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Unravelling treatment success in enterococcal prosthetic joint infection: a systematic review and meta-analysis with individual patient data

Background

Enterococcal prosthetic joint infection (PJI) is often associated with polymicrobial co-infection, antimicrobial resistance and limited treatment options, resulting in a poor prognosis.

Aim

This review estimates the outcome of enterococcal PJI in different subgroups, focusing on methodological quality of included studies.

Methods

- PubMed and Embase until 8 January 2025
- Adults with PJI caused by Enterococcus spp.; two reviewers screened, extracted and appraised quality (Newcastle–Ottawa)
- Outcome: treatment success as defined by each study
- Pooled proportion — random effects, Freeman–Tukey, REML, Hartung–Knapp, with a 95% prediction interval

Snapshot

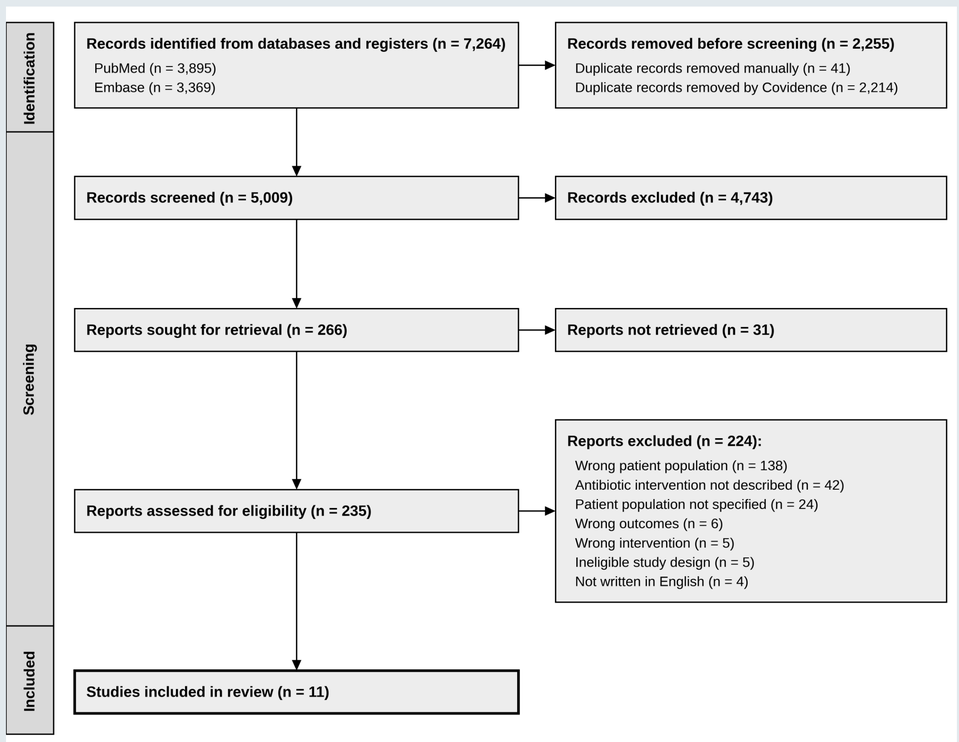
11 studies included in the review

638 enterococcal PJI episodes (10 studies)

194 patients with individual patient data (5 studies)

53% of infections polymicrobial

Figure 1 · Study selection (PRISMA 2020)



7,264 records identified · 5,009 screened · 235 full texts assessed · 11 studies included

