

Pediatric Anti-bacterial and Anti-fungal Trials from 2007 to 2015: A Systematic Review of **ClinicalTrials.gov**

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April 5, 2016



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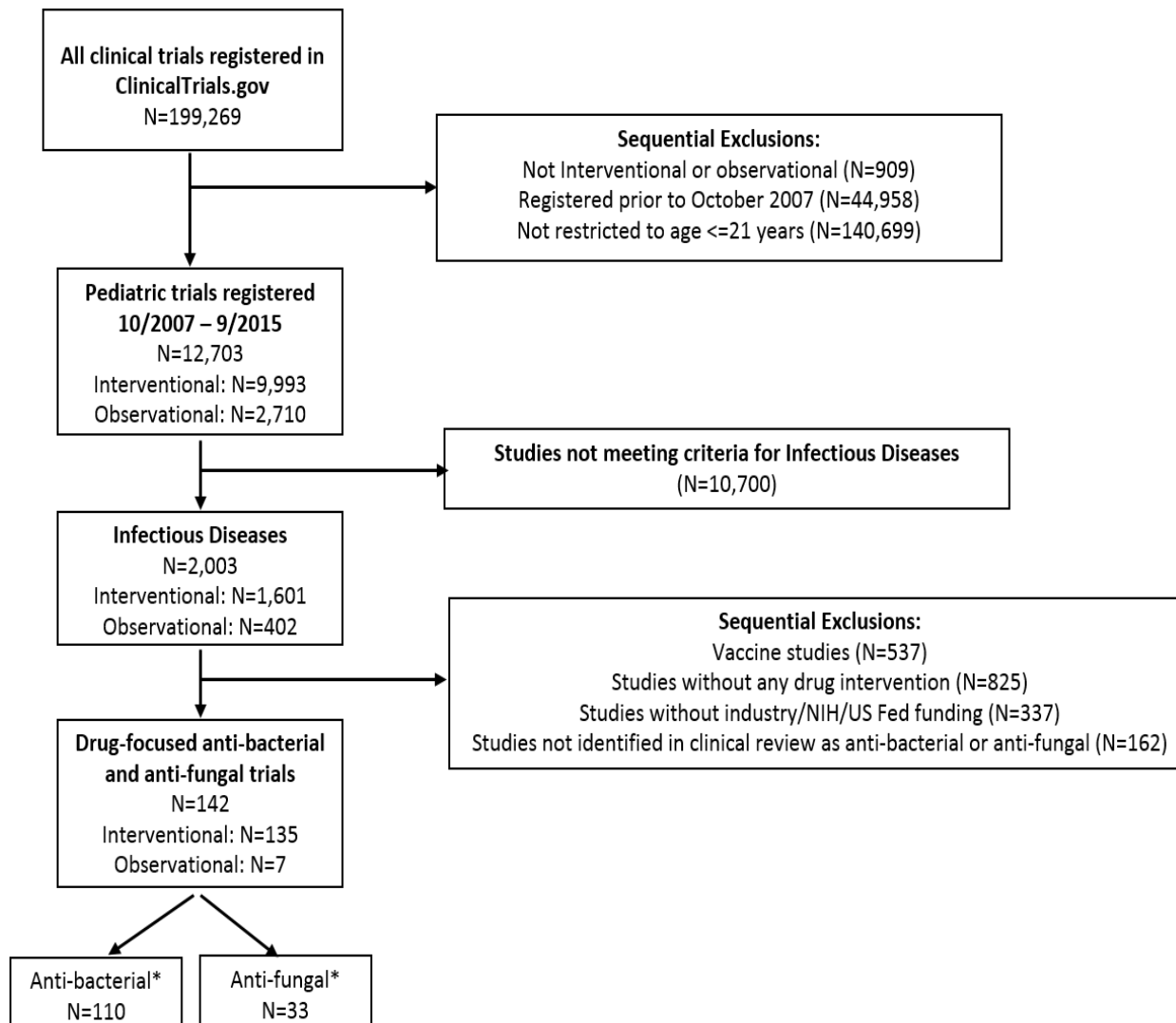
Objectives

- ▶ Characterize the current state of pediatric anti-bacterial and anti-fungal clinical trials
- ▶ Identify gaps in the clinical trials enterprise
- ▶ Inform efforts to address disparities in the evaluation and development of pediatric drugs

What is ClinicalTrials.gov?

