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Antimicrobial strategies and multidisciplinary care in prosthetic joint infections

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Chapter 6

Practice variation, outcomes and definitions of suppressive antimicrobial therapy for prosthetic joint infections: a systematic review and expert consensus statement

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Abstract

Background Literature on periprosthetic joint infection (PJI) contains varying strategies and definitions of suppressive antimicrobial therapy (SAT). This study aimed to describe current SAT strategies, evaluate their clinical outcomes, and establish a consensus definition of SAT for research and clinical purposes.

Methods Following PRISMA guidelines, a systematic review was performed by searching PubMed and EMBASE from their inception to March 10, 2025. All trials and observational studies including ≥10 patients with PJI treated with SAT were eligible. Data on study, patient, and treatment characteristics, definitions and outcomes were extracted. Study quality was appraised using the Methodological Index for Non-randomized Studies tool. A random effects model was used to pool success rates. Definitions were developed through a modified Delphi process.

Results Forty-two studies (n = 2524 patients) were included: 25 from the United States (U.S.) and 17 from Europe. In U.S. literature, SAT was predominantly prescribed for acute PJI managed with debridement, antibiotics, and implant retention (DAIR), whereas European studies primarily involved PJI managed without curative intent. The pooled reported success rate of SAT was 74% (95% CI: 63-85%) for acute PJI treated with DAIR and 70% (95% CI: 63-78%) for chronic PJI treated with DAIR or without surgery. Definitions of SAT were inconsistently reported. Consensus was achieved, resulting in definitions distinguishing SAT from extended antimicrobial therapy (EAT).

Conclusion SAT is inconsistently defined in PJI literature with variation of practice between the U.S. and Europe. To harmonize research and clinical communication, we advocate the use of consensus definitions of SAT and EAT.

Introduction

Periprosthetic joint infection (PJI) is a serious complication of arthroplasty necessitating antibiotics and surgical debridement with or without exchange arthroplasty to achieve cure. After completion of the initial therapeutic antimicrobial regimen, physicians often continue antimicrobial treatment, commonly referred to as suppressive antimicrobial therapy (SAT). The indications for this treatment strategy vary worldwide and no uniform definition of SAT currently exists (1). For example, the Infectious Diseases Association of America (IDSA) in their 2012 guideline recommends indefinite SAT for PJI treated with Debridement, Antibiotics and Implant Retention (DAIR), implying this is a non-curative strategy (2). From a European perspective, however, DAIR is generally regarded as a curative procedure for acute PJI and is therefore not standardly followed by suppressive therapy. In Europe, the term SAT is used only for long-term antimicrobial strategies in situations considered non-curative—such as in patients who would normally have an indication for exchange arthroplasty but are nonetheless treated with DAIR, or in those managed without surgical debridement (3-5). To our knowledge, national guidelines specifically addressing PJI management are not available outside Europe and the United States (U.S.). These differences in clinical practice are reflected in the heterogeneous methodology of studies evaluating SAT. Across studies, SAT is variably defined and considered as a treatment strategy or as a marker for treatment failure. This inconsistency introduces misclassification bias and limits comparability of data on PJI treated with SAT. We therefore performed a systematic review to (1) characterize current SAT practices, (2) summarize and compare reported clinical outcomes, and (3) ultimately propose a consensus based definition of SAT through a modified Delphi process for future research and patient management.

Methods

Search strategy and selection criteria

This systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and registered in the PROSPERO database (registration number CRD420251011557). The population of interest consisted of patients with PJI treated with SAT. Clinical trials, observational studies and case series containing more than ten PJI treated with SAT were eligible for selection. Studies that also included other antimicrobial strategies, or other infections (i.e., other implant-associated infections, osteomyelitis, or septic arthritis) were only included if the variables of interest were reported separately for

PJI. Studies that included fewer than 10 patients with PJI treated with SAT, or that considered SAT as a failure of treatment, were excluded.

The literature search was designed in collaboration with a medical librarian from the Leiden University Medical Center. PubMed and EMBASE databases were searched from inception to March 10, 2025. The complete search terms and strategy are provided in supplementary table 1.

Study selection and data extraction

Literature screening and data extraction were performed with the use of Covidence systematic review software (Veritas Health Innovation Ltd, Melbourne, Australia. Available at www.covidence.org). Two reviewers independently screened titles, abstracts, and full texts of potentially relevant studies to assess eligibility. Data extraction was performed by one reviewer (JLJH). A random 25% sample of included studies was verified by a second reviewer (HS). No discrepancies necessitating third-reviewer adjudication were identified.

Assessment of quality of evidence

The Methodological Index for Non-Randomized Studies (MINORS) assessment tool was used to assess the methodology and quality of the included studies used for quantitative analysis (6).

Data analysis

Data extracted from eligible studies included study characteristics (country or continent, year of publication), patient characteristics (chronicity of infection and the indication for initiating SAT), treatment characteristics (surgical strategy, pre-SAT antimicrobial regimen, SAT dosing, duration, and treatment goals), and outcomes (definition of SAT, definition of failure, reported success rate, and relapse rate after discontinuation). Definitions of acute and chronic infection, as well as failure criteria, were adopted as reported by the original authors; acute infection included both postoperative and hematogenous cases.

The primary quantitative outcome was the reported success rate of SAT in each study. Reported numbers of successful and total treated patients were aggregated across studies at the patient level and within predefined subgroups (based on PJI chronicity, SAT dosing, and treatment duration) to calculate pooled success rates. Due to expected heterogeneity in study populations, treatment protocols, and follow-up durations, a random effects meta-analysis was performed using metafor package in R with Re-

stricted maximum-likelihood estimation (REML) for estimating heterogeneity (I^2) (7). All descriptive statistics were performed using SPSS 23.0 (IBM Corp., Armonk, NY).

Approach for defining SAT

Qualitative data were analyzed by comparing definitions, indications, and treatment strategies across studies and regions to identify recurring concepts and differences. These data were used to inform the expert consensus process described below. The assembled expert panel was based on recognized clinical and academic PJI expertise among investigators who previously collaborated on an international SAT survey that formed the foundation for this consensus effort (1).

