Maternal and Pediatric Precision in Therapeutics Knowledge Portal (MPRINT-KP)

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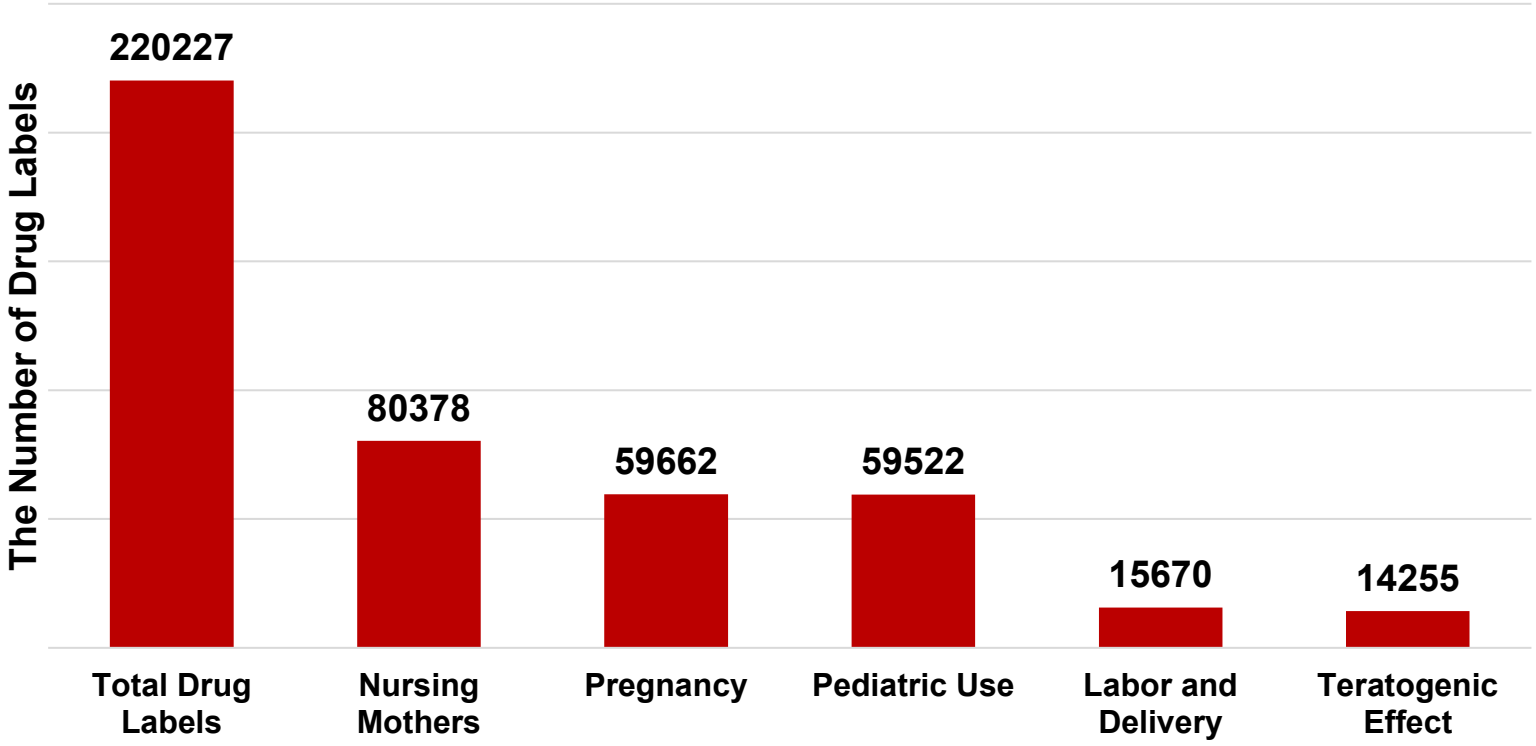
September 15, 2025

mprint

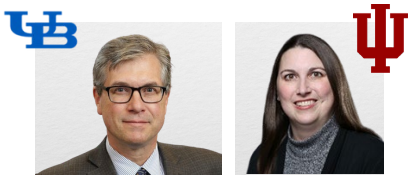
The Ohio State University
Wexner Medical Center

Knowledge gap of drug labels in maternal and pediatric patient populations (https://dailymed.nlm.nih.gov/dailymed/)



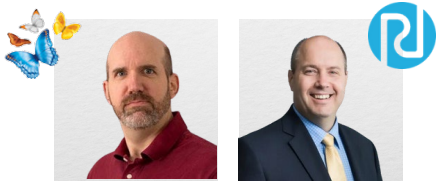
Maternal and Pediatric Precision in Therapeutics (MPRINT)

Data, Modeling, Knowledge, & Research Coordinating Center

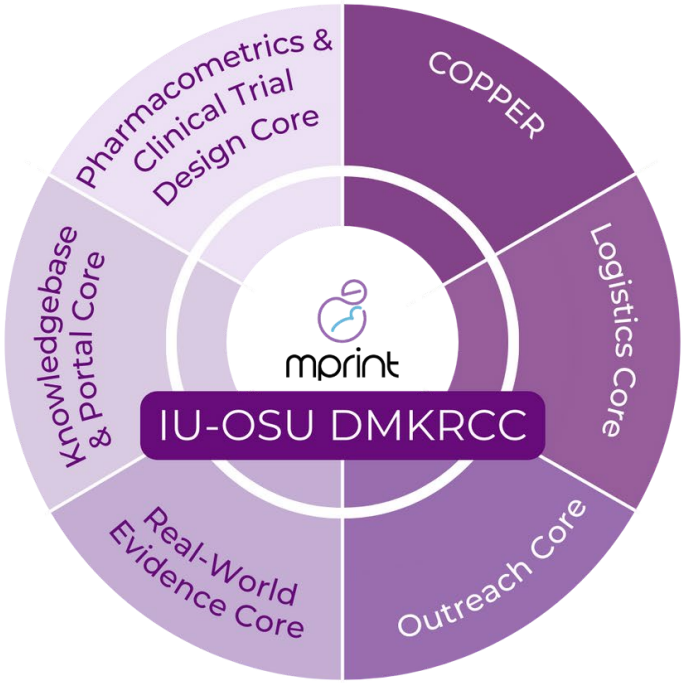


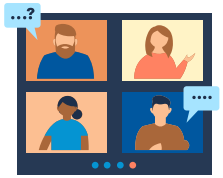
Pharmacometrics &
Clinical Trial Design Core

