PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Development and evaluation of an algorithm to link mothers and children in a US commercial claims database

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Background

- Current mother-offspring pairs (MOPs) in US databases lack generalizability to the commercial claims population

- Our MOP linkage algorithm measures linkage confidence and establishes an evaluation framework for assessing generalizability to the US commercial claims population

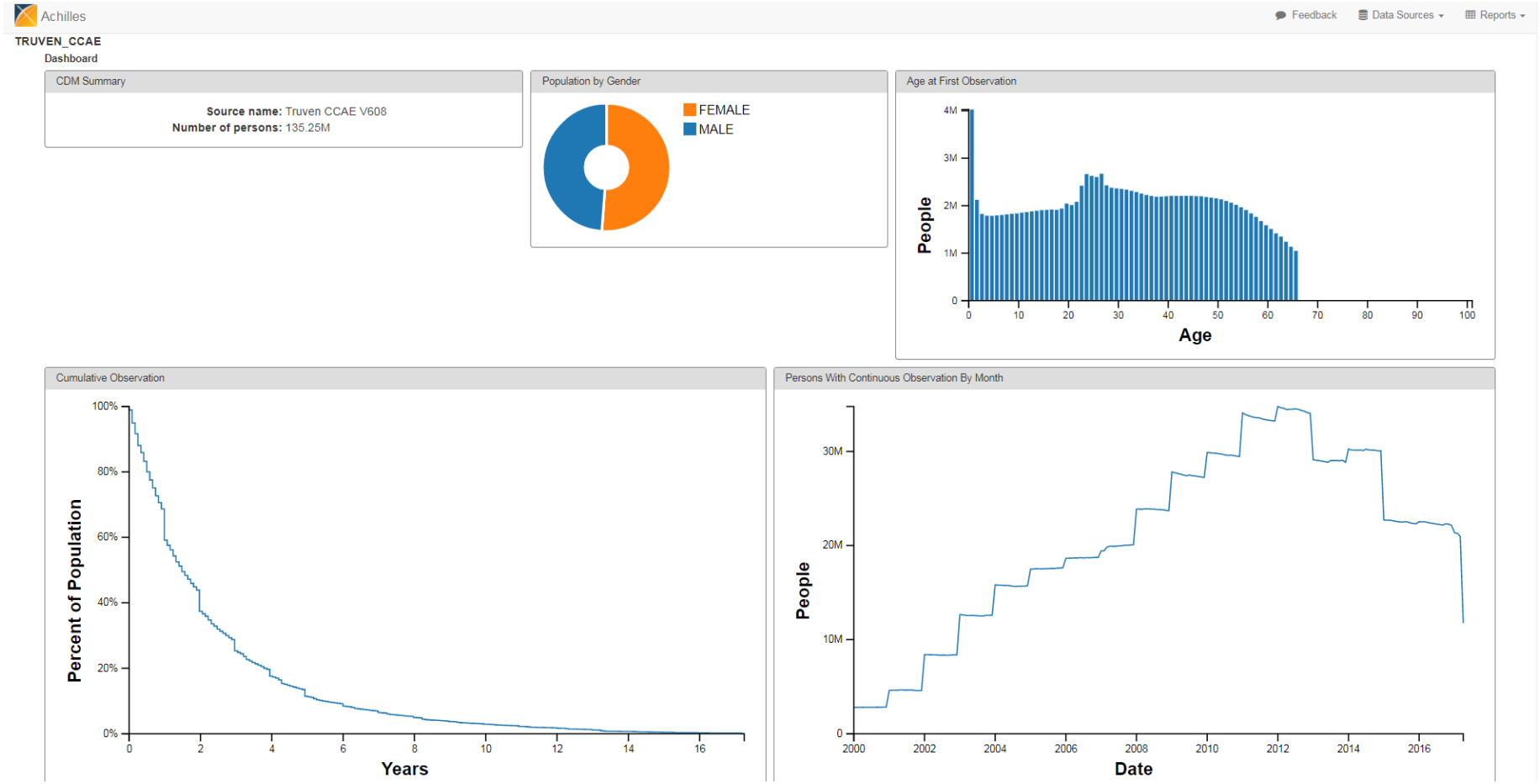
- Observational database studies of pregnancy exposures will address:
  - gap of drug safety information during pregnancy due to trial exclusions of pregnant women
  - lack of evidence on benefits and risks of drug use during pregnancy and resultant birth outcomes
  - Insufficient sample sizes, difficult and expensive new data collection, recall bias
  - includes longitudinal follow up, real-world treatment practice patterns

