Review

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Abstract: Background/Objectives: The optimal duration of antibiotic therapy, a cornerstone of PJI treatment, remains a topic of considerable debate, with current recommendations often based on limited evidence and expert consensus. Emerging evidence suggests that shorter antibiotic courses may be as effective as prolonged therapies in select cases, provided thorough surgical debridement is performed and biofilm-active agents are used.We aimed to synthesize available data on antibiotic therapy duration based on the surgical technique, along with recall of definitions, diagnosis criteria and classification. Future perspectives on PJI diagnosis have been also presented. **Methods**: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), databases were searched using predefined medical subject headings (MeSH) and PUBMED. Randomized controlled trials (RCTs), observational studies, and expert guidelines have been synthetized.**Results**: A total of 2305 articles involving observational studies and randomized controlled trials were reviewed. We summarized the results of studies that have compared shorter antibiotic courses to prolonged therapies according to the surgical procedure. Forty five studies were analyzed. Definitions and classification of PJI were mentioned for a better analysis. Future perspectives were also noted.**Conclusions**: This review highlights the limited data available for evaluating antibiotic duration in the setting of PJI. The most studies found that a shorter antibiotic duration was non-inferior to a longer duration in selected cases but evidence-based guidelines to harmonize practices and improve outcomes for PJI patients are needed.

Keywords: PJI; BJI; treatment; antibiotic duration; DAIR; surgery; one-step exchange; two-step exchange; arthroplasty

1. Introduction

Prosthetic joint infections (PJI) represent a severe and complex complication in orthopedic surgery, significantly impacting patient morbidity and healthcare systems with 15-year incidences of 1.5–2% and a 5-year mortality exceeding 20% [1]. In 2017, the incidence of hip and knee PJI in the United States was 2.1% and 2.3%, respectively, with comparable rates observed in Korea [1]. In France, PJIs account for approximately 4% of all osteo-articular infections [2]. By 2030, hospital costs related to hip and knee PJI in the United States are projected to reach $1.85 billion annually [1].

PJI are foreign-body associated infections that often necessitate a surgical approach, typically involving the removal of the foreign body and extended antibiotic treatment duration [2]. Standard surgical procedures include the removal of the arthroplasty, usually followed by the implantation of a new prosthetic device in a one- or two-stage exchange procedure [3]. A more conservative surgical approach that involves debridement, antibiotics, and retention of the implant (DAIR) is proposed for selected patients with acute PJI. It can offer a reasonable chance of success in managing the infection [3]. According to the IDSA guidelines of 2013, the treatment duration of PJI ranges from 3 to 6 months [4]. These extended durations were recommended due to biofilm-embedded bacteria. Recently, there

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were trends to shorten antibiotic length. In 2018, the International Meeting on Musculoskeletal Infections recommended to reduce the antibiotic duration for PJI managed with DAIR to 6 weeks [5,6].

Our primary objective in this narrative review is to evaluate the effectiveness of the total duration of antimicrobial therapy in treating PJI according to the surgical approach.

2. Methods

2.1. Literature Search Strategy

We carried out this systematic review out following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [7]. An extensive search was conducted over four medical electronic databases (PubMed, Embase Science Direct, and Cochrane Library) from the 1st of January 1998 to the 1st of April 2025.

To optimize our search strategy, we integrated these key words: 'antibiotic duration', 'antibiotic lengh', 'short duration antibiotic', 'short course antibiotic', 'prolonged antibiotic', 'prosthetic joint infection', 'periprosthetic joint infection', 'bone and joint infection', 'arthroplasty infection, 'surgery', 'DAIR', 'one-step exchange', 'two-step exchange' and 'biofilm'.

2.2. Selection Criteria

Abstracts were screened; studies and clinical trials evaluating the impact of antibiotic duration on clinical outcomes were selected. We also reviewed additional references cited within these articles to identify relevant earlier studies. Exclusion criteria included case reports, conference presentations, studies focused on antibiotic prophylaxis, chronic suppressive therapy, microbiological and radiological diagnosis. Fungal or mycobacterial PJI were either excluded as well as articles written in languages other than English, French. Osteoarticular infections without a hardware implant were not retained for analysis.

2.3. Data Extraction and Criteria Appraisal

We gathered the data from article texts, abstracts, tables, and figures. For data extraction we followed the Population, Intervention, Comparison, Outcome (PICO) structure and included information such as the title, author name, year of publication, study structure, sample size, patient characteristics, antibiotics (molecules and their duration, routes of administration), surgery intervention, outcomes, and conclusions.

3. Results

A total of **n = 2305 studies** were initially identified from the databases based on the redefined inclusion and exclusion criteria. After removing articles that met the exclusion criteria, **n = 45** articles were ultimately selected for inclusion in our systematic review. The study selection and screening process is illustrated in the **PRISMA [7] flow diagram (Figure 1)**.

For our narrative review, we will begin with a brief overview of the definitions and classifications of PJI to provide a clearer understanding of the treatment strategies.

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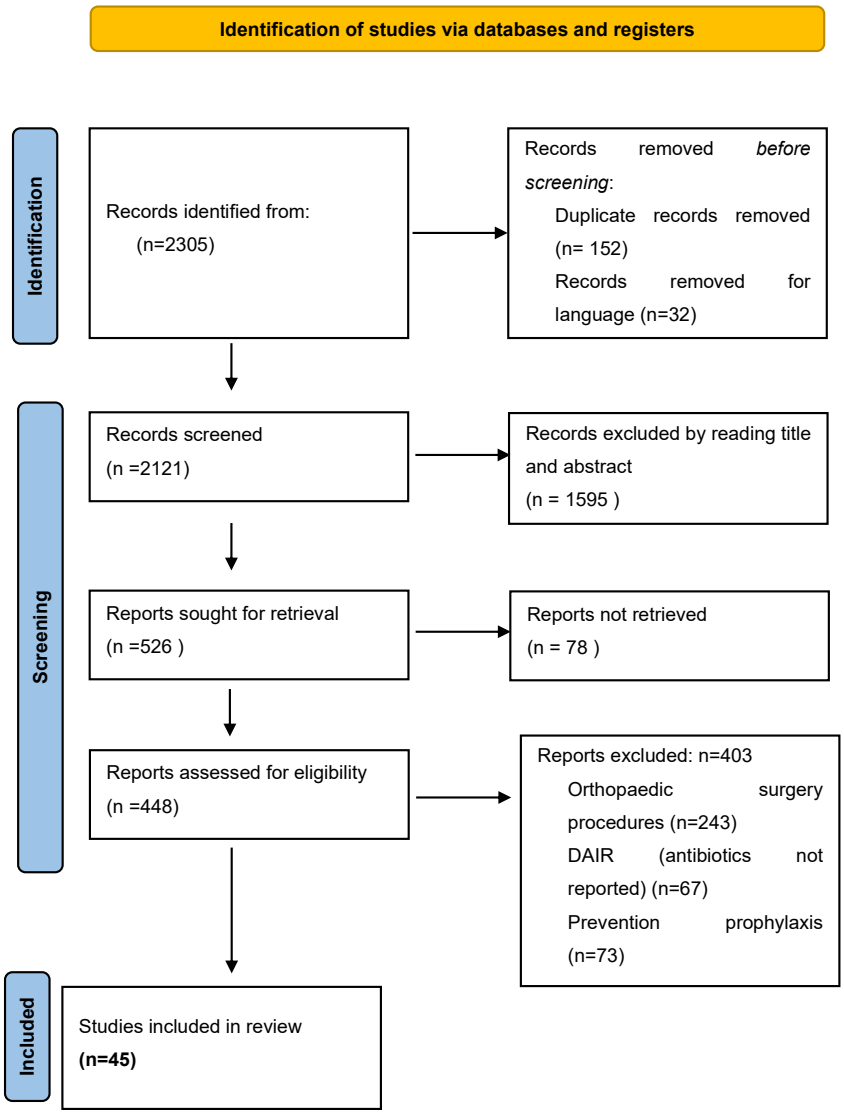

Figure 1. PRISMA Flow Diagram of PJI Systematic Review.

