# Topical Antibiotics in Orthopedic Surgeries

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October 3, 2023

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# Disclosures

- None

# Acknowledgements


- Adam Kantor, MD – content and references
- Jeremy Gililland, MD – spacer pictures

# Types and routes of topical antibiotics

- Bone cement (polymethylmethacrylate = PMMA)
- Powder placed directly into the surgical site
- Calcium sulfate beads (Stimulan)
- Intra-osseous

# Bone cement

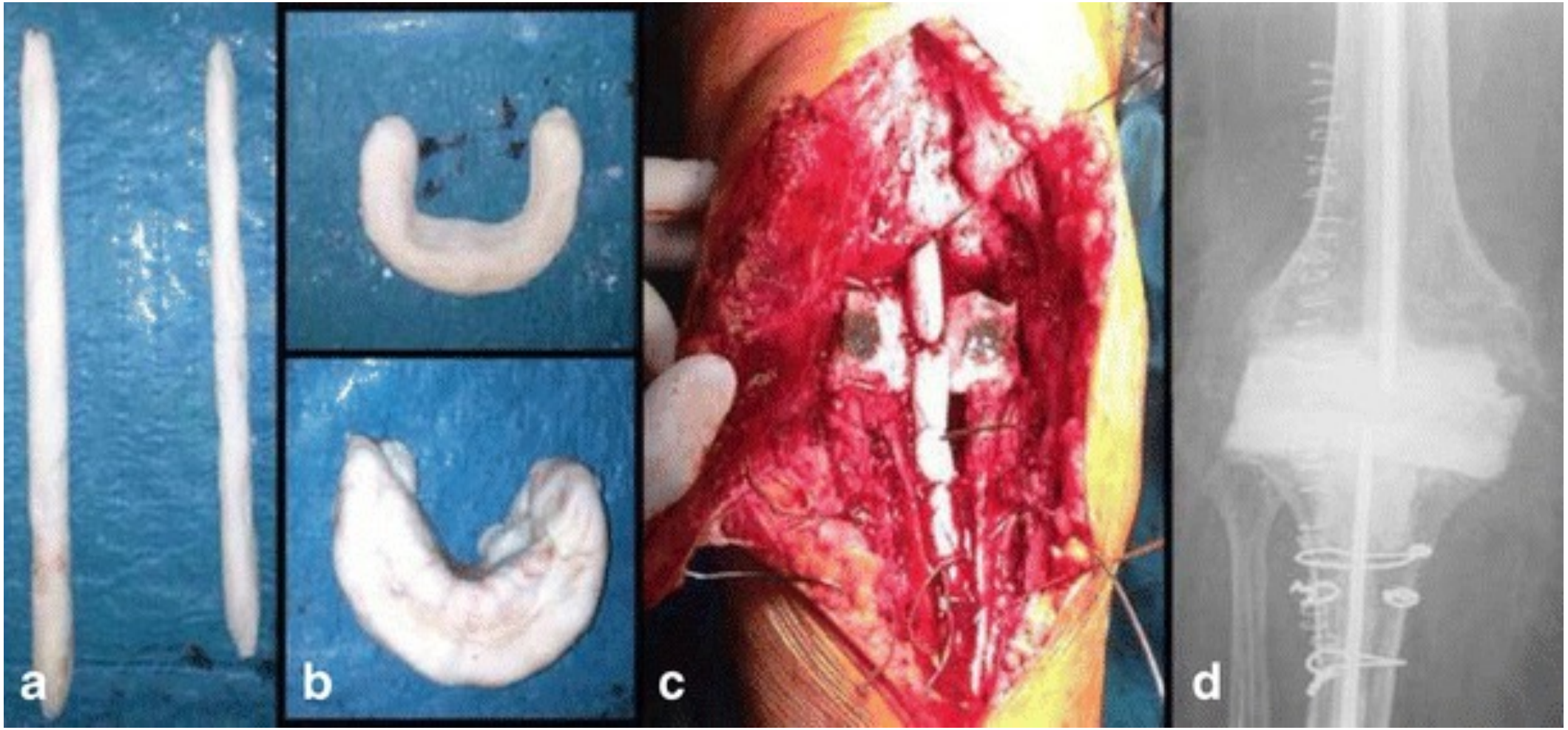
Three purposes:

- Fix prostheses in place
- Deliver local antibiotics
- Fill dead space

Mostly used in:

- Arthroplasty
  - Prevention and treatment of PJI (periprosthetic joint infection)
- Trauma
  - Treatment of infected fractures, chronic osteomyelitis

# Spacers can be all cement and static.




Curr Rev Musculoskelet Med. 2015; 8(4): 373–382.