- ▶ Registry and results database of publicly and privately supported clinical studies of human participants conducted around the world
- ▶ Interventional trials of drugs, biologics, or devices initiated after September 27, 2007 are required to register

Generating the dataset



Generating the dataset

Algorithm

- ▶ Study Type
- ▶ Registration date, Study start year
- ▶ Enrollment status, Planned or actual # of participants
- ▶ Planned or actual completion year for collection of primary endpoint
- ▶ Planned or actual study duration
- ▶ Eligibility (age ranges, healthy volunteers)
- ▶ # of sites, locations
- ▶ Regulatory / oversight authority, lead sponsor, funding source
- ▶ Intervention type
- ▶ Results reported

Manual Review

- ▶ Antibacterial or Antifungal study
- ▶ Infection type
- ▶ Scientific question addressed
- ▶ Outcome measures and data types
- ▶ Study Interventions
- ▶ Conducted under PREA or BPCA
- ▶ Results publication in a Peer-Reviewed journal

Anti-bacterial pediatric drug trials

Infection type	Number (%) studies N=110	Number (%) participants N=23,773
Otitis media	25 (23)	8179 (34)
Pneumonia	16 (15)	2353 (10)
Skin	10 (9)	3343 (14)
Intra-abdominal	9 (8)	1377 (6)
Urinary tract infection	6 (5)	3252 (14)
Sepsis	6 (5)	1073 (5)
CNS	2 (2)	52 (<1)
Bacteremia/CLABSI	1 (1)	75 (<1)
Other	40 (36)	8760 (37)

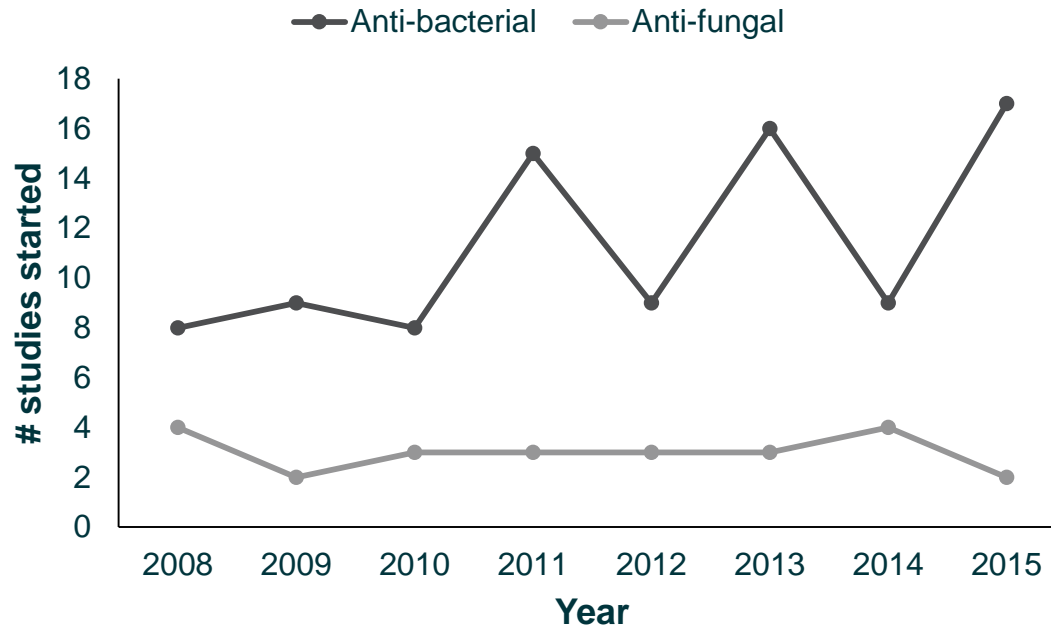
Very low numbers of CNS and bacteremia/CLABSI trials

