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1. Introduction

Sterile body fluid infections – such as blood stream infections (BSI) and prosthetic joint infections (PJI) – are a major cause of morbidity and mortality globally.



BSI have an estimated annual burden of **1.2 million** episodes in the European region alone (1).

PJI are the second leading cause of revisions in hip and knee arthroplasties occurring in **1% - 2%** of primary arthroplasties (2-4).

Clinical outcomes and prognosis of BSI have been closely linked to the **time and accuracy** of the diagnosis with complications such as septicshock and organ failure being averted with timely delivery of targetedantimicrobial agents (5).



For this reason, recent innovations in the diagnostics for sterile bodyfluid infections target a reduction in the time to results (TTR), fromrapid antimicrobial specificity tests to DNA-based identification from whole blood (4).

While there has been some work done on clinical outcomes associated with the early diagnosis of bloodstream infections, specific data on how the early diagnosis of BSI and PJI affect clinical outcomes is lacking.

Aim

This living systematic review aims to evaluate the impact of early diagnosis of infections in normally sterile body fluids on clinical outcomes.

2. Methods

- In accordance with PRISMA and Cochrane LSR guidelines.
- Prospectively registered with PROSPERO (CRD42024574733).
- Databases: PubMed, Embase, Web of Science, and Cochrane Central (Trials).
- January 2000-present (monthly automated database updates).
- Risk of bias: Cochrane's Risk of Bias 2 (RoB-2) for randomized controlled trials and ROBINS-I for non-randomized studies.
- Primary outcomes: length of hospital stay, total treatment days, time to optimal antimicrobial therapy, and mortality.
- Meta analysis: random effects model using weakly informative priors.

3. Preliminary Results

Systematic Review

- 66 studies met the set inclusion criteria.
- Range of rapid diagnostic methods used across studies (e.g., multiplex PCR and phenotypic susceptibility platforms).
- Gram-positive bacteria were the most frequently reported pathogens (e.g., Staphylococcus aureus).
- Consistent findings indicate there is an association between rapid diagnostics and time to optimal antimicrobial therapy as well as mortality rate.

Meta Analysis

- Rapid diagnostic interventions are associated with a lower rate of mortality compared to standard diagnostic methods (Odds ratio = 0.83 ; 95% CrI (0.71-0.94))

