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Study Protocol for National Health Insurance Claims-based Literature Evaluation for Risk of Bias in Korean Medicine (CLEAR-KM)

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Piloting of the study selection process.

Conflicts of interest - This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health and Welfare, Republic of Korea (grant number: RS-2020-KH087602). The funders had no role in study design, investigation of data, statistical analyses, interpretation of data, and preparation of the manuscript.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 February 2026 and was last updated on 25 February 2026.

INTRODUCTION

Study aim To conduct a methodological review evaluating the risk of bias in Korean Medicine studies using National Health Insurance claims data in the Republic of Korea from 2012 to 2025.

Background In contrast to the limitation of traditional randomized controlled trials (RCTs), such as high resource demands and limited generalizability, real-world evidence (RWE) has increasingly solidified its position in healthcare research. Real-world data (RWD) offers multiple advantages, including the reflection of actual clinical settings, the capture of long-term effectiveness, nationwide-scale surveillance, the assessment of multiple alternative interventions, and the evaluation of clinical and economic outcomes associated with implementation of new policies. Furthermore, RWD enable the assessment of effectiveness and safety in clinical fields such as rare diseases, cancer, and precision medicine, including chimeric antigen receptor T-cell therapy, where RCTs are infeasible.

The use of real-world evidence (RWE) in health technology assessment (HTA) has expanded across multiple countries, including Australia, Canada, England, France, Germany, Ireland, Italy, the Netherlands, and the United States. In the Republic of Korea, the Ministry of Food and Drug Safety published the guidelines on the use of RWE to support the regulatory process for drugs and medical devices. The recognition and application of RWD, especially administrative claims data, in Korean medicine (KM) research are also increasing, ranging from descriptive and comparative effectiveness analyses in a wide range of patients

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to nationwide pharmacovigilance following policy implementation.

However, as RWE is primarily derived from observational studies based on data not collected for research purposes, the use of inappropriate analytic methods can compromise the validity of the findings. A previous review of HTA reports incorporating observational studies found that multiple regression analysis was the most frequently used method to control for confounding or effect modifiers, while most studies did not perform analyses to assess key assumptions. Current guidelines therefore suggest methodological techniques, including propensity score matching, confounding control, sensitivity analyses, and target trial emulation. The inherent characteristics of KM, including highly individualized treatment patterns in real-world clinical practice and a relatively low National Health Insurance (NHI) coverage rate in the KM hospitals (47.2%), add further complications to research based on NHI claims data. To address treatment heterogeneity and data incompleteness due to non-reimbursed services, KM researchers need to adopt appropriate statistical methods and implement strategies such as the linkage of multiple databases.

Therefore, this study aims to evaluate the methodological quality of NHI claims data-based research in KM as a foundational study to support the establishment of an RWD-based TCIM research support system.

METHODS

Search strategy Two international databases including PubMed/MEDLINE and EMBASE, and four Korean publication databases including ScienceON, Research Information Sharing Service (RISS), Oriental Medicine Advanced Searching Integrated System (OASIS) and Korean Medical Database (KMBASE) will be systematically searched in January 2026. The following search terms, including relevant Medical Subject Headings (MeSH) terms, will be combined by Boolean operators: 'National Health Programs', 'health insurance claims data', 'Korea', 'traditional Korean medicine', 'acupuncture', 'moxibustion', 'chuna', 'herbal medicine', and additional terms related to KM practices reimbursed by the NHI service.

Eligibility criteria This study will include all studies utilizing Korean NHI claims data that are related to KM, regardless of population, disease, exposure, or analysis method. Publications from 2012 to 2025 will be eligible for assessment, as the HIRA initiated the provision of NHI databases to researchers in 2012. Studies using both representative sample cohorts and complete (customized) datasets will be included. Studies involving linkage between NHI claims data and other databases will be eligible for inclusion. Eligible study types will include outcome research, hypothesis evaluating treatment effectiveness (HETE) studies, healthcare utilization patten analyses, and studies predicting factors associated with KM use.

Full-text articles published in either Korean or English will be included, given that access to NHI claims data for academic and scientific research is restricted to researchers based in Korea under the Personal Information Protection Act, which strictly regulates the cross-border provision of personal data.

Studies using only registry or EMR datasets established by individual hospitals and communities, panel survey data, or private automobile insurance datasets without linkage to NHI data will be excluded.

Data extraction Descriptive information, including authors, title, publication year, language, journal name, impact factor, and funding source, will be extracted. Study characteristics will include study design, study objectives, data type and provider, study population, and KM practices of interest. Disease and procedure codes used to define study population, exposure, interventions, outcomes, confounders, and effect modifiers will be collected from the included studies.

To assess methodological quality, information on control group, handling of confounders or effect modifiers, management of missing or incomplete data, and analytic methods will be extracted. When available, the original study protocols will be reviewed to assess selective outcome reporting. All extracted data will be entered into a pre-designed electronic spreadsheet.

Outcome definitions The methodological quality of the included studies will be evaluated in accordance with the Revised Risk of Bias Assessment Tool for Nonrandomized Studies of Interventions (RoBANS 2). RoBANS 2 consists of eight domains: comparability of the target group, target group selection, confounders, measurement of intervention and/or exposure, blinding of assessors, outcome assessment, incomplete outcome data, and selective outcome reporting. The blinding of assessors domain will not be assessed in this study, as it is not applicable to analyses based on NHI claims data. For each domain, the risk of bias will be judged as low, high, or unclear. The primary outcome of this study is the proportion of low risk of bias across included

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studies. To identify methodological flaws, the proportion of studies classified at each risk of bias level will be calculated for each domain.

Strategy of data synthesis / Statistical analysis
In the descriptive analysis, absolute numbers and relative proportions for categorical variables and means and 95% confidence intervals for continuous variables will be presented. If continuous variables do not satisfy the assumption of normality, medians and interquartile ranges will be reported. The primary analysis will summarize the overall completeness of reporting across all included studies.
Included studies will be classified according to study design and type of database used. Differences in study characteristics and methodological quality between groups will be assessed using: Chi-squared tests or Fisher's exact tests for categorical variables; independent t-tests or Mann–Whitney U tests for continuous variables with two groups; or one-way analysis of variance or Kruskal–Wallis tests when comparing more than two groups.
Where applicable, regression analyses will be conducted with the methodological quality as the dependent variable to identify factors associated with risk of bias.

Country(ies) involved The Republic of Korea.

Keywords Risk of Bias; Validity; Real-world data; National Health Insurance claims data; Korean medicine; Traditional, Complementary, and Integrative Medicine.

Dissemination plans The results of study will be disseminated through submission as part of the terms of reference of the WHO Collaborating Centre for Traditional Medicine and publication in a peer-reviewed journal.

Contributions of each author
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