RQ 33: Is there a routine role for local antibiotic delivery in the management of open fractures?

Section 1: Background

Open fractures remain highly vulnerable to fracture-related infection because contamination, devitalized tissue, dead space, and impaired perfusion reduce the effectiveness of systemically delivered antibiotics to the wound/implant interface. While early systemic antibiotics, careful debridement, skeletal stability, and timely soft-tissue coverage remain the foundations of care,local antibiotic delivery is attractive because it can generate very high local concentrations with minimal serum exposure; platforms in the uploaded corpus include PMMA beads and strips, collagen sponges, aqueous aminoglycoside injection, antibiotic-coated nails and plates, and absorbable calcium sulfate or hydroxyapatite composites. Observational studies and meta-analyses generally suggest lower infection rates with adjunctive local antibiotics, especially in Gustilo III injuries. However, the evidence base is heterogeneous and dominated by retrospective studies, case series, and tibial-fracture cohorts. Furthermore, a large matched nationwide study found no benefit when using non-standardized prophylactic local antibiotic therapy over modern standard care. There is no definitive completed randomized trial specifically testing routine prophylactic local antibiotics in open fractures is available in the uploaded corpus. The key unanswered question is therefore not whether local delivery can work, but whether it should be used routinely in all open fractures, or selectively in the highest-risk wounds where dead space, implant surfaces, vascular compromise, and delayed coverage make systemic prophylaxis least reliable. Clinically, this matters because fracture-related infection drives reoperation, delayed union, nonunion, limb loss, and cost, while local antibiotic delivery adds material choice, stewardship considerations, and sometimes removal procedures [1, 2, 3, 8, 9, 10]]

Section 2: Data Extraction

This manuscript follows the uploaded Open Injury International Consensus Meeting template and adapts the data-extraction format to the specific question of local antibiotic delivery. [13]

For this synthesis, the uploaded local-antibiotic/open-fracture corpus was treated as the review universe. Duplicate uploads were merged, leaving 41 topic-relevant records for analysis. Data were extracted, where reported, for study design, sample size, fracture severity, local antibiotic type and carrier, timing relative to debridement or fixation, comparator, major outcomes, follow-up, and adverse events. When a field was not clearly reported in the accessible text of the uploaded record, it is listed as unspecified.

Study	Design	Sample	Population	Local antibiotic strategy and comparator	Key outcomes and main findings	Follow-up	Risk of bias
Henry et al., 1990, USA [5]	Retrospective comparative cohort	404 open fractures in 339 patients	Grade I–III open fractures	Tobramycin PMMA bead chains + systemic cefazolin/tobramycin/penicillin vs systemic antibiotics alone after irrigation/debridement	Wound infection 2.7% with beads vs 11.4% without; chronic osteomyelitis 2.4% vs 14.3%; greatest excess risk in grade III fractures	Unspecified	High

Study	Design	Sample	Population	Local antibiotic strategy and comparator	Key outcomes and main findings	Follow-up	Risk of bias
					without beads		
Ostermann et al., 1995, USA [6]	Retrospective comparative cohort	1085 fractures in 914 patients	Type I–III open limb fractures	Aminoglycoside-PMMA beads + systemic antibiotics vs systemic antibiotics alone	Overall infection 3.7% with beads vs 12% without; benefit most apparent in severe injuries	Mean 19.2–23.6 months	High
Lawing et al., 2015, USA [7]	Retrospective cohort	351 fractures	Open fractures treated operatively within 36 h	Local aqueous aminoglycoside (2 mg/mL) at index surgery + systemic antibiotics vs systemic antibiotics alone	Overall infection 9.5% vs 19.7%; deep infection 6.0% vs 14.2%; no nonunion difference	Unspecified	Moderate
Pinto et al., 2019, India [14]	Alternate-allocation comparative study	28	GA I–II open tibia fractures	Gentamicin-coated IMIL nail vs regular IM nail	0 infections with coated nail vs 4 in controls; better 6-month healing markers and bone healing	6 months	Moderate–high
Greco et al., 2021, Italy [15]	Retrospective comparative cohort	46	Open diaphyseal tibial fractures (AO 42), GA I–III	Gentamicin-coated tibial nail vs uncoated tibial nail	12-month healing 18/23 vs 16/23; infections 3 superficial in coated group vs 4 total including 1 osteomyelitis in uncoated group; no	Minimum 18 months	Moderate–high