Objectives

- Develop an algorithm to identify MOPs in a large, observational, US healthcare claims database

- Compare linked MOPs to all-mothers and all-offspring to evaluate generalizability to the US commercial claims population

Data Source


Achilles
Feedback
Data Sources
Reports
TRUVEN_CCAE
Dashboard
CDM Summary
Source name: Truven CCAE V608
Number of persons: 135.25M
Population by Gender
FEMALE
MALE
Age at First Observation
People
Age
Cumulative Observation
Percent of Population
Years
Persons With Continuous Observation By Month
People
Date

Cohort Construction - overview

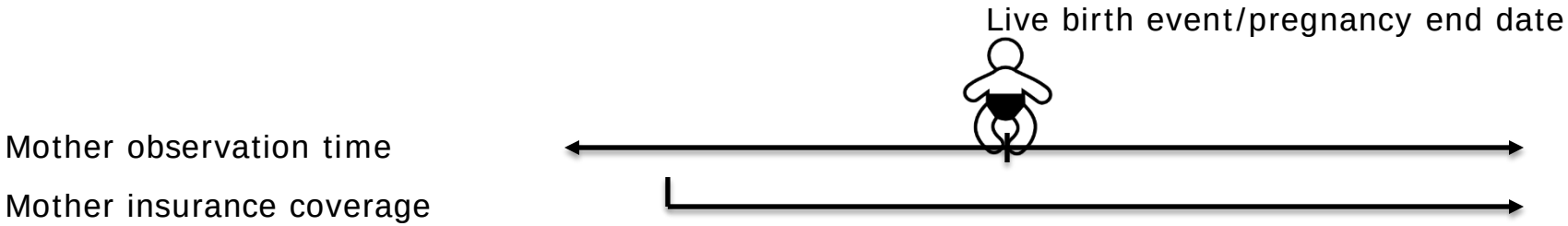
- Constructed 3 cohorts:
  1. MOPs, mothers and their associated offspring
  2. All-mothers
  3. All-offspring

- All mothers
  - Women with live birth outcome using pregnancy episode identification algorithm

- All offspring
  - People 0 years of age at observation period start

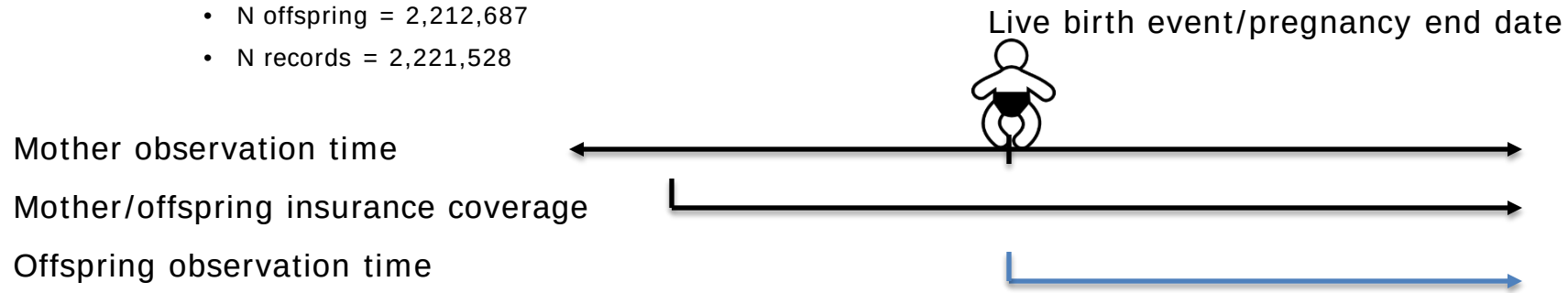
Cohort Construction

- MOP mothers
  - i. Pregnancy episodes with live birth outcome
    - N mothers = 2,378,762
  - ii. Have family identifier code (PAYER_PLAN_PERIOD.FAMILY_SOURCE_VALUE) and birth during insurance coverage period
    - N mothers = 2,378,234



