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MEDICINE

# Antibiotic Stewardship in Preterm Infants

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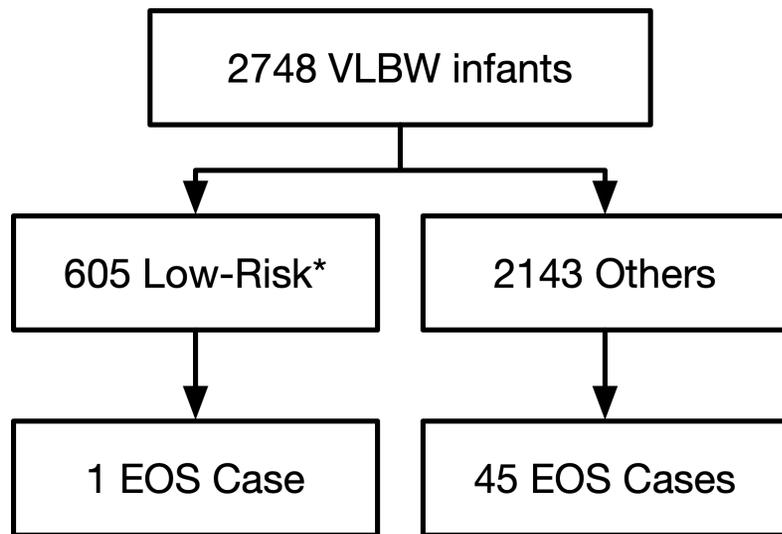


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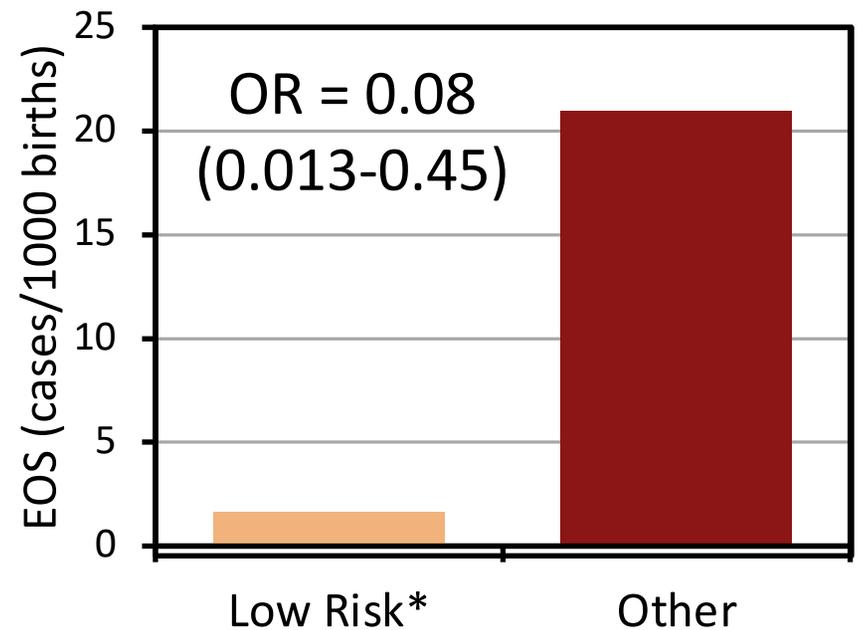
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## Antibiotic Stewardship in Preterm Infants