4. Definitions and Classifications

4.1. Defining Prosthetic Joint Infections and Clinical Presentation

Accurate diagnosis of PJI is a challenging issue and requires a combination of clinical signs, microbiological evidence, and imaging findings.

In 2011, the diagnosis of PJI was established through standards suggested by The Musculoskeletal Infectious Society (MSIS) that underwent un update by the International Consensus Meeting on PJI [8,9]. Two years later in 2013, the Infectious Diseases Society of America (IDSA) published definitions of PJI with a slight distinction [4]. In a more recent publication with evidence-based data, the MSIS and the International Consensus Meeting (ICM) have developed in 2018 a more updated version [5]. These criteria and definitions are outlined in Table 1.

Table 1. Proposed definitions of prosthetic joint infections.

Musculoskeletal Infection	**International Consensus Meeting 2013** [9]	**IDSA 2013** [4]	**Musculoskeletal Infection Society (MSIS) 2018** [5]

 doi:10.20944/preprints202505.2388.v1

Society (MSIS) 2011 [8]			
Infected if at least one **major criteria** is present: - Two positive periprosthetic cultures with phenotypically identical organisms - A sinus tract communicating with the joint - Presence of purulence in the affected joint - Positive histologic analysis of periprosthetic tissue - A single positive culture	Infected if at least one **major criteria** is present: - Two positive periprosthetic cultures with phenotypically identical organisms - A sinus tract communicating with the joint	Infected if one of the following criteria is present: - Sinus tract communicating with prosthesis - Presence of purulence - Acute inflammation on histopathologic evaluation of periprosthetic tissue - Two or more positive cultures with the same organism (intra-operatively and/or pre-operatively) - Single positive culture with virulent organism	Infected if at least one **major criteria** is present: - Two positive cultures of the same organism - Sinus tract with evidence of communication to the joint or visualization of the prosthesis
Infected if at least four out of six **minor criteria** exist: - Elevated CRP and ESR - Elevated synovial fluid PMN%	Infected if three out of five **minor criteria** exist**:** - Elevated CRP and ESR - Elevated synovial fluid WBC count or ++ change on leukocyte esterase test strip -Elevated synovial fluid PMN% -Positive histologic analysis of periprosthetic tissue -A single positive culture		Infected if **preoperative diagnosis** score ≥ 6 / Possibly infected if **preoperative diagnosis** score between 2 and 5: - Elevated CRP or D-Dimer (Serum): 2 - Elevated ESR (Serum): 1 - Elevated synovial WBC count or LE (Synovial): 3 - Positive alpha-defensin (Synovial): 3 - Elevated synovial PMN (%): 2 - Elevated synovial CRP: 1 Infected if **intraoperative diagnosis** score ≥ 6 / Possibly infected if **intraoperative diagnosis** score between 4 and 5: - Positive histology: 3 - Positive purulence: 3 - Single positive culture: 2

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; WBC: white blood cells, PMN%, polymorphonuclear neutrophils percentage. Proceed with caution in: adverse local tissue reaction, crystal deposition disease, slow growing organisms. ; LE, leukocyte esterase; . a For patients with inconclusive minor criteria, operative criteria can also be used to fulfill definition for PJI. b Consider further molecular diagnostics such as next-generation sequencing.

4.2. Classification of Prosthetic Joint Infections

Management of PJIs is a challenge and various classification systems have been introduced, which consider variables such as onset of symptoms, pathogenesis and clinical manifestations.

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Classifications for PJI were established to predict the most appropriate treatment strategy according to physiopathology of infection.

Mainly, classifications are based on the time of symptom onset: early (within three months post-surgery), delayed (3–12 months post-surgery), or late (beyond 12 months). Early infections are often caused by virulent organisms such as Staphylococcus aureus, whereas delayed and late infections frequently involve less aggressive pathogens like coagulase-negative staphylococci [3,10] (Table 2).

Table 2. Classification and clinical presentation of prosthetic joint infections.

Type of Infection	Time of presentation	Mechanism of infection	Clinical Presentation		Organisms
Early	< 3 months	Intraoperative contamination	Acute	Acute Sudden onset erythema, edema, warmth, and tenderness	Virulent bacteria (i.e., *Staphylococcus aureus*)
Delayed	3-12 months	Intraoperative contamination	Chronic	Joint pain and stiffness	Low virulent bacteria (coagulase-negative staphylococci)
Late	>12 months	Hematogenous Seeding	Acute	Sudden-onset erythema, edema, tenderness and warmth,	Virulent bacteria (i.e., *S.aureus*)
		Intraoperative contamination	Chronic	Joint pain, sinus tract	Low virulent bacteria (i.e., *Propionibacterium acnes*)

These physiopathology classifications are important for well-designed clinical trials and set the rationale for prolonged treatment, based on the difficulty of treating biofilm-embedded bacteria and surgical treatment or conservative strategy like DAIR (debridement, antibiotics and implant retention).

Coventry proposed a classification of PJI. He devided infections into three stages according to the onset timing: Stage I (acute), within the first three months; Stage II, more than three months post-surgery intervention; and Stage III, two years after the initial infection [10,11]. Tsukayama et al. [12] classified infections into four categories: 1) Positive intraoperative cultures; 2) Early postoperative infection occurring within four weeks; 3) Late chronic infection (beyond four weeks); 4) Acute hematogenous infection.

Theses classifications help to determining the optimal surgical technique, the appropriate duration of antibiotic therapy, and the prognosis of PJI, limiting the development of evidence-based approaches and accurate prognostic assessments [13].

To address this gap, the PJI-TNM classification was introduced by Alt et al. in 2020 [4]. One of the most widely used and successful classification systems in medicine is the TNM classification for malignant tumors in oncology that was developed by Pierre Denoix in the late 1940s and early 1950s [14]. Beyond treatment planning, the TNM system provides valuable prognostic information and enables clinical and scientific comparisons of treatment outcomes. These principles are also relevant for PJI. The commonly stated phrase “treat the infection like a tumor” highlights similarities between PJIs and malignancies, particularly the necessity for surgical resection of affected tissue, the optimal choice of antibiotics and their duration. This system applies the principles of the well-established oncological TNM classification to better reflect the severity and complexity of PJIs. The three key factors defining PJIs were mapped to the TNM framework:

- T (Tissue & Implant) – Condition of the infected implant and periarticular soft tissues.
- N (Non-human Cell) – The causative microorganism.

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- M (Morbidity of the Patient) – The host's overall health and comorbidities.

Each category is further subdivided by a number (0–3) and a letter (a–c) to distinguish between various situations. A lowercase "r" is placed in front of the TNM classification in case of recurrent infection in the same joint.