Knowledgebase &
Portal Core



Real-World Evidence
Core



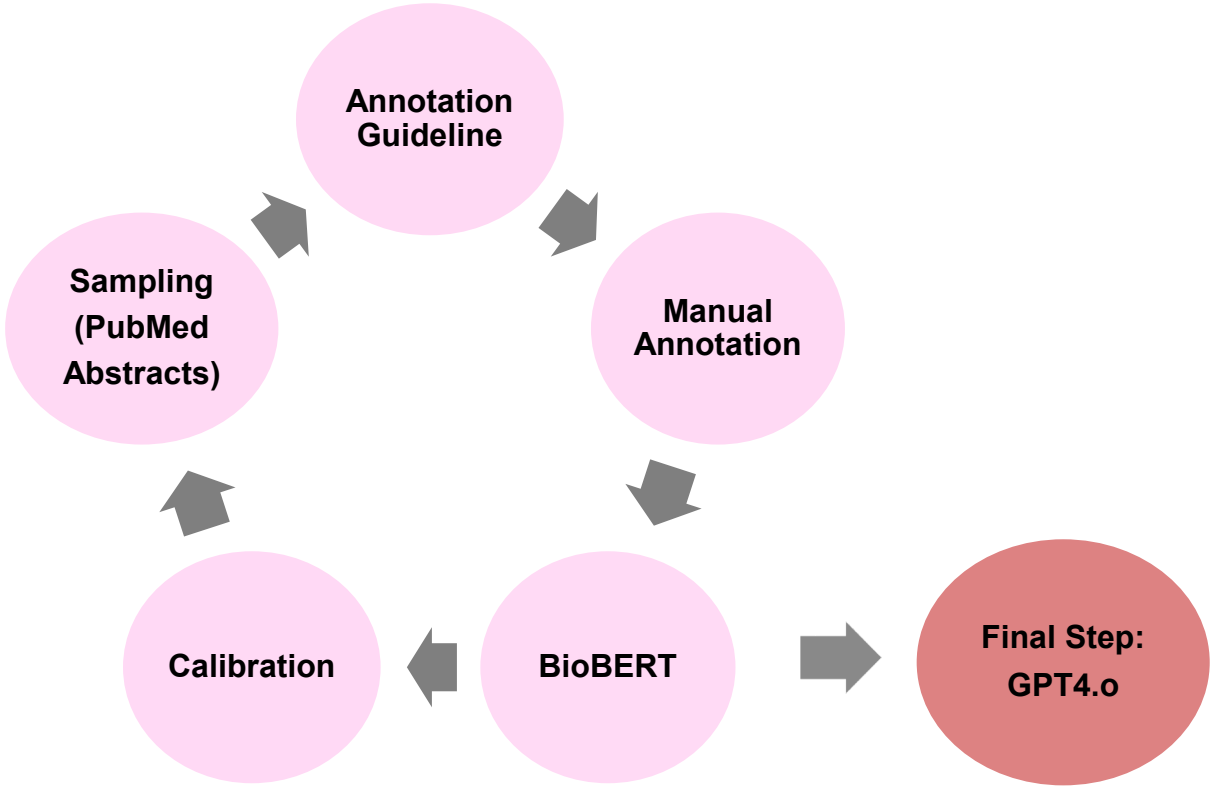


MPRINT Knowledge Portal

- Co-Learning and large language model applications in MPRINT-KP development for classifying published pharmacokinetics, pharmaco-epidemiology and clinical trial papers.

- Pharmacotherapy knowledge landscape and gap analysis in pediatric and maternal patient populations.

Co-Learning: how do we extract and classify maternal/pediatric related paper in pharmacokinetics, pharmacoepidemiology and clinical trials?



Annotation Guideline: Inclusion Criteria

Version 1

- Maternal patients
- Pediatric patients
- Drug therapies, including cell therapies, are the primary object of study.
- Include PK and PD modeling paper.

Version 2 (edits)

- Drug therapies are both the primary and **secondary** object of study.
- **Include assay development paper.**
- **Include epidemiological survey paper on medication frequencies**

Version 3 (edits)

- Maternal patients **(pregnant, lactation, fertility treatment, postpartum)**
- Drugs, **endogenous, exogenous compounds (e.g. chemicals) and nutrition.**
- Include assay **(e.g. LC/MS)** development papers **if some mention of maternal/pediatric population.**
- **Studies evaluating breastfeeding (if there is a comparator group).**

Version 4 (edits)

- Maternal patients (pregnant, lactation, fertility treatment, postpartum, **contraceptives**).
- Include assay (e.g. LC/MS) development papers **for drug/metabolite measurement** if some mention of maternal/pediatric population.

Version 5 (edits)

- Drugs, endogenous, exogenous compounds (e.g. chemicals) and **oxygen**.
  - Include cell therapy.
  - **Include vaccine.**
  - **Include cell type biomarker.**
  - **Include a protein/peptide.**
  - **Include smoking.**

Version 6/7/8 (no edit)

Annotation Guideline: Paper Classification Criteria

Version 1

- **Clinical trial (CT):** It is typically a randomized clinical trial comparing a drug treatment's efficacy and/or toxicity to control and/or placebo.
- **Pharmacokinetics (PK):** It studies drug exposure in patients or healthy volunteers in mothers and/or their babies during pregnancy, labor, delivery, postpartum or lactation.
- **Pharmacoepidemiology (PE):** It studies a drug's pharmacodynamic endpoints, biomarkers, efficacy, or adverse drug events in an observational study.

Version 2 (edits)

- **CT and PE are mutually exclusive.**

Version 3 (no edit)

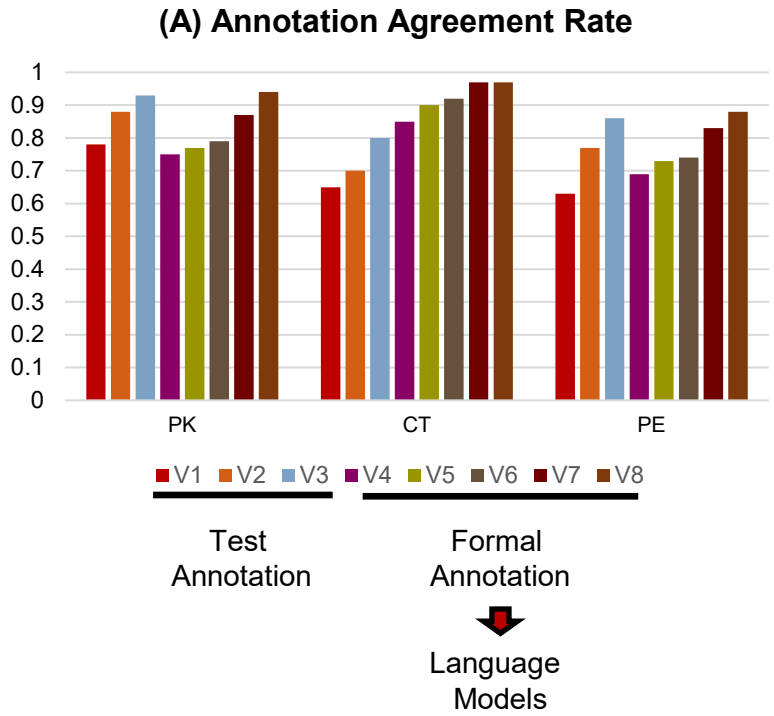
Version 4/5 (edits)

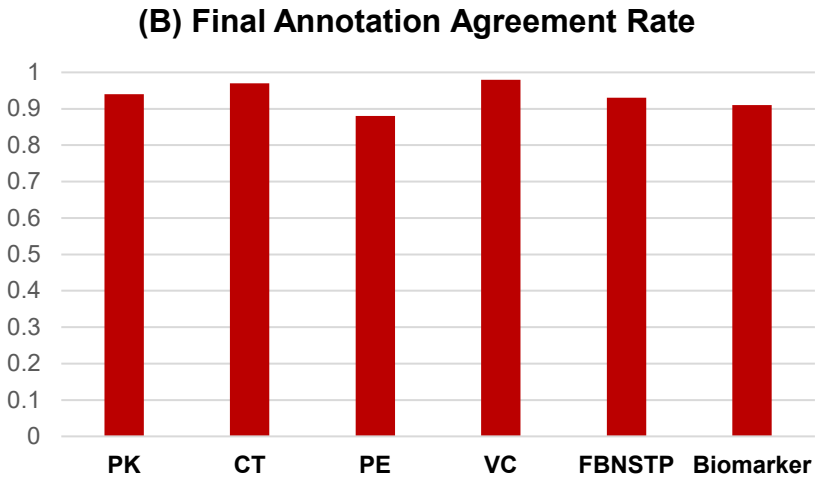
- **CT:** CT must include randomization.
- **PK**: It studies drug exposure, **endogenous, exogenous compounds, (e.g. chemicals), or nutrition.**
- **It can be either a drug or a biomarker.**

Version 6/7/8 (edits)