# More often, patients have “articulating” spacers


Curr Rev Musculoskelet Med. 2015; 8(4): 373–382.

# Or can have a more durable “spacer.”


Photos from Dr. Jeremy Gililland

# Antibiotic cement elutes for a long time.

- 49 patients undergoing two-stage exchange with spacer placement
- Synovial fluid concentration measured at the time of the second surgery

| Time Between Stages (d) | Tobramycin Level (mg/L) | Vancomycin Level (mg/L) |
|---|---|---|
| ≤60 | 6.88 (3.33–10.43) | 2.28 (1.68–2.88) |
| 61–90 | 8.66 (6.09–11.24) | 1.95 (1.22–2.56) |
| 91–130 | 4.35 (3.36–5.35) | 1.49 (1.03–1.95) |
| >130 | 1.98 (1.32–1.98) | 0.97 (0.77–1.17) |

Masri. 1998. The Journal of Arthroplasty, 13(3)

# Serum concentrations persist as well

- 21 patients undergoing two-stage exchange with spacer placement
- Serum antibiotic concentration measured weekly

| | Vancomycin µg/mL Mean (SD) | | Tobramycin µg/mL Mean (SD) |
|---|---|---|---|
| | On IV Vancomycin | Not on IV Vancomycin | |
| Week 1 | 18.70 (3.45) | 14.38 (0.94) | 0.27 (0.10) |
| Week 2 | 16.17 (5.86) | 13.10 (11.34) | 0.35 (0.08) |
| Week 3 | 16.35 (4.58) | 7.76 (7.73) | 0.41 (0.18) |
| Week 4 | 13.26 (5.76) | 7.21 (8.61) | 0.39 (0.14) |
| Week 5 | 13.08 (6.24) | 7.89 (7.77) | 0.32 (0.21) |
| Week 6 | 15.55 (2.46) | 6.05 (8.64) | 0.38 (0.15) |
| Week 7 | 8.35 (6.66) | 1.80 (0.94) | 0.30 (0.20) |
| Week 8 | 21.50 (0) | 7.53 (8.04) | 0.59 (0.58) |

Edelstein. 2018. Journal of Arthroplasty 33(3): 835-839

# Typical antibiotics in bone cement

- Vancomycin + gram negative agent
- Tobra and gent most commonly
- Can also add antifungals (vori, ampho)

- Total amount typically ≤15% (≤ 2g per 40 g of cement)
- Elution kinetics depend on cement viscosity

# U of U Hip/Knee Protocol

| Standard antimicrobials used in cement | Amount per 40 g cement | Typical dose for infected joints at stage 1 (spacer placement) | Typical dose for infected joints at stage 2 (permanent prosthesis) |
|---|---|---|---|
| Vancomycin | ≤ 2 g | 2 g | 1 g |
| Ceftazidime | ≤ 4 g | 3 g | 2 g |
| OR | | | |
| Tobramycin | ≤ 3.6 g | 3.6 g | 1.2 g |

**TABLE 1. Available antibiotics and anti-fungals which can be used in spacers**

| Antibiotic Group | Type of Antibiotic | Activity Against | Dose per 40 gm cement (in grams) |
|---|---|---|---|
| Aminoglycoside | Tobramycin | Gram-negative bacteria such as *Pseudomonas* | 1 to 4.8 |
| Aminoglycoside | Gentamicin | Gram-negative bacteria-*Escherichia coli, Klebsiella* and particularly *Pseudomonas aeruginosa*. Also aerobic bacteria (not obligate/ facultative anaerobes) | 0.25 to 4.8 |
| Cephalosporin, 1st gen | Cefazolin | Gram-positive infections, limited gram-negative coverage | 1 to 2 |
| Cephalosporin, 2nd gen | Cefuroxime | Reduced gram-positive coverage, improved gram-negative coverage | 1.5 to 2 |
| Cephalosporin, 3rd gen | Ceftazidime | Gram-negative bacteria, particularly *Pseudomonas* | 2 |
| Cephalosporin, 4th gen | Cefotaxime | Gram-negative bacteria, no activity against *Pseudomonas* | 2 |
| Cephalosporin, 5th gen | Ceftaroilne | Gram-negative bacteria, no activity against *Pseudomonas* | 2 to 4 |
| Fluoroquinolone | Ciprofloxacin | Gram-negative organisms including activity against *Enterobacteriaciae* | 0.2 to 3 |
| Glycopeptide | Vancomycin | Gram-positive bacteria, including methicillin-resistant organisms | 0.5 to 4 |
| Lincosamide | Clindamycin | Gram-positive cocci, anaerobes | 1 to 2 |
| Macrolide | Erythromycin | Aerobic gram-positive cocci and bacilli | 0.5 to 1 |
| Polymyxin | Colistin | Gram-negative | 0.24 |
| β-lactam | Piperacillin- not available Piptzobactam | Gram-negative bacteria (particularly *Pseudomonas*), Enterobacteria and anaerobes | 4 to 8 |
| β-lactam | Aztreonam | Only gram-negative bacteria | 4 |
| β-lactamase inhibitor | Tazobactam | Gram-negative bacteria (particularly *Pseudomonas*), Enterobacteria, and anaerobes in combination with Piperacillin | 0.5 |
| Oxazolidinones | Linezolid | Multidrug-resistant gram-positive cocci such as MRSA | 1.2 |
| Carbapenem | Meropenem | Gram-positive and gram-negative bacteria, anaerobes, *Pseudomonas* | 0.5 to 4 |
| Lipopeptide | Daptomycin | Only gram-positive organisms | 2 |
| Antifungale | Amphotericin | Most fungi | 200 |
| Antifungal | Voricanazole | Most fungi | 300-600 mg |

