5 PRACTICE-CHANGING PAPERS

Orthopaedic Trauma

2020 – 2025

High-energy lower extremity trauma · Open fracture management
Fracture-related infection · Limb viability decisions

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The Arc of Treatment

Each paper overturns a long-held dogma — following the patient from initial wound management through fixation, complication, and the ultimate limb decision.

1
PREVENT
Skin antisepsis
PREPARE + Aqueous-PREP
NEJM 2024 · Lancet 2022

2
PROTECT
VTE prophylaxis
PREVENT CLOT
NEJM 2023

3
FIXATE
Open tibia fixation
FIXIT
JBJS 2022

4
TREAT
Fracture infection Rx
POvIV
JAMA Surg 2025

5
DECIDE
Salvage vs amputation
OUTLET
JBJS 2021

Skin Antisepsis Before Fracture Fixation

PREPARE (NEJM 2024) + Aqueous-PREP (Lancet 2022) · PREP-IT Investigators · Cluster-RCTs

What they found

PREPARE (closed and open fractures): Iodine-in-alcohol significantly reduced SSI vs chlorhexidine-in-alcohol (25 hospitals, n ≈ 6,900 with closed fractures). Rate: 2.4% vs 3.3% (RR 0.74, p=0.049)

Aqueous-PREP (open fractures): Neither aqueous povidone-iodine nor aqueous chlorhexidine was superior — both acceptable (14 hospitals, n ≈ 1,100)

Combined message: A complete, evidence-based antisepsis protocol now exists for the full spectrum of extremity fractures

TAKE HOME

Switch to iodine-in-alcohol for closed fracture prep.

For open fractures: either aqueous antiseptic is acceptable.

Why this overturns practice

Chlorhexidine had been the assumed standard — championed in surgical infection guidelines — without fracture-specific RCT evidence. These trials, together, constitute the only cluster-randomized antisepsis program ever conducted in orthopaedic trauma. Directly actionable for every open or closed lower extremity case.

PREVENT CLOT: Aspirin vs LMWH After Fracture

METRC · O'Toole RV et al. · N Engl J Med 2023;388(3):203–213 · Multicenter RCT · n = 12,211 · 21 centers

12,211

patients randomized

largest orthopaedic trauma RCT ever

0.78%

90-day mortality (ASA)

vs 0.73% LMWH — non-inferior

≈equal

PE rates

1.49% in each group

Important nuance

DVT was modestly higher with aspirin **(2.51% vs 1.71%, Δ0.80%)** — but PE and mortality were equivalent. The trial was powered for mortality as primary endpoint (with FDA exemption for off-label aspirin use), reflecting real-world practice design. Mean patient age 45 — results may not fully apply to elderly high-risk patients.

TAKE HOME —

Aspirin 81 mg BID is a safe, inexpensive, patient-preferred alternative to enoxaparin for VTE prophylaxis after operatively treated extremity or pelvic/acetabular fractures. Surgeons should review institutional protocols — this challenges two decades of LMWH dogma.

FIXIT: External Ring vs Internal Fixation — Open Tibial Fractures

METRC · J Bone Joint Surg Am 2022;104(12):1061–1067 · Multicenter RCT · n = 260 · 20 centers · Gustilo IIIA/IIIB tibial shaft

Outcome at 1 Year	External Ring Fixation	Internal Fixation
Major limb complication	**62.1%**	**43.7%**
Risk difference (favoring IF)	—	**18.4% (95%CI 5.8–30.4, p=0.005)**
Primary driver of EF failures	Malreduction requiring conversion to IF	N/A
SMFA function at 12 months*	**Inferior**	**Superior**

**JBJS 2025 functional outcome secondary analysis*

TAKE HOME —

The first adequately powered RCT confirms: modern external ring fixation should NOT be used routinely for severe open tibial fractures. Intramedullary nailing or plating yields significantly fewer major complications. The debate is settled.

POvIV: Oral vs IV Antibiotics for Fracture-Related Infection

METRC · Obremskey WT, O'Toole RV et al. · JAMA Surgery 2025;160(3):276–284 · Multicenter RCT · n = 233 · 24 centers

Current Standard of Care

6 weeks IV antibiotics via PICC line

after debridement for FRI

Complications:
PICC-related DVT, line sepsis,
line occlusion, prolonged hospitalization,
high cost, poor quality of life

POvIV Trial Evidence (2025)

Oral antibiotics NON-INFERIOR to IV

for reoperation, reinfection, treatment failure, and nonunion

Benefits:
Eliminates PICC risk, reduces cost,
improves patient experience,
supports antibiotic stewardship

Caveat: patients without radiographic osteomyelitis only. Pathogen-specific oral bioavailability must be confirmed.

TAKE HOME —
Six weeks of PICC-line IV antibiotics is no longer the required standard for FRI without osteomyelitis. Transition to oral step-down therapy: fewer complications, lower cost, same outcomes.

OUTLET: Limb Salvage vs Transtibial Amputation — Severe Distal Tibial, Ankle & Hindfoot Injuries

METRC · Bosse MJ et al. · J Bone Joint Surg Am 2021;103(17):1588–1597 · Prospective multicenter observational · n = 639 · 32 centers

Study design note: Randomization to amputation vs salvage is ethically unfeasible — this prospective observational study with causal inference modeling represents the highest achievable evidence level for this question.

Primary finding

Salvage patients would have gained a 7-point SMFA mobility improvement had they undergone amputation (95%CI 2.0–10.7). Largest benefit in pilon/ankle fractures and complex multi-segment injuries.

Who benefits most from amputation

Type III pilon & ankle (OTA/AO 43C3), Type III talar & calcaneal fractures, open/crush foot injuries with vascular compromise or severe soft-tissue loss.

The paradigm shift

Amputation is a treatment option, not a last resort or failure. This reframes the consent conversation: salvage carries real functional trade-offs that must be shared with patients honestly.

TAKE HOME — Amputation is not failure. For the most complex distal lower extremity injuries, early amputation may yield better functional outcomes than heroic salvage. Share this data with patients before choosing a path.

Take-Home Messages

1. Switch your surgical prep: iodine-in-alcohol for closed fractures, either aqueous antiseptic for open. (PREPARE / Aqueous-PREP)

2. Aspirin 81 mg BID is non-inferior to enoxaparin for VTE prophylaxis — simpler, cheaper, patient-preferred. (PREVENT CLOT, NEJM)

3. Internal fixation is decisively superior to modern ring external fixation for severe open tibial fractures. The debate is over. (FIXIT, JBJS)

4. Oral antibiotics are non-inferior to IV for fracture-related infection without osteomyelitis. Eliminate the PICC. (POvIV, JAMA Surgery)

5. For the most severe distal lower extremity injuries: tell your patients that early amputation may outperform salvage. (OUTLET, JBJS)

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