Study	Design	Sample	Population	Local antibiotic strategy and comparator	Key outcomes and main findings	Follow-up	Risk of bias
					adverse events		
Burtt et al., 2019, USA [27]	Retrospective cohort	73 lower extremities	Open lower-extremity fractures requiring soft-tissue coverage	Antibiotic beads and/or NPWT before reconstruction	Infection 6.4% with beads vs 30.7% without; longer delay to coverage associated with infection	Unspecified	High
Bhogadi et al., 2023, USA [10]	Propensity-matched database cohort	2304 matched from 61,337 OLBF patients	Adult isolated open long-bone fractures	Any prophylactic local antibiotic therapy vs none	Infectious complications similar (3.5% vs 2.5%); unplanned return to OR similar; hospital LOS longer with local therapy	Inpatient database outcomes	Moderate

Study	Design	Sample	Population	Local antibiotic strategy	Key outcomes and main findings	Follow-up	Risk of bias
Eckman et al., 1986, USA [28]	Pharmacokinetic case series	70 fractures; 27 assayed for levels	Compound fractures after debridement	Tobramycin-PMMA beads	High wound/drainage tobramycin concentrations with nontoxic serum levels	Immediate/short-term	High; indirect
Chaudhary et al., 2011, India [21]	Case series	35 enrolled; 31 with adequate follow-up	Open fractures treated with immediate plate fixation	Gentamicin-loaded collagen sponge around plate + systemic antibiotics	Local wound complications 9.7%; deep infection 6.45%; delayed	Mean 40 weeks	High

Study	Design	Sample	Population	Local antibiotic strategy	Key outcomes and main findings	Follow-up	Risk of bias
					union 16.1%; no nonunion or implant failure		
Stinner et al., 2010, USA [29]	Animal study	Goat model, n unspecified in abstract	Contaminated musculoskeletal wounds	Chitosan sponge loaded with amikacin or vancomycin after debridement/irrigation	Lower bacterial burden than controls; serum levels <15% of systemic targets; biodegradable carrier	48 h	Not directly clinical
Metsemakers et al., 2015, Belgium [30]	Retrospective case series	16	Acute GA II–III open tibia fractures and complex revision cases	Gentamicin-coated tibial nail	No deep infections; nonunion 25%	Unspecified	High
Jahangir et al., 2019, UK [16]	Prospective review/case series	51	GA IIIB open fractures managed in orthoplastic unit	Cerament G in bone voids during single-stage fix-and-flap + systemic antibiotics until closure	No deep infection; primary union 84.3%; mean union 32.5 weeks; amputation 1.9%	Mean 13.9 months	High
Aljawadi et al., 2020, UK [17]	Retrospective case series	80	GA IIIB open fractures with single-stage fix-and-flap	Adjuvant local antibiotic hydroxyapatite/calcium sulfate biocomposite (Cerament G)	Successful union 96.1%; 1 deep infection; 4 amputations	Until union/complication review; exact mean unspecified	High
Perisano et al., 2021, Italy [19]	Retrospective case series	38	Open tibial fractures	Gentamicin-coated ETN Protect nail	34/38 unions; 2 septic nonunions; no systemic toxicity or hypersensitivity	Minimum 18 months	High

Study	Design	Sample	Population	Local antibiotic strategy	Key outcomes and main findings	Follow-up	Risk of bias
Freischmidt et al., 2020, Germany [25]	Technical case series	3 cases	Fracture fixation or revision cases	Individual implant coating with antibiotic-loaded hydroxyapatite/calcium sulfate	No recurrence reported; no adverse events; osseointegration achieved	Unspecified	High; very indirect
Jia et al., 2024, China [31]	Translational mechanistic study	Unspecified in abstract	Open-fracture macrophage analysis	Vancomycin-loaded calcium sulfate with and without NPWT	Suggested M2 polarization and improved infection resistance, strongest with combined treatment	Mechanistic endpoint study	Not directly clinical
Kang et al., 2023, China [22]	Retrospective case series	20	GA IIIB/C lower-extremity open fractures	Temporary antibiotic cement-coated locking plate after initial debridement	2 wound infections and 1 severe bone infection; all achieved union by 1 year	1 year	High
Lamay et al., 2023, India [23]	Case series	105	Type I–IIIC open fractures	PMMA-vancomycin strips after definitive stabilization	4.6% subclinical infection; no osteomyelitis or nonunion reported	1 year	High
Kumar et al., 2023, India [24]	Case series	24	Grade II, IIIA, IIIB compound long-bone fractures	Antibiotic-coated beads after debridement and stabilization	1 superficial and 1 deep infection; union typically 12–22 weeks; mostly good/excellent outcomes	At least 6 months	High

