

# Antibiotics: IV, Oral, or Local

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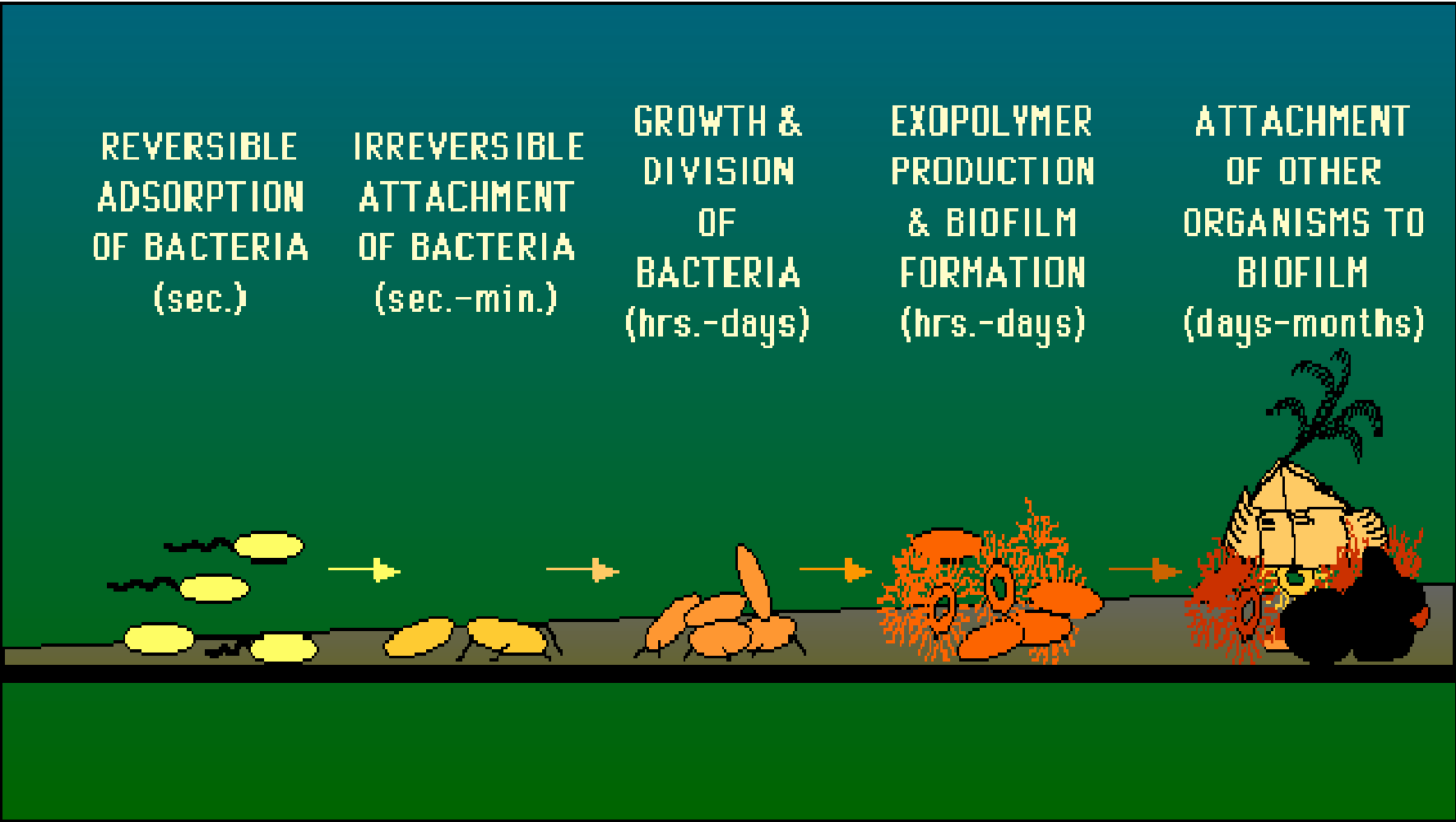
University of California, San Francisco