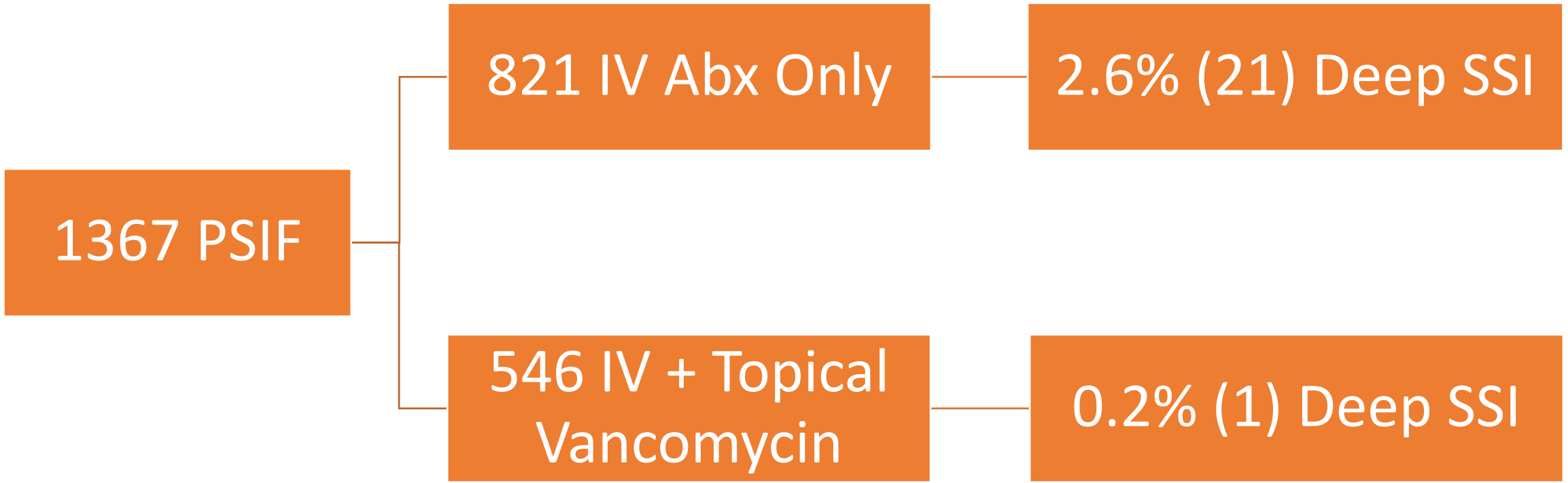
2018 International Consensus Statement on Musculoskeletal Infections. https://icmphilly.com/document/

# Intra-wound antibiotics

- Usually vancomycin powder
- Sometimes Gram negative agent added (gent, tobra, ceftaz)
- Most evidence comes from the spine surgery literature

# First study of topical vancomycin – 2009

- Retrospective cohort study, Sweet et al.



# Two meta-analyses in 2019 both showed a benefit.

**The effect of prophylactic vancomycin powder on infections following spinal surgeries: a systematic review**

Vincent Dodson, Neil Majmundar, Vanessa Swantic, Rachid Assina

> Neurosurg Focus. 2019 Jan 1;46(1):E11. doi: 10.3171/2018.10.FOCUS18470.