Table 1 · Study population — all studies vs IPD cohort

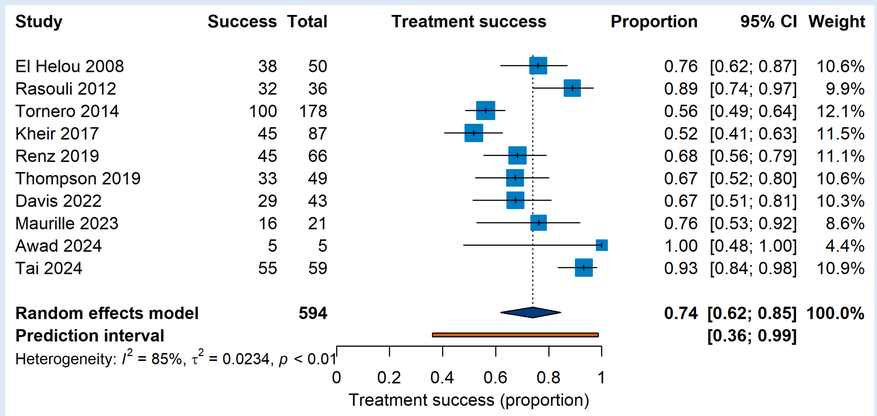
Characteristic	All studies k = 10 · n = 638	IPD cohort k = 5 · n = 194
Age, years — mean (range)	65.9 (30–90)	68.1 (37–88)
Female sex	366/638 (57.4%)	81/158 (51.3%)
Knee	259/638 (40.6%)	124/194 (63.9%)
Hip	369/638 (57.8%)	70/194 (36.1%)
E. faecalis	409/483 (84.7%)	123/194 (63.4%)
E. faecium	51/483 (10.6%)	11/194 (5.7%)
Polymicrobial infection	335/638 (52.5%)	107/194 (55.2%)
DAIR	293/534 (54.9%)	93/192 (48.4%)
Two-stage revision	140/534 (26.2%)	71/192 (37.0%)
Monotherapy	205/359 (57.1%)	128/184 (69.6%)
Combination therapy	154/359 (42.9%)	56/184 (30.4%)
Treatment duration, weeks — median	11.5	10.8

N differs per row: only episodes for which the characteristic was reported are counted (available-case analysis).

Figure 2 · Pooled treatment success — primary analysis

74.0% pooled treatment success

95% CI 61.9–84.6% · 95% prediction interval 36.2–98.7% · I^2 = 84.9% · k = 10, n = 594



Random-effects model (Freeman–Tukey, REML, Hartung–Knapp). Wouthuyzen-Bakker excluded from pooling (cohort overlap with Tai), retained in the IPD analysis. With heterogeneity this high, the prediction interval — not the point estimate — is what a clinician should read as the expected range in a new cohort.

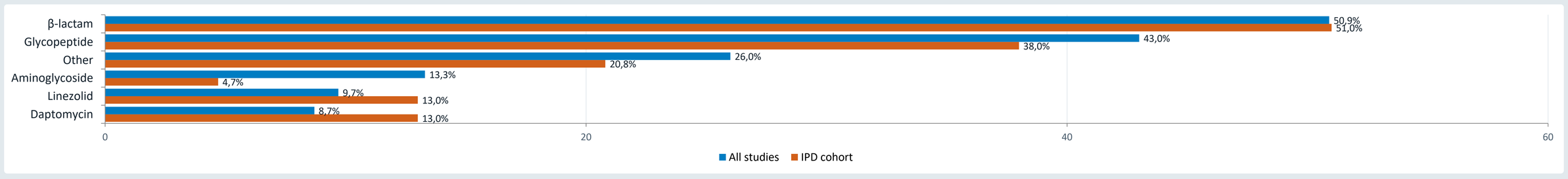
Methodological considerations about included studies

- Treatment groups not mutually exclusive in 8 of 11 studies
- No comparative study exists: all 11 cohorts are observational and single-arm studies
- Confounding by indication present in all studies
- Newcastle–Ottawa quality assessment: of 7 studies assessed, 5 FAIR and 2 GOOD
- GRADE certainty for the comparative questions expected to be very low — observational design, high heterogeneity, small numbers
- Publication bias not formally tested: with 11 studies a funnel plot is not interpretable

Pre-specified contrasts — in progress

- B1 · Monotherapy vs combination therapy — El Helou, Kheir, Renz, Maurille (k = 4), pooled as a risk ratio
- B2 · With vs without rifampicin — Tornero, Thompson, Maurille, Davis (k = 4), pooled as a risk ratio
- Individual studies point in opposite directions and none reached significance

Used antimicrobial strategies targeting enterococcal PJI



Percentage of episodes in which each class was used. Denominators overlap — a patient on combination therapy appears in more than one bar — so these bars describe use, not effectiveness.

Conclusions

- 11 studies, including 638 enterococcal PJI episodes, with individual patient data for 194 patients from 5 studies.
- Pooled treatment success: 74.0% (95% CI 61.9–84.6%), with a 95% prediction interval of 36.2–98.7% reflecting substantial heterogeneity (I^2 = 84.9%) across studies.
- Significant methodological constraints across the included studies mean that no scientific conclusions can be drawn about the most adequate antimicrobial treatment strategy for enterococcal PJI.

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