International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

INPLASY202630033

doi: 10.37766/inplasy2026.3.0033

Received: 9 March 2026

Published: 9 March 2026

Corresponding author:
Jing-Ren Tseng

drtsengjr@gmail.com

Author Affiliation:
Department of Nuclear Medicine, New Taipei Municipal TuCheng Hospital (Built and Operated by Chang Gung Medical Foundation), No. 6, Sec. 2, Jincheng Rd., Tucheng Dist., New Taipei City 236, Taiwan.

Comparative detection performance of PET and conventional scintigraphy tracers for inflammation and infection in bone and soft tissue: A systematic review and network meta-analysis

Wang, HN; Huang, CK; Huang, YE; Huang, YT; Chan, SH; Tseng, JR.

ADMINISTRATIVE INFORMATION

Support - Nil.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202630033

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 9 March 2026 and was last updated on 9 March 2026.

INTRODUCTION

Review question / Objective The network meta-analysis employed the PICO model (population, intervention, comparison, outcome), featuring the subsequent criteria: (1) P: human participants with inflammation and infection in bone and soft tissue region (2) I: PET and traditional radiotracers in detection of inflammation and infection in osseous and soft tissue structures; (3) C: 67Ga-citrate as the reference tracer; and (4) O: diagnostic accuracy in the management of infection and inflammation. Eligible study designs included prospective and retrospective comparative studies, controlled clinical trials, pragmatic clinical trials, randomized controlled trials. We excluded case reports, case series with fewer than 10 patients, meta-analyses, review articles, and non-human studies. Both reviewers independently screened titles and abstracts of all identified records. A third author (JRT) independently assessed full-text articles for eligibility, with any discrepancies resolved by consensus among all investigators. No restrictions on language were imposed on this research.

Rationale In nuclear medicine, clinically approved radiopharmaceuticals—compounds integrating a medical radionuclide with a pharmaceutical ligand—are utilized to identify inflammation and infection by detecting pathophysiological changes such as elevated metabolic activity, increased regional perfusion, and enhanced capillary permeability. These radionuclides generally emit low-dose gamma (γ) photons, which are captured by a scintillation gamma camera and translated into diagnostic images. While the growing variety of PET and conventional radiotracers has greatly improved our ability to detect infections in osseous and soft tissues, a lack of robust head-to-head comparisons makes it difficult to determine the most effective option. To address this, our study employs Network Meta-analysis (NMA), a sophisticated statistical approach that synthesizes both direct and indirect trial data. By leveraging NMA, we aim to rank these radiotracers based on

their diagnostic accuracy, thereby providing an evidence-based hierarchy to help clinicians select the optimal radiopharmaceutical for managing infectious and inflammatory conditions.

Condition being studied This network meta-analysis provides robust evidence supporting the diagnostic accuracy of infection imaging, thereby informing and enhancing clinical decision-making.

METHODS

Search strategy Two authors (HNW and CKH) independently performed systematic electronic searches of PubMed, Embase, Cochrane Library, and ClinicalTrials.gov databases through Feb 2026. We used the following search strategy: ((infection) OR (inflammation) OR infectious) OR (inflammatory)) AND ((Ga-67) OR (In-111) OR (Tc-99m) OR (FDG) OR (PET) OR (Ga-68) OR (FAPI)) AND (comparison). Our search strategy was conducted without restrictions on language or publication year. We included clinical studies that provided head-to-head comparisons of the diagnostic performance of at least two PET or conventional radiotracers for detecting inflammation and infection in osseous and soft tissues.

Participant or population The systematic search yielded 1,671 results. After duplicate removal, 1,504 records underwent title and abstract screening, of which 306 met initial inclusion criteria by comparing at least two radiotracers. A further title screening excluded 223 records, leaving 83 full-text articles assessed for eligibility. Of these, 45 were excluded – comprising meta-analyses (n = 13), non-human studies (n = 29), and case images (n = 4) – yielding 37 studies that fulfilled the predefined criteria. An additional 24 were excluded due to insufficient data, resulting in 13 studies included in the final NMA.

Intervention Two authors (H.N.W. and C.K.H.) independently collected data from each included study using a standardized form. Extracted variables included study design, patient demographics, imaging acquisition parameters, and radiotracer characteristics. All procedures for data handling, transformation, and synthesis were performed in accordance with the Cochrane Handbook for Systematic Reviews of Interventions and relevant methodological literature. When data required for analysis were unavailable in published reports, the corresponding authors were contacted to request original source materials.