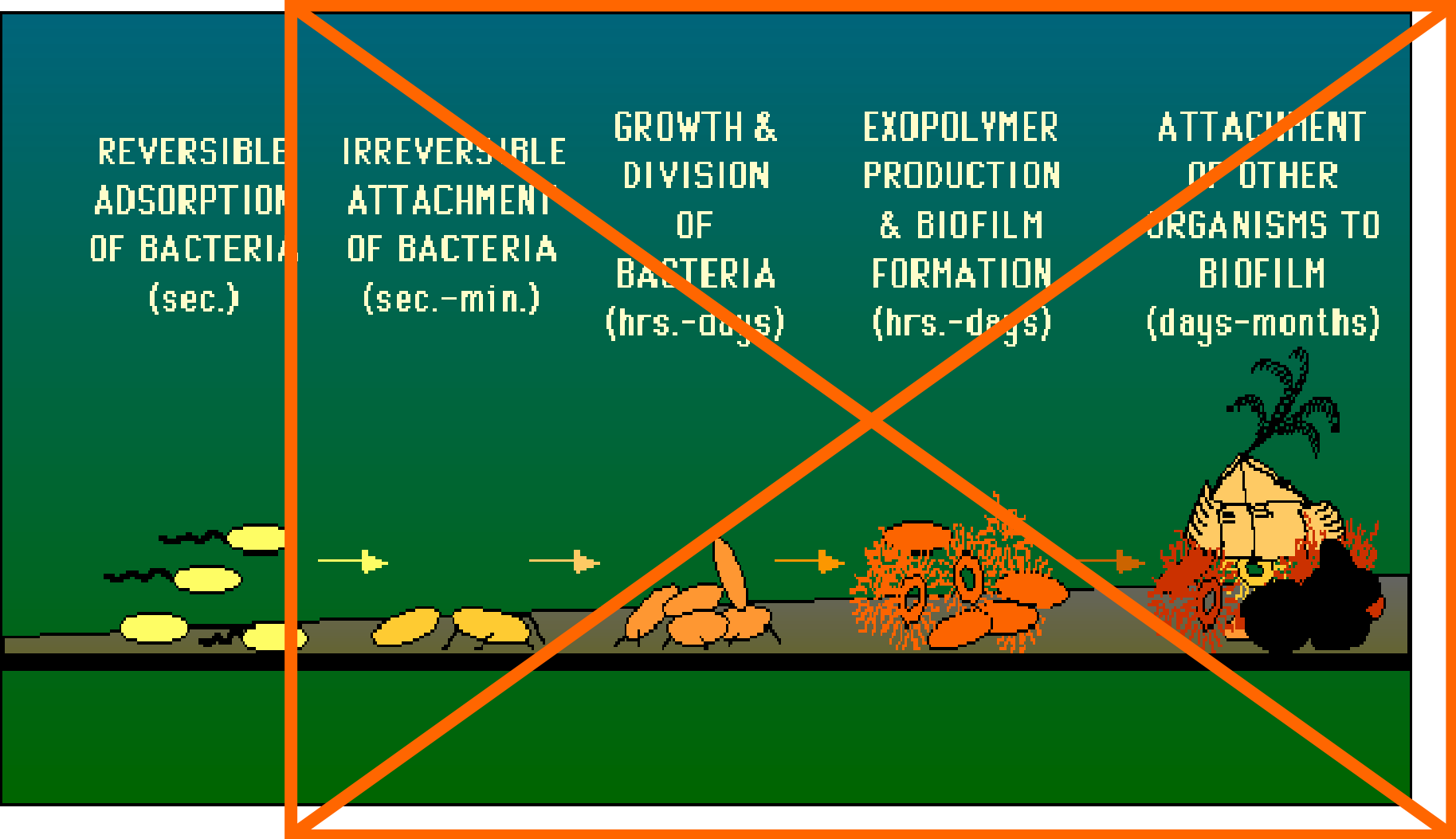
# Learning objectives

- Preop IV antibiotics to prevent infection
- Potential for local antibiotics in high risk cases for both prevention and treatment
- Question the dogma of 6 weeks IV antibiotics

