# Effectiveness Comparison on Different Antibiotics in the Management of Odontogenic Infections – A Systematic Review

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**Abstract**

Odontogenic infections can be effectively treated through dental care and surgical treatment, and antibiotic therapy remains useful for the treatment of several odontogenic infections.

This review conduct a systematic literature comparing the effectiveness of different antibiotics in treating odontogenic infections. This review uses PubMed, SpringerLink, SCOPUS, and Embase databases as the bibliographic resources. Studies with matching keywords were analyzed and filtered using PRISMA guidelines. Thirteen of the 596 studies reviewed were included in this review. The total number of odontogenic infection cases is 4824 cases treated with different antibiotics. The antibiotics discussed in this review are penicillin, penicillin combined with beta-lactamase inhibitors, metronidazole, and clindamycin.

The conclusion is penicillin combined with a beta-lactamase inhibitor (ampicillin-sulbactam or amoxicillin/clavulanic acid) is the most effective antibiotic for odontogenic infections treatment. Their combination with metronidazole is not necessary for healthy patients. Patients who are allergic to penicillin can use clindamycin as an alternative antibiotic.

**Review (J Int Dent Med Res 2023; 16(3): 1361-1368)**

**Keywords:** Infection Control, Dental, Periapical Abscesses, Periodontal Abscess, Pericoronitis, Anti-Bacterial Agents.

**Received date:** 12 July 2023. **Accept date:** 19 August 2023

## Introduction

Odontogenic infections are a frequent reason for consulting the emergency service.[1–3] Despite the improvement of health care services, morbidity and mortality remain occur in spite of the decrease in prevalence and complication rates.[4,5] Odontogenic infections include alveolar, jaw, or face infections derived from tooth or supporting structures.[3,6] These infections arise from several cases, including carious or necrotic pulp, defective root canal treatment, or an infection of the periodontium from a deep periodontal pocket.[1,4,6,7] In the United States and other countries, both periodontal disease and dental cavities are widespread conditions, and odontogenic infections are a globally major source of burden of disease.[3,8,9]

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The pathogenesis of odontogenic infection is polymicrobial.[1,6,10,11] Bacterial inoculation into sterile tissues results in a focal infection and induces immune responses in the patient.[1,4] Pain, swelling, and erythema/redness are the main resulting symptoms.[3,6] These infections must be treated as soon as possible, as they may potentially spread, resulting in severe conditions such as fever, trismus, dysphagia, and even serious complications, such as airway obstruction, brain affection, descending mediastinitis, orbital abscess leading to vision loss, and sepsis.[1,4,12,13]

Management of odontogenic infections has improved over the years.[4,14] Even though odontogenic infections can be effectively treated through dental care and surgical treatment, antibiotic therapy remains useful for the treatment of several odontogenic infections.[1,2,4,11] It depends on various factors, including the primary source and severity of infection.[3,6] Extracting non-preservable teeth focuses on focal infection elimination, which has proven to be the key step for treating odontogenic infections. For several cases, it may include debridement, irrigation, incision, and drainage.[3,6,7,10,15,16]

Due to the high number of odontogenic infections cases, dentists have to be familiar with the appropriate use of antibiotics.[12,16] In many dental infections, antibiotics are necessary to limit the spread of infection and quicken complete resolution.[6,11] However, it is important to know that not all infections require antibiotics.[16] Recent guidelines suggest that antibiotic therapy should be prescribed after eliminating the source of infection. Antibiotics are commonly indicated for treating immunocompromised patients. Major issues from inappropriate use of antibiotics lead to bacterial resistance toward the prescription of broadspectrum regimens.[10–12] Unnecessary and overuse of antibiotics may lead to adverse effects such as gastrointestinal disorders, anaphylactic shock, and other complications.[11,12,16] Moreover, World Health Organization (WHO) reported that the morbidity and mortality rate due to antimicrobial resistance would cause enormous global economic loss estimated at around 100 trillion US dollars by 2050.[17] Because most of the pathogens involved in odontogenic infections are known, it seems sensible to start therapy empirically with one of the antibiotics recognized as highly effective.[6]

This study conducted a systematic literature review assessing the effectiveness comparison of different antibiotics for the treatment of odontogenic infections, as well as to review patient evaluations.