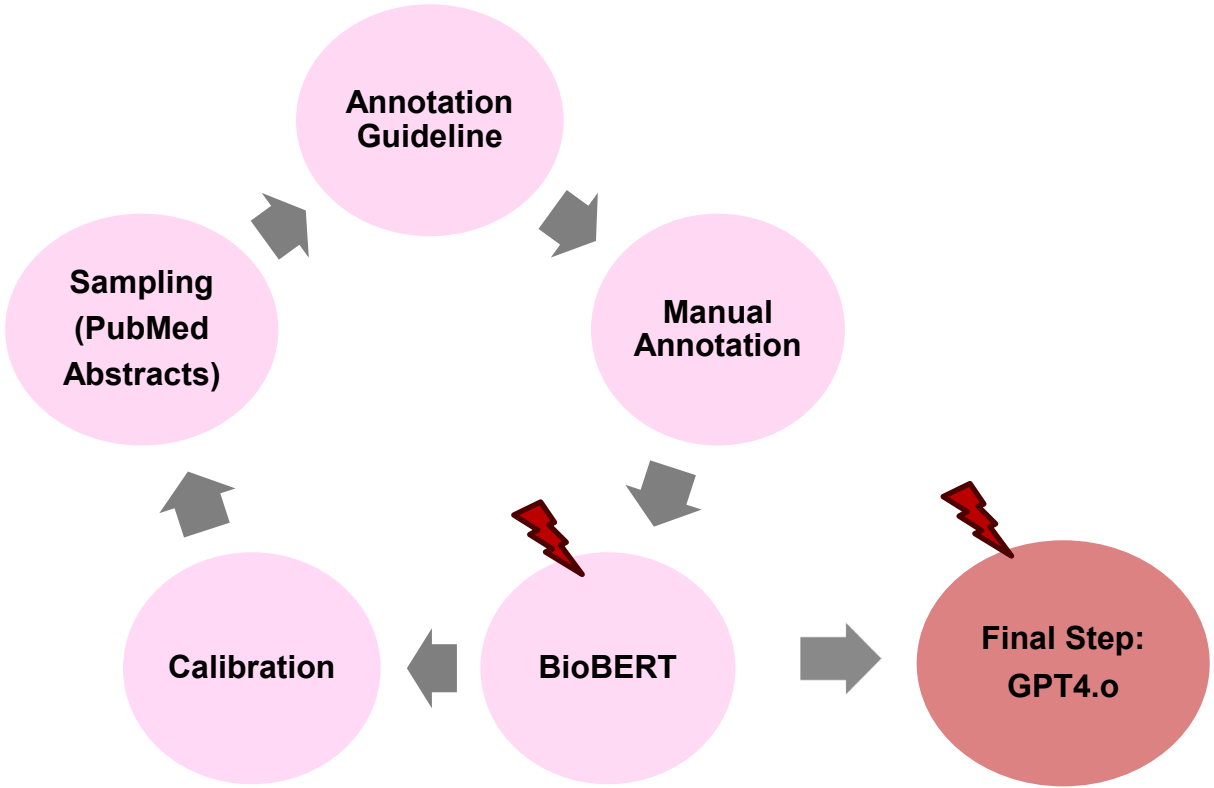
- **Vaccine (VC):**
- **Food, breastfeeding, nutrition, smoking, environmental toxin, pollutant, and oxygen (FBNSTP):**
- **Biomarker**: No drug in the study. Biomarker is for disease diagnosis, prognosis, or progression.

Annotation agreement rates among multiple versions of annotation guideline

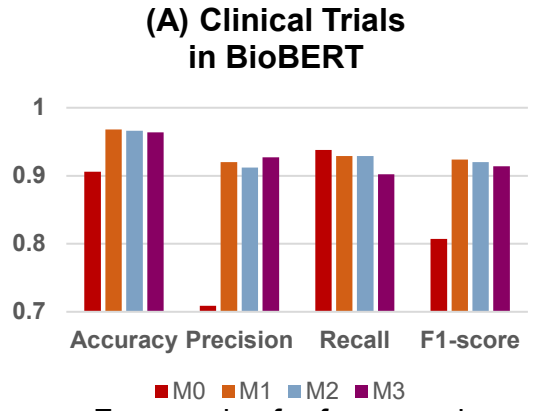




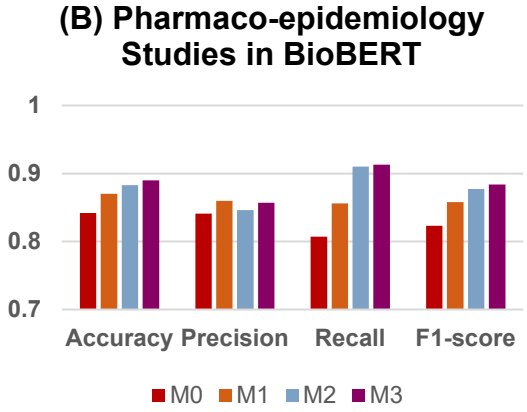
Four rounds of co-learning in classifying PK/PE/CT papers

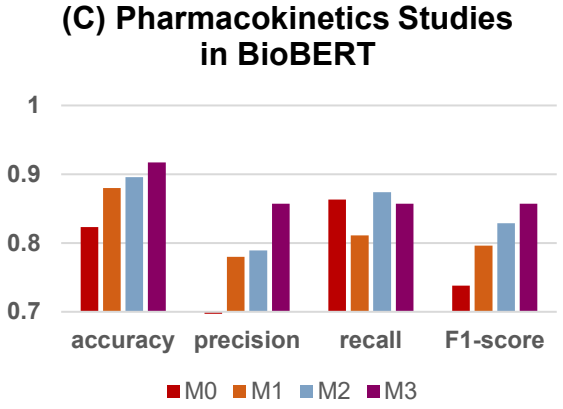


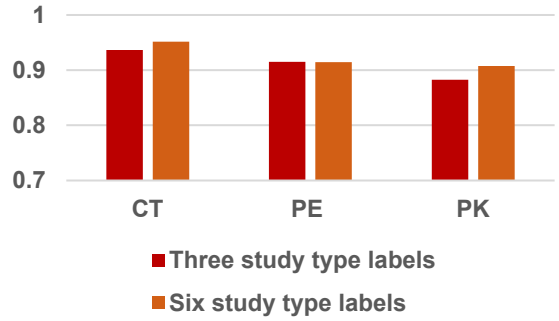
Co-Learning and Large Language Model Performance

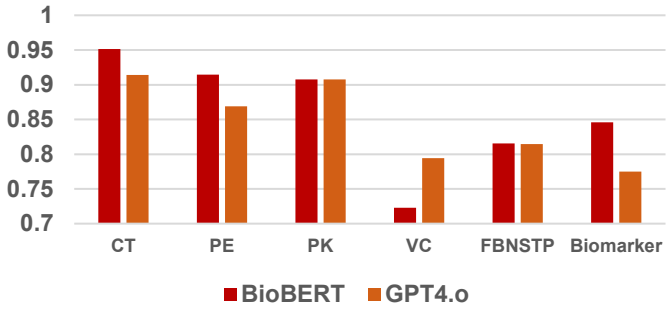


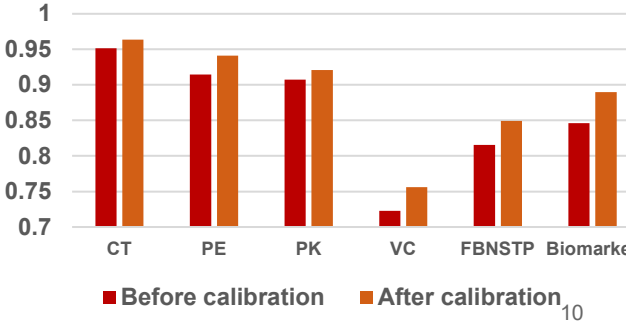
Four modes for four rounds of formal annotations



