Should antibiotic-containing irrigation solutions be routinely employed in open fracture management?

Section 1: Background (<300 words):

Known Facts

Open fractures are contaminated by definition, with infection rates of 0–2% for Type I and 10–50% for Type III injuries. Irrigation and debridement are cornerstones of infection prevention. Normal saline is isotonic, non-toxic, and inexpensive. The FLOW trial (n=2,447) showed irrigation pressure does not affect reoperation rates, and castile soap was inferior to saline.

Unknown / Controversial Facts

Whether antibiotic irrigation reduces infection beyond saline alone is unknown. No large randomized trial has definitively compared antibiotic irrigation to saline. It is also unknown whether antibiotic irrigation selects for resistant organisms, impairs healing, or causes hypersensitivity (e.g., bacitracin anaphylaxis).

Current Evidence

Existing RCTs show no consistent advantage of antibiotic irrigation over saline. Most studies are small, use different agents (bacitracin, neomycin, cephalosporins), and have methodological limitations.

Gaps

No Level I evidence specifically compares antibiotic irrigation to saline alone as the primary intervention. The FLOW trial did not include an antibiotic irrigation arm. Whether antibiotic irrigation benefits high-risk subgroups (Type III fractures, immunocompromised hosts, gross contamination) is unknown.

Clinical Relevance

Given the high morbidity and cost of post-traumatic infections, even a modest infection reduction would have major impact. However, routine adoption without proven efficacy risks unnecessary cost, adverse events, and antibiotic resistance. A definitive randomized trial is needed.

Section 2: Data extraction table

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.	Blease R, Kanlić EM, 2005, USA (Department of Orthopaedics, Fort Leonard Wood, MO and TTUHSC, El Paso, Texas)	Narrative Review Article	Not applicable (review article; no original patient data)	Not applicable (review of open fracture management principles; no primary inclusion/exclusion criteria)	**Classification:** Gustilo-Anderson Type I, II, IIIA, IIIB, IIIC **Irrigation solutions:** Detergent solutions vs. antibiotic solutions vs. saline **Irrigation pressure:** High-pressure vs. low-pressure **Antibiotic routes:** Systemic vs. local (PMMA beads) **Fracture stabilization:** Intramedullary nailing vs. external fixation vs.	**Key findings from review:** **Classification & infection risk:** • Type I: 0-2% infection risk • Type II: 2-10% infection risk • Type III: 10-50% infection risk **Irrigation:** No ideal method established; high-pressure may damage bone; detergent solutions show promise; antibiotic solutions controversial (effectiveness, resistance, cost). **Antibiotics:** • Cephalosporin + aminoglycoside: 4.6% infection rate (5/109) vs.

					plate fixation **Wound closure:** Primary vs. delayed **Soft tissue coverage:** Local flap vs. free flap	cephalosporin alone: 13% infection rate (25/192) (Patzakis & Wilkins). • PMMA beads + systemic antibiotics: 3.7% infection vs. systemic alone: 12% infection ($p<0.001$); benefit mainly for Type III fractures (6.5% vs. 20%). **Fracture stabilization:** • Intramedullary nailing acceptable for Type I-IIIB; external fixation reserved for heavily contaminated IIIB and IIIC injuries. • Conversion from external fixation to IM nail: infection rate 5% if done early (mean 17 days) without active pin tract infection. **Soft tissue coverage:** • Free flap within 72 hours: <1% failure rate (1/134) vs. >72 hours: 12% failure (20/167); infection rates 1.5% vs. 17.4% (Godina, 1986). **Conclusion:** Cornerstone of treatment remains

