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# Effectiveness of Postoperative Systemic Antibiotic Prophylaxis Following Cardiovascular Implantable Electronic Device Implantation: A Systematic Review and Meta-Analysis

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**Abstract**

Background

Cardiac implantable electronic devices (CIED) represent established life-sustaining interventions for various cardiac conditions, but post-placement infections are associated with high morbidity and mortality. Although pre-procedural antibiotic prophylaxis effectively reduces CIED infection rates, limited data exist on post-procedural antibiotic use, especially beyond 24 hours. This study assesses the efficacy of post-procedural antibiotic usage in preventing CIED placement-related infections.

Methods

We conducted a systematic review and meta-analysis, including studies that examined the comparative outcomes among patients. The study cohorts were divided into two groups: (1) those who underwent preoperative antibiotic prophylaxis followed by a continuation of 24 hours or more postoperatively (intervention group); and (2) those who received either preoperative-only antibiotic prophylaxis or preoperative prophylaxis with a duration of less than 24 hours postoperatively (control group). Risk of bias was assessed with ROBINS-I and ROB-2 tools. Risk ratio (RR) was pooled using random-effect or fixed-effect meta-analyses with inverse variance method.

Results

Our analysis of ten studies, including four randomized controlled trials and six cohort studies with 27,375 participants, revealed no statistically significant differences in outcomes between two groups. These outcomes included (CIED) infection rates (RR 0.83, 95% CI 0.47, 1.44), mortality (RR 1.22, 95% CI 0.66, 2.25), pocket hematoma (RR 1.01, 95% CI 0.54, 1.92) and re-intervention (RR 0.71, 95% CI 0.20, 2.50). The larger randomized controlled trial had an obvious impact on the overall findings.

Conclusions

The present systematic review and meta-analysis found no advantage in extending postoperative antibiotic prophylaxis for more than 24 hours following (CIED) implantation. These findings align with prevailing guidelines which support antibiotic stewardship practices. This approach has the ability to reduce adverse drug events, curb the potential for antibiotic resistance and alleviate the financial burdens associated with prolonged postoperative antibiotic prophylaxis.

**Key words:** infection; post-operative; antibiotic; cardiovascular

## Introduction

Cardiac implantable electronic devices (CIEDs) were initially introduced for therapeutic applications in the 1960s[2,1] . Subsequently, there has been steady growth in CIED implantation worldwide due to the wide spectrum of clinical indications and an augmented prevalence of cardiovascular comorbidities within the public [3, 4]. Besides the escalating utilization of CIEDs, there has been a surge in the frequency of CIED infections [5, 6].

As CIED infection usually mandates complete device removal, efforts to prevent infection are paramount[7]. In addition to optimizing modifiable risk factors, patients identified as at higher risk of infection are likely to have benefit from infection prevention strategies, such as antibiotic-eluting envelopes, pre-operative antiseptic preparation, sterile techniques, leadless device systems or preoperative and postoperative antibiotic regimens[8].

Preoperative antibiotic prophylaxis has consistently been shown efficacy in diminishing the occurrence of cardiac implantable electronic device (CIED) infections[1]. A previous meta-analysis and a substantial randomized, double blinded, controlled trial have provided obvious evidence that preoperative systemic antibiotic prophylaxis obviously reduces the risk of cardiac implantable electronic device (CIED) infection[9]. Furthermore, in 2009 a randomized controlled trial which aimed at assessing the efficacy of antibiotic prophylaxis proved reduced rates of CIED infection in patients administered preoperative Cefazolin compared to those receiving a placebo[10]. Consequently, existing guidelines universally endorse the administration of a singular preoperative systemic antibiotic prophylaxis dose, ideally administered 1-2 hours prior to CIED implantation [1, 11].

In accordance with clinical surveys, the utilization of postoperative systemic antibiotic prophylaxis persists as a prevalent practice across numerous institutions globally[2, 12]. This approach entails the administration of supplementary doses of antibiotic prophylaxis after the surgical procedure or the continuation of antibiotic prophylaxis for more than 24 hours after the moment of implantation [13, 14]. Realistically, there is no available data to advocate for the impact of post-procedural antibiotic therapy on rates of CIED infection when used in addition to pre-procedural therapy.

Given the limited available data on the efficacy of Post-operative antibiotic therapy, Our study is supposed to conduct a systematic review comparing outcomes associated with two distinct strategies of systemic antibiotic prophylaxis: (1) administration preoperatively with continued dosage for 24 hours or more postoperatively, and (2) preoperative administration alone or preoperative administration followed by less than 24 hours of postoperative dosage.

## Methods

### Design of the examination

We executed a systematic review and meta-analysis, including studies that compared the results of two patient cohorts: (1) those subjected to preoperative antibiotic prophylaxis along with 24 hours or more of postoperative administration (intervention group); and (2) those administered either preoperative-only prophylaxis or preoperative plus postoperative prophylaxis for less than 24 hours (control group). Risk of bias was assessed with ROBINS-I and ROB-2 tools. Risk ratio (RR) was pooled using random-effect or fixed-effect meta-analyses with inverse variance method. Multiple databases, such as OVID, PubMed, the Cochrane Library and Google Scholar, were systematically utilized to gather and scrutinize data. These datasets were employed to analyses that compared and evaluated the consequences of prolonging antibiotic administration beyond the initial 24 hours post-operatively.

