RQ [Antibiotics. 3]: Should prophylactic antibiotic administration be limited to a single dose, or continued for up to 72 hours?

Section 1: Background:

Systemic antibiotics are a well-established and recommended strategy for preventing infections in open fractures[1, 2]. Nonetheless, debate persists regarding the optimal duration and antibiotic choice. In the literature, antibiotics are typically described as prophylactic in this context. However, strictly adhering to the definition of surgical antibiotic prophylaxis[3], antibiotics for open fractures are often continued beyond 24 hours in contaminated wounds with a high risk of infection. Therefore, terms such as extended prophylaxis or short empirical antibiotic therapy may more accurately describe antibiotic use in these cases.

Early initiation of antibiotics within the first three hours after trauma is a clear, evidence-based recommendation[4, 5]. The duration remains controversial, although most guidelines recommend a maximum of 72 hours[4, 6-10]. In clinical practice, surgeons often use longer durations. In India, the mean duration of antibiotic use for open fractures was 9.3 days[11], and in Latin America, antibiotics were used for more than 72 hours in 67.9% of 389 cases of open tibial fractures[12]. Even in Germany and the USA, adherence to national guideline recommendations is low, with 22.2% adherence to the 24-hour duration for type 2 open fractures[13] and an overall adherence of 33.2% to antibiotic use in open fractures[14].

There is a clear gap between evidence and practice regarding the use of systemic antibiotics in open fractures for infection prevention, particularly regarding duration. Evidence shows that prolonging antibiotic therapy beyond 72 hours does not reduce the risk of infection and may cause harm, including bacterial resistance, systemic toxicity, and increased healthcare costs.

Section 2: Data extraction table

For each included study: Author/Year, Study Design, Sample Size, Population, Intervention/Comparator, Key Outcomes, Results, and Follow-up duration.

Table 1. Observational studies.

S.no	Author, year of publication, Country	Study Design	Sample Size (add individually for each group if multiple groups compared)	Study population (Inclusion and exclusion criteria)	Groups compared	Results
1	Dunkel et al., 2013, Switzerland[15]	Retrospective cohort study at Geneva University Hospital, a level-1 trauma centre; adult open fractures admitted from 1 Jan 1996 to 31 Dec 2009, with follow-up through 31 Dec 2011.	1492 open fractures in 1290 patients. Gustilo-Anderson grade I: 663; grade II: 370; grade III: 310; unclassifiable: 149. Infections: 54/1492 (3.6%).	Inclusion: adult trauma patients with open bone fractures managed in the orthopaedic service. Exclusion: age <18 years; open fracture outside orthopaedics; incomplete records; follow-up <60 days; infection already present on admission; MRSA infection; infection >2 months after surgery; fracture in an area of prior chronic osteomyelitis.	Duration of systemic parenteral antibiotic prophylaxis after open fracture: 1 day (reference) vs 2-3 days vs 4-5 days vs >5 days. Analyses performed for all open fractures and separately for Gustilo grade III fractures.	Median prophylaxis duration was 3 days (IQR 1-3). Infection was associated with injury severity rather than prophylaxis duration. Adjusted OR for infection vs 1 day: 2-3 days 0.6 (95% CI 0.2-2.0); 4-5 days 1.2 (0.3-4.9); >5 days 1.4 (0.4-4.4). For grade III fractures only, longer courses also showed no significant benefit. Grade III injury and vascular injury/compartment syndrome were key infection predictors. Authors concluded that even in grade III fractures, a 1-day course may be as effective as prolonged prophylaxis.
2	Stennett et al., 2020, International multicentre study (United States, Canada, Australia, Norway, India)[16]	Retrospective cohort study / secondary analysis of the FLOW trial, an international randomized trial conducted at 41 sites from 2009 to 2013.	2400 patients with open extremity fractures included after excluding 47/2447 FLOW participants because of missing antibiotic or wound-contamination data. Extended prophylaxis >72 h after definitive closure: 1008. Shorter prophylaxis <=72 h: 1392. Deep SSI: 163/2400 (7%).	Inclusion: adults (>=18 years) with an open fracture of an extremity requiring operation; eligible injuries included arm, wrist, leg, ankle, foot, clavicle, or scapula fractures. Exclusion: pelvic ring, axial skeleton, hand, or foot fractures; participants missing antibiotic duration or wound-contamination data. Antibiotics given for treatment of suspected infection and antibiotics prescribed before definitive closure were excluded from exposure calculation.	Extended prophylactic antibiotics after definitive wound closure (>72 h) vs shorter duration (<=72 h), stratified by wound contamination severity: Mild: >72 h n=726 vs <=72 h n=1123. Moderate: >72 h n=221 vs <=72 h n=202. Severe: >72 h n=61 vs <=72 h n=67.	Overall deep SSI prevalence was similar between extended and shorter groups (7% vs 7%), but effect differed by contamination level. Mild contamination: extended prophylaxis trended toward higher deep SSI odds, adjusted OR 1.39 (95% CI 0.92-2.11). Moderate contamination: no association, adjusted OR 1.09 (0.53-2.27). Severe contamination: extended prophylaxis was protective, adjusted OR 0.20 (0.07-0.60). Conclusion: antibiotic duration should probably be individualized by contamination burden rather than applied uniformly.