**Selection pressures of vancomycin powder use in spine surgery: a meta-analysis**

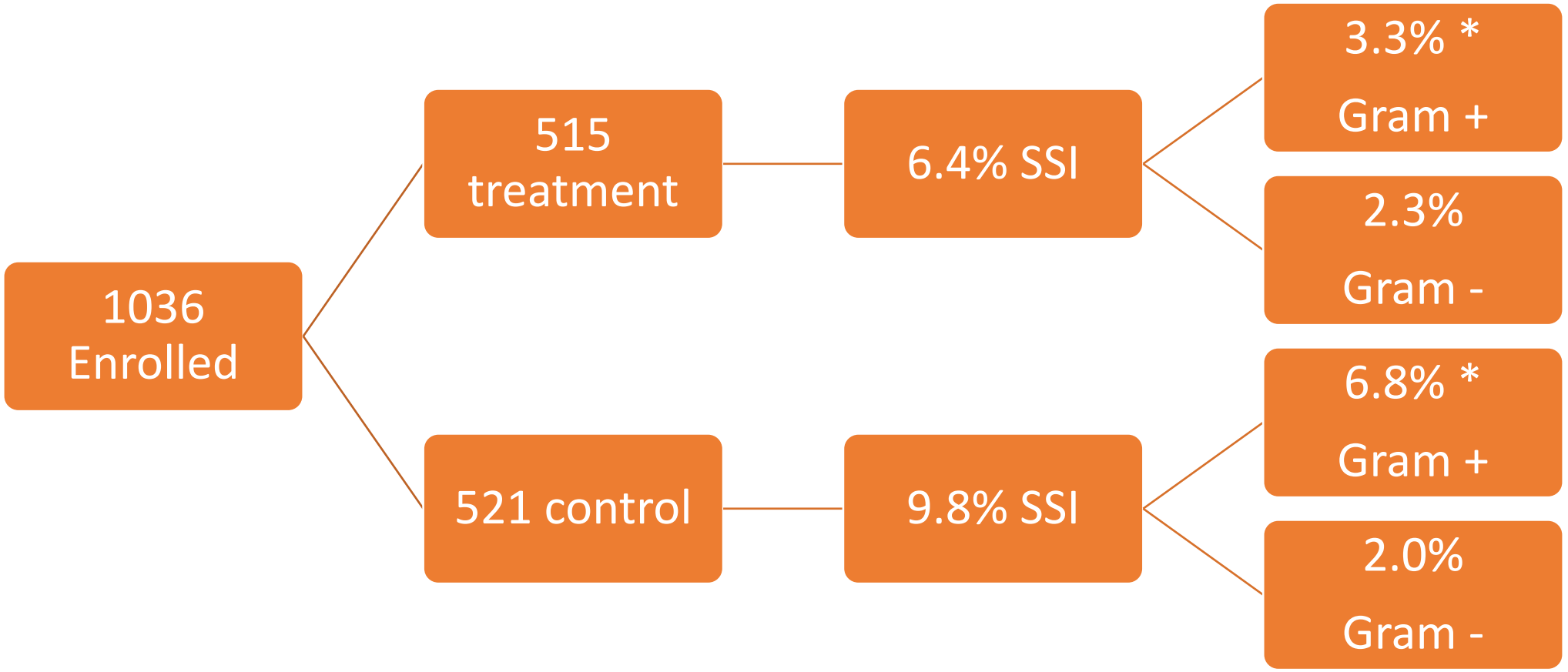
Abhiram Gande [1], Alex Rosinski [2], Torin Cunningham [3], Nitin Bhatia [4], Yu-Po Lee [4]

Meta-Analysis > Spine J. 2019 Jun;19(6):1076-1084. doi: 10.1016/j.spinee.2019.01.002.

Epub 2019 Jan 17.

# Also studied in tibia fracture – VANCO study

- Prospective RCT in 34 trauma centers (O'Toole et al. 2021)



# Dissolvable beads (calcium sulfate)

- Only purpose is to deliver antibiotics locally
  - Generally used by trauma surgeons for infected fracture fixation
- Any antibiotic can be mixed in
  - Vanc, gent, rifampin most common
- Dissolve over days to weeks
  - Can cause wound drainage

# Intra-osseous antibiotics

- Newer idea in the prosthetic joint infection literature
- Typically vancomycin (500 mg) or cefazolin (1 g)
- Injected into the tibial plateau (for knees) after the tourniquet is inflated

Clin Orthop Relat Res (2021) 479:2504-2512
DOI 10.1097/CORR.0000000000001919

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## Intraosseous Regional Prophylactic Antibiotics Decrease the Risk of Prosthetic Joint Infection in Primary TKA: A Multicenter Study

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