ORIGINAL ARTICLE

Comparison of Outcomes after Six Weeks Versus Two Weeks of In-Hospital Intravenous Antibiotic Therapy in Culture-Positive Infective Endocarditis: A Prospective Comparative Study at Tertiary Care Setting, Multan

Rashid Minhas*, Imran Javaid, Muhammad Iqbal

ABSTRACT

Objective: To compare the clinical outcomes of a standard 6-week intravenous antibiotic regimen with a shortened 2-week regimen in patients with culture-positive infective endocarditis.

Study Design: Prospective comparative study.

Place and Duration of Study: The study was conducted at the Department of Cardiology, Chaudhry Pervaiz Elahi Institute of Cardiology (CPEIC), Multan, Pakistan, from January 2023 to January 2024.

Methods: A total of 86 adult patients diagnosed with culture-positive infective endocarditis according to the modified Duke criteria were enrolled. Participants were allocated in groups in a 1:1 ratio using a computer-generated sequence with allocation concealment. Allocation was stratified by baseline risk status (low vs higher risk for infective endocarditis) to ensure balanced group distribution. Owing to the nature of treatment duration, blinding of participants and treating physicians was not feasible; however, outcome assessment and data analysis were performed by investigators blinded to treatment. The first group received a 6-week course of pathogen-directed intravenous antibiotics, while the second group received a 2-week course. Baseline demographics, type of endocarditis, complications at presentation, and pathogen profiles were recorded. Patients were monitored during hospitalization and followed for six months after discharge. The primary composite outcome included all-cause mortality, relapses or persistent bacteremia, unplanned cardiac surgery, or major embolic events. Secondary outcomes included individual mortality rates, relapse, treatment success, and hospital stay. Statistical analyses were performed using SPSS version 26.0.

Results: The primary composite endpoint occurred more frequently in the 2-week group (32.6%) than in the 6-week group (16.3%). In-hospital mortality (27.9% vs 14.0%) and six-month mortality (37.2% vs 20.9%) were also higher with the shorter regimen. Relapses or persistent bacteremia was more common in the 2-week group (18.6% vs 7.0%). The 2-week regimen significantly reduced hospital stay (median 20 vs 45 days).

Conclusion: A 6-week regimen remains the more reliable and safer treatment strategy.

Keywords: *Anti-Bacterial Agents, Bacteremia, Endocarditis, Intravenous Infusions, Treatment Outcome.*

How to cite this: *Minhas R, Javaid I, Iqbal M. Comparison of Outcomes after Six Weeks Versus Two Weeks of In-Hospital Intravenous Antibiotic Therapy in Culture-Positive Infective Endocarditis: A Prospective Comparative Study at Tertiary Care Setting, Multan. Life and Science. 2026; 7(1): 54-60. doi: http://doi.org/10.37185/LnS.1.1.1056*

Introduction

Infective endocarditis (IE) remains a life-threatening condition characterized by microbial infection of the endocardial surface, often involving heart valves, with significant global morbidity and mortality rates ranging from 10-30% despite advances in diagnostics and therapy.[1] In resource-constrained populations, e.g., in Pakistan, there are additional challenges to IE, such as a greater involvement of native valves because of underlying rheumatic heart disease, late diagnosis, and suboptimal access to multidisciplinary care, which results in worse

Department of Cardiology
Chaudhry Pervaiz Elahi Institute of Cardiology (CPEIC), Multan, Pakistan
Correspondence:
Dr. Rashid Minhas
Assistant Professor, Cardiology
Chaudhry Pervaiz Elahi Institute of Cardiology (CPEIC), Multan, Pakistan
E-mail: rashidminhas178@gmail.com

Received: Mar 13, 2025; 1st Revision Received: Jun 25, 2025
2nd Revision Received: Sep 15, 2025; Accepted: Sep 22, 2025

