



# The Operating Room Global Journal (TORGJ)

<https://torgjournal.org/>

ISSN: 3105-3262



## Managing Recurrent Osteomyelitis in the Context of Antimicrobial Resistance in Sub-Saharan Africa: A Narrative Review.

Emmanuel Abiodun Owolabi<sup>1\*</sup>, Priscilla Olaoluwa Bakare<sup>1</sup>, Winifred Olajumoke Fagbenro<sup>1</sup>

<sup>1</sup>Benjamin S. Carson (SNR) College of Health and Medical Sciences, Babcock University, Ilishan-Remo, Ogun State, Nigeria.

### ABSTRACT

#### Corresponding Author\*:

Emmanuel Abiodun Owolabi  
[abiodunowolabi2000@gmail.com](mailto:abiodunowolabi2000@gmail.com)

#### Declaration:

**Authors' Contribution:** Emmanuel A. Owolabi conceived and designed the study, developed the methodology, wrote the original draft, supervised the project, and led the review, editing, and overall project administration, while Priscilla O. Bakare and Winifred O. Fagbenro conducted the literature search and contributed to the review and editing of the manuscript.

**Conflict of Interest:** No conflict of interest.

**Funding:** No funding received by the authors.

#### Article History:

Received: 07-10-2025  
Accepted: 14-12-2025  
Available Online : 14-12-2025

QR access this Article



**Background:** Chronic osteomyelitis (COM) persists globally as a challenging surgical infection, with recurrence rates remaining high, especially in resource-constrained Sub-Saharan Africa (SSA). The rise of antimicrobial resistance (AMR) further complicates effective management, necessitating practical and scalable solutions.

**Methods:** We conducted a narrative review using studies published between 2000 and 2025 from PubMed, AJOL, Google Scholar, and WHO resources, with terms such as "chronic osteomyelitis," "recurrent osteomyelitis," "AMR," and "Sub-Saharan Africa." Inclusion criteria encompassed recurrence rates, AMR profiles, treatment strategies, simulation-based training (SBT), and low-cost interventions in SSA.

**Results:** The recurrence rates of COM in SSA range from 2.8% to 16.7%, with adolescents and young adults being the predominant affected group. High burdens of *Staphylococcus aureus* (including methicillin-resistant *Staphylococcus aureus*) and extended-spectrum  $\beta$ -lactamase-producing Gram-negative bacteria complicate treatment in settings with limited microbiology and surgical infrastructure. Low-cost innovations, such as locally produced antibiotic-impregnated beads and biodegradable carriers, have demonstrated improved outcomes; however, systematic evidence of scalability remains limited. Simulation-based training (SBT) and context-specific antimicrobial stewardship are underutilized despite their potential to improve infection prevention.

**Conclusions:** Practical solutions such as low-cost antibiotic delivery, SBT integration, and tailored stewardship should be prioritized to reduce recurrence and improve outcomes.

**Keywords:** Chronic Osteomyelitis, Recurrent Osteomyelitis, Antimicrobial Resistance, Sub-Saharan Africa, Simulation-Based Training.

## INTRODUCTION

Osteomyelitis, first described by Hippocrates, is an ancient disease with evidence of similar bone infections in prehistoric fossils. It currently affects approximately 13 per 100,000 people annually worldwide, with higher rates in settings with increased trauma and limited healthcare access.<sup>1</sup> It is characterized by progressive bone inflammation, necrosis, and sequestrum formation resulting from disrupted blood supply and biofilm formation, which protects pathogens from host immunity and antibiotics.<sup>1,2</sup> Despite standard treatment combining surgical debridement and prolonged antibiotic therapy, recurrence rates remain high, particularly in low-resource environments like Sub-Saharan Africa (SSA).<sup>3</sup>

The rising threat of antimicrobial resistance (AMR) complicates treatment further, as *Staphylococcus aureus* acquires resistance to beta-lactam antibiotics, thereby increasing the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA), and multidrug-resistant Gram-negative bacteria add complexity to management.<sup>4,5</sup> SSA faces additional challenges due to inadequate diagnostics, surgical capacity, and infection prevention practices, necessitating the exploration of low-cost, scalable interventions and context-adapted antimicrobial stewardship.