### Data pooling

Temporal constraints were imposed within the years 2000 to 2023, excluding animal model studies. Language restrictions were not applied. The outcomes were confined to randomized controlled trials (RCTs) or cohort studies. A controlled vocabulary, complemented by relevant keywords, was employed to search for studies explaining postoperative antibiotic prophylaxis subsequent to Cardiac Implantable Electronic Device (CIED) implantation. Figure 1 illustrates the complete process of examination identification.

### Inclusion criteria:

Inclusion criteria involved randomized controlled trials (RCTs) or cohort studies conducted between 2000 and 2023, as routine antibiotic prophylaxis did not constitute standard care before 2000. The eligible studies investigated outcomes in patients undergoing Cardiac Implantable Electronic Device (CIED) implantation, distinguishing between those in the "intervention group" who received preoperative antibiotic prophylaxis along with 24 hours or more of postoperative systemic administration and those in the "control group" who received either solely preoperative prophylaxis or preoperative plus postoperative prophylaxis lasting less than 24 hours. Cardiac Implantable Electronic Devices (CIED) covered automated implantable cardioverter defibrillators (AICD), dual chamber implanted cardioverter defibrillator system, cardiac resynchronization therapies (CRT) either up-grade or generator replacement and permanent pacemakers (PPM). CIED implantation, constituting initial implantation, re-implantation, device upgrade, device revision and generator exchange, formed the scope of our study. The primary endpoint of this study was the occurrence of Cardiac Implantable Electronic Device (CIED) infection necessitating the removal of the system within 6 months post-procedure. CIED infection was comprehensively defined to include CIED pocket infection or erosion, CIED device and lead-related endocarditis on the right side, native valve endocarditis on the left side or recurrent occult gram-positive bacteremia lacking an evident source.

A secondary outcome of interest in this investigation pertained to hematoma formation. Hematoma was characterized by persistent pocket swelling with ecchymosis documented in a digital photograph of the chest wall taken during the 2- to 4-week follow-up visit.

### Exclusion criteria:

The exclusion criteria were defined as follows: (1) studies incorporating left ventricular assisted devices (2) studies employing only non-systemic antibiotic prophylaxis, such as topical antibiotic irrigation or antibiotic envelopes without concurrent systemic antibiotic prophylaxis (3) studies conducted on animal models and (4) conference

abstracts lacking sufficient data.

**Screening of studies**

The titles and abstracts obtained by the search underwent screening, with subsequent review of full texts for potentially eligible studies. Data extraction from eligible studies included baseline demographic information, CIED type and procedures, antibiotic prophylaxis class and duration and pertinent outcomes, facilitated through the utilization of a standardized electronic spreadsheet. Two unidentified reviewers assessed the potential bias and methodological quality of each study. They objectively evaluated the methods employed in each examination.

**Statistical analysis**

The quantification of outcomes in both the intervention and control groups was extracted. The calculation of the Risk Ratio (RR) with a corresponding 95% confidence interval (CI) was performed. The collective RR and 95% CI from all studies were pooled through random-effect or fixed-effect meta-analyses utilizing the inverse variance method. Construction of a Forest plot ensued. The I2 statistic was employed to assess statistical heterogeneity of effect size across the incorporated studies. Predefined subgroup analyses were performed based on study design, the number of antibiotic doses in the control group, the presence or absence of antibiotic pocket irrigation and the presence of hematoma. Sensitivity analysis was also conducted to explore heterogeneity. All statistical analyses were conducted using Review Manager (RevMan) version 5.4, developed by The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen.

**Results**

In our search, a total of 1173 articles were identified. Subsequently, 100 articles underwent full-text review, with ten studies meeting the eligibility criteria for inclusion in the final analysis.