# Theoretical Timeline



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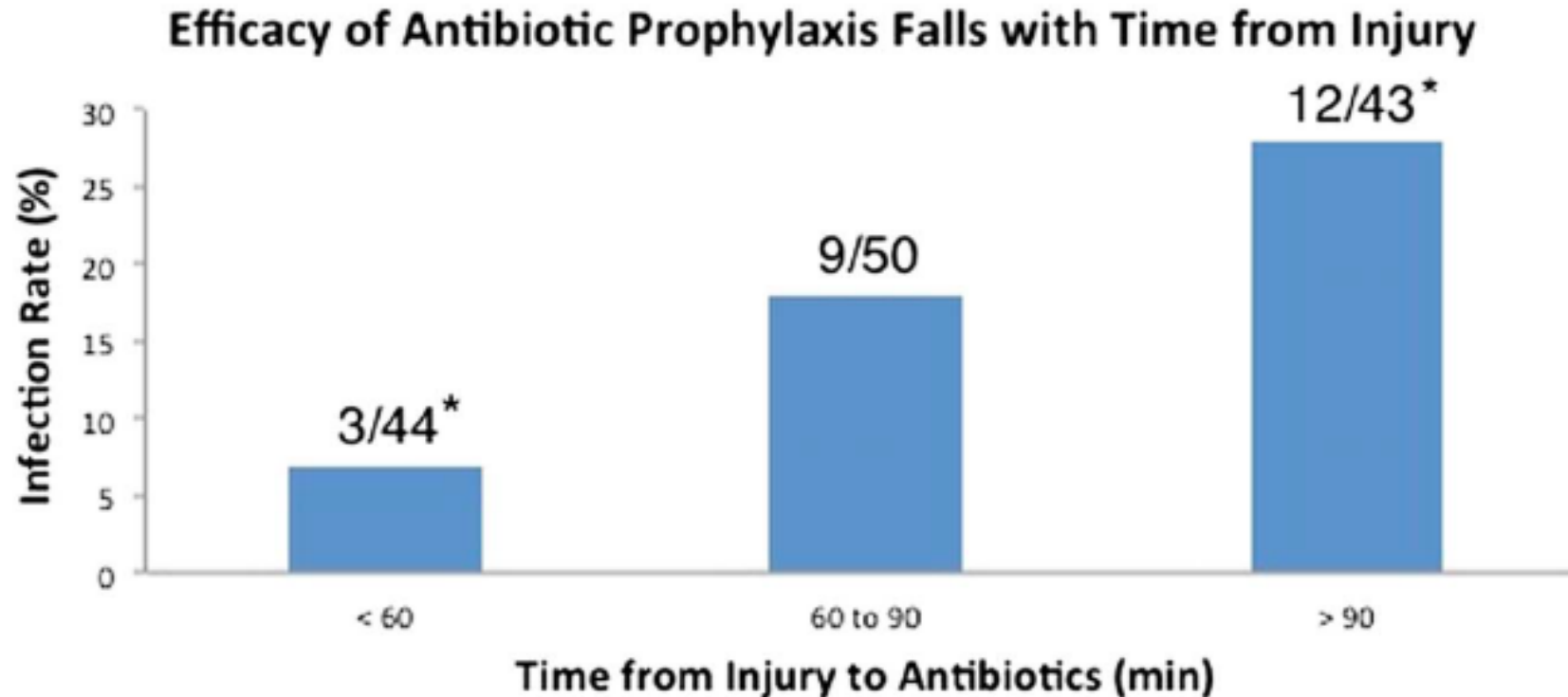


# Pre-operative Antibiotics: Closed Fractures

- IV within 60 minutes of incision
- 1<sup>st</sup> gen cephalosporin unless allergy, MRSA colonized
- Strong evidence, CMS quality metric

# Pre-operative Antibiotics: Open Fractures

- IV ASAP



# Antibiotic Prophylaxis

- Type 1/2: Gram positive
- Type 3: + **Gram negative**
- “Barn Yard Contamination”  
(Soil/fecal/standing water)  
+ **Anaerobic Coverage**



# Post-operative Antibiotics

- Less than 24hrs
- Consider 48-72hrs Type 3 open injuries
- Local antibiotics may have a role intraop





# Local Antibiotics

- Low risk fractures – not necessary
- High risk fractures – Consider “Naked” powdered antibiotic
- High risk open fractures with bone loss – Consider adding a carrier (e.g. PMMA)

# Effect of Intrawound Vancomycin Powder in Operatively Treated High-risk Tibia Fractures A Randomized Clinical Trial

The Major Extremity Trauma Research Consortium (METRC)

- 980 patients from 36 US Trauma Centers
- High-risk fractures (plateau and pilon, staged, plated)
- Intervention: 1g intrawound vancomycin powder
- Control: Standard prevention protocol
- Outcome: Deep infection @ 6 months