Table 3. provides a summary of the original PJI-TNM classification introduced by Alt et al. in 2020 [14].

Table 3. The original PJI-TNM classification as introduced by Alt et al. in 2020 [14].

T/N/M	Classification	Subclassification	Descriptive
T: Tissue and Implant Conditions	T0	a	Stable standard implant without important soft tissue defect
		b	Stable revision implant without important soft tissue defect
	T1	a	Loosened standard implant without important soft tissue defect
		b	Loosened revision implant without important soft tissue defect
	T2	a	Severe soft tissue defect with standard implant
		b	Severe soft tissue defect with revision implant
N: Non-human Cells (Bacteria and Fungi)	NO	a	No mature biofilm formation (former: acute), directly postoperatively
		b	No mature biofilm formation (former: acute), late hematogenous
	N1	a	Mature biofilm formation (former: chronic) without 'difficult to treat bacteria'
		b	Mature biofilm formation (former: chronic) with culture-negative infection
	N2	a	Mature biofilm formation (former: chronic) with 'difficult to treat bacteria'
		b	Mature biofilm formation (former: chronic) with polymicrobial infection
		c	Mature biofilm formation (former: chronic) with fungi
M: Morbidity of the Patient	M0		Not or only mildly compromised (Charlson Comorbidity Index: 0–1)
	M1		Moderately compromised patient (Charlson Comorbidity Index: 2–3)
	M2		Severely compromised patient (Charlson Comorbidity Index: 4–5)
	M3	a	Patient refuses surgical treatment
		b	Patient does not benefit from surgical treatment
		c	Patient does not survive surgical treatment

T – Tissue and implant conditions. For this item: standard implants ('a') versus revision implants ('b'); N – Non-human cells (bacteria and/or fungi), M – Morbidity of the patient, r: recurrent infection.

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5. Prosthetic Joint Infection Surgery Options

A collaborative approach involving orthopedic surgeons, infectious disease specialists, and patients is essential in managing PJI. Treatment typically combines surgical intervention with antibiotic therapy. Surgery is a major pillar in the management of PJI. Surgical treatment options include DAIR, one-stage or two-stage exchange, resection arthroplasty, arthrodesis, and amputation [3, 13, 15]. Among these, the surgical treatment of reference is removal of the arthroplasty [2].

DAIR consist of debridement, antibiotics and implant retention. Debridement involves the removal of infected, devitalized bone and soft tissue, hematomas, fibrous membranes and sinus tracts. It should be undertaken to reduce the bioburden of the pathogens and to improve the efficiency of the patient's immune system [16].

In one-stage revision, within the same surgical intervention, a new prothesis is implanted after removing all the foreign material and full debridement. Antibiotics is administered for two to three weeks prior to the prosthesis exchange if the pathogen is identified before the surgery intervention and the patient had no signs of sepsis [3]. By contrast, the two-stage exchange procedure includes a delayed reimplantation of a new prothesis. Resection arthroplasty allows for the definitive removal of the prosthesis, along with debridement, without reimplantation thereafter [3]. In certain cases, surgery options are not possible and conservative treatment is recommended with long term suppressive antibiotics [2].

For the radical surgery approaches (DAIR or prosthesis removal) long-term antibiotics are prescribed for certain duration that could be extended due to the challenge of treating biofilm-associated bacteria. However, treatment duration is not well established and it is in most of cases empirical [2]. It differs based on the surgical approach and the underlying cause of the infection.

Antibiotic selection is a multifactorial decision, influenced by the identified pathogen, its antibiotic susceptibility profile, its capacity to form a biofilm, the severity of the infection, and host-related factors [17].

Here we will discuss the duration of antibiotics based on the surgical procedure performed.

6. Antibiotic Duration of PJI According to the Surgery Options

Orthopedic infectious disease specialists collaborate with surgeons and microbiologists to determine antibiotic regimens. They are based on the patient's overall health status, clinical context, detected microorganism, its susceptibility and the surgery procedure [18]. Empirical antibiotics are given usually 72 to 144 hours before microbiology data are available. The therapy duration is measured from the surgery date to the discontinuation date [18]. The type of microorganism might also influence treatment duration. Generally, treatment lasts 6 to 12 according to surgical management [17].

6.1. Prosthetic Joint Infection Treated with DAIR

6.1.1. The Recommended Duration of Antibiotics

The optimal length of antibiotic therapy after PJI surgery remains debated, depending on the chosen medical–surgical strategy (implant retention versus removal) and the practices of individual treatment teams [17].

Treatment begins during the first-stage procedure. The approach should be individualized based on the infecting organism and patient factors. Intravenous administration is often recommended for the first week, followed by oral therapy if an appropriate agent is available and the organism's sensitivity allows [16,19].

The antibiotic duration for DAIR was about 3 to 6 months in old guidelines [4]. Some observational studies without a control group have tried to treat patients with a shorter duration of 8 to 12 weeks with a rate success of 57 to 88%. These studies are summarized in Table 4.

Table 4. Summary of Non-Comparative Studies on Antibiotic Treatment Duration in Prosthetic Joint Infections Managed with DAIR.

 doi:10.20944/preprints202505.2388.v1

Author Year Reference	Study design	Patients N	Bacteria Major strains isolated	Antibiotics	Antibiotic duration (mean)	Follow-up (mean) Months	Success treatment rate (%)
Berdal et al. 2005 [20]	Prospective	29	Staphylococcus aureus	Rifampicin plus Cirpofloxacin	3 Months	22.5	83
Soriano et al. 2006 [21]	Prospective	39	Gram positive Cocci	Levofloxacin plus Rifampicin	2.7 +/-1 Months	24	76.6
Martínez-Pastor et al. 2009 [22]	Prospective	47	Enterobacteriaceae family	Bata-lactam for IV Fluoroquinolones for oral	Intravenous 14 days Oral 2.6 months	15.4	74.5
Cobo et al. 2010 [23]	Prospective	117	Gram negative strains Gram positive cocci	Not reported	2.5 Months	25	57.3
Vilchez et al. 2011 [24]	Prospective	53	Staphylococcus aureus		IV: 11 ± 7 days and oral 88 ± 46 days	24	75.5
Tornero et al. 2015 [25]	Prospective	143	Gram negative strains Gram positive cocci	Fluoroquinolones Rifampicin in combination	IV: 8 days Oral 69 days	48	88.2

6.1.2. Comparative Studies to Shorten the Antibiotic Duration for PJI

Numerous studies have been undertaken to evaluate the reduction of antibiotic treatment duration from six months to three months, and in some cases to six weeks, depending on the type of surgical procedure. The main findings of these key studies are summarized in Table 5.

Table 5. Summary of Studies on Antibiotic Treatment Duration for Prosthetic Joint Infections managed by DAIR.