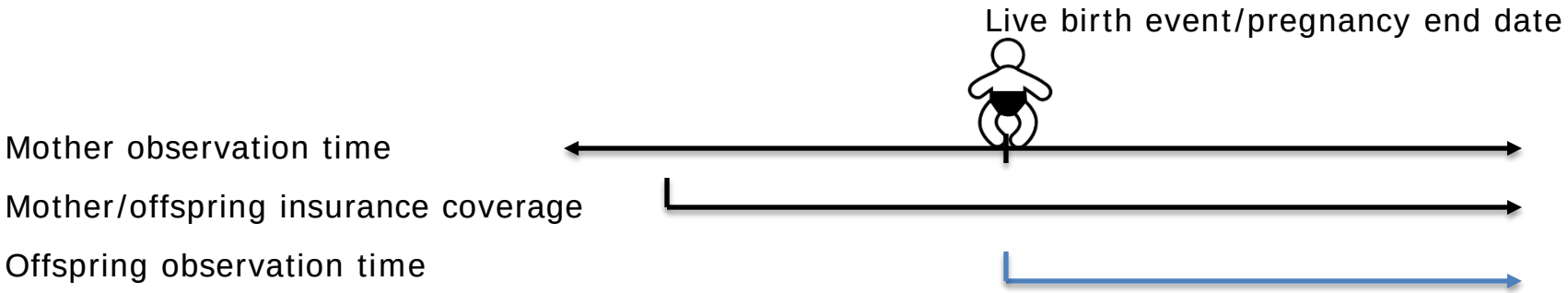
Cohort Construction

- MOP offspring
  - i. Share family identifier code (PAYER_PLAN_PERIOD.FAMILY_SOURCE_VALUE) and overlapping observation time with mother, 0 years of age at observation period start
    - Mother family_source_value = offspring family_source_value
  - ii. Insurance coverage start date within mother's observation period
    - N mothers = 1,742,530
    - N offspring = 2,212,687
    - N records = 2,221,528



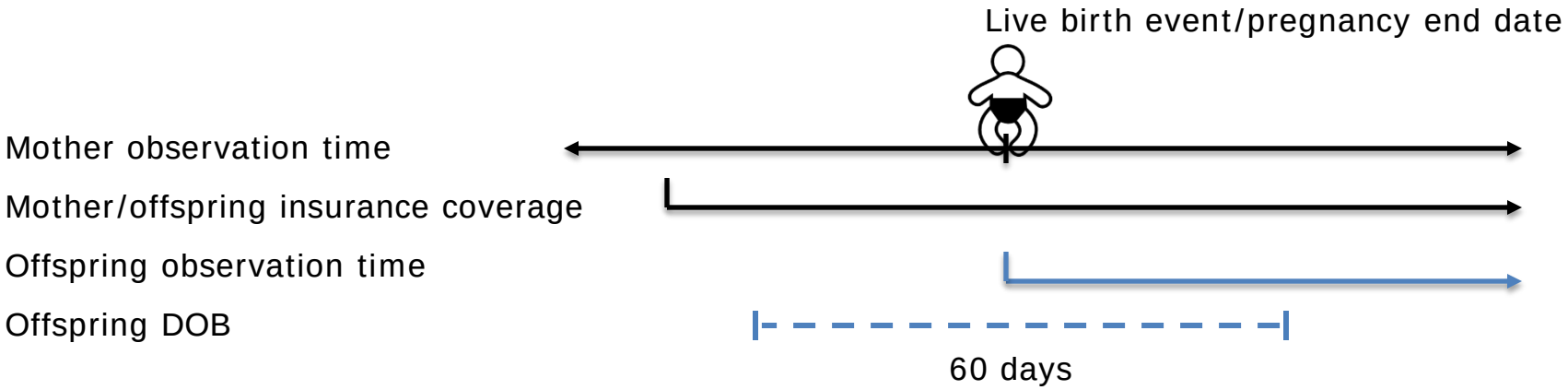
Cohort Construction

- MOP offspring
  - iii. Exclude inaccurate linkages, duplicate records; e.g. 1 offspring associated with multiple mothers
    - N mothers = 1,729,530
    - N offspring = 2,203,687
    - N records = 2,203,687