# Effect of Intrawound Vancomycin Powder in Operatively Treated High-risk Tibia Fractures A Randomized Clinical Trial

The Major Extremity Trauma Research Consortium (METRC)

- Results:

- Vanco: 29/481 (6%)
- No Vanco: 46/499 (9.2%)

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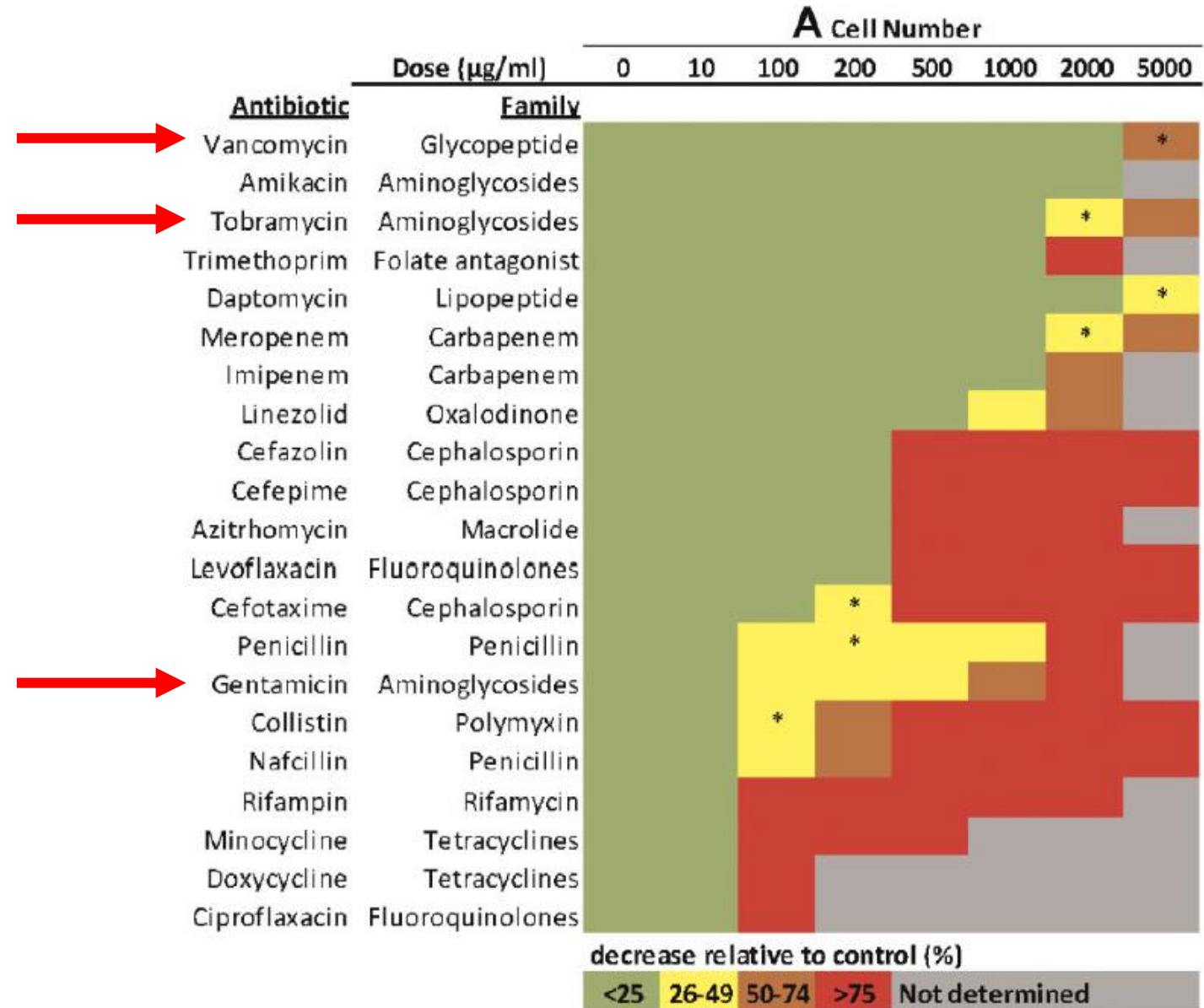
- Reduced Gram positive infection

- 16/481 (3.3%) vs 34/499 (6.8%)