Consensus definitions were developed through a modified Delphi process. Preliminary findings from the literature review were summarized and distributed to all co-authors (i.e., panel members) together with a structured questionnaire consisting of 13 questions addressing potential definitional domains and their formulation. All panel members provided feedback, which was collated and used to construct a draft definition accompanied by a summary of comments and rationale for each choice. The draft and accompanying rationale were then redistributed for a second full round of review and feedback. In this round, all panelists re-evaluated each proposed element and provided additional input. A final proposal was then developed with this feedback, and panel members were polled for their approval.

Results

Overview of included studies

The literature search retrieved 2076 articles, of which 91 full-text articles were assessed for eligibility (Figure 1). In total, 42 observational studies, published between 1988 and 2025, comprising 2524 patients, were included (Supplementary file). All studies were from either the U.S. (n=25; 1528 patients) or Europe (n=17; 996 patients). No eligible studies from regions outside the U.S. and Europe were identified through our search strategy. No randomized trials were identified. Forty studies containing 2467 patients reported clinical outcome of included patients and were available for quantitative analysis. According to MINORS assessment, methodological quality was generally low to moderate (Supplementary table 2).

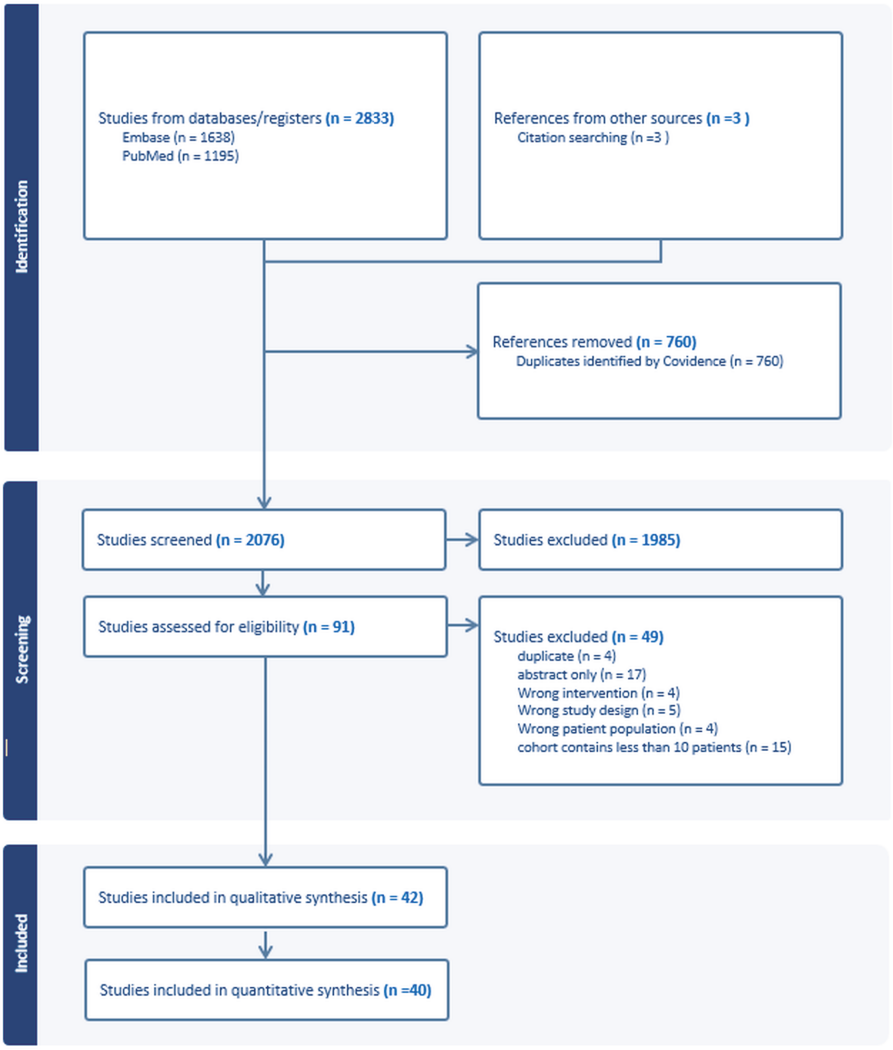

Figure 1. *PRISMA flowchart for the identification, screening, and inclusion of studies. Abbreviations: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis.*

Clinical aspects of SAT

Reported indications for SAT

Of the 25 studies from the U.S., ten reported exclusively on acute PJI managed with DAIR, nearly all published between 2017 and 2024 (Supplementary Refs 1-10). Seven studies included mixed acute and chronic infections (Supplementary Refs 11-17), and five described a reason for SAT beyond implant retention—such as non-surgical man-

agement or DAIR performed in the presence of risk factors like immunosuppression or after failure of a prior DAIR (Supplementary Refs 18-22). Three studies did not report infection chronicity (Supplementary Refs 23-25).

Among the 17 European studies, 15 described SAT as being prescribed in one of two clinical contexts as stated by the authors (Supplementary Refs 26-40). First, to mitigate a high relapse risk following procedures that were not expected to be curative—such as non-surgical management or DAIR performed in the presence of risk factors for failure. Second, in patients who underwent potentially curative surgery (DAIR for acute PJI or exchange arthroplasty) but for whom a relapse was considered unacceptable because of frailty, advanced age, or other comorbidities.

Studies were categorized according to the patient characteristics and indications reported by the authors, reflecting the dominant clinical context within each study (Figure 2).

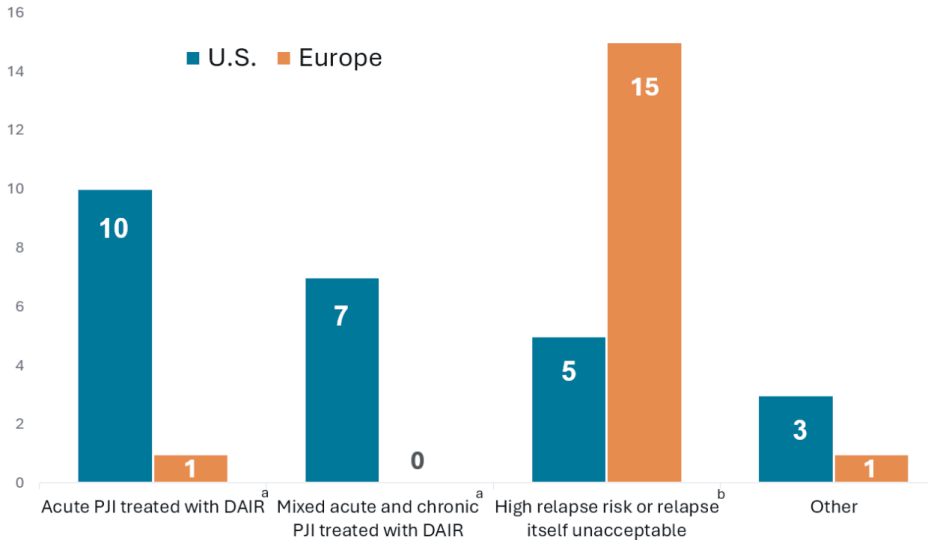

Figure 2. *Reported dominant clinical contexts in which SAT was applied in U.S. and European studies (n = 42)*

Abbreviations: PJI, periprosthetic joint infection; DAIR, debridement, antibiotics and implant retention.