Author Year (Reference)	Study design	Bacteria (Major Strains Isolated)	Antibiotics (Major prescribed)	Antibiotic duration	Patients in each arm	Outcome & Conclusion
Bernard et al. 2010 [30]	Prospective observational, non-randomized monocentric	Staphylococci (66%)	Rifampicin (n=58, always in combination and only for staphylococcal infections), Ciprofloxacin (n=42), vancomycin	6 weeks vs 12 weeks	144 episodes -6 weeks: 70 episodes	Overall cure in 115 episodes (80%) -6 weeks: 90% cure vs. -12 weeks: 55%

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			(n=40), and amoxicillin/clavulanic acid (n=25).		(70/144, 49%) -12 weeks: 74 episodes (74/144, 51%)	Failure 29 (20%) antibiotic therapy might be able to be limited to a 6-week course Randomized trials are needed
Puhto et al., 2012 [26]	Retrospective observational, pre-post-design monocentric	Staphylococcus aureus (42%)	Rifampicin and fluoroquinolones for GP strains	2-3 months vs 3-6 months	ITT: long n= 60 Short n= 72 PP: long n=38 Short n=48	Non-inferiority of short treatments. Cure rates: ITT—Long 57%, Short 58% (p = 0.85) PP—Long 89%, Short 87% (p = 0.78) Short antibiotic treatment seems to be a good alternative for patients treated with DAIR prospective randomized controlled trials are urgently needed
Lora-Tamayo. et al., 2013 [27]	Retrospective observational, multicenter	Staphylococcus aureus	(>75% rifampin-based combinations)	<61 days 61–90 days >90 days	231 patients n=52 n=52 n=127	Cure rate: <61 days—75% 60–90 days—77% >90 days—77% (p = 0.434)
Lora-Tamayo. et al., 2016 [28]	Randomized, open clinical trial,	Staphylococci	Levofloxacin and Rifampicin	8 weeks vs 3–6 months	N= 63 ITT: long n= 33	Non-inferiority. Cure rates:

 doi:10.20944/preprints202505.2388.v1

	multicenter			3 months for hip prostheses and 6 months for knee prostheses	Short n= 30 PP: long n=20 Short n=24	ITT—Long 58%, Short 73% (Δ = −15.7 95% CI −39.2% to +7.8%) PP—Long 95%, Short 92% (Δ = +3.3% 95% CI −11.7%to +18.3%) 8 weeks of L+R could be non-inferior to longer standard treatments for acute staphylococcal PJI managed with DAIR
Chaussade et al. 2017 [31]	Retrospective observational, multicenter	Staphylococci (40%)	Rifampin-based combinations for GP and fluoroquinolones	6 weeks vs. 12 weeks	N= 87 -6 weeks n=44 -12 weeks n=43	Cure rates: 67.4% in the long treatment group 70.5% in the short treatment group (aOR 0.76, 95%CI 0.27–2.10) Prospective randomized trials are required
Bernard et al. 2021 DATIPO [32]	Randomized, open clinical trial, multicenter	Staphylococcus aureus (30-40%)	Rifampin-based combinations and fluoroquinolones	6 weeks vs. 12 weeks	N= 151 -6 weeks n=75 -12 weeks n=76	Failure rate for 6 weeks: 30.7% Failure rate for 12 weeks: 14.5% Difference: 16.2% (95% CI: 2.9% to 29.5%)

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						Non inferiority was not shown

DAIR—debridement, antibiotics, and implant retention. GP: Gram-positive microorganisms. ITT: intention-to-treat analysis. PP: per-protocol analysis. 95% CI: 95% confidence interval.

Twelve Weeks Versus Eight Weeks

Puhto et al. have conducted a study in which they aimed to evaluate the effect of shortening antibiotic treatment duration in PJI managed with DAIR [26]. In 2006, the standard antibiotic regimen was reduced from 6 to 3 months for total knee arthroplasty (TKA), and from 3 to 2 months for total hip arthroplasty (THA) in their hospital [26]. They conducted a retrospective review of all DAIR-treated TKA and THA PJIs between February 2001 and August 2009. Of 132 patients, 86 (65%) completed the full antibiotic course and were included in the analysis. Among them, 32 (37%) had THA and 54 (63%) had TKA. Treatment success was observed in 34 patients (89.5%) in the longer-duration group and in 42 patients (87.5%) in the shorter-duration group (p = 0.78). These results suggest that, when antibiotic therapy is completed as planned, shorter treatment duration 3 months for TKA and 2 months for THA is as effective as longer courses [26].

In a more recent study, Tornero et al. have prospectively collected and retrospectively reviewed from 1999 to 2013 143 cases of PJI managed with DAIR with minimum follow-up of 2 years. The failure rate after a median duration of oral antibiotic treatment of 69 days (IQR 45–95 days) was 11.8%. They have concluded that the only factor associated with failure was the oral antibiotic selection, not the duration of treatment. Thus, duration of 8 weeks seems to be a good alternative to prolonged regimens [25].

A Spanish team, have published in 2013 a retrospective, multicenter, observational study of cases of PJI by *S. aureus* that were managed with DAIR (2003–2010). The success rate was 55%. There were no differences in relapse that were observed between patients regardless of treatment duration, which ranged from 60 to more than 90 days [27].

The same team has conducted a more recent randomized clinical trial in 2016 comparing short versus long duration of levofloxacin plus rifampicin for acute staphylococcal PJI managed with DAIR [28]. Sixty three patients were included. The primary endpoint of the study was the cure rate with a median follow-up duration of 540 days. In the intention-to-treat analysis, cure rates were 58% in the long-schedule group and 73% in the short-schedule group (difference: 15.7%, 95% CI: 39.2% to 7.8%). Among the 44 patients (70%) included in the per-protocol analysis, cure rates were 95.0% for the long schedule and 91.7% for the short schedule (difference: 3.3%, 95% CI: 11.7% to 18.3%). Thus, they suggest that an 8-week course of levofloxacin and rifampicin may be non-inferior to longer standard regimens for acute staphylococcal PJI managed with DAIR [28].

Considering these studies, in 2024, the American Academy of Orthopaedic Surgeons have published that there is no difference in outcomes between antibiotic protocols lasting 8 weeks versus those lasting 3 to 6 months [2].

Twelve Weeks Versus Six Weeks

In 2010, Bernard et al. included in their study 144 PJI cases, consisting of 62 hip arthroplasties, 62 knee arthroplasties, and 20 hip hemiarthroplasties, with a follow-up period ranging from 26 to 65 months. Surgical interventions comprised 60 DAIR, 10 one-stage prosthesis exchanges, 57 two-stage exchanges, and 17 Girdlestone procedures or knee arthrodeses. Antibiotic therapy lasted 6 weeks in 70 episodes (49%) and 12 weeks in 74 episodes. Overall, cure was achieved in 115 cases (80%). Only two patients failed in the short-term group (90% cure rate) [30].

In 2017, Chaussade et al. in the same French team have included in a multicenter retrospective study 87 episodes of PJI with debridement performed within 3 weeks of symptom onset [31]. Sixty patients (69%) sustained remission after a mean follow-up of 52.1 months. In a multivariate analysis no statistical difference was demonstrated difference between hip and knee cases (73.3% vs. 59.3%, 95% confidence interval (CI), 0.20–1.38), or between patients receiving 6 weeks versus 12 weeks of

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antibiotic treatment (70.5% vs. 67.4%, 95% CI 0.27–2.10, p = 0.60). Therefore, as conclusion there were no difference in long-term remission between patients treated with DAIR who received either 6 or 12 weeks of antibiotic therapy [31]. Further prospective randomized trials were recommended [31].