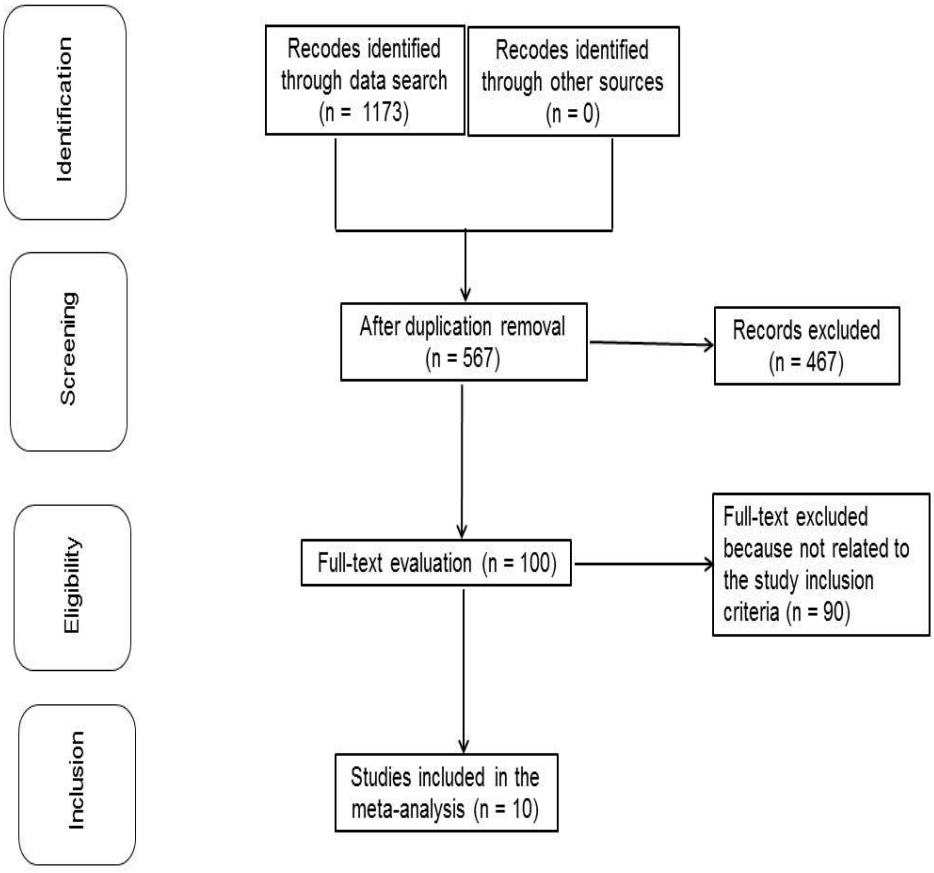


Figure 1: The PRISMA 2020 flow diagram for a new systematic review which included searches of databases only.

**Studies characteristics:**

The included studies comprised six cohort studies [20-15] and four randomized controlled trials (RCTs) [21-24] as shown in table 1. All publications fell within the timeframe of the past two decades, with the earliest study being conducted in 2001. A comprehensive analysis involved a total of 27,375 patients, with 14,275 in the intervention group and 13,100 in the control group. Within the intervention group, the postoperative systemic antibiotic prophylaxis duration spanned from more than 2 days to 14 days, with one study omitting the reporting of this specific duration[20]. Variability was observed in the route of administration and class of antibiotic across the studies. In the control

group, four studies employed a singular preoperative systemic antibiotic prophylaxis dose [17, 20, 21, 24]. Another four studies adopted a two-dose regimen, wherein the initial dose was administered preoperatively, followed by a postoperative dose within 24 hours [15, 16, 18, 19]. A singular study integrated a three-dose protocol, involving one preoperative administration and two postoperative doses within 24 hours [23]. An additional study implemented a five-dose regimen, consisting of one preoperative dose and four postoperative doses [25]. Preoperatively, intravenous Cefazolin was utilized in all cases except for three, In the initial case [18], intravenous amoxicillin-clavulanate was administered, the second instance [25], involved the use of cloxacillin, while the third [24] did not specify the type of cephalosporin employed. In instances involving penicillin-allergic patients, two studies [18, 19] employed clindamycin, three studies [16, 21, 24] opted for vancomycin, and the remaining studies lacked information on this aspect. Moreover, four studies [16, 20, 21, 24] incorporated alternative non-systemic antibiotic prophylaxis, which consisted of pocket irrigation with Bacitracin [16, 21], Vancomycin powder [16], Polymyxin-B/bacitracin [24], Neomycin/bacitracin [24], Amikacin/bacitracin [24] and unspecified antibiotic solutions [20].

**TABLE 1.** Baseline characteristic of included studies

| Year | Study | Country | Total |
|---|---|---|---|
| 2001 | Dwivedi, 2001 [25] | India | 90 |
| 2012 | Uslan, 2012 [20] | California | 586 |
| 2013 | Chiang, 2013 [15] | Taiwan | 136 |
| 2014 | Senaratne, 2014 [19] | Canada | 1972 |
| 2017 | Lee, 2017 [17] | Taiwan | 257 |
| 2018 | Krahn, 2018 [21] | Canada | 9976 |
| 2019 | Kabulski, 2019 [16] | USA | 401 |
| 2019 | Madadi, 2019 [23] | Iran | 150 |
| 2022 | Malagù, 2022 [18] | Italy | 202 |
| 2023 | Ellis, 2023 [24] | U.S | 505 |
| | | **Total** | **14275** |

**Risk of bias:**

Regarding cohort studies, three studies [15, 18, 19] were classified as presenting a substantial risk of bias primarily attributed to pre-intervention confounding factors, such as vivid distinctions in clinical characteristics between the two groups, comparisons involving disparate sets of historical data or the selection of intervention types based on patient preference. The remaining studies [16, 17, 20] exhibited a moderate risk of bias due to confounding and challenges in the outcome measurement.

Concerning randomized controlled trials (RCTs), one study [23] raised some concerns regarding the risk of bias associated with the randomization process (including allocation sequence randomization, concealment, and blinding), outcome measurement issues (unclear pre-specified analysis plan) and the selection of reported results (as it remained unclear whether all results were reported). The second study [24] raised concerns about potential biases due to the non-standardized use of intraoperative antibiotic wash, influenced by hospital pharmacy committee decisions and physician preferences, suggesting more favorable outcomes with specific regimens, compounded by the lack of placebo control or blinding for postoperative oral antibiotic use, and further impacted by enrollment slowdown from the COVID-19 pandemic and supply chain issues, potentially limiting the sample size. Another one study [21] was considered to have a low risk of bias. The remaining study [25] did not mention it.