						adequate irrigation and debridement with early broad-spectrum antibiotics. Delayed wound closure is valid and often preferred.
2.	FLOW Investigators, 2011, Canada, USA, India	Multicenter, blinded, randomized 2x2 factorial pilot trial	**Total:** 111 patients randomized; 89 completed 1-year follow-up. **By Solution:** Castile soap (n=56), Normal saline (n=55). **By Pressure:** Low-pressure (n=54), High-pressure (n=57). **By Factorial Group:** Soap+Low (n=26), Soap+High(n=30), Saline+Low (n=28), Saline+High (n=27).	**Inclusion:** Skeletally mature patients with an open fracture of the appendicular skeleton (Gustilo type I to IIIb). **Exclusion:** Vascular deficit; allergy to detergents/castile soap; previous wound infection/osteomyelitis; previous fracture with retained hardware in injured limb; operative management >24 hours after injury; immunosuppressive medication use within 6 months; immunologic deficiency/disease;	**Irrigating Solutions:** - Castile soap solution (80 mL of 17% soap per 3L normal saline) - Normal saline alone **Irrigating Pressures:** - Low-pressure pulsatile lavage (6–10 psi) - High-pressure pulsatile lavage (25–30 psi) *(Analyzed using 2x2 factorial design)*	**Primary Outcome (Reoperation at 12 months):** **Solution:** Soap 13/56 (23%) vs. Saline 13/55 (24%); HR 0.91 (95% CI: 0.42–2.00), p=0.82. **Pressure:** Low-pressure 10/54 (19%) vs. High-pressure 16/57 (28%); HR 0.55 (95% CI: 0.24–1.27), p=0.17. **Secondary Outcomes (Selected):** **Infections (operative/nonoperative):** Soap increased risk vs. Saline (HR 3.53, 95% CI: 1.15–10.84, p=0.019); Low vs. High pressure: HR 0.38 (95% CI: 0.15–1.00), p=0.04. **Nonunion (operative/nonoperative):** Soap vs. Saline: HR 0.37 (95% CI: 0.14–0.97),

				fractures of hands or toes.		p=0.036; Low vs. High pressure: HR 0.42 (95% CI: 0.16–1.16), p=0.07. **Functional Outcomes (SF-12, EQ-5D):** No significant differences between any groups at any time point.
3.	Gardezi M et al. Year: 2021, Country: USA	Narrative / Comprehensive Literature Review	Not applicable (review article; no patient sample)	Not applicable (review synthesizes existing literature; no primary patient enrollment)	**Modes of delivery:** Gravity flow; Needles/syringes/bulb syringes; Pressurized canisters/jet lavage. **Physical factors:** Volume (<3L, >6L); Pressure (ultra-low/low 1-12 psi vs. high >12 psi); Temperature (cold vs. warm); Timing (<6h vs. >6h). **Solution types:** Chemically inert (saline, sterile water, tap water); Antibiotics; Castile soap; Benzalkonium chloride; Chlorhexidine; Hydrogen peroxide; Povidone-iodine.	**Key findings per comparison:** **Pressure:** Low pressure (1-12 psi) overcomes bacterial adhesion and shows similar reoperation rates vs. high pressure, with less tissue/bone damage. **Solution - Saline vs. others:** Saline is isotonic, non-toxic, inexpensive, current standard of care; equally effective as most active agents. **Solution - Tap vs. sterile water vs. saline:** Tap water is least expensive; no difference in infection vs. saline; water toxicity risk with large volumes. **Solution - Antibiotics:** No consistent advantage over

						saline; risks include anaphylaxis, resistance, cost. **Solution - Castile soap:** Loosens bacteria but has higher reoperation rates vs. saline; skin irritant; not effective against S. aureus; avoid except for grease-contaminated wounds. **Solution - Benzalkonium chloride:** Effective against S. aureus but causes skin breakdown with some bacteria. **Solution - Chlorhexidine:** No advantage over saline; host cell toxicity. **Solution - Hydrogen peroxide:** Cheap, decomposes safely, but catalase reduces efficacy; toxicity; gas embolism risk. **Solution - Povidone-iodine:** Effective against broad pathogens but mixed results; possible thyroid effects; low concentrations maintain efficacy with less toxicity.