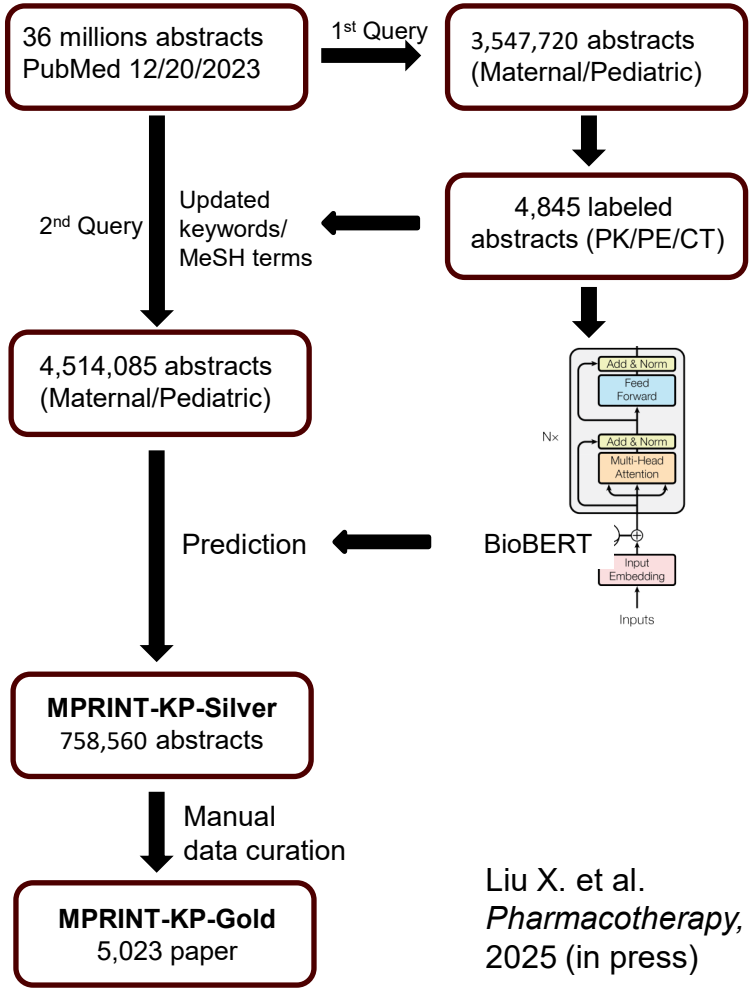






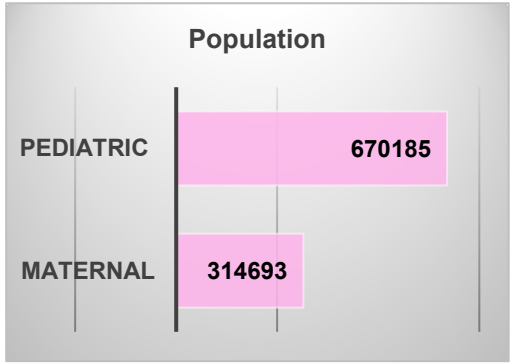


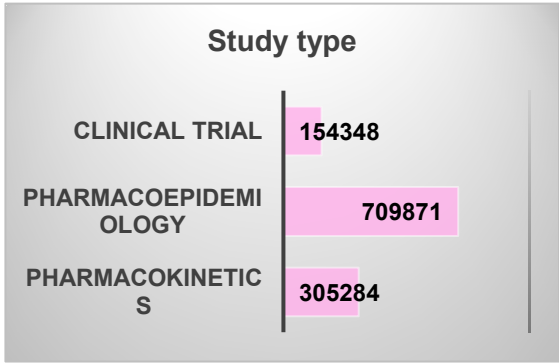
(A) MPRINT-KP Consort Diagram

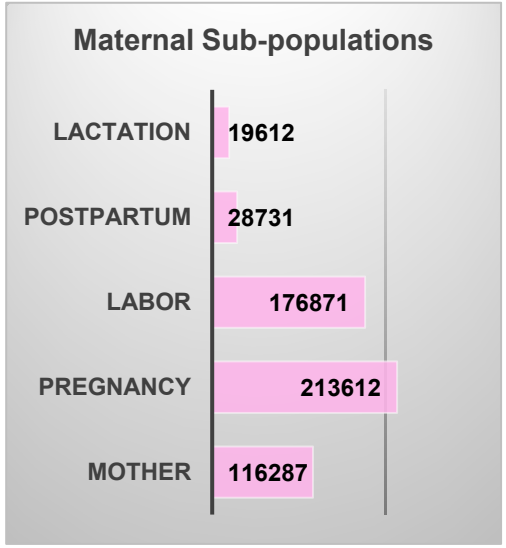


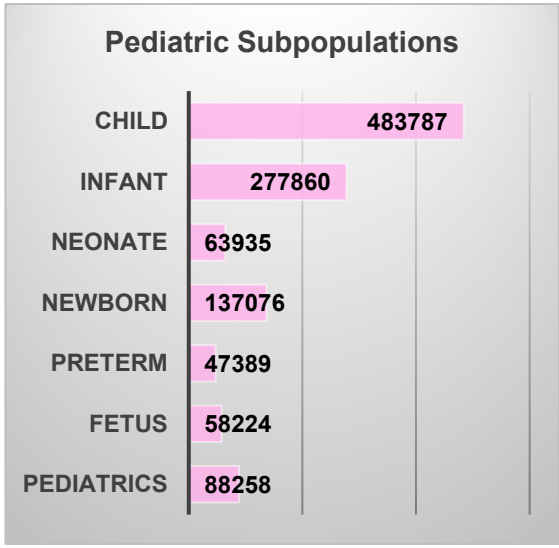
Liu X. et al.
Pharmacotherapy,
2025 (in press)

(B) MPRINT-KP Silver Statistics

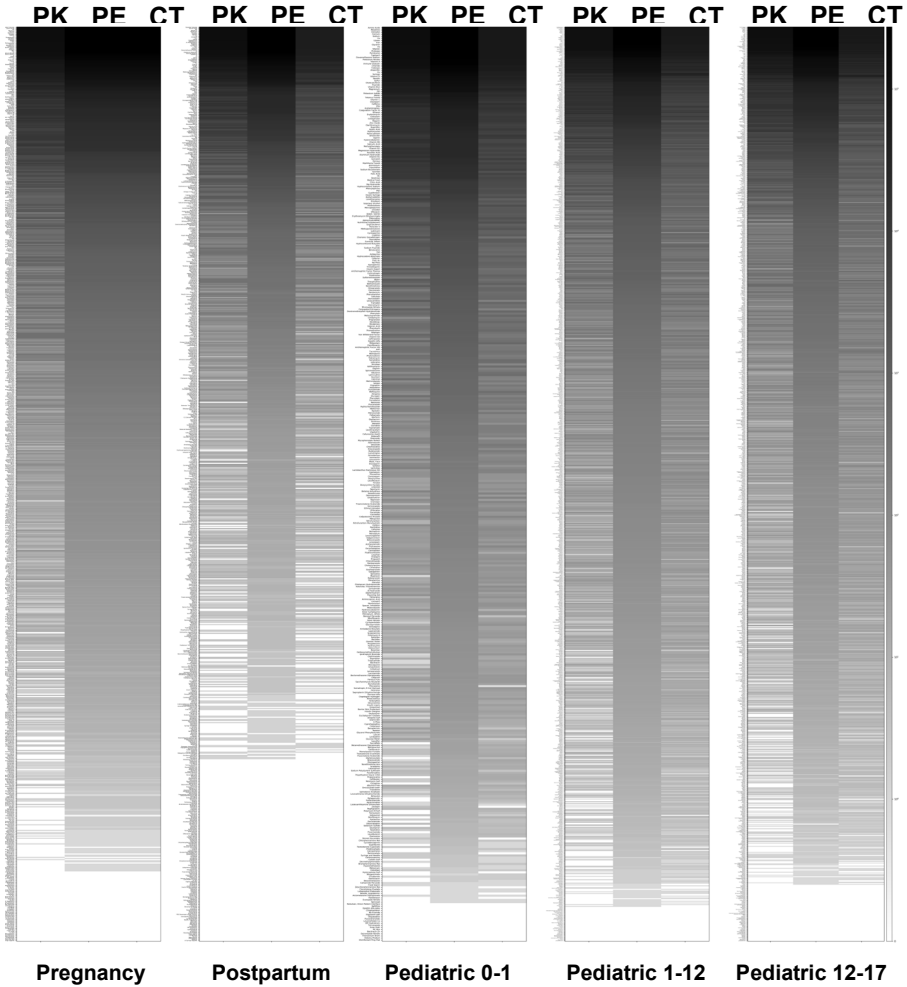




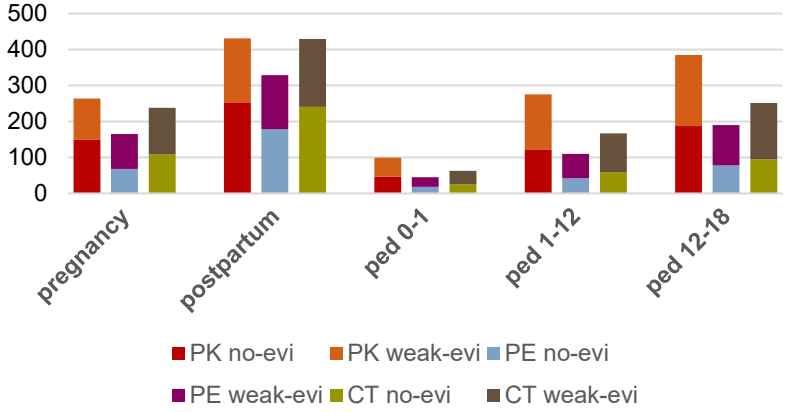




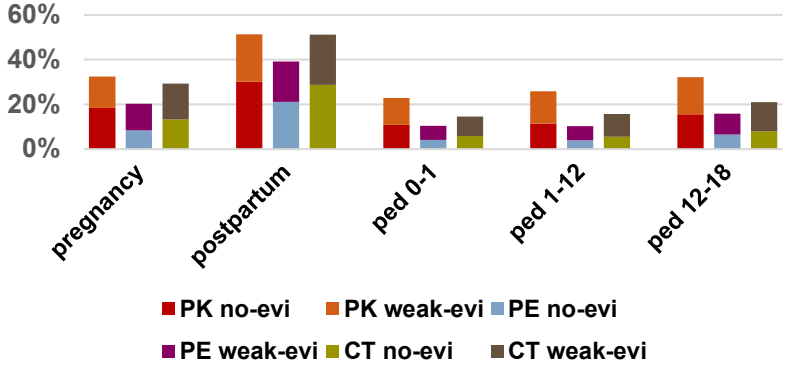
(A) Knowledge Landscape of Pharmacotherapy Publications