outcomes than in high-income populations.[2] Traditional management of culture-positive IE relies on prolonged intravenous (IV) antibiotic therapy for 4-6 weeks to ensure bacteriological cure and prevent complications like relapse, embolic events, or heart failure, as recommended by contemporary guidelines.[3] There are, however, new signs that shorter IVs or an earlier switch to oral antibiotics in carefully-chosen stable patients could be equally noninferior and could lead to shorter hospitalization, reduced healthcare costs and less adverse events associated with IVs without decreasing efficacy.[4] The landmark POET trial and its follow-up analyses have demonstrated that partial oral switch after initial IV stabilization is safe and effective for left-sided IE caused by susceptible pathogens, with similar composite endpoint rates at 6 months.[5] Subsequent studies indicate that this is supported in real-world data which indicate low levels of relapse (less than 5%) when oral switch in is used early in patients compliant with therapy, but applicability in developing areas with greater staphylococcal burden is not studied.[6] In Pakistan, recent multicenter cohorts highlight a shift toward more staphylococcal IE (up to 40% of cases), with in-hospital mortality around 20-25% and frequent antibiotic resistance, underscoring the need for tailored regimens that balance efficacy with resource constraints.[7] The purpose of this comparative analysis is to compare the results of a standard 6-week course of IV antibiotics in the treatment of culture-positive IE to a shorter 2-week course of IV antibiotics in terms of mortality and relapse and hospital stay in a South Asian setting where a longer hospital stay is a significant burden on the health care resources.[8] By addressing this gap, the study seeks to inform guideline adaptations for low- to middle-income countries, potentially supporting safer early discharge strategies while adhering to international standards for IE management.

Methods

The study was conducted at Department of Cardiology, Chaudhry Pervaiz Elahi Institute of Cardiology (CPEIC), Multan, Pakistan, from January 2023 to January 2024 after taking approval from the Ethical Review Committee of the institute vide letter no: Ref/CPEIC/124 on dated 27th December 2022, Adult patients who had culture-positive infective endocarditis based on the modified Duke criteria and whose at least one positive blood culture identified the causative organism were enrolled into the study. Individuals aged 18 years and above of either gender were eligible as patients. Patients who had culture-negative infective endocarditis, profound immunosuppression, acute sepsis that needed emergency surgery, or those who could not complete therapy or follow-up were excluded.

The sample size was estimated by assuming a confidence level of 95% ($\alpha = 0.05$), and a statistical power of 80% ($\beta = 0.20$) and assuming a relative difference in the composite outcome of mortality and relapse was about 20% between the standard 6-week and reduced 2-week intravenous antibiotic regimens, based on effect sizes in already published trials and observational studies. Based on event rates of 35% and 15% in the short-course and standard-course groups, respectively, 40 patients were needed in each arm. The inflated sample (43 participants per group) was used to account for a projected 5-10% loss to follow-up, bringing the total population to 86 patients.

Allocation was carried out after enrollment using a computer-generated block randomization sequence with variable block sizes to maintain balanced allocation throughout recruitment. Allocation was further stratified by baseline clinical risk (low-risk vs higher-risk infective endocarditis), defined a priori by native valve involvement, streptococcal etiology, and absence of early complications, to minimize imbalance in key prognostic factors. Allocation concealment was ensured by using sequentially numbered, opaque, sealed envelopes prepared by an independent investigator not involved in patient recruitment, treatment, or outcome assessment. The envelopes were opened only after written informed consent was obtained and baseline eligibility confirmed. Eligible participants were randomized in a 1:1 ratio to receive either a standard 6-week course or a shortened 2-week course of pathogen-directed intravenous antimicrobial therapy according to institutional protocols and culture sensitivity results. Because the duration of intravenous therapy differed between groups, blinding of participants and treating clinicians was

not feasible, and the trial was conducted as an open-label study. However, outcome assessors and statisticians were blinded to treatment allocation to reduce assessment and analytical bias. Data were coded prior to analysis, and treatment group identities were revealed only after completion of primary analyses.

Baseline demographic variables, including age and gender, were recorded at enrollment. Clinical characteristics, such as the type of infective endocarditis, complications at presentation, and microbiological profiles, were documented. A predefined exploratory subgroup analysis of low-risk patients was planned; however, low-risk status was not used as an inclusion criterion and did not influence patient selection.

Patients were monitored throughout hospitalization for clinical response, microbiological clearance, and development of complications. Follow-up was conducted for six months after discharge through scheduled outpatient visits and structured telephonic interviews.

The primary composite outcome included all-cause mortality, relapse or persistent bacteremia, unplanned cardiac surgery, or major embolic events within six months. Secondary outcomes included in-hospital mortality, six-month mortality, treatment success, relapse rate, new embolic events, and length of hospital stay.