						Timing: Delaying irrigation beyond 6 hours may NOT increase infection rate (contrary to historical "6-hour rule"). **Volume & Temperature:** No established optimal values; larger wounds need more volume; warm fluid may reduce hypothermia; cold irrigation reduces bleeding/pain but may slow healing.
4.	Not able to open the file					
5.	Karuppasamy K, et al., 2004, UK (West Suffolk Hospital, Bury St. Edmunds)	Experimental / Laboratory comparison of irrigation techniques (Technical note)	Not applicable (no patients enrolled; timed flow rate comparison of different irrigation devices/methods)	Not applicable (in vitro mechanical testing; no human or animal subjects)	**Groups compared (irrigation techniques):** 1. 60 mL syringe with 19-gauge needle 2. Giving set (gravity) - bag at 3 ft height 3. Giving set with pressure cuff (400 mm Hg) 4. Pulsatile lavage (Microaire system) 5. **Novel**	**Primary outcome: Flow rate (liters/min)** • Syringe (60 mL/19G needle): 0.05 L/min • Giving set + gravity: 0.32 L/min • Giving set + pressure cuff (400 mm Hg): 0.38 L/min • Pulsatile lavage: 0.75 L/min • **Novel technique: 2.00 L/min**

					technique: Sterile 1L bag of saline/Hartmann's with outflow port cut to form nozzle; pressure and flow altered by manually squeezing bag and partially occluding nozzle	**Secondary outcome: Time to irrigate 10 Liters** • Syringe: 200 minutes • Giving set + gravity: 32 minutes • Giving set + pressure cuff: 26 minutes • Pulsatile lavage: 14 minutes • **Novel technique: 5 minutes** **Conclusion:** The novel technique (cut bag with manual compression) was fastest (2 L/min), simple, low-pressure, cost-effective, and avoided potential bone/soft tissue damage associated with pulsed lavage. The technique was adopted in the hospital's A&E department and by pre-hospital BASICS doctors for primary decontamination of dirty wounds.
6.	Klinge SA, 2020, USA (Lahey Hospital	Commentary / Expert Opinion / CORR	Not applicable (no original patient data; commentary on	Not applicable (discusses management of superficial SSIs	Not applicable (no direct group comparison; discusses antibiotic treatment success	**Key Points from the Commentary:** **Main finding (citing Prada**

	and Medical Center, Burlington, MA)	Insights® (Secondary analysis of FLOW trial cohort)	Prada et al.'s study)	after open fractures; no primary inclusion/exclusion criteria)	based on timing of SSI diagnosis)	**et al.):** Superficial SSIs diagnosed **≥90 days** after open fracture had only a **50%** chance of resolution with antibiotics alone, compared to **71-72%** for those diagnosed earlier. **Clinical recommendation:** Surgeons should consider early operative irrigation & debridement (rather than initial antibiotic treatment) for late superficial SSIs (especially those diagnosed after 3 months). **Identified knowledge gaps:** 1. Are late SSIs (>90 days) reliably superficial? 2. Need for noninvasive means to detect deep infection underlying superficial SSIs. 3. Role of anatomic region (femur vs. distal tibia/ankle) in predicting deep infection. 4. Pathogen patterns and antibiotic susceptibility in late SSIs.

						5. Role of presurgical skin biome analysis. **Suggested future research:** Prospective, multicenter cohort analysis at tertiary trauma centers with formal I&D, superficial + deep cultures, and advanced imaging (contrast MRI/CT) prior to reoperation.
7.	FLOW Investigators (Bhandari M, Jeray KJ, Petrisor BA, et al.), 2015, Multicenter (USA, Canada, Australia, Norway, India)	Multicenter, randomized (allocation concealed), blinded (patients, outcome assessors, data analysts), controlled trial with 12-month follow-up	**Total analyzed:** 2,447 patients (mean age 45.2 yrs; 69% men) **By Pressure:** - High (>20 psi): n=859 - Low (5-10 psi): n=846 - Very low (1-2 psi): n=846 **By Solution:** - Castile soap (0.45% in normal saline): n=1,275	**Inclusion:** Patients ≥18 years with an open fracture of arm, wrist, leg, ankle, foot, clavicle, or scapula. **Exclusion:** Fractures of pelvic ring, axial skeleton, hand, or toes; Gustilo-Anderson Type IIIC open fractures.	**Irrigation Pressure:** - High (>20 psi) - Low (5-10 psi) - Very low (1-2 psi) **Irrigation Solution:** - Castile soap (0.45% in normal saline) - Normal saline alone	**Primary Outcome (Reoperation at 12 months):** **By Pressure:** No significant difference among high, low, and very low pressure groups ($p=0.80$ for 3-way comparison). **By Solution:** Castile soap was associated with **higher reoperation rate** than normal saline alone ($p=0.01$). **Secondary Outcomes:** No significant differences between groups for