**P=0.02**

# Potential Issues

- Inhibition of bone healing
- Nephrotoxicity
- Selection of bacteria



# Potential Issues

- Inhibition of bone healing
- **Systemic toxicity**
- Selection of bacteria

## Systemic Absorption and Nephrotoxicity Associated With Topical Vancomycin Powder for Fracture Surgery

*Robert V. O'Toole, MD,<sup>a</sup> Yasmin Degani, MPH,<sup>a</sup> Anthony R. Carlini, MS,<sup>b</sup> Renan C. Castillo, PhD,<sup>b</sup> Nathan N. O'Hara, MHA,<sup>a</sup> and Manjari Joshi, MBBS,<sup>c</sup> and METRC<sup>d</sup>*

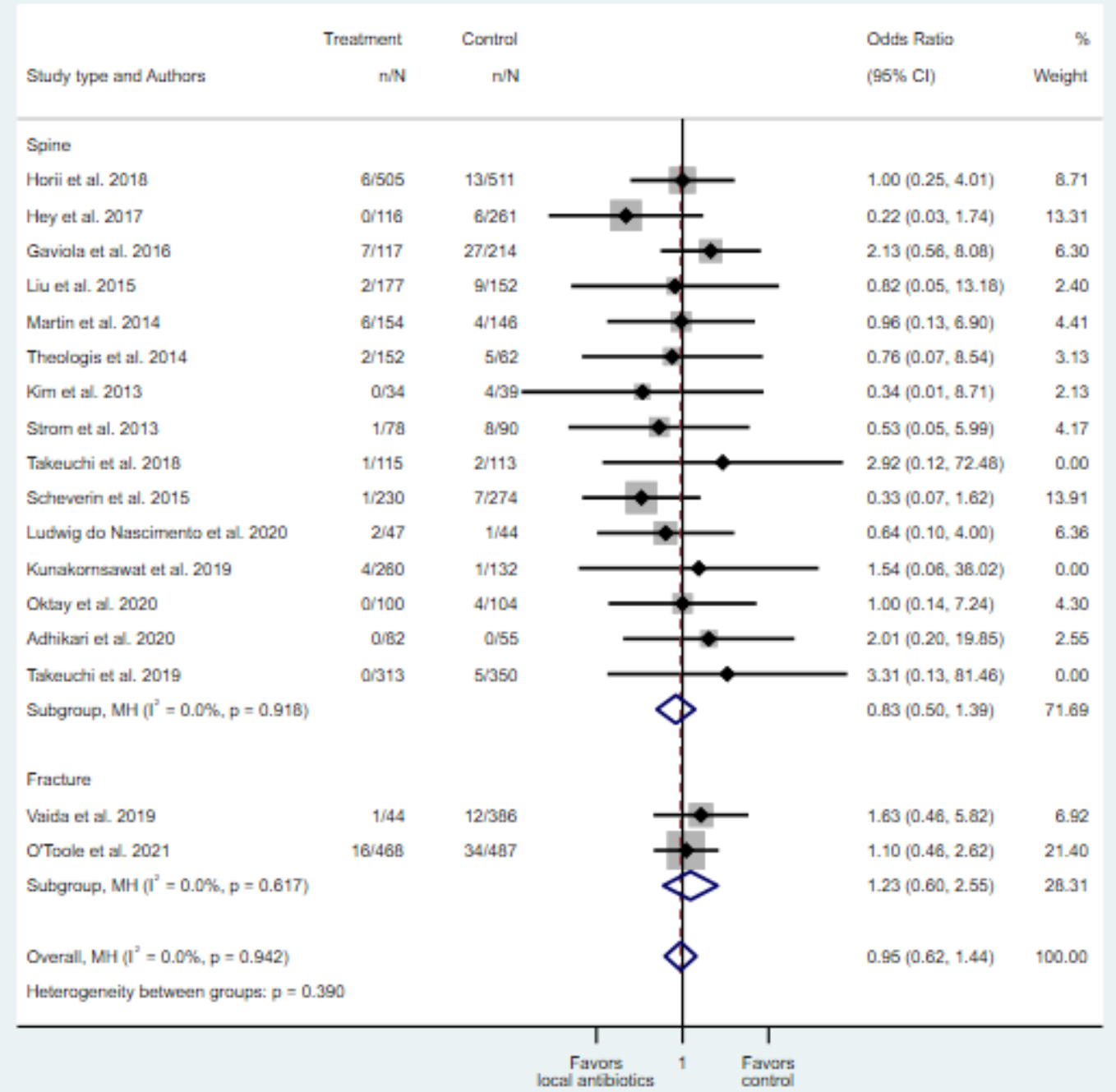
*J Orthop Trauma* • Volume 35, Number 1, January 2021

