

PEDIATRIC TRIALS NETWORK

Making drugs safer & more effective for use in the youngest patients

Updates from 2024 and 2025

COMBINED ANNUAL REVIEW

A MESSAGE FROM PTN LEADERSHIP

Over the past two years, the PTN continued its mission to ensure better health outcomes for children. We did this by contributing data to the U.S. Food and Drug Administration (FDA) that informed label changes, performing research in multiple studies, and connecting with partners. The goals that we met in 2024 and 2025 would not have been possible without the support of PTN study participants, families, researchers, and partners.

In 2024 and 2025, we contributed data leading to seven FDA medication label changes. The changes we made to medication labels provided health care professionals with the necessary information to prescribe the safest, most effective dosages of medicines to children. These label changes bring the total number of label changes informed by PTN research to 26.

In our ongoing studies, we met several important milestones in 2024 and 2025. The Pharmacokinetics and Safety of Antiretroviral and Related Drugs in Lactating Women and Breastmilk Fed Infants (BMS02) study began in 2024, closed enrollment in 2025, and is now in the analysis phase. The Sildenafil in Premature Infants study also closed enrollment in 2025 and we are now analyzing the data for submission to FDA and publication. Additionally, the PTN submitted eight clinical study reports (CSRs) for FDA review during this period.

The PTN presented at the International Children's Advisory Network (iCAN) Annual Summits in 2024 and 2025, the Pediatric Academic Societies Meeting in 2024, and the Maternal and Pediatric Precision in Therapeutics (MPRINT) Hub meeting in 2024. PTN and iCAN collaborated on Results-at-a-Glance video summaries and a digital anthology of art by pediatric advocates. In 2024 and 2025, the PTN released two dozen new publications and nine new Results-at-a-Glance summaries.

Please read on for more details and thank you for your continued commitment to advancing the important work of PTN.

Sincerely,



Danny Benjamin, MD, PhD, MPH
Pediatric Trials Network,
Principal Investigator



Rachel Greenberg, MD, MB, MHS
Pediatric Trials Network,
Multiple Principal Investigator

IN 2024 AND 2025, THE PTN...

...CHANGED LABELS

Topiramate label change

Topiramate is a common anti-seizure medication. The PTN used data from the Pharmacokinetics of Understudied Drugs Administered to Children per Standard of Care (POP01) and Pharmacokinetics of Anti-epileptic Drugs in Obese Children (AED) studies to investigate how children with and without obesity under 21 years old processed topiramate. The study showed that adjusting the dose based on obesity status was not necessary. This was the 26th label change informed by PTN research.

Ondansetron label change

Ondansetron is a drug used to treat nausea and vomiting. The PTN study called Commonly Used Drugs During Lactation and Infant Exposure (CUDDLE) sought to learn how much ondansetron breastfeeding infants are exposed to through breastmilk. The study confirmed that ondansetron passes into breast milk, but at low levels. There were no adverse effects observed in infants exposed to ondansetron. This was the 25th label change informed by PTN research.

Metronidazole label change

Metronidazole is an antibiotic that is often used when treating infants with complicated intra-abdominal infections (cIAIs). The PTN study Antibiotic Safety in Infants with Complicated Intra-Abdominal Infections (SCAMP) evaluated how metronidazole affects infants and the safest, most effective dosage of metronidazole for treating infants with cIAIs. The study determined that antibiotic treatment including metronidazole was safe in this group of infants. This was the 24th label change informed by PTN research.

Furosemide label change

Furosemide is a drug that is often used to treat and prevent bronchopulmonary dysplasia, a lung disease that affects infants born prematurely. The PTN study called Safety of Furosemide in Premature Infants at Risk of Bronchopulmonary Dysplasia evaluated the safety and ideal dosage of furosemide for infants. The label for furosemide now includes information to help clinicians determine the best dose for premature infants. This was the 23rd label change informed by PTN research.

Oxcarbazepine label change

Oxcarbazepine is an anti-seizure medication that is commonly prescribed to children. The PTN study Pharmacokinetics of Anti-epileptic Drugs in Obese Children (AED) evaluated the way that a child's obesity status may affect what dosage of oxcarbazepine they need. The updated oxcarbazepine label includes guidance for dosing the medicine for children who are obese; the label change applies to the medicine in both the form of a tablet and oral suspension. This was the 22nd label change informed by PTN research.