			- Normal saline alone: n=1,276			nonoperatively managed infections, wound-healing problems, or bone-healing problems. **Commentary note (Schottel):** Subgroup analysis suggested very-low-pressure irrigation decreased reoperation rates for open tibial fractures but increased rates for non-tibial fractures (p=0.053) — not deemed significant due to multiple comparisons. **Conclusion:** Irrigation pressure did not affect reoperation rate; normal saline solution was better than castile soap.
8.	Stinner DJ, Noel SP, Haggard WO, Watson JT, Wenke JC, 2010, USA	Randomized controlled animal study (goat model)	**Study I (P. aeruginosa):** n =10 goats (5 control, 5 experimental) **Study II (S. aureus):** n=10 goats (5 control, 4 experimental;	**Inclusion:** Adult goats with a complex musculoskeletal wound created on proximal left hindlimb. **Exclusion:** None specified; one goat	**Control group:** Standard debridement + irrigation with 9L normal saline using bulb syringe irrigation (no adjunctive treatment). **Experimental group:** Standard	**Primary Outcome (Bacterial reduction at 48 hours):** **Study I (P. aeruginosa):** • Control group rebounded to 82% ± 35% of 6-hour post-debridement levels. • Amikacin-loaded sponge group: **0.5% ± 0.3%** of 6-

			1 death from pneumonia excluded)	died from pneumonia before study completion.	debridement + irrigation + antibiotic-loaded chitosan sponge (amikacin for P. aeruginosa; vancomycin for S. aureus) placed in wound before closure.	hour levels (P < 0.05). **Study II (S. aureus):** • Control group rebounded to 677% ± 448% of 6-hour post-debridement levels. • Vancomycin-loaded sponge group: **18% ± 15%** of 6-hour levels (P < 0.05). **Secondary Outcomes:** **Serum antibiotic levels:** Peak at 6 hours (amikacin 0.53 ± 0.48 µg/mL; vancomycin 1.63 ± 0.65 µg/mL), remained <15% of target systemic levels. **Sponge degradation:** At 48 hours, sponges were 87% ± 13% (amikacin) and 86% ± 3% (vancomycin) degraded. **Antibiotic persistence:** Detectable in all recovered sponges at 12 hours post-removal.

						Conclusion: Chitosan sponges effectively delivered local antibiotics, significantly reduced bacterial load, and were biocompatible and resorbable without need for surgical removal.
9a.	Sendi P, McNally MA, 2016, Switzerland & UK	Letter to the Editor / Commentary on FLOW trial (2015)	Not applicable (commentary; no original patient data)	Not applicable (discusses FLOW trial patients with open fractures)	**Conceptual comparison:** Patients receiving vacuum-assisted closure (VAC) vs. no VAC	**Key points from letter:** **Concerns raised:** 1. Whether FLOW investigators adhered to protocol for definitive wound coverage (7-14 days). 2. Number and duration of VAC procedures not reported. 3. Prolonged VAC may facilitate superinfection and polymicrobial colonization. 4. Skin flora may migrate into wound, adhere to hardware, leading to nonunion or recurrent infection. **Request:** Information on VAC use to understand association with later infection.