## Materials and methods

1. Searching Strategy

The search strategy was carried out through database searching in PubMed, Embase, Scopus, and SpringerLink. The keyword used in the literature search was "effectiveness or efficacy or use", "tooth and bacterial infections or periapical abscesses or periodontal abscess or infection control, dental or pericoronitis or odontogenic infections", and "anti-bacterial agents or antibiotics". In each database, the search line is adjusted, as shown in Table 1.

2. Inclusion and Exclusion Criteria

The PICOS (Population, Intervention, Comparator, Outcomes, Study Design) framework was used to identify articles that could be included. Population (P) includes patients with odontogenic infection, and Intervention (I) are patients treated with antibiotics. For Comparison (C), the effectiveness of various antibiotics. Outcome (O) was an evaluation and effectiveness of various antibiotics. Study Design (S) is a Controlled Clinical Trial, Retrospective, Prospective, Randomized Control Trial (RCT) design. Exclusion criteria for this review are systematic review, literature review, letter to the editor, and non-English studies.

| Database | Line of Search |
|---|---|
| Pubmed | Effectiveness OR efficacy OR use AND (tooth [MeSH Terms]) AND bacterial infections[MeSH Terms])) OR periapical abscesses[MeSH Terms]) OR periodontal abscess[MeSH Terms]) OR infection control, dental[MeSH Terms]) OR pericoronitis[MeSH Terms]) OR odontogenic infections[Title/Abstract]) AND anti-bacterial agents[MeSH Terms] |
| SpringerLink | 'Effectiveness OR Effectiveness OR Efficacy OR Use AND ((tooth AND bacterial infections) OR periapical abscesses OR periodontal abscess OR infection control, dental OR pericoronitis OR odontogenic infections) AND (anti-bacterial agents OR Antibiotics)' |
| Scopus | 'Effectiveness OR Effectiveness OR Efficacy OR Use AND tooth AND bacterial infections OR periapical abscesses OR periodontal abscess OR infection control, dental OR pericoronitis OR odontogenic infections AND anti-bacterial agents OR Antibiotics' |
| Embase | (effectiveness OR 'efficacy'/exp OR efficacy OR use) AND ('tooth'/exp OR tooth) AND ('bacterial infections'/exp OR 'bacterial infections' OR (bacterial AND ('infections'/exp OR infections)) OR 'periapical abscesses' OR (periapical AND abscesses) OR 'periodontal abscess'/exp OR 'periodontal abscess' OR (periodontal AND ('abscess'/exp OR abscess)) OR 'infection control, dental' OR 'infection'/exp OR infection) AND ('anti-bacterial agents'/exp OR 'anti-bacterial agents' OR ('anti bacterial' AND agents) OR 'antibiotic agent'/exp OR 'antibiotic agent') |

**Table 1.** Line of Search Used for Each Database

3. Data Collection

To collect sufficient data, we followed the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) report procedure. Data were taken from each study based on: author, year, study design, surgical intervention, number of dental infections, number of dental infections; antibiotic administered, the effectiveness of antibiotic use, and patient evaluation and comment (Table 2).

4. Methodological Quality Assessment

Methodological quality assessment evaluations were performed using the Newcastle Ottawa Scale (NOS). The criteria used in analyzing the potential risk classification of bias were: Selection, Comparability, and Results, as shown in Table 3.