(B) Number of Drugs with No or Weak Publication (<5 papers) Evidence

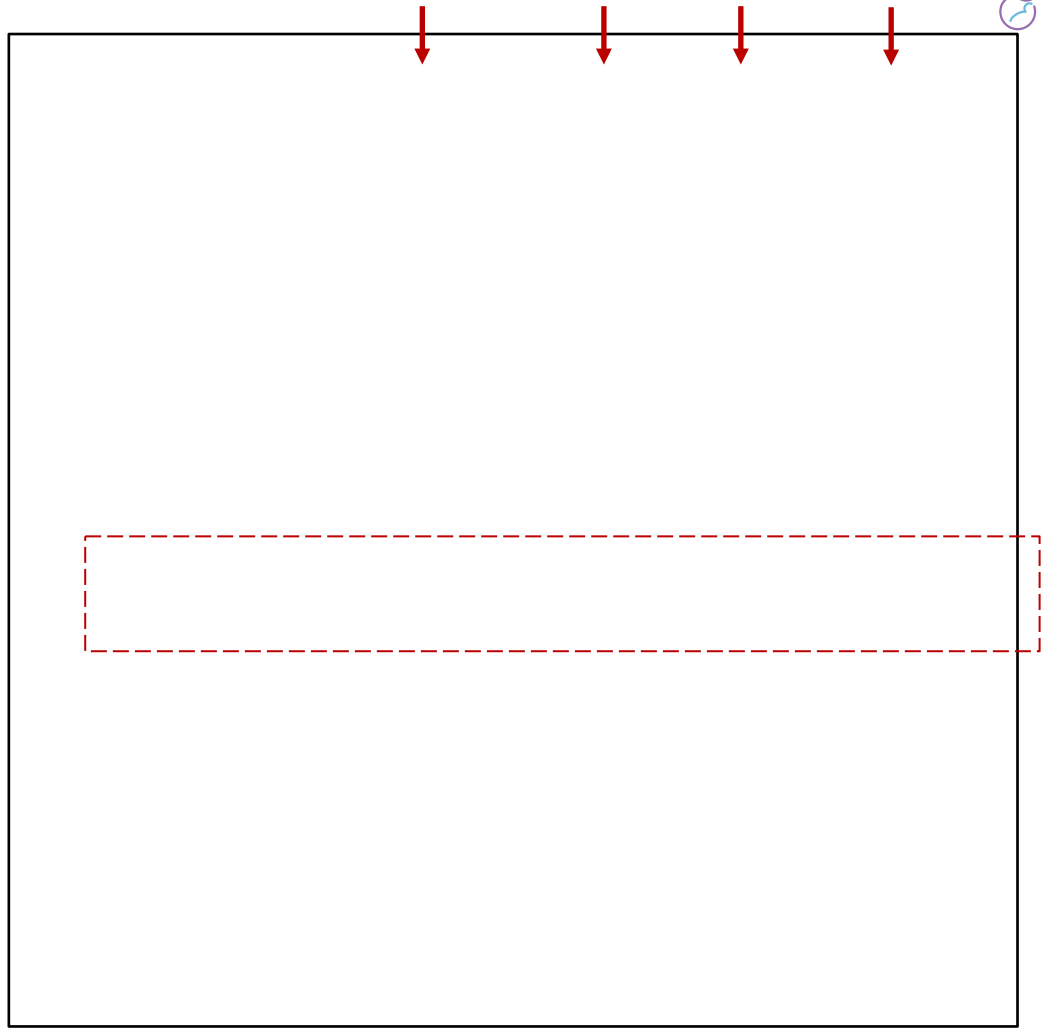


(C) Relative Frequency of Drugs with No or Weak Publication (<5 papers) Evidence



Liu X. et al. *Pharmacotherapy*, 2025 *(in press)*

Pharmacotherapy research landscape and knowledge gaps of opioids in **pediatric populations**

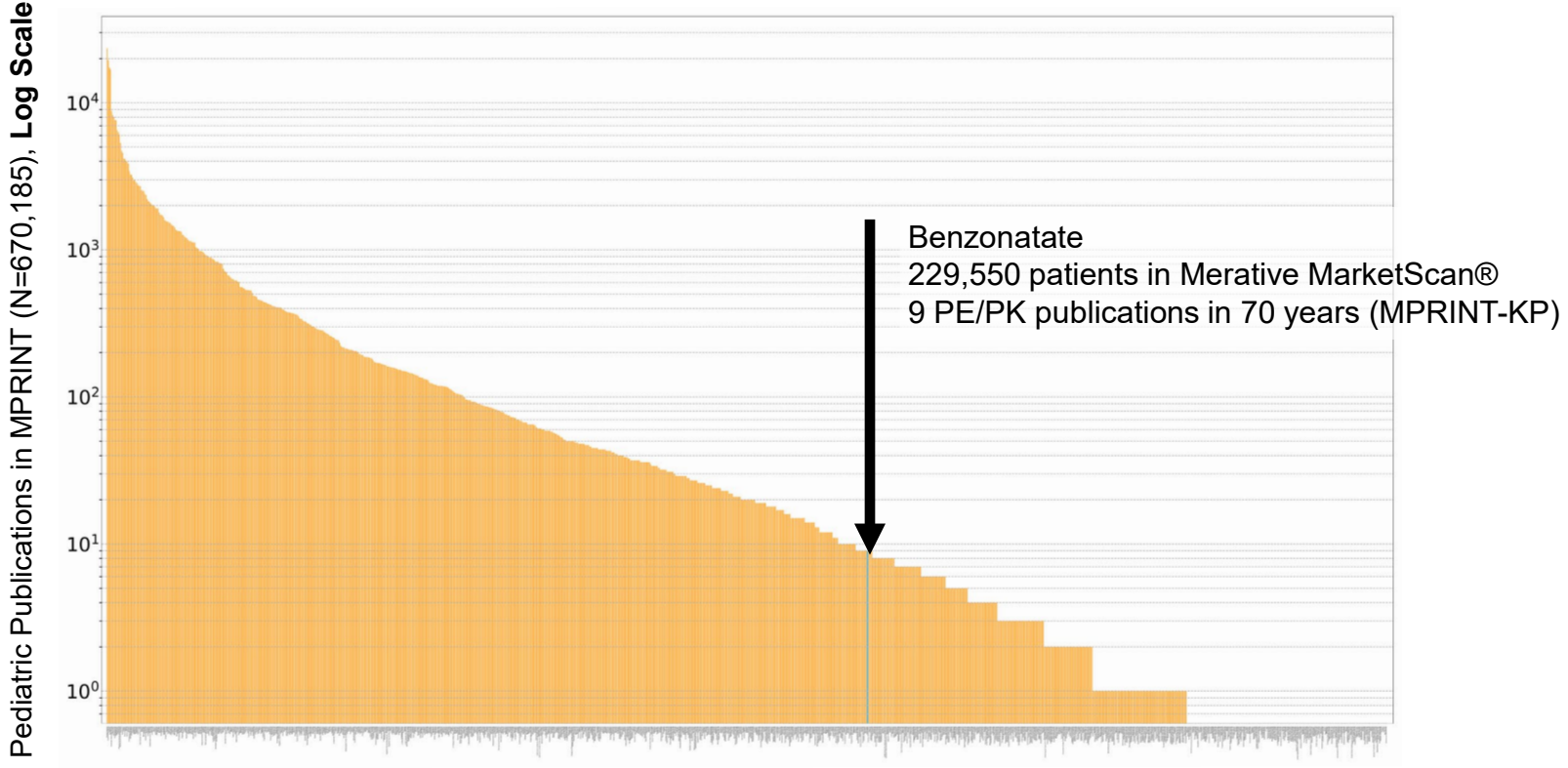


(Shendre *et al, Pharmacotherapy*, 2025 May 15;45(6):367–385)

Saurabh
Rahurkar, PhD
Assistant Professor
Ohio State Univ.

