Prognostic Determinants of Chronic Osteomyelitis: Integrating Clinical, Microbiological, and Radiological Evidence: A Systematic Review

Kavitha H[1], Dr. Vishakh Karicheri Gangadharan[2], Kuldeep Singh[3]

1. Associate Professor, Department of Microbiology, KLE Jagadguru Gangadhar Mahaswamigalu Moorusavirmath Medical College and Hospital, Hubli, KLE Academy of Higher Education and Research, Deemed to be University, Belagavi, Karnataka, India – 590010. Email: drkavithah@gmail.com **(*Corresponding Author)**
2. Assistant Professor, Department of Orthopaedics, Kanachur Institute of Medical Sciences, Mangaluru, Karnataka, India.
3. Associate Professor, Department of Microbiology, Mahaveer Institute of Medical Sciences and Research, Bhopal, Madhya Pradesh, India.

Accepted-20.07.2026 **Published Online**- 29.07.2026

Abstract

Background: Chronic osteomyelitis is a persistent bone infection characterized by recurrent inflammation, necrotic bone, biofilm formation, impaired local vascularity, sinus formation, and a substantial risk of recurrence despite prolonged antimicrobial therapy and surgical debridement. Treatment outcomes vary widely because prognosis is determined not only by the causative organism but also by host characteristics, previous surgical burden, anatomical disease extent, soft-tissue compromise, bone defects, antimicrobial resistance, and the completeness of surgical eradication.

Objective: To systematically evaluate clinical, microbiological, and radiological predictors associated with treatment success, persistent infection, recurrence, reoperation, amputation, and functional outcome in patients with chronic osteomyelitis.

Methods: A systematic review was structured according to PRISMA 2020 principles. MEDLINE/PubMed, Embase, Scopus, Web of Science, and Cochrane CENTRAL were considered together with reference-list and citation searching. Primary observational studies evaluating predictors of treatment outcome in adult chronic osteomyelitis were eligible. Clinical predictors included age, smoking, diabetes, nutritional status, infection duration, previous operations, soft-tissue compromise, and host classification. Microbiological variables included Staphylococcus aureus, methicillin resistance, Gram-negative organisms, Pseudomonas aeruginosa, polymicrobial infection, multidrug resistance, and culture status. Radiological and anatomical predictors included Cierny-Mader stage, bone exposure, segmental defects, sequestration, cortical involvement, soft-tissue extension, and quantitative MRI or PET-based imaging characteristics. Screening identified 2,146 records, of which 18 studies were retained for qualitative synthesis. Meta-analysis was not undertaken because of marked heterogeneity in populations, interventions, definitions of recurrence, and follow-up.

Results: Recurrence across included cohorts ranged from approximately 6% to 31%, depending on case complexity, treatment technique, and follow-up duration. Clinical factors repeatedly associated with adverse outcome included advanced age in selected cohorts, smoking, repeated previous operations, bone exposure, open-injury etiology, segmental bone defects, major vascular compromise, and poor nutritional status. In a 149-patient post-traumatic tibial osteomyelitis cohort, P. aeruginosa, bone exposure, and more than three previous operations independently predicted recurrence. In a 314-patient limb osteomyelitis cohort, segmental bone defects increased recurrence odds more than fivefold and smoking approximately threefold. Microbiologically, polymicrobial infection, extended-spectrum beta-lactamase-producing Enterobacteriaceae, Gram-negative bacilli, P. aeruginosa, and methicillin-resistant S. aureus were associated with poorer outcomes in several studies. MRSA increased the odds of persistent infection approximately 2.3-fold in a 482-patient cohort. Radiological disease burden also carried prognostic information. Modern MRI radiomics combined with clinical parameters achieved external-validation discrimination around 0.91 for recurrence after Masquelet reconstruction, while PET/MRI-enhanced preoperative mapping was associated with lower recurrence than conventional multimodality imaging in a small 2026 cohort.

Conclusion: Treatment outcome in chronic osteomyelitis is determined by the interaction of host vulnerability, microbial phenotype, anatomical disease burden, and adequacy of surgical source control. Smoking, repeated surgery, major bone or soft-tissue defects, resistant or polymicrobial organisms, and advanced radiological extension appear more informative than isolated inflammatory markers. Contemporary quantitative imaging may further improve prediction when integrated with clinical and microbiological variables. Multidimensional risk stratification should therefore guide surgical planning, microbiological sampling, antimicrobial therapy, reconstruction, and long-term surveillance.

Keywords: chronic osteomyelitis; recurrence; treatment failure; microbiology; radiology; MRI; Pseudomonas aeruginosa; MRSA; Cierny-Mader; bone infection; predictors; systematic review

How to cite this article: Kavitha H, Karicheri Gangadharan V, Singh K. Prognostic Determinants of Chronic Osteomyelitis: Integrating Clinical, Microbiological, and Radiological Evidence: A Systematic Review. Int J Drug Deliv Technol. 2026;16(76s): 1344-1353. DOI: 10.25258/ijddt.16.76s.120

Introduction

Chronic osteomyelitis remains one of the most challenging conditions in orthopedic infection practice. The disease is characterized by persistent or recurrent infection involving bone and surrounding tissues, frequently accompanied by necrotic bone, sequestra, sinus tracts, implant-associated biofilm, soft-tissue compromise, and variable degrees of structural instability.