## Results

Electronic literature research was performed in May 2023 and identified 596 studies. Four databases were reviewed in this study, i.e., PubMed, SpringerLink, SCOPUS, and Embase. Forty-six studies were eliminated for duplication. Studies excluded due to inappropriate titles were 323 studies. The abstract screening was performed on 550, then 212 studies were excluded. After checking the design study, 202 were eliminated. One study was eliminated because the discussion was not appropriate, seven studies were eliminated because the results of the importance of this review were not included in the study, and 2 studies were eliminated because they were non-English. There are just 13 included in this review to be analyzed. The PRISMA flowchart of this systematic review is given in Figure 1.

## Discussion

Odontogenic infections can be caused by pericoronitis, dental caries, deep periodontal pockets, trauma, surgery, or foreign body impaction.[1,18–20] This infection is characterized by inflammation and/or abscess formation primarily caused by polymicrobial flora remaining in the oral cavity entering sterile tissue.[1] Treatment of infection depends on the severity. If the infection is local, it can be treated simply, whereas if the infection has spread to the head and neck space, then treatment requires hospitalization and even treatment in the operating room.[18]

Definitive management of odontogenic infections requires intervention on the cause, i.e., root canal treatment or tooth extraction, and often hospitalization. Appropriate antibiotics can shorten the period of infection and minimize associated risks such as bacteremia.[2,21]

This study aims to see the differences in the effectiveness of various antibiotics in managing odontogenic infections. The review aggregated data from 13 studies that involved 4824 patients with odontogenic infections who used various antibiotics in their treatment, such as penicillin, amoxicillin, metronidazole, ampicillin-sulbactam, clindamycin, ceftriaxone, cefazolin, cefalexin, cefadroxil, moxifloxacin, cotrimoxazole, cephalosporin, and macrolide.

The antibiotic most commonly used in managing odontogenic infections was penicillin.[1,22,23] Penicillins are antibiotics that can fight most oral micro-organisms. The side effects of penicillin are usually minimal, but they can cause allergies.[15,23] Opitz et al.[22] reported that 814 patients with severe odontogenic infections who were treated with penicillin combined with adequate surgical treatment recovered completely, with an average length of hospital stay of 19.9 days. Complications in odontogenic surgery patients were experienced only in 1.7% of all patients. Patients who experience these complications have typical comorbidities that reduce the patient's immunocompetence.

The penicillin derivatives most widely used for the treatment of odontogenic infections are amoxicillin and ampicillin. Mahmoodi et al.[1] stated that the use of amoxicillin alone can fight orofacial infection pathogens, which show good antimicrobial activity. In the study by Eroglu et al.[24], the use of amoxicillin alone can cure lymphadenopathy with a high rate of healing of 90% at the end of the seventh day. However, the current use of penicillin derivatives is mostly combined with beta-lactamase inhibitors due to bacterial resistance.[21]

Liau et al.[21] reported that the penicillin antibiotic resistance rate was 10.8% and amoxicillin was 9.7%, whilst amoxicillin/clavulanic acid rate antibiotic resistance was relatively low (3.2%). The addition of a beta-lactamase inhibitor (sulbactam or clavulanic acid) will inhibit the beta-lactamase mechanism.[23] The combination of amoxicillin and clavulanic acid has been reported to treat severe odontogenic infections.[1] Besides, Rothamel et al.[13] showed that ampicillin, in combination with sulbactam, displayed high susceptibility rates (98.73%). This is in line with research by El-Ma'aita et al. which shows that amoxicillin/clavulanic acid is the first choice for treating odontogenic infection by 49.2% of endodontists in Jordan.[25]