**CIED infection:**

All studies designated CIED infection as their primary outcome. The duration of follow-up post-implantation varied across studies, ranging from 3 months to 5 years. No significant difference in the risk of CIED infection was observed between the intervention and control groups, yielding a pooled Risk Ratio (RR) of 0.83 (95% CI 0.47, 1.44, p-value = 0.50, I2 = 63%) as shown in figure 2. The combined relative risks (RRs) remained consistent across subgroup analyses, when they were stratified based on the number of antibiotic doses in the control group. They produced a pooled Risk Ratio (RR) of 0.82 (95% CI 0.63, 1.09, p-value = 0.17, I2 = 0%) in investigations which used only one dose in the control group as shown in figure 3, at the same time, studies where control group had more than one antibiotic dose yielded a pooled Risk Ratio (RR) of 0.68 (95% CI 0.23, 2.01, p-value = 0.48, I2 = 77%) as shown in figure 4. Additionally, there was no alteration in the pooled RRs when considering the presence of antibiotic pocket irrigation with a pooled Risk Ratio (RR) of 0.80 (95% CI 0.61, 1.03, p-value = 0.09, I2 = 0%) as shown in figure 5 or absence of antibiotic pocket irrigation with a pooled Risk Ratio (RR) of 0.83 (95% CI 0.21, 3.27, p-value = 0.79, I2 = 78%) as shown in figure 6. This indicates a stable and uniform effect regardless of variations in the number of doses or the use of antibiotic pocket irrigation.

A sensitivity analysis was performed by excluding a study [19] with an extreme outlier result to investigate

heterogeneity. The pooled risk ratios did not show significant changes, but the I2 statistic shifted to zero as shown in figure 7.

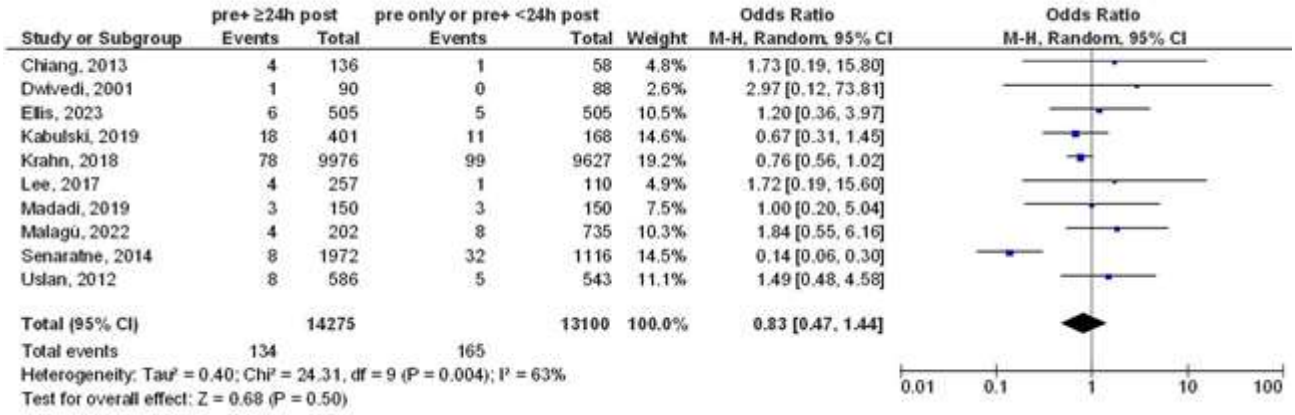


Figure 2: Forest plots display pooled risk ratios for CIED infection.

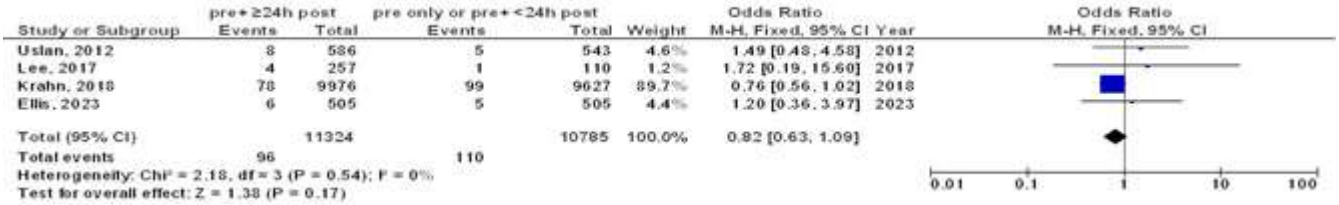


Figure 3: Control groups administered a single antibiotic dose.

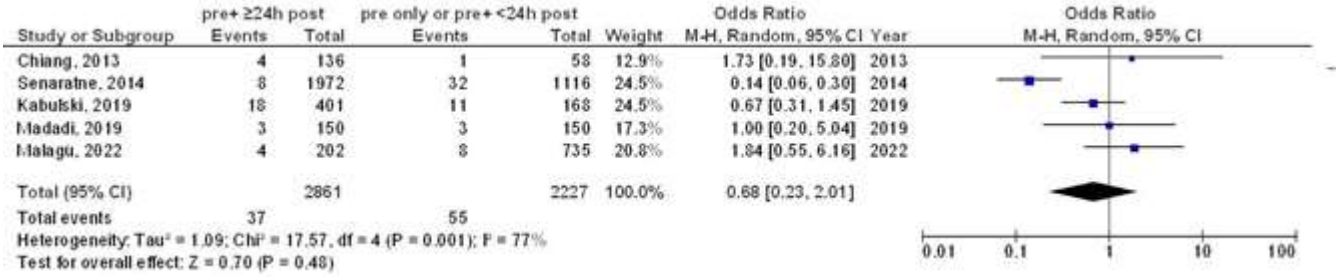


Figure 4: Control groups administered more than one antibiotic dose.