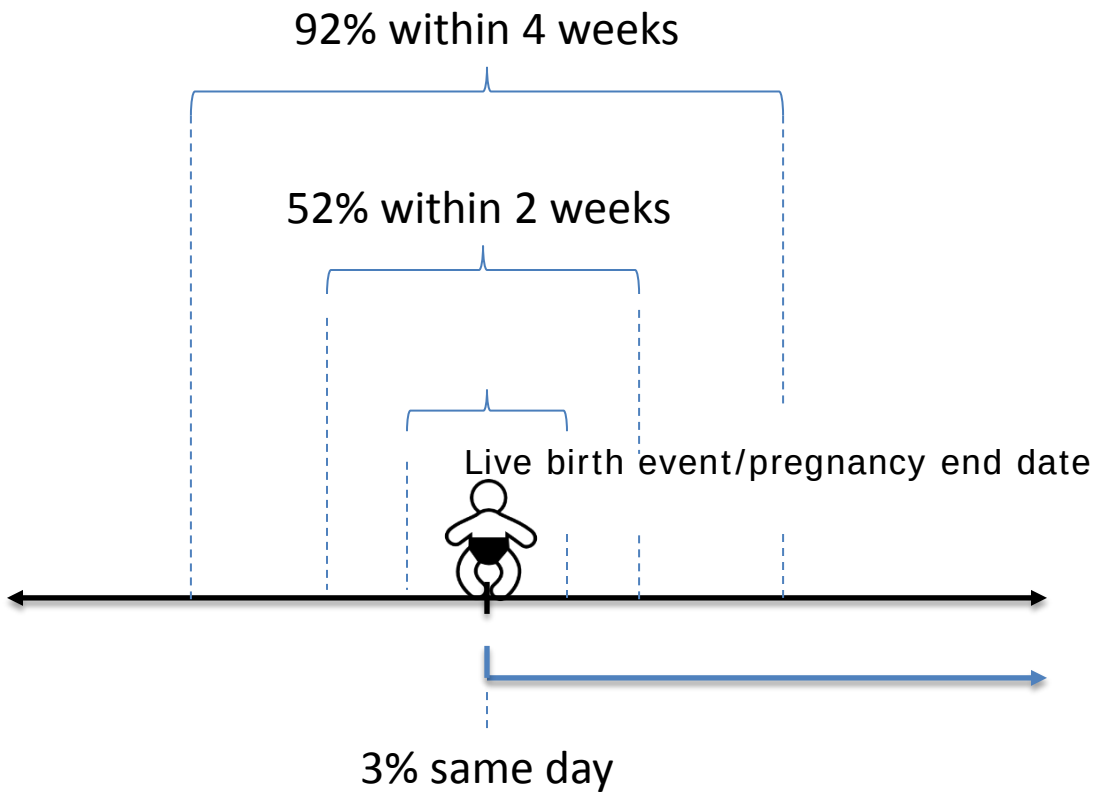
Cohort Construction

- MOP offspring
  - iv. Restrict where DOB is within 60 days of pregnancy episode end date
    - N mothers = 1,661,987
    - N offspring = 1,928,114
    - N records = 1,928,114



Cohort Construction

- Correspondence between algorithm birthdate and inferred birthdate
  - 92% within 4 weeks



Cohort Characterization

- Observation time, days from index

		MOPs	All	Std. diff.
Mothers	*Before birth*	-1029	-1074	0.06
	After birth	1071	997	0.07
Offspring	*After birth*	1054	1003	0.05

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Cohort Characterization

- Demographics
  - 5 year age categories
  - Index month and year

- Condition occurrence, procedure occurrence, and drug exposure covariates
  - Proportion of persons with event observed in 365 days before index for mothers and 365 days after index for offspring
  - Conditions and procedures were coded using the SNOMED-CT ontology
  - Drugs aggregated at 3rd, 4th, and 5th levels of the ATC and RxNorm ingredient level

- 54,779 and 46,130 covariates constructed for mother and offspring cohorts, respectively

Cohort Characterization

- R package and Shiny application for constructing cohorts, constructing covariates, evaluating MOP generalizability to all-mother and all-offspring, and populating MOPs information in FACT_RELATIONSHIP