Thus, Bernard in 2021 published DATIPO, a large French open-label, randomized, non-inferiority trial comparing 6 weeks versus 12 weeks of antibiotic therapy for patients with PJI, with 205 patients in each group [32]. The study did not confirm the non-inferiority of 6-week therapy, as 18% of patients in the 6-week group experienced persistent infection, compared to 9% in the 12-week group. Subgroup analyses highlighted significant differences based on the surgical approach: for patients managed with DAIR, the 6-week regimen resulted in notably worse outcomes than the 12-week regimen (30.7% vs. 14.5%, respectively). No significant difference was observed for patients who underwent one-stage exchange (4% vs. 2.8%). However, for patients receiving a two-stage exchange, those treated with 6 weeks of antibiotics had more adverse outcomes (15% vs. 4.9%) [32].

Table 5 provides an overview of these studies.

6.2. PJI Treated with Single-Step Exchange Procedure

Single-stage revision surgery has recently experienced interest as a treatment strategy for PJI [33]. The success of a one-stage exchange arthroplasty depends heavily on careful patient selection, precise surgical technique, and coordinated perioperative management by a multidisciplinary team. Similar to the two-stage exchange, the effectiveness of this approach is closely tied to the thoroughness of debridement and the extent to which the microbial load is reduced [16].

Rowan et al. have published a review in 2018 assessing evidence that single-step exchange for PJI has an increased interest since the last 5 years [34]. The reinfection rates (RR) were of 7.6% (95% CI 3.4–13.1) and 8.8% (95% CI 7.2–10.6) for single-stage and two-stage revisions respectively [33]. Thus, they advocate for recommanding of single-stage revision in cases of significant bone loss and atypical PJI, such as fungal infections [34].

In our review of PJI managed by single-step exchange procedure, the reported RRs for this technique range from 5% to 25% [35-43], which are comparable to those observed with two-stage revisions (9% to 20%) [44]. For instance, a study involving 28 patients who underwent single-stage revision for chronic knee arthroplasty infections reported no reinfections at a three-year follow-up [35]. Similarly, another study examining 50 knee revisions with an average follow-up of 10.5 years found a reinfection rate of only 2% [45]. However, Buchholz et al. reported a reinfection rate of 23% when using single-stage revision. It was explained that the patients were managed without systemic antibiotics [46]. Similarly, Ammon and Stockley observed a 14% recurrence rate (8 out of 57 cases) following staged revision procedures performed without systemic antibiotic therapy in patients who required impaction allografting as part of their reconstruction [47, 48].

According to IDSA guidelines published in 2013, current recommendations suggest that one-stage exchange should be followed by 4 to 6 weeks of pathogen-specific antimicrobial therapy, based on limited but existing evidence, with an additional 3 months of oral suppressive therapy [4].

The Endo-Klinik in Germany has reported using a shorter course 10 to 14 days of antibiotics post–one-stage exchange except in cases involving streptococcal infections [48]. Over their 35 years of experience, they have claimed success rates ranging from 75% to 90% [49].

Studies that tried to shorten antibiotic duration for PJI managed by single-step exchange are mentioned in table 6.

Table 6. Summary of Studies on Antibiotic Treatment Duration for Prosthetic Joint Infections managed by single-step exchange

Table 6. Summary of Studies on Antibiotic Treatment Duration for Prosthetic Joint Infections managed by single-step exchange.

Author (year, reference)	Patients N	Study design	Antibiotics (major prescribed)	Antibiotic duration	Local antibiotics or suppressive	Follow-up (mean)	Outcome	Conclusion

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						Years		
Whiteside et al. (2011) [50]	18	Retrospective Cohort	Not reported	Intravenous 2-4 weeks	Local Vancomycin : intraaticular	5.1	RR = 5.5% FO: Mean KSS was 78 ± 8 at 1year, 83 ± 9 at 2 years, 84 ± 8 at 5years, 85 ± 10 at 6 years, and 84 at 8 years	A single-stage revision total TKA for MRSA infection, managed with six weeks of intra-articular vancomycin administration, effectively controlled the infection
Singer at al. (2012) [41]	57	Retrospective	Rifampicin fluoro-quinolones Combination : 50.8%	Overall duration : 6 weeks -2 weeks IV after surgery – 4 weeks : oral antibiotics	Local Gentamicin	3	RR = 15% FO: KSS after surgery was 72 points (range, 20–98 points), the Knee Society function score was 71 points (range, 10–100 points), and the Oxford–12 knee score was 27 points (range, 13–44 points).	One-stage revision of knee PJI leads to a high rate of infection control of 95% and reasonable patient function when the pathogen is identifiable and when MRSA and MRSE infections are excluded. Recurrence is about 15% in

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								hinged prothesis
Jenny et al. (2013) [38]	47	Observational Cohort Prospective	-IV : vancomycin, teicoplanin -Oral Rifampicin Levofloaxcin	-IV : 3.5 (1–16 weeks), -Oral : 12 (3–16 weeks)	Suppressive ATB : not reported	3	RR = 12% FO: The median preoperative KSS function score was 42 points. 56% of the patients had a KSS of >150 points postoperatively	Single-stage exchange may offer a viable alternative for managing chronically infected TKA, providing a more convenient approach for patients by avoiding the risks associated with two separate surgeries and hospitalizations, while also reducing overall healthcare costs.
Baker et al (2013) [51]	33	Prospective	Not reported	Not reported	Not reported	0.5 (7 months)	RR = 21% FO: The mean pre– and post–operative OKS were 15 (95% CI, 13–18) and 25 (95% CI, 21–29), respectively,	No difference between single-stage and two-stage revision of the infected knee replacement

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							giving a mean improvement of 10 (95% CI, 5–14)	
Shanmugasundaram et al. (2014) [42]	5	Retrospective	Not reported	Not reported	Antibiotic spacers	2	RR = 17.2% FO: Not reported	In hip prosthetic joint infections (PJI), the initial success rate was 60% for one-stage exchange and 70% for two-stage exchange. For knee PJI, success rates were higher—80% for one-stage exchange and 75% for two-stage exchange. Future advances in microbiological diagnosis are needed
Tibrewal et al. (2014) [45]	50	Prospective	Not reported	-IV : 2 weeks -Oral : 3 months	Antibiotic-impregnated cement	10	RR = 2% FO: the mean OKS increased by a factor of 2.4 from 14.5 (6 to 25) pre–operative	Single-stage revision may achieve clinical outcomes comparable to those of two-stage

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							ly to 34.5 (26 to 38) one year after surgery. This represents a mean absolute improvement of 20.0 points (95% CI: 17.8 to 22.2, $p < 0.001$).	revision. Additionally, the single-stage approach is associated with reduced healthcare costs, lower patient morbidity, and decreased overall inconvenience.
Cury Rde P et al. (2015) [52]	6	Retrospective	Not reported	-IV : 2-4 weeks -Oral : 6 months	Suppressive : 4 patients	3	RR = 16.7% FO: WOMAC score 49.5 (47–55)	The DAIR, one-stage revision and two-stage revision success rates were 75%, 83.3%, and 100%, respectively
Haddad et al. (2015) [35]	28	Retrospective	Not reported	-6 Weeks (IV and/or Oral)	antibiotic-loaded cement Gentamicin Vancomycin	2	RR = 0% FO: KSS was higher in the single–stage group than in the two–stage group (mean, 88; range, 38–97 versus 76; range,	Single-stage approach can be an alternative to the two-stage procedure in carefully selected patients with chronically infected TKA.

