INPLASY

Low-Dose Trimethoprim-Sulfamethoxazole Prophylaxis for Pneumocystis jirovecii Pneumonia in Kidney Transplant Recipients: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Review stage at the time of initial registration - Completed but not published.

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 15 November 2026 and was last updated on 15 November 2026.

INTRODUCTION

Review question / Objective What is the incidence of Pneumocystis jirovecii pneumonia (PJP) and the safety profile of low-dose trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis in kidney transplant recipients?

Rationale Pneumocystis jirovecii pneumonia (PJP) remains a life-threatening opportunistic infection in kidney transplant recipients (KTRs), with reported mortality exceeding 30% in untreated cases. Trimethoprim-sulfamethoxazole (TMP-SMX) is the recommended prophylactic agent; however, standard-dose regimens are frequently discontinued due to adverse effects including nephrotoxicity, hyperkalemia, and hematologic suppression. Low-dose TMP-SMX regimens have been proposed as a pragmatic alternative to improve tolerability while maintaining prophylactic efficacy. Despite increasing clinical adoption, the pooled incidence of PJP breakthrough and the safety profile of low-dose TMP-SMX in KTRs have not been systematically quantified. Existing evidence is fragmented across heterogeneous single-center studies with variable dosing definitions and follow-up durations. This systematic review and meta-analysis aims to synthesize the best available evidence on the efficacy and safety of low-dose TMP-SMX prophylaxis in KTRs to inform evidence-based clinical practice and transplant guideline development.

Condition being studied Pneumocystis jirovecii pneumonia (PJP) in kidney transplant recipients receiving low-dose TMP-SMX prophylaxis.

METHODS

Search strategy Five electronic databases (PubMed, Europe PMC, Epistemonikos, ScienceDirect, Scopus) were systematically searched from inception through October 2026.

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Participant or population Adult kidney transplant recipients receiving low-dose TMP-SMX prophylaxis.

Intervention Low-dose trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis, defined as ≤560 mg trimethoprim/week, including single-strength thrice-weekly (SS-TIW), single-strength daily (SS-daily), and double-strength thrice-weekly (DS-TIW) regimens.

Comparator No comparator; this is a single-arm meta-analysis of proportions estimating pooled PJP incidence in kidney transplant recipients receiving low-dose TMP-SMX prophylaxis.

Study designs to be included Randomized controlled trials, prospective cohort studies, retrospective cohort studies, and case-control studies with ≥10 participants.

Eligibility criteria Inclusion criteria: Adult kidney transplant recipients receiving low-dose TMP-SMX prophylaxis (≤560 mg trimethoprim/week); reporting PJP incidence and/or adverse effects; sample size ≥10 participants; any study design (RCT, prospective or retrospective cohort, case-control).

Exclusion criteria: Non-kidney transplant populations; standard-dose or high-dose TMP-SMX only; non-TMP-SMX prophylaxis; duplicate publications or overlapping cohorts; case reports or series <10 participants; no extractable PJP incidence data.

Information sources PubMed, Europe PMC, Epistemonikos, ScienceDirect, Scopus; supplemented by manual reference checking.

Main outcome(s) Pooled incidence of PJP in kidney transplant recipients receiving low-dose TMP-SMX prophylaxis.

Additional outcome(s) Adverse effects: nephrotoxicity (creatinine elevation), hyperkalemia, hematologic adverse effects (leukopenia, anemia), discontinuation due to adverse effects.

Data management Management Rayyan for title/abstract screening; standardized data extraction form; dual independent extraction with discrepancies resolved by consensus or arbitration by a third reviewer.

Quality assessment / Risk of bias analysis Bias Newcastle-Ottawa Scale for observational studies; Cochrane RoB 2.0 for randomized controlled trials and the Newcastle-Ottawa Scale for observational studies.

Strategy of data synthesis Synthesis Generalized linear mixed model (GLMM) binomial-normal random-effects meta-analysis with Freeman-Tukey double arcsine transformation as cross-check; heterogeneity assessed by I^2 and Cochran's Q test to assess statistical heterogeneity; a random-effects model will be applied when I^2 >50%.

Subgroup analysis No formal subgroup analysis was performed due to limited number of studies and insufficient data heterogeneity.

Sensitivity analysis Analysis Leave-one-out (LOO) sensitivity analysis to assess the influence of individual studies on the pooled estimate using leave-one-out analysis.

Language restriction English language only.

Country(ies) involved Indonesia.

Other relevant information Protocol registered retrospectively in accordance with transparency-oriented reporting recommendations (Canellas & Borges, 2026). Review conducted and reported per PRISMA 2020 guidelines.

Keywords kidney transplantation; Pneumocystis jirovecii pneumonia; trimethoprim-sulfamethoxazole; low-dose prophylaxis; PJP prophylaxis; systematic review; meta-analysis.

Dissemination plans Submission to a peer-reviewed transplantation journal (Transplantation Proceedings, Elsevier); potential presentation at national nephrology and urology conferences in Indonesia.

Contributions of each author

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