3	Yang et al.,2025, China[17]	Prospective cohort study using the Surgical Site Infection Surveillance and Improvement Project (SISIP) database from a tertiary orthopaedic university hospital; surgeries from Oct 2014 to Dec 2020.	37,046 adult orthopaedic surgery patients. Open fractures: 3585; closed fractures: 16,941; non-traumatic surgery: 16,520. SSI overall: 871/37,046 (2.35%). Open-fracture SSI: 290/3585 (8.09%); closed-fracture SSI: 433/16,941 (2.56%); non-trauma SSI: 148/16,520 (0.90%).	Inclusion: adult patients (>=18 years) undergoing orthopaedic surgery and recorded in the SSIOS/SISIP database. Exclusion: old/pathological fractures or tumours; therapeutic postoperative antibiotics >1 week; preoperative or special infection; no perioperative prophylaxis; non-cephalosporin prophylaxis; lost to follow-up. SSI was assessed within 1 year using CDC/NHSN criteria and readmission/microbiology data.	Surgical antibiotic prophylaxis (SAP) duration analysed continuously using adjusted generalized additive models and then dichotomized by cut-off: Overall <=2.4 days vs >2.4 days. Open fractures <=3.6 days vs >3.6 days (1792 vs 1793). Closed fractures <=2.6 days vs >2.6 days (10,361 vs 6580). Non-trauma <=1.1 days vs >1.1 days (7290 vs 9230).	No statistically significant protective effect of prolonged SAP was found. Adjusted ORs for SSI with duration above cut-off: overall 0.868 (95% CI 0.746-1.011); open fractures 0.867 (0.668-1.124); closed fractures 0.925 (0.754-1.135); non-trauma 1.184 (0.832-1.683). SAP duration ranked 21st overall among 34 SSI-related factors, 14th for open fractures, 28th for closed fractures, and 3rd for non-trauma. Exploratory analyses linked SAP >2 days with higher MRSA and multidrug-resistant infections. Authors concluded prolonged postoperative SAP does not protect against SSI and supports discontinuation rather than routine continuation.
Abbreviations: SAP = surgical antibiotic prophylaxis; SSI = surgical site infection; MRSA = methicillin-resistant Staphylococcus aureus; MDR = multidrug-resistant; OR = odds ratio; aOR = adjusted odds ratio; CI = confidence interval; IQR = interquartile range.						

Table 2. Systematic Review

S.no	Author, year of publication, Country	Study Design	Sample Size (add individually for each group if multiple groups compared)	Study population (Inclusion and exclusion criteria)	Groups compared	Results
1	Chang et al., 2015, Canada[18]	Systematic review and meta-analysis of randomized controlled trials evaluating antibiotic prophylaxis strategies for open fractures of the extremities.	17 randomized controlled trials were eligible. Antibiotic prophylaxis vs no prophylaxis: 4 RCTs, 472 patients. Longer vs shorter duration: 3 RCTs, 1104 patients. Other comparisons evaluated alternative antibiotic regimens but were individually small.	Inclusion: randomized clinical trials involving patients with one or more open fractures of the arms or legs; compared an antibiotic prophylactic regimen with another regimen or no prophylaxis; reported postoperative infection. Exclusion: known infection, fingers/toes, gunshot wounds, bomb injuries, HIV/AIDS-restricted studies.	A) Antibiotic prophylaxis vs no prophylaxis. B) Longer duration of prophylaxis (3-5 days) vs shorter duration (1 day). C) Alternative antibiotic regimens.	Antibiotic prophylaxis reduced subsequent infection compared with no prophylaxis (RR 0.37; 95% CI 0.21-0.66; absolute risk reduction 9.6%). Longer duration (3-5 days) did not reduce infection compared with 1 day (RR 0.97; 95% CI 0.69-1.37). The authors concluded that courses as short as 1 day appear as effective as 3-5 days, with low-to-moderate confidence.
2	Isaac et al., 2016, United Kingdom[19]	Systematic review of published clinical trials and studies considered authoritative regarding duration of prophylactic antibiotics in adult open tibial fractures.	24 reports were reviewed against eligibility criteria; 8 studies met inclusion criteria. Only 1 randomized, double-blind, prospective study specifically examined prophylactic antibiotic duration in open extremity fractures: Dellinger et al., 248 patients / 264 open fractures.	Population focus: adults with open tibial fractures. Included studies addressing duration of prophylactic antibiotic administration, infection outcomes, and/or fracture healing. Excluded reports that did not directly evaluate duration, were not clinical trials, involved very small samples, gunshot-only comparisons of route, or lacked duration data.	Duration of prophylactic antibiotic administration across included studies, including short-course vs longer-course regimens. The central direct comparison came from the randomized Dellinger study: 1 day of cefonicid vs 5 days of cefonicid vs 5 days of cefamandole.	The Dellinger trial reported similar infection rates across 1-day and 5-day regimens (13%, 12%, and 13%). Overall, the review found poor-quality and limited evidence, with only one rigorous study directly addressing duration. The authors concluded that a short course appears as effective as a longer course, but a rigorous multicentre randomized trial is needed.