Metronidazole was more often used in combination with broad-spectrum antibiotics such as clindamycin, penicillin, or cephalosporin.[15,23,26] Kumari et al.[27] reported that all patients with odontogenic infections responded rapidly to ampicillin-sulbactam added with metronidazole as observed by a reduction in discharge, swelling, pain, and improvement in mouth opening on the seventh day. Igoumenakis et al.[4] reported that all the patients with odontogenic infections resolved with ampicillin-sulbactam plus metronidazole treatment. Bowe et al.[28] also showed that 125 patients responded well to the combination of ampicillin-sulbactam with metronidazole, but successful resolution requires surgical intervention with a combination of intravenous antibiotics in the majority of patients. However, Bali et al.[29] stated that metronidazole was not fundamental in healthy patients after drainage, but the prescription of this antimicrobial ought to still be based on the assessment of clinical symptoms and adjunctive examination. The statement is based on the results of their research, which showed no significant differences between amoxicillin/clavulanic acid alone and amoxicillin/clavulanic acid with metronidazole for the perception of pain, size of swelling, improvement in dysphagia, or discharge of pus.[29]

Clindamycin is the most frequently used first choice for penicillin-allergic patients.[4,22,28,30] Bhagania et al.[15] compared the use of clindamycin and penicillin with metronidazole. The results show that a combination of penicillin with metronidazole and clindamycin alone had similar antimicrobial effectiveness for odontogenic infections. The antibiotic failure rate was 3.5% in the clindamycin group and 4.7% for the penicillin with the metronidazole group. The study by Igoumenakis et al.[4] also showed that clindamycin had good clinical resolution and no severe adverse effects of clindamycin, such as pseudomembranous colitis. Bowe et al.[28] reported that all the patients responded well to clindamycin.

A study by Liau et al.[21] and Rothamel et al.[13] revealed resistance to clindamycin at a rate of 3.8%[21] and 22.78%.[30] Rothamel et al.[13] recommended an alternative antibiotic to clindamycin, namely moxifloxacin, because of its almost equal effectiveness in terms of reducing clinical outcomes, pain, and safety. Cotrimoxazole may also be an alternative to clindamycin, but cotrimoxazole usage in severe odontogenic infections requires further clinical evaluation. This is because research related to alternative empiric antibiotics continues. Moreover, cefuroxime and cefotaxime can be alternative antibiotics for individuals who are allergic to penicillin.[30]

Igoumenakis et al.[31] compared the treatment of odontogenic infections using ampicillin/sulbactam plus metronidazole with tooth extraction and without tooth extraction. The result is that there was a statistically significant association between extraction and infection resolution time. On the contrary, a study by Kumari et al.[27] showed no significant differences between the surgical intervention with antibiotics group and the one without antibiotics group for any category of clinical outcome. It shows that the elimination of causation is associated with a faster clinical and biological outcome of the infection than by only using antibiotics. Thus, the main treatment of odontogenic infection is to eliminate the cause, namely removing the tooth if it cannot be restored or performing root canal treatment when the tooth is deemed to be restorable.[31]

## Conclusions

This review concludes that a combination of penicillin with a beta-lactamase inhibitor such as amoxicillin/clavulanic acid or ampicillin-sulbactam is the most effective antibiotic for odontogenic infections treatment. Their combination with metronidazole is not necessary. however, the assessment of clinical and laboratory markers of infection is mandatory for the prescription. Patients who are allergic to penicillin can use clindamycin as an alternative antibiotic. Other antibiotic alternatives are moxifloxacin, cefuroxime, cefotaxime, and cotrimoxazole. Cotrimoxazole usage in severe odontogenic infections requires further clinical evaluation.

## Declaration of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.[21]

| Author, Year | Study Design | Surgical Intervention | Number of Dental Infections (DIs) 4824 | Number of DIs; Antibiotic Administered | Effectiveness of Antibiotic Use | Patient Evaluations and Comments |
|---|---|---|---|---|---|---|
| Bali, Sharma, and Gaba, 2014[29] | Randomized prospective study | I&D and/or extraction or surgical debridement | 60 | 30; Inj AMC and Inj MET<br>30; Inj AMC | There were no significant differences between groups for the size of swelling, perception of pain, discharge of pus, or improvement in dysphagia, at any time. Only three patients (two in the 2-antimicrobial group and one in the ampicillin/clavulanate alone group) complained of mild dyspnoea on admission | In healthy subjects, metronidazole is not necessary for the period after drainage, but its prescription should be based on an assessment of clinical and laboratory markers of infection |