Anti-fungal pediatric drug trials

Infection type	Number (%) studies N=33	Number (%) participants N=4877
Candidiasis	12 (36)	886 (18)
Invasive fungal infections	10 (30)	3034 (62)
Skin	4 (12)	2164 (44)
Bacteremia/CLABSI	2 (6)	45 (1)
Urinary tract infection	1 (3)	2000 (41)
Sepsis	1 (3)	145 (3)
Pneumonia	0 (0)	0 (0)
Intra-abdominal	0 (0)	0 (0)
CNS	0 (0)	0 (0)
Otitis media	0 (0)	0 (0)
Other fungal infections	8 (24)	668 (14)

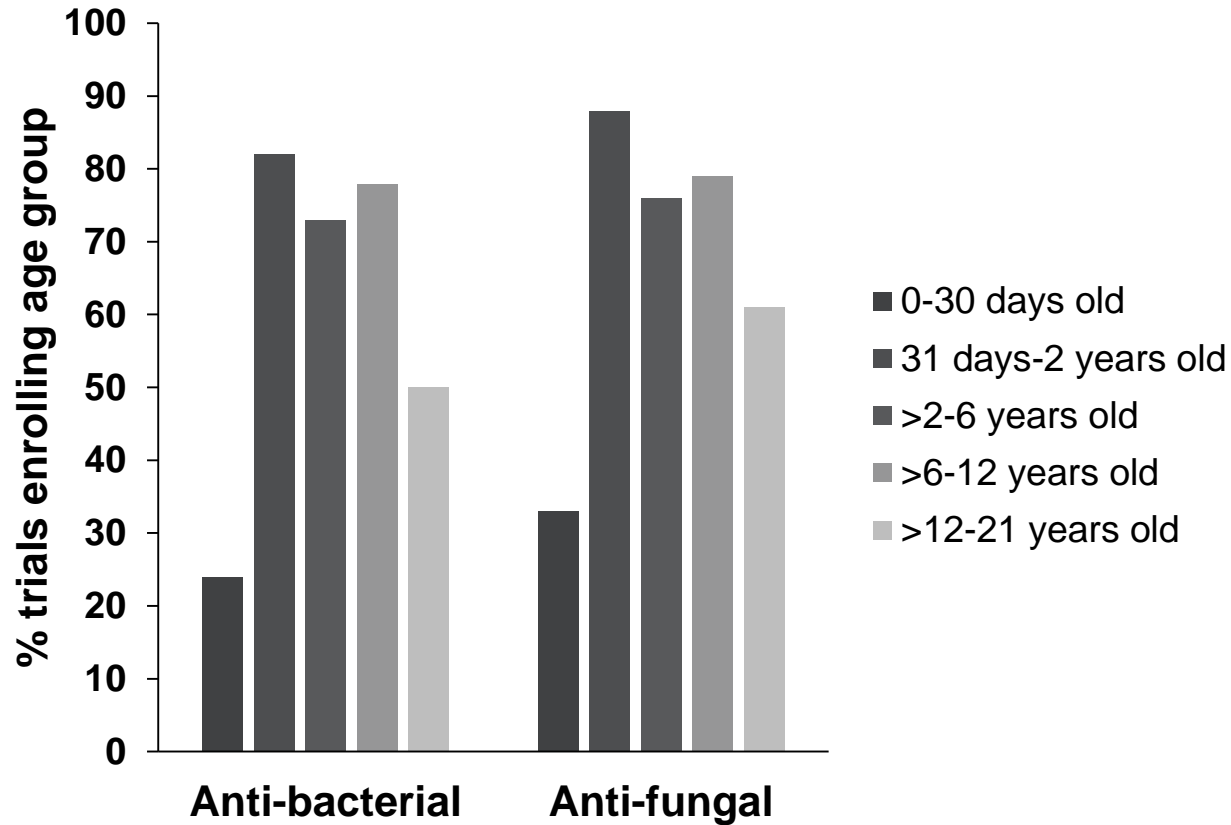
Trials involve primarily candidiasis and invasive fungal infections

