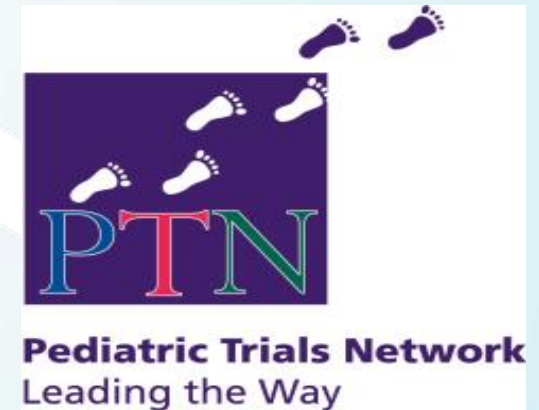


Addressing the Challenges in Neonatal Infection Studies

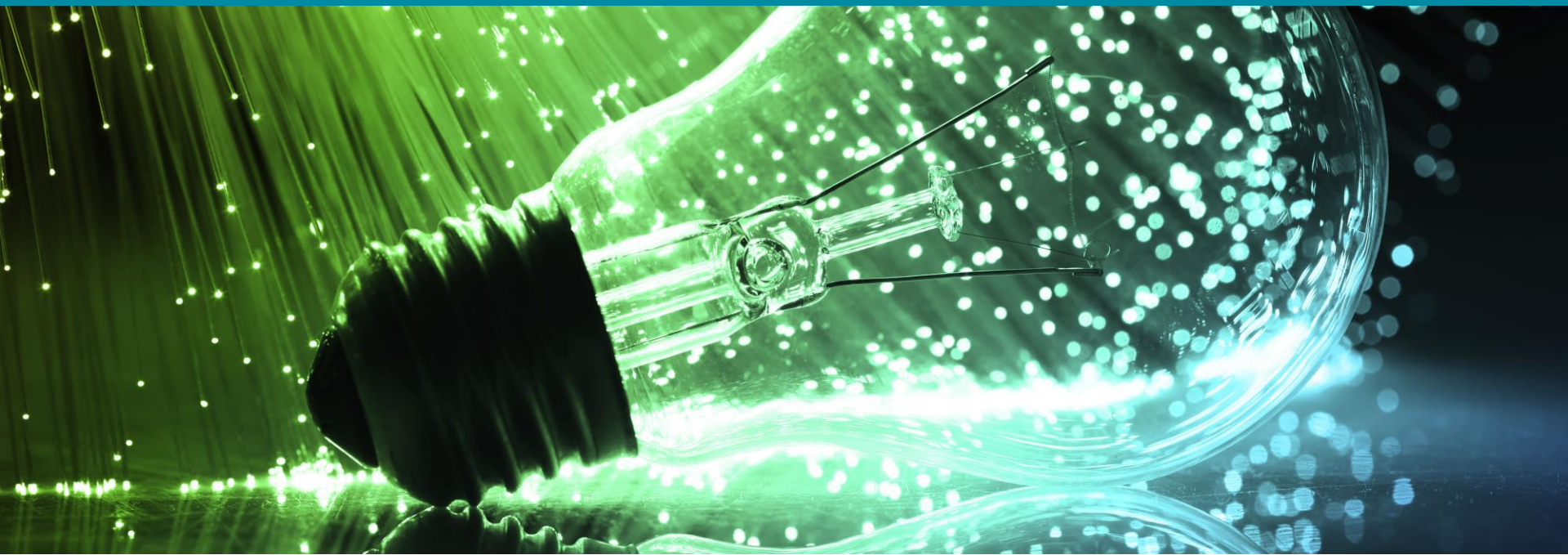
P. Brian Smith MD MPH MHS

Duke Clinical Research Institute

April 5, 2016



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Disclaimer