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|---|---|---|---|---|---|---|
| Bhagania et al., 2018[15] | Retrospective study | I&D | 78 | 57; IV CLI (group A)<br>21; IV PNC and IV MET (group B) | The average white cell count at the time of admission count was higher in Group I (19.3) versus Group II (17.4). The antibiotic failure rate was 3.5% in Group I and 4.7% for Group II patients. | CLI alone and a combination of PNC with MET are both effective pharmaceutical regimes for Dis. |
| Bowe et al., 2018[28] | Prospective study | I&D and/or extraction or no intervention | 125 | 15; AMC or CLI and MET<br>110; AMC or CLI and MET with surgical intervention | All patients infected with Streptococcus milleri group (SMG) bacteria responded well to AMC, or CLI. | Early aggressive surgical drainage, with adjunctive intravenous antibiotics and supportive care, is critical to ensuring successful treatment. Most patients require surgical intervention in combination with intravenous antibiotics for successful resolution. |
| Connors et al., 2017[2] | Prospective study | Not Mentioned | 348 | ED/UC (IV):<br>60; CZ and MET<br>22; CLI<br>13; CRO and MET<br>OPAT (IV):<br>84; CZ and MET<br>22; CLI<br>13; CRO and MET<br>OPAT (PO):<br>64; CN or CFR and MET<br>24; AMC<br>16; CLI | No difference between antibiotic treatment on balance and the antibiotic regimens used. Although, when using the duration of parenteral therapy as a substitute for early therapy effectiveness, broader spectrum therapy (ceftriaxone or clindamycin-based regimes) appeared to be more effective, shorter mean duration of parenteral treatment. This effect is more likely explained by OPAT practice patterns rather than differential antibiotic efficacy. | - |
| Eroglu et al., 2018[24] | Randomized clinical trial | No Intervention | 40 | 20; AMX, indocyanine green, and antimicrobial photodynamic therapy<br>20; AMX | In the antimicrobial photodynamic therapy group, 100% improvement was achieved regarding pain and lymphadenopathy at the end of the seventh day. | Antimicrobial photodynamic therapy combined with antibiotic therapy for pericoronitis treatment was found to be more successful compared to antibiotic therapy alone regarding clinical and histological outcomes. |
| Igoumenakis et al., 2015[31] | Prospective clinical trial | Extraction or no intervention | 179 | 91; AMP-SULB MET, and exodontia<br>88; AMP-SULB and MET | There was a statistically significant association between extraction and infection resolution time. | Extraction of the causative tooth is associated with a faster clinical and biological resolution of the infection than the use of antibiotics only. |
| Igoumenakis et al., 2014[4] | Retrospective study | I&D and/or removal of the cause (extraction) during study | 212 | 199; AMP-SULB and MET<br>13; CLI | AMX-SULB coupled with MET was curative of infection in the vast majority of cases in this study. All patients that received CLI had clinical resolution of their infections. No incidence of pseudomembranous colitis, the most severe adverse effect of clindamycin was recorded. | One of the effective management protocols in cases of maxillofacial infection is the use of intravenous antibiotics with aerobic and anaerobic coverage and the adaptation of these antibiotics on the basis of sensitivity testing. |
| Kumari et al., 2018[27] | Prospective, randomized clinical study | I&D and/or extraction or endodontics | 40 | 20; AMC and MET, surgical intervention<br>20; no antibiotic and surgical intervention | Pain: The majority of patients in both groups were pain-free by the seventh day. The difference in the mean pain scores between groups A and B was clinically significant at any visit. Mouth opening: the percentage increase in mouth opening was 25% for the antibiotic group and 21% for the group without antibiotics between day one and day seven. Purulent discharge stopped within three days for 75% of the patients. Return to normal life: 47.5% of the patients reported a return to normal life on the seventh day. | No significant differences between both groups for any category of clinical outcome. |
| Liau et al., 2018[21] | Retrospective study | I&D and/or removal of the cause (extraction) | 447 | Not mentioned | 185 patients resistant to antibiotics in which PNC-resistant organisms were identified in 10.8% of patients, AMX-resistant organisms were identified in 9.7% of patients, AMC-resistant organisms were identified in 3.2% of patients. | Effective treatment of odontogenic infections involves early operative intervention, with adjunctive use of appropriate antibiotic therapy that involves close monitoring of response to the removal of the cause and use of first-line antibiotic agents. |

