studies that only report unadjusted effect estimates (after attempts to obtain adjusted data from authors), compared to the primary analysis based solely on adjusted estimates.
4. Model choice
Comparing results from the primary random-effects model with those from a fixed-effect model when heterogeneity is low-to-moderate, to check for consistency.
All sensitivity analyses will be performed using R software (version 4.4.4 or later). The results of these analyses will be interpreted descriptively. If the direction, magnitude, or statistical significance of the primary pooled estimate meaningfully changes in any sensitivity analysis, this will be highlighted and discussed as a limitation affecting the certainty of the evidence.

Language restriction Yes, to Chinese and English only.

Country(ies) involved China.

Other relevant information Supplementary Information
Theoretical Framework: The identification and synthesis of prognostic factors will be conceptually organized using a health-ecological model. This framework will guide the mapping of factors across individual, interpersonal, organizational, community, and policy levels to inform multi-level interventions.
Data from RCTs: As per the eligibility criteria, randomized controlled trials (RCTs) will be included only if they report multivariable, observational analyses of baseline prognostic factors (not intervention effects).
Search Strategy Specificity: The search strategy for Chinese databases will utilize professionally translated, conceptually equivalent terms to ensure accuracy and comprehensiveness alongside the English search.
Publication Bias Assessment: If a meta-analysis includes 10 or more studies, publication bias will be assessed using a funnel plot and Egger's statistical test.
Conflict of Interest: The authors declare no competing interests related to this systematic review protocol.

Keywords hip fracture; aged; prognostic factors; systematic review; mortality; activities of daily living; observational study.

Dissemination plans The findings of this systematic review will be disseminated through multiple channels to reach academic, clinical, and public audiences:
Peer-reviewed Publication: The primary results will be submitted for publication in a reputable, peer-reviewed international journal within the fields of geriatrics, orthopedics/trauma, or rehabilitation medicine.
Academic Conferences: Key findings will be presented at relevant national and international scientific conferences (e.g., in geriatric medicine, orthopedic surgery, or evidence synthesis).
Open Science Platforms: The finalized review protocol and the completed review manuscript will be made publicly available. A pre-print version may be deposited on servers such as medRxiv or Research Square upon completion.
Professional and Public Outreach: A plain-language summary of the main findings will be prepared for dissemination through institutional news channels, relevant professional society newsletters, and academic social media platforms (e.g., ResearchGate, X) to engage clinicians, policymakers, and the interested public.
Data Sharing: The data extraction forms and analysis codes developed for this review will be made available upon reasonable request to facilitate transparency and reproducibility.

Contributions of each author
Author 1 - LuJin Lian - The author contributed to the conception of the study, the development of the protocol, the design of the search strategy, the screening process, the data extraction, the risk of bias assessment, the data synthesis plan, and drafted the manuscript.
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Author 2 - Yuan Gao - The author contributed to the development of the search strategy, the formal screening of studies, data validation, and reviewed and edited the manuscript.
Author 3 - QingQing Su - The author contributed to the data extraction, the risk of bias assessment of included studies, assisted in the data analysis plan, and reviewed and edited the manuscript.