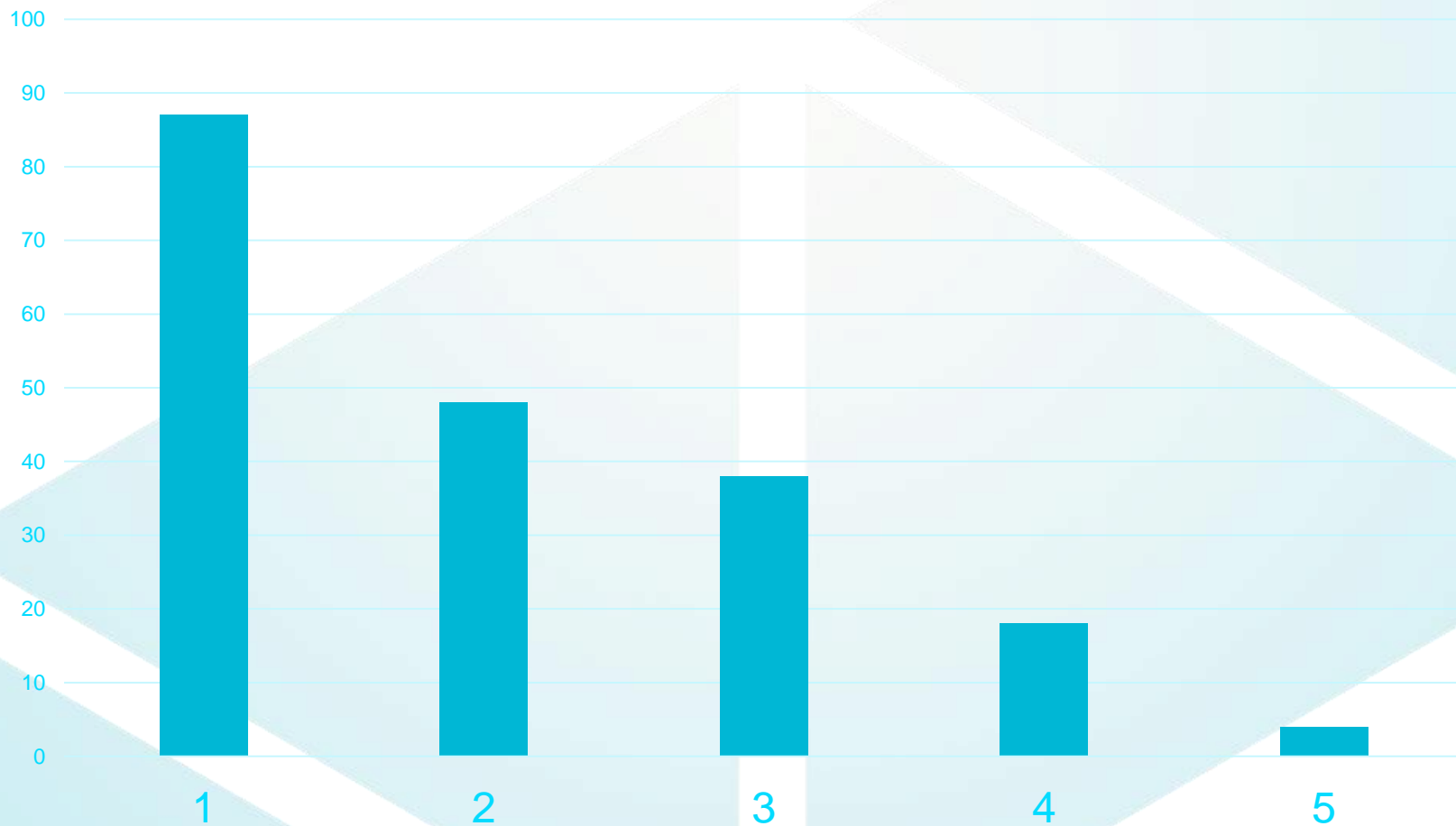
The views and opinions expressed in this presentation are those of the individual presenter and do not necessarily reflect the views of the Clinical Trials Transformation Initiative.

The presenter is an Employee of Duke University.

Why are labeling studies in infants difficult?