### Selection of Preterm Infants at Low Risk for Early Onset Sepsis Brigham and Women's Hospital 1999 - 2012

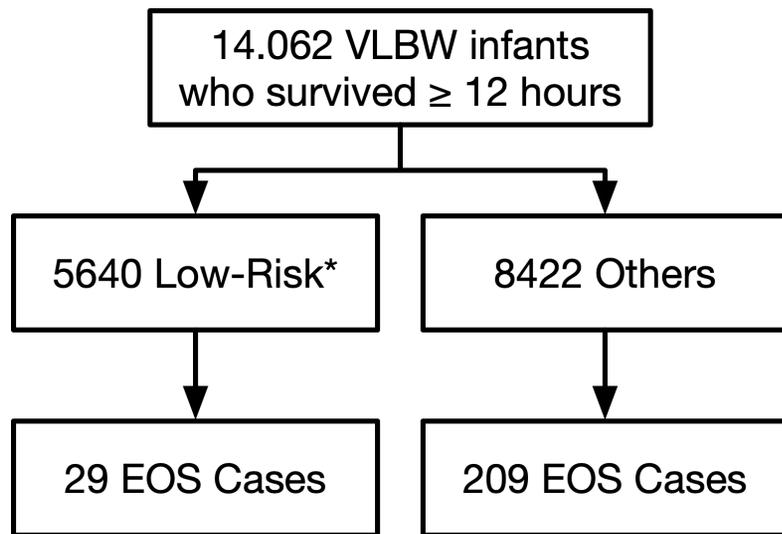


\* Born to mothers with pre-eclampsia delivered by Cesarean section, without preterm rupture of membranes or chorioamnionitis.

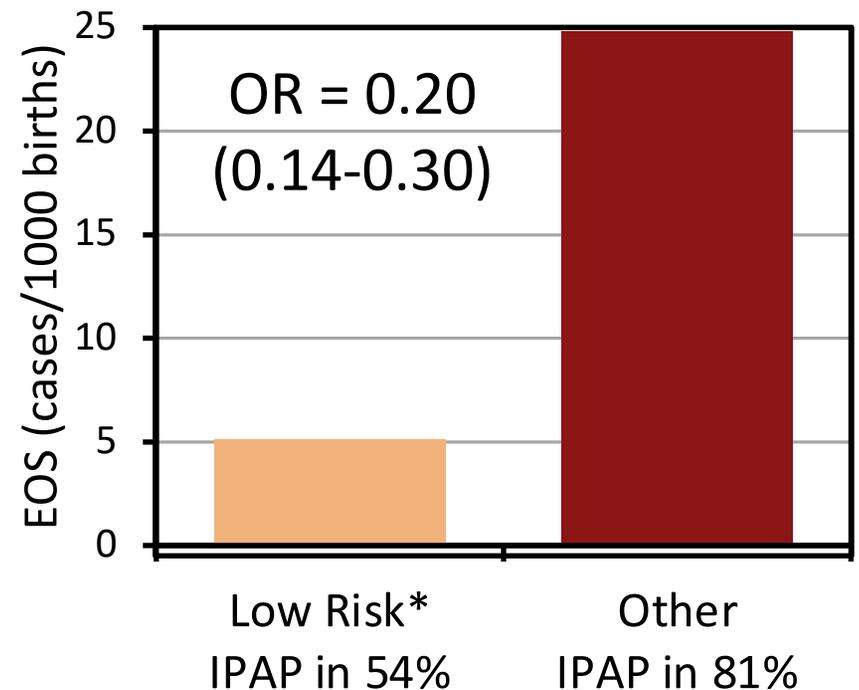


## Antibiotic Stewardship in Preterm Infants

### Selection of Preterm Infants at Low Risk for Early Onset Sepsis NICHD Neonatal Research Network 2006 - 2014



\* Born to mothers delivered by Cesarean section, rupture of membranes at delivery, and no documented chorioamnionitis.