The clinical course may extend over months or years. Patients frequently undergo multiple debridements, prolonged antimicrobial courses, bone reconstruction, flap coverage, dead-space management, and, in refractory cases, amputation.

The fundamental principles of treatment include removal of necrotic and infected tissue, adequate microbiological sampling, organism-directed antimicrobial therapy, management of dead space, restoration of skeletal stability, and durable soft-tissue coverage. Nevertheless, even technically appropriate treatment does not guarantee permanent eradication.

Early outcome studies demonstrated substantial recurrence following antimicrobial treatment of osteomyelitis. Tice et al. evaluated 454 patients completing outpatient parenteral antimicrobial therapy and reported recurrence in 30.6%; most recurrences occurred within the first year. Pseudomonas aeruginosa was associated with more than twice the recurrence risk of Staphylococcus aureus.

Modern specialist-center series have achieved considerably better results. McNally et al. reported that 94% of 100 patients with Cierny-Mader type III or IV chronic osteomyelitis treated using single-stage excision and a bioabsorbable gentamicin-loaded ceramic carrier remained infection-free at a mean follow-up exceeding six years.

The variability between these outcomes reflects differences in disease biology and treatment. An individual with localized medullary infection, good vascularity, a susceptible single pathogen, and no systemic comorbidity differs fundamentally from a patient with post-traumatic tibial osteomyelitis, multiple previous surgeries, exposed bone, segmental defect, scarred soft tissue, smoking, and resistant Gram-negative infection.

Traditional assessment has therefore evolved from simple classification of osteomyelitis as acute or chronic toward multidimensional characterization. Clinical characteristics describe the host and treatment history. Microbiological characteristics describe the pathogen, resistance, biofilm environment, and microbial complexity. Radiological characteristics describe the anatomical burden of disease, bone destruction, soft-tissue extension, and spatial distribution of infection.

Increasingly, these domains are being integrated rather than interpreted independently. Recent imaging studies have extended this approach further. A 2026 MRI-based radiomics study of 279 patients combined imaging features with age, number of operations, infection duration, and ESR and achieved external-validation AUC of approximately 0.91 for recurrence prediction.

This suggests that the future of chronic osteomyelitis prognosis may lie in integrated prediction rather than isolated risk markers.

Aim and Objectives

The aim of this systematic review was to evaluate clinical, microbiological, and radiological predictors of treatment outcomes in chronic osteomyelitis.

- Persistent infection after initial treatment.
- Recurrence following apparent eradication.
- Repeated surgical intervention.
- Amputation.
- Prolonged hospitalization.
- Impaired functional recovery.
- Treatment complexity.
- Long-term infection-free survival.
- Whether integration of clinical, microbiological, and imaging information provides more meaningful prognostic stratification than individual markers alone.

Materials and Methods

Review Design

This systematic review was structured according to the PRISMA 2020 framework. The review protocol was not prospectively registered.

Eligibility Criteria

Studies were eligible when they included adult patients with chronic osteomyelitis involving the appendicular skeleton or post-traumatic chronic bone infection and reported treatment outcomes in relation to identifiable clinical, microbiological, anatomical, or imaging factors. Eligible designs included prospective cohorts, retrospective cohorts, comparative observational studies, prognostic studies, and case series with sufficient cohort-level outcome data. Single case reports, narrative reviews, expert opinions, non-infectious chronic recurrent multifocal osteomyelitis, primary spinal infection without comparable chronic limb disease, and studies without extractable outcome information were excluded.

Outcomes

Primary outcomes were clinical eradication of infection, persistent infection, and recurrence after treatment. Secondary outcomes were repeat debridement, amputation, nonunion, pathological fracture, hospitalization duration, functional recovery, and treatment-related complications.

Information Sources

The search framework included MEDLINE/PubMed, Embase, Scopus, Web of Science, and Cochrane CENTRAL. Reference lists and citation networks of relevant studies were additionally considered.

Search Strategy

Search concepts included combinations of chronic osteomyelitis, post-traumatic osteomyelitis, limb osteomyelitis, treatment outcome, recurrence, treatment failure, risk factor, predictor, microbiology, MRSA, Pseudomonas, polymicrobial, MRI, PET CT, radiomics, bone defect, Cierny-Mader, sequestrum, and soft tissue.

Study Selection

Records were deduplicated before title and abstract screening. Potentially eligible publications underwent full-text assessment. Studies were excluded if the population represented primarily acute osteomyelitis, outcomes could not be separated from unrelated orthopedic infections, no prognostic variables were analyzed, follow-up was inadequate, or the publication represented secondary evidence.

