

Time to rethink?

Prophylactic Antibiotics for Upper GI Bleed in Patients with Cirrhosis

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Background

- Infections are the leading cause of death in cirrhosis
- GI bleeding associated with a historical infection rate of 45% - 66%
 - But this was before modern treatment (banding, TIPS, restrictive transfusion, IV PPI)
- Quinolones were the originally studied prophylaxis, replaced by ceftriaxone when resistance developed

What do the guidelines say

- From the AGA on Gastric Variceal bleed

Antibiotic prophylaxis²⁶

- Prophylactic antibiotics reduce infections, rebleeding, and mortality.
- Intravenous ceftriaxone 1 g/24 h (maximal duration 7 d).

The History

2011 Cochrane Review - 12 trials
Decreased mortality
Decreased bacterial infections
Decreased rebleeding
Decreased LOS

2015 – 2025
Increasing recognition that this
might not benefit lower Child-Pugh

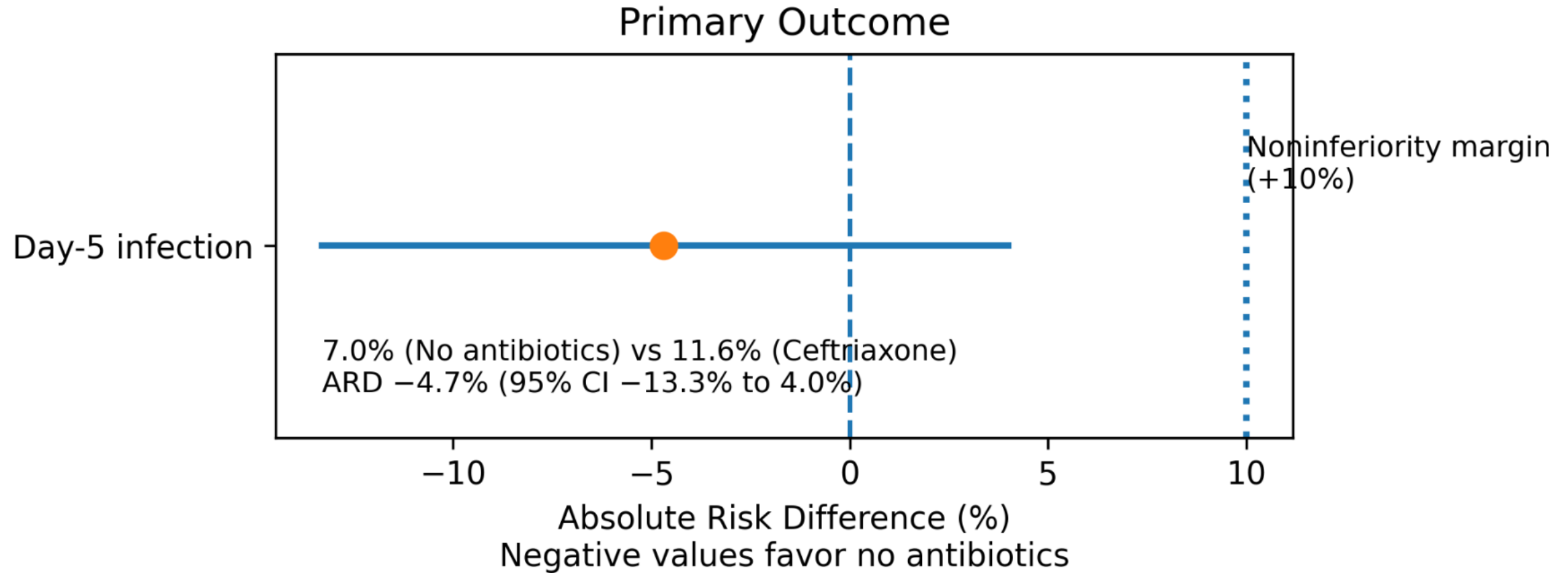
2002 Cochrane Review - 8 trials
Decreased mortality
Decreased bacterial infections
Mostly FQ

Rising FQ resistance, transition to IV
cephs

1. Soares-Weiser. 2002, Cochrane review
2. Chavez-Tapia. 2011, Cochrane review.
3. Gao, 2022, PLOS One

RCT Investigating Prophylaxis in Child-Pugh A

- Single-center, open-label, non-inferiority RCT
- 180 pts Child-Pugh A cirrhosis with UGIB, hemodynamically stable
- No prophylactic antibiotics (test) vs. ceftriaxone x 72 h
- Primary Outcome: infection at day 5
- Secondary Outcome: Failure to control bleed, mortality (d5, w6)



Systematic Review & Bayesian Meta-Analysis

- Objective: does current evidence continue to support recommended 5-7 days of antibiotics for UGIB in cirrhosis
- 14 RCTs (1322 patients), all with variceal bleeding
- Primary outcome: all-cause mortality (5% noninferiority)
- Secondary outcome: early rebleed, bacterial infections
 - Bacterial infections – heterogeneously defined