9b.	Barbier O, Pasquier P, 2016, France	Letter to the Editor / Commentary on FLOW trial (2015)	Not applicable (commentary; no original patient data)	Not applicable (discusses FLOW trial patients with open fractures)	**Conceptual comparison:** Débridement quality across Gustilo-Anderson types	**Key points from letter:** **Concerns raised:** 1. Débridement is more important than irrigation. 2. FLOW protocol lacked information on how quality of initial débridement was evaluated. 3. Débridement should be extensive for type III fractures but limited for type I fractures. 4. Culture specimens should be obtained before and after irrigation to assess bacteriologic load reduction.
9c.	Bhandari M, Petrisor BA, Jeray KJ (FLOW Investigators), 2016, Canada & USA	Authors' Reply (Post-hoc analysis of FLOW trial data)	**VAC analysis:** 331 patients underwent VAC **By fracture type (infection rates):** Type I: VAC (n=10), No VAC (n=629) Type II: VAC (n=62), No VAC (n=834)	Same as FLOW 2015 trial: Patients ≥18 years with open extremity fracture; excluded pelvic ring, axial skeleton, hand, toes, and Type IIIC fractures.	**VAC vs. No VAC** (stratified by Gustilo-Anderson type)	**Primary finding (Infection rates):** VAC use was associated with **significantly higher infection rates** across all fracture types ($p < 0.001$ for comparison; odds ratio 2.39, 95% CI: 1.76-3.26 after adjustment for fracture type). **Infection rates by fracture type:** • Type I: VAC 30.0% vs. No

			Type IIIA: VAC (n=10), No VAC (n=519) Type IIIB: VAC (n=130), No VAC (n=103)			VAC 5.7% • Type II: VAC 27.4% vs. No VAC 11.2% • Type IIIA: VAC 70.0% vs. No VAC 14.6% • Type IIIB: VAC 31.5% vs. No VAC 21.4% **Reply to débridement concern:** Débridement approach was left to surgeon discretion but was standardized to extent feasible; similar amounts of tissue were debrided across treatment groups and increased with fracture severity. Stratification by Gustilo-Anderson type ensured balance across groups. **Conclusion:** VAC use was proportional to fracture severity but associated with increased infection. Further analysis of factors associated with reoperation is ongoing.

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

Summary of Available Evidence

The available evidence on antibiotic-containing irrigation solutions for open fractures comes predominantly from large trials comparing other irrigants (normal saline, castile soap) rather than directly testing antibiotics. Critically, **no high-quality randomized controlled trial has directly compared antibiotic irrigation to normal saline alone** as the primary intervention.

The FLOW Trial (2015) – Highest Level Evidence

The Fluid Lavage of Open Wounds (FLOW) trial, a multicenter, blinded randomized controlled trial of 2,447 patients, represents the largest and most rigorous study on open fracture irrigation. This trial compared irrigation pressures (high, low, very low) and solutions (castile soap vs. normal saline). **Antibiotic-containing solutions were not studied.** Key findings included: (1) irrigation pressure did not affect reoperation rates ($p=0.80$); (2) castile soap was associated with significantly higher reoperation rates than normal saline alone ($p=0.01$). The trial established normal saline as the standard of care.

Indirect Evidence from Other Studies

The FLOW pilot trial (2011, n=111) similarly compared castile soap to saline, with no significant difference in reoperation (23% vs. 24%). A goat model study (2010) demonstrated that antibiotic-loaded chitosan sponges (amikacin for *P. aeruginosa*, vancomycin for *S. aureus*) significantly reduced bacterial load compared to controls ($p<0.05$), but this represents sustained local delivery—distinct from irrigation.

Evidence from Reviews and Commentaries

A 2005 review concluded that antibiotic-containing irrigation solutions remain controversial due to questions about effectiveness, selection of resistant organisms, and cost-benefit ratio. A 2016 letter to NEJM raised concerns about vacuum-assisted closure potentially increasing infection risk (OR 2.39, $p<0.001$), but did not address antibiotic irrigation.

Gaps in the Literature

No Level I evidence directly compares antibiotic irrigation to saline. Existing studies are small, heterogeneous, use different antibiotic agents (bacitracin, neomycin, cephalosporins), and have methodological limitations. Potential harms—including anaphylaxis (reported with bacitracin), impaired wound healing, and antibiotic resistance—remain inadequately studied.

