Review

Suppressive Antibiotic Therapy in Prosthetic Joint Infections: A Contemporary Overview

Hejer Harrabi *, Eloïse Meyer, Nathalie Dournon, Frédérique Bouchand, Christel Mamona, Véronique Perronne, Karim Jaffal, Emma d'Anglejan Chatillon, Aurélien Dinh *

Posted Date: 14 February 2025

doi: 10.20944/preprints202502.1139.v1

Keywords: bone and joint infection; suppressive antibiotic treatment; mobility; mortality; dalbavancin

Review

Suppressive Antibiotic Therapy in Prosthetic Joint Infections: A Contemporary Overview

Hajer Harrabi, Eloïse Meyer, Nathalie Dournon, Frédérique Bouchand, Christel Mamona Kilu, Véronique Perronne, Karim Jaffal, Emma d'Anglejan and Aurélien Dinh *

Infectious Disease department, University Hospital R. Poincaré, Garches, APHP, Versailles Paris Saclay University

* Correspondence: aurelien.dinh@aphp.fr; Tel.: + 33 1 47 10 77 67

Abstract: The management of prosthetic joint infections (PJIs) poses significant challenges, requiring a multidisciplinary approach involving surgical, microbiological, and pharmacological expertise. Suppressive antibiotic therapy (SAT) has emerged as a viable option in cases where curative interventions are deemed unfeasible. This review provides an updated synthesis of recent evidence on SAT, including its indications, efficacy, practical considerations, and associated challenges. We aim to highlight the nuances of this therapeutic approach, discuss the factors influencing its success, and propose future directions for research to optimize patient outcomes.

Keywords: bone and joint infection; suppressive antibiotic treatment; mobility; mortality; dalbavancin

1. Introduction

The management of prosthetic joint infections (PJIs) is a complex process that requires the integration of surgical, microbiological, and pharmacological considerations, all of which must be tailored to each individual patient to achieve the best possible outcome.

The primary objective in treating PJIs is to eradicate the infection while preserving or restoring joint functionality. While surgical options such as debridement, antibiotics, and implant retention (DAIR), or one- and two-stage revisions, remain mainstays, some clinical scenarios contraindicate their use [1,2].

Indeed, in some cases, curative treatment of the infection may not be feasible, while in others, the likelihood of surgical success is deemed very low. As a result, the prolonged use of antibiotics to suppress the infection's progression becomes a valuable option. This strategy is called suppressive antibiotic therapy (SAT) [3,4].

Historically, SAT for PJI has been linked to poor outcomes. However, success rates over the past decade have varied between 60% and 93% [4]. Suppressive antibiotic therapy has gained traction as a strategy to control infection and alleviate symptoms when curative surgery is impractical or has a high likelihood of failure. The prolonged use of antimicrobials to suppress infection without achieving eradication represents a paradigm shift in PJI management [5].

2. Concept and Definition of SAT

SAT entails long-term or indefinite administration of antibiotics aimed at mitigating symptoms and delaying disease progression. It is typically employed when surgical intervention is not feasible due to patient-related factors or when curative strategies have limited success potential [1]. In the area of PJI, SAT is considered a "noncurative" strategy [3]. A significant challenge in treating infections associated with prosthetic materials is the ability of many bacteria to form biofilms. These bacterial biofilms are microscopic matrices that adhere to both living tissue and prosthetic surfaces [4,6], often forming rapidly after infection. This impairs achieving a complete cure, as these biofilms protect bacteria from both antimicrobial agents and the host immune system [7]. Bacteria in biofilms

 doi:10.20944/preprints202502.1139.v1

on prosthetic materials can evade detection by standard microscopy and culture techniques [4]. Biofilms necessitate suppressive strategies to manage persistent infections and prevent their escalation [6,8].

However, there is no global consensus on what constitutes SAT, with definitions varying significantly across studies and clinical settings. In most European publications, SAT refers to lifelong antibiotic treatment for 'incurable infections,' typically in patients who receive suboptimal or no surgical intervention [9]. Conversely, studies from the United States primarily use the term SAT to describe extended antibiotic treatment following DAIR. These two concepts of SAT represent distinct treatment strategies with differing goals and durations:

1. Fixed-term SAT: Prolonged antimicrobial therapy for a defined duration of 6–24 months, with the primary aim of curing the infection.
2. Indefinite SAT: Antimicrobial therapy for an undetermined duration, intended to prevent relapse.

In both approaches, SAT is initiated after the infection has been clinically controlled in accordance with standard treatments outlined by national, international, or local guidelines [9]. This variability complicates efforts to standardize treatment and assess outcomes effectively.

3. Indications for SAT, Dosage, Duration

3.1. Indications

SAT is primarily indicated in:

- **Acute PJIs:** Particularly when DAIR fails or has limited likelihood of success [10].
- **Chronic PJIs:** Where resection arthroplasty or revision surgery is not an option due to high surgical risk, short life expectancy, or other contraindications [11].
- **Failed prior treatments:** Cases involving recurrent infection or unsuccessful curative attempts [12].

Despite limited literature supporting its utility, SAT is frequently employed following DAIR in clinical practice, even by experienced Orthopedic Infectious Diseases specialists. Decisions to initiate and continue SAT should be guided by a comprehensive risk-benefit assessment that considers multiple factors. These include the perceived risk of failure based on patient and infection characteristics known to predict treatment outcomes, the feasibility of further surgical intervention given anatomic and implant conditions, the patient's willingness to undergo additional surgery if necessary, and the potential adverse effects of prolonged antimicrobial therapy [13].

Interestingly, regional practices vary widely. An online survey investigating clinicians' approaches to SAT for PJI revealed that North American physicians are significantly more likely to prescribe SAT for acute PJIs following DAIR compared to their European counterparts (38% versus 6%) [9]. For patients with PJI not managed surgically, the majority of respondents in this study indicated that SAT is appropriate, provided the patient does not have a fistula. The host risk factors for failure that were considered indications for initiating SAT in acute PJI treated with DAIR were frail patients, megaprothesis, chemotherapy, no change of modular components during surgery, poor soft tissue, immunosuppressive drugs, a second debridement less than 3 weeks after DAIR, rheumatoid arthritis and no use of rifampicin in staphylococcal PJI. The top five microbiological factors cited as indications for SAT were: Infection with *Candida species*, *Pseudomonas species*, rifampicin-resistant *Staphylococci,* methicillin-resistant *Staphylococcus aureus* (MRSA) and Enterococci [9].

In a recent review published by Cortes-Penfield *et al*., the authors propose risk–benefit stratification criteria to guide the use of SAT following DAIR for PJI.

- Indications Strongly Supporting SAT: SAT is recommended when surgical revision is not an option, as recurrent infection would require amputation, arthrodesis, or complex wound

 doi:10.20944/preprints202502.1139.v1

reconstruction (a). It is also favored in cases of recurrent PJI or previous treatment failure (b). Infections caused by difficult-to-treat pathogens (S. aureus, P. aeruginosa, Candida) have higher recurrence risks, justifying prolonged suppression (a, b). Additionally, severe immunosuppression (solid organ/stem cell transplant, chemotherapy, chronic steroids, TNF inhibitors, advanced HIV) increases the likelihood of treatment failure, making SAT beneficial (a). Patients who underwent arthroscopic DAIR or retained the polyethylene liner are also at higher risk of relapse and may benefit from SAT (b).