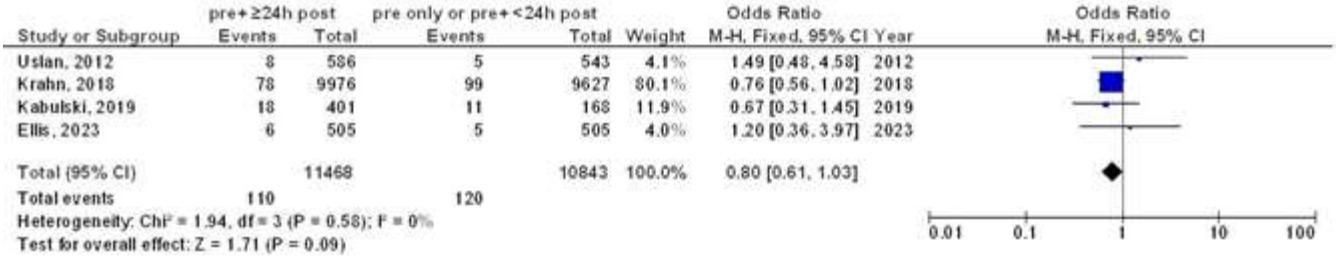


Figure 5: The presence of antibiotic pocket irrigation.

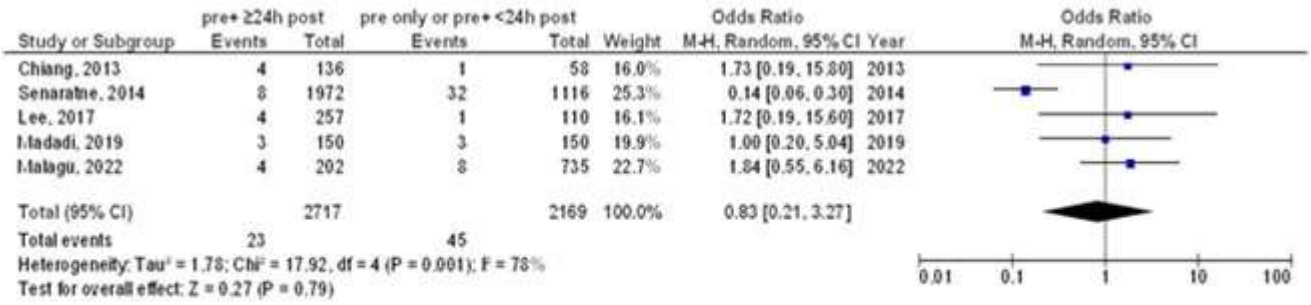


Figure 6: The absence of antibiotic pocket irrigation.

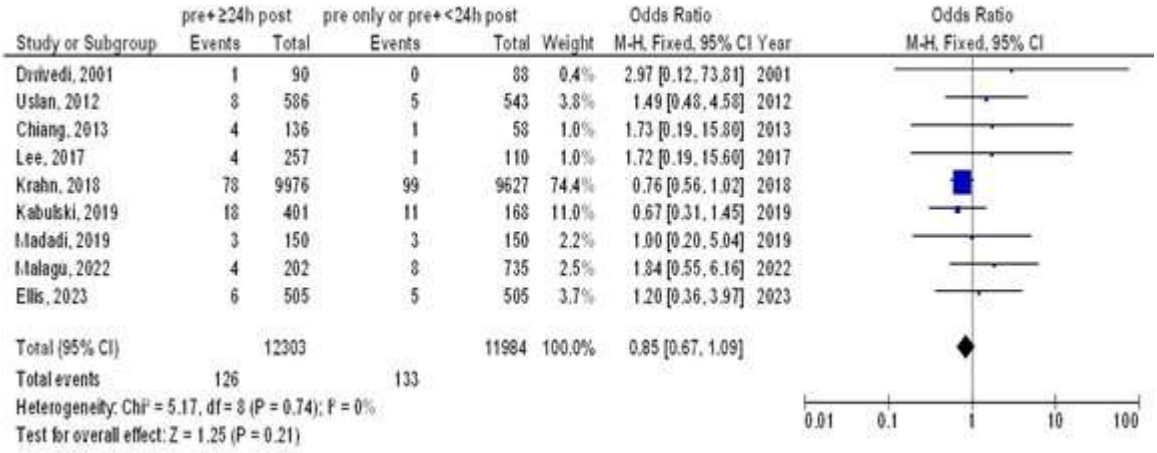


Figure 7: Forest plots of pooled risk ratios for CIED infection after excluding the outlier study.

**Mortality:**

Two studies involving 20,540 patients documented instances of all-cause mortality as shown in figure 8. One study continued for a follow-up period of 250 days[18], while the other extended to 1-year observation duration[21]. The comparative risk assessment revealed no difference in mortality outcomes between the two groups, yielding a pooled risk ratio (RR) of 1.22 (95% CI 0.66, 2.25, p-value = .53, I2 = 85%).