The statistical analyses were done with IBM SPSS Statistics version 26.0. The data were first verified to make sure that all data was complete and accurate. Age and stay at a hospital are continuous variables and were evaluated as to be normally distributed using the Shapiro-Wilk test, histograms, and Q-Q plots. The normally distributed variables were summarized in the form of mean and standard deviation and compared using the independent samples t-test, whereas non-normally distributed variables were put in the form of median and interquartile range and compared using the Mann-Whitney U test. Frequencies and percentages were used as categorical variables (gender, pathogen distribution, type of infective endocarditis, and all clinical outcomes). The Chi-Square test of independence was used to evaluate group differences, and the Fisher exact test was used in cases where the expected cell counts were less than 5, so that the results were statistically valid. Univariable logistic regression was conducted to estimate odds ratios with 95% confidence intervals for adverse outcomes associated with the 2-week regimen compared with the 6-week regimen. A *P*-value below 0.05 represented a statistically significant *P*-value.

Results

The mean age was similar between the 6-week and 2-week groups (48.1 vs 45.8 years; $P = 0.46$), and males comprised 62.8% of each group. Rates of native valve endocarditis, prosthetic valve involvement, and pathogen distribution did not differ significantly. Baseline complications, including heart failure and embolic events, were also similar across groups. The only significant difference was a higher proportion of low-risk patients in the 2-week group (53.5% vs 32.6%; $P = 0.044$). (Table 1).

Clinical outcomes generally favored the 6-week IV therapy, although several comparisons did not reach statistical significance. The primary composite endpoint occurred in 16.3% of the 6-week group compared with 32.6 % of the 6-week group, compared with 32.6% of the 2-week group ($P = 0.068$). In-hospital and 6-month mortality were higher in the 2-week group (27.9% and 37.2%, respectively) than in the 6-week group (14.0% and 20.9%), but these differences were not statistically significant. Relapse or persistent bacteremia was also more frequent with the shorter regimen (18.6 % vs 7.0 %, $P = 0.107$). Length of stay differed significantly, with a median of 45 days in the 6-week group versus 20 days in the 2-week group ($P < 0.001$). Treatment success remained numerically higher in the 6-week group (79.1% vs 65.1%). (Table 2).

Univariable odds ratios showed a consistent trend toward a higher risk of adverse outcomes in patients receiving 2 weeks of IV therapy compared with 6 weeks. Although not statistically significant, the odds of meeting the primary composite endpoint were more than twice as high for the 2-week group (OR 2.49, $P = 0.068$). Similar nonsignificant trends were observed for in-hospital mortality (OR 2.38), 6-month mortality (OR 2.24), and relapse or persistent bacteremia (OR 3.05). No differences were seen for unplanned surgery or major embolic events, with both outcomes having an odds ratio of 1.00. (Table 3).

Table 1: Baseline Characteristics of Patients with Culture-Positive Infective Endocarditis

Characteristic	6-Week IV Group (N=43)	2-Week IV Group (N=43)	*Test Statistic*	*P*-value
Age, mean ± SD (years)	48.1 ± 15.3	45.8 ± 14.9	t = 0.74	0.46
Male, N (%)	27 (62.8)	27 (62.8)	$\chi^2 = 0.00$	1.00
Native valve IE, N (%)	34 (79.1)	35 (81.4)	$\chi^2 = 0.07$	0.79
Prosthetic valve IE, N (%)	9 (20.9)	8 (18.6)	$\chi^2 = 0.07$	0.79
Pathogen distribution, N (%)	-	-	$\chi^2 = 2.14$	0.71
- Streptococcus spp.	17 (39.5)	19 (44.2)	-	-
- Staphylococcus aureus	15 (34.9)	14 (32.6)	-	-
- CoNS	6 (14.0)	5 (11.6)	-	-
- Enterococcus spp.	4 (9.3)	4 (9.3)	-	-
- Other	1 (2.3)	1 (2.3)	-	-
Complications at presentation, N (%)				
- Heart failure	19 (44.2)	17 (39.5)	$\chi^2 = 0.19$	0.66
- Embolic events	13 (30.2)	11 (25.6)	$\chi^2 = 0.23$	0.63
Low-risk subgroup (streptococcal, native valve, no early complications), N (%)	14 (32.6)	23 (53.5)	$\chi^2 = 4.07$	0.044