Conclusion of Evidence

Based on the articles reviewed, there is **no direct high-quality evidence supporting routine use of antibiotic-containing irrigation solutions** for open fractures. Normal saline alone is supported by large RCT evidence as safe, effective, and the current standard of care

Section 4: Discussion (<1000 words):

The available evidence addressing whether antibiotic-containing irrigation solutions should be routinely employed in open fracture management is notable more for its **gaps than its definitive answers.** After a comprehensive review of the literature provided—including the landmark FLOW trial (2015, n=2,447), the FLOW pilot trial (2011, n=111), multiple review articles, a goat model study on local antibiotic delivery, and several expert commentaries—several key observations emerge.

First, **no high-quality randomized controlled trial has directly compared antibiotic-containing irrigation solutions to normal saline alone** as the primary intervention. The FLOW trial, which represents the largest and most methodologically rigorous study on open fracture irrigation to date, compared castile soap to normal saline and different irrigation pressures. Antibiotic solutions were not included in the study design. This absence of direct evidence is a critical gap that must be acknowledged.

Second, the available evidence establishes **normal saline as an effective, safe, and inexpensive standard of care.** The FLOW trial demonstrated that irrigation pressure (high, low, or very low) does not affect reoperation rates ($p=0.80$), and that castile soap was associated with significantly higher reoperation rates than normal saline alone ($p=0.01$). These findings reinforce that normal saline is not merely a neutral comparator but an active, effective irrigant that should be considered the benchmark against which any new irrigation solution must prove superiority.

Evidence from Indirect Sources

The FLOW pilot trial (2011) similarly compared castile soap to normal saline, showing no significant difference in reoperation rates (23% vs. 24%). While this smaller study did not demonstrate superiority of one solution over the other, it further validated the use of normal saline as a control group and established the feasibility of large-scale irrigation trials.

Review articles from 2005 and the recent CORR Insights® commentary (2020) consistently highlight that antibiotic-containing irrigation solutions remain **controversial**. The 2005 review by Blease and Kanlić explicitly notes that questions persist regarding effectiveness, selection of resistant organisms, and the cost-benefit ratio of antibiotic irrigation. The CORR Insights® piece emphasizes diagnostic challenges in differentiating superficial from deep surgical site infections and notes that a large percentage of pathogens in superficial SSIs remain unidentified, making targeted antibiotic selection difficult.

The Distinction Between Irrigation and Sustained Local Delivery

A critical distinction must be made between **brief irrigation** with antibiotic-containing solutions and **sustained local antibiotic delivery** using vehicles such as PMMA beads or biodegradable chitosan sponges. The goat model study (Stinner et al., 2010) demonstrated that antibiotic-loaded chitosan sponges (amikacin for *P. aeruginosa*, vancomycin for *S. aureus*) significantly reduced bacterial load compared to controls ($p<0.05$). Serum antibiotic levels remained low (<15% of target systemic levels), and sponges were >85% degraded by 48 hours.

However, this evidence applies to **sustained local delivery**, not to irrigation. Irrigation involves brief (seconds to minutes) contact of the antibiotic solution with the wound surface, after which the solution is aspirated or drained. In contrast, local delivery vehicles remain in the wound for hours to days, providing prolonged antibiotic concentrations. These two interventions should not be conflated. The absence of evidence for antibiotic irrigation does not preclude potential benefit from sustained local delivery, and vice versa.

Potential Harms and Downsides

Even if antibiotic irrigation were effective, potential harms must be considered. **Anaphylactic shock** has been reported with bacitracin irrigation during orthopedic procedures (Antevil et al., 2003; Sprung et al., 1990). While rare, such events are life-threatening and avoidable if non-antibiotic irrigants are used. Additionally, routine use of topical antibiotics may contribute to the growing crisis of **antibiotic resistance**. Subtherapeutic concentrations achieved by brief irrigation (as opposed to sustained delivery) could theoretically select for resistant organisms, although this has not been definitively proven.

Cost is another consideration. Antibiotic additives increase the cost of irrigation without proven benefit. In resource-limited settings or high-volume trauma centers where thousands of liters of irrigation fluid are used annually, even small per-liter cost differences translate into substantial expenditure.

Clinical Relevance and the Need for Further Research

Given that open fracture infection rates remain as high as 10–50% for Type III injuries, even a modest reduction in infection rate would have substantial clinical and economic impact. However, adopting an intervention without evidence of efficacy—especially one with potential harms and costs—is not justified.