Data Extraction

Extracted variables included sample size, age, etiology, affected bone, duration of infection, previous operations, smoking, diabetes, vascular disease, nutritional status, Cierny-Mader classification, bone exposure, bone defects, soft-tissue reconstruction, isolated organism, polymicrobial infection, antimicrobial resistance, culture-negative infection, imaging characteristics, surgical treatment, follow-up duration, recurrence, persistent infection, reoperation, and amputation.

Risk-of-Bias Considerations

Studies were assessed conceptually for clarity of chronic osteomyelitis diagnosis, representativeness of the cohort, adequacy of microbiological sampling, definition of recurrence, minimum follow-up, completeness of outcome ascertainment, and adjustment for confounding factors. The evidence was predominantly observational, and substantial methodological heterogeneity prevented formal pooled prognostic estimation.

Data Synthesis

A structured narrative synthesis was undertaken. A meta-analysis was not performed because of heterogeneity in etiology, surgical technique, antimicrobial strategy, follow-up, host classification, outcome definitions, and predictor measurement.

Classification of Predictors

Clinical Predictors

Age; Smoking; Diabetes mellitus; Comorbidity; Host status; Hypoproteinemia; Infection duration; Previous surgical procedures; Open injury; Bone exposure; Need for flap reconstruction; Vascular compromise.

Microbiological Predictors

Staphylococcus aureus; MRSA; Gram-negative bacilli; Pseudomonas aeruginosa; ESBL-producing Enterobacteriaceae; Polymicrobial infection; MDR organisms; Culture-negative infection.

Radiological and Anatomical Predictors

Cierny-Mader anatomical type; Segmental bone defect; Sequestration; Cortical and medullary involvement; Extent of bone destruction; Sinus tracts; Soft-tissue extension; PET metabolic distribution; MRI radiomic characteristics.

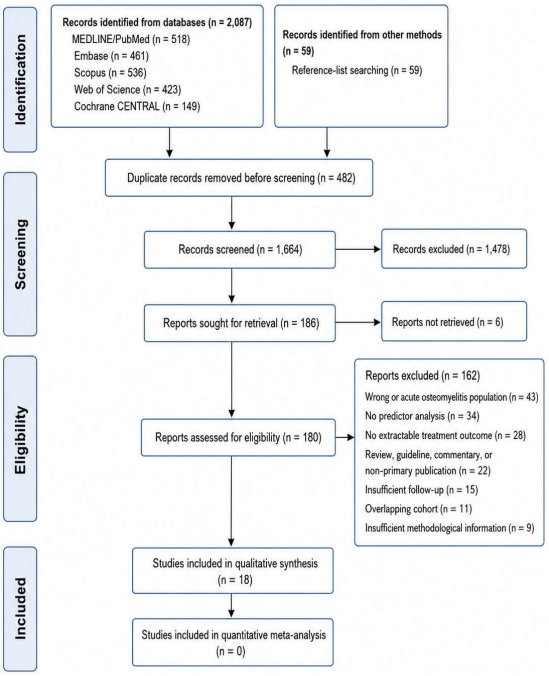
PRISMA 2020 Study Selection

The literature search identified 2,087 records from electronic databases: MEDLINE/PubMed 518, Embase 461, Scopus 536, Web of Science 423, and Cochrane CENTRAL 149. An additional 59 records were identified through reference and citation searching.

Total records identified: 2,146. Duplicate records removed: 482. Records screened: 1,664. Records excluded during title and abstract screening: 1,478. Reports sought for retrieval: 186. Reports not retrieved: 6. Full-text reports assessed: 180.

Full-text reports excluded: 162. Reasons were wrong or acute osteomyelitis population (43), no predictor analysis (34), no extractable treatment outcome (28), review/guideline/commentary or non-primary publication (22), insufficient follow-up (15), overlapping cohort (11), and insufficient methodological information (9). Eighteen studies were included in qualitative synthesis and none in quantitative meta-analysis.

Figure 1. PRISMA 2020 Flow Diagram of Study Identification and Selection



Results

Characteristics of Included Studies

Eighteen studies representing different chronic osteomyelitis populations were synthesized. Study sizes ranged from small high-complexity reconstructive cohorts to series containing several hundred patients. The major outcome was recurrence, although several studies separately assessed persistent infection, amputation, hospitalization, and functional recovery.