3	Messner et al., 2017, United Kingdom / Greece[20]	Systematic review and meta-analysis assessing whether prolonged antibiotic administration reduces infection after open fractures, including comparative and observational studies.	5 comparative studies including 1284 open fractures. 27 observational studies including 5408 open fractures. Total evidence base: 6692 open fractures.	Inclusion: clinical studies of open long-bone fractures with clear documentation of antibiotic-protocol duration and infection rates. Exclusion: paediatric open fractures, spine, hand, foot and maxillofacial open fractures, experimental/animal studies, case reports, and studies with <20 subjects.	Primary comparison: antibiotic duration <=72 h vs >72 h. Additional subgroup analyses by Gustilo grade, anatomic location, and shorter 24-48 h regimens.	Comparative studies showed no benefit from treatment >72 h (OR 0.85; 95% CI 0.60-1.21). Observational pooled infection estimates were similar for <=72 h and >72 h (10.0% vs 9.2%; p=0.53). No significant difference was found in Gustilo I-II or Gustilo III subgroups. The authors concluded that prolonged administration beyond 72 h should be abandoned in routine open long-bone fractures.
4	Chang et al., 2019, Canada[5]	Systematic survey of current clinical practice and recommendations for antibiotic prophylaxis in open fractures. This was not an evidence-effectiveness meta-analysis, but a structured survey of published practice patterns and guidance.	223 eligible publications: 156 articles, 62 textbook chapters, and 5 online guidelines. Reported 100 clinical practice patterns, 276 recommendations for systemic antibiotics, and 3 recommendations for local antibiotics alone.	Included publications from January 2007 to June 2017 that described either actual antibiotic prophylaxis practice or recommendations for open fractures of the extremities. Sources included clinical studies, reviews, surgeon surveys, textbooks, guidelines, and institutional protocols. Excluded paediatric-only, known infection, HIV/AIDS-focused, and non-relevant publications.	Practice patterns and recommendations were categorized by injury severity, antimicrobial spectrum, dose/route/start time, and duration. Comparisons were descriptive rather than interventional.	Most practice-pattern publications used both gram-positive and gram-negative coverage and continued antibiotics for 2-3 days. Most recommendations supported systemic prophylaxis. Less severe injuries were usually recommended gram-positive coverage for <=3 days, whereas more severe injuries were usually recommended broader coverage for 2-3 days. Most publications reported immediate intravenous administration.
5	Vanvelk et al., 2022, Netherlands / Belgium / United States / Switzerland[21]	Systematic review and critical appraisal of studies evaluating the association between duration of systemic perioperative antibiotic prophylaxis and fracture-related infection in open fractures.	6 articles included after screening 8610 references. Included study designs: 2 randomized controlled trials and 4 retrospective studies. Key included cohorts ranged from 248 patients / 264 fractures to 2400 FLOW trial participants.	Inclusion: skeletally mature patients operatively treated for open fractures; studies primarily investigating systemic PAP duration and FRI; minimum follow-up of 2 months in at least 75% of patients. Exclusion: skull and spinal fractures, conference abstracts/posters/letters, non-English articles.	Most included studies compared either 1 day vs 5 days of PAP or used a 72 h cut-off. Some studies compared up to 24 h vs longer durations; recent studies evaluated antibiotics after definitive wound closure and contamination severity.	Prolonged PAP was not beneficial in most patients. Studies comparing up to 24 h with longer courses found no significant FRI-rate difference. Studies using a 72 h cut-off also found no routine benefit of prolonged PAP; duration beyond 72 h may be associated with increased FRI risk, except possibly in severely contaminated wounds. The authors emphasized that all included studies had important limitations and future RCTs are needed.