Pediatric Drug Safety Study Using MPRINT-KP and RWD - A Benzonatate Story

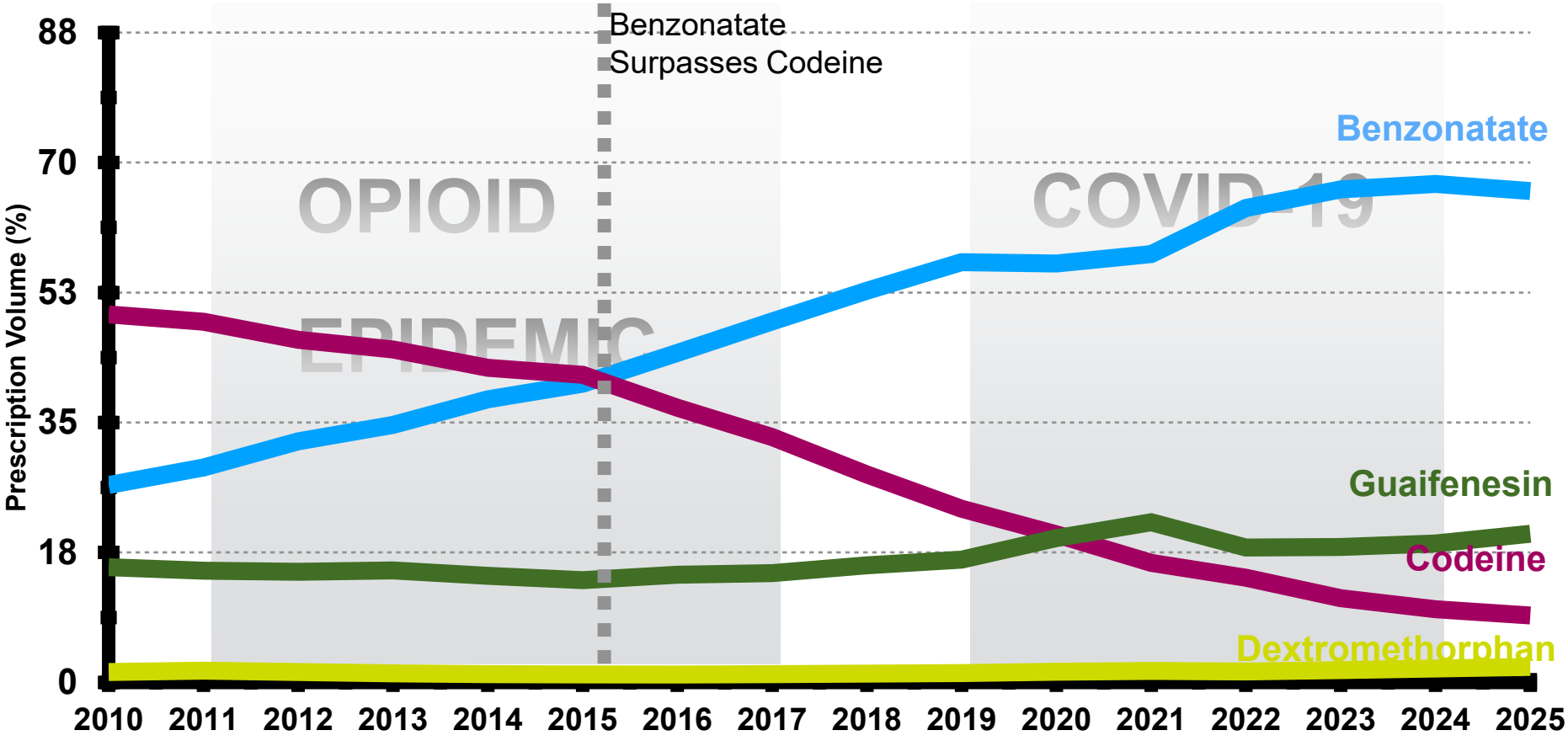
mprint



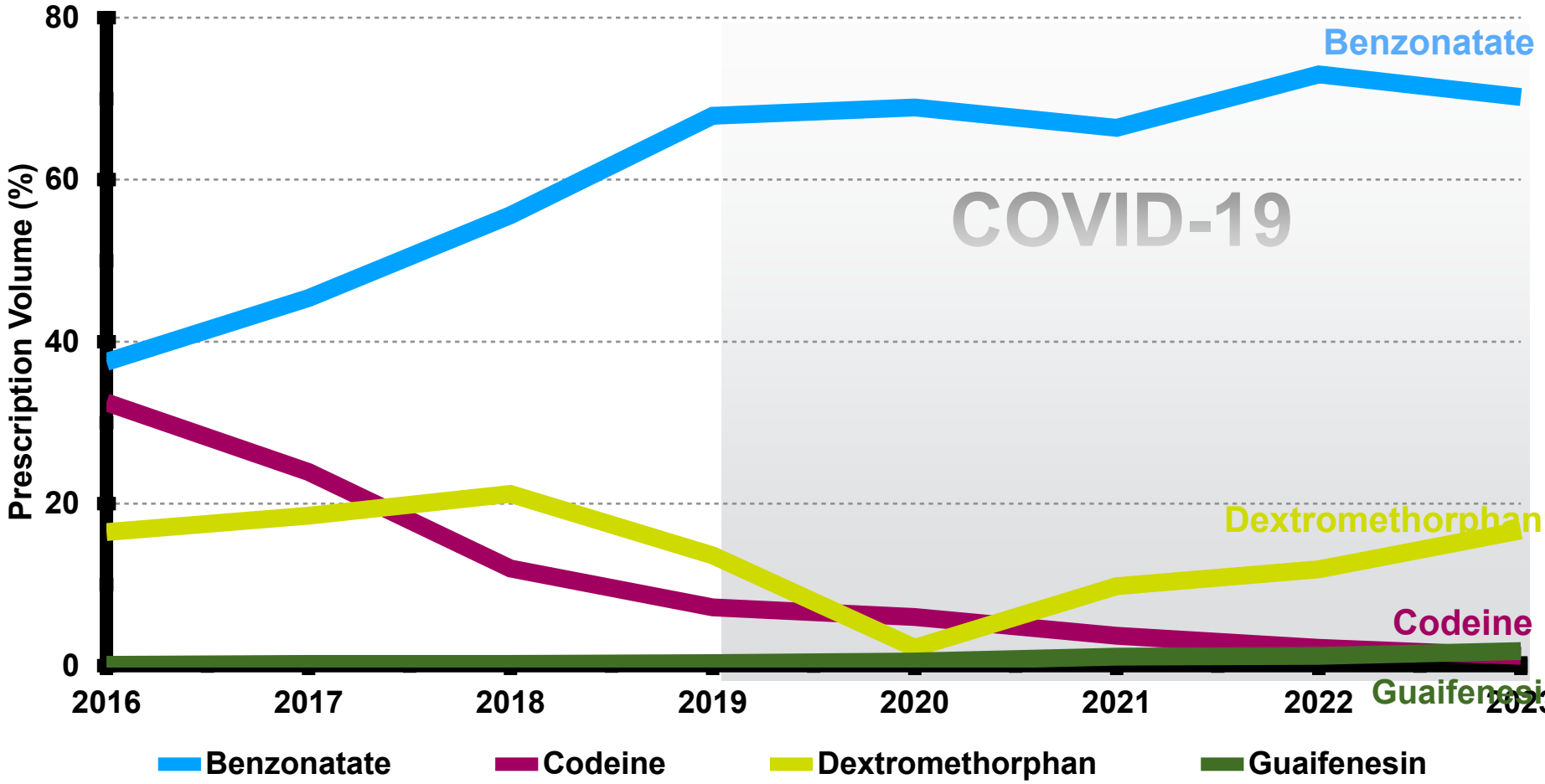
Benzonatate: Why it matters?