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|---|---|---|---|---|---|---|
| Mahmoodi et al., 2015[1] | Retrospective study | I&D and/or trepanation, subgingival curettage | 2058 | 31; PNC<br>380; AMX<br>199; AMC<br>52; CLI<br>10; Cephalosporin<br>2; Macrolide<br>2; MET | 35.5% of abscess patients were treated with a combination of antibiotics and incision; 13.8% of the abscess collectively got antibiotics as sole therapy. Prescription of antibiotics in pulpitis patient does not relieve pain. | Amoxicillin alone was the most commonly used antibiotic in this trial, followed by amoxicillin in combination with clavulanic acid. Both have been shown to possess good antimicrobial activity against pathogens of orofacial infections, though the combination with clavulanic acid should be administered for the management of severe cases of odontogenic infections. |
| Mutwiri et al., 2021[23] | Retrospective study | I&D | 129 | 17; AMC<br>46; AMC and MET<br>38; CRO and MET<br>7; CLI<br>6; AMC, CRO, MET | Treatment outcomes were favorable, with complete resolution of infection in 92.5% (n=198) of patients. | The treatment outcome was good in most patients. However, there was 7% mortality from the infections. |
| Opitz et al., 2015[32] | Retrospective study | I&D | 814 | 814; PNC or CLI | 14 patients required postoperative intensive medical treatment due to various complications that they had that are typical predisposing factors such as diabetes mellitus, obesity, immunosuppression, and arterial hypertension with its systemic consequences. In addition, long-term alcohol and nicotine abuse and inadequate oral hygiene were noted. | - |
| Rothamel et al., 2016 [30] | Retrospective study | I&D | 294 | 282; AMP-SULB<br>12; CLI | Tested ampicillin in combination with sulbactam (or without) and cephalosporins displayed high susceptibility rates, revealing distinguished results regarding clindamycin ($p<0.05$). MOX and COTRIM showed high overall susceptibility rates (MOX: 94.7%, COTRIM: 92.6%). | AMP-SULB proves itself to be good for empiric antibiosis in severe odontogenic infections. Furthermore, cephalosporins could be considered as another option in treatment. However, MOX and COTRIM deserve further investigation as empiric antibiosis in odontogenic infections if beta-lactam allergy is diagnosed. |

**Table 2.** Included Studies Characteristics.

| Author | Selection | | | | Comparability | Outcome | | | Total | Risk of Bias |
|---|---|---|---|---|---|---|---|---|---|---|
| | Representative of the exposed cohort | Selection of external control | Ascertainment of exposure | The Outcome of interest not present at the start of the study | Control for treatment | Assessment of outcomes | Sufficient follow-up time | Adequacy of follow-up | | |
| **Bali, Sharma, and Gaba, 2014[29]** | c | a | a | a | a | a | a | a | 8 | Low |
| **Bhagania et al., 2018[15]** | c | a | a | a | a | a | a | a | 8 | Low |
| **Bowe et al., 2018[28]** | b | a | a | a | a | a | a | a | 9 | Low |
| **Connors et al., 2017[2]** | b | a | a | a | a | b | a | b | 9 | Low |
| **Eroglu et al., 2018[24]** | c | a | a | a | a | a | a | a | 8 | Low |
| **Igoumenakis et al., 2014[4]** | b | a | a | a | a | a | a | b | 9 | Low |
| **Igoumenakis et al., 2015[31]** | b | a | a | a | a | a | a | b | 9 | Low |
| **Kumari et al., 2018[27]** | c | a | a | a | a | a | a | a | 8 | Low |
| **Liau et al., 2018[21]** | b | a | a | a | b | a | a | a | 7 | Low |
| **Mahmoodi et al., 2015[1]** | b | a | a | a | b | b | a | b | 7 | Low |
| **Mutwiri et al., 2021[23]** | b | a | a | a | b | b | a | b | 7 | Low |
| **Opitz et al., 2015[32]** | b | a | a | a | b | b | a | a | 7 | Low |
| **Rothamel et al., 2016 [30]** | b | a | a | a | b | b | a | a | 7 | Low |