This review synthesizes evidence on recurrent Chronic osteomyelitis (COM) within the AMR context in SSA, highlighting pathogen profiles, recurrence rates, barriers to effective care, and low-cost innovations while identifying critical gaps to guide policy, practice, and research priorities.

## METHODS

A narrative review approach was adopted, targeting English-language publications from 2000 to 2025, using PubMed, AJOL, Google Scholar, and WHO resources. Search terms included “chronic osteomyelitis,” “recurrent osteomyelitis,” “antimicrobial resistance,” and “Sub-Saharan Africa.” Grey literature and WHO reports were also reviewed.

Inclusion criteria:

- Studies reporting prevalence and recurrence rates of COM in SSA.
- Articles discussing pathogen profiles and AMR patterns.
- Studies detailing treatment strategies, low-resource innovations, and SBT in orthopedic infections.

Exclusion criteria:

- Studies unrelated to osteomyelitis or antimicrobial resistance in orthopedic infections.
- Studies outside Sub-Saharan Africa unless they provide insights which can be applied to SSA countries.
- Case reports without broader epidemiological or treatment strategy insights.
- Editorials, commentaries, and opinion pieces lacking empirical data or policy analysis.
- Studies focusing exclusively on acute osteomyelitis without discussion of chronic or recurrent aspects.

### Selection process

1. Identification: 120 identified records from databases and grey literature.
2. Screening: 20 duplicates removed; 100 titles/abstracts screened; 50 excluded
3. Eligibility: 50 Full-text articles reviewed; 25 excluded.
4. Included: 25 publications

The findings were narratively synthesized to align with SSA's context, emphasizing practical insights for clinicians and policymakers.

Two reviewers (PB and WOF) independently assessed the methodological quality of included studies. For randomized controlled trials we used the Cochrane Risk of Bias tool; for non-randomized cohort and case-control studies we used the Newcastle–Ottawa Scale (NOS); for cross-sectional and case series we used the Joanna Briggs Institute (JBI) critical appraisal checklists; and for qualitative or implementation studies we used the CASP qualitative checklist. Disagreements were resolved by discussion and, if needed, by arbitration with a third reviewer (EAO). Each study was assigned a certainty rating (High / Moderate / Low / Very low) adapted from GRADE principles for narrative synthesis: randomized trial evidence was rated higher than observational evidence, and risk of bias downgraded certainty where appropriate. Results of the critical appraisal are summarized in Supplementary Table S1.

**Table 1: Summary of Studies on Recurrent Osteomyelitis in Sub-Saharan Africa**

AUTHORS	STUDY DESIGN	SAMPLE SIZE	FINDINGS
Achor MT, Aaron FE, Obene TA (2025, Nigeria)	Hospital-based retrospective study	Not specified	Reported recurrence rate ~16.7%, identified <i>S. aureus</i> , <i>Pseudomonas</i> , <i>Klebsiella</i> ; highlighted AMR challenges.
Tesfaye Bizuneh B, Kassahun Tarekegn T, et al. (2023, Ethiopia)	Retrospective study	Hospital records (2018–2021)	Prevalence of acute and chronic osteomyelitis; recurrence rate 2.89%; pathogens mainly <i>S. aureus</i> .
Mantero E, Carbone M, Calevo MG, Boero S (2011, Kenya)	Prospective study	96 pediatric patients	Diagnosis and treatment of pediatric chronic osteomyelitis; recurrence rate ~12.2%; <i>S. aureus</i> predominant.
Ouedraogo S, Zida M, Walla A, Tall M (2017, Burkina Faso)	Epidemiological, bacteriological and therapeutic study	Not specified	Reported recurrence rate 5.3%; common pathogens included ceftriaxone-resistant <i>Salmonella</i> and <i>Staphylococcus</i> .
Nacoulma SI, Ouédraogo DD, et al. (2007, Burkina Faso)	Retrospective study	102 cases (1996–2000)	Chronic osteomyelitis cases described; resistant pathogens noted.
Ikpeme IA, Oku EO, Ngim NE, Ilori IU, Abang IE (2013, Nigeria)	Comparative study (with/without local antibiotic delivery)	Not specified	Antibiotic beads improved outcomes (77.8% cure) compared to debridement alone (57.7%).