[a]These cohorts included both acute postoperative PJI (within 3–4 weeks after total joint arthroplasty [TJA]) and acute hematogenous PJI (developing > 1 month after TJA but with symptom duration < 3–4 weeks). No reason other than implant retention was provided by the authors.

[b]This high risk was explicitly stated by the authors.

Treatment goals

Treatment goals were variably reported and included: infection control, symptom reduction, prevention of progression, prevention of further surgery, and prosthesis retention. For studies exclusively including acute PJI managed with DAIR, the goal, when specified, was to maximize reoperation-free survival and to prevent recurrence.

Treatment duration

All except one U.S. and one European study reported on treatment duration. Most U.S. studies (n=19) reported that the intended treatment duration was indefinite and the majority of patients were still receiving SAT at final follow-up (average follow-up 51 months, based on reported means or medians). Four studies reported a finite SAT duration (mean 6–18 months), mainly for acute PJI treated with DAIR (Supplementary Refs 1, 3, 4, 8). In one study, patients managed by DAIR who discontinued SAT after a median of six months were compared with those with indefinite therapy (showing no difference in success rate).

In European studies, treatment was intended to be indefinite in 12 and most patients were still on SAT at the end of follow-up (average follow-up 25 months, based on reported means or medians) . Two studies compared patients treated with DAIR who stopped SAT after a defined period (ranging from 6 to 36 months) with those on indefinite therapy; one found no difference in outcome, while one reported a higher success rate in the ongoing SAT group (Supplementary Refs 27, 30). In the only study focusing primarily on acute PJI, SAT was intended for a minimum of 12 months and discontinued in 81% of patients after mean 18 months (Supplementary Ref 41).

Pre-SAT antimicrobial strategy

In U.S. studies, antimicrobial treatment before starting SAT was exclusively intravenous (IV) in 23 studies, and one study initiated SAT orally without any reported pre-treatment.

In European studies, pre-SAT therapy was administered solely IV in eight studies, whereas seven studies reported IV therapy followed by oral antibiotics before transitioning to SAT. The remaining studies in both regions did not specify their pre-SAT regimen.

Dosing

Nine U.S. and ten European studies described SAT dosing. Regimens were interpreted in relation to the 2013 IDSA PJI guideline recommendations for chronic oral antimicrobial suppression (2). Of the nine U.S. studies providing dosing information, five

referenced the IDSA guideline (Supplementary Refs 2, 9, 13, 16, 17, 41). Four used a combination of IDSA-concordant and lower-than-IDSA regimens (Supplementary Refs 11, 15, 21, 22).

Within the ten European studies, exclusively IDSA-concordant regimens were observed in two (Supplementary Refs 30, 36). Both higher-than-IDSA dosing and IDSA-concordant regimens were described in two studies (Supplementary Refs 33, 38), whereas three studies used IDSA-concordant and lower-than-IDSA regimens, with lower dosing predominating (Supplementary Refs 27, 28, 33, 34, 39). One study used tedizolid for suppression, a regimen not included in the IDSA dosing recommendations (Supplementary Ref 38). Two European studies reported the use of therapeutic drug monitoring (TDM); one for dosing IV dalbavancin and the other for subcutaneous beta-lactams (Supplementary Refs 37, 42).

Outcomes of SAT

Forty of 42 included studies reported treatment outcomes. Definitions of treatment success and failure were highly heterogeneous across studies. Most defined failure as reoperation for infection, clinical recurrence or persistence of infection, or infection-related death. Detailed study-specific definitions are provided in Supplementary Table 3.

Pooled analysis of 40 studies (2467 patients) yielded an overall reported success rate of 74% (95% confidence interval (CI) 70%-79%). Acute PJI treated with DAIR had a similar success rate of SAT (74% (95% CI 63%-85%)) compared to chronic PJI (70% (95% CI 63%-78%)). Continent and SAT duration did not alter pooled success rates (Table 1). Patient population, surgical treatment, duration of treatment and follow-up, and success rate for each individual study included in the pooled analysis are summarized in supplementary Table 4. Eight studies on PJI treated with DAIR included a comparator group of patients managed without SAT; their reported outcomes are summarized descriptively in Supplementary Table 5. Five studies reported higher success rates with SAT, whereas three found no significant difference, including the largest cohort (n=510).

Table 1. Pooled data of studies reporting individual patient data regarding suppressive antimicrobial therapy

	N studies	N patients	Pooled success rate N, % [95%CI]
All PJI	40	2467	1806, 74 [70-79]
Indication			
Acute PJI treated with DAIR	11[a]	711	538, 74 [63-85]
Chronic PJI with implant retention	13[a,b]	732	507, 70 [63-78]
Continent			
United States	24	1483	1089, 73 [66-79]
Europe	16	984	717, 77 [70-83]
Duration SAT			
ongoing at final follow-up	25	944	693, 74 [69-80]
discontinued[c]	21	526	410, 74 [64-84]

Abbreviations: PJI, periprosthetic joint infection; DAIR, debridement, antibiotics and implant retention; SAT, suppressive antimicrobial therapy; IDSA, Infectious Diseases Society of America.
Except for the therapeutic dose subgroup, all pooled success rates showed relevant between study variation (heterogeneity) of more than 40%.
[a]One study (Kildow), included both acute and chronic PJI but reported patient outcome for these two groups separately.
[b]One study (Hanssen) individual patient data on chronic PJI was available.
[c]all patients who stopped SAT combined; both pre-emptively planned to stop as those who stopped for example due to side effects or because physicians believed the patient was cured.

