

## Prevalence of infective endocarditis in streptococcal bloodstream infections is dependent on streptococcal species

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**Background:** Streptococci frequently cause infective endocarditis (IE), yet the prevalence of IE in patients with bloodstream infections (BSIs) caused by different streptococcal species is unknown.

**Purpose:** To investigate the prevalence of IE in BSIs with different streptococcal species.

**Methods:** We included all patients with streptococcal BSIs, from 2008 to 2017, in a population-based setup. Based on microbiological identification of phylogenetic relationship, streptococcal species were classified into eight main groups: Anginosus, Bovis, Mitis, Mutans, Salivarius, Pyogenic, *S. pneumoniae*, and "other streptococci". Using nationwide registries, we determined the prevalence of IE at streptococcal group level and at species level. In a multivariable logistic regression analysis, we investigated the risk of IE according to streptococcal species with *S. pneumoniae* as reference and adjusted for age, sex,  $\geq 3$  positive blood culture (BC) bottles, native valve disease, prosthetic valve, previous IE, and cardiac device.

**Results:** In 6,506 cases with streptococcal BSIs (mean age 68.1 years (SD 16.2), 52.8% men), the IE prevalence was 7.1% (95% CI: 6.5–7.8%). For the most common streptococcal species ( $>5\%$  of BSIs), the IE prevalence was: *S. pneumoniae* 1.2% (95% CI: 0.8–1.6%), *S. dysgalactiae* 6.4% (95% CI: 4.9–8.2%), *S. pyogenes* 1.9% (95% CI: 0.9–3.3%), *S. agalactiae* 9.1%

(95% CI: 6.6–12.1%), *S. anginosus* 4.8% (95% CI: 3.0–7.3%), and *S. mitis/oralis* 19.4% (95% CI: 15.6–23.5%) (Figure 1). For moderately common streptococcal species (1–5% of BSIs), the IE prevalence was: *S. gallolyticus* 30.2% (95% CI: 24.3–36.7%), *S. salivarius* 5.8% (95% CI: 2.9–10.1%), *S. sanguinis* 34.6% (95% CI: 26.6–43.3%), *S. parasanguinis* 10.3% (95% CI: 5.2–17.7), and *S. gordonii* 44.2% (95% CI: 34.0–54.8%). For uncommon streptococcal species (0.1–1% of BSIs), the highest IE prevalence was in *S. mutans* with 47.9% (95% CI: 33.3–62.8%). In a multivariable adjusted analysis using *S. pneumoniae* as a reference, we identified that all species except *S. pyogenes* were associated with a significantly higher IE risk (Figure 1). The highest associated IE risk was found in *S. mutans* (OR 81.3, 95% CI: 37.6–176), *S. gordonii* (OR 80.8, 95% CI: 43.9–149), *S. sanguinis* (OR 59.1, 95% CI: 32.6–107), *S. gallolyticus* (OR 31.0, 95% CI: 18.8–51.1), and *S. mitis/oralis* (OR 31.6, 95% CI: 19.8–50.5) (Figure 1).

**Conclusion:** The prevalence of IE in streptococcal BSIs is highly species dependent with the lowest IE prevalence observed in *S. pneumoniae* and *S. pyogenes* BSIs, whereas *S. mutans*, *S. gordonii*, *S. sanguinis*, *S. gallolyticus* and *S. mitis/oralis* had the highest IE prevalence and the highest associated IE risk after adjusting for IE risk factors.

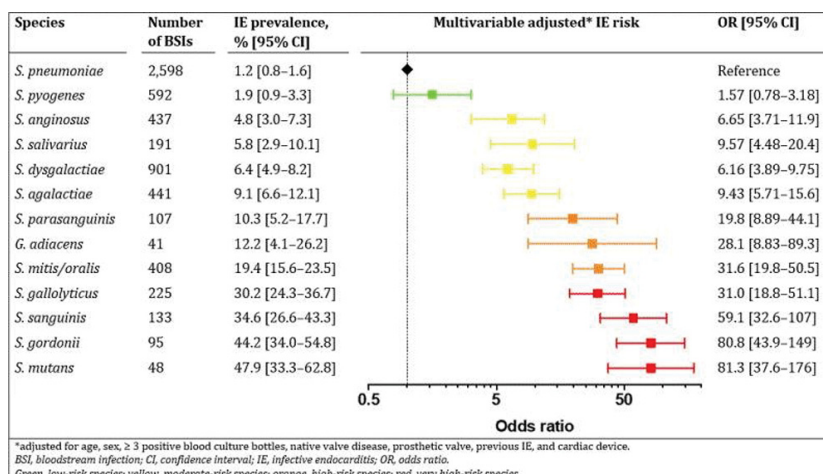


Figure 1. Risk of IE in streptococcal BSIs