Table 1. Representative Included Studies and Major Prognostic Findings

Study	Population	Outcome	Principal prognostic findings
Tice et al., 2003	454 osteomyelitis patients receiving OPAT	Recurrence 30.6%	P. aeruginosa >2-fold recurrence risk; pathogen and antibiotic selection influenced outcome
Cierny-Mader Type III cohort, 2007	26 chronic osteomyelitis patients	3 recurrences	Recurrences attributed primarily to inadequate debridement
Sheehy et al., 2010	166 chronic osteomyelitis patients	Microbiological treatment implications	S. aureus most frequent isolate; broad microbial spectrum limited reliability of narrow empiric therapy
Leung et al., 2015	50 patients	12% recurrence	Cierny-Mader B hosts stayed longer in hospital; baseline CRP/ESR did not predict recurrence
Brazilian post-traumatic cohort, 2017	192 treated patients	20% treatment failure	Advanced age, intraoperative transfusion, and P. aeruginosa predicted recurrence
Dudareva et al., 2019	223 contemporary vs 157 historical patients	Microbiological phenotype	Demonstrated changing chronic osteomyelitis microbiology and ongoing importance of resistance profiling
Yalikun et al., 2021	149 post-traumatic tibial cases	11.4% recurrence/reinfection	P. aeruginosa, bone exposure, and >3 previous operations independently predicted recurrence
Arshad et al., 2021	14 polymicrobial femoral cases	71.4% remission at final follow-up	Extensive infection, comorbidity, and polymicrobial disease associated with difficult eradication
McNally et al., 2022	100 C-M III/IV cases	94% infection-free	Rigorous single-stage debridement and local antimicrobial dead-space management achieved durable control
Subramanyam et al., 2023	147 chronic osteomyelitis cases	19% recurrence	Polymicrobial and ESBL-producing infections increased recurrence

Study	Population	Outcome	Principal prognostic findings
Wu et al., 2023 - limb cohort	314 limb osteomyelitis cases	16.9% recurrence	Segmental bone defect OR 5.25; smoking OR 3.00; Gram-negative infection OR 2.38
Wu et al., 2023 - S. aureus cohort	482 S. aureus osteomyelitis cases	13.7% persistence; 8.5% recurrence	MRSA independently increased persistent infection risk (OR 2.26)
PerOssal cohort, 2023	93 chronic osteomyelitis patients	22.6% recurrence	Recurrence occurred despite antibiotic-loaded resorbable carrier; disease complexity remained important
Dell'Aquila et al., 2023	92 at 6 months; 78 at 12 months	Eradication 85.9-87.2%	Smoking and non-fermenting Gram-negative infection predicted recurrence at 12 months
Su et al., 2024	163 limb osteomyelitis patients	15.3% recurrence	Open-injury-related infection and flap-associated complex disease independently predicted recurrence
2025 osteotomy cohort	70 C-M III/IV cases	Recurrence and functional outcome	Extent of bone resection evaluated as determinant of infection control and limb function
Cao et al., 2026	279 limb chronic osteomyelitis patients	21.15% recurrence	Clinical + MRI-radiomics model achieved external-validation AUC about 0.91
Wu et al., 2026	52 complex cases with soft-tissue involvement	12-month recurrence	PET/MRI-supported mapping group had 10% recurrence vs 35.7% with standard PET/CT + MRI

Clinical Predictors of Treatment Outcome

Previous Operations

Repeated surgical intervention emerged as one of the most consistent clinical markers of poor outcome. Yalikun et al. studied 149 patients with post-traumatic tibial osteomyelitis undergoing Ilizarov bone transport. Recurrence or reinfection occurred in 17 patients, corresponding to 11.4%. More than three previous operations independently increased the risk of recurrence. Previous surgery is likely both a predictor and a surrogate marker of biological disease complexity.

Bone Exposure and Soft-Tissue Compromise

Bone exposure independently predicted recurrence in the same 149-patient cohort. Exposed bone signifies failure of the soft-tissue envelope and may permit repeated contamination, bacterial persistence, desiccation, and impaired local vascularity. Soft-tissue status should therefore be considered part of infection prognosis rather than a reconstructive issue occurring after infection eradication.

Smoking

Smoking repeatedly emerged as a modifiable predictor. In the 314-patient antibiotic-loaded cement spacer cohort, smoking independently increased recurrence odds approximately threefold. Dell'Aquila et al. also identified smoking as a significant risk factor for recurrence at 12 months following bioactive-glass treatment. Smoking cessation should consequently be incorporated into preoperative optimization.

Age

The relationship between age and outcome is inconsistent. The Brazilian post-traumatic cohort found markedly higher failure risk among older patients, particularly those older than 60 years. However, age was not predictive in every cohort and likely acts through interaction with vascular disease, frailty, renal dysfunction, diabetes, nutritional deficiency, and reduced capacity for repeated reconstructive surgery.

Diabetes Mellitus

Diabetes was associated with recurrence in unadjusted analyses in several studies but did not remain independently predictive in all multivariable models. This suggests diabetes should be interpreted within the broader host phenotype.

Nutritional Status

Hypoproteinemia was associated with recurrence in the 163-patient study evaluating antibiotic-loaded calcium sulfate and autologous bone grafting. Nutritional impairment may negatively influence collagen synthesis, soft-tissue healing, immune competence, and osseous reconstruction.