Assessment of publication bias

The funnel plot showed a broad, symmetrical distribution of studies, consistent with the substantial between-study variation (Supplementary Figure 1). Trim-and-fill analysis detected no missing studies and did not alter the pooled estimate.

Definition of SAT

Reported definitions in included literature

Most studies (n=23) did not report a definition of SAT. Definitions were heterogeneous, typically one or more of three aspects differed: (1) the starting point of SAT (i.e., the transition from therapeutic to suppressive treatment), (2) the intended duration (fixed, indefinite, or lifelong), and (3) the treatment goal (curative versus non-curative). Supplementary table 6 contains all reported definitions from included studies.

In the U.S. literature, eight studies provided a definition. Of these, seven studies defined the starting point, four the intended duration, and one the treatment goal as

part of the definition. In the remaining U.S. studies, any prolonged oral antibiotic use in PJI was referred to as "SAT" or "chronic suppression". Eleven studies from Europe provided a definition. Five defined the starting point, seven the intended duration (six: indefinite/lifelong, one: treatment over six months), and six the treatment goal as part of the definition.

SAT definition by modified Delphi process

To address the substantial heterogeneity in how SAT was defined across the included studies, all components of the reported definitions were extracted and subsequently refined through the modified Delphi procedure described in the Methods section. This process yielded final consensus definitions of *suppressive antimicrobial therapy* (SAT) and the related term *extended antimicrobial therapy* (EAT). Agreement among panel members for individual definitional components ranged from 78% to 100%, with full consensus ultimately achieved on the final definitions (table 2).

Table 2. Consensus Definitions for Suppressive and Extended Antimicrobial Therapy in Periprosthetic Joint Infection.

Suppressive antimicrobial therapy (SAT):
A non-curative antimicrobial regimen continued beyond the recommended therapeutic treatment duration according to (inter)national guidelines, with the goal of suppressing a latent infection (i.e., preventing symptoms and potential consequences thereof).
a. When prescribed indefinitely, SAT is intended to be continued without a planned stop, because curative surgery will not be performed.
b. When prescribed for a fixed term, SAT is intended to be discontinued once conditions have improved to allow for curative surgery.
Extended antimicrobial therapy (EAT):
A curative-intent antimicrobial regimen continued for a fixed term beyond the recommended therapeutic treatment duration according to (inter)national guidelines to increase the likelihood of infection eradication without additional surgery.

Discussion

The need for a standardized definition of SAT

This review demonstrates that the commonly used term 'SAT' in PJI literature refers to varying treatment strategies used in heterogenous patient populations. This lack of conceptual uniformity complicates interpretation of reported outcomes and limits comparability between studies, underscoring the need for a standardized definition of SAT. Importantly, long-term antimicrobial therapy may be used both in situations where cure remains the goal of treatment and in situations where cure is unlikely and treatment is intended to suppress infection. By distinguishing suppressive an-

timicrobial therapy from extended antimicrobial therapy with curative intent, the consensus definitions proposed in this study aim to improve clarity in future research and facilitate more consistent reporting of treatment strategies and outcomes.

Treatment duration

For chronic PJI managed without exchange arthroplasty, SAT was usually prescribed indefinitely. However, two studies reported that even in this high-risk population, discontinuing SAT after two years did not result in worse outcomes compared to indefinite therapy . In clinical practice, discontinuation of SAT (regardless of the indication) after several years is relatively common both in Europe, the U.S. and Oceania, yet criteria for cessation remain poorly defined and largely clinician- or patient-driven (1).

Whether extending antimicrobial therapy beyond 12 weeks is beneficial for acute PJI treated with DAIR without risk factors for failure remains debated. Also, the optimal duration of such prolonged treatment is uncertain. Antimicrobial treatment beyond one or two years did not further improve failure-free survival in observational studies.

Overall, establishing objective criteria for discontinuing long-term antibiotics and identifying which patients may safely stop therapy remain important unresolved clinical challenges.

Outcome

The overall pooled success rate of SAT (74%) appeared relatively high compared with succes rates reported in the literature after DAIR (55–90%) or revision surgery (≈85%) (8-10). Success rates were equal for acute PJI managed with DAIR and chronic PJI treated with DAIR or without surgery. However, these findings should be interpreted with caution, as reported success rates are strongly influenced by study methodology and patient selection, and should not be interpreted as reflecting treatment efficacy alone. Definitions of treatment failure differed considerably across studies and such heterogeneity in outcome definitions affects pooled estimates. In addition, patients selected for SAT are typically clinically stable and able to tolerate prolonged therapy, introducing selection and survivorship bias that may inflate reported success rates. Of note, in other studies on PJI (outside the scope of this review), initiation of SAT is sometimes classified as treatment failure or treated as a competing endpoint rather than as a therapeutic strategy, further complicating interpretation of SAT outcomes.

Australasian perspective

A prospective PJI cohort study from Australia and New Zealand, published after completion of our literature search, provides additional insight of contemporary SAT

practice from a different region (11). In this study (n = 720), SAT was prescribed in 31% of patients, predominantly in those who were older, comorbid, had chronic PJI, a sinus tract, or were managed with DAIR or without surgery. SAT was defined as therapy extending beyond 12 months or initiated with an early intent for long-term suppression. The goals were symptom control and avoidance of further surgery rather than cure. SAT was associated with failure (adjusted OR 2.5, 95% CI 1.7–3.7), likely reflecting confounding by indication. These findings further illustrate the heterogeneity in SAT practice internationally and highlight the need for clear definitions and risk stratification in future studies.

Framework for future SAT research

Taken together, the present review demonstrates that —beyond the absence of a uniform definition of SAT—interpretation of SAT data is further complicated by heterogeneous study populations and varying outcome definitions. The observed differences between U.S. and European studies should be interpreted with caution though. As our review was designed to synthesize data from studies on PJI treated with SAT rather than DAIR management more broadly, we did not collect data on patients undergoing DAIR without SAT. The categories presented in Figure 2 therefore reflect how study populations and indications were described in the included reports, rather than representing how patients treated with DAIR are generally managed (i.e., with or without SAT). While clinical decision-making is usually more nuanced than reflected in published reports, our findings highlight differences in the types of SAT populations studied in the existing literature. Stratifying patients according to relapse risk may therefore enable a more individualized interpretation of SAT strategies and improve the translation of study findings to clinical practice. We therefore propose an expert opinion-based risk classification based on expected relapse risk if SAT would be withheld, with elements partly adapted from the European Bone and Joint Infection Society (EBJIS) position paper on DAIR as curative strategy for acute periprosthetic hip and knee infection (Fig 3) (5).