Salawu ON, Babalola OM, et al. (2017, Nigeria)	Comparative clinical study	Not specified	Better outcomes with antibiotic beads vs gentamicin-saline after sequestrectomy.
Alonge TO, Ogunlade SO, et al. (2002, Nigeria)	Clinical trial (initial study)	Not specified	Ceftriaxone-PMMA beads were effective in management of chronic osteomyelitis.
Fonkoue L, Tissingh EK, et al. (2024, Cameroon)	Cohort study	Not specified	66% Gram-negative fracture-related infections; high resistance to fluoroquinolones/rifampicin, carbapenems moderately effective.
Alamarat ZI, Babic J, et al. (2020, Nigeria case)	Case report (compassionate drug use)	Single pediatric case	Cefiderocol successfully used for resistant <i>Pseudomonas</i> and <i>Klebsiella</i> osteomyelitis.
Venter RG, Tanwar YS, et al. (2020, South Africa)	Retrospective cohort study	80 patients	Debridement and dead space management used. 6% recurrence successfully treated with bio-glass

## RESULTS

### RECURRENCE RATES AND EPIDEMIOLOGY

Chronic osteomyelitis (COM) recurrence rates in Sub-Saharan Africa (SSA) vary across regions:

- Nigeria: 16.7%<sup>6</sup>
- Ethiopia: 2.89%<sup>7</sup>
- Burkina Faso: 5.3%<sup>8</sup>
- Kenya: 12.2%<sup>9</sup>
- South Africa: 6%<sup>26,27</sup>

Adolescent and young adult males are commonly affected due to open fractures and hematogenous spread, with the tibia and femur frequently involved.<sup>10,11</sup>

**Table 2: Recurrent Osteomyelitis: Recurrence Rates, Pathogen Profiles, and Innovations in Sub-Saharan Africa**

Country	Recurrence Rate (%)	Common Pathogens	AMR Challenges	Innovations
---------	---------------------	------------------	----------------	-------------

Nigeria	16.7	<i>Staphylococcus aureus</i> (MRSA, MSSA), <i>Pseudomonas</i> , <i>Klebsiella</i>	MRSA, extended-spectrum $\beta$ -lactamase-producing Gram-negatives	Antibiotic-impregnated polymethylmethacrylate (PMMA) beads, biodegradable carriers
Ethiopia	2.89	Likely <i>Staphylococcus aureus</i>	Likely AMR (details not specified)	N/A
Burkina Faso	5.3	<i>Salmonella</i> spp. (ceftriaxone-resistant), <i>Staphylococcus</i>	Ceftriaxone-resistant <i>Salmonella</i>	N/A
Kenya	12.2	<i>Staphylococcus aureus</i>	MRSA, limited AMR data	N/A
Cameroon	N/A	Gram-negative (66%)	High resistance to fluoroquinolones and rifampicin; moderate efficacy of carbapenems	Limited stewardship; local antibiotic delivery challenges
Zaire	N/A	N/A	N/A	Plaster-of-Paris antibiotic systems, collagen fleece
South Africa	6%	<i>Klebsiella Pneumoniae</i> (70%), <i>Staphylococcus aureus</i> (17%)	High resistance to cephalosporins carbapenems; 17% <i>Staphylococcus aureus</i> infections are non-susceptible to cloxacillin (MRSA)	Bioactive glass (S53P4)

## PATHOGEN PROFILES AND AMR CHALLENGES

*Staphylococcus aureus* (including methicillin-sensitive *Staphylococcus aureus*[MSSA] and methicillin-resistant *Staphylococcus aureus*[MRSA]) remain the leading pathogen in bone and joint infections, accounting for up to 75% of cases worldwide. In SSA, the emergence of MRSA and ESBL-producing Gram-negative bacteria significantly complicates treatment options.<sup>12</sup> In Cameroon, Gram-negative pathogens accounted for 66% of fracture-related infections, exhibiting high resistance (>60%) to fluoroquinolones and rifampicin, with only carbapenems, amikacin, and vancomycin showing moderate efficacy. A study in Nigeria also showed an adolescent male with chronic osteomyelitis caused by a resistant *Pseudomonas aeruginosa* and a *Klebsiella pneumoniae* strain, which was treated using Cefiderocol.<sup>13</sup> A case of osteomyelitis caused by ceftriaxone-resistant *Salmonella* was reported in a study in Burkina Faso.<sup>14</sup>