Comparator Studies were included if they (1) directly compared at least two radiotracers – whether PET or conventional scintigraphy agents – for infection and inflammation detection, and (2) enrolled 10 or more patients. Eligible designs included randomized controlled trials, controlled clinical trials, pragmatic trials, and prospective or retrospective comparative studies. Case reports, case series with fewer than 10 patients, meta-analyses, review articles, and non-human studies were excluded.

Study designs to be included Eligible designs included randomized controlled trials, controlled clinical trials, pragmatic trials, and prospective or retrospective comparative studies. Case reports, case series with fewer than 10 patients, meta-analyses, review articles, and non-human studies were excluded.

Eligibility criteria Eligible study designs comprised prospective and retrospective comparative studies, controlled and pragmatic clinical trials, and randomized controlled trials. Conversely, we excluded case reports, case series involving fewer than 10 patients, meta-analyses, review articles, and non-human studies. During the initial phase, two reviewers independently screened the titles and abstracts of all identified records. Subsequently, a third author (JRT) independently evaluated the full-text articles for final eligibility. Any discrepancies that arose during the selection process were resolved through consensus among all investigators. No language restrictions were imposed on this review.

Information sources Two independent reviewers (HNW and CKH) conducted a comprehensive electronic literature search of the PubMed, Embase, Cochrane Library, and ClinicalTrials.gov databases, covering records from their inception up to February 2026. The specific search strategy employed was as follows: ((infection) OR (inflammation) OR infectious) OR (inflammatory)) AND ((Ga-67) OR (In-111) OR (Tc-99m) OR (FDG) OR (PET) OR (Ga-68) OR (FAPI)) AND (comparison).

Main outcome(s) The primary endpoint of this study was the detection rate (DR), defined as the proportion of patients or lesions exhibiting true-positive findings on imaging. For the purposes of our analysis, any equivocal or indeterminate scan results were strictly classified as negative.

Additional outcome(s) Nil.

Data management Data were extracted independently by two authors (HNW and CKH), capturing study characteristics, patient demographics, imaging parameters, and radiotracer types. All procedures for data extraction, conversion, and synthesis strictly adhered to the Cochrane Handbook for Systematic Reviews of Interventions and pertinent medical guidelines. If essential information was missing from the publications, we contacted the corresponding authors to request the original data.

Quality assessment / Risk of bias analysis Two independent authors critically appraised the methodological quality of the included studies using the revised Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool. This instrument evaluates both the risk of bias and applicability concerns across four key domains: patient selection, index test, reference standard, and flow and timing. We utilized the tool's standard signaling questions to guide our judgments. For each domain, the risk of bias and applicability concerns were systematically categorized as low, high, or unclear.

Strategy of data synthesis Because of the variety of PET and conventional scintigraphy radiotracers included, we employed a random-effects model for the network meta-analysis (NMA) under a frequentist framework, using MetaInsight software (version 6.4.1, Complex Reviews Support Unit, National Institute for Health Research, London, UK). Studies that formed isolated, unconnected nodes within the network were excluded. To compare the detection rates (DRs) of different tracers, we calculated the relative risk (RR) and 95% confidence intervals (CIs), using the most frequently applied tracer as the control. An RR greater than 1 indicates a higher DR than the control, an RR less than 1 indicates a lower DR, and an RR of 1 signifies equivalence. Results were visualized with forest plots displaying point estimates and 95% CIs. Finally, tracers were ranked based on both direct and indirect comparisons, and inconsistency tests were performed to check for data disparities.

Subgroup analysis Nil.

Sensitivity analysis We performed a leave-one-out sensitivity analysis to verify the robustness of our results. Systematically excluding individual studies allowed us to confirm the stability of the overall diagnostic efficacy estimates and the consistency of the tracer hierarchy.

Language restriction No language limit.

Country(ies) involved Taiwan.

Other relevant information Nil

Keywords positron emission tomography, network meta-analysis, infection, inflammation, leukocyte scintigraphy, 67Ga-citrate, 68Ga-citrate, 68Ga-FAPI, 18F-FDG.

Dissemination plans Nil.

Contributions of each author

Author 1 - Hsin-Ning Wang - Author 1 drafted the study design, manuscript, data collection, and data analysis.
Email: wangeinstein@gmail.com
Author 2 - Cheng-Kai Huang - Author 2 collected data, and data analysis.
Email: changkai0906@gmail.com
Author 3 - Yu-Erh Huang - Author 3 reviewed manuscript.
Email: nuclearye@yahoo.com.tw
Author 4 - Ya-Ting Huang - Author 4 reviewed manuscript.
Email: frankie7451@gmail.com
Author 5 - Shan-Ho Chan - Author 5 reviewed manuscript.
Email: shchan@ms.szmc.edu.tw
Author 6 - Jing-Ren Tseng - Author 6 contributed to the study conception and design.
Email: drtsengjr@gmail.com