- Situations Where SAT May Be Considered: Major comorbidities (cirrhosis, ESRD, heart failure) contribute to poor outcomes, supporting SAT in select cases (b). Older patients (>75 years) or those with limited life expectancy (<10 years) may also benefit (a, b). Late hematogenous infections (>2 years post-arthroplasty) with active bacteremia and gram-negative infections untreatable with fluoroquinolones are additional considerations (b). SAT may also be appropriate when patients prioritize infection suppression over surgical revision (a).
- Factors Suggesting Limited Benefit of SAT: SAT is unlikely to benefit patients who have completed six weeks of rifampin for monomicrobial coagulase-negative Staphylococcus PJIs (b), or those who have received a full fluoroquinolone-based regimen for gram-negative infections (b). Culture-negative PJIs, where targeted suppression is impossible, also do not typically warrant SAT (b).

These criteria are based on the limited literature reviewed and reflect their consensus practice [13]. They are designed to support decision-making by considering the patient's individual risk of recurrent infection, the potential consequences of treatment failure, and their values and preferences. They recommend that SAT is most appropriate for patients at the highest risk of failure (e.g., those with limited surgical source control, recurrent PJI, and/or difficult-to-treat pathogens) and for those where further failure could result in catastrophic functional outcomes due to limited surgical alternatives [13]. Currently, there are no specific recommendations for SAT use in guidelines.

3.2. Antibiotic Dose in SAT

IDSA recommendations for lower doses of some antimicrobials are primarily based on expert opinion, as studies specifically evaluating SAT dosing remain limited [14]. While many physicians worldwide commonly use relatively low antibiotic doses for SAT, there is currently only one retrospective study addressing this approach [15]. This study compared patients with orthopedic implant infections treated with low-dose versus normal-dose SAT, after an initial standard treatment of 1 to 2 weeks of intravenous antibiotics followed by 4 to 11 weeks of targeted oral antimicrobial therapy (for a total duration of 6 to 12 weeks) [15]. Low dose SAT following initial treatment varied depending on antibiotics, but was approximately half of standard dose.

No significant difference in failure free survival between patients on low-dose SAT and those on standard-dose SAT was observed. Lower dose did not seem to reduce side effects. Additional research is needed to better understand the efficacy of low-dose SAT and its potential impact on the development of antimicrobial resistance.

3.3. Duration

Once SAT is initiated, the decision to continue or discontinue therapy should be regularly reevaluated [13]. Although earlier studies did not define a point beyond which SAT ceases to delay or prevent infection, two recent retrospective cohort studies found no difference in treatment failure rates between PJI patients receiving 1 year of oral antimicrobial suppression versus those receiving longer durations following DAIR [16,17]. This indicates that the majority of SAT's benefit likely occurs within the initial months, and a defined-duration approach may be as effective as lifelong SAT [16,17].

 doi:10.20944/preprints202502.1139.v1

Rather than considering SAT as a lifelong commitment, it is advisable to inform patients that its continuation will be reassessed after 1 year, with discontinuation being a reasonable option for most individuals at that point [13]. Regular monitoring of SAT should be maintained through outpatient visits, typically annual or biannual after an initial phase of closer follow-up. These visits should include symptom evaluation and laboratory testing to detect potential adverse reactions to antibiotics or signs of relapse or reinfection [13].

The heterogeneity of patient populations between studies makes it difficult to provide recommendations for clinical practice. There are currently no definitive guidelines to determine a clinically relevant stopping point, nor a biomarker that may indicate to stop safely SAT. Some authors have also suggested radiolabeled leukocyte scintigraphy as possible methods for monitoring response to SAT but this strategy need to be confirmed in larger studies [18].

4. Efficacy of SAT

4.1. Does SAT Work?

Evidence supporting SAT remains heterogeneous and predominantly observational. Studies indicate variable success rates ranging from 23% to 84%, depending on the criteria used to define efficacy [19,20]. For patients treated with DAIR, SAT has been associated with reduced odds of treatment failure, with one meta-analysis reporting a 4-fold reduction in recurrence risk [20].

Recent large cohort studies have demonstrated success rates of approximately 58% to 75% within 2 years of SAT initiation, dropping to around 50% at 5 years, indicating its potential for long-term infection control [21]. The variability in outcomes highlights the importance of tailoring SAT protocols to individual patient needs and infection profiles. Notably, patients in settings with robust multidisciplinary teams (MDTs) may experience better outcomes due to coordinated care and comprehensive follow-up [13].

Interpreting the efficacy of SAT is challenging for several reasons: the lack of controlled studies, the inclusion of patients with acute infections who may be cured by DAIR alone, and inconsistencies in the criteria used to evaluate efficacy across published studies summarized in Table 2. For instance, some authors defined success as avoiding surgery, even if the infection was not fully controlled [5], whereas others also required symptom control as part of their efficacy criteria [12,20,22,23]. Reported success rates ranged from 23% to 84%, but the studies with the highest success rates predominantly included patients with early PJI [12,20,23], many of whom might have achieved similar outcomes with significantly shorter treatment durations.

4.2. Predictors of Success and Failure

Factors influencing SAT outcomes include:

- **Pathogen type:** Gram-positive organisms (enterococci), especially *Staphylococcus aureus*, *Candida* spp, *Pseudomonas aerugionsa* are associated with higher failure rates [24].
- **Biofilm formation:** Infections involving biofilm-associated organisms are less likely to respond to SAT [25].
- **Patient demographics:** Advanced age and severe comorbidities such as cirrhosis or chronic kidney disease increase the likelihood of SAT failure [26].
- **Regional variability:** Practices differ significantly, with variations in antimicrobial selection, dosing, and duration reflecting differences in regional guidelines and microbial resistance patterns [13].

Failures are often due to antibiotic-resistant organisms, inadequate adherence to prescribed regimens, or the emergence of unsuspected pathogens. Incorporating biomarkers like C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) into monitoring protocols can aid in assessing treatment response and identifying early signs of relapse [27].

 doi:10.20944/preprints202502.1139.v1

Few studies have evaluated the factors associated with SAT failure. However, failure rates appear to be higher in patients with a sinus tract and in those with infections caused by *S. aureus* [19,20,27].

In a multicenter study published by Escudero-Sanchez *et al.*, predictors of failure were analyzed, with failure defined as either persistent, uncontrolled symptoms of PJI (including a sinus tract) or the need for additional surgery (such as debridement or prosthesis removal) due to infection [28]. A multivariate analysis identified the following factors as being associated with SAT failure:

- Infection etiology other than Gram-positive cocci (e.g., Gram-negative rods, fungi, or negative cultures): This may be due to the limited availability of orally active antimicrobials for Gram-negative bacilli.
- Prosthesis located in the upper limbs: Although this finding is difficult to explain, it may be influenced by the relatively small number of upper-limb PJI cases.
- Age under 70 years: This seemingly paradoxical finding might reflect that younger patients managed with SAT are more likely to be immunosuppressed or have "tumoral" prostheses, which are associated with a worse prognosis [25].

At present, there are no definitive predictors of SAT failure. Therefore, SAT should not be excluded as a treatment option for patients who meet the appropriate conditions despite the factors mentioned above [3].

5. Practical Considerations

5.1. Is Debridement Necessary?

While debridement reduces bacterial load and provides microbiological samples, its necessity prior to SAT initiation is debated. Retrospective studies indicate that SAT can succeed even without debridement in patients with stable symptoms [29]. However, surgical intervention is recommended to optimize infection control when feasible [30].

5.2. Optimal Antibiotic Regimens

Selection of antibiotics for SAT prioritizes oral bioavailability, tolerability, and efficacy against causative pathogens. Common regimens include monotherapy with beta-lactams, tetracyclines, or combinations involving rifampin [31]. Long-acting agents like dalbavancin have emerged as promising options for patients with limited compliance [32].