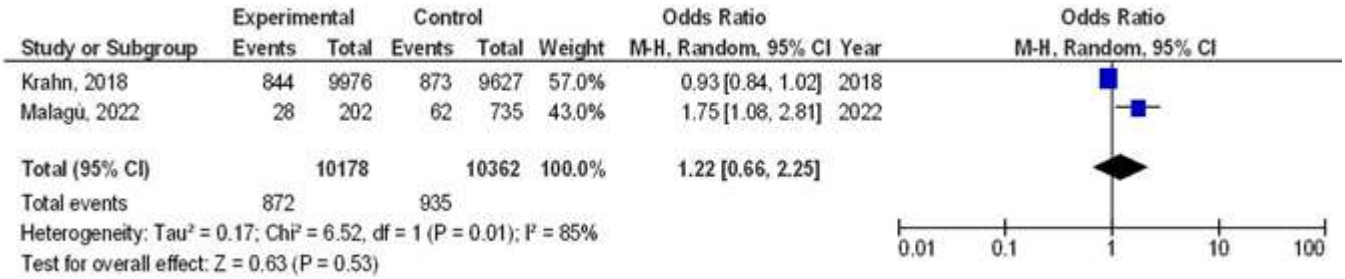


Figure 8: the pooled risk ratio for mortality.

**Other outcomes:**

Three investigations [16, 18, 24] containing a collective participant pool of 2516 individuals, documented the frequency of re-intervention with a pooled risk ratio (RR) of 0.71 (95% CI 0.20, 2.50, p-value = .59, I2 = 70%). as shown in figure 9. Regarding the first investigation [18] the control cohort experienced early reoperation in 14 cases, while the

intervention group encountered 7 instances. In the second study [24] the control group exhibited early reoperation (pocket reentry <2 weeks) in two instances, whereas none were noted in the study group. As for the third study [16], about 15 cases of the control group required re-intervention, while 16 of the intervention group did.
Moreover, five studies, comprising a cumulative cohort of 3077 patients, documented the incidence of pocket hematoma with a pooled risk ratio (RR) of 1.01 (95% CI 0.54, 1.92, p-value = .97, I2 = 61%)[15-18, 24] as shown in figure 10. Additionally, a singular study [21] exclusively reported adverse drug events related to antibiotic prophylaxis. The recorded incidence of adverse drug events, inclusive of renal failure, gastrointestinal upset, diarrhea, allergic reactions, and Clostridioides difficile infection, stood at 0.26%. Importantly, no statistically significant difference was observed between the intervention and control groups.

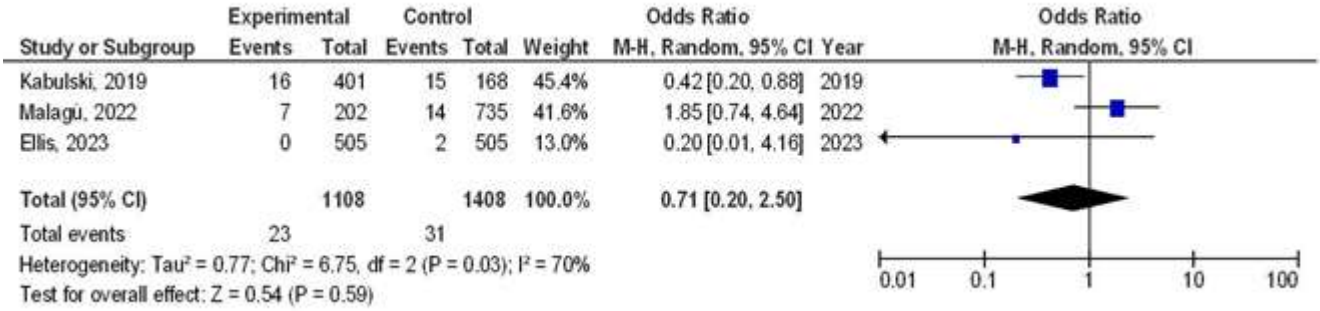


Figure 9: the pooled risk ratio for re-intervention.

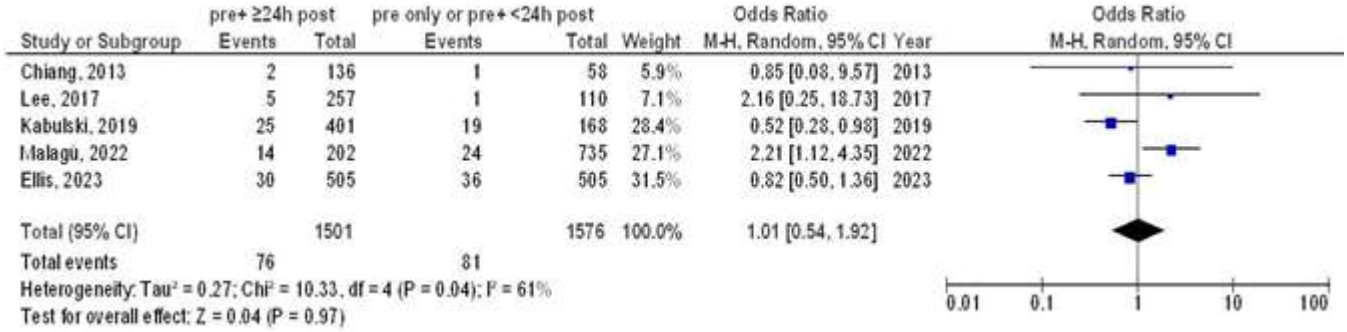


Figure 10: the pooled risk ratio for pocket hematoma.