Oxycodone label change

Oxycodone is a medication used for pain management. The PTN study called Commonly Used Drugs During Lactation and Infant Exposure (CUDDLE) looked at how oxycodone transferred to infants through breastmilk. The study reported no adverse events attributed to oxycodone, indicating it is safe for mothers to take it while breastfeeding. The FDA updated the oxycodone label with this information. This was the 21st label change informed by PTN research.

Fluconazole label change

Fluconazole is an anti-fungal medication used to treat *Candida* (yeast) infections in neonatal and pediatric intensive care units. PTN's analysis of several completed studies, listed below, evaluated the pharmacokinetics, dosing, safety, and efficacy of fluconazole for treating *Candida* infections in premature infants. The fluconazole label now includes this information.

The studies that contributed to this label change are:

1. Fluconazole Prophylaxis for the Prevention of Candidiasis in Infants < 750 Grams Birth Weight
2. Pharmacokinetics of a Fluconazole Loading Dose in Infants and Toddlers
3. Safety and Pharmacokinetics of Fluconazole in Children Supported by Extracorporeal Membrane Oxygenation (ECMO)
4. A Multicenter, Open Label Pharmacokinetics Study of Fluconazole in Infants

This was the 20th label change informed by PTN research.

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...CHANGED LABELS (continued from page 2)

PTN label changes to date

Under the Best Pharmaceuticals for Children Act (BPCA), the PTN provides the FDA with research and data to inform updates to medication labels so that health care providers can prescribe the most effective doses of medications to children. The research performed through the BPCA program and led by the PTN has resulted in label changes for the following drugs and devices:

- Acyclovir
- Ampicillin
- Caffeine
- Clindamycin (2)
- Diazepam
- Doxycycline
- Fluconazole
- Furosemide
- Levetiracetam
- Lisinopril
- Lithium
- Lorazepam
- Mercy babyTAPE
- 2D and 3D Mercy TAPE
- Meropenem
- Metronidazole
- Ondansetron
- Oxcarbazepine
- Oxycodone
- Propylthiouracil
- Pralidoxime
- Rifampin
- Sodium nitroprusside
- Topiramate
- Trimethoprim-Sulfamethoxazole (TMP-SMX)

...PERFORMED RESEARCH

BMS02 study update

The PTN began the Pharmacokinetics and Safety of Antiretroviral and Related Drugs in Lactating Women and Breastmilk Fed Infants (BMS02) study in January 2024. It closed to enrollment in 2025 and is now in analysis. This study is testing how several medicines used to treat HIV/AIDS might transfer from mother to baby through breastmilk. A better understanding of the safety of common antiretroviral medications in breastfeeding infants will provide data to help clinical professionals everywhere advise breastfeeding mothers who live with HIV/AIDs.

Sildenafil II study update

This study aimed to describe the safety of sildenafil in premature infants at risk of bronchopulmonary dysplasia (BPD) and determine preliminary effectiveness and pharmacokinetics of sildenafil. Sildenafil II closed to enrollment in 2025 and is now in analysis.

TBS02 study update

The PTN paused the study A Prospective, Blinded, Cross-Over Trial of the Exposure-Response Relationship of Terbutaline Sulfate in Adults with Asthma (TBS02) in 2025.

HYP01 study update

The PTN study Guanfacine for Hyperactivity in Children with Down Syndrome (HYP01) began enrollment in 2024 and concluded in 2025. This study investigated the pharmacokinetics and safety of guanfacine for treating hyperactivity or Attention Deficit Hyperactivity Disorder (ADHD) in children with Down Syndrome.

Ongoing PTN studies (2024 and 2025)

Anesthetics and Analgesics in Children (ANA01).

Commonly Used Drugs During Lactation and Infant Exposure (CUDDLE).

Guanfacine for Hyperactivity in Children With Down Syndrome (HYP01).

Pharmacokinetics, Pharmacodynamics, and Safety Profile of Understudied Drugs Administered to Children per Standard of Care (POP02).

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...PERFORMED RESEARCH (continued from page 3)

Clinical study reports

The PTN has eight CSRs that are with the FDA for review.

- Nifedipine (breast milk)
- Valproic acid
- Timolol
- Digoxin
- Piperacillin-tazobactam
- Metformin Extended Release
- Hydromorphone
- Clindamycin

...CONNECTED WITH PARTNERS

Duke's STAR Program

The Summer Training in Academic Research (STAR) Program provides a high-quality research experience for high school, undergraduate, and medical students during the summer academic break.