Tetracyclines and cotrimoxazole are particularly favored for their tolerability and low risk of resistance development. However, care should be taken when selecting antibiotics for polymicrobial infections or gram-negative pathogens, as these cases often require combination therapy [33].

Dalbavancin is a broad-spectrum lipoglycopeptide effective against Gram-positive infections, including MRSA. Due to its spectrum, prolonged action, and favorable tolerability, dalbavancin appears promising for suppressive antibiotic as reported in a pilot study [34].

5.3. Role of Initial Intravenous Therapy

Although initial intravenous therapy is commonly employed, its necessity remains unclear. Clinical guidelines recommend at least 6 weeks of intravenous antibiotics for severe cases before transitioning to oral SAT [35]. Evidence suggests that shorter intravenous durations may be sufficient for stable infections, provided oral alternatives are effective and well-tolerated [36].

5.4. Treatment Interruptions

Antibiotic-free intervals are generally discouraged due to high failure rates associated with treatment discontinuation, particularly within the first four months [37]. Long-term suppressive regimens ensure continuous bacterial suppression and reduce the risk of relapse. However,

 doi:10.20944/preprints202502.1139.v1

intermittent SAT strategies may be considered for patients experiencing significant side effects or adherence challenges [38].

6. Safety and Adverse Events

Prolonged antibiotic use carries risks, including gastrointestinal disturbances, skin reactions, and nephrotoxicity. Notably, *Clostridioides difficile* infections and antimicrobial resistance have been documented, necessitating careful monitoring [35]. Adverse events are reported in up to 41% of SAT patients but rarely lead to discontinuation [27].

In a multicenter cohort study, SAT was discontinued due to adverse events in only 5.6% of patients, demonstrating its overall safety when carefully managed [39]. Nevertheless, the emergence of resistant pathogens underscores the need for antimicrobial stewardship and periodic reassessment of treatment efficacy.

Emerging concerns include the potential for microbiome disruption and its long-term implications. Future research should explore strategies to mitigate these risks while preserving SAT efficacy [28].

7. Conclusions and Future Directions

SAT represents a viable, albeit non-curative, option for managing complex PJIs. It has shown promise in extending infection-free intervals and improving quality of life for patients ineligible for surgical interventions. However, its long-term benefits must be weighed against risks such as antimicrobial resistance and adverse events [40].

The global heterogeneity in SAT practices underscores the need for standardization. Future research should prioritize defining optimal indications, antimicrobial regimens, and monitoring protocols. Large-scale randomized controlled trials and international collaborations will be instrumental in addressing these gaps [13].

Table 2. Published Series on SAT in PJI.

Author (Ref) Methods	Type of Infection	Indication	Previous surgical treatment	Bacteria Major strains isolated	Suppressive antibiotics (N patients)	Duration Mean (Mo)	Follow up Mean (Mo)	Success criteria	Success rate (%)	Side effects	Outcome	Conclusion
Johnson and Bannister (1986) [41] Retrospective 25 cases SAT 9 cases	56% acute 44% chronic	-Patients who are too infirm for surgery and have limited life expectancy	Excision of sinus tract, debridement, exchange arthroplasty	*S. aureus* (52%), CoNS (28%), *Streptococ-cus spp*. (20%)	No data	15.6 (1.2-59)	15.6 (1.2-59)	Resolution of the pain and discharge	8	No data	Handicap by their knee: 9/9 intermittent discharge from the knee 7/9 Painful knees 5/9 A mean fixed flexion deformity of knees 9/9	SAT very rarely eradicate deep infection in a cemented prosthesis
Goulet *et al*. (1988) [5] Retrospective (1972-1982) 19 cases	90% chronic 10% acute	-Infection that had not yet become well-established 3/19 -Surgery risk 4/19 -Patient decision 4/19 -Strain sensitive to ATB with good initial result -Multifactorial 4/19	DAIR (11/19; 57.9%)	*S. aureus* (21%), CoNS (21%), *Streptococcus spp*. (32%)	Penicillin 8 Ampicillin 5 Cefazolin 4 Gentamicin 3 Oxacillin/Dicloxacillin 3 Clindamycin 1 Erythromycin: 1	-14 patients (73.7%): without a planned endpoint -4 patients (21%) 39 (12-104) -1 patient (5.3%): 6	49.2 (24-120)	Retention of the implant	63.2	no antibiotic-related morbidity	-No deterioration (9/19; 47.7%) -Failure (7/19, 36.7%) with progressive hip sepsis in 5 cases of them (5/7) -Increasing symptoms without prosthesis removal (3/19, 15.6%)	-SAT is indicated in old, frail patients -SAT may also be considered for an otherwise compliant patient who refuses removal of an infected prosthesis
Tsukayama *et al.* (1991) [21] Retrospective 13 cases	100% chronic	No data	DAIR	*S. aureus*, (54%), CoNS (46%)	No data	No data	37.2 (24 -55)	Retention of the implant	23	38% antibiotic needed to be changed	-Success: Implant retention (3/13, 33%) -Failure (10/13, 67%) recurrent infection with prosthesis removal	-SAT has limited clinical efficacy -SAT is associated with a substantial risk of adverse effects
Segreti *et al*. (1998) [23] Retrospective (1986-1992) 18 cases	50% chronic 50% acute	No data	DAIR in all cases	*S. aureus* (44%), CoNS (44%)	Minocycline 5 Dicloxa/Oxa 5 Penicillin 2 Ampicillin 1 TMP/SMX 1 Other ATB: 4	48.9 (4-103)	48.9 (4-103)	Remained asymptomatic and functional prosthesis	83.3	4; 22% -CDI: 4/4 -Drug rush: 2/4 No discontinuation	-Success (15/18; 83.3%) -Clinical failure (3/18; 16.7 %), 1 with prosthesis removal -ATB discontinuation (7/18; 38.9%: *failure 3/18 *4 patient decisions without relapse after a follow-up (36–86 months later)	SAT is a reasonable alternative to surgery in selected patients with infected orthopedic prostheses
Rao *et al*. (2003) [20] Retrospective 36 cases (1995-2001)	53% chronic 47% acute	-Patient decision -Poor general condition and a stable functioning prosthesis	DAIR in all cases	*S. aureus* (26%), CoNS (50%)	Minocycline/ Rifampin: 11 Levofloxacin: 5 Cephalexin: 4 Dicloxacillin: 3 Sulfamethoxazole/Trimethoprim: 2	52.6 (6–128)	60 (16-128)	Remained asymptomatic and functional prosthesis	86.2	Diarrhea (3/36; 8%)	-Failure (5/36; 13.8%): *Chronic sinus drainage 1/5 *Painful, loose prostheses 4/5	-The ideal regimen and optimal duration of oral SAT is not well-established - Prospective studies are needed