Studies per year



No major increases in anti-bacterial or anti-fungal trials

Age enrollment criteria



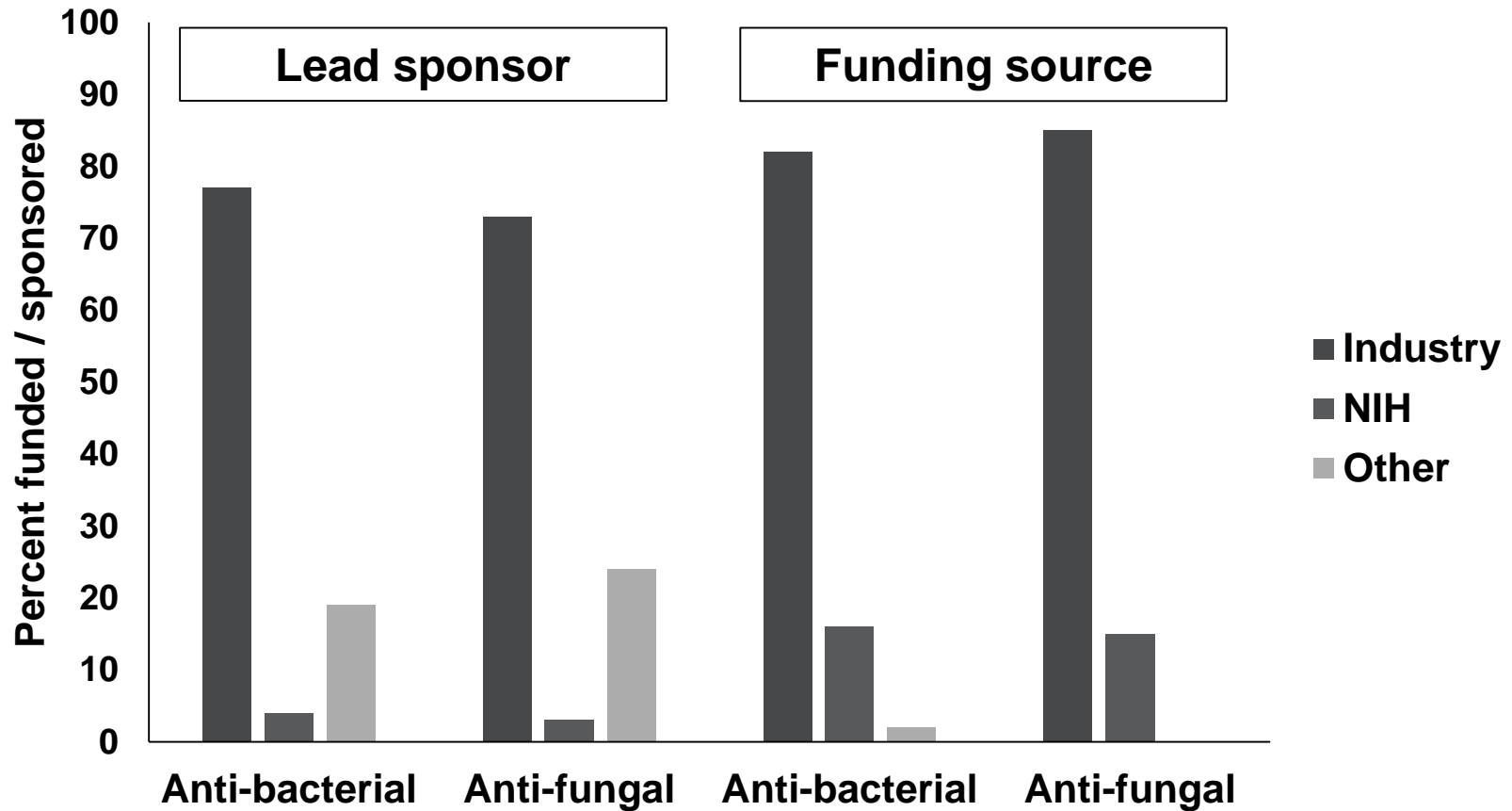
Few studies are enrolling neonates

Study size

Study characteristic	Anti-bacterial N=110 n (%)	Anti-fungal N=33 n (%)
Planned or actual number of participants		
Mean (SD)	216 (293)	148 (355)
Median (25th, 75th)	70 (35, 331)	42 (21, 90)
Min, Max	0, 2000	0, 2000
Number of sites		
Single site	25 (25%)	6 (21%)
Multiple sites	74 (75%)	23 (79%)

