

Real World Data and Real World Evidence Regarding Research Specific to Lactating Persons: Challenges and Opportunities

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Electronic Medical Records as a Source of Data

- Electronic medical records are not routinely structured to properly identify breastfeeding habits of infants/children and link these to maternal exposures from the medical record and ultimately to infant health outcomes
- However, this would likely be feasible within many health systems

Electronic Medical Records as a Source of Data



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ORIGINAL ARTICLE

WILEY

The most common medications dispensed to lactating persons: An electronic health record-based approach

Kristin Palmsten¹  | Gabriela Vazquez-Benitez¹ | Meghan M. JaKa² |
Gretchen Bandoli^{3,4} | Katherine A. Ahrens⁵ | Elyse O. Kharbanda¹ 

Abstract

Purpose: Using a novel, electronic health record (EHR)-based approach, to estimate the prevalence of prescription medication use at 2, 4, and 6 months postpartum among lactating individuals.

Methods: We utilized automated EHR data from a US health system that records infant feeding information at well-child visits. We linked mothers who received prenatal care to their infants born May 2018–June 2019, and we required infants to have ≥ 1 well-child visit between 31 and 90 days of life (i.e., 2-month well-child visit with a ± 1 month window). Mothers were classified as lactating at the 2-month well-child visit if their infant received breast milk at the 2-month well-child visit. For subsequent well-child visits at 4 and 6 months, mothers were considered lactating if their infant was still receiving breast milk.

Results: We identified 6013 mothers meeting inclusion criteria, and 4158 (69.2%) were classified as lactating at the 2-month well-child visit. Among those classified as lactating, the most common medication classes dispensed around the 2-month well-child visit were oral progestin contraceptives (19.1%), selective serotonin reuptake inhibitors (8.8%), first generation cephalosporins (4.3%), thyroid hormones (3.5%), nonsteroidal anti-inflammatory agents (3.4%), penicillinase-resistant penicillins (3.1%), topical corticosteroids (2.9%), and oral imidazole-related antifungals (2.0%). The most common medication classes were similar around the 4 and 6-month well-child visits although prevalence estimates were often lower.

Challenges & Opportunities with Electronic Health Records

Challenges

- not knowing if a medication documented as dispensed in the maternal record was actually taken and when
- many medications/vaccines would not be documented in medical record, e.g., OTC
- details about breastfeeding exposure may not be available

Opportunities

- electronic health care systems could be expanded to capture additional information as well as samples if desired

Real World Data from Stand-Alone Biorepositories for Research

Nationwide Mommy's Milk Human Milk Research Biorepository (HMB) established at UC San Diego in 2014



Breastfeeding Medicine, Vol. 15, No. 3 | Clinical Research

The Design and Mechanics of an Accessible Human Milk Research Biorepository

Gretchen Bandoli ✉, Kerri Bertrand, Maryana Saoor, and Christina D. Chambers

Published Online: 9 Mar 2020 | <https://doi.org/10.1089/bfm.2019.0277>

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Objectives of HMB

- To provide a nationwide platform to study the safety of medications in lactation
 - Rx medications
 - OTC medications
 - Vaccines, herbal products
- To examine prevalence and potential consequences of environmental contaminants
- To serve as a resource for other research teams and networks to address key questions about human milk
- To advance human research and best practices regarding breastfeeding through community partnerships

HMB Study Design

Samples

- 50 mL milk sample up to full expression, can be repeated samples – local collection or shipped overnight on ice packs
- Samples aliquoted and stored at -80° C at UC San Diego biobank
- Addition of paired blood samples self-collected from mothers/infants using a Tasso device