doi:10.20944/preprints202502.1139.v1

					Minocycline:2 Oxacillin:2 Penicillin: 2 Clindamycin:1 Amoxicillin/Doxycycline: 1 Fluconazole: 1 Linezolid: 1					-Death: 1/5 unrelated death	
Marculescu *et al.* (2006) [19] Retrospective (1995–1999) 99 episodes in 91 patients	No data	-Conservative surgical approach (55; 56%) -None of the prostheses were found to be loosen intraoperatively (47; 48%) -An exchange of the modular polyethylene parts was performed in addition to debridement	-DAIR in all cases -A median of 1 surgical debridement per patient (range, 1–4 debridement)	*S. aureus* (32%), CoNS (23%)	Oral b-lactam antibiotics 53% (penicillins in 17 episodes and cephalosporins in 36 episodes) -Minocycline 7% - Trimethoprim-sulfamethoxazole 10% -Quinolones: 8%	23.3 (0.33–92.6) 0.03 Mo =1 day	23.3 (0.16-89.1)	Absence of the following: Relapse, reinfection, presence of acute inflammation in the periprosthetic tissue or at any subsequent surgery on the joint, development of a sinus tract, death from prosthesis-related infection, or indeterminate clinical failure	57	-Delayed hypersensitivity reaction (11, 11%) (1%) -Diarrhea (3; 3%) -CDI (1;1%) Leukopenia (vancomycin) (1; 1%) Nephrotoxicity (vancomycin) (1;1%) Skin discoloration (minocycline) (1;1%)	Failure (53 %) -Indeterminate clinical failure: 7 -Relapse of Infection due to the same microorganism:19 -Reinfection: 22 episodes -Acute inflammation: 2 -Death related to PJI: 3	-The role of a sinus tract and duration of symptoms are important to predict the success of debridement and retention of prosthesis -Future clinical trial studies
Byren *et al.* (2009) [12] Retrospective 112 cases (1998-2003)	31% chronic 69% acute	No data	-Open debridement (97; 87% -Arthroscopic washout (15; 13%) -Multiple procedures (24; 21%)	*S. aureus* (40%), CoNS (23%)	FQ/RFP combinations of doxycycline, fusidic acid, rifampicin, clindamycin or amoxicillin	12 months at least	27.6	Absence of the following: Recurrence, wound or sinus drainage recurring or persisting for 3 months beyond the index debridement procedure or requirement for revision surgery (irrespective of the indication)	82	No data	Treatment failures (18%) during a mean follow-up of 2.3 years 89%, 81% and 78% of joints had not failed at 1, 2 and 3 years, respectively	The length of duration of antibiotic prescribing beyond 6 months is not critical to the outcome - Prospective controlled trials
Prendki *et al.* (2014) [8] Retrospective (2004-2011) 38 cases	61% chronic 39% acute	-Very high operative risk (20; 52.6%) -Very complex surgical intervention (9; 23.7%) -Patient refusal (9; 23.7%)	(9; 23.7%) -Synovectomy 6/9 -- Abscess drainage 3/9 -Partial exchange 1 - Excision of fistula 1	*S. aureus* (39%), *Streptococcus spp.* (18%), GNB (17%)	Amoxicillin (8), amoxicillin–clavulanate (1), cloxacillin (4), clindamycin (7), co-trimoxazole (1), fusidic acid (5), minocycline (1), levofloxacin (1), peflacin (2), and rifampin (13)	59 (15–90)	24 (6–98)	Absence of the following: Persisting infection, relapse, new infection, treatment discontinuation because of severe adverse events, or related or unrelated death	60	1 case of recurrent CDI	-Event-free at 24 months (23. 60.5%) -Failure (6; 15.7%): *Persisting infection: 1, *relapses 3, *related death 1, * treatment discontinuation: 1 -Unrelated deaths (9; 23.6%)	SAT is an alternative therapy in elderly patients with PJI when surgery is contraindicated
Siqueira *et al.* (2015) [24] Retrospective (1996 to 2010) 92 cases	61% chronic 39% acute	-A history of multiple joint infections, -Previous failed surgery for PJI, -Retained implants and/or -Immunosup	All cases -Irrigation and debridement with polyethylene exchange (54; 58.8%), -2-stage revision (38; 41.2%)	*S. aureus* (48%), CoNS (35%)	Dicloxacillin (13) Doxycycline (29) Cephalexin (8) Trimethoprim/sulfamethoxazole (12) Amoxicillin (6) Clindamycin 300 mg bid (4) RFP (2) FQ (2) Other ATB	63.5 ± 38.3 (6-165.1)	69.1 ± 38.2 (2.2 - 168.3)	Absence of the following: Subsequent surgical intervention for infection after the index procedure, persistent sinus tract, drainage, or	68.5	No data	34.8% Subsequent surgical intervention for infection after the index procedure persistent fistula, drainage, or joint pain at the last follow-up	Chronic suppression with oral antibiotics increased the infection-free prosthetic survival rate following surgical treatment

doi:10.20944/preprints202502.1139.v1

		pression					joint pain at the last follow-up visit, or death related to the PJI			visit; or death related to the periprosthetic joint infection.	
Prendki *et al.* (2017) [37] Retrospective cohort 21	No data	Palliative intent in all cases	No data	*S. aureus* (62%), CoNS (21%)	-Monotherapy clindamycin (5/21), beta-lactams (4/21), co-trimoxazole (4/21), pristinamycin (4/21), and fluoroquinolones (4/ 21) -Dual therapy: (4/21) fluoroquinolone + rifampicin, fluoroquinolone + clindamycin, co-trimoxazole + fusidic acid, and amoxicillin + clindamycin.	12.7 (1.3-56.5)	Over follow-up 17.3 (1.3–56.6) Follow-up under SAT 9.2 (1.3-56.5)	Absence of the following: Local or systemic progression of the infection, death, or discontinuation because an adverse drug reaction	66	Adverse drug reaction 1/21	-Death unrelated to PJI (2; 9.5%) -- Discontinuation or switch of SAT (1; 4.8%) -Local worsening (2; 9.5%) -Systemic progression of inflammation (3; 14.3%)	SAT appeared to be an effective and safe option in this cohort
Pradier *et al.* (2017) [11] Retrospective cohort (2006-2014) 39 cases	61% delayed or late 39% acute	-Suboptimal surgery or curative antibiotic therapy (26; 66.6% and 6; 15.4%, respectively) -Complex orthopedic surgery (4; 10%) - Immunosup pressive status (3; 7.7%)	-DAIR (32 ;82.1%) -Implant exchange (7; 17.9%)	*S. aureus* (79%), CoNS (10%)	Doxycycline	-Mean duration 22.5 ± 20.6 (17-28) Two-year duration of SAT (13, 33.3%) A continued SAT (26; 67.7%)	24	Absence of the following: Local or systemic progression of the infection, death, or discontinuation because an adverse drug reaction	74,4	Side effects (10; 25.6%) in 6 patients (15.4%), Photosensitization (4/39), Nausea/vomiting (2/39) Cycline-induced skin problems and SAT discontinuation (2/39)	-Event-free (29; 74.4%), -Failure (10; 25.6%): * relapses 8; 20.5%, and *superinfections 2 ; 5.1% Overall, 8 out of the 10 failure cases were related to a doxycycline-susceptible pathogen.	-Oral doxycycline used as SAT in patients treated for *S. aureus* -PJI has an acceptable tolerability and effectiveness, and appears to be a reasonable option in this setting
Wouthuyzen-Bakker *et al.* (2017) [25] Retrospective (2009-2015) 21 cases	62% late or delayed 38% early	-Poor bone stock and/or severe tissue Injury (10; 48%) -A poor prognosis and/or severe comorbidity (10; 48%) -Patient decision: (2; 9.5%)	A debridement and/or lavage of the affected joint (14; 67%)	*S. aureus* (33%), CoNS (38%)	Clindamycin (83%) minocycline (67%) Amoxicillin 4/21 19% Amoxicillin/acide clavulanique 2*21 (9.5%) Moxifloxacine 2/21 (9.5%)	No data	21 (3-81).	Absence of the following: Pain during follow-up, surgical intervention is needed to control the infection, or death related to PJI	67	10; 43% reported side effects and needed change or adjustment of SAT	Failure (7; 33%) was due to persistent joint pain (n=1), surgical intervention because of an uncontrolled infection (n=3), Death related to the infection (n=3).	SAT is a reasonable alternative treatment option in a subgroup of patients with a PJI who are no candidate for revision surgery, in particular in patients with a 'standard' prosthesis and/or CoNS as the causative micro-organism
Pradier *et al.* (2018) [26] Retrospective (2006-2014) 78 cases	60% delayed or late 40% early	-Suboptimal surgery or (Curative antibiotic therapy (48; 61.5 % and 11; 14% respectively), -Complex orthopedic surgery (11; 14%)	-DAIR 59; 75.6% -Implant exchange 19;24.4% including 1SE (10.3%) and 2SE (11.5%) -and Resection	*S. aureus* (40%), CoNS (32%)	Doxycycline (72; 93.6%) Minocycline 6; 6.7%)	22.2 ± 17.9	34 ± 19.9	Absence of the following: Signs of infection assessed ≥24 months after the end of the curative treatment and then at the last contact with the patient, or	71.8	14; 18%) leading to SAT discontinuation in 6 cases of them (8%)	Failure (22; 28.2%) In 3 cases of them (3.8%) documented acquisition of tetracycline resistance in initial pathogen(s).	Oral cyclins used as SAT in patients treated for PJI have an acceptable tolerability and effectiveness a reasonable option