## Antibiotic Stewardship in Preterm Infants

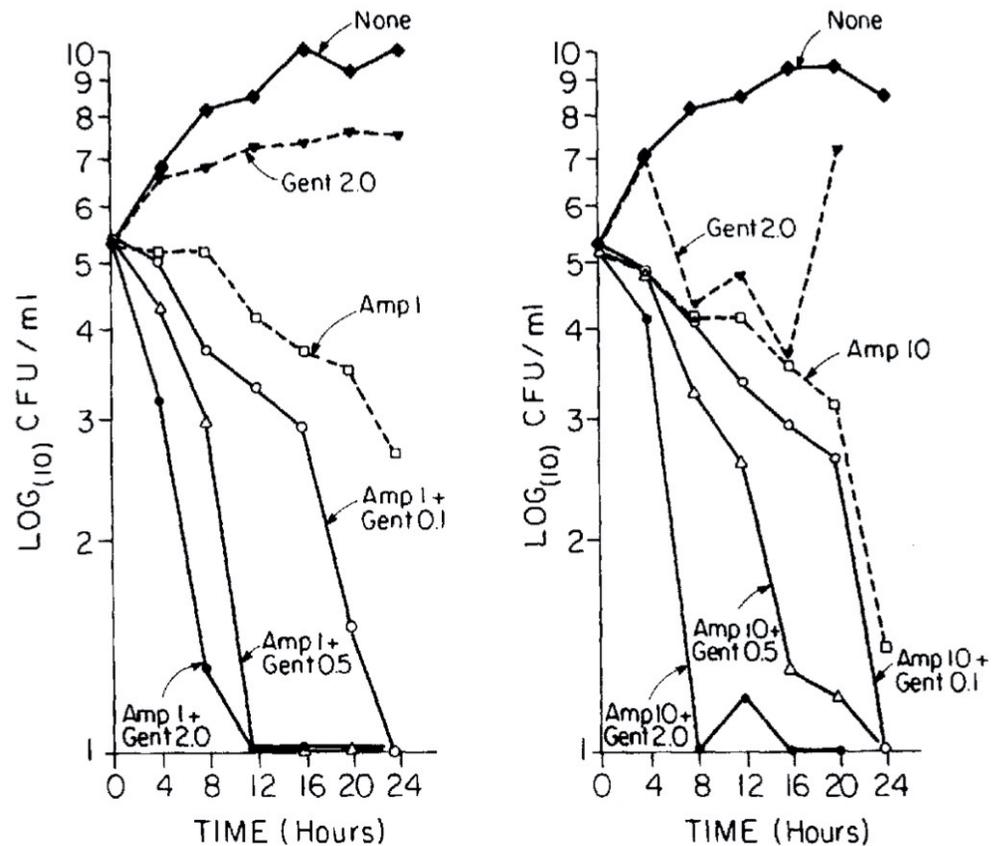
### Indications for Intrapartum Antibiotic Prophylaxis: Preterms

- Cesarean section surgical prophylaxis
  - Single dose of first generation cephalosporin with 60 minutes before delivery
- Preterm labor with intact membranes if qualified for GBS prophylaxis (GBS bacteriuria, prior affected infant, GBS colonization status unknown or positive in previous pregnancy)
  - Ampicillin every 4 hours until delivery
- Preterm prelabor rupture of membranes before 34 weeks
  - 2 days of intravenous ampicillin and erythromycin followed by a 5 days of oral amoxicillin and erythromycin