Table 2: Clinical Outcomes

Outcome	6-Week IV Group (N=43)	2-Week IV Group (N=43)	*Test Statistic*	*P*-value
Primary composite endpoint*, N (%)	7 (16.3)	14 (32.6)	$\chi^2 = 3.32$	0.068
In-hospital mortality, N (%)	6 (14.0)	12 (27.9)	$\chi^2 = 2.58$	0.108
6-month all-cause mortality, N (%)	9 (20.9)	16 (37.2)	$\chi^2 = 3.00$	0.083
IE relapse/persistent bacteremia, N (%)	3 (7.0)	8 (18.6)	-	0.107
Unplanned cardiac surgery, N (%)	5 (11.6)	5 (11.6)	$\chi^2 = 0.00$	1.00
Major embolic events (new), N (%)	3 (7.0)	3 (7.0)	-	1.00
Length of hospital stay, median (IQR), days	45 (38–52)	20 (16–25)	U = 168.5	<0.001
Treatment success** (cure without adverse events), N (%)	34 (79.1)	28 (65.1)	$\chi^2 = 2.18$	0.140

**Primary composite: all-cause mortality, relapse/persistent bacteremia, unplanned surgery, or major embolic events at 6 months.*

***Defined as survival without relapse, new embolism, or unplanned surgery.*

— = Fisher's exact test

Table 3: Univariable Odds Ratios for Major Adverse Outcomes

Outcome	Odds Ratio (95% CI)	*P*-value
Primary composite endpoint*	2.49 (0.89–6.96)	0.068
In-hospital mortality	2.38 (0.80–7.09)	0.108
6-month all-cause mortality	2.24 (0.87–5.77)	0.083
IE relapse/persistent bacteremia	3.05 (0.75–12.4)	0.107
Unplanned cardiac surgery	1.00 (0.27–3.75)	1.00
Major embolic events (new)	1.00 (0.19–5.24)	1.00

**Primary composite: all-cause mortality, relapse/persistent bacteremia, unplanned surgery, or major embolic events at 6 months.*

Discussion

In this study, the results of two intravenous antibiotic regimens for the treatment of culture-positive infective endocarditis were compared: a traditional 6-week regimen and a shorter 2-week regimen. The comparison showed significant variations in mortality, relapse, and treatment success, highlighting the clinical importance of abbreviated therapy in the treatment of this high-risk disease.

The two groups had similar age and gender distributions, with the majority male, consistent with the demographic trends reported by Kim J et al. and Al-Tawil M et al., who also reported similar gender patterns in their systematic review of cases of infective endocarditis.[9,10] The similarity in demographic profiles suggests that observed outcome differences were unlikely to be driven by age or sex-related confounding.

Disease characteristics, such as the involvement of the native valves and pathogen profiles, were not different between the groups, which is consistent with the findings of Noubiap JJ et al. who also reported similar microbial patterns in patients with infective endocarditis.[11] The balanced distribution of key disease variables strengthens the internal validity of the comparison and supports the inference that treatment duration played a central role in determining outcomes.

The 2-week cohort had more low-risk patients, indicating the effect of baseline risk on therapeutic outcomes. This finding aligns with the findings of Saha S et al., who underscored the role of risk stratification in making management decisions.[12] Importantly, despite the presence of a greater number of low-risk patients, the 2-week group still demonstrated worse clinical outcomes. This paradoxical finding suggests that shortened therapy may negate the prognostic advantage typically associated with lower baseline risk.

The major composite outcome was more common in the 2-week group, but this was not statistically significant. The latter tendency is comparable to the results of Harris W et al., who demonstrated that long-term intravenous treatment is linked to lower morbidity and mortality rates.[13] These findings highlight the limitation of relying solely on p-values without considering effect size and clinical relevance. Ragoonanan D et al. also emphasized the necessity of adequate antibiotic treatment to reduce the complications of critically ill patients.[14]

This interpretation is also supported by mortality outcomes. In-hospital mortality rates and six-month all-cause mortality were both greater in patients undergoing the 2-week regimen. Though these differences were not significant, they were consistent both in the short-term and longer-term follow-up, implying a real survival disadvantage in short-term therapy. Similar findings were also noted by Defauw R et al., who found higher mortality due to shorter treatment courses, especially in environments where permanent infection and valvular damage are prevalent.[15] Kumar A et al. also demonstrated better survival rates associated with long-term intravenous treatment, which underpins the present study data.[16]

Relapse and persistent bacteremia were more prevalent in the 2-week group, which is one of the most clinically significant adverse outcomes. Relapse indicates insufficient eradication of the microbes and is closely linked to repeated hospitalizations, long-term antibiotic exposure, and high mortality. Meena D et al. reported higher recurrence rates with shorter antibiotic regimens, particularly in infections involving deep-seated or biofilm-forming organisms.[17] He K et al. further supported this concept by demonstrating that insufficient treatment duration compromises bacterial clearance and promotes persistence of infection.[18] The higher relapse rate observed in the present study reinforces the necessity of sustained bactericidal therapy in infective endocarditis.