doi:10.20944/preprints202502.1139.v1

		- Immunosuppressive status (8; 9%)	arthroplasty management (2; 2.6%)					death related to the PJI				
Weston *et al.* (2018) [38] Retrospective 134 cases	Acute 100% Acute postoperative infection 17% Acute hematogenous infection 83%	-Prosthesis salvage - Minimize morbid-ity.	DAIR 100%	*S. aureus* 29% CoNS 23%	No data	No data	60 (25.2-156)	Implant retention	66	No data	Death (45; 34%) Subsequent or recurrent infection (45; 34%) The infection involved a recurrence of the original organism 26; 57.7%) a new organism 4; 8%	The greatest risk factor for SAT failure was an infection with a staphylococcal species, followed by age of < 60 years
Pouderoux *et al.* (2019) [35] Single-center prospective cohort study (2010–18) 10 cases	Acute 7; 70% Chronic 3; 30%	Prothesis retention Ineligible for explanation (2/10)	DAIR 6; 60%	Gram negative bacilli 5; 50% Polymicrobial 4; 40% *Streptococcus spp* 1; 10%	Ertapenem 7; 70% Ceftriaxone 2; 20% Ceftazidim 1; 10%	14.4 (IQR 6.98–23.7), for a total of _6000 subcutaneous injections.	14	Implant retention	60	Skin necrosis ceftriaxone injection; non controlled epilepsy, cutaneous rash and pruritus under ertapenem hyper eosinophilia under ertapenem	Failure 1; 10% (Relapse under ertapenem) Discontinuation of SAT (3; 30% for side effects)	As salvage therapy, subcutaneous SAT delivered by gravity infusion is a safe and interesting alternative when an optimal surgical strategy is not feasible and no oral treatment is available
Leijtens *et al.* (2019) [27] Retrospective (2006-2013) 23 cases	30% early 70% late or delayed	Surgical complexity with poor bone stock and severe soft tissue injury (29%), Patient decision (13%) Poor general medical condition (21%) A combination of reasons . (38%)	20; 87.5% underwent surgery before the start of AST DAIR 13; 56.5%	*S. aureus* (2%), CoNS (61%)	Doxycycline 14; 60.8% TMP/SMX 6; 26%	38 (1–151)	33	Absence of the following: Reoperation for PJI or death related to PJI	56.5	Adverse events 6; 26.1%: gastrointestinal problems 4/6 a rash or itching 2/6	-Failure 10; 43.5% -Relapse of infection with the same micro-organism 7;29.2% -A new infection with a different micro-organism 3; 13 %	SAT an alternative treatment in selected patients with a PJI There is a persisting and considerable number of failures, particularly in PJI caused by S. aureus and in patient with an antibiotic-free period before the start of SAT
Renz *et al.* (2019) [39] Prospective cohort study (2016-2018) with a retrospective control group (2009-2015) 69 cases SAT 24 cases (35%)	Early 12; 17% Delayed 27; 39% Late 30; 43%	No data	-DAIR 27;39% -One-stage exchange in 5 ;7%, -Multi-stage exchange 31; 44% -Prosthesis removal 6; 9%	Beta-hemolytic *Streptococci spp.* 43;62% *S. viridans* group 26; 38%	Amoxicillin 22/24 doxycycline 1/24 Clindamycin 1/24	13 (0.5-111)	13 (0.5-111)	Infection-free status No subsequent surgical intervention for persistent or perioperative infection after re-implantation No PJI-related death (within 3 months)	95	Allergic skin rash under Amoxicillin 4 Switch doxycycline (n=2) and clindamycin (n=2). CDI 2 clindamycin	Failure 1; 5%	SAT was associated with higher success rate compared with no suppression (93% vs. 57%, p=0.002) SAT should be strongly considered in streptococcal PJI.

doi:10.20944/preprints202502.1139.v1

Sandiford *et al.* (2020) [7] Retrospective (2012-2017) 24 cases	No data	No data	DAIR 15; 62.5% Single-stage revision 4;16.6%, two-stage revision 4; 16.6%	*S. aureus* (25%), CoNS (21%)	Amoxicillin (no data) Doxycycline (no data) Fluconazole 1 case	No data	122.8 (15.6–68.4)	Absence of the following: Sepsis arising from the affected joint, no progression to further surgery, or death related to PJI.	83	4.2% rash 4.2% rifampicin interaction	PSAT successful 20;83% Episodes of sepsis from joint 2; 8% Progression to further surgery 2; 8% Persistent wound discharge 1; 4%	SAT is a viable option for the management of PJI with a low incidence of complications
Escudero-Sánchez *et al.* (2020) [28] Retrospective multicenter cohort (2003-2016) 302 cases	73% chronic 11% hematogenous 16% early postoperative	-Decision of the surgeon 82;27.2% -High surgical risk 80;26.5% -Advanced age 71; 23.5% -Patient's decision 70; 23.2% -Anticipation of poor functional results 69; 22.8% -Presence of minor symptoms 35; 11.6%)	Debridement with partial removal 24; 7.9%) Debridement without removal 143; 47.4% Non-surgical 132; 43.7%	*S. aureus* (31%), CoNS (33%)	Tetracyclin 39.7% TMP/SMX 35.4% Rifampicin in combination with another antibiotic 23.2%	36.5; IQR 20.75-59.25	36.5	Absence of the following: Appearance or persistence of a sinus tract, need for debridement or replacement of the prosthesis due to persistence of the infection, or the presence of uncontrolled symptoms, death related to PJI	58.6	104 adverse effects in 81;26.8%-gastrointestinal (16.9%) -Cutaneous (5.3%). SAT was suspended in only 17; 5.6%, while 46; 15.2% changed antibiotics to avoid the adverse effect. -CDI 3; 1%	-Failure 125; 41.4%: Need to remove the prosthesis 61/125 (48.8%) Presence of a fistula 31/125 (24.8%) need for debridement 19/125 (15.2%) poor symptoms control 14/125 (11.2%) -Resistance 15 of 65 (23.1%) of the microbiologically documented cases -Unrelated death to PJI 46/302 (15.2%) -Hospitalization after initiating SAT for a cause related to the PJI 92/302 (15.2%)	SAT offers acceptable results for patients with PJI when surgical treatment is not performed or when it fails to eradicate the infection
Lensen *et al.* (2020) [32] Multicenter, retrospective observational cohort study (2008-2018) 72 cases SAT 63 cases	Chronic 100%	Common practice in the participating hospital (22; 35 %) Intention to stop the drainage or close the sinus tract in (6, 9.5 %) Intention to prevent bacteremia (5;3, 8 %) A combination of the previous reasons (10; 16 %) No indication was specified (20;31.7%)	No data	Cocci G positive (70%) Gram negative bacilli (24%)	TMP/SMX 25% Fluoroquinolones 7%	No data	54.4	-Implant retention -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 when treated with SAT.	No data	27%	-Implant retention 79.4% -Sinus tract closed in SAT group 42% -Resolution of pain 35% -No bacteremic episodes were observed in SAT group	SAT is not able to fully prevent complications in patients with a draining sinus. However, it may be beneficial in a subset of patients
Ferry *et al.* (2021) [40]	Chronic 100%	Cases not eligible for further surgery	LysinDAIR	*S epidemidis*	Tedizolid in the 4 cases	>12 months	>12 months	Implant retention	50	No adverse event	Relapsing PJI: 3/4	Exebacase has the potential to be used in