## Antibiotic Stewardship in Preterm Infants

### Ampicillin Killing Kinetics: GBS

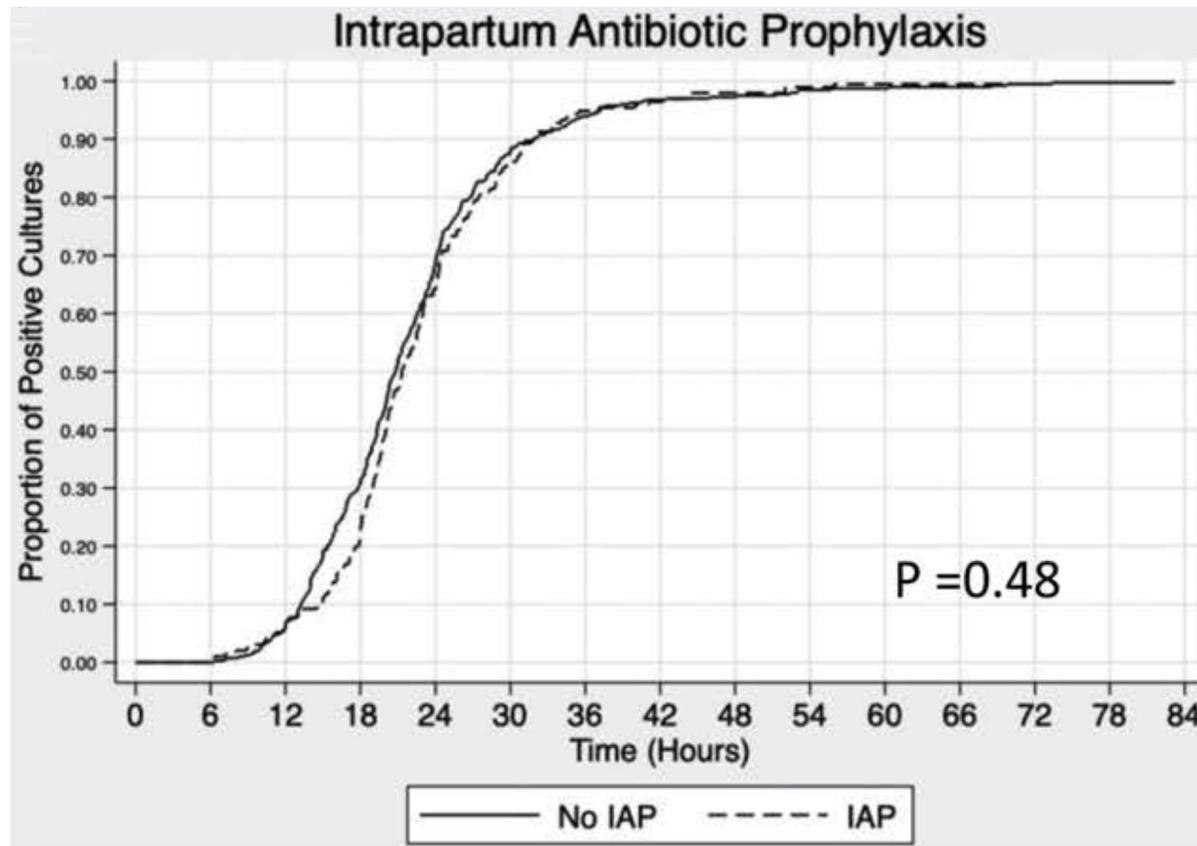
**Figure 2.** Timed killing of a strain of GBS by ampicillin at a concentration of 1.0  $\mu\text{g}/\text{ml}$  (left) and 10.0  $\mu\text{g}/\text{ml}$  (right) with various concentrations of gentamicin. The MIC of ampicillin was 0.015  $\mu\text{g}/\text{ml}$  and of gentamicin, 2.5  $\mu\text{g}/\text{ml}$ .