The letters to the editor regarding the FLOW trial (Sendi & McNally, 2016; Barbier & Pasquier, 2016) raise important additional considerations. Sendi and McNally questioned whether vacuum-assisted closure (VAC) therapy, which was used in 331 FLOW trial patients, might influence infection rates. The FLOW investigators' post-hoc analysis revealed that VAC use was associated with significantly higher infection rates (OR 2.39, $p<0.001$), though this association may reflect confounding by injury severity rather than causation. Barbier and Pasquier emphasized that **debridement quality** may be more important than irrigation solution choice—a point with which most surgeons would agree.

Limitations of the Available Evidence

The studies provided have several limitations. The FLOW trial, while large and rigorous, did not include an antibiotic irrigation arm. The smaller studies are underpowered for detecting differences in infection rates. The goat model, while valuable for proof-of-concept, may not generalize to human clinical practice. The review articles, while synthesizing available knowledge, do not provide primary evidence.

Conclusion of Discussion

Based on the articles reviewed, there is **no direct high-quality evidence supporting the routine use of antibiotic-containing irrigation solutions** for open fractures. Normal saline alone is supported by large RCT evidence as safe, effective, and the current standard of care. The distinction between brief irrigation and sustained local delivery is critical and should not be overlooked. Potential harms—including anaphylaxis, antibiotic resistance, and cost—argue against routine adoption without proven benefit. A definitive randomized trial comparing antibiotic irrigation to normal saline is needed before any recommendation can be made for routine use.

Section 5: Risk of bias of included studies:

Risk of Bias	Number of Studies	Study Identifiers

LOW	2 (3 including Anglen 2005)	FLOW 2015, FLOW 2011, (Anglen 2005 - cited)
MODERATE	2	Stinner 2010 (animal), Karuppasamy 2004 (lab)
HIGH	4	Blease 2005 (review), Klinge 2020 (commentary), Sendi 2016 (letter), Barbier 2016 (letter)

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

Antibiotic-containing irrigation solutions should NOT be routinely employed in open fracture management. Normal saline alone is the standard of care, supported by high-level evidence, while antibiotic irrigation lacks proven benefit and carries risks of anaphylaxis and resistance.

Section 7: Level/ strength of Evidence:

The overall strength of evidence supporting a recommendation against routine use of antibiotic-containing irrigation solutions is **LOW** .

Domain	Assessment	Justification
Number of studies	Insufficient	No randomized controlled trial has directly compared antibiotic irrigation to normal saline. The available evidence is indirect (saline vs. soap) or non-comparative.
Risk of bias	Moderate to High	Only 2 studies have LOW risk of bias (FLOW 2015, FLOW 2011), but neither directly addressed antibiotic irrigation. Four studies have HIGH risk of bias (reviews, letters, commentaries).
Study design	Indirect evidence	The highest-quality evidence comes from the FLOW trial (2015), which compared castile soap to saline—not antibiotics. No Level I RCT exists for the PICO question.

Sample size	Inadequate for direct comparison	FLOW trial (n=2,447) is large but does not answer the question. No study with adequate sample size has directly compared antibiotic irrigation vs. saline.
Key outcomes	No direct outcome data	Infection rates, reoperation rates, and adverse events (anaphylaxis, resistance) have not been directly compared between antibiotic irrigation and saline in a prospective RCT.

Conclusion on Strength of Evidence

The **LOW** strength of evidence reflects that:

1. **No high-quality RCT** has directly compared antibiotic-containing irrigation solutions to normal saline for open fractures.
2. The best available evidence is **indirect** (saline vs. soap from FLOW trials) or **limited** (one older RCT by Anglen, 2005).
3. Potential harms (anaphylaxis, resistance) are **theoretically supported** but lack rigorous comparative study.
4. A **large, well-designed RCT** directly comparing antibiotic irrigation to saline is needed to upgrade the strength of evidence.

Reference List

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9. Barbier O, Pasquier P. Wound irrigation in initial management of open fractures [Letter]. *N Engl J Med*. 2016;374(18):1788-1789