Low risk	Medium risk	High risk	Very high risk	Indeterminate
PJI treated with exchange arthroplasty PJI treated with DAIR under the following conditions: • Well-fixed prosthesis • Acute PJI: – Early acute: ≤4 weeks after index arthroplasty – Late acute: < 3 weeks of symptoms after an uneventful postoperative period • Good conditions of the surrounding soft tissue without a sinus tract	PJI treated with DAIR with the following risk factors: • Early acute: 4–12 weeks after index arthroplasty • Multiple previous revision surgeries • Host and clinical factors: – Rheumatoid arthritis – COPD – Immunosuppressive therapy • *S. aureus* infection (late acute PJI) • Difficult to treat microorganism – no biofilm active antimicrobial therapy available – and fungal infections • Bacteraemia	PJI treated with DAIR despite not recommended due to: • Loose prosthesis • > 12 weeks after index arthroplasty • > 3 weeks of symptoms • Presence of a sinus tract • Compromised soft tissue	PJI treated without surgery – antimicrobial treatment only	Low-risk profile, but SAT started because of old age or frailty

Figure 3. *Expert opinion-based classification of risk for failure in patients receiving SAT*. *This classification can be used for research purposes and is adapted from the European Bone and Joint Infection Society (EBJIS) position paper on debridement, antimicrobial therapy, and implant retention (DAIR) as a curative strategy for acute periprosthetic hip and knee infection (5). The "very high-risk" (purple column) and "indeterminate" (blue column) categories were added based on the current systematic review. Patients are classified according to the highest risk factor present; the presence of a single factor in a given column places the patient in that risk category.*

This proposed classification aligns with clinical practice and is feasible for research purposes. The EBJIS position paper was not intended to provide a formal risk stratification, but it offers a comprehensive overview of risk factors for DAIR failure, which makes it a useful reference for the proposed classification. Stratifying patients by risk profile is essential, as the likelihood of persistent biofilm and relapse after initial treatment varies across these groups. In addition to risk stratification, interpretation of SAT success also depends on patient preferences. In frail patients prioritizing symptom control and avoidance of surgery, long-term suppression may represent a favorable outcome. Conversely, in younger or surgically fit patients, continued SAT may be less desirable compared with curative strategies. Incorporating Desirability of Outcome Ranking frameworks in future studies would further strengthen evaluation of SAT by explicitly integrating clinical context and treatment goals.

Strengths and limitations

This systematic review is the first to comprehensively evaluate definitions and practices of SAT and included the largest number of studies on SAT in PJI to date. Strengths include a comprehensive literature search, combined qualitative and quantitative analysis, and practical recommendations for SAT definitions and patient stratification.

Limitations include the heterogeneity in study design and patient populations, variability in outcome reporting, and the overall low methodological quality of the included studies according to the MINORS tool, indicating a considerable risk of bias. Not all data were extracted in duplicate; however, verification of a random sample of 25% of the included studies did not reveal discrepancies. Since our literature search specifically targeted suppressive therapy, we may have missed studies on long-term antibiotic treatment for PJI that did not explicitly label their approach as SAT. Moreover, in our qualitative synthesis of SAT indications and patient populations, we primarily captured chronicity-based indications, whereas other potential risk factors such as host immunocompromise, specific pathogens, or local surgical complexity were not always systematically reported and therefore not analyzed in detail. Lastly, the expert panel comprised more European than American or Australian participants, which may have influenced the consensus-derived definition.

Conclusion

Definitions and reported practices of suppressive antimicrobial therapy for PJI vary widely. This complicates data interpretation and hampers communication among clinicians and researchers. Implementation of standardized definitions and risk-based patient stratification will improve research comparability, enable better clinical decision-making, and allow more accurate assessment of SAT effectiveness and treatment strategies in distinct patient populations.

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Supplement

Supplementary Table 1. Search strategy

Databases:	Pubmed, Embase
Search terms:	("prosthetic joint infection*"[tiab] OR "prosthetic joint infection"[tiab:~2] OR "prosthetic joint infections"[tiab:~2] OR "PJI"[tiab] OR "arthroplast*"[tiab] OR "implant-related"[tiab] OR "implant related"[tiab] OR "periprosthetic joint infection*"[tiab] OR "peri-prosthetic joint infection*"[tiab] OR "arthroplasty"[mesh] OR "Prosthesis-Related Infections"[Mesh] OR "prosthesis-related infection*"[tiab] OR "prosthesis-related infection"[tiab:~2] OR "prosthesis-related infections"[tiab:~2]) AND ("suppress*"[tiab] OR "prolonged antibiotic"[tiab] OR "extended antibiotic"[tiab] OR "SAT"[tiab] OR "long term antibiotic"[tiab] OR "chronic antibiotic"[tiab] OR "lifelong antibiotic"[tiab])