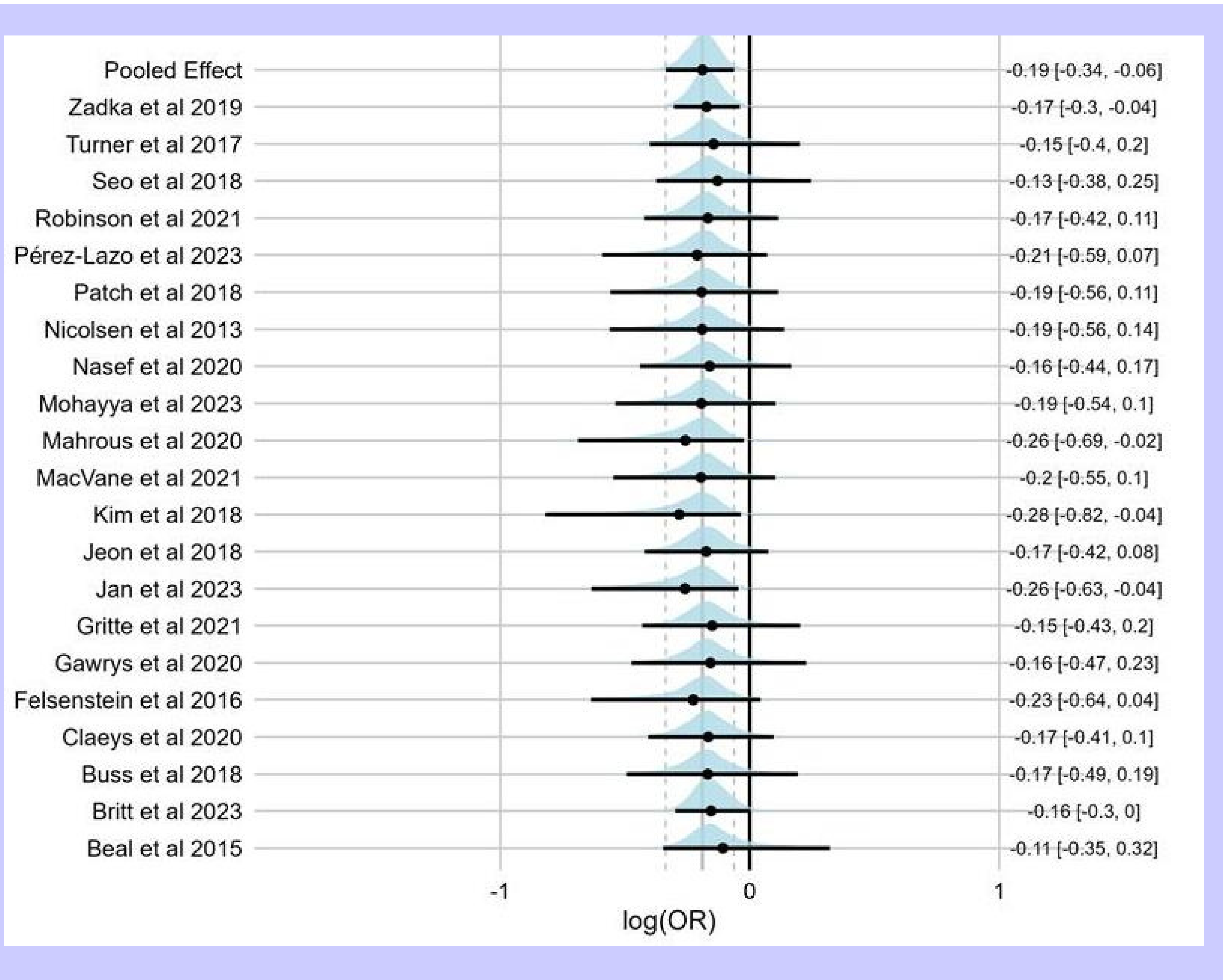


Figure 1. Bayesian Random-effects Meta-analysis for Mortality

References

1. Lamy B, Sundqvist M, Idelevich EA, ESCMID Study Group for Bloodstream Infections, Endocarditis and Sepsis (ESGBIES). Bloodstream infections - Standard and progress in pathogen diagnostics. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. 2020 Feb;26(2):142-50.
2. Siljander MP, Sobh AH, Baker KC, Baker EA, Kaplan LM. Multidrug-Resistant Organisms in the Setting of Periprosthetic Joint Infection—Diagnosis, Prevention, and Treatment. J Arthroplasty. 2018;33(1):185-94.
3. McNally M, Sigmund I, Hotchen A, Sousa R. Making the diagnosis in prosthetic joint infection: a European view. EFORT Open Rev. 2023 May 9;8(5):253-63.
4. Gonzalez MR, Bedi ADS, Karczewski D, Lozano-Calderon SA. Treatment and Outcomes of Fungal Prosthetic Joint Infections: A Systematic Review of 225 Cases. J Arthroplasty. 2023 Nov 1;38(11):2464-2471.e1.
5. Leal HF, Azevedo J, Silva GEO, Amorim AML, de Roma LRC, Arraes ACP, et al. Bloodstream infections caused by multidrug-resistant gram-negative bacteria: epidemiological, clinical and microbiological features. BMC Infect Dis. 2019 Jul 11;19:609.

5. Conclusion

This living systematic review and meta-analysis offers a continuously updated synthesis of the clinical benefits of early diagnosis of infections in normally sterile body fluids. Consistent findings across studies indicate the association of rapid diagnostic interventions with improved clinical outcomes. These findings will directly inform the economic evaluation of an emerging Alguided whole genome sequencing (WGS) diagnostic tool by providing key model parameters, estimating its cost-effectiveness compared to standard diagnostics.



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