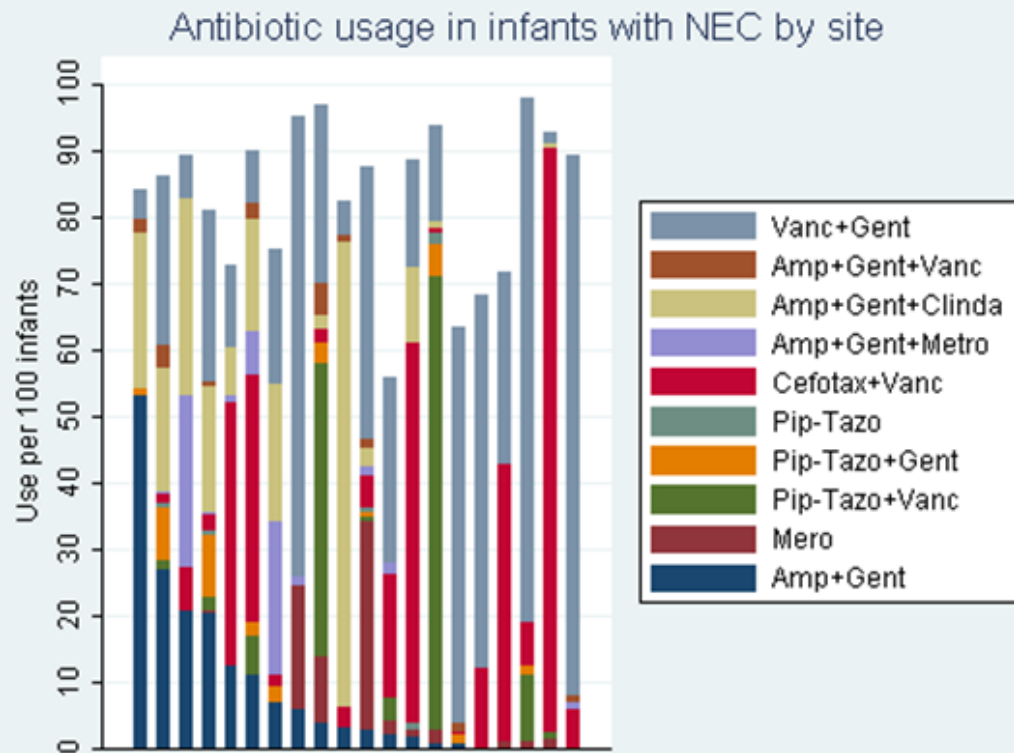
- ▶ Limited number of patients with the disease
- ▶ No “healthy baby volunteer”
- ▶ Low rates of parental informed consent
- ▶ Perceived study risks
- ▶ Limited blood volume
- ▶ Sick population – increases variability
- ▶ Lack of clinical pharmacology expertise
- ▶ Clinician beliefs about therapies and trials
- ▶ What conditions can efficacy be extrapolated (e.g. meningitis, necrotizing enterocolitis, complicated UTI, etc.)

Problem – enrollment – 200 patient study (quintiles)



Empirical Therapy for Necrotizing Enterocolitis

Antibiotic prescribing practices vary by center



Problem - # of eligible subjects

PTN - Microtrial Inclusion/Exclusion Criteria

Inclusion Criteria

1. <121 days PNA
2. Sufficient intravascular access
3. Suspected systemic infection

Exclusion Criteria

1. History of an allergic reaction
2. Urine output <0.5 mL/hr/kg over the prior 24 hours
3. Serum creatinine >1.7 mg/dl

POPS Inclusion/Exclusion Criteria

Inclusion Criteria

1. < 21 years of age and receiving drug of interest per standard of care

Exclusion Criteria

1. Known pregnancy as determined via interview or testing if available

Questions for Consideration

- ▶ *What would you recommend to improve the feasibility of conducting neonatal PK trials and obtaining CSF samples?*
 - *How could opportunistic sampling studies be improved?*
 - *What could networks do that they are not doing at present?*
 - *Could in-vitro and animal model data better inform the design of neonatal CSF PK trials?*

Questions for Consideration

- *Should neonates be enrolled at the same time as older children in PK trials or only after safety/PK is assessed in older children?*

Questions for Consideration

➤ *Should PK trials be single or multiple dose in neonates?*

Questions for Consideration

- ▶ *What would you recommend to streamline neonatal safety trials (e.g. changes in I/E criteria, data collection requirements, sample size, comparator arm, timing of endpoints, logistics)?*

Questions for Consideration

- ▶ *How long should safety follow-up be for neonatal trials (e.g. weeks, months, years)?*

Questions for Consideration

▶ *Are master protocols feasible for any indications in this population?*

Questions for Consideration

➤ *If the available data for neonates does not include CSF data, should dosing recommendations based on that data be included in the labeling? What are the pros and cons in terms of usefulness for pediatricians?*

Thank you.



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P. Brian Smith MD MPH MHS

Duke Clinical Research Institute

brian.smith@duke.edu