Barriers to effective antimicrobial stewardship include:

- Limited microbiology capacity and diagnostics<sup>15</sup>
- Bacteria evolving into minor colony variants (SCV) or forming biofilm<sup>16-18</sup>
- Unregulated antibiotic sales<sup>15,19</sup>
- Outpatient poor adherence to the antibiotic regimen<sup>20</sup>
- Weak prescribing oversight and inadequate healthcare training<sup>12</sup>

## TREATMENT STRATEGIES AND INNOVATIONS

### Standard Management

Standard treatment for chronic osteomyelitis (COM) typically involves surgical debridement and prolonged parenteral antibiotic therapy, often hindered by limited surgical resources and inadequate sterile conditions in SSA.<sup>21</sup> A systematic review reported no significant differences in recurrence rates between single-stage and two-stage surgeries for long-bone COM.<sup>22</sup> Oral versus parenteral antibiotic effectiveness shows no significant differences if pathogens are sensitive; however, limitations in oral formulations remain in availability and spectrum.<sup>2</sup>

### Low-Resource Innovations

#### Clinically Tested in SSA:

- Locally produced antibiotic-impregnated polymethylmethacrylate (PMMA) beads: Studies in Nigeria demonstrated a 77.8% cure rate with antibiotic beads versus 57.7% with debridement alone.<sup>21,23</sup>

#### Experimental/Limited to Case Series:

- Biodegradable carriers (e.g., plaster-of-Paris antibiotic systems): Plaster-of-Paris antibiotic systems in Zaire achieved wound healing in 16 of 18 patients with radiographic bone regeneration within six weeks.<sup>24</sup>
- Collagen fleece filled with antibiotics: Emerging reports suggest higher antibiotic dispersion rates than PMMA beads, but current data are largely observational and not yet supported by large-scale clinical trials.<sup>25</sup>

These innovations reduce recurrence while minimizing hospital stays and systemic antibiotic use; however, they lack evidence of region-wide scalability, standardization, and long-term safety.

## SIMULATION-BASED TRAINING (SBT)

SBT is underutilized in SSA but offers a promising adjunct to infection prevention education. A study revealed that SBT improved infection prevention compliance, reduced healthcare-associated infections, and enhanced learners' confidence and competence in infection control measures<sup>28</sup>.

Simulation-based training (SBT) has demonstrable effects on improving infection-prevention knowledge, adherence to practices (including hand hygiene and aseptic technique), and learner confidence; several systematic reviews and meta-

analyses report improved compliance and reductions in healthcare-associated infection rates after institution-wide SBT programmes<sup>29</sup>. In low-resource and SSA settings, pilot simulation modules (e.g., hand-hygiene scenarios and PPE donning/doffing training) have shown feasibility, increased adherence and improved skills scores, though larger scale effectiveness studies with patient-level outcomes remain limited<sup>28,29</sup>. Given this evidence, SBT is a promising adjunct to stewardship and surgical training but should be implemented alongside robust monitoring and outcome measurement.

Similar SBT adaptation in SSA could address infection prevention deficits and reduce the recurrence of COM.

## IDENTIFIED GAPS IN SSA CONTEXT

Despite available insights, critical gaps persist:

- Lack of systematic synthesis on recurrence rates, treatment outcomes, and AMR patterns across SSA, hindering informed policy development.
- The underexplored scalability of low-cost interventions like local antibiotic delivery systems across diverse SSA contexts<sup>15</sup>
- Minimal SBT integration in orthopedic infection prevention within SSA despite demonstrated effectiveness elsewhere
- Limited antimicrobial stewardship models tailored to recurrent COM in SSA's low-resource orthopedic settings.<sup>20</sup>
- Absence of patient-centered outcome measures (quality of life, functional recovery, financial burden) in studies, limiting comprehensive disease impact assessment.<sup>15</sup>

## DISCUSSION

COM recurrence remains a significant burden in SSA, driven by high AMR prevalence and limited healthcare resources. Local innovations, such as PMMA beads and biodegradable carriers, offer cost-effective solutions; however, a systematic evaluation across diverse SSA contexts is necessary to determine their effectiveness and applicability.