 doi:10.20944/preprints202505.2388.v1

							29–93; p < 0.001) Preoperative mean KSS was 32 in the single–stage group (range, 18–65)	Prospective trials are needed.
Zahar et al. (2016) [53]	46	Retrospective	Not reported	14.2 (10–17 days)	Antibiotic-loaded cement Gentamicin Clindamycin Vancomycin	10	RR = 7% FO: HSS score improved significantly from a mean preoperative value of 35 (±24.2 SD; range, 13–99) to an average of 69.6 (±22.5 SD; range, 22–100)	The overall infection control rate was of 93% and good clinical results Further research into one-stage exchange techniques for PJI in TKA are needed
Cochran et al. (2016) [39]	3069	Retrospective Observational Database	Not reported	Not reported	Not reported	6	RR = 24.6% at 1 year and 38.25% at 6 years FO: Not reported	Two-stage reimplantation, despite 19% recurrence, had the highest success rateover single-stage and DAIR.
Jenny et al. (2016) [43]	Intervention group	Retrospective	Not reported	3 months	Not reported	2	RR = Intervention	When a single-stage

 doi:10.20944/preprints202505.2388.v1

	= 54, Control group = 77,	case-control					group: 15% Control group: 22% FO: KSS over 160 points (80%). No significant difference between the two groups	exchange is performed, patient selection does not appear to influence the outcome.
Massin et al. (2016) [40]	108	Retrospective	Not reported	Not reported	Not reported	2	RR = 24% FO: IKS 88.6 ± 9.4	One-stage procedures are preferable in women, because they offer greater comfort without increasing the risk of recurrence. Routine one-stage procedures may be a reasonable option in the treatment of infected TKR
Li et al. (2017) [37]	22	Retrospective	Vnacomycin	4-6 weeks	Not reported	5	RR = 9.1% FO: Not reported	No significant difference between single–stage and

 doi:10.20944/preprints202505.2388.v1

								two–stage revision in terms of satisfaction rates, and overall infection control rates.
Castellani et al. (2017) [36]	14	Retrospective	Not reported	Not reported	Not reported	1	RR = 7.2% FO: Not reported	Superiority of one- versus two-stage revision and the value of antibiotic-free periods prior to definitive revision remain unclear. Large prospective studies or randomized controlled trials are needed

RR: reinfection rate, FO: functional outcome, HSS: Hospital for Special Surgery knee score, IKS: International Knee Society Score, KSS: Knee Society Score, OKS: Oxford Knee Score, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index, TKR : total knee replacement, TKA : total knee arthroplasty, DAIR : debridement, antibiotics and implant retention, MRSA Methicillin-resistant Staphylococcus aureus, MRSE Methicillin-resistant Staphylococcus epidermidis .

6.3. PJI treated With Two-Step Exchange Procedure

A review of some former studies, highlights significant variability in treatment protocols, ranging from no antibiotic use at all [46, 47] to extended intravenous courses lasting up to 9 weeks, often followed by oral therapy for varying durations [54,55,35]. According to the IDSA guidelines published in 2013, the typical duration of systemic antibiotics for PJI managed with a two-stage exchange procedure ranges from 4 to 6 weeks [4]. However, some studies suggest that this duration could be significantly reduced. Hoed-Reddick et al. achieved an 89% success rate in eradicating infection during staged revision for infected total knee arthroplasty, using only 24 hours of intravenous cefuroxime in a cohort of 53 patients [56].

 doi:10.20944/preprints202505.2388.v1

The same team reported on a cohort of 114 patients who underwent two-stage revision procedures utilizing antibiotic-impregnated cement beads and only 24 hours of intravenous antibiotic prophylaxis [57]. With a minimum follow-up of two years, they achieved a success rate of 87.7%. These results suggest that radical debridement combined with local antibiotic delivery via cement beads may offer comparable efficacy to that of prolonged systemic antibiotic regimens [57].

While conceptually similar to the study of McKenna et al. [58], there were several important differences. The protocol of Hoad-Reddick employed vancomycin alone within biconcave cement beads, whereas Mc Kenna et al used a combination of tobramycin and vancomycin embedded in a contoured cement spacer. They believe that the spacer not only helps preserve soft tissue tension but also improves interim joint function and patient mobility, potentially contributing to a shorter hospital stay. Furthermore, their approach included a 5-day course of intravenous antibiotics, intended to eliminate residual bacteria dislodged during surgery, missed during debridement, or located in areas beyond the reach of the cement spacer [57,58].

The two-stage protocol, involving prosthesis removal and the placement of an antibiotic-loaded cement spacer, is considered the gold standard for managing late PJI in Europe and North America [59]. The most commonly used local antibiotics include vancomycin and aminoglycosides, primarily gentamicin, although tobramycin is also employed [2].

In 2019, a Swiss open-label randomized controlled trial involving 123 patients with bone and joint infections treated with hardware removal, a 4-week antibiotic regimen was shown to be non-inferior to a 6-week course. The study included 39 cases of PJI treated with a two-stage exchange [60]. Notably, only two patients (5%) received local antibiotic treatment with tobramycin. After a median follow-up of 2.2 years, no significant difference was observed between the groups, with microbiological cure rates of 98% in the 4-week group and 94% in the 6-week group [60].

6.4. PJI Treated with Total Removal Without Implantation

6.4.1. Permanent Resection Arthroplasty

Permanent resection arthroplasty is a definitive surgery intervention in PJI. It consists in a total remove of all components along with soft-tissue and bone debridement without re-implantation of new prothesis. Excision arthroplasty may be a suitable option for low-demand patients whose primary functional requirement is comfortable sitting, as this is often more easily attained compared to outcomes following knee arthrodesis [3, 16, 61].

As a salvage procedure, infection can be eradicated in 50% to 89% of patients [62, 63]. Wasielewski et al. have managed seventy-six consecutive infected total knee arthroplasties in 74 patients. Intravenous antibiotics were administered perioperatively for a minimum duration of 3 weeks and up to 3 months. Eighty two percent of patients (41/50) received intravenous antibiotic therapy for approximately 6 weeks (±6 days). Subsequent oral antibiotics were not prescribed in all cases. Their duration varied, ranging from no oral treatment to indefinite antibiotic suppressive antibiotherapy. The cure rate was 94% [63].

Table 7 provides a synthesis of studies examining the duration of antibiotic therapy in cases of PJI managed through implant removal.

Table 7. Summary of Studies on Antibiotic Treatment Duration for Prosthetic Joint Infections managed by implant removal.