Anti-bacterial trials are larger than anti-fungal trials

Study sponsor and funding



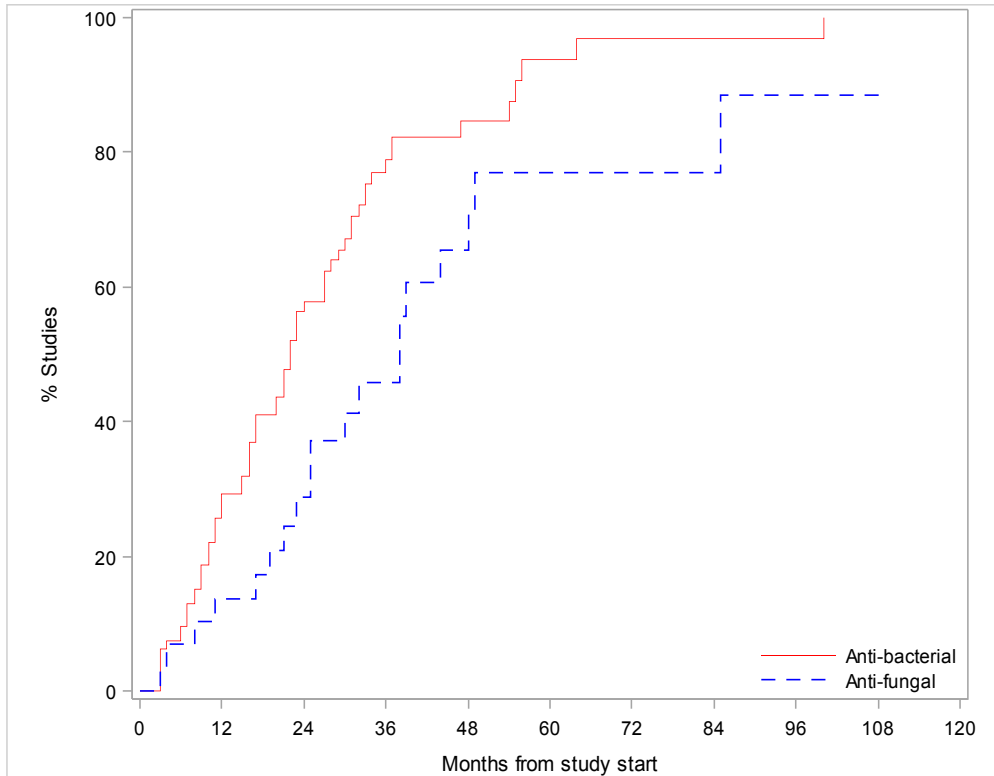
Industry is sponsoring and funding the majority of studies

Pharmacokinetics

Infection type	Anti-bacterial N=110 n (%)	Anti-fungal N=33 n (%)
PK sampling		
None	65 (59%)	15 (45%)
1-2	13 (12%)	3 (9%)
3-5	3 (3%)	1 (3%)
6-9	6 (5%)	4 (12%)
Variable	1 (1%)	1 (3%)
Number not reported	22 (20%)	9 (27%)
PK source matrix		
No PK sampling	65 (59%)	15 (45%)
CSF	5 (5%)	0 (0%)
Dried blood spot	2 (2%)	1 (3%)
Plasma	45 (41%)	18 (55%)
Serum	1 (1%)	1 (3%)
Urine	2 (2%)	1 (3%)
Stool	1 (1%)	0 (0%)