Addressing these challenges requires:

1. Expand local antibiotic delivery systems (PMMA beads / biodegradable carriers) - Evidence: Moderate (observational comparative studies in Nigeria reported improved cure rates). Implementation: surgical training on bead implantation, local production protocols, hospital infection control review<sup>6</sup>. (Responsible: Hospital surgical departments, national orthopedic societies).
2. Strengthen microbiology capacity and local antibiograms - Evidence: Strong indirect (surveillance data indicate variable resistance). Implementation: standardize specimen transport, subsidize basic AST panels, connect sentinel labs to NICD/GERMS networks. (Responsible: Ministries of Health, NHLS/NICD)<sup>27</sup>.
3. Integrate context-appropriate SBT into surgical/IPC training - Evidence: Moderate (SBT improves IPC practices; SSA pilots feasible). Implementation: start with low-cost scenarios (hand hygiene, aseptic technique), evaluate impact on IPC metrics, scale iteratively<sup>28</sup>.
4. Implement antimicrobial stewardship tailored to orthopedic services - Evidence: Low to Moderate; implementation studies show feasibility. Implementation: develop standard empiric protocols updated by local hospital antibiograms, audit prescribing, provide targeted education. (Responsible: Hospital stewardship teams).
5. These strategies will improve patient outcomes, reduce recurrence, and support AMR containment.

## LIMITATIONS

The inherent constraints of narrative synthesis limit this narrative review, as it lacks quantitative meta-analysis and a formal risk of bias assessment. The review may have missed unpublished data or region-specific reports not indexed in major databases. Additionally, antimicrobial resistance patterns can vary significantly across local contexts within Sub-Saharan Africa, potentially affecting the generalizability of the findings.

## CONCLUSION

This narrative review synthesizes published evidence on recurrent chronic osteomyelitis in Sub-Saharan Africa and highlights the interaction between recurrence and antimicrobial resistance. Observational studies and local innovations (e.g., locally produced antibiotic-impregnated beads) suggest potential benefits in reducing recurrence, but the overall evidence base is limited by heterogeneity and moderate to high risk of bias. Surveillance data from regional programs indicate a persistent burden of resistant *S. aureus* and resistant Gram-negative pathogens that should inform empiric therapy and stewardship<sup>2</sup>. Consequently, we recommend prioritizing strengthening microbiology capacity and local antibiograms, pragmatic local antibiotic delivery strategies evaluated in prospective studies, and integration of simulation-based infection prevention training with monitoring of clinical outcomes. Future research should include multicentre prospective studies with standardized outcome measures and implementation research to test scalability.

## ETHICS STATEMENT

This study is a narrative review of published data and did not require institutional ethics approval.

## DATA AVAILABILITY STATEMENT

Data sharing does not apply to this article as no new data were created or analyzed in this study.

## FUNDING STATEMENT

This work received no specific funding.

## ACKNOWLEDGEMENT

We acknowledge the Benjamin S. Carson (SNR) College of Health and Medical Sciences at Babcock University for providing an enabling environment for this research. We also thank colleagues who contributed insights during the early drafting stages.

## CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

## REFERENCES

1. Panteli M, Giannoudis PV. Chronic osteomyelitis: what the surgeon needs to know. *EFORT Open Rev* [Internet]. 2016 May 31 [cited 2025 Jul 7];1(5):128–35. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5367612/>
2. Haddad N, Ajaz J, Mansour L, Kasemodel R, Jarvis J, Jarad J, et al. A review of the clinical utilization of oral antibacterial therapy in the treatment of bone infections in adults. *Antibiotics (Basel)*. 2023;13(1):4. doi: 10.3390/antibiotics13010004
3. 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):228–35. doi: 10.1016/j.cjtee.2023.01.003
4. Lari A, Esmaeil A, Marples M, Watts A, Pincher B, Sharma H. Single versus two-stage management of long-bone chronic osteomyelitis in adults: a systematic review and meta-analysis. *J Orthop Surg Res*. 2024;19(1):351. doi: 10.1186/s13018-024-04832-7