Study	Design	Sample	Population	Local antibiotic strategy	Key outcomes and main findings	Follow-up	Risk of bias
Pandoh et al., 2023, India [26]	Mixed orthopedic case series	50 total, including 13 open fractures	Osteomyelitis, periprosthetic infection, open fractures, degloving	Vancomycin-impregnated calcium sulfate pellets	Overall 45/50 successful outcomes; open-fracture subgroup not separately quantified for infection/union	8 months	High; indirect
Zamorano et al., 2025, Chile [20]	Prospective cohort	139 analyzed	Open tibial fractures treated under standardized protocol	Gentamicin-coated tibial nails	Overall FRI 8.8%; nonunion 2.2%; average healing 34.3 weeks; poorer outcomes in IIIB/C; no adverse effects	Minimum 24 months	Moderate–high
Asano et al., 2025, UK [18]	Retrospective descriptive cohort	76 patients, 78 fractures	GA IIIB open fractures	Cerament G adjunct to conventional fix-and-flap	Primary union 83.3%; osteomyelitis 5.1%; 4 amputations; no local/systemic adverse reactions	Mean 88.7 months	Moderate–high

Study	Type and scope	Main local-antibiotic focus	Main take-home for the consensus question	Limitations / indirectness
Bowyer/Sawyer, 1993, UK [32]	Technique report / military application	Bead-pouch technique with aminoglycoside PMMA	Positions beads as useful adjunct for temporary wound management until closure or flap coverage	Not a controlled efficacy study
Seligson & Berling, 2015 [33]	Narrative review	PMMA bead chains	Concludes bead chains are practical, provide high local levels, and support infection	Review-level evidence

Study	Type and scope	Main local-antibiotic focus	Main take-home for the consensus question	Limitations / indirectness
			prevention in open fractures	
Greco et al., systematic review [34]	Systematic review	Antibiotic-coated tibial nails	Included 5 studies/146 fractures; suggests promise but emphasizes small, heterogeneous, low-level literature	No high-level comparative evidence
Zalavras et al., 2007 [35]	Narrative review	Local antibiotic therapy in open fractures/osteomyelitis	Calls local therapy safe and potentially useful, but notes limited level I evidence	Review-level evidence
Hake et al., 2015 [36]	Practical review	PMMA, cement nails, dosing, toxicity	States local antibiotics are well established in open fractures and osteomyelitis; provides practical dosing and carrier information	Narrative synthesis
Zalavras et al., 2005 [37]	Review of open-fracture management	Severe injuries and bead-pouch technique	Places local antibiotics within severe open-fracture infection-prevention strategy	Broader management review
Coates & Ziran, 2003 [38]	Narrative review	Historical role of local antibiotics	Describes local antibiotic therapy as an adjunct within infection prevention	Indirect
Zalavras, 2017 [2]	Review	Prevention of infection after open fractures	Recommends local antibiotic delivery, especially bead-pouch, in severe injuries	Narrative, not comparative
Rupp et al., 2019 [12]	Review	Current prevention strategies	Notes newer literature suggests benefit of local antibiotics and coated implants, but controversy persists	Review-level evidence
Carver et al., 2017 [3]	Review	Systemic plus local antibiotics	Emphasizes high local concentration with minimal systemic toxicity and renewed interest in many delivery modes	Narrative review
Seligson & Henry, 1991 [39]	Narrative review	PMMA beads in compound fractures	States supplemental local PMMA beads appear to reduce morbidity in high-grade injuries	Historical review
"ABP and VAC" review, 2009 [40]	Narrative review	Antibiotic bead pouches and VAC	Concludes ABPs can reduce infection in severe open fractures and may help when	Review; older literature

Study	Type and scope	Main local-antibiotic focus	Main take-home for the consensus question	Limitations / indirectness
			primary closure is not possible	
Halawi & Morwood, 2015 [1]	Evidence-based review	Antibiotic-impregnated devices	Frames such devices as important adjuncts in highly contaminated or comminuted injuries	Broader rather than focused review
Whiting et al., 2023 [4]	OTA best-practice proceedings	FRI prevention	Reinforces systemic prophylaxis, debridement, and coverage; local antibiotics appear within selected prevention strategies	Consensus-style, not original comparative study
Craig et al., 2014 [8]	Systematic review / meta-analysis	Local prophylactic antibiotics in open tibia fractures treated with IM nailing	Infection lower with local antibiotics, especially severe GA III fractures; authors call for direct comparative trial	Meta-analysis of heterogeneous observational studies
Morgenstern et al., 2018 [9]	Systematic review / meta-analysis	Open limb fractures	Local prophylaxis associated with lower pooled infection, but heterogeneity and bias are substantial	Secondary synthesis limited by poor primary studies
Aneja et al., protocol [11]	Phase 3 trial protocol	Local aqueous tobramycin injection	Demonstrates that a definitive randomized question is recognized, but provides no efficacy data yet	No results available
Burbank et al., 2020 [41]	Concept / hypothesis paper	Very early topical antibiotic powder	Suggests timing may matter because of biofilm formation; supports early local application conceptually	No clinical efficacy data
You & Schneider, 2020 [42]	Contextual review	Standard open-fracture timing principles	Useful for framing standard care comparator: early IV antibiotics, OR within 24 h, coverage within 7 days	No direct local-antibiotic efficacy data