Noninferior pause

Noninferior =

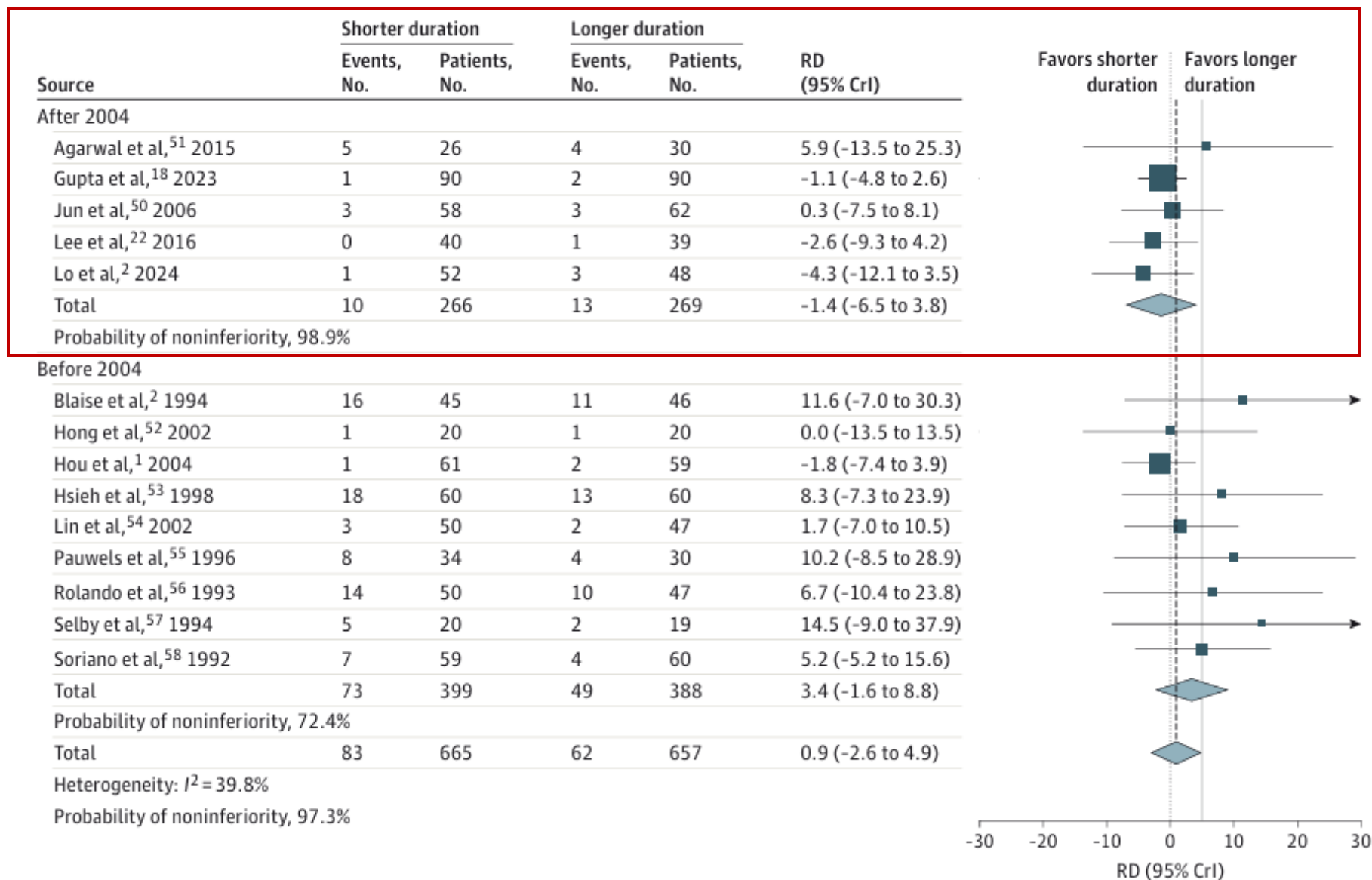
Are no/short antibiotics not worse? =

Are no/short antibiotics as good as long antibiotics

Probability of non-inferiority

- Higher % means greater chance that not/short antibiotics is not worse

Figure 2. All-Cause Mortality Among Patients With Cirrhosis and Upper Gastrointestinal Bleeding, by Studies Published Before vs After 2004



Systematic Review & Bayesian Meta-Analysis

- Secondary outcomes:
- Early rebleed: Did not meet criteria for non-inferiority
- Bacterial infection: Shorter durations were inferior for study-defined bacterial infections (27.4 vs 15.2%)

Systematic Review & Bayesian Meta-Analysis

- Stated conclusion: HIGH probability (>97%) that shorter (including no) antibiotic was noninferior to longer duration for all-cause mortality, particularly in more recent studies
- We need a large RCT
 - With modern bleeding treatments
 - And properly defined, clinically meaningful, infectious outcomes

Takeaways

- Nursing/Pharmacy:
 - We will likely continue to see this practice
 - Low Childs-Pugh class, might be worth asking why?
- “Clinicians should be aware that the current guideline recommendations are not based on high-quality evidence”
 - Prosty 2025
- We don’t need long therapy