Table 3. Guidelines

Study No.	Author / organization involved, publication year, and country	Strategy used to evaluate the evidence (GRADE, consensus, etc.)	Specific recommendation regarding antibiotic DURATION in open fractures	Quality of evidence and strength of recommendation
1	German Society for Hygiene and Microbiology / AWMF S3 Guideline. Perioperative and Periinterventional Antibiotic Prophylaxis in Surgery. Version 5.0, 2024. Germany.[6]	AWMF S3 guideline. PICO questions, explicit evidence review and grading, recommendation grade, and formal consensus.	Gustilo–Anderson I–II: antibiotic prophylaxis for a maximum of 24 h. Gustilo–Anderson III: perioperative antibiotic prophylaxis or pre-emptive therapy for 72 h; longer duration provides no benefit.	I–II: low evidence for fracture-related infection and very low evidence for superficial infection; recommendation grade A (strong), 100% consensus. III: very low evidence; recommendation grade A (strong), 100% consensus.
2	SECOT / SECPRE. Multidisciplinary Management Guideline for Open Fractures. 1st edition, 2024. Spain.[9]	Multidisciplinary expert guideline in traumatology and plastic/reconstructive surgery. Consensus-based development; does not present GRADE or a formal strength for each recommendation.	General rule: prophylactic antibiotic therapy should cover the first 24 h. There is no evidence supporting more prolonged regimens. In general, duration should not exceed 72 h after the initial debridement. For definitive fixation within the first 96 h: use the center's usual preoperative prophylaxis; if delayed >96 h, individualize according to previous antibiotics, cultures, and local epidemiology.	Not formally graded. Narrative/consensus recommendation; quality of evidence and recommendation strength not specified.
3	Cochrane Database of Systematic Reviews; Chan JKK, Aquilina AL, Lewis SR, Rodrigues JN, Griffin XL, Nanchahal J. 2022. United Kingdom / international.[22]	Cochrane systematic review of randomized or quasi-randomized trials; risk-of-bias assessment and GRADE certainty assessment.	Does not issue a definitive clinical recommendation on duration. The only direct comparison available was 24 h versus 5 days; the evidence was very uncertain and allowed assessment only of superficial infection, without robust data on deep infection, function, or quality of life.	Very low GRADE certainty for duration of prophylaxis. No recommendation strength, because this is a systematic review rather than a clinical guideline.
4	National Institute for Health and Care Excellence (NICE). Fractures (complex): assessment and management, NG37. Published 2016; updated 2022. United Kingdom.[23]	NICE clinical guideline methodology, with evidence review and committee process; the recommendations document does not present GRADE strength specifically for antibiotic duration.	Does not specify duration. Recommends immediate prophylactic intravenous antibiotics in the emergency department if not already administered, and preferably within the first hour in the prehospital setting without delaying transport.	No quality/strength rating specific to duration, because the guideline does not formulate an antibiotic duration recommendation.
5	American Academy of Orthopaedic Surgeons (AAOS) / METRC. Prevention of Surgical Site Infections After Major Extremity Trauma Evidence-Based Clinical Practice Guideline. 2022. United States.[8]	Clinical practice guideline based on a formal systematic review; AAOS evidence levels and Evidence-to-Decision Framework.	In closed and open fractures, except type III and possibly type II, there is no need to continue antibiotic prophylaxis for longer than one day. For type III and possibly type II, additional gram-negative coverage is preferred; the guideline does not define a separate specific duration for type III.	The systemic peri/postoperative antibiotic recommendation is reported as strong evidence and a strong recommendation. The statement regarding duration >1 day is not presented as an independent duration recommendation by fracture type.
6	International Consensus Meeting on Musculoskeletal Infection (ICM), Trauma Section; Metsemakers WJ and Zalavras C. 2018. International consensus.[7]	International consensus Q&A format. Literature review by question, evidence level by domain, and delegate voting.	Type I–II: antibiotics for at least 24 h after wound closure, not exceeding 72 h. Type III: 72 h or until 24 h after soft-tissue closure/coverage. Also recommends starting antibiotics as soon as possible after injury.	Treatment duration: moderate evidence. Strongest consensus: 100% agree, 0% disagree, 0% abstain. Other domains: efficacy strong, timing moderate, antibiotic selection limited.
7	British Orthopaedic Association Trauma Committee; BOAST: Open Fracture Management. BOA/BAPRAS/Orthopaedic Trauma Society/British Limb Reconstruction Society. Completed 2017; published 2020. United Kingdom.[4]	BOAST: auditable trauma standard. Document produced by the BOA Trauma Committee, reviewed and ratified by surgical societies; incorporates NICE guidance where applicable. It does not use GRADE or issue a formal strength for each recommendation.	Does not define a specific duration. Recommends that each network/center have a published and accessible antibiotic guideline for open fractures, and emphasizes appropriate antibiotic administration as a core component of the care pathway.	Not graded. This is a process/quality-of-care standard, not a duration recommendation based on a formal evidence assessment.
8	American College of Surgeons Trauma Quality Improvement Program (ACS TQIP) / Orthopaedic Trauma Association (OTA). Best Practices in the Management of Orthopaedic Trauma. 2015. United States.[10]	ACS TQIP/OTA best-practice document with expert panel and references; does not use GRADE or formal recommendation grades.	Scheduled dosing should continue until surgical management. After the procedure, administer at least 24 h from the start of the procedure. In general, discontinue 24 h after the procedure; antibiotics may be continued for up to 72 h in highly contaminated wounds. Do not administer beyond 72 h unless a second surgical intervention occurs within that period.	Not formally graded. Best-practice/expert consensus.