The in-person program, held at the Duke Clinical Research Institute in Durham, NC, lasts five weeks and gives participants interested in science and medicine hands-on experience in research methodology and writing. The program places participants in teams and matches them with Duke faculty mentors to work on an original project, originating as a one-page summary and culminating in a complete research paper. A goal of the program is to have every participant qualify for co-authorship on a peer-reviewed manuscript related to their team's project.

In 2024 and 2025, the STAR program partnered with Montana State University (MSU) and U Washington-WWAMI (Washington, Wyoming, Alaska, Montana and Idaho).

In 2024, the program expanded to include a five-week program specifically designed for medical students. After receiving more than 1,000 applications, the program included 22 participants: three high school teachers, three medical students, six college students, and 10 high school students.

In 2025, the program received 1,200 applications and accepted 25 participants: 7 medical students, 11 college students, and 7 high school students.

PTN at Annual iCAN Summits

In July 2025, PTN members presented at the International Children's Advocacy (iCAN) 2025 Summit. Members also attended the iCAN Ask the Experts Webinar in August 2025. In July 2024, members of the PTN attended the 10th Annual iCAN Summit. Program Manager Cheryl Alderman, Program Manager Zoe Sund, and Associate Director of PTN and iCAN Board Member Phyllis Kennel, presented on the ways iCAN and the PTN collaborate. Over the course of the Summit, the PTN team distributed 90 hardcopies of the iCAN and DCRI Anthology.

MPRINT Hub Annual Meeting

In May 2024, PTN researcher Liz Thompson attended the virtual Maternal and Pediatric Precision in Therapeutics (MPRINT) Hub annual conference. The conference focused on how emerging discoveries in maternal and pediatric pharmacology can translate into real-world clinical care. Dr. Thompson presented "Human Milk Transfer and Infant Exposure to Sertraline."

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...CONNECTED WITH PARTNERS (continued from page 4)

PTN and MPRINT investigators present at PAS

At the 2024 Pediatric Academic Societies (PAS) Annual Meeting, in Toronto, Canada, the PTN and the Maternal and Pediatric Precision in Therapeutics (MPRINT) Hub hosted an ancillary session and lunch. The session, titled "Mom/Baby Shark Tank: Pediatrics and Maternal Therapeutics Edition," featured two investigators pitching their ideas for solutions to issues in maternal and pediatric care to a panel of "sharks." The Shark Tank panel included three researchers, as well as a pediatric patient advocate from iCAN.

PTN and iCAN Anthology

The PTN partnered with iCAN to produce an anthology that highlights iCAN members' perspectives on the pediatric clinical research process.
View the digital version.

Duke-North Carolina Central University (NCCU) Bridge Office Internship

Over summer 2024, the PTN supported an intern through the Duke-NCCU Bridge Office. This program gives university students the opportunity for hands-on clinical research experience. The PTN worked with Zhani Swailes, a student pursuing her master's degree in public health at the University of North Carolina at Chapel Hill. At the conclusion of her internship in early August, Swailes presented the work she did and what she took away from it.

PTN and iCAN create videos

The PTN and iCAN teamed up to create video versions of PTN's Results-at-a-Glance Summaries. Each video features an iCAN youth advocate describing the purpose, process, and outcomes of a PTN study. The team created ten video summaries in 2024-2025.

...SHARED SCIENCE

PTN methods for analyzing drug concentration

Many PTN studies measure the concentration of medicines in children's bodies. The PTN collaborates with several laboratories to develop and validate methods for analyzing biological samples. The PTN is now sharing these methods with the research community. The PTN Methods webpage contains a list of drugs studied by the PTN along with the type of sample (plasma, dried blood spot, urine, cerebrospinal fluid, and breastmilk) used to evaluate drug concentration. There are over 200 methods available for 90 drugs.

Results-at-a-Glance

The PTN shares what it's learning with research participants and the public through Results-at-a-Glance summaries. These summaries describe the key information, including results, of PTN studies and publications in a format that is quick and easy to read. The PTN continues to develop Results-at-a-Glance summaries for publications to share the knowledge generated from the PTN, especially with study participants who make it possible. In 2024 and 2025, the PTN created nine summaries. Read them and all the PTN's Results-at-a-Glance summaries.

Published research in 2024 and 2025

Metronidazole exposure-response and safety in infants. Randell RL et. al. *Antimicrobial Agents and Chemotherapy*, 2025 Nov 5;69(11):e0037725.