- Subset 58 patients Vanco trial
- 1g intrawound powder
- No detectable serum vanco @1hr and 6-8hrs
- No significant change creatinine



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- Inhibition of bone healing
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- **Selection of bacteria**



# More evidence is coming

- **TOBRA Trial**

- Vanco + Tobra vs. Vanco alone
- Study Site: METRC
- Target enrollment: 1900
- Estimated completion: June 2024

- **GO-Tibia**

- Liquid gentamicin vs placebo saline
- Study Site: Tanzania
- Target enrollment: 890
- Estimated completion: 2027

# Role of Oral Antibiotics in Prevention

- Open fractures managed outpatient
  - Low-energy GSWs without indication for surgery
  - Low-grade pediatric open fractures
  - Open fractures of the phalanges
- 7-10 days 1<sup>st</sup> gen cephalosporin
- Not strongly supported by evidence



# Treatment of Infection (Chronic Osteomyelitis)

1. Debride
2. Manage dead space
3. Soft-tissue Coverage
4. Bony Reconstruction

Debridement >> Antibiotics

# Treatment of Infection: IV or oral antibiotics

- Historically 6 weeks IV antibiotics
- Increasing evidence for early transition to oral antibiotics
- Must be bioavailable and sensitive

## Oral Antibiotics and Their Coverage and Bioavailability (%)

<i>Staphylococcus</i>	<i>Enterococcus</i>	<i>Streptococcus</i>	<i>Enterobacteriaceae</i>	<i>Pseudomonas</i>
<b>MRSA</b>	Linezolid <sup>a</sup> (100%)	<b>GAS/GBS</b>	Ciprofloxacin <sup>c</sup> (70%)	Ciprofloxacin <sup>c</sup> (70%)
Linezolid <sup>a</sup> (100%)	Ampicillin <sup>d</sup> (50%)	Penicillin VK (50%)	Levofloxacin <sup>c</sup> (99%)	Levofloxacin <sup>c</sup> (99%)
TMP/SMX (90%-100%)	Nitrofurantoin (80%)	Amoxicillin (85%)	Moxifloxacin (90%)	Delafloxacin (60%)
Clindamycin <sup>b</sup> (90%)	Amox/Clav (85%)	Cephalexin (90%)	Amox/Clav (85%)	
Doxycycline <sup>c</sup> (95%)		Levofloxacin <sup>c</sup> (99%)	Amoxicillin (85%)	
		Clindamycin <sup>b</sup> (90%)	Cefixime (40%-50%)	
		Linezolid <sup>a</sup> (100%)	Cefuroxime <sup>b</sup> (70%)	
<b>MSSA</b>			Cephalexin (90%)	
Cephalexin (90%)		<b>S Pneumoniae</b>	TMP/SMX (90%-100%)	
Dicloxacillin <sup>d</sup> (50%-75%)		Amoxicillin (85%)		
		Doxycycline <sup>c</sup> (95%)		
		Azithromycin (30%-50%)		
		Levofloxacin <sup>c</sup> (99%)		

<sup>a</sup> Concurrent ingestion of foods rich in tyramine or tyrosine could lead to hypertensive crisis or serotonin syndrome.

<sup>b</sup> Take with food.

<sup>c</sup> Oral absorption is decreased with concurrent calcium/magnesium-containing foods and products. Avoid taking with antacids and separate 2 h before or 6 h after calcium foods.

<sup>d</sup> Take on empty stomach.

Amox/Clav: amoxicillin/clavulanate; GAS/GBS: group A Streptococcus/group B Streptococcus; MRSA: methicillin-resistant S aureus; MSSA: methicillin-resistant susceptible S aureus; TMP/SMX: trimethoprim/sulfamethoxazole.

Source: Reference 18.