- Very common indication: Cough
- Use has increased dramatically since 2010 especially as a substitute for opioid antitussives
  - 70% of all pediatric antitussive prescriptions
- Perception of safety
  - No population-based drug safety study
  - Inadequate safety label. No black box, no contraindication except hypersensitivity
- Extremely resistant to de-prescribing
  - Prescription is against evidence-based guidelines: American College of Emergency Physicians recommends not prescribing in pediatric populations

Benzonatate Prescription Trend in Epic Cosmos

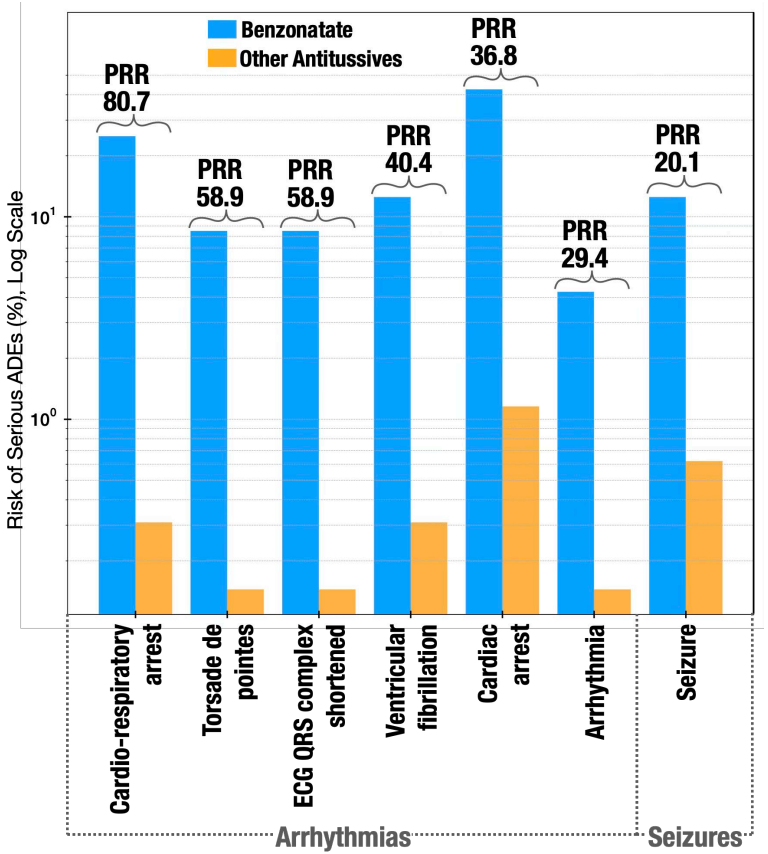


Benzonatate Prescription Trend in Merative MarketScan



Benzonatate Associated ADEs

ADEs in FAERS



ADE in MarketScan

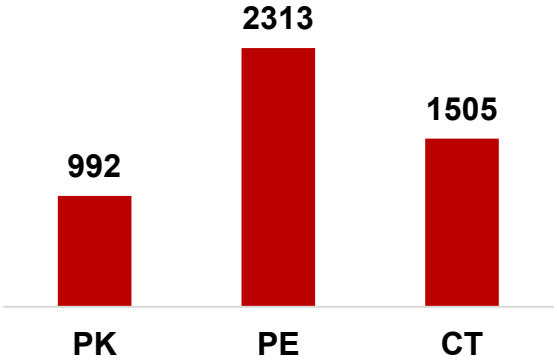
- Benzonatate vs. Standard of Care (i.e., no treatment)
  - 68% higher odds of seizure for Benzonatate
  - Age, sex, geographic region, care setting, provider type, Dx at encounter, Hx of chronic conditions

Rahurkar *et al, Pharmacotherapy.* 2025 Oct;45(10):667-676.

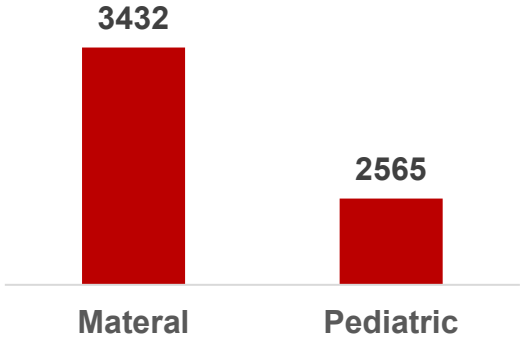
MPRINT-KP Gold Statistics
(manual data curation)