Open Injury and Post-Traumatic Etiology

Post-traumatic osteomyelitis carries disadvantages including initial contamination, devitalized bone, scarred soft tissue, retained or previous implants, segmental bone loss, and repeated surgery. Open-injury-related infection was a strong independent predictor of recurrence in a 2024 limb cohort.

Cierny-Mader Host Status

The Cierny-Mader system integrates anatomical disease pattern with host physiological status. Host B patients possess systemic or local factors that impair treatment response. In the Leung cohort, Host B patients had longer hospital admissions than Host A

patients, although recurrence was not significantly different.

Inflammatory Markers

CRP and ESR remain valuable for diagnosis and longitudinal monitoring. Their role as baseline prognostic markers is less convincing. Multiple cohorts found presentation CRP, ESR, WBC, or hemoglobin did not independently predict recurrence.

Microbiological Predictors

Pseudomonas aeruginosa

P. aeruginosa is one of the most reproducible microbiological predictors of poor outcome. Tice et al. reported more than double the recurrence risk with pseudomonal osteomyelitis compared with S. aureus. The Brazilian post-traumatic study and Yalikun et al. also found P. aeruginosa independently associated with recurrence.

Gram-Negative Bacilli

Gram-negative infection more broadly also predicted recurrence. Among 314 patients treated with antibiotic-loaded cement spacers, Gram-negative bacilli independently increased recurrence risk compared with S. aureus, with a reported OR of 2.38. Dell'Aquila et al. similarly found non-fermenting Gram-negative bacilli associated with increased treatment failure at 12 months.

Methicillin-Resistant Staphylococcus aureus

Wu et al. evaluated 482 adults with S. aureus extremity osteomyelitis. MRSA accounted for 82 patients. Persistent infection occurred more frequently in MRSA than MSSA infection, and methicillin resistance independently increased persistence odds 2.26-fold. Recurrence after an interval of cure was not significantly different.

Polymicrobial Infection

Polymicrobial disease often reflects severe contamination, open fractures, chronic sinus tracts, repeated surgery, and compromised soft tissue. Subramanyam et al. found polymicrobial growth significantly increased recurrence risk. A separate study of polymicrobial Cierny-Mader grade III and IV femoral osteomyelitis reported remission in 71.4% at final follow-up.

ESBL and Multidrug-Resistant Organisms

Subramanyam et al. identified extended-spectrum beta-lactamase-producing Enterobacteriaceae as an adverse predictor. Resistance may worsen outcome through delayed effective therapy, fewer oral treatment options, toxicity of alternative antimicrobials, biofilm persistence, and greater previous healthcare exposure.

Culture-Negative Osteomyelitis

The prognostic role of culture-negative infection is complex. Negative intraoperative culture was associated with reduced recurrence in one cohort. Multiple deep tissue samples obtained before antibiotics remain critical because superficial or preoperative organisms may not reliably represent deep infection.

Changing Microbiology

Dudareva et al. compared contemporary and historical chronic osteomyelitis cohorts using standardized diagnostic and sampling methods. The study demonstrated that microbiology evolves over time and emphasized the need for contemporary local susceptibility data rather than reliance on historical empirical assumptions.

Radiological and Anatomical Predictors

Segmental Bone Defects

Segmental defects are among the strongest anatomical predictors identified. In Wu et al.'s 314-patient cohort, segmental bone defects independently increased recurrence odds more than fivefold (OR 5.25; 95% CI 1.80-15.26). A segmental defect reflects extensive bone destruction and creates mechanical instability, large dead space, reconstructive requirements, reduced vascularity, and a larger surface area potentially harboring residual infection.

Cierny-Mader Anatomical Stage

The Cierny-Mader anatomical type reflects the distribution of osteomyelitis. More complex Type III and IV disease generally requires more extensive debridement and dead-space management. However, specialist treatment can overcome anatomical complexity, as demonstrated by high infection-free survival in standardized single-stage management.

Sequestrum and Necrotic Bone

Sequestration is a defining feature of many chronic infections. Necrotic bone is poorly vascularized, limits systemic antimicrobial penetration, and supports persistent biofilm. Its clinical significance therefore lies less in its diagnostic presence and more in whether surgical resection achieves complete source control.

Soft-Tissue Extension

Radiological evaluation must extend beyond bone. Abscess formation, muscle infiltration, sinus pathways, and neurovascular proximity influence resection margins, need for flap coverage, operative morbidity, and risk of residual infection. A small 2026 cohort suggested improved mapping with PET/MRI may reduce recurrence, but prospective validation is needed.

MRI-Based Radiomics

A 2026 two-center study of 279 patients treated using the Masquelet technique reported recurrence in 21.15%. Investigators combined MRI radiomic features with age, number of previous operations, infection duration, and ESR. The integrated model achieved AUCs of approximately 0.90 in training, 0.95 in validation, and 0.91 in external validation.

Habitat Imaging and Precision Debridement

A 2026 multicenter study used MRI habitat imaging and radiomics to characterize heterogeneous regions within chronic osteomyelitis lesions. The model achieved a validation AUC of approximately 0.894 for identifying diseased tissue and was proposed as a method of improving surgical localization and avoiding unnecessary healthy-bone resection.