Swingle 1985

## Antibiotic Stewardship in Preterm Infants

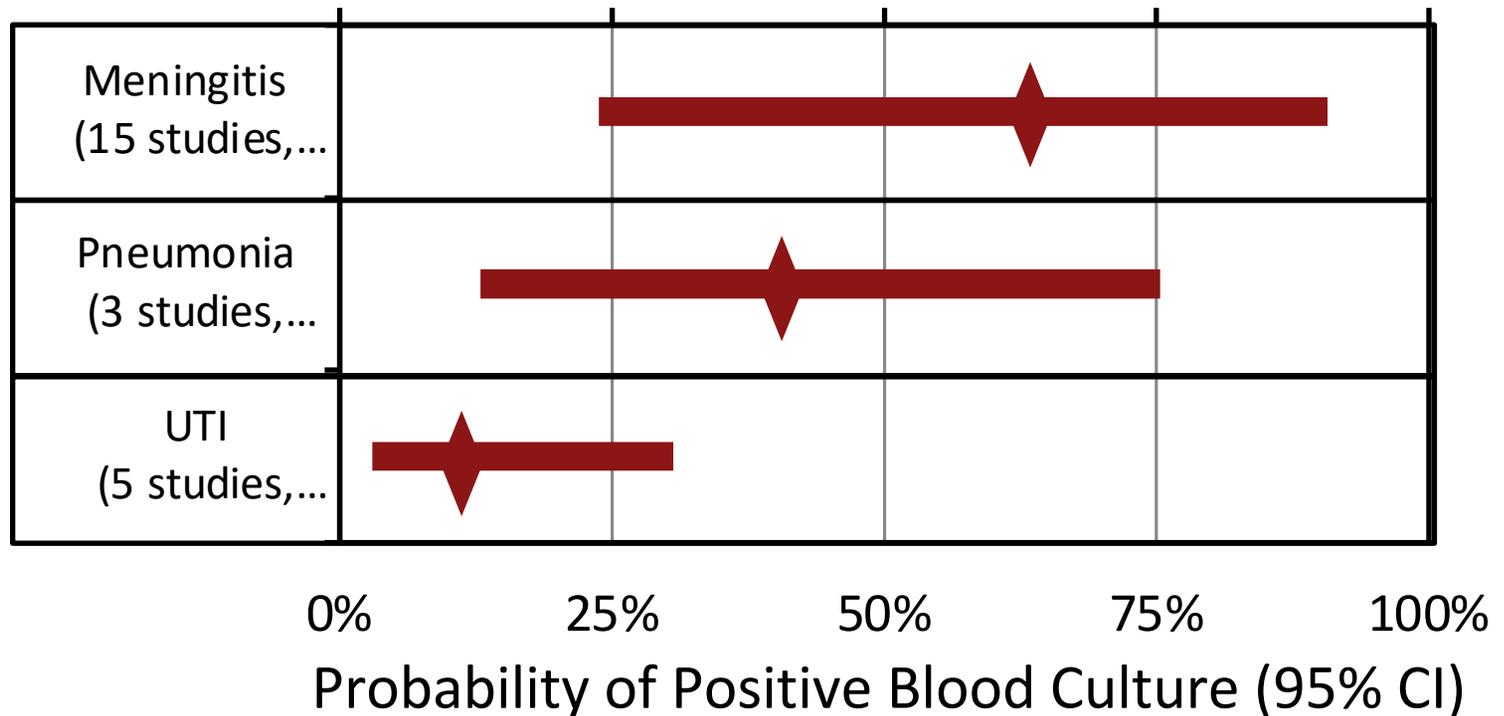
### Effects of IPAP on Blood Culture Time to Positivity



Kuzniewicz 2018

## Antibiotic Stewardship in Preterm Infants

### Serious Bacterial Infection Without Bacteremia



Visser 1980; Bell 1989; Isaacs 1989; Franco 1992; Shattuck 1992; Wiswell 1995; Ansong 2009; Aletayeb 2010; Berardi 2010; Lin 2012; Ecker 2013; Tan 2015; Ouchenir 2017; Aronson 2018; Woll 2018; Sherman 1980; Webber 1990; Booth 2009; Maherzi 1978; Visser 1979; Bachur 1995; Magin 2007; Bonadio 2014

## Antibiotic Stewardship in Preterm Infants

### Impact of Early Discontinuation of Antibiotics: SCOUT Study

- Empirical antibiotics discontinued with negative cultures at 48 hrs in 95% (850) of 895 intervention subjects
- Antibiotics were reinitiated within 14 days in only 3 subjects, all of whom received only 48 hours of treatment and had negative repeat cultures

	Baseline (n=1607)	Intervention (n=895)	p value
Number of infants $\leq$ 32 weeks' gestation	246	133	
Late-onset sepsis (95% CI)	11.4% (7.4–15.4)	7.5% (3–12)	0.23
$\geq$ Stage 2 necrotising enterocolitis (95% CI)	3.7% (1.3–6)	5.3% (1.5–9.1)	0.43
Mortality (95% CI)	6.1% (3.1–9.1)	6.8% (2.5–11.1)	0.69
Composite late-onset sepsis, necrotising enterocolitis, or mortality	17.1% (12.4–21.8)	15.8% (9.7–21.9)	0.75

**Table 2: Outcome data for study infants during baseline and intervention periods**

### The Rise of *H. influenzae* in Early Onset Neonatal Sepsis

- Recent surveys indicate the *Haemophilus influenzae* account for up to 7% of cases of culture-positive early onset sepsis in preterm infants
- The isolated strains are non-typeable, not type B, and most are susceptible to ampicillin (although spread of resistant strains is being reported, especially outside the US and Europe)