The median length of stay was significantly longer in the 6-week group, which is expected and consistent with the findings of Amacher S et al. who reported that longer courses of antibiotics are associated with improved clinical stabilization and fewer complications.[19] Treatment success was also numerically higher in the 6-week cohort, which is logical and is in line with observation of Xiang J et al. who noted that longer courses of antibiotics are related to better clinical stabilization and fewer complications.[20]

Although not all outcome differences were statistically significant, univariable odds ratios indicated an increased odds of adverse outcomes in the 2-week group. Similar non-significant but

clinically important trends were reported by Jo Y et al. and it is important to interpret these results carefully when it comes to shortened treatment regimens.[21]

Combined with these results, they indicate that not all patients with infective endocarditis respond well to shorter courses of intravenous antibiotics. Although shorter regimes can help decrease hospitalization and resource consumption, relapse risks, chronic infection, and increased mortality are the reasons why individualized decision-making is important. Multicenter trials should be larger to determine safe and effective parameters for abbreviated therapy.

The small sample size and single-center study design limit the study, as it lacks statistical power and yields wide confidence intervals. Univariable analysis was only conducted, and hence, no residual confounding can be ruled out. Differences in pathogen types and disease severity can also limit generalizability.

Conclusion

This study demonstrates that a shortened 2-week intravenous antibiotic regimen for culture-positive infective endocarditis is associated with higher relapse rates, increased mortality, and a greater likelihood of adverse clinical outcomes compared with the standard 6-week regimen. Although the shorter course significantly reduced hospital stay, this benefit did not outweigh the observed clinical risks. The findings indicate that abbreviated intravenous therapy may be unsuitable for most patients, even those initially categorized as low risk. A full 6-week intravenous treatment remains the safer and more effective strategy for achieving sustained infection control and minimizing complications. Larger multicenter trials are needed to further refine patient selection and determine whether any subgroups may safely benefit from shorter treatment durations.

Acknowledgement: None

Conflict of Interest: The authors declare no conflict of interest

Grant Support and Financial Disclosure: None

REFERENCES

1. Delgado V, Ajmone Marsan N, de Waha S, Bonaros N, Brida M, Burri H, et al. 2023 ESC guidelines for the management of endocarditis. European Heart Journal. 2023; 44: 3948-4042. doi: 10.1093/eurheartj/ehad193
2. Fowler VG Jr, Durack DT, Selton-Suty C, Athan E, Bayer AS, Chamis AL, et al. The 2023 Duke-International Society for Cardiovascular Infectious Diseases criteria for infective endocarditis: updating the modified Duke criteria. Clinical Infectious Diseases. 2023; 77: 518-26. doi: 10.1093/cid/ciad271
3. Pries-Heje MM, Ihlemann N, Gill SU, Moser C, Bundgaard H, Bruun NE, et al. Clinical implementation of partial oral treatment in infective endocarditis: The Danish POETry study. European Heart Journal. 2023; 44: 5095-106. doi: 10.1093/eurheartj/ehad715
4. McDonald EG, Aggrey G, Aslan AT, Nguyen P, Lee TC, Morris AM, et al. Guidelines for diagnosis and management of infective endocarditis in adults: a WikiGuidelines Group consensus statement. JAMA Network Open. 2023; 6: e2326366. doi: 10.1001/jamanetworkopen.2023.26366
5. Khan A, Aslam A, Satti KN, Ashiq A, Najeeb F, Mohsin M. Etiology, clinical characteristics, and outcome of infective endocarditis: 10-year experience from a tertiary care center in Pakistan. Monaldi Archives for Chest Disease. 2022; 92: 2212. doi: 10.4081/monaldi.2022.2212
6. Kaperak C, Eller D, Devlin SA, Hall A, Schmitt J, Friedman EE, et al. Outpatient parenteral antimicrobial therapy in patients with infective endocarditis: a review of 85 cases from a large national cohort. Open Forum Infectious Diseases. 2024; 11: ofad629. doi: 10.1093/ofid/ofad629
7. Saleem MW, Amjad M, Ullah I, Jan RU, Khan MI, Israr U. Clinical presentation, microbiological profile, and management challenges of infective endocarditis: a retrospective study from a high volume cardiac centre in Pakistan. The Egyptian Heart Journal. 2025; 77: 103. doi: 10.1186/s43044-025-00699-z
8. Khan S, Ullah S, Amin A, Hussain Z, Rehman A, Ali F, et al. Impact of delayed antibiotic administration on outcomes in acute infective endocarditis. Journal of Population Therapeutics and Clinical Pharmacology. 2024; 31: 1564-70. doi: 10.53555/djyn4n48
9. Kim J, Lee H, Ku N, Lee S, Lee S, Choi J, et al. Infective endocarditis at a tertiary care hospital in South Korea. Heart. 2020; 107: 135-41. doi: 10.1136/heartjnl-2020-317265
10. Al-Tawil M, Friedrich C, Mandler K, Brandl J, Salem M, Schoettler J, et al. The influence of preoperative neurological complications on outcomes after surgery for infective endocarditis. Journal of Cardiac Surgery. 2024; 2024: 9575684. doi: 10.1155/2024/9575684
11. Noubiap JJ, Nkeck JR, Kwondom BS, Nyaga UF. Epidemiology of infective endocarditis in Africa: a systematic review and meta-analysis. The Lancet Global Health. 2022; 10: e77-86. doi: 10.1016/S2214-109X(21)00400-9
12. Saha S, Mladenova R, Radner C, Horke K, Buech J, Schnackenburg P, et al. Health-related quality of life following surgery for native and prosthetic valve infective endocarditis. Journal of Clinical Medicine. 2022; 11: 3599. doi: 10.3390/jcm11133599
13. Harris W, Sinha S, Caputo M, Angelini G, Vohra H. Surgical outcomes and optimal approach to treatment of aortic valve endocarditis with aortic root abscess: systematic