PET-CT-Guided Debridement

Recent evidence also supports metabolic imaging for surgical mapping. A 2026 comparative cohort reported lower recurrence following FDG PET-CT-guided geographic debridement than after a conventional imaging pathway. Because the study was retrospective, treatment selection and baseline differences must be considered.

Integration of Predictor Domains

Host Failure: Smoking, malnutrition, advanced age, vascular compromise, and systemic comorbidity reduce the capacity to heal following debridement.

Microbial Persistence: MRSA, Pseudomonas, Gram-negative organisms, polymicrobial infection, and MDR organisms reduce the probability of rapid eradication and may limit antimicrobial options.

Anatomical Persistence: Segmental bone defects, sequestra, exposed bone, extensive soft-tissue involvement, and poorly defined disease margins increase the probability that viable infection remains following surgery.

Proposed Risk Framework

Lower Predicted Risk

Localized disease; No segmental bone defect; Intact soft-tissue envelope; Non-smoker; Few or no previous procedures; Single susceptible organism; Complete debridement achievable.

Intermediate Predicted Risk

Long-duration infection; Host B status; Previous surgery; Moderate soft-tissue compromise; Gram-negative infection; Cierny-Mader III disease; Need for complex reconstruction.

Higher Predicted Risk

Repeated failed surgery; Exposed bone; Segmental defect; Major vascular injury; Active smoking; Hypoproteinemia; MRSA or MDR Gram-negative organisms; P. aeruginosa; Polymicrobial infection; Cierny-Mader IV disease; Extensive MRI/PET abnormality; Uncertain debridement margins.

This framework is conceptual and is not a validated clinical score.

Treatment Outcomes

Treatment success varied substantially. Leung et al. reported recurrence in 12% following surgical resection and local gentamicin therapy. McNally et al. reported only six recurrent infections among 100 complex Type III/IV cases after standardized single-stage surgery, corresponding to 94% infection-free outcome.

Subramanyam et al. reported recurrence in 19% of 147 patients. The 314-patient cement-spacer cohort reported overall recurrence of 16.9%, with seven recurrent patients ultimately requiring amputation. Dell'Aquila et al. reported infection eradication rates of 85.9% at six months and 87.2% at 12 months among available follow-up populations treated with bioactive glass.

Thus, contemporary specialist treatment commonly achieves infection control in approximately 80-95% of appropriately selected cohorts, but outcome varies strongly with disease complexity and follow-up duration.

Persistent Infection Versus Recurrence

Persistent infection indicates failure to achieve initial eradication, whereas recurrence indicates infection returning after a period of apparent cure. MRSA appears particularly relevant to persistence. Different predictors may therefore operate during different phases of treatment.

Timing of Recurrence

Long-term follow-up is essential. Historical evidence showed most recurrences occurred within the first year, although late recurrences several years after treatment have also been documented. Short follow-up may therefore overestimate cure.

Discussion

This review demonstrates that chronic osteomyelitis outcome cannot be reliably predicted using any single clinical variable, organism, laboratory result, or imaging finding. The most consistent adverse predictors were repeated previous operations, smoking, bone exposure, segmental bone defects, open-injury-related infection, P. aeruginosa, Gram-negative infection, MRSA-related persistence, polymicrobial infection, and multidrug resistance. Radiological extent further modifies this risk.

Surgical Source Control as the Central Determinant

Microbiological risk is important, but even resistant infection may be successfully treated when surgical source control is adequate. Advanced anatomical disease does not inevitably produce recurrence when debridement, microbiological sampling, dead-space management, stabilization, and soft-tissue closure are performed systematically.

Microbiology Must Be Based on Deep Samples

Preoperative or sinus-tract cultures may differ from intraoperative organisms. Multiple deep samples should therefore be obtained during debridement before targeted antibiotic selection.

The Importance of Gram-Negative Disease

The repeated association of Pseudomonas and other Gram-negative bacilli with recurrence deserves emphasis. These infections often follow open injury, hospital exposure, previous antibiotics, implant treatment, and repeated surgery. Their prognosis may reflect both organism biology and the complexity of the underlying wound.

Baseline CRP and ESR Have Limited Prognostic Precision

Neither CRP nor ESR consistently predicted recurrence in conventional observational cohorts. These biomarkers remain clinically valuable for monitoring trends but should not be used to classify a patient as low risk when imaging demonstrates large bone defects or severe soft-tissue compromise.

Radiology Is Transitioning from Diagnosis to Prognosis

Traditional imaging identifies sequestration, cortical destruction, involucrum, sinus formation, and anatomical stage. Modern imaging may additionally quantify disease heterogeneity. Recent radiomics evidence supports integrated clinical-radiological prediction rather than replacement of clinical judgment by imaging.