**Discussion**

Cardiac implantable electronic devices (CIED) are crucial interventions for various heart conditions [26]. However, infections following CIED placement can lead to serious health issues and increased mortality[27]. In accordance with findings from two recent randomized controlled trials, the incidence of CIED infection at 12 months is estimated to vary widely (range 1%–7%) [4, 28]. Considering the substantial morbidity, mortality and financial healthcare implications associated with CIED infections [1], there exists a pivotal imperative for the development and implementation of effective, evidence-based preventive measures and management strategies [29].
CIEDs consist of two principal components: the pulse generator, typically housed within a subcutaneous or sub-muscular pocket, and the leads [9]. Therefore, infections related to CIED can be obviously categorized into three main types: superficial infections, isolated pocket infections, and lead infections, the latter potentially associated with bacteremia and/or endocarditis[1]; however, the majority of CIED infections are attributed to the pocket [1, 5, 30]. Lead infection may manifest independently of pocket infections, highlighting the potential for separate occurrences of these distinct infection types [2, 31].
The majority of cardiac implantable electronic device (CIED) infections are associated with gram-positive microorganisms [32], particularly Coagulase-Negative Staphylococci (CoNS) species followed by Staphylococcus aureus (S. aureus) as the predominant isolates [4, 6, 33]. Methicillin-resistant Staphylococcus aureus (MRSA) represents approximately one third of S. aureus infections and is indicative of a more unfavorable clinical outcome [6]. Non-Staphylococcal CIED infections, accounting for up to 20% of cases, involve diverse pathogens such as gram-negative bacilli, Enterococci, Streptococci and fungal species [34]. Notably, about 15% of CIED infections present as culture-negative [6], attributed to factors such as prior antibiotic therapy to blood culture, localized pocket-site infections and the involvement of fastidious or atypical bacteria. It is documented that there is a 16% overall 1-year mortality rate in patients with Staphylococcal-related CIED infections, underscoring the severity of such cases [31, 33]. In contrast, non-Staphylococcal CIED infections exhibit a more favorable prognosis, with an overall mortality rate of 4% [31].

The clinical manifestation of cardiac implantable electronic device (CIED) infections exhibits considerable variability and is dependent on several factors, including site of infection and the virulence of the causative organism [2, 6]. Infections can be classified temporally: early infections occur within 1 month of the procedure, late infections within 1-12 months, and delayed infections occur 12 months following the procedure [5, 35]. Predominantly, CIED infections manifest within the first 6 months [2]. While early infections frequently present as localized pocket infections, and late infections tend to manifest as systemic infections [5, 36], the timing of infection following procedure alone does not reliably discriminate between localized or systemic infections [28].

Risk factors for CIED infection can be subdivided into patient-related, procedure-related, and device-related [1, 2, 37]. These can be further classified as being modifiable or non-modifiable [38].

Postoperative hematoma stands out as an identified risk factor for CIED infection [39]. The Bridge or Continue Coumadin for Device Surgery Randomized Controlled trial (BRUISE-CONTROL) provided evidence that individuals with a history of clinically significant hematoma—defined by the necessity for further surgery and/or prolongation of hospitalization of >24 hours and/or necessitating coagulation interruption—exhibited a CIED infection rate of 11% in contrast to the 1.5% rate observed in those without hematoma[13]. Re-intervention, conducted for hematoma and lead displacement, also correlates with higher risk of subsequent device infection [2].

Considering the seven-fold augmented risk of subsequent device infection associated with postoperative hematoma, imperative measures for hematoma reduction are important. These include the application of pressure dressings, electro-cauterization, hemostatic agents, and the appropriate management of antiplatelet and anticoagulant therapy as well as the application of antibiotic-impregnated sponges within the pocket is undertaken to furnish tamponade during the insertion of leads [40].

The complete and immediate removal of all hardware is the recommended treatment for patients with established cardiovascular implantable electronic device infection [33, 34]. Although antimicrobial therapy serves as an adjunct in the management of Cardiac Implantable Electronic Device (CIED) infections, the removal of the device is imperative and should not be deferred, irrespective of the timing of antimicrobial therapy initiation. In order to avoid the elevated relapse rates of infection associated with retained hardware [1, 41].

Current international guidelines, informed by primary literature and meta-analyses, advocate for the administration of pre-procedural antibiotics to prevent infectious complications post-Cardiac Implantable Electronic Device (CIED) implantation [1, 11]. In contrast, there is limited supportive evidence for the use of postoperative antibiotics, and the decision seems to be influenced by physician preference and, potentially, a subjective evaluation of patient risk, as observed in various institutions.