Physiologically Based Pharmacokinetic Modeling of Oxcarbazepine to Characterize Its Disposition in Children with Obesity. Maglalang PD et. al. *Journal of Clinical Pharmacology*. 2025 Sept;66(2):e70107.

Physiologically Based and Population Pharmacokinetic Modeling of Midazolam in Children With Obesity Using Real-World Data. McCann SM et. al. *Clinical and Translational Science*. 2025 May;18(5):e70247.

Expansion of a Pharmacokinetic Model for Diazepam to Characterize Real-World IV and Oral Data in Children with and Without Obesity. McCann SM et al. *Journal of Clinical Pharmacology*. 2025 Sep;65(9): 1135-1149.

Furosemide Safety in Preterm Infants at Risk for Bronchopulmonary Dysplasia: A Randomized Clinical Trial. Greenberg RG et al. *Journal of Pediatrics*. 2025 Aug;283:114629.

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...SHARED SCIENCE (continued from page 5)

Sponsor- vs. FDA-Initiated Changes to Pediatric Clinical Trial Protocols: A Comparison of Associated Participant Burden. Abdel-Rahman S et. al. *Therapeutic Innovation & Regulatory Science*. 2025 May;59(3):558-565.

Population Pharmacokinetics of Meropenem Across the Adult Lifespan. Boutzoukas AE et. al. *Clinical Pharmacokinetics*. 2025 Feb;64(2):229-241.

Medical treatment of gastroesophageal reflux in the neonatal intensive care unit: current practice. Lockyear C et. al. *Journal of Perinatology*. 2025 May;45(5):616-621.

Predictors of Potentially Inappropriate Stimulant Prescribing Among Adults. Thakkar PV et. al. *Pharmacoepidemiology and Drug Safety*. 2025 Jan;34(1):e70079.

Pharmacoepidemiology of combination pulmonary vasodilator therapy in critically ill infants. Kumar KR et. al. *Cardiology in the Young*. 2025 Jan;35(1):93-101.

Trends in Gabapentin Use in Neonatal Intensive Care Units from 2005 to 2020. Roberts AG et. al. *American Journal of Perinatology*. 2025 Jun;42(8):1017-1023.

Pharmacokinetics of Dexamethasone in Children and Adolescents with Obesity. Wen J et. al. *Journal of Clinical Pharmacology*. 2024 Dec;64(12):1491-1504.

Physiologically-based pharmacokinetic modeling of pantoprazole to evaluate the role of CYP2C19 genetic variation and obesity in the pediatric population. Thompson EJ et. al. CPT: Pharmacometrics & Systems Pharmacology. 2024 Aug;13(8):1394-1408.

Using Real-World Data to Externally Evaluate Population Pharmacokinetic Models of Dexmedetomidine in Children and Infants. McCann SM et. al. *Journal of Clinical Pharmacology*. 2024 Aug;64(8):963-974.

Epidemiology and outcomes of bacterial meningitis in the neonatal intensive care unit. Aleem S et. al. *Journal of Perinatology*. 2024 Dec;44(12):1822-1826.

Acyclovir Dosing Practices Across a Multicenter Cohort of Neonatal Intensive Care Units. Foote HP et. al. *The Pediatric Infectious Disease Journal*. 2024 Dec;43(12):1156-1161.

Postdiscontinuation Antibiotic Exposure in Hospitalized Infants at Risk for Late-onset Sepsis in the Neonatal intensive care unit. Wade KC et. al. *The Pediatric Infectious Disease Journal*. 2024 Oct;43(10):991-996.

Application of Physiologically Based Pharmacokinetic Modeling to Characterize the Effects of Age and Obesity on the Disposition of Levetiracetam in the Pediatric Population. Maglalang PD et. al. *Clinical Pharmacokinetics*. 2024 Jun;63(6):885-899.

Urinary Tract Infection Epidemiology in NICUs in the United States. Kilpatrick R et. al. *American Journal of Perinatology*. 2024 May;41(S 01):e2202-e2208.

Opportunistic dried blood spot sampling validates and optimizes a pediatric population pharmacokinetic model of metronidazole. Randell RL et. al. *Antimicrobial Agents and Chemotherapy*. 2024 Apr;68(4):e0153323.

Risk factors and epidemiology of spontaneous intestinal perforation among infants born at 22-24 weeks' gestational age. Thakkar PV et. al. *Journal of Perinatology*. 2024 Jan;44(1):94-99.

View a full list of publications from the PTN.