Author year Reference	Study design	Patients/ Prothesis site	Bacteria (major strains isolated)	Systemic antibiotics	Systemic antibiotics duration (days)	Local antibiotics	Mean follow up (Months)	Outcome Additional Intra operative positive Persistence/ Relapse

 doi:10.20944/preprints202505.2388.v1

								debridement cultures at reimplantation
Taggart et al., 2003 [64]	Prospective observational, single-center, non-comparative	33/Hip & Knee	93% Gram-positives 71% staphylococci	Not reported	5	Vancomycin	67	0% 9% 3%
Hoad-Reddick et al., 2005 [56]	Prospective observational, single-center, non-comparative	52/knee	63% staphylococci	None Cefuroxime as prophylaxis	1	Various	56	12% 16% 9%
Hart & Jones, 2006 [65]	Prospective observational, single-center, non-comparative	48/knee	96% Gram-positives 76% staphylococci	Vancomycin	14	Vancomycin+ gentamicin	49	13% 23% 13%
Stockley et al., 2008 [57]	Prospective observational, single-center, non-comparative	114/hip	61% staphylococci	None Cephalosporin as prophylaxis	1	Various	74	4% 16% 12%
Whittaker et al., 2009 [66]	Prospective observational, single-center, non-comparative	44/Hip	All Gram-positives 72% staphylococci	Vancomycin	14	Vancomycin+ gentamicin	49	7% 2% 7%

 doi:10.20944/preprints202505.2388.v1

McKenna et al., 2009 [58]	Retrospective, observational, single-center, non-comparative	31/Hip	All Gram-positives 77% staphylococci	Vancomycin	5	Various	35	0% 0% 0%
Mittal et al., 2007 [67]	Retrospective, observational, multicenter, comparative	37/knee	Methicillin-resistant staphylococci	Not reported	≥6 weeks IV vs. <6 weeks IV	Various	51	- 0% Short: 2/15 (13%) Long: 2/22: (9%) (p = 0.07)
Hsieh et al., 2009 [68]	Retrospective, observational, single-center, comparative	99/knee	67% Gram-positives 53% staphylococci	A first-generation cephalosporin and gentamicin	4–6 weeks vs. 7 days	Various	43	Long 2/46 (4%) - Long: 2/46 (4%) Short 1/53 (2%) Short: 3/53 (6%)
El Helou et al., 2011 [69]	Retrospective, observational, single-center, comparative, propensity score-adjusted	208/hip and knee	Mainly Gram-positives. 62% staphylococci	Not reported	4 weeks +/-7 d vs. 6 weeks +/-7 d	Vancomycin +/- Tobramycin	60	- Short: 6.1% Short: 16% Long: 8.7% Long: 27%
Benkabouche et al., 2019 [60]	Single-center, open, randomized clinical trial	39 /Hip & Knee	Various	Vancomycin IV Fluoroquinolones Oral	6 weeks (39-45 days) Vs 4 weeks (27–30 days)	Only 2 cases (5%); tobramycin	26	No significant difference was observed in the PJI group
Ma et al, 2020 [70]	Retrospective,	64/knee		Not reported	4–6 weeks vs.	Vancomycin (◎}	75	Need for salvage antimicrobi

 doi:10.20944/preprints202505.2388.v1

	observational, single-center, comparative		69% staphylococci		≤7 days	aminoglycosides)		als or surgery Long: 11/43 (26%); Short: 3/21 (14%)
Bernard et al., 2021 [32]	Multicenter, open, randomized clinical trial	81/Hip & knee	40% *S. aureus*	Rifampicin Fluoroquinolones	6 weeks vs. 12 weeks	Not reported	≥24	Failure: 6 w: 6/40 (15%); 12 w: 2/41 (5%) (p > 0.05) Difference: 10.1% (95%CI −0.9–22.2), longer antibiotic duration is recommended

RR: reinfection rate, FO: functional outcome, HSS: Hospital for Special Surgery knee score, IKS: International Knee Society Score, KSS: Knee Society Score, OKS: Oxford Knee Score, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index, TKR : total knee replacement, TKA : total knee arthroplasty, DAIR : debridement, antibiotics and implant retention, MRSA Methicillin-resistant *Staphylococcus aureus*, MRSE Methicillin-resistant *Staphylococcus epidermidis* 6.4.2. Arthrodesis.

This procedure was the traditional treatment of PJI. It is suitable for young, active patients in whom reconstructive alternatives have failed, particularly those presenting with osteoarticular infection, chronic pain, leg-length discrepancy, or rotational malalignment with success rates for infection control and fusion range from 88% to 94% and 75% to 88%, respectively [71-73].

Antibiotic duration is controversial for arthrodesis. Kutscha-Lissberg et al. have treated their patients with parenteral antibiotics, according to the resistance of germs. It was initiated just before the operation for at least 10 days and was continued up to 6 weeks orally [72].

6.4.3. Amputation

Above-knee amputation is considered an absolute last resort in the management of PJI following total knee arthroplasty, and is rarely indicated [16]. It may be the only viable treatment in cases of life-threatening systemic sepsis which can be managed with aggressive open debridement, continuous lavage, and the use of suction drains. When bone loss is so severe that arthrodesis is no longer feasible, amputation may be the only remaining option [16]. According to IDSA guidelines published in 2013, antibiotic therapy following amputation, generally only needs to be continued for 24 to 48 hours provided that all infected tissue has been completely removed and there is no evidence of ongoing infection elsewhere in the body, such as bacteremia or a deep-seated abscess [4].

These all studies tried to reduce the antibiotic duration for PJI, but they are faced to failure rate in some cases due to the difficulty in targeting biofilm-associated bacteria.

6.5. Discussion

In the past, we used to treat people for PJI for at least 3 months much longer than the 4 to 6 weeks normally recommended for bone and joint infections without orthopedic hardware [74]. The duration is essentially due to the difficulty in eradicating bacteria within biofilms [75].

In France, Bernard et al. undertook a multi-center, randomized controlled trial (DATIPO), in which they enrolled 410 patients suffering from hip or knee PJI. Participants were randomized to

 doi:10.20944/preprints202505.2388.v1

receive either 6 weeks or 12 weeks of antibiotic therapy, following surgical source control [32]. The primary outcome was infection persistence or recurrence within two years following cessation of antibiotic therapy, reported in 18.1% of the 6-week group vs. 9.4% of the 12-week group. The risk difference confidence interval precluded non-inferiority for the shorter course. Sub-group analysis revealed that inferior outcomes were accentuated in patients treated with DAIR, with an absolute risk difference of 16.2%. However, no significant differences in outcomes between 6- and 12-week regimens were observed in patients managed with one- or two-stage revision. These observations demonstrate the importance of retained infected hardware, as vital to determine the prognosis of treatment of PJI [32].

In a multicenter randomized controlled trial conducted in Spain, Lora-Tamayo and collaborators evaluated an 8-week antibiotic duration compared with 3- and 6-month length regimens in the treatment of staphylococcal PJI of the hip or knee treated with DAIR [28]. The intention-to-treat analysis showed non-inferiority of clinical cure, but the trial was conducted using fluoroquinolone–rifampicin treatment groups, and excluded patients with poor initial prognosis or high risk of early treatment failure [28].

Single-stage revision surgery has gained increasing popularity in the management of PJI. Studies on single-stage revision have reported promising results, with reinfection rates ranging from 5% to 25% [35-43], which are comparable to those seen with two-stage revision procedures (9% to 20%) [44].

The randomized controlled trial conducted by Benkabouche et al. found no significant difference in recurrence rates between 4- and 6-week antibiotic courses following the removal of orthopedic hardware [60].

In summary of these studies, the overall evidence suggests that antibiotic duration may be safely reduced to 6 weeks in selected patient groups particularly those with acute PJI at low risk of failure following DAIR, and those with chronic infections managed through revision surgery. The results of the SOLARIO trial are awaited [76]. It is a multicenter, open-label, randomized controlled non-inferiority study designed to compare short versus long systemic antibiotic therapy in conjunction with local antibiotic treatment for orthopedic infections. Participants will be randomized 1:1 to receive either a short course (≤ 7 days) or a standard long course (≥ 4 weeks) of systemic antibiotics. The primary endpoint is treatment failure within 12 months post-surgery, evaluated by an independent, blinded Endpoint Committee. A non-inferiority margin of 10% will be applied in both per-protocol and intention-to-treat analyses. One potential limitation of this study is that it encompasses all bone and joint infections, which may reduce the specificity of the findings for particular subgroups, such as PJI [76].