doi:10.20944/preprints202502.1139.v1

Prospective 4 cases			Several previous prosthetic knee revisions without prosthesis loosening								Clinical signs of septic arthritis 2/4 (complete disappearance of clinical signs of septic arthritis>12 months) Sinus tract recurrence 2/4 (6 months	patients with staphylococci PKI during arthroscopic DAIR as salvage therapy to improve the efficacy of suppressive antibiotics and to prevent major loss of function
Burr *et al.* (2022) [42] Retrospective (2007-2020) 45 cases	Chronic 100%	Multiple comorbidities Patient decision	No data	*S. aureus* (62% 27/45) CoNS (17.7% 8/45) Gram Positive 9% (5/45)	Doxycycline 11; 24.4% Cephalexin 9; 20% TMP/SMX 7;15.5 Combination with RFP 4;9% Amoxicilline/Amox-clav : 4;9% Clindamycin 3; 7%	50	50	Avoid reoperation after SAT	67	Diarrhea (3), tooth discoloration (2) nausea (2) Acute kidney injury (2), neurotoxicity (1), hallucinations (1),	-Failure 15: 33% -Death unrelated to SAT: 3; 6.6%	SAT is a reasonable strategy in patients with PJI who lack or refuse further surgical treatment options
Ceccarelli *et al.* (2023) [43] Retrospective study 16 cases	Chronic 100%	Cases not eligible for standard surgery Severe comorbidity Significant surgical risk	DAIR in all cases	CoNS13 (82%) CoNS + *E. coli* 1 (6%) MRSA 2 (12%)	Minocyclin 100%	15 (6-30)	15 (6-30)	Absence of: severe joint pain, warmth, redness, tenderness, effusion, restricted active and passive motion, and presence of new fistula or local dehiscence or decubitus	62.5	Minocycline-induced teeth staining 1/12 Epigastric pain related to drug: 2/12	Failure with a relapse of the infection 6; 37.5%	SAT can be considered as an interesting approach in patients not suitable for standard treatments of PJI Requires careful monitoring
Tai *et al.* (2024) [44] Multicenter retrospective Europe 2005-2016 USA 2008-2018 510 patients	Acute 100% Early acute infection (367; 62%) Late acute infection (143; 38%)	No data	DAIR in all cases	*S. aureus* (38%) CoNS (29%) *Streptococcus spp* (19%) Polymicrobial (31%)	Rifampicin 282 (55%) Quinolone 221 (43%)	No data	26.7 (3-136)	No data	Overall succes rate 87.7% Succes rate SAT76.6%	No data	Overall failure 66;13% Failure under SAT (39, 23.3%)	SAT's benefits might be restricted to specific groups of patients, underscoring the need for randomized controlled trials
Lafon-Desmurs *et al.* (2024) [45] Retrospective bicentric study (2021-2023) 15 cases 12 cases of PJI	No data	Nonremovable implants (14; 93.3%) Resistance to other oral SAT (8; 53.3%) or intolerance (6; 40%), and/or to preserve the patient's quality of life (5; 33.3%).	No data	*S. aureus* (20%), CoNS (33.3%) Polymicrobial (33.3%)	Dalbavancin The median number of injections received as SAT and excluding the loading dose was 4 (IQR 2–7)	The median time between two reinjections was 1.9 (IQR 1–2.7) with a maximum of 4.7 days	9.9	No data	80%	Bronchospasm-type event during dalbavancin infusion that required discontinuation of treatment	Failure (3; 20%) Superinfection caused by microorganisms naturally resistant to dalbavancin 3/3 A superinfection with S. aureus 1/3	These results support the use of dalbavancin SAT for implant-related infections

CDI: *Clostridoides difficile* infection; CoNS: coagulase-negative staphylococci, Mo: months; IQR: interquartile, GNB: Gram negative bacilli.