Recruitment Sources

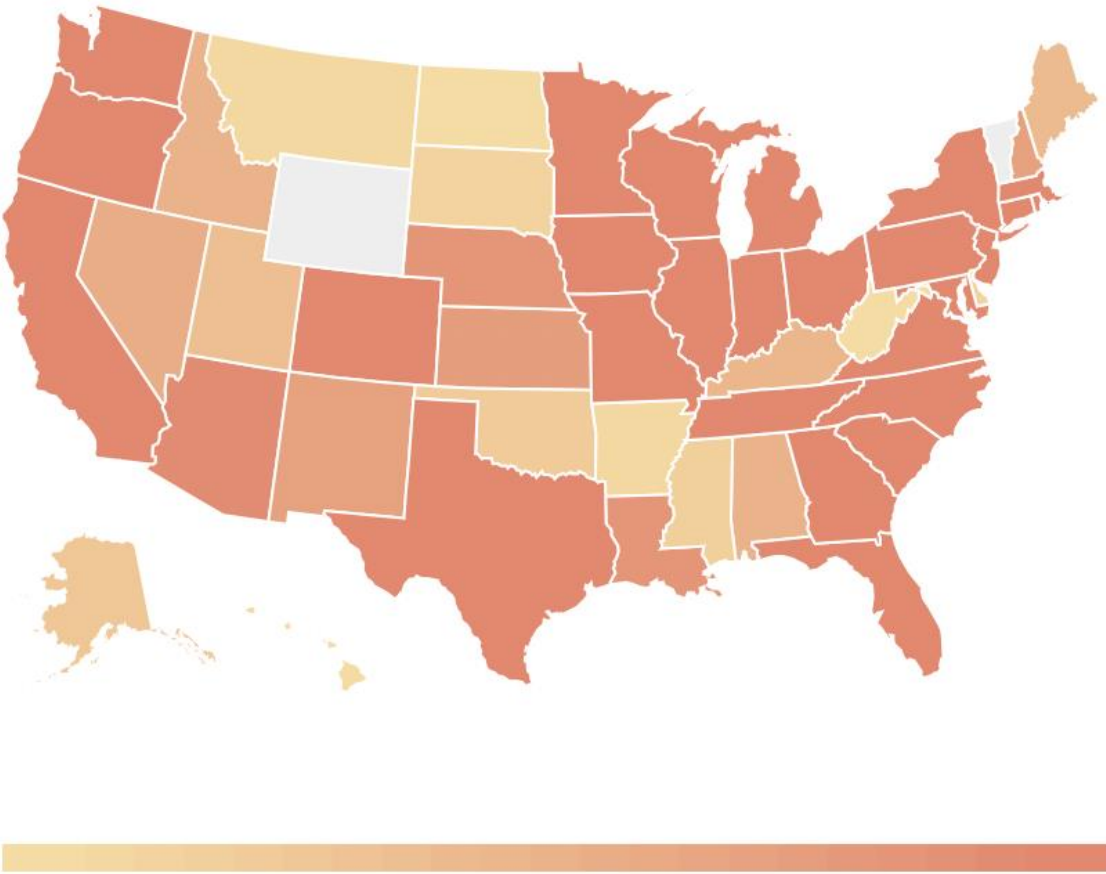
- MotherToBaby Services and MotherToBaby Pregnancy Studies (US and Canada)
- Social media
- Lactation consultants, Donor Milk Banks, pediatric/pharmacy referrals

Meta-Data

- Demographics, maternal and child health, and detailed breastfeeding habits
- Exposure to recreational drugs, alcohol, tobacco, caffeine, and all Rx & OTC medications, supplements, herbal products, vaccines day-by-day over past 14 days
- Infant adverse reaction checklist
- Stress, anxiety, depression screening, food frequency questionnaires
- Neurobehavioral questionnaires 12-36 months; face-to-face testing for subset
- Medical records abstraction for mother and infant annually

Growth Trajectory

MOTHERS DISTRIBUTION BY STATES



| Psychother | N | Immune | N | Pain/Antibiotic | N | Other | N |
|----------------|-----|--------------------|-----|-------------------|-----|---------------|-----|
| sertraline | 296 | infliximab | 14 | oxycodone | 123 | atorvastatin | 1 |
| citalopram | 32 | etanercept | 10 | hydrocodone | 127 | rosuvastatin | 2 |
| duloxetine | 6 | abatacept | 3 | acyclovir | 23 | enalapril | 3 |
| clonazepam | 10 | tocilizumab | 7 | oseltamivir | 15 | labetalol | 73 |
| fluoxetine | 46 | adalimumab | 34 | cephalexin | 62 | levothyroxine | 232 |
| gabapentin | 13 | methotrexate | 3 | amoxicillin | 44 | metformin | 25 |
| lamotrigine | 23 | prednisone | 102 | azithromycin | 39 | mesalamine | 16 |
| desvenlafaxine | 3 | dupilimab | 6 | clindamycin | 22 | metoprolol | 13 |
| pregabalin | 2 | tofacitinib | 2 | doxycycline | 3 | nifedipine | 54 |
| trazodone | 9 | ustekinumab | 19 | levofloxacin | 7 | riveroxban | 1 |
| bupropion | 42 | certolizumab | 39 | metronidazole | 13 | domperidone | 19 |
| lorazepam | 23 | mepolizumab | 1 | methylphenidate | 5 | zolpidem | 11 |
| respiridone | 1 | apremilast | 2 | amphetamine salts | 15 | ondansetron | 23 |
| aripipazole | 5 | vedolizumab | 19 | sumatriptan | 23 | prucalopride | 3 |
| escitalopram | 50 | hydroxychloroquine | 46 | naltrexone | 4 | Covid Vaccine | 742 |