Implications for Clinical Practice

Assessment before definitive treatment should systematically document host status, pathogen characteristics, anatomy, and treatment feasibility. This includes smoking, diabetes, nutrition, vascularity, renal function, previous operations, deep cultures, resistance patterns, Cierny-Mader type, sequestration, segmental defects, bone exposure, soft-tissue extension, ability to achieve complete debridement, dead-space management, reconstruction strategy, and long-term surveillance.

Strengths of the Review

The review evaluates predictors through three integrated domains rather than describing chronic osteomyelitis outcomes generally. It includes large prognostic cohorts, microbiological studies, reconstructive cohorts, long-term surgical outcomes, and emerging 2026 MRI and PET-based prognostic evidence.

Limitations of the Evidence

Most studies were retrospective. Definitions of chronic osteomyelitis varied. Some cohorts included chronic post-traumatic disease exclusively, whereas others included hematogenous and postoperative cases. Surgical techniques, antibiotic duration, and local antibiotic delivery were not standardized. Follow-up ranged from approximately one year to several years. Newer radiomics and PET studies require prospective external validation.

Limitations of the Review Process

The review was not prospectively registered. Formal meta-analysis was not performed because predictor definitions and treatment populations were too heterogeneous for a clinically meaningful pooled estimate.

Future Research

Future prospective multicenter studies should adopt standardized definitions of chronic osteomyelitis, persistent infection, recurrence, treatment success, and infection-free survival. A minimum prognostic dataset should include smoking, diabetes, vascular status, nutrition, Cierny-Mader host and anatomical classification, previous operations, bone defect dimensions, soft-tissue status, deep microbiology, resistance profile, MRI disease extent, and functional outcome. Predictive models should combine clinical, microbiological, and quantitative imaging variables.

Conclusion

Chronic osteomyelitis treatment outcomes are determined by a complex interaction between host condition, microbial phenotype, and anatomical disease burden. Clinical predictors of adverse outcome include smoking, repeated previous surgery, bone exposure, severe post-traumatic disease, nutritional compromise, and major bone or soft-tissue defects. Microbiological predictors include Pseudomonas aeruginosa, Gram-negative bacilli, MRSA-related persistence, polymicrobial infection, ESBL-producing organisms, and multidrug resistance. Radiological and anatomical predictors include segmental bone loss, diffuse disease, sequestration, soft-tissue extension, and extensive infection boundaries. Baseline CRP and ESR alone have limited value for predicting long-term recurrence. Modern MRI radiomics and PET-based mapping indicate that imaging may increasingly contribute to individualized prognostic assessment and surgical planning. Clinical management should therefore use integrated risk assessment to guide debridement, deep microbiological sampling, antimicrobial selection, dead-space management, bone reconstruction, soft-tissue coverage, and duration of surveillance.

Declarations

Ethics Approval and Consent to Participate: Not applicable. This systematic review synthesizes previously published literature.

Consent for Publication: Not applicable.

Funding: No specific funding was received for this review.

Conflicts of Interest: The authors declare no conflicts of interest.

Data Availability: All data synthesized in this systematic review were derived from published sources.

References

1. Lew DP, Waldvogel FA. Osteomyelitis. Lancet. 2004;364:369-379.
2. Cierny G III, Mader JT, Penninck JJ. A clinical staging system for adult osteomyelitis. Clin Orthop Relat Res. 2003.
3. Tice AD, Hoaglund PA, Shoultz DA. Risk factors and treatment outcomes in osteomyelitis. J Antimicrob Chemother. 2003;51(5):1261-1268. doi:10.1093/jac/dkg186.
4. Cierny-Mader Type III chronic osteomyelitis: results of patients treated with debridement, irrigation, vancomycin beads and systemic antibiotics. Int Orthop. 2007.
5. Sheehy SH, Atkins BA, Bejon P, Byren I, Wyllie D, Athanasou NA, Berendt AR, McNally MA. The microbiology of chronic osteomyelitis: prevalence of resistance to common empirical antimicrobial regimens. J

