

# Evaluation Of The BPCA Priority List

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Why do infants need to be prioritized separately?

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## Conflict of Interest/Disclosures

- Mr. Gostelow and Drs. Tripathi, Hornik, Benjamin, Laughon, Clark have documented no financial relationships to disclose or Conflicts of Interest (COIs) to resolve
- Dr. Benjamin is a consultant for Astellas Pharma US, Cempra Pharmaceuticals, Cubist Pharmaceuticals, Johnson and Johnson Pharmaceutical Research & Development, Merck & Co., Pfizer, and The Medicines Company
- Dr. Cohen-Wolkowicz is a consultant for Cempra Pharmaceuticals, GlaxoSmithKline, Janssen Research and Development, Special Products Ltd., Tetrphase Pharmaceuticals, and The Medicines Company
- Dr. Smith is a consultant for Astellas Pharma US, GlaxoSmithKline, and Pfizer.
  - \* Complete list of disclosures can be found at the conclusion of the powerpoint



# Background

- Majority of drugs used in premature infants lack specific US FDA labeling for dosing, safety, and efficacy
  - Nearly all infants in NICU are exposed to at least one off-label drug during hospitalization
- Off-label use of drugs is associated with higher rates of adverse events and therapeutic failure.
- Trials are difficult to conduct in children
  - Ethical issues
  - Technical issues
  - Sample size
  - Funding



# Background: BPCA Legislation (2002)

- Charged NIH with developing a priority list of drugs to study in children
  - Goal: to identify drugs in need of further study and prioritize needs
  - NIH uses a panel of experts to identify drugs to be placed on the priority list based on knowledge gaps in therapeutic areas
- In 2007, the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) recognized that drug development was leaving infants behind and prioritized them separately.
- BPCA renewed in FDA Safety and Innovation Act (2012)



# Aims

1. Determine the frequency with which drugs on the 2012 BPCA priority list are used in VLBW infants
2. Determine the proportion of commonly used drugs in the NICU that are labeled for use in VLBW infants



# Dataset

- **Pediatrix Medical Group database**
  - De-identified dataset including all infants discharged from 333 NICUs
- **Dataset includes:**
  - Admission notes, daily progress notes, discharge summaries
  - Demographics, medications, laboratory results, culture results, procedures, daily growth parameters, diagnosis



# Methods

- Inclusion criteria
  - All VLBW infants <32 weeks gestation at birth from 333 NICUs managed by the Pediatrix Medical Group from 2011-12
  - Collected demographics and drug exposures
- Exclusion criteria
  - Vitamins (except vitamin A)
  - Nutritional supplements
  - Vaccines
  - Eye drops
  - Topical drugs



# Methods

- Described drug exposure
  - Number of unique individuals exposed to a drug during hospitalization
- Compared drug exposure in the NICU to the 2012 BPCA priority list
- Reviewed the drug labels of the 100 most commonly used drugs in the NICU





# Results

- N = 20,293 VLBW infants
- Total number of exposures = 161,756
- Number of drugs = 225

<b>Demographics, median (interquartile range)</b>	
Gestational age	28 weeks (26-29)
Birth weight	1020 g (776-1260)
Length of stay	55 days (35-81)
Drug exposures	6 drugs (4-11)



# Results

- 2012 BPCA priority list – 70 drugs
- 21/70 (30%) of prioritized drugs are used in >1% of premature infants



# Results

100 most commonly used drugs

- 87/100 not labeled in premature infants
- 64% of all drug exposures not labeled
- 64/100 not labeled and not prioritized
- 34% of all drug exposures not labeled and not prioritized



# BPCA progress in premature infants

- As a result of the ongoing efforts of the NICHD and the Pediatric Trials Network (PTN), data has been submitted to FDA for 5 drugs for consideration of labeling change for premature infants.
  - Meropenem – dosing, safety
  - Fluconazole – dosing, safety, efficacy
  - Acyclovir – dosing, safety
  - Ampicillin – dosing, safety
  - Metronidazole – dosing, safety
- Several drugs currently under study by NICHD and the PTN in premature infants include: sildenafil, loop diuretics, piperacillin-tazobactam, clindamycin, rifampin, ticarcillin-clavulanate



# Limitations

- Did not have access to indication for drug or drug dose – therefore the proportion of exposures that are off-label is likely higher than what we report
- Example
  - Indomethacin for prevention of intraventricular hemorrhage



# Discussion

- Majority of the most commonly used drugs in the NICU are not labeled for use in premature infants
- The NICHD decision to prioritize infants separately was critical for ongoing drug development in this population



# Questions?



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