**Table 3** Quality assessment of the studies.

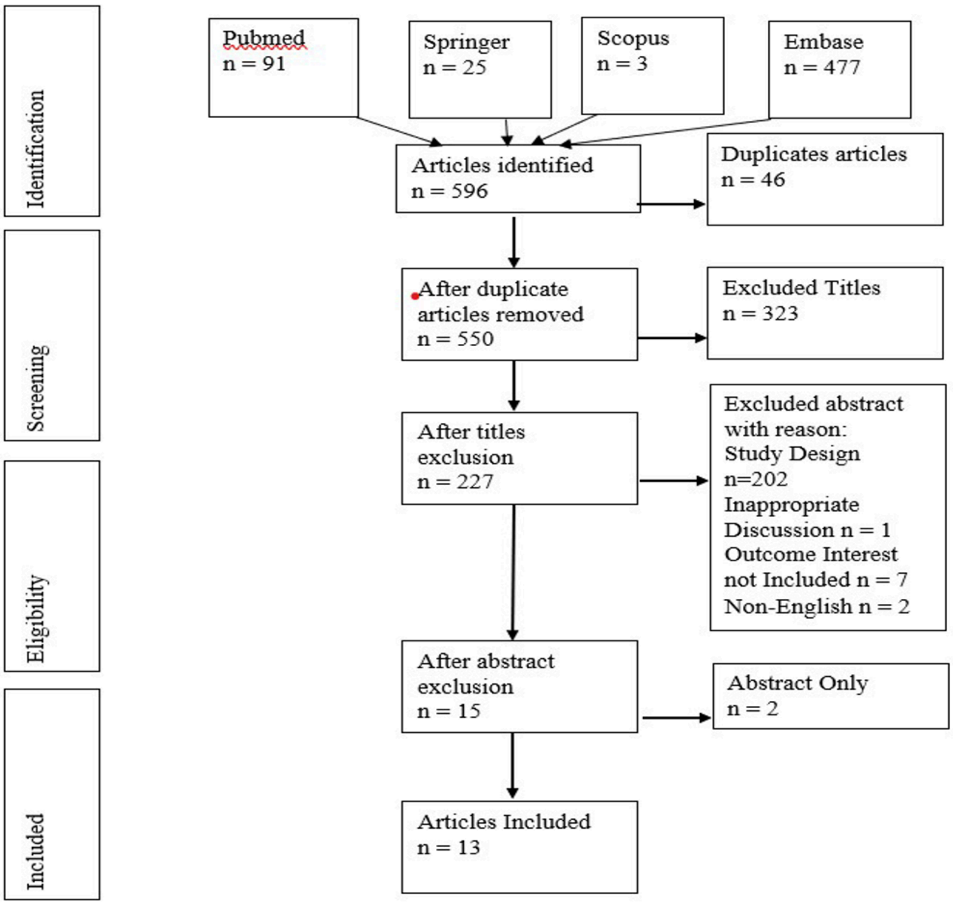


**Figure 1.** Flowchart of the Systematic Review.

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