Total number of drugs: 237
Total number of publications: 5034

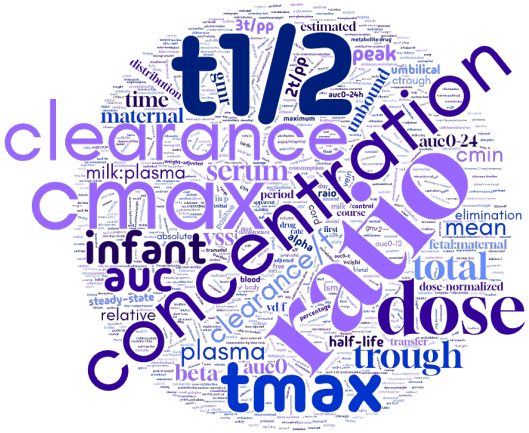
Study Type



Populations

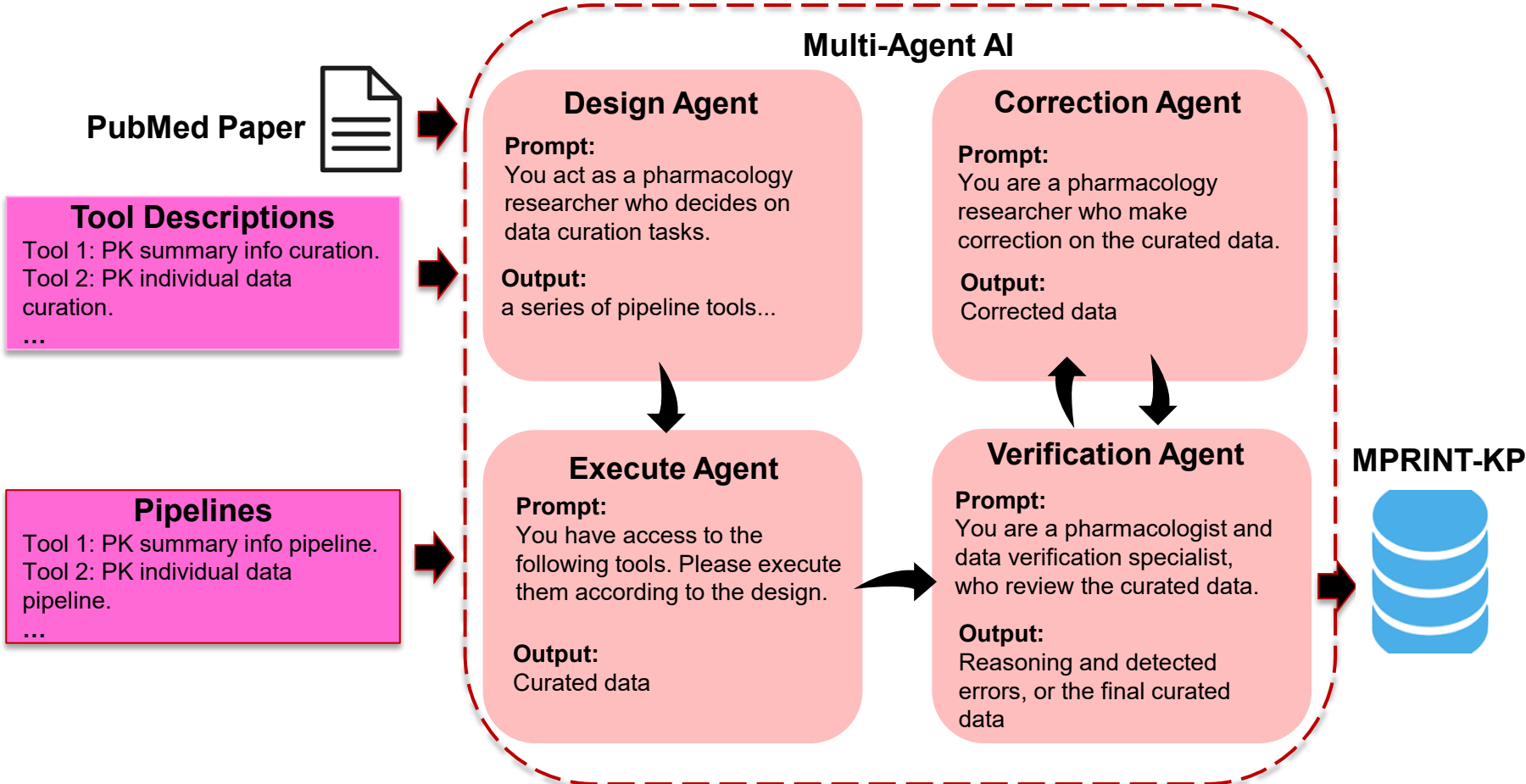


(B) PK Parameters



(C) Clinical Variables

Multi-Agent Data Curation System

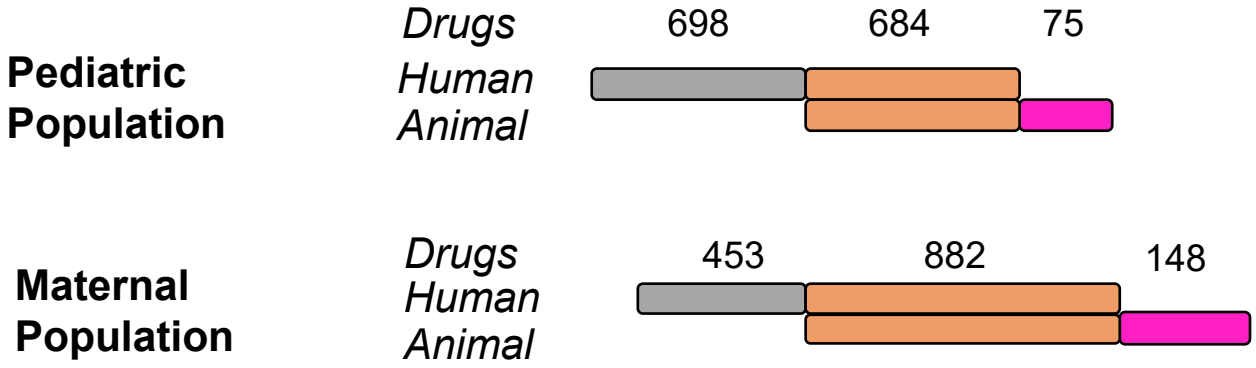


Translational Drug Safety Data between Human and Animal Studies in Maternal and Pediatric Populations

- Data sources
  - PubMed: 95,443 pediatric PE study abstracts; 47,787 maternal PE study abstracts; and 6,951 pregnant/juvenile animal studies.
  - Drug Labels: 9,520 labels on maternal data, and 15,220 labels on pediatric data (human/animal combined).

- Data extraction AI method
  - Multi-Agent AI systems
  - Performance: F1-score = 0.95.

Translational Drug Safety Data between Human and Animal Studies in Maternal and Pediatric Populations

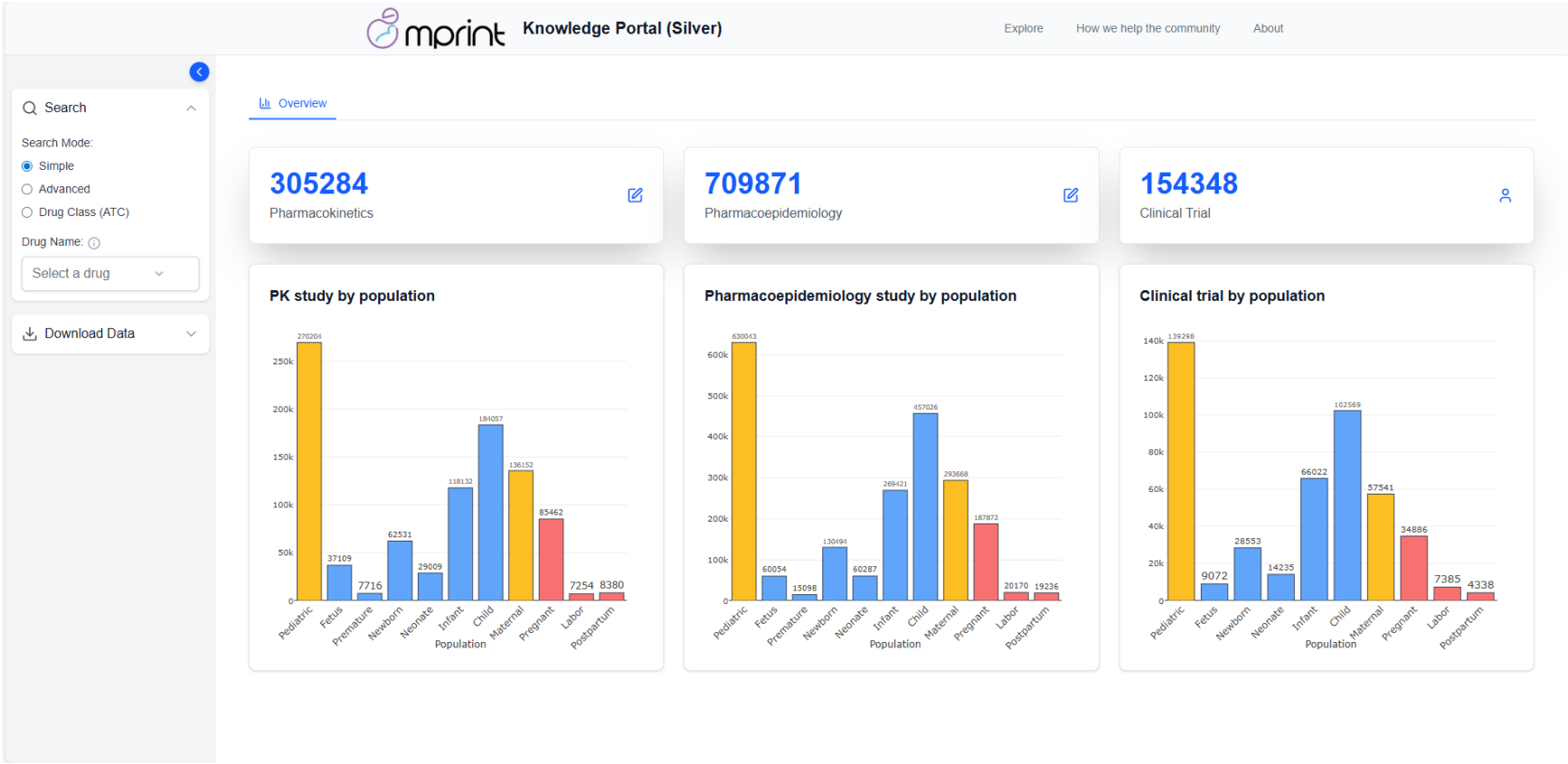


Note:
(1) The drug safety definitions between maternal and pediatric depend on who have the symptom.
(2) The overlapping drugs between human and animal do not mean they share the same ADEs.
(3) These data are not yet in MPRINT-KP Silver, but available upon request.

Pharmacokinetics Models Extraction from PubMed

- PK Models in all patient populations (2017~2025): 5,798.
  - Non-compartment PK: 2,160
  - One-compartment PK: 548
  - Multi-compartment PK: 1,551
  - Physiologically based PK: 293
  - PK/PD: 390
  - Non-standard PK: 523
  - Others: 333

- Data extraction AI method
  - Multi-Agent AI systems
  - Performance: F1-score = 0.98.



https://silver-staging.mprintkb.org/

MPRINT-KP Summery

- MPRINT-KP Silver is a great tool in knowledge gap discovery in maternal and pediatric populations.
- Together, MPRINT-KP Silver and RWD are powerful resources for discover and validate drug safety signals.
- Multi-Agent AI is an efficient and scalable technology in data curation for MPRINT-KP.
- MPRINT-KP needs significant more research and effort in the following tasks.
  - Data curation on data sources, study design, analysis methods, outcomes and risk factors.
  - Disease and drug response data mapping between PubMed reported data and RWD.
  - Systematic review and meta-analysis.
  - Pharmacology evidence summary.

Acknowledgement

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- **University of Buffalo**

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- **MD Anderson**

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