Examples of HMB Primary Work



Letter | Letter

The Concentration of Etanercept in Human Milk and Infant Outcomes

Kerri Bertrand, Steven Rossi, Alan Wells, Brookie Best and Christina D. Chambers

The Journal of Rheumatology November 2022, jrheum.220724; DOI: <https://doi.org/10.3899/jrheum.220724>

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Clinical Research

Maternal and Child Outcomes Reported by Breastfeeding Women Following Messenger RNA COVID-19 Vaccination

Kerri Bertrand,¹ Gordon Honerkamp-Smith,¹ and Christina D. Chambers^{1,2}



[PEDIATRICS](#). 2018 Sep; 142(3): e20181076.
Published online 2018 Aug 31. doi: [10.1542/peds.2018-1076](https://doi.org/10.1542/peds.2018-1076)

PMCID: PMC6317767

NIHMSID: [NIHMS992391](#)

PMID: [30150212](#)

Marijuana Use by Breastfeeding Mothers and Cannabinoid Concentrations in Breast Milk

[Kerri A. Bertrand](#), MPH,^a [Nathan J. Hanan](#), PharmD,^{a,b} [Gordon Honerkamp-Smith](#), MS,^a [Brookie M. Best](#), PharmD, MAS,^{a,b} and [Christina D. Chambers](#), PhD, MPH^{a,b,c}

www.nature.com/pr



CLINICAL RESEARCH ARTICLE OPEN

Check for updates

No infectious SARS-CoV-2 in breast milk from a cohort of 110 lactating women

Paul Krogstad^{1,2,3,4}, Deisy Contreras¹, Hwee Ng¹, Nicole Tobin¹, Christina D. Chambers^{3,4}, Kerri Bertrand^{3,4}, Lars Bode^{3,5} and Grace M. Aldrovandi¹

CLINICAL RESEARCH ARTICLE OPEN

Check for updates

Metabolomic and exposomic biomarkers of risk of future neurodevelopmental delay in human milk

Kefeng Li^{1,2}, Kerri Bertrand³, Jane C. Naviaux^{1,4}, Jonathan M. Monk⁵, Alan Wells³, Lin Wang^{1,2}, Sai Sachin Lingampelly^{1,2}, Robert K. Naviaux^{1,2,3,6,8} and Christina Chambers^{3,7,8}

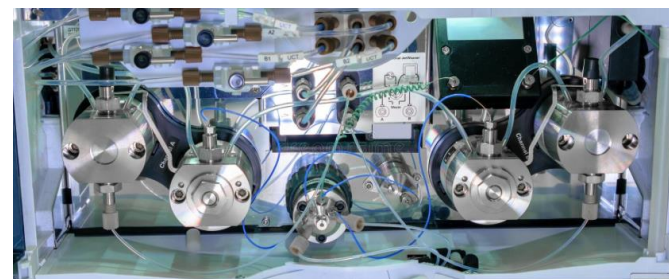
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BACKGROUND: The chemical composition of human milk has long-lasting effects on brain development. We examined the prognostic value of the human milk metabolome and exposome in children with the risk of neurodevelopmental delay (NDD).
METHODS: This retrospective cohort study included 82 mother-infant pairs (40 male and 42 female infants). A total of 59 milk samples were from mothers with typically developing children and 23 samples were from mothers of children at risk. Milk samples were collected before 9 months of age (4.6 ± 2.5 months, mean ± SD). Neurocognitive development was assessed by maternal report at 14.2 ± 3.1 months using the Ages and Stages Questionnaires-2.
RESULTS: Metabolome and exposome profiling identified 453 metabolites and 61 environmental chemicals in milk. Machine learning tools identified changes in deoxysphingolipids, phospholipids, glycosphingolipids, plasmalogens, and acylcarnitines in the milk of mothers with children at risk for future delay. A predictive classifier had a diagnostic accuracy of 0.81 (95% CI: 0.66–0.96) for females and 0.79 (95% CI: 0.62–0.94) for males.

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EU ConcePTION Project with a Similar Model: Multiple EU Countries, Samples Analyzed and Banked in Uppsala Sweden



<https://www.imi.europa.eu/projects-results/project-factsheets/conception>
<https://www.imi-conception.eu/general/>



efpia



innovative
medicines
initiative

The research leading to these results has received support from the EU/EFPIA Innovative Medicines Initiative [2] Joint Undertaking ConcePTION grant n° 821520



concePTION

Challenges & Opportunities with Human Milk Biobanks

Challenges

- potential variability in sample integrity for various medications with home collection (being tested)
- Sustainability of the biobank as a resource

Opportunities

- could potentially be used to address efficacy if desired
- can fulfill post-marketing commitments/requirements for new medications