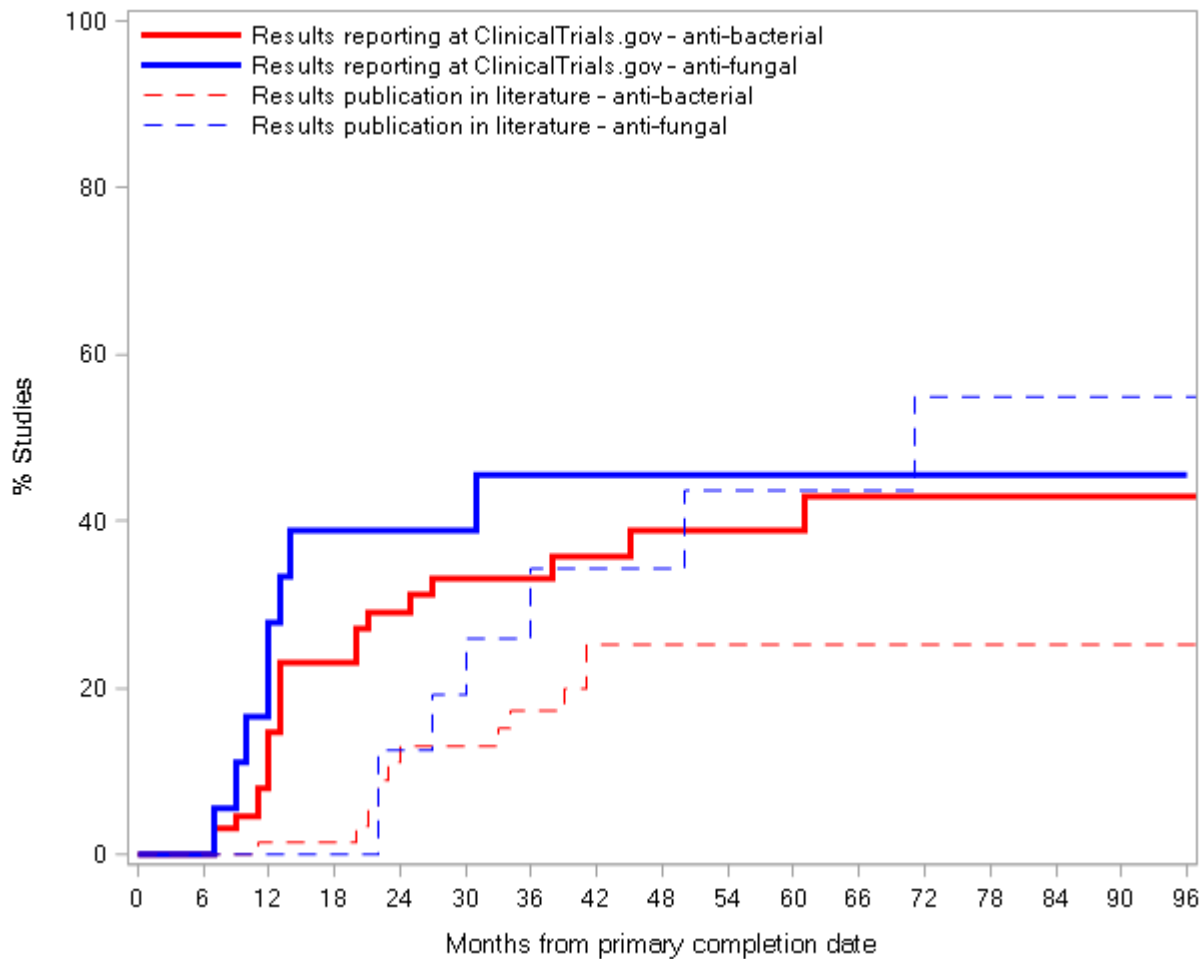
PK sampling generally involves a small number of samples from the plasma

Duration of drug trials



Anti-fungal trials take longer

Reporting results to CT.gov or through scientific literature



Low frequency of reporting trial results to ClinicalTrials.gov or through scientific publication

Big picture points

- Overall number of pediatric anti-bacterial and anti-fungal drug trials is low
- No clear upward trend in number of trials per year
- Few studies enrolling neonates
- Industry sponsored and funded the majority of trials

Next steps

- ▶ Link this data from ClinicalTrials.gov to the FDA data regarding BPCA/PREA
- ▶ Manuscript preparation

Thanks

Investigators

- Stephen Bergin
- Jamie Roberts
- Brian Smith
- Ephraim Tsalik
- William Yang

Statistics

- Karen Chiswell

Entire CTTI Pediatric ID team

Thank you.



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