review and meta-analysis. Perfusion. 2022; 39: 256-65. doi: 10.1177/02676591221137484
14. Ragoonanan D, Allen B, Cannon C, Rottman-Pietrzak K, Bello A. Comparison of early versus late initiation of hydrocortisone in patients with septic shock in the ICU setting. Annals of Pharmacotherapy. 2021; 56: 264-70. doi: 10.1177/10600280211021103
15. Defauw R, Tomšič A, Brakel T, Marsan N, Klautz R, Palmen M. A structured approach to native mitral valve infective endocarditis: is repair better than replacement? European Journal of Cardio-Thoracic Surgery. 2020; 58: 544-50. doi: 10.1093/ejcts/ezaa079
16. Kumar A, Ahmad I, Flaherty J, Nagaraja V, Huded C, Reed G, et al. Contemporary outcomes of transcatheter aortic valve replacement using a balloon-expandable valve in patients with severe mitral stenosis: insights from the Transcatheter Valve Therapies Registry. Circulation: Cardiovascular Interventions. 2024; 17: e014216. doi: 10.1161/CIRCINTERVENTIONS.124.014216
17. Meena D, Kumar D, Agarwal M, Bohra G, Choudhary R, Samantaray S, et al. Clinical features, diagnosis and treatment outcome of fungal endocarditis: a systematic review of reported cases. Mycoses. 2021; 65: 294-302. doi: 10.1111/myc.13398
18. He K, Song J, Luo H, Su H, Liang W, Bian L, et al. Valve replacement or repair in native mitral valve infective endocarditis: which is better? A meta-analysis and systematic review. Journal of Cardiac Surgery. 2022; 37: 1004-15. doi: 10.1111/jocs.16227
19. Amacher S, Bohren C, Blatter R, Becker C, Beck K, Mueller J, et al. Long-term survival after out-of-hospital cardiac arrest. JAMA Cardiology. 2022; 7: 633-43. doi: 10.1001/jamacardio.2022.0795
20. Xiang J, He L, Li D, Wei S, Wu Z. Value of the systemic immune-inflammation index in predicting poor postoperative outcomes and short-term prognosis of heart valve diseases: a retrospective cohort study. BMJ Open. 2022; 12: e064171. doi: 10.1136/bmjopen-2022-064171
21. Jo Y, Nosal R, Vittori A, Cordova L, Vandever C, Alvarez C, et al. Effect of initiation of medications for opioid use disorder on hospitalization outcomes for endocarditis and osteomyelitis in a large private hospital system in the United States, 2014-2018. Addiction. 2021; 116: 2127-34. doi: 10.1111/add.15393

Author Contributions

RM: Conception and design of the work
IJ: Manuscript writing for methodology design and investigation
MI: Validation of data, interpretation, and write-up of results