Section 3: Results

The available literature under consideration exhibits a clinically heterogeneous evidence base. The strongest evidence in favor of local antibiotics comes from comparative cohort studies. According to Henry, et al (19990), adding tobramycin PMMA beads to systemic prophylaxis in 404 open fractures was associated with lower acute wound infection and chronic osteomyelitis than systemic prophylaxis alone, with the largest excess infection burden observed in severe grade III injuries when beads were not used. In the larger Osterman, et al (1995) study of 1085 open fractures, supplementary aminoglycoside-PMMA beads were again associated with lower infection than systemic antibiotics alone. A more recent retrospective cohort study by Lawing, et al (2015) demonstrated that local aqueous aminoglycoside injection reduced both overall and deep infection without affecting rates of nonunion. Smaller implant-specific comparative studies of gentamicin-coated tibial nails also reported fewer infections than uncoated nails, although these results were limited by cohort size and design. [5, 6, 7, 14, 15]

The available meta-analytic evidence is also consistent with these findings. Craig et al. reported that in severe open tibial fractures, infection was reduced with adjunctive local antibiotics than with systemic antibiotics alone, but emphasized the lack of direct head-to-head trials. Morgenstern et al. pooled eight comparative studies and observed a lower infection rate with local prophylaxis, while explicitly warning that the pooled literature was heterogeneous and at considerable risk of bias. [8, 9]

Single-arm series are most encouraging in selected high-risk settings rather than as proof of the potential benefit with more routine use. Cerament G or related absorbable gentamicin-eluting composites used during fix-and-flap management of Gustilo IIIB injuries reported less deep infection and acceptable rates of union in single-center series from the UK, with Asano, et al's long-term follow-up demonstrating osteomyelitis in 5.1% after a mean of 88.7 months. Antibiotic-coated tibial nail studies also suggest acceptable union and low device-related toxicity but outcomes were less impressive with IIIB/IIIC injuries, and the evidence remains mostly uncontrolled. Other platforms (such as collagen sponges, temporary antibiotic cement-coated plates, PMMA strips, generic antibiotic beads, custom implant coatings, and mixed calcium-sulfate series) are promising, but substantially more indirect. [16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26]

In contradistinction, the large propensity-matched database study by Bhogadi, et al evaluated 61,337 open long bone fractures, and reported no reduction in either the incidence of infections or return to the operating room with nonspecific prophylactic local antibiotic therapy. The available literature contains only a phase 3 study protocol for local aqueous tobramycin, and together with the absence of a definitive randomized trial, this prevents a recommendation for routine use in all open fractures. [10, 11]

Section 4: Discussion

The central clinical issue is whether a recurring benefit in demonstrated in observational studies is strong enough to justify recommending “routine” local antibiotic delivery. On balance, the literature support a selective role, but not a universal routine role. The biological rationale is compelling, as open fractures are contaminated, perfusion is impaired, implants introduce biofilm-prone surfaces, and local depots can expose the wound or implant interface to concentrations that systemic therapy may not achieve. Older pharmacokinetic and technique papers, the historical PMMA bead literature, and newer carrier-based or coated-implant studies all align with that rationale. [28, 32, 33, 35]

The best clinical support is not evenly distributed across all open fractures. It is heavily concentrated in more severe injuries and in implant-associated or dead-space–rich scenarios. Henry, Ostermann, Lawing, and the two meta-analyses consistently indicate reduced rates of infection with adjunctive local antibiotics, and that effect appears largest in Gustilo III fractures. UK orthoplastic series using Cerament G within single-stage fix-and-flap pathways also report very low deep infection or osteomyelitis in IIIB injuries, while coated-nail studies suggest that local antibiotic surfaces may help in open tibial fractures treated with intramedullary fixation. This pattern makes clinical sense, as the more severe the wound and the more compromised the local biology the stronger the rationale for augmenting systemic prophylaxis. [5, 6, 7, 8, 9, 16, 17, 18, 19, 20]