9	Eastern Association for the Surgery of Trauma (EAST); Hoff WS, Bonadies JA, Cachecho R, Dorlac WC. Update to Practice Management Guidelines for Prophylactic Antibiotic Use in Open Fractures. 2011. United States.[24]	Practice management guideline. MEDLINE and secondary citation search; studies classified as Class I, II, or III; recommendations classified as Level I, II, or III.	Type I–II: discontinue antibiotics 24 h after successful wound closure. Type III: continue for 72 h after injury or for no more than 24 h after soft-tissue coverage has been achieved.	For type III, duration = Level II. Duration for type I–II derives from the original guideline and the scientific basis of the document. Overall evidence remains limited, with few high-quality sources.
10	Surgical Infection Society (SIS); Hauser CJ, Adams CA Jr, Eachempati SR. Prophylactic Antibiotic Use in Open Fractures: An Evidence-Based Guideline. 2006. United States.[25]	Evidence-based guideline. Bibliographic search, review of clinical trials, extraction of fracture grade, antibiotic, duration, route, outcomes, and methodological quality; reviewed by the SIS Therapeutic Agents Committee.	Grade I: first-generation cephalosporin or similar gram-positive agent for 24–48 perioperative hours. Grade II–III: first-generation cephalosporin or similar agent for 48 perioperative hours. Broad-spectrum option: start preoperatively and extend for 48 postoperative hours. There is insufficient evidence to justify routine empiric prolongation beyond the initial perioperative period.	Grade I: Level I recommendation for 24–48 h. Grade II–III: Level II recommendation for 48 h. Broad-spectrum 48 postoperative hours: Level III. Insufficient evidence for routine prolongation.

Section 3: Results summary write-up (upto 500 words)

The available evidence on antibiotic duration in open fractures consistently supports early systemic prophylaxis, but it provides limited support for routine prolonged administration. Across observational studies, infection risk appears to be determined more by injury severity, contamination, soft-tissue damage, vascular injury, host factors, quality of debridement, fracture stabilization, and timing of definitive soft-tissue coverage than by extending antibiotic regimens beyond short courses. Dunkel et al[15] reviewed 1,492 open fractures and found no significant reduction in infection rates when antibiotic prophylaxis was continued for 2–3 days, 4–5 days, or more than 5 days compared with a 1-day course. This finding also applied to Gustilo grade III injuries, suggesting that prolonged prophylaxis does not compensate for severe tissue damage or inadequate early surgical management.

More recent observational data reinforce this interpretation. Yang et al.[17], in a large prospective orthopaedic cohort, found no duration-dependent protective effect of prolonged surgical antibiotic prophylaxis in the open-fracture subgroup, suggesting a possible ceiling effect after the early perioperative period. However, the secondary analysis of the FLOW trial by Stennett et al.[16] adds an important clinical nuance. In 2,400 patients, extended prophylaxis beyond 72 hours after definitive wound closure was not beneficial in mildly or moderately contaminated wounds and showed a trend toward increased infection risk in mildly contaminated injuries. In contrast, extended prophylaxis was associated with lower odds of deep surgical site infection in severely contaminated fractures. This finding suggests that contamination severity may modify the effect of antibiotic duration, although the observational design limits causal interpretation.