doi:10.20944/preprints202502.1139.v1

 doi:10.20944/preprints202502.1139.v1

References

1. Tsang, S.-T.J.; Ting, J.; Simpson, A.H.R.W.; Gaston, P. Outcomes Following Debridement, Antibiotics and Implant Retention in the Management of Periprosthetic Infections of the Hip: A Review of Cohort Studies. *The Bone & Joint Journal* **2017**, *99-B*, 1458–1466, doi:10.1302/0301-620X.99B11.BJJ-2017-0088.R1.
2. Zimmerli, W.; Ochsner, P.E. Management of Infection Associated with Prosthetic Joints. *Infection* **2003**, *31*, 99–108, doi:10.1007/s15010-002-3079-9.
3. Cobo, J.; Escudero-Sanchez, R. Suppressive Antibiotic Treatment in Prosthetic Joint Infections: A Perspective. *Antibiotics* **2021**, *10*, 743, doi:10.3390/antibiotics10060743.
4. Horne, M.; Woolley, I.; Lau, J.S.Y. The Use of Long-Term Antibiotics for Suppression of Bacterial Infections. *Clin Infect Dis* **2024**, *79*, 848–854, doi:10.1093/cid/ciae302.
5. Goulet, J.A.; Pellicci, P.M.; Brause, B.D.; Salvati, E.M. Prolonged Suppression of Infection in Total Hip Arthroplasty. *The Journal of Arthroplasty* **1988**, *3*, 109–116, doi:10.1016/S0883-5403(88)80075-5.
6. Patel, R. Periprosthetic Joint Infection. *N Engl J Med* **2023**, *388*, 251–262, doi:10.1056/NEJMra2203477.
7. Sandiford, N.A.; Hutt, J.R.; Kendoff, D.O.; Mitchell, P.A.; Citak, M.; Granger, L. Prolonged Suppressive Antibiotic Therapy Is Successful in the Management of Prosthetic Joint Infection. *Eur J Orthop Surg Traumatol* **2020**, *30*, 313–321, doi:10.1007/s00590-019-02559-4.
8. Prendki, V.; Zeller, V.; Passeron, D.; Desplaces, N.; Mamoudy, P.; Stirnemann, J.; Marmor, S.; Ziza, J.-M. Outcome of Patients over 80 Years of Age on Prolonged Suppressive Antibiotic Therapy for at Least 6 Months for Prosthetic Joint Infection. *International Journal of Infectious Diseases* **2014**, *29*, 184–189, doi:10.1016/j.ijid.2014.09.012.
9. Hanssen, J.L.J.; Gademan, M.G.J.; Wouthuyzen-Bakker, M.; Davis, J.S.; Dewar, D.; Manning, L.; Campbell, D.; van Prehn, J.; Miller, A.O.; van der Wal, R.J.P.; et al. Global Practice Variation of Suppressive Antimicrobial Treatment for Prosthetic Joint Infections: A Cross-Sectional Survey Study. *J Infect* **2024**, *89*, 106316, doi:10.1016/j.jinf.2024.106316.
10. Furman, D.; Campisi, J.; Verdin, E.; Carrera-Bastos, P.; Targ, S.; Franceschi, C.; Ferrucci, L.; Gilroy, D.W.; Fasano, A.; Miller, G.W.; et al. Chronic Inflammation in the Etiology of Disease across the Life Span. *Nat Med* **2019**, *25*, 1822–1832, doi:10.1038/s41591-019-0675-0.
11. Pradier, M.; Nguyen, S.; Robineau, O.; Titecat, M.; Blondiaux, N.; Valette, M.; Loïez, C.; Beltrand, E.; Dézeque, H.; Migaud, H.; et al. Suppressive Antibiotic Therapy with Oral Doxycycline for Staphylococcus Aureus Prosthetic Joint Infection: A Retrospective Study of 39 Patients. *Int J Antimicrob Agents* **2017**, *50*, 447–452, doi:10.1016/j.ijantimicag.2017.04.019.
12. Byren, I.; Bejon, P.; Atkins, B.L.; Angus, B.; Masters, S.; McLardy-Smith, P.; Gundle, R.; Berendt, A. One Hundred and Twelve Infected Arthroplasties Treated with "DAIR" (Debridement, Antibiotics and Implant Retention): Antibiotic Duration and Outcome. *J Antimicrob Chemother* **2009**, *63*, 1264–1271, doi:10.1093/jac/dkp107.
13. Cortes-Penfield, N.; Krsak, M.; Damioli, L.; Henry, M.; Seidelman, J.; Hewlett, A.; Certain, L. How We Approach Suppressive Antibiotic Therapy Following Debridement, Antibiotics, and Implant Retention for Prosthetic Joint Infection. *Clinical Infectious Diseases* **2024**, *78*, 188–198, doi:10.1093/cid/ciad484.
14. Osmon, D.R.; Berbari, E.F.; Berendt, A.R.; Lew, D.; Zimmerli, W.; Steckelberg, J.M.; Rao, N.; Hanssen, A.; Wilson, W.R. Diagnosis and Management of Prosthetic Joint Infection: Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA). *Clinical Infectious Diseases* **2013**, *56*, e1–e25, doi:10.1093/cid/cis803.
15. Hanssen, J.L.J.; van der Wal, R.J.P.; van der Linden, H.M.J.; van Prehn, J.; Scheper, H.; de Boer, M.G.J. Dosing and Treatment Duration of Suppressive Antimicrobial Therapy in Orthopedic Implant Infections: A Cohort Study. *Journal of Bone and Joint Infection* **2024**, *9*, 149–159, doi:10.5194/jbji-9-149-2024.
16. Shah, N.B.; Hersh, B.L.; Kreger, A.; Sayeed, A.; Bullock, A.G.; Rothenberger, S.D.; Klatt, B.; Hamlin, B.; Urish, K.L. Benefits and Adverse Events Associated With Extended Antibiotic Use in Total Knee Arthroplasty Periprosthetic Joint Infection. *Clin Infect Dis* **2020**, *70*, 559–565, doi:10.1093/cid/ciz261.

17. Tai, D.B.G.; Berbari, E.F.; Suh, G.A.; Lahr, B.D.; Abdel, M.P.; Tande, A.J. Truth in DAIR: Duration of Therapy and the Use of Quinolone/Rifampin-Based Regimens After Debridement and Implant Retention for Periprosthetic Joint Infections. *Open Forum Infect Dis* **2022**, *9*, ofac363, doi:10.1093/ofid/ofac363.
18. Valero-Martínez, C.; Castillo-Morales, V.; Gómez-León, N.; Hernández-Pérez, I.; Vicente-Rabaneda, E.F.; Uriarte, M.; Castañeda, S. Application of Nuclear Medicine Techniques in Musculoskeletal Infection: Current Trends and Future Prospects. *Journal of Clinical Medicine* **2024**, *13*, 1058, doi:10.3390/jcm13041058.
19. Marculescu, C.E.; Berbari, E.F.; Hanssen, A.D.; Steckelberg, J.M.; Harmsen, S.W.; Mandrekar, J.N.; Osmon, D.R. Outcome of Prosthetic Joint Infections Treated with Debridement and Retention of Components. *Clinical Infectious Diseases* **2006**, *42*, 471–478, doi:10.1016/S0276-1092(08)70277-3.
20. Rao, N.; Crossett, L.S.; Sinha, R.K.; Le Frock, J.L. Long-Term Suppression of Infection in Total Joint Arthroplasty. *Clinical Orthopaedics and Related Research* **2003**, *414*, 55–60, doi:10.1097/01.blo.0000087321.60612.cf.
21. Tsukayama, D.T.; Wicklund, B.; Gustilo, R.B. Suppressive Antibiotic Therapy in Chronic Prosthetic Joint Infections. *Orthopedics* **1991**, *14*, 841–844.
22. Pavoni, G.L.; Giannella, M.; Falcone, M.; Scorzolini, L.; Liberatore, M.; Carlesimo, B.; Serra, P.; Venditti, M. Conservative Medical Therapy of Prosthetic Joint Infections: Retrospective Analysis of an 8-Year Experience. *Clin Microbiol Infect* **2004**, *10*, 831–837, doi:10.1111/j.1469-0691.2004.00928.x.
23. Segreti, J.; Nelson, J.A.; Trenholme, G.M. Prolonged Suppressive Antibiotic Therapy for Infected Orthopedic Prostheses. *Clinical Infectious Diseases* **1998**, *27*, 711–713, doi:10.1086/514951.
24. Siqueira, M.B.P.; Saleh, A.; Klika, A.K.; O'Rourke, C.; Schmitt, S.; Higuera, C.A.; Barsoum, W.K. Chronic Suppression of Periprosthetic Joint Infections with Oral Antibiotics Increases Infection-Free Survivorship. *J Bone Joint Surg Am* **2015**, *97*, 1220–1232, doi:10.2106/JBJS.N.00999.
25. Wouthuyzen-Bakker, M.; Nijman, J.M.; Kampinga, G.A.; van Assen, S.; Jutte, P.C. Efficacy of Antibiotic Suppressive Therapy in Patients with a Prosthetic Joint Infection. *J Bone Jt Infect* **2017**, *2*, 77–83, doi:10.7150/jbji.17353.
26. Pradier, M.; Robineau, O.; Boucher, A.; Titecat, M.; Blondiaux, N.; Valette, M.; Loïez, C.; Beltrand, E.; Nguyen, S.; Dézeque, H.; et al. Suppressive Antibiotic Therapy with Oral Tetracyclines for Prosthetic Joint Infections: A Retrospective Study of 78 Patients. *Infection* **2018**, *46*, 39–47, doi:10.1007/s15010-017-1077-1.
27. Leijtens, B.; Weerwag, L.; Schreurs, B.W.; Kullberg, B.-J.; Rijnen, W. Clinical Outcome of Antibiotic Suppressive Therapy in Patients with a Prosthetic Joint Infection after Hip Replacement. *J Bone Jt Infect* **2019**, *4*, 268–276, doi:10.7150/jbji.37262.
28. Escudero-Sanchez, R.; Senneville, E.; Digumber, M.; Soriano, A.; Del Toro, M.D.; Bahamonde, A.; Del Pozo, J.L.; Guio, L.; Murillo, O.; Rico, A.; et al. Suppressive Antibiotic Therapy in Prosthetic Joint Infections: A Multicentre Cohort Study. *Clinical Microbiology and Infection* **2020**, *26*, 499–505, doi:10.1016/j.cmi.2019.09.007.
29. Malahias, M.-A.; Gu, A.; Harris, E.C.; Adriani, M.; Miller, A.O.; Westrich, G.H.; Sculco, P.K. The Role of Long-Term Antibiotic Suppression in the Management of Peri-Prosthetic Joint Infections Treated With Debridement, Antibiotics, and Implant Retention: A Systematic Review. *J Arthroplasty* **2020**, *35*, 1154–1160, doi:10.1016/j.arth.2019.11.026.
30. Rao, K.; Young, V.B. Fecal Microbiota Transplantation for the Management of Clostridium Difficile Infection. *Infect Dis Clin North Am* **2015**, *29*, 109–122, doi:10.1016/j.idc.2014.11.009.
31. Akinyoola, A.L.; Adegbehingbe, O.O.; Aboderin, A.O. Therapeutic Decision in Chronic Osteomyelitis: Sinus Track Culture versus Intraoperative Bone Culture. *Arch Orthop Trauma Surg* **2009**, *129*, 449–453, doi:10.1007/s00402-008-0621-y.
32. Lensen, K.-J.; Escudero-Sanchez, R.; Cobo, J.; Soriano, A.; Wouthuyzen-Bakker, M. Chronic Prosthetic Joint Infections with a Draining Sinus. Who Should Receive Suppressive Antibiotic Treatment? *J Bone Jt Infect* **2020**, *6*, 43–45, doi:10.5194/jbji-6-43-2020.
33. Dinh, A.; Duran, C.; Pavese, P.; Khatchatourian, L.; Monnin, B.; Bleibtreu, A.; Denis, E.; Etienne, C.; Rouanes, N.; Mahieu, R.; et al. French National Cohort of First Use of Dalbavancin: A High Proportion of off-Label Use. *International Journal of Antimicrobial Agents* **2019**, *54*, 668–672, doi:10.1016/j.ijantimicag.2019.08.006.