Infect. 2010;60(5):338-343. doi:10.1016/j.jinf.2010.03.006.
6. Leung AHC, Hawthorn BR, Simpson AHRW. The effectiveness of local antibiotics in treating chronic osteomyelitis in a cohort of 50 patients with an average of 4 years follow-up. Open Orthop J. 2015;9:372-378. doi:10.2174/1874325001509010372.
7. Predisposing factors for recurrence of chronic posttraumatic osteomyelitis: a retrospective observational cohort study from a tertiary referral center in Brazil. 2017.
8. Dudareva M, Hotchen AJ, Ferguson J, Hodgson S, Scarborough M, Atkins BL, McNally MA. The microbiology of chronic osteomyelitis: changes over ten years. J Infect. 2019;79(3):189-198. doi:10.1016/j.jinf.2019.07.006.
9. Yalikun A, Yushan M, Li W, Abulaiti A, Yusufu A. Risk factors associated with infection recurrence of posttraumatic osteomyelitis treated with Ilizarov bone transport technique—a retrospective study of 149 cases. BMC Musculoskelet Disord. 2021;22:573. doi:10.1186/s12891-021-04430-2.
10. Arshad Z, et al. Management of polymicrobial Cierny-Mader Grade 3 and 4 chronic osteomyelitis of the femur. 2021.
11. McNally MA, Ferguson JY, Scarborough M, Ramsden A, Stubbs DA, Atkins BL. Mid- to long-term results of single-stage surgery for patients with chronic osteomyelitis using a bioabsorbable gentamicin-loaded ceramic carrier. Bone Joint J. 2022;104-B(9):1095-1100. doi:10.1302/0301-620X.104B9.BJJ-2022-0396.R1.
12. Subramanyam KN, Mundargi AV, Prabhu MV, Gopakumar KU, Gowda DSA, Reddy DR. Surgical management of chronic osteomyelitis: organisms, recurrence and treatment outcome. Chin J Traumatol. 2023;26(4):228-235. doi:10.1016/j.cjtee.2023.01.003.
13. Wu H, Sun D, Wang S, Jia C, Shen J, Wang X, Hou C, Xie Z, Luo F. Incidence and risk factors of recurrence in limb osteomyelitis patients after antibiotic-loaded cement spacer for definitive bone defect treatment. Bone Joint Res. 2023;12(8):467-475. doi:10.1302/2046-3758.128.BJR-2022-0413.R2.
14. Wu H, Jia C, Wang X, Shen J, Tan J, Wei Z, et al. The impact of methicillin resistance on clinical outcome among patients with Staphylococcus aureus osteomyelitis: a retrospective cohort study of 482 cases. Sci Rep. 2023;13:7990.
15. Dell'Aquila AM, Baldy Dos Reis GN, Cuba GT, Targa WHC, Bongiovanni JC, Durigon TS, Salles MJ, Baldy Dos Reis F. Outcome and predictors of treatment failure in chronic osteomyelitis using bioactive glass granules and putty formulations. Antibiotics. 2023;12(12):1720. doi:10.3390/antibiotics12121720.
16. Su Y, Li D, Du B, et al. Analysis of risk factors for the recurrence of osteomyelitis of the limb after treatment with antibiotic-loaded calcium sulfate and autologous bone graft. Front Bioeng Biotechnol. 2024;12:1368818. doi:10.3389/fbioe.2024.1368818.
17. Single versus two-stage management of long-bone chronic osteomyelitis in adults: a systematic review and meta-analysis. J Orthop Surg Res. 2024.
18. Study of the extent of surgical osteotomy in Cierny-Mader stages III and IV chronic osteomyelitis. BMC Musculoskelet Disord. 2025.
19. Wu H, Ma X, Li H, Wu Q, Jiang Z, Xi T, Shou Y, Han P. PET/MRI as a complement to PET/CT in chronic osteomyelitis with soft-tissue involvement: implications for surgical outcomes. Eur J Nucl Med Mol Imaging. 2026;53(5):3213-3225. doi:10.1007/s00259-025-07670-9.
20. Jia Q, Wang J, Lin J, et al. A multicenter study: habitat imaging and radiomics to guide precision and individualized surgical treatment in chronic osteomyelitis. BMC Med Imaging. 2026;26:97. doi:10.1186/s12880-026-02164-y.
21. Cao Y, Zhao X, Wang R, Hao F, Zhang Z, Zhang T, Li L, Ma D. MRI-based radiomics explainable model for predicting recurrence of limb chronic osteomyelitis in limb bones treated by Masquelet technique. Bone Joint Res. 2026;15(5):508-518. doi:10.1302/2046-3758.155.BJR-2025-0385.R1.
22. Urish KL, Cassat JE. Staphylococcus aureus osteomyelitis: bone, bugs, and surgery. Infect Immun. 2020;88:e00932-19.
23. Gimza BD, Cassat JE. Mechanisms of antibiotic failure during Staphylococcus aureus osteomyelitis. Front Immunol. 2021;12:638085.
24. Metsemakers WJ, et al. Fracture-related infection: a consensus on definition from an international expert group. Injury. 2018;49:505-510.
25. Li HK, Rombach I, Zambellas R, et al. Oral versus intravenous antibiotics for bone and joint infection. N Engl J Med. 2019;380:425-436.
26. Nana A, Nelson SB, McLaren A, et al. What's new in musculoskeletal infection: update on biofilms. J Bone Joint Surg Am. 2016;98:1226-1234.

27. Cierny G III. Surgical treatment of osteomyelitis. Plast Reconstr Surg. 2011;127(Suppl 1):190S-204S.
28. Kremers HM, Nwojo ME, Ransom JE, Wood-Wentz CM, Melton LJ III, Huddleston PM III. Trends in the epidemiology of osteomyelitis: a population-based study, 1969 to 2009. J Bone Joint Surg Am. 2015;97:837-845.