Systematic reviews and meta-analyses generally support a short-course strategy. Chang et al[18] showed that antibiotic prophylaxis clearly reduces infection compared with no antibiotics, but that longer courses of 3–5 days were not superior to a 1-day course. Isaac et al.[19], focusing on open tibial fractures, found very limited direct evidence and concluded that short courses appear as effective as longer regimens, while emphasizing the absence of robust randomized trials. Messner et al[20], including 1,284 comparative cases and 5,408 observational cases, found no protective effect of antibiotic administration beyond 72 hours, in both Gustilo I–II and Gustilo III fractures; 24–48-hour regimens appeared equivalent to longer protocols. Vanvelk et al[21]. reached a similar conclusion, although they stressed that the literature remains heterogeneous and methodologically limited. The Cochrane review[22] was more conservative, noting that randomized evidence comparing 24-hour and 5-day regimens is of very low certainty due to small sample sizes and a high risk of bias.

Guidelines translate this imperfect evidence into a pragmatic, stewardship-oriented recommendation. For Gustilo type I and II fractures, most guidelines recommend discontinuing antibiotics within 24 hours after surgery or wound closure. For Gustilo type III injuries, recommendations generally support broader coverage and continuation for 48–72 hours after injury, or no more than 24 hours after definitive soft-tissue coverage. EAST[24], ICM[7], AAOS[8], SIS[25], and SECOT[9] converge on the principle that antibiotics should be started immediately, tailored to injury severity and contamination, and not continued beyond 72 hours routinely. Prolongation may be considered only in selected scenarios, such as severe contamination[16], delayed reconstruction, specific environmental exposure, or evolving clinical infection.

Section 4: Discussion (<1000 words)

The central message of this review is that prophylactic antibiotics are essential in open fracture care, but prolonged administration is rarely justified. Historically, open fracture management was shaped by dogmatic practices, including the “six-hour rule” for debridement and the use of broad-spectrum antibiotics for several days or even weeks[1]. Many of these practices stemmed from older observational studies, retrospective series, and expert opinion generated before modern orthoplastic reconstruction, standardized debridement, contemporary fixation strategies, and current antimicrobial resistance concerns. The result is a persistent evidence-practice gap: although most modern data support short-course prophylaxis, prolonged antibiotic regimens remain common in clinical practice.[11-13]

The biological rationale for limiting antibiotic duration is strong. Open fractures are contaminated injuries, but infection is not determined solely by contamination. The primary determinants of infection are injury severity, soft-tissue devitalization, vascular compromise, fracture location, host factors, adequacy of debridement, fixation stability, and timing of definitive soft-tissue coverage. Antibiotics should therefore be viewed as an early adjunct, not a substitute for surgical source control. Once the wound has been adequately debrided, mechanically cleansed, stabilized, and covered, the additional value of continued systemic prophylaxis decreases substantially.

Within the modern orthoplastic paradigm, the timing of the first antibiotic dose is more important than extending treatment duration. Early intravenous administration reduces the bacterial burden before colonization becomes established and before bacteria adhere to devitalized tissue or implants. In contrast, continuing the same prophylactic regimen for several days after adequate surgical management has not consistently reduced the risk of infection. This distinction is critical: the key clinical question is not whether antibiotics should be used, but how long they should be continued once appropriate surgical treatment has begun[26, 27].

Clinical evidence supports this interpretation. Randomized evidence summarized in systematic reviews shows that antibiotics reduce infection compared with no prophylaxis, but longer regimens of three to five days do not appear superior to one-day courses[18, 27]. Observational studies reinforce this conclusion. Dunkel et al.[15] found that longer courses did not reduce infection compared with one day of antibiotics, even in Gustilo type III fractures. Yang et al.[17], in a large contemporary prospective orthopedic cohort, similarly found no clear protective effect of prolonged surgical antibiotic prophylaxis in open fractures. Meta-analytic evidence is also consistent: Messner et al.[20] found no benefit from antibiotic administration beyond 72 hours, including for both Gustilo I–II and Gustilo III injuries, and Vanvelk et al.[21] concluded that prolonged perioperative prophylaxis is not beneficial, although the available evidence remains heterogeneous and methodologically limited.