This comprehensive systematic review and meta-analysis including ten studies and involving a total of 27,375 patients was undertaken to address a pertinent clinical question—whether prolonged postoperative systemic antibiotic prophylaxis following cardiac implantable electronic device (CIED) implantation offers any benefits. Despite the prevalent practice of employing postoperative antibiotic prophylaxis [38], our study findings revealed that the addition of post-procedural antibiotics would yield no significant benefits and no difference in the risk of CIED infection, mortality, pocket hematoma, or the need for re-intervention between patients receiving preoperative plus 24 hours or more of postoperative systemic antibiotic prophylaxis and those receiving either only preoperative prophylaxis or preoperative plus less than 24 hours of systemic antibiotic prophylaxis. Furthermore, the investigation delved into the impact of postoperative antibiotic prophylaxis specifically within a high-risk cohort across three studies [18, 21, 24], revealing an absence of demonstrable benefits in this subgroup of patients. It is clear to highlight that the outcomes derived from our examination predominantly originated from a comprehensive Randomized Controlled Trial (RCT): Prevention of Arrhythmia Device Infection Trial (PADIT) [21]. The trial revealed that postoperative antibiotic prophylaxis did not effectively prevent CIED infection. Our analysis indicated a consistency in the risk ratio across all studies, aligning closely with the PADIT trial's effect estimate. Additional Randomized Controlled Trials (RCT) [22, 24] yielded concordant results, albeit with a smaller sample size. Even though the PADIT study showed a lower CIED infection rate than expected, the overall absolute effect, calculated from the data of six other cohort studies, suggests that around 120 patients would need postoperative antibiotic prophylaxis to prevent one CIED infection. When considering individual cohort studies reflecting real-world practice, five studies [15-18, 20] did not find any advantage in postoperative antibiotic prophylaxis, while one study [19] showed a positive result with a lower CIED infection rate. This study contrasted patients undergoing CIED implantation in the "perioperative antibiotic-only era" (1993-1999) with those in the "postoperative antibiotics era" (1999-2009). The findings revealed a decreased rate of CIED infection in the "postoperative antibiotics era" group. However, the authors acknowledged in the limitation section that changes in CIED implantation practices over the years might introduce bias, making it challenging to extrapolate and apply the study's results effectively. All six studies exhibit a moderate to serious risk of bias, primarily attributed to pre-intervention unadjusted confounders—a common occurrence in non-Randomized Controlled Trial (RCT) studies. Hence, the findings from the PADIT trial alone should be considered adequate to inform current clinical practices.

Preoperative antibiotic prophylaxis has proven effective in various studies [42] and is recommended by the current Centers for Disease Control and Prevention Guideline for preventing surgical site infections, including in CIED implantation [37]. Our review found no convincing support for the use of postoperative systemic antibiotic prophylaxis, both short and long term. Although the PADIT trial showed no difference in adverse events, unnecessary antibiotic

use can lead to substantial costs, patient burden, and antibiotic resistance.

In contrast to the PADIT trial, a recent large Randomized Controlled Trial (RCT), the Antibacterial Envelope to Prevent Cardiac Implantable Device Infection (WRAP-IT) [30], revealed a lower incidence of CIED infection at the 1-year follow-up for patients who received an adjunctive, absorbable, antibiotic-eluting envelope compared to those without the envelope. The envelope releases minocycline and rifampin locally within the pocket for a minimum of 7 days post-operatively. The study authors noted that pre- and post-operative systemic antibiotic prophylaxis was not controlled, leaving uncertainty about its impact on outcomes. This prompts the question of whether local postoperative antibiotic prophylaxis reduces the risk of CIED infection, a benefit not observed with systemic antibiotic prophylaxis beyond 24 hours. Speculation arises about potential differences in tissue concentrations of antibiotics at the implantation site between local and systemic prophylaxis [7, 43, 44], potentially explaining the variation in efficacy. However, direct comparisons of tissue concentrations at the time of device implantation are lacking in current studies.

A recent study [24] indicates that the utilization of TYRX-a, an antibiotic envelope containing minocycline and rifampin, led to a decreased incidence of major Cardiac Implantable Electronic Device (CIED) infections compared to standard infection prevention strategies alone. These conventional strategies include peri-procedural antibiotics, pocket wash, or post-procedure antibiotics.

Our study presents several limitations. Firstly, heterogeneity among the studies was observed, mainly stemming from one outlier study [19] that demonstrated the benefit of postoperative antibiotic prophylaxis, as discussed earlier. Upon its exclusion, the overall I2 shifted to zero. Secondly, variations in antibiotic class and timing may have influenced the results. An ideal scenario would involve a direct comparison between patients receiving preoperative antibiotic prophylaxis and those with a similar duration of postoperative antibiotic prophylaxis. However, most studies administered antibiotic doses post-surgery with varying durations, making it challenging to find studies meeting these strict criteria. Additionally, factors such as the type of device, diverse patient populations and disparate follow-up times contribute to the complexity. Thirdly, the certainty of evidence across all studies remained low, primarily due to the risk of bias in cohort studies. Nevertheless, this should not undermine the overall message conveyed by our investigation.

In conclusion, despite being a widespread practice, our study highlights that postoperative antibiotic prophylaxis following Cardiac Implantable Electronic Device (CIED) implantation, especially when administered beyond 24 hours, does not contribute to a reduction in the risk of CIED infection, mortality, pocket hematoma, and re-intervention. The current evidence does not support the necessity of prolonged postoperative antibiotic prophylaxis in the context of CIED implantation.

**Conclusions**

The present systematic review and meta-analysis revealed no advantage associated with postoperative antibiotic prophylaxis exceeding 24 hours following Cardiac Implantable Electronic Device (CIED) implantation. These findings match with the recommendations outlined in contemporary guidelines, advocating for antibiotic regulation. Implementation of such practices may yield reductions in adverse drug events, mitigate the potential for antibiotic resistance and alleviate the financial burdens associated with prolonged postoperative antibiotic prophylaxis.

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