5. World Health Organization. Antimicrobial resistance [Internet]. Geneva: WHO; 2023 [cited 2025 Jul 7]. Available from: <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>
6. Achor MT, Aaron FE, Obene TA. Presentation and outcome of treatment of chronic osteomyelitis at the Rivers State University Teaching Hospital, Port Harcourt, Nigeria. *Int J Health Pharm Res* [Internet]. 2025 [cited 2025 Jul 7];10(3):64–74. Available from: <https://www.iiardjournals.org/get/IJHPR/VOL.%2010%20NO.%203%202025/Presentation%20and%20Outcome%2064-74.pdf>
7. Hassan A, Gayus D, Abdulrasheed I, Umar M, Ismail D, Babadoko A. Chronic leg ulcers in sickle cell disease patients in Zaria, Nigeria. *Arch Int Surg* [Internet]. 2014;4(3):141. Available from: <https://go.gale.com/ps/i.do?p=AONE&sw=w&issn=22789596&v=2.1&it=r&id=GALE%7CA394843092>
8. Tesfaye Bizuneh B, Kassahun Tarekegn T, Melake Weldeslassie F, Abebaw Tsehay S, Kiflom Gaim T, Sium Mesfin S, et al. A retrospective study on assessment of prevalence and treatment outcome of acute and chronic osteomyelitis at surgical ward in HFUSH from 2018–2021. *J Surg*. 2023;11(2):12. doi: 10.11648/j.js.20231102.12
9. Mantero E, Carbone M, Calevo MG, Boero S. Diagnosis and treatment of pediatric chronic osteomyelitis in developing countries: prospective study of 96 patients treated in Kenya. *Musculoskelet Surg*. 2011;95(1):13–8. doi: 10.1007/s12306-011-0104-0
10. Ouedraogo S, Zida M, Walla A, Tall M. Epidemiological, bacteriological and therapeutic aspects of chronic osteomyelitis in a sub-Saharan environment. *Med Sante Trop*. 2017;27(3):292–5. doi: 10.1684/mst.2017.0705
11. Ikpeme IA, Oku EO, Ngim NE, Ilori IU, Abang IE. Comparison of the outcome of treatment of chronic osteomyelitis by surgical debridement with and without local antibiotic delivery system: experience from a Nigerian teaching hospital. *Int J Clin Med* [Internet]. 2013 [cited 2025 Jul 7];4(7):313–8. Available from: <https://www.scirp.org/journal/paperinformation?paperid=33913>
12. Salawu ON, Babalola OM, Kadir DM, Ibraheem GH, Ahmed BA, Mejabi JO, et al. Chronic osteomyelitis: comparison of outcome following the use of antibiotic impregnated beads and gentamycin-saline solution after sequestrectomy. *Niger J Orthop Trauma* [Internet]. 2017 [cited 2025 Jul 7];16(1):13–7. Available from: <https://www.ajol.info/index.php/njotra/article/view/199037>
13. Alamarat ZI, Babic J, Tran TT, Wootton SH, Dinh AQ, Miller WR, et al. Long-term compassionate use of cefiderocol to treat chronic osteomyelitis caused by extensively drug-resistant *Pseudomonas aeruginosa* and extended-spectrum- $\beta$ -lactamase-producing *Klebsiella pneumoniae* in a pediatric patient. *Antimicrob Agents Chemother*. 2020;64(4):e01872-19. doi: 10.1128/AAC.01872-19
14. Nacoulma SI, Ouédraogo DD, Nacoulma EWC, Korsaga A, Drabo JY. [Chronic osteomyelitis at the Ouagadougou teaching hospital (Burkina Faso): a retrospective study of 102 cases (1996–2000)]. *Bull Soc Pathol Exot*. 2007;100(4):264–8.
15. Rolfe R, Kwobah C, Muro F, Ruwanpathirana A, Lyamuya F, Bodinayake C, et al. Barriers to implementing antimicrobial stewardship programs in three low- and middle-income country tertiary care settings: findings