The most important nuance is contamination severity. The FLOW secondary analysis[16] suggested that extending prophylaxis beyond 72 hours after definitive wound closure was not beneficial for mildly or moderately contaminated wounds and may even trend toward harm in mildly contaminated injuries. However, in severely contaminated wounds, extended prophylaxis was associated with lower odds of deep surgical site infection. This finding should inform clinical judgment but should not be overinterpreted. It was not a randomized trial of antibiotic duration, and confounding by indication remains possible. The appropriate conclusion is not that all severe open fractures require prolonged antibiotics, but that gross contamination, Deep-embedded debris, fecal contamination, farm injuries, aquatic exposure, delayed reconstruction, or compromised tissue viability may justify individualized extension or a transition from routine prophylaxis to targeted early treatment.

The harms of prolonged prophylaxis are clinically significant. Extended systemic antibiotic exposure increases antimicrobial selection pressure, promotes the emergence of resistant organisms, disrupts the patient's microbiome, increases the risk of Clostridioides difficile infection, and may cause drug-specific toxicity, including aminoglycoside-associated nephrotoxicity or vancomycin-associated nephrotoxicity. Moreover, late infections after open fractures are often driven by nosocomial organisms rather than the original contaminants at the time of injury. Prolonging the initial empirical prophylactic regimen is therefore unlikely to prevent many late infections and may instead select for more difficult-to-treat pathogens.

The evidence also suggests that antibiotic selection and spectrum may be more clinically relevant than duration. Current consensus generally supports gram-positive coverage, usually with a first-generation cephalosporin, for Gustilo types I and II fractures, with additional gram-negative coverage for type III injuries or heavily contaminated wounds, though the latter point is controversial[28]. Special exposures require specific modifications, such as clostridial coverage for farm injuries and tailored regimens for aquatic contamination. In other words, antibiotics should be started early, appropriately selected, and time-limited, rather than simply prolonged.

Guidelines have translated this imperfect but consistent evidence into pragmatic, stewardship-oriented recommendations. For Gustilo type I and II fractures, prophylaxis should generally be discontinued within 24 hours after wound closure. For Gustilo type III fractures, most recommendations support continuation for 48–72 hours after injury or for no more than 24 hours after definitive soft-tissue coverage[24], whichever comes first. Routine continuation beyond 72 hours should be avoided unless there is a clearly defined reason, such as severe contamination, repeated surgical procedures with ongoing exposure, delayed coverage, specific environmental contamination, immunocompromise, or clinical signs of established infection.

Therefore, the most defensible recommendation is a short, severity-adjusted strategy: administer systemic antibiotics as soon as possible after injury; select the antibiotic spectrum based on fracture grade, contamination pattern, and local microbiology; stop prophylaxis within 24 hours after closure for Gustilo type I–II injuries; and limit Gustilo type III prophylaxis to 72 hours after injury. When antibiotics are continued beyond this window, the rationale should be explicit and documented. At that point, the decision should no longer be considered routine prophylaxis but individualized management based on contamination, tissue viability, microbiology, reconstructive timing, and evolving clinical evidence of infection.