As mentioned earlier, the duration of antibiotics was prolonged due to biofilm-embedded bacteria. The switch to oral therapy is now possible and it has gained interest after the British randomized controlled trial OVIVA conducted in 2019 [19]. This study involved 1,054 patients with BJI. Participants were randomized to either switch to oral therapy within 7 days after surgery or continue with a full 6-week course of intravenous antibiotics, followed by additional oral therapy if necessary. Among the randomized patients, 61% had infections related to a foreign body, including prosthetic joints. The surgery procedures included DAIR, implant removal, or one- or two-stage exchange procedures [19]. The results showed that early oral treatment, administered to approximately 90% of patients in the oral therapy arm, was non-inferior to the prolonged intravenous antibiotic regimen in terms of treatment failure. This trial supports the early transition to oral antibiotics for complex orthopedic implant-related infections, provided that adequate surgical debridement is performed and an oral antibiotic with antibiofilm properties and sufficient bioavailability is available [19].

7. The Role of Biofilms in PJI Treatment

The formation of biofilms on implanted devices plays a crucial role in the onset and persistence of infections [15].

Biofilm formation is a key factor complicating PJI management, as bacteria within biofilms exhibit significant resistance to both antibiotics and host immune responses [1, 77]. The biofilm protects the bacteria via its matrix against antibiotics or immune cell attacks. This matrix is a polarized

 doi:10.20944/preprints202505.2388.v1

and contains proteins, polysaccharides, nucleic acids and lipids [78]. To penetrate biofilm, antibiotics should have proteins as a target and an extended duration is required. For more antibiotic efficiency, it is valuable to measure the biofilm matrix, biomass and viability [78].

Anti-biofilm molecules usually combine various compounds inhibiting the biofilm formation. They are mainly isolated from natural sources, or can be synthetic compounds. Chelating agents and antibiotics have also been found to possess anti-biofilm activity [78].

Studies have highlighted the importance of combining surgical debridement with biofilm-active antibiotics, such as rifampin in combination with a fluoroquinolone, to improve treatment outcomes [79,80].

Despite these strategies, the persistence of biofilm-related infections underscores the need for novel therapeutic approaches and further research into biofilm-targeted treatments [81].

Recently a phase 1 clinical study analyzing TRL1068, a native human monoclonal antibody that destabilize bacterial biofilms yielded promising results [81]. This is the first in-human research. It has the advantage of a broad-spectrum activity against both Gram-positive and Gram-negative species in PJI [81].

8. Future Perspectives

In recent years, artificial intelligence (AI) has become very popular in medical imaging, and convolutional neural networks have been widely used for their excellent performance, high accuracy, and short response time.

The diagnosis of PJI is challenging and costly. A missed or delayed diagnosis can have a tremendous impact on patients and put high financial strain on our healthcare budget. Advancements in artificial intelligence, molecular diagnostics and pathogen-specific treatments offer promising avenues for improving PJI management.

The BIOFIRE® Joint Infection Panel is a diagnostic test that utilizes multiplex PCR technology to identify microorganisms in synovial fluid samples from patients suspected of having septic arthritis in native joints or PJI with high sensitivity and specificity [82]. It allows a rapid microbiological diagnosis which could reduce empirical antibiotic treatment. Moreover, it improves bacterial identification especially in case with previous antibiotic treatment.

Next-generation sequencing (NGS) is being increasingly adopted for the diagnosis of PJI; however, its clinical value remains inadequately defined [83]. Shotgun metagenomic sequencing (sNGS) has shown promise in identifying pathogens in sonicate fluid that are missed by conventional culture methods. Despite its diagnostic potential, sNGS remains technically demanding and expensive. In this context, Hong et al. conducted a study in which 16S ribosomal RNA (rRNA) gene-based targeted metagenomic sequencing (tNGS) was evaluated alongside sNGS for microbial detection and identification in sonicate fluid samples from patients with failed total THA and TKA. 16S rRNA gene-based tNGS represents a promising diagnostic approach for identifying pathogens in sonicate fluid from failed total hip and knee arthroplasties, particularly in culture-negative PJI cases. Its performance characteristics are comparable to those of sNGS [83].

The integration of AI and machine learning (ML) into clinical decision-making could further sharpen PJI management by analyzing patient-specific factors and predicting optimal treatment strategies.

Machine learning is a subset of artificial intelligence that can mimic human thought processes and, in some cases, even surpass human capabilities. Developing an ML model typically involves dividing large datasets and their outcomes into training and test sets, which are then fed into a computer system. The system analyzes the data to identify patterns and creates an algorithm based on these associations. It generates an algorithm that can then be applied to make predictions or decisions on new, previously unseen data [84].

In a systematic review conducted by Chong et al. numerous parameters were discussed: prediction, diagnosis, treatment and prognosis [84]. The prediction of the early preoperative risk of PJI may help for a better optimization of surgery decisions. Machine learning may assist in the diagnosis of PJI in a manner distinct from the 2018 International Consensus Meeting (ICM) and the 2021 European Bone and Joint Infection Society (EBJIS) definitions, as they rely on neutrophil count

 doi:10.20944/preprints202505.2388.v1

and the positive high-power field number. In contrast, the ML model may bypass these parameters, as the diagnosis is not exclusively based on neutrophil count, but also incorporates several other infection indicators, such as tissue edema, capillary hyperplasia, and neutrophil infiltration and proliferation [5, 84, 85]. With regard to antibiotic prescription, as ML can generate infection predictions in a short time frame, it allows the early prescription of antibiotics [84]. Several ML models exhibit microbiological capabilities, including the identification of antibiotic susceptibility in pathogens associated with clinical failure, particularly non-culturable PJI pathogens, which are implicated in 5%–42% of PJI cases [84].

To improve treatment outcomes, it is essential to make an early and accurate decision regarding the appropriate therapeutic approach and to optimize the patient's condition preoperatively. ML may assist in identifying patients who require such optimization to ensure a better prognosis [84, 86].

Recently a novel ML-derived PJI "in-time" diagnostic system constructed by Chen et al. have demonstrated significantly improved diagnostic potency for surgical decision-making compared with the commonly used criteria [86]. The sensitivity and precision of this model were significantly higher than those observed in the ICM 2018 in their development cohort (90.6% vs. 76.1%, p = 0.032; 94.5% vs. 86.7%, p = 0.020) and in the internal validation cohort (84.2% vs. 78.6%; 94.6% vs. 81.8%) [86].

9. Conclusions

This review underscores the complexity and variability of antibiotic therapy duration in PJI management, highlighting the need for a more standardized and evidence-based approach. While current practices often rely on prolonged courses, emerging data suggest that shorter durations may be effective in select cases, reducing the risks associated with extended antibiotic use. Future research should focus on multicenter trials, advanced diagnostics, and innovative therapeutic strategies to address the persistent challenges in PJI treatment. By leveraging technological advancements and fostering collaboration, the orthopedic and infectious disease communities can improve outcomes for patients with this challenging condition.

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