- from a multi-site qualitative study. *Antimicrob Resist Infect Control* [Internet]. 2021 [cited 2025 Jul 8];10:60. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7993456/>
16. Driche EH, Badji B, Mathieu F, Zitouni A. In-vitro antibacterial and antibiofilm activities and in-silico analysis of a potent cyclic peptide from a novel *Streptomyces* sp. strain RG-5 against antibiotic-resistant and biofilm-forming pathogenic bacteria. *Arch Microbiol*. 2024;206(11):450. doi: 10.1007/s00203-024-04174-2
  17. del Pozo EG, Collazos J, Cartón JA, Camporro D, Asensi V. Bacterial osteomyelitis: microbiological, clinical, therapeutic, and evolutive characteristics of 344 episodes. *Rev Esp Quimioter* [Internet]. 2018 [cited 2025 Jul 8];31(3):217–25. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6166254/>
  18. Oliveira P, Carvalho V, Lima A. Optimizing the treatment of osteomyelitis with antimicrobial drugs: current concepts. *Curr Orthop Pract*. 2017;28(1):1.
  19. Raka L, Kurti A. Addressing barriers in antimicrobial stewardship: a guide from research to implementation. *J Glob Antimicrob Resist*. 2024;39:26. doi: 10.1016/j.jgar.2024.10.005
  20. Masetla MA, Ntuli PN, Abraham V, Godman B, Witika BA, Mudenda S, et al. Antimicrobial stewardship for outpatients with chronic bone and joint infections in the orthopaedic clinic of an academic tertiary hospital, South Africa. *Antibiotics (Basel)*. 2023;12(7):1142. doi: 10.3390/antibiotics12071142
  21. Fonkoue L, Tissingsh EK, Ngouateu MT, Muluem KO, Ngongang O, Mbouyap P, et al. The microbiological profile and antibiotic susceptibility of fracture-related infections in a low-resource setting differ from high-resource settings: a cohort study from Cameroon. *Antibiotics (Basel)* [Internet]. 2024 [cited 2025 Jul 7];13(3):236. Available from: <https://www.mdpi.com/2079-6382/13/3/236>
  22. Jerzy K, Francis H. Chronic osteomyelitis – bacterial flora, antibiotic sensitivity and treatment challenges. *Open Orthop J* [Internet]. 2018 [cited 2025 Jul 6];12:153–63. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5925860/>
  23. Alonge TO, Ogunlade SO, Omololu AB, Fashina AN, Oluwatosin A. Management of chronic osteomyelitis in a developing country using ceftriaxone–PMMA beads: an initial study. *Int J Clin Pract*. 2002;56(3):181–3. doi: 10.1046/j.1368-5031.2002.00363.x
  24. Geurts J, Hohnen A, Vranken T, Moh P. Treatment strategies for chronic osteomyelitis in low- and middle-income countries: systematic review. *Trop Med Int Health*. 2017;22(9):1054–62. doi: 10.1111/tmi.12921
  25. El-Husseiny M, Patel S, MacFarlane RJ, Haddad FS. Biodegradable antibiotic delivery systems. *J Bone Joint Surg Br*. 2011;93(2):151–7. doi: 10.1302/0301-620X.93B2.24844
  26. Venter RG, Tanwar YS, Grey JP, Ferreira N. The management of chronic osteomyelitis in adults: outcomes of an integrated approach. *SA Orthopaedic Journal* [Internet]. 2021 [cited 2025 Sep 26];20(1):33–8. Available from: [http://www.scielo.org.za/scielo.php?script=sci\\_arttext&pid=S1681-150X2021000100007&lng=en&nrm=iso&tlng=en](http://www.scielo.org.za/scielo.php?script=sci_arttext&pid=S1681-150X2021000100007&lng=en&nrm=iso&tlng=en)

27. National Department of Health. Surveillance for Antimicrobial Resistance and Consumption of Antibiotics in South Africa 2018-2022 [Internet]. 2024 Mar [cited 2025 Sep 26]. Available from: <https://www.nicd.ac.za/wp-content/uploads/2024/04/South-African-AMR-Surveillance-Report-2022.pdf>
28. Kang M, Nagaraj MB, Campbell KK, Nazareno IA, Scott DJ, Arocha D, et al. The role of simulation-based training in healthcare-associated infection (HAI) prevention. *Antimicrobial Stewardship & Healthcare Epidemiology : ASHE* [Internet]. 2022 Feb;2(1):e20. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9614911/>
29. Yoshikawa A, Ohtsuka H, Aoki K, Tashiro N, Togo S, Komaba K, et al. Simulation-based infection prevention and control training for medical and healthcare students: a systematic review. *Front Med (Lausanne)*. 2025 May 14;12.