Supplementary Table 2. MINORS Item-by-Item Assessment of Included Studies

author	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	Total Score
Barry	2	2	1	2	0	2	1	0	2	2	1	1	16/24
Bene	2	2	1	1	0	2	2	0	-	-	-	-	10/16
Bene	2	2	1	1	0	2	2	0	-	-	-	-	10/16
Brandt	2	0	1	2	0	2	1	0	-	-	-	-	8/16
Bryan	2	2	1	2	0	2	2	0	-	-	-	-	11/16
Burr	2	2	1	1	0	2	2	0	-	-	-	-	10/16
Byren	2	2	1	2	2	2	1	0	-	-	-	-	12/16
Ceccarelli	2	0	1	1	0	1	2	0	-	-	-	-	7/16
Chao	2	0	2	2	0	2	2	0	2	1	1	2	16/24
Dos Santos	2	0	2	2	1	2	1	0	2	1	2	2	17/24
Escudero-Sanchez	2	0	1	2	1	2	2	0	-	-	-	-	10/16
Ferry	1	0	2	2	0	1	2	0	-	-	-	-	8/16
Furukawa	2	2	0	1	0	2	2	0	1	2	2	1	14/24
Goulet	1	0	0	1	0	2	2	0	-	-	-	-	6/16
Goutelle	1	0	1	1	0	1	2	0	-	-	-	-	6/16
Hanssen	2	0	2	2	0	1	2	0	-	-	-	-	9/16
Huotari	2	0	2	2	0	1	2	0	-	-	-	-	9/16
Kherabi	2	2	2	2	0	2	2	0	-	-	-	-	11/16
Kildow	2	0	2	2	0	2	2	0	-	-	-	-	10/16
Koeppe	2	0	0	1	0	2	2	0	-	-	-	-	7/16
Lafon	1	0	0	0	0	1	2	0	-	-	-	-	4/16
Leijtens	2	0	0	2	0	1	2	0	-	-	-	-	7/16
Lensen	2	0	2	2	0	1	2	0	2	2	1	1	15/24
Marculescu	2	0	2	2	0	2	2	0	-	-	-	-	10/16
Nandi	2	2	2	2	0	2	2	0	-	-	-	-	10/16
Pradier	2	0	2	2	0	2	2	0	2	1	2	1	16/24
Prendki ('14)	2	0	2	2	0	2	2	0	-	-	-	-	10/16
Prendki ('17)	2	0	2	2	0	2	1	0	-	-	-	-	9/16
Rao	2	0	2	2	0	2	1	0	-	-	-	-	9/16
Salmons	2	0	2	2	0	2	2	0	-	-	-	-	10/16
Sandiford	2	0	2	2	0	2	2	0	-	-	-	-	10/16
Segreti	2	0	0	2	0	2	2	0	-	-	-	-	8/16
Shah	2	0	2	2	0	2	2	0	2	0	1	2	15/24
Siquera	2	2	2	2	0	2	2	0	2	2	2	2	20/24
Spichler	2	0	2	1	0	1	2	0	-	-	-	-	8/16
Tai ('22)	2	0	2	2	0	2	2	0	-	-	-	-	8/16
Tai ('24)	2	0	2	2	0	2	2	0	1	2	1	2	16/24
Vahedi	2	0	2	2	0	1	2	0	1	0	2	1	13/24

Supplementary Table 2. MINORS Item-by-Item Assessment of Included Studies *(Continued)*

author	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	Total Score
Valencia	2	0	2	2	0	2	1	0	2	0	0	2	13/24
Weston	2	0	2	2	0	2	1	0	-	-	-	-	9/16
Wolff	2	0	0	1	0	2	2	0	-	-	-	-	7/16
Wouthuyzen	2	0	2	2	0	1	2	0	-	-	-	-	9/16

-: not applicable. *The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The global ideal score being 16 for non-comparative studies and 24 for comparative studies.

Items of MINORS

Methodological items for non-randomized studies

(1) A clearly stated aim: the question addressed should be precise and relevant in the light of available literature.

(2) Inclusion of consecutive patients: all patients potentially fit for inclusion (satisfying the criteria for inclusion) have been included in the study during the study period (no exclusion or details about the reasons for exclusion).

(3) Prospective collection of data: data were collected according to a protocol established before the beginning of the study.

(4) Endpoints appropriate to the aim of the study: unambiguous explanation of the criteria used to evaluate the main outcome, which should be in accordance with the question addressed by the study. Also, the endpoints should be assessed on an intention-to-treat basis.

(5) Unbiased assessment of the study endpoint: blind evaluation of objective endpoints and double-blind evaluation of subjective endpoints. Otherwise, the reasons for not blinding should be stated.

(6) Follow-up period appropriate to the aim of the study: the follow-up should be sufficiently long to allow the assessment of the main endpoint and possible adverse events.

(7) Loss to follow-up less than 5%: all patients should be included in the follow-up. Otherwise, the proportion lost to follow-up should not exceed the proportion experiencing the major endpoint.

(8) Prospective calculation of the study size: information on the size of detectable difference of interest with a calculation of 95% confidence interval, according to the expected incidence of the outcome event, and information about the level for statistical significance and estimates of power when comparing the outcomes.

Additional criteria in the case of comparative study

(9) An adequate control group: having a gold standard diagnostic test or therapeutic intervention recognized as the optimal intervention according to the available published data.

(10) Contemporary groups: control and studied groups should be managed during the same time period (no historical comparison).

(11) Baseline equivalence of groups: the groups should be similar regarding the criteria other than the studied endpoints. Absence of confounding factors that could bias the interpretation of the results.

(12) Adequate statistical analyses: whether the statistics

Supplementary Table 3. Reported definitions of SAT failure (n=42)

Author	year	region	Reported definition of SAT failure
Goulet	1988	US	Not reported
Brandt	1996	US	relapse of S. aureus PJI or occurrence of culture-negative PJI during continuous antistaphylococcal therapy
Segreti	1998	US	removal or revision of their prostheses, sepsis
Rao	2003	US	the development of progressive pain, loosening of the implant, or drainage despite antibiotic therapy.
Wolff	2003	US	recurrence of infection
Marculescu	2006	US	Occurrence of a PJI due to the original microorganism at any time after the surgical procedure (relapse of infection); Occurrence of a PJI due to a different strain or different microorganism (reinfection) at any time after the surgical procedure; Presence of acute inflammation in the periprosthetic tissue on histopathological examination or at any subsequent surgery on the joint; Development of a sinus tract; Death from prosthesis-related infection;
Koeppe	2008	US	loss of a functional prosthesis due to infection.
Siquera	2015	US	subsequent surgical intervention for infection after the index procedure; (2) persistent fistula, drainage, or joint pain at the last follow-up visit; or (3) death related to the periprosthetic joint infection.