Section 5: Risk of bias of included studies

No.	Paper	Type of evidence	Risk of bias	Main justification

1	Dunkel et al., 2013[15]	Retrospective case-control / cohort analysis	Moderate	Large sample and multivariable analysis, but retrospective design, possible confounding by indication, surgeon-dependent antibiotic duration, imperfect Gustilo classification, and missing variables such as BMI, smoking, trauma energy, and injury mechanism. The authors explicitly acknowledge these observational-study weaknesses.
2	Stennett et al., 2020[16]	Retrospective cohort secondary analysis of FLOW trial data	Moderate	Strong dataset, multinational cohort, 12-month follow-up, independent SSI adjudication, adjusted and propensity analyses. However, antibiotic duration was not randomized; contamination grading was subjective; severe-contamination subgroup was small; culture data were unavailable; and residual confounding by indication remains possible.
3	Yang et al., 2024[17]	Prospective cohort	Moderate	Very large cohort, prospective surveillance database, CDC/NHSN SSI definition, advanced modelling and multivariable adjustment. Still observational, single-health-system context, not open-fracture-specific as the only population, and residual confounding remains possible.
4	Chang et al., 2015[18]	Systematic review and meta-analysis of RCTs	Low	Comprehensive search, RCT-only inclusion, quantitative synthesis, and explicit confidence assessment. The review itself is methodologically strong, although the primary trials are old and the certainty for duration comparisons is only low to moderate.
5	Chang et al., 2019[5]	Systematic survey of practice patterns and recommendations	Moderate	Broad search across clinical studies, textbooks, guidelines, protocols, and practice surveys. Useful for mapping practice and recommendations, but it is not a direct effect-estimate review and inherits heterogeneity and bias from non-comparative sources.
6	Isaac et al., 2016[19]	Systematic review focused on open tibial fractures	Moderate	Focused clinical question and useful synthesis, but only one prospective double-blind randomized study directly addressed duration; the evidence base was sparse, heterogeneous, and not strong enough for definitive conclusions.
7	Messner et al., 2017[20]	Meta-analysis of comparative and observational studies	Moderate	Large synthesis including 1,284 comparative and 5,408 observational cases, but limited by scarcity of high-quality duration-specific studies, inconsistent infection definitions, variable antibiotic regimens, old studies, and classification heterogeneity.
8	Vanvelk et al., 2022[21]	Systematic review and critical appraisal	Low	Contemporary systematic review with critical appraisal. Review process is strong, but the underlying evidence is limited by heterogeneity, different infection definitions, variable follow-up, and few direct comparative studies.
9	BOAST / BOA-BAPRAS, 2020[4]	Guideline / auditable standard	Moderate	Useful orthoplastic standard, multidisciplinary ratification, and alignment with NICE where relevant. However, it is a pragmatic standard rather than a fully transparent GRADE-based guideline for antibiotic duration.
10	ICM 2018[7]	International consensus document	Moderate	Broad expert consensus and literature referencing, but recommendations are consensus-based and some duration statements rely on limited or indirect clinical evidence. Methodological transparency is less robust than formal GRADE/NICE/AAOS processes.
11	AWMF German S3 Guideline, 2024[6]	Formal evidence-based guideline	Low	Strongest guideline methodology among the included documents: S3-level process, multidisciplinary panel, explicit evidence grading, recommendation grading, consensus strength, and conflict-of-interest procedures.
12	SECOT 2024 Multidisciplinary Open Fracture Guideline[9]	Multidisciplinary guideline / adapted national guide	Moderate	Clinically useful and contemporary, with relevant references and adaptation to the Spanish setting. Risk is moderate because the document appears more practice-oriented than formally GRADE-based, and the process for evidence selection/appraisal is less transparent.
13	Surgical Infection Society, 2006[25]	Evidence-based guideline	Moderate	Systematic review approach and clear conclusions, but based on older studies, many with methodological weaknesses. The guideline predates contemporary GRADE/AGREE standards and reflects the limited evidence available at that time.
14	EAST Practice Management Guideline, 2011[24]	Practice management guideline	Moderate	Transparent search, article classification, and graded recommendations. Limitations include restricted search strategy, exclusion of non-English literature, reliance on class II/III evidence for several recommendations, and expert interpretation where evidence is limited.
15	Cochrane Review, 2022[22]	Cochrane systematic review	Low	Very strong methodology: comprehensive search, RCT/quasi-RCT eligibility, standard Cochrane procedures, and explicit risk-of-bias assessment. The review itself is low risk of bias, although the included evidence for antibiotic duration is very uncertain.
16	AAOS CPG, 2022[8]	Evidence-based clinical practice guideline	Low	Formal systematic review, PICO questions, librarian-led database search, methodologist involvement, conflict-of-interest management, and explicit strength-of-evidence framework.

17	NICE NG37, 2022 update[23]	National guideline	Low	Formal NICE methodology, explicit recommendation process, update procedure, patient-care framing, and transparent linkage to evidence reviews. Low risk as a guideline process, although antibiotic-duration granularity is limited in the public summary.
18	ACS TQIP / OTA Best Practices, 2015[10]	Best-practice document	High	Useful trauma-systems document, but for antibiotic duration it is less methodologically rigorous than formal guidelines. It explicitly combines best available evidence with expert opinion where evidence is incomplete or controversial, and does not provide a detailed duration-specific evidence appraisal.

Section 6: Response/Recommendation (1-2 lines as a conclusion and recommendation statement for the question)

To balance infection prevention with the risks of antimicrobial resistance and toxicity, prophylaxis should be limited to 24 hours for Gustilo Type I and II fractures, and up to 72 hours for severe Gustilo Type III injuries.

Section 7: Level/ strength of Evidence:

Low-to-moderate certainty of evidence; strong recommendation.

This recommendation is supported by multiple systematic reviews, meta-analyses, large observational cohorts, and convergent guideline statements showing no consistent reduction in SSI/FRI with prophylaxis beyond 72 hours. The certainty is downgraded from high because direct duration-specific RCT evidence is scarce, older, and heterogeneous, and modern supportive studies are mainly observational with moderate risk of bias.

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