A stronger universal recommendation is prevented by the quality and consistency of the evidence. The device literature is divided between beads, strips, collagen sponges, aqueous injections, coated nails, temporary cement-coated plates, and absorbable biocomposites. Many studies are limited to the tibia. Definitions of infection vary, timepoints differ, and some modern studies are vulnerable to indication bias because surgeons are more likely to deploy local antibiotics in their worst injuries. The large TQIP study diverges from the favorable single-center studies, though it is also limited by non-standardized intervention details, inpatient outcomes, and lack of granularity regarding agent, dose, carrier, and timing. This conflict is exactly why the current evidence supports selective adoption rather than a universal quality metric. [10, 34, 12]

The literature also suggests that modality matters. PMMA beads provide the strongest direct comparative evidence, but they may require removal and are less attractive when one wants a resorbable dead-space filler. Aqueous aminoglycoside injection offers a simple, low-hardware option, and is supported by one relatively strong retrospective cohort. Coated nails appear most useful in tibial fractures when internal fixation is already planned, but current data are insufficient to infer benefit in the most extreme IIIB/IIIC patterns. Absorbable calcium sulfate or hydroxyapatite composites are particularly attractive in orthoplastic fix-and-flap pathways because they can fill bone voids while avoiding a second procedure for removal, but the supporting data remain predominantly single-center and uncontrolled. Experimental ideas such as earlier topical powder placement, biodegradable chitosan delivery, or macrophage-modulating calcium sulfate platforms are interesting, but not yet enough data is available to support routine consensus practice. [36, 7, 15, 19, 16, 17, 18, 41, 29, 31]

Safety reporting is overall reassuring but still incomplete. Multiple series found no systemic toxicity or hypersensitivity, Cerament G cohorts reported no local or systemic adverse reactions, and the practical review literature notes that systemic serum levels are usually low when local delivery is used appropriately. However, underreporting of nephrotoxicity, long-term stewardship consequences, and cost-effectiveness is common, and arthroplasty spacer literature cautions that very high antibiotic loads are not biologically trivial. As a result, a consensus statement should emphasize antimicrobial stewardship and careful agent choice, rather than regarding local antibiotic delivery as risk free. [19, 20, 18, 36]

Section 5: Risk of bias summary.

Risk of bias was judged pragmatically by study design. Small randomized or quasi-randomized studies were judged for allocation and sample-size limitations; nonrandomized comparative cohorts were judged mainly for confounding and selection bias; single-arm case series were rated high risk because they lacked controls; narrative reviews and guidelines were treated as contextual evidence rather than primary efficacy evidence; and translational, animal, or protocol papers were classified as indirect for the specific clinical question under consideration.

Evidence layer	Quantity in corpus	Main limitations	Overall judgment
Comparative primary clinical studies	7	Confounding by injury severity, device selection, small size, nonrandomized allocation, inconsistent infection definitions	Moderate to high risk
Single-arm clinical/device studies	15	No control groups, single centers, tibia-heavy populations, underreporting of systemic antibiotic regimens and adverse events	High risk
Systematic reviews/meta-analyses	4	Depend heavily on observational and heterogeneous primary studies	Moderate quality, but limited by indirectness
Narrative reviews/guidelines/context papers	13	Not primary efficacy evidence	High indirectness
Experimental / mechanistic / protocol papers	2 plus 1 trial protocol	Nonhuman, mechanistic, or no outcomes yet	Not directly applicable to routine-use decision

Across the uploaded corpus, no completed low-risk definitive randomized trial establishes routine prophylactic local antibiotic delivery for all open fractures. That is the main reason the overall certainty remains low, despite a recurrent favorable signal when used in the management of severe injuries. [11, 8, 9]

Section 5: Response / recommendation statement.

Local antibiotic delivery should not be recommended as a routine universal requirement for all open fractures. It has a selective adjunctive role in high-risk open fractures, particularly Gustilo type III injuries, with gross contamination, dead space, staged orthoplastic reconstruction, or with implant-intensive fixation. This recommendation provided that early systemic antibiotics, meticulous debridement, stable fixation, and timely coverage are already optimized. [10, 7, 8, 9, 2, 4]

Section 6: Level / strength of evidence.

LOW overall. Support for local antibiotics is consistent across PMMA bead studies, modern cohort studies, and two meta-analyses, but the primary literature is dominated by retrospective designs, small single-center studies, severe-tibia–heavy populations, and substantial heterogeneity in carrier, agent, timing, and infection definitions. The only large nationwide matched cohort evaluated here was neutral, and the available randomized trial for prophylactic local tobramycin is still only a published study protocol without results. [5, 6, 7, 8, 9, 10, 11]

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