Supplementary Table 3. Reported definitions of SAT failure (n=42) *(Continued)*

Author	year	region	Reported definition of SAT failure
Bryan	2017	US	failure to eradicate infection characterized by a wound fistula, drainage, intolerable pain, or infection recurrence caused by the same organism strain; subsequent removal of any component for infection; unplanned second wound debridement for ongoing deep infection; and/or occurrence of periprosthetic joint infection-related mortality,
Weston	2018	US	subsequent or recurrent infection
Bene	2018	US	reoperation for infection recurrence
Bene	2018	US	reoperation for infection recurrence
Vahedi	2019	US	reinfection
Valencia	2019	US	Fulfilling the Musculoskeletal Infection Society criteria for PJI
Barry	2020	US	reoperation for infection)
Shah	2020	US	occurrence of PJI that occurred any time after the primary antibiotic therapy period, as well as any further surgical procedure on the operative knee due to infection
Kildow	2021	US	occurrence of PJI that occurred any time after the primary antibiotic therapy period, as well as any further surgical procedure on the operative knee excluding manipulation under anesthesia, periprosthetic fracture, and extensor mechanism disruption.
Tai	2022	US	(1) recurrence of PJI as defined, (2) unplanned reoperation (DAIR, implant resection, amputation) secondary to infection, or (3) infection-related death.
Burr	2022	US	reoperation after starting CAS therapy or if they died of causes directly related to their PJI.
Spichler	2023	US	Not reported
Salmons	2023	US	any reoperation for infection
Tai	2024	US	recurrence of PJI, unplanned reoperation secondary to infection, or infection-related death
Nandi	2024	US	reoperation for infection recurrence
Furukawa	2024	US	repeat surgery for clinical suspicion of infection leading to repeat treatment with a prolonged course of antibiotics
Chao	2024	US	occurrence of PJI, based on the modified MSIS criteria, that occurred any time after the primary antibiotic therapy period as well as any further surgical procedure on the operative knee, due to infection
Byren	2009	Europe	infection recurrence with positive cultures from peri-prosthetic samples or an aspirate; wound or sinus drainage recurring or persisting for 3 months beyond the index debridement procedure; or a requirement for revision surgery
Prendki	2014	Europe	persisting infection, relapse, new infection, treatment discontinuation because of severe adverse events, or related death
Prendki	2017	Europe	(i) local or systemic progression of the infection (failure), (ii) death and (iii) discontinuation or switch of PSAT

Supplementary Table 3. Reported definitions of SAT failure (n=42) *(Continued)*

Author	year	region	Reported definition of SAT failure
Wouthuyzen	2017	Europe	1) the patient still reported joint pain during follow-up visits at the outpatient clinic, 2) when surgical intervention was needed to control the infection (i.e. removal of the prosthesis (Girdlestone or arthrodesis), revision surgery and/or amputation/ dysarticulation) and/or 3) when death occurred due to the infection
Pradier	2018	Europe	signs of infection
Leijtens	2019	Europe	death related to PJI or new surgical intervention at prosthesis side due to persistent or recurrent infection
Escudero	2020	Europe	no admissions due to sepsis arising from the affected joint; no progression to further surgery or death from related causes
Sandiford	2020	Europe	appearance or persistence of a fistula, the need for debridement or replacement of the prosthesis due to persistence of the infection or the presence of uncontrolled symptoms. OR PJI related death
Goutelle	2021	Europe	Not reported
Ferry	2021	Europe	the presence of clinical signs suggestive of uncontrolled infection and the need for a new surgical procedure.
Lensen	2021	Europe	Failure of: retention of the implant during follow-up. Secondary end points consisted of failure of: the prevention of prosthetic loosening in initially fixed implants, the need for surgical debridement during follow-up, closing of the sinus tract, resolution of pain, the development of bacteremia, the resolution of inflammation and anaemia, and side ffects when treated with SAT
Kherabi	2022	Europe	Reinfection
Huotari	2023	Europe	No removal of the implant, no infection-related death, or active infection at the end of follow-up
Ceccarelli	2023	Europe	severe joint pain, warmth, redness, tenderness, effusion, restricted active and passive motion, and presence of new fistula or local dehiscence or decubitus. Fever and signs of sepsis were considered indicators of possible systemic spread through bacteremia. Additionally, a new positive result of the LS was considered a sign of failure
Hanssen	2024	Europe	the appearance or persistence of a fistula, unplanned surgical intervention or admission for IV antibiotics, increasing the low-dosage SAT to standard dosage, restart of antimicrobial treatment after stopping SAT, uncontrolled symptoms, or death related to the infection
Lafon	2024	Europe	Not reported
Dos Santos	2025	Europe	(i) sinus tract and/or discharge, and signs of PJI recurrence, (ii) further surgical intervention for persistent or perioperative infection, (iii PJI-related death within 3 months

Supplementary Table 4. Studies on SAT that reported an outcome of SAT (n=40)

author	year	region	N	N acute	N chronic	% DAIR	duration SAT (months)	follow-up (months)	Success rate (%)
Goulet	1988	US	19	2	17	58	48 (mean)	48 (mean)	63
Brandt	1996	US	18	n.a.	n.a.	100	n.a.	78 (median)	39
Segreti	1998	US	18	8	10	100	49 (mean)	n.a.	83
Siquera	2015	US	92	n.a.	n.a.	59	64 (mean)	69 (mean)	65
Bryan	2017	US	69	69	0	100	72 (mean)	72 (mean)	97
Bene	2018	US	76	76	0	100	12 (mean)	42 (mean)	72
Bene	2018	US	26	26	0	100	20 (mean)	49 (mean)	92
Weston	2018	US	129	129	0	100	n.a.	60 (mean)	66
Vahedi	2019	US	24	24	0	100	n.a.	46 (mean)	71
Valencia	2019	US	11	n.a.	n.a.	0	36 (median)	31 (median)	91
Shah	2020	US	51	17	34	100	28 (median)		69
Barry	2021	US	56	41	15	100	n.a.	37 (median)	63
Kildow	2021	US	35	26	9	100	16 (mean)	17(mean)	80
Burr	2022	US	45	0	45	0	50 (median)	50 (median)	67
Tai	2022	US	227	170	57	100	25 (median)	48 (median)	78
Salmons	2023	US	40	40	0	100	84 (mean)	84 (mean)	68
Chao	2024	US	35	35	0	100	12	36	61
Furukawa	2024	US	90	63	27	100	6 (median)	27 (median)	89
Nandi	2024	US	115	115	0	100	11 (median)	33 (mean)	77
Tai	2024	US	167	167	0	100	n.a.	27 (median)	77
Byren	2009	Europe	112	93	19	100	18 (mean)	28 (mean)	82
Prendki	2014	Europe	38	15	23	18	24 (median)	24 (median)	84
Prendki	2017	Europe	136	n.a.	n.a.	58	6 (median)	6 (median)	93