34. Lafon-Desmurs, B.; Gachet, B.; Hennart, B.; Valentin, B.; Roosen, G.; Degrendel, M.; Loiez, C.; Beltrand, E.; D'Elia, P.; Migaud, H.; et al. Dalbavancin as Suppressive Therapy for Implant-Related Infections: A Case Series with Therapeutic Drug Monitoring and Review of the Literature. *Eur J Clin Microbiol Infect Dis* **2024**, *43*, 1475–1480, doi:10.1007/s10096-024-04849-0.
35. Pouderoux, C.; Becker, A.; Goutelle, S.; Lustig, S.; Triffault-Fillit, C.; Daoud, F.; Fessy, M.H.; Cohen, S.; Laurent, F.; Chidiac, C.; et al. Subcutaneous Suppressive Antibiotic Therapy for Bone and Joint Infections: Safety and Outcome in a Cohort of 10 Patients. *J Antimicrob Chemother* **2019**, *74*, 2060–2064, doi:10.1093/jac/dkz104.
36. Escudero-Sánchez, R.; Ponce-Alonso, M.; Barragán-Prada, H.; Morosini, M.I.; Cantón, R.; Cobo, J.; Del Campo, R. Long-Term Impact of Suppressive Antibiotic Therapy on Intestinal Microbiota. *Genes* **2020**, *12*, 41, doi:10.3390/genes12010041.
37. Prendki, V.; Sergent, P.; Barrelet, A.; Oziol, E.; Beretti, E.; Berlioz-Thibal, M.; Bouchand, F.; Dauchy, F.A.; Forestier, E.; Gavazzi, G.; et al. Efficacy of Indefinite Chronic Oral Antimicrobial Suppression for Prosthetic Joint Infection in the Elderly: A Comparative Study. *Int J Infect Dis* **2017**, *60*, 57–60, doi:10.1016/j.ijid.2017.05.008.
38. Weston, J.T.; Watts, C.D.; Mabry, T.M.; Hanssen, A.D.; Berry, D.J.; Abdel, M.P. Irrigation and Debridement with Chronic Antibiotic Suppression for the Management of Infected Total Knee Arthroplasty: A Contemporary Analysis. *Bone Joint J* **2018**, *100-B*, 1471–1476, doi:10.1302/0301-620X.100B11.BJJ-2018-0515.R1.
39. Renz, N.; Rakow, A.; Müller, M.; Perka, C.; Trampuz, A. Long-Term Antimicrobial Suppression Prevents Treatment Failure of Streptococcal Periprosthetic Joint Infection. *Journal of Infection* **2019**, *79*, 236–244, doi:10.1016/j.jinf.2019.06.015.
40. Ferry, T.; Batailler, C.; Souche, A.; Cassino, C.; Chidiac, C.; Perpoint, T.; le Corvaisier, C.; Josse, J.; Gaillard, R.; Roger, J.; et al. Arthroscopic "Debridement and Implant Retention" With Local Administration of Exebacase (Lysin CF-301) Followed by Suppressive Tedizolid as Salvage Therapy in Elderly Patients for Relapsing Multidrug-Resistant S. Epidermidis Prosthetic Knee Infection. *Front Med (Lausanne)* **2021**, *8*, 550853, doi:10.3389/fmed.2021.550853.
41. Johnson, D.P.; Bannister, G.C. The Outcome of Infected Arthroplasty of the Knee. *J Bone Joint Surg Br* **1986**, *68*, 289–291, doi:10.1302/0301-620X.68B2.3958017.
42. Burr, R.G.; Eikani, C.K.; Adams, W.H.; Hopkinson, W.J.; Brown, N.M. Predictors of Success With Chronic Antibiotic Suppression for Prosthetic Joint Infections. *J Arthroplasty* **2022**, *37*, S983–S988, doi:10.1016/j.arth.2022.02.003.
43. Ceccarelli, G.; Perciballi, B.; Russo, A.; Martini, P.; Marchetti, F.; Capparuccia, M.R.; Iaiani, G.; Fabris, S.; Ciccozzi, M.; Villani, C.; et al. Chronic Suppressive Antibiotic Treatment for Staphylococcal Bone and Joint Implant–Related Infections. *Antibiotics* **2023**, *12*, 937, doi:10.3390/antibiotics12050937.
44. Tai, D.B.G.; Tande, A.J.; Langworthy, B.; Abdel, M.P.; Berbari, E.F.; Ten Have, B.; Jutte, P.; Soriano, A.; Suh, G.A.; Zijlstra, W.; et al. Role of Routine Suppressive Antibiotic Therapy After Debridement, Antibiotics, and Implant Retention for Acute Periprosthetic Joint Infections. *Open Forum Infect Dis* **2024**, *11*, ofae216, doi:10.1093/ofid/ofae216.
45. Lafon-Desmurs, B.; Gachet, B.; Hennart, B.; Valentin, B.; Roosen, G.; Degrendel, M.; Loiez, C.; Beltrand, E.; D'Elia, P.; Migaud, H.; et al. Dalbavancin as Suppressive Therapy for Implant-Related Infections: A Case Series with Therapeutic Drug Monitoring and Review of the Literature. *Eur J Clin Microbiol Infect Dis* **2024**, *43*, 1475–1480, doi:10.1007/s10096-024-04849-0.