ORIGINAL ARTICLE

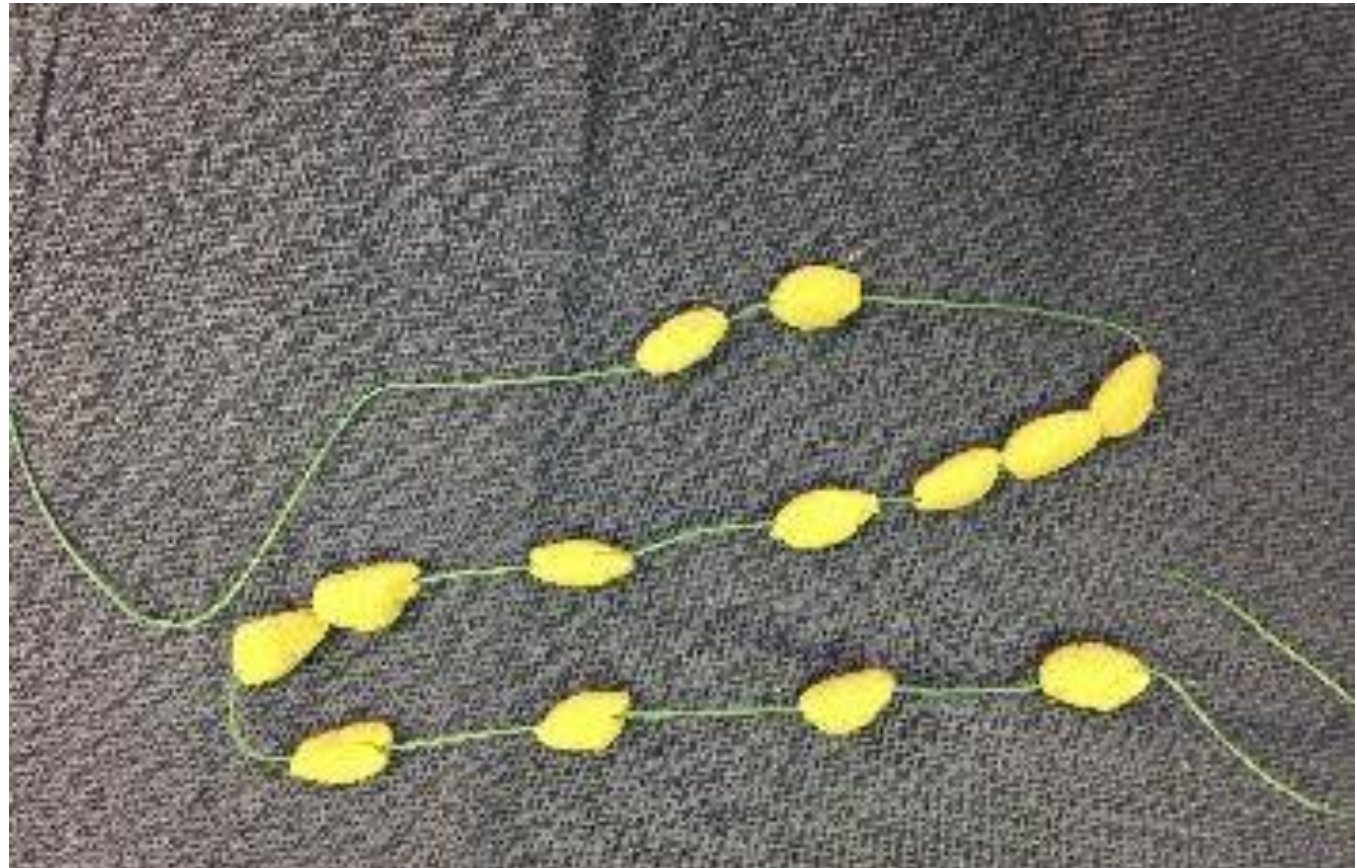
Oral versus Intravenous Antibiotics for Bone  
and Joint Infection

N ENGL J MED 380;5 NEJM.ORG JANUARY 31, 2019

- 1057 randomized to oral or IV antibiotics
  - ~10% in oral group received IV
- Heterogeneous population (extremity osteo, PJI, diskitis)
- Treatment failure in 14.6% IV vs 13.2% Oral

# Local Antibiotics + Carrier

- PMMA
- Calcium sulfate
- Hydrogels



No amount of antibiotics will overcome  
an inadequate surgical debridement



# Take-home messages

- IV antibiotics prevention
- Likely role for local antibiotics in high-risk cases
- Chronic osteo treat culture specific IV + local antibiotics with carrier
- Early transition to oral antibiotics non-inferior\* to 6 weeks IV

Thank you!

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