Supplementary Table 4. Studies on SAT that reported an outcome of SAT (n=40) *(Continued)*

author	year	region	N	N acute	N chronic	% DAIR	duration SAT (months)	follow-up (months)	Success rate (%)
Wouthuyzen	2017	Europe	21	n.a.	n.a.	29	21 (median)	21 (median)	67
Pradier	2018	Europe	78	n.a.	n.a.	76	22 (mean)	34 (mean)	78
Leijtens	2019	Europe	23	0	23	44	38 (mean)	33 (median	57
Escudero	2020	Europe	302	82	220	56	36,5(median)	37 (median)	59
Sandiford	2020	Europe	24	n.a.	n.a.	65	37 (mean)	38 (mean)	83
Goutelle	2021	Europe	10	0	10	n.a.	34 (median	34 (median)	80
Ferry	2021	Europe	16	0	16	81	6 (median)	8 (median)	75
Lensen	2021	Europe	63	0	63	0	54 (mean)	54 (mean)	79
Kherabi	2022	Europe	31	n.a.	n.a.	0	13	13	84
Ceccarelli	2023	Europe	11	0	11	100	21 (median)	n.a.	64
Huotari	2023	Europe	22	22	0	100	n.a.	n.a.	100
Hanssen	2024	Europe	67	28	39	79	20 (median)	22 (median)	60
Dos Santos	2025	Europe	30	13	17	43	42 (median)	48 (median)	73

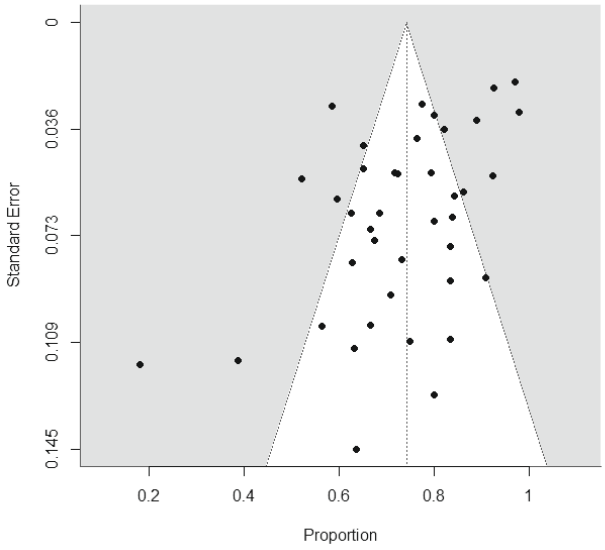
Supplementary Table 5. Studies Comparing SAT versus No SAT in Patients with PJI Treated with DAIR (n=8)

author	year	region	N SAT	% acute PJI, SAT	% DAIR	N no SAT	% acute PJI, no SAT	% DAIR, no SAT	Success rate SAT (%)	Succes rate, no SAT (%)	P
Brandt	1996	US	18	n.a.	100	15	n.a.	100	39	33	0.79
Siquera	2015	US	54	n.a.	100	152	n.a.	100	65	30	<0.01
Bryan	2017	US	69	100	100	9	100	100	97	89	0.3
Shah	2020	US	51	n.a.	100	57	n.a.	100	69	39	0.009
Chao	2024	US	35	100	100	39	100	100	65[a]	38[a]	0.02
Tai	2024	US	167	100	100	343	100	100	77	92	0.27
Huotari	2023	Europe	22	100	100	61	100	100	100	74	n.a.
Dos Santos	2025	Europe	30	43	43	33	24	24	73	42	0.02

[a]Survival probability at 24 months

Supplementary Table 6. Studies on SAT that reported a definition of SAT

Author	year	region	Reported definition
Brandt	1996	US	oral antimicrobial therapy of indefinite duration following the completion of iv antimicrobial therapy
Marculescu	2006	US	Orally administered antimicrobial therapy of indefinite duration received after completion of intravenous antimicrobial therapy
Koeppe	2008	US	use of oral antibiotics for the prevention of relapse, rather than the treatment of the underlying infection. It is assumed in these patients that the prosthesis remains infected, and oral antibiotics are given indefinitely to keep the symptoms under control but not cure the infection.
Siquera	2015	US	treatment with oral antibiotics for a minimum of six months following the initial course of intravenous antibiotics.
Shah	2020	US	any antibiotics that were provided beyond 6 weeks after DAIR
Burr	2022	US	chronic control clinical symptoms rather than to cure infection.
Chao	2024	US	Extended antibiotic therapy included any oral antibiotics that were provided beyond 6 weeks for one year after the initial DAIR procedure.
Tai	2024	US	antibiotic therapy after 12 weeks of therapy
Furukawa	2024	US	oral antibiotics given after completion of IV therapy.
Prendki	2014	Europe	an oral antibiotic therapy prescribed for a duration longer than a curative treatment
Prendki	2017	Europe	an antimicrobial therapy with a lifelong planned duration, even if it could be secondarily discontinued by the physician in charge of the patient.
Wouthuyzen	2017	Europe	antibiotic treatment that was started after the standard 3 months of 'regular' antibiotic treatment (in most cases 2 weeks of intravenous therapy and 10 weeks of oral therapy)
Pradier	2018	Europe	oral antibiotic therapy following curative therapy
Leijtens	2019	Europe	oral antibiotic therapy without an end date, started with the intention to control the infection where curative treatment seems unachievable
Escudero-Sanchez	2020	Europe	indefinite administration of antibiotics with a non-curative intention, in the context of either a PJI for which cure would require complete removal of the implant (as occurs for late chronic infections) or an acute infection for which conservative treatment such as DAIR has failed.
Sandiford	2020	Europe	oral antibiotic therapy continuing beyond 12 weeks with an intention to continue lifelong as documented at the time of starting therapy.
Ferry	2021	Europe	indefinite administration of antibiotics without curative intention in the context of a chronic infection that would normally require implant removal;
Lensen	2021	Europe	a period of >6 months of oral antibiotic therapy.
Ceccarelli	2023	Europe	a strategy based on a suppressive antibiotic treatment in which the administration of antibiotics occur in the long term or indefinitely over time with the aim of reducing symptoms and delaying or preventing the progression of PJI in cases not eligibile for standard surgical treatment
Hanssen	2024	Europe	prolonged oral antimicrobial therapy after the initial standard treatment of 6 to 12 weeks.



Supplementary Figure 1. Funnel plot assessing publication bias among the included studies

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