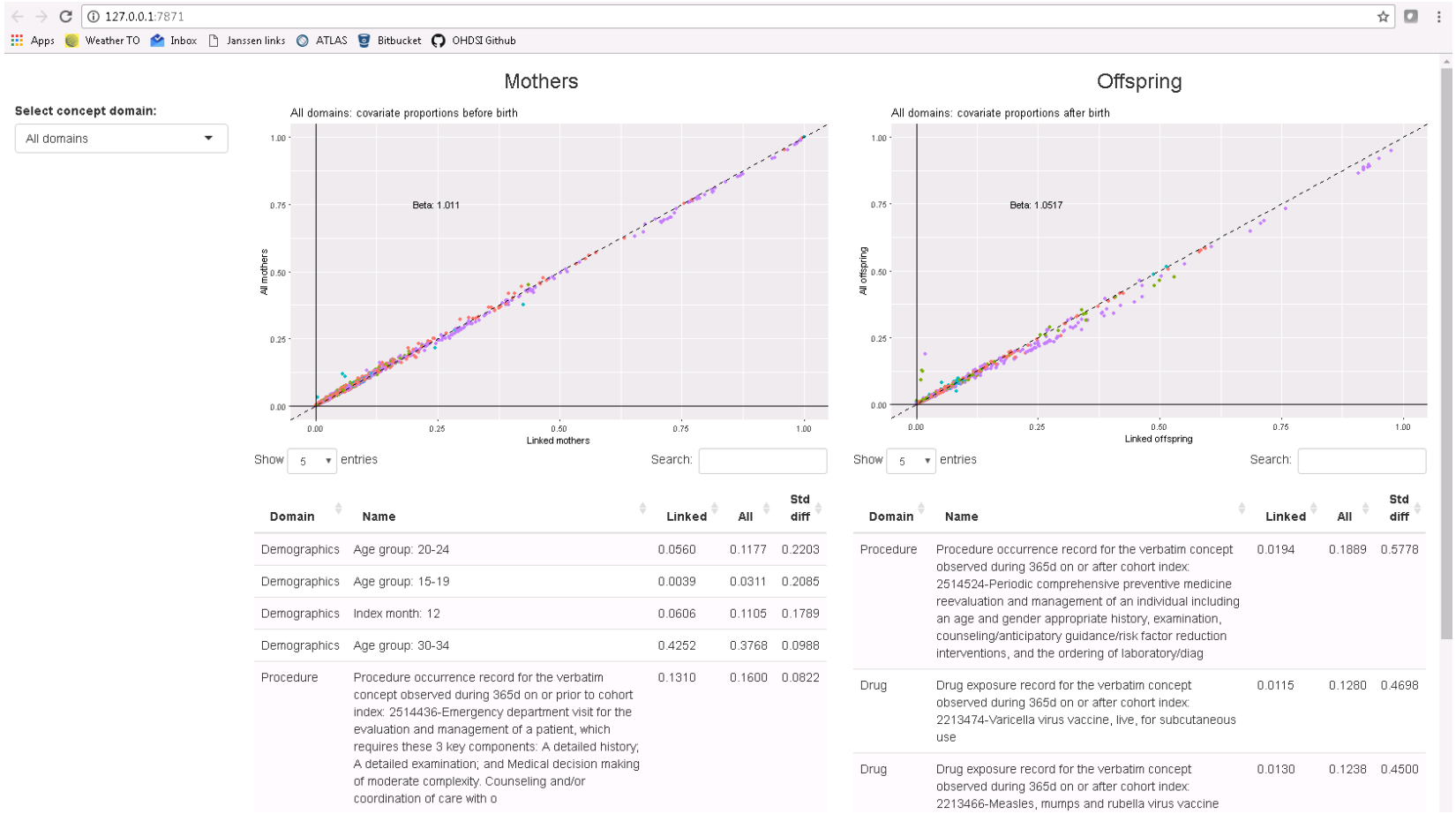
- Similarity suggests MOP generalizability to the commercial claims population

- High similarity supports use of MOP sample for teratogenic exposure studies

- Demo

Results – Interactive visualization

Figure 3. Application screen shot



Discussion & Next Steps

- Quick and inexpensive assembly of large MOPs cohorts for investigating maternal drug exposures and associated offspring outcomes

- Potential for pharmacoepidemiology studies of maternal drug exposures to be conducted outside the context of formal pregnancy registries while being HIPAA compliant

Discussion & Next Steps

FDA Drug Safety Communication: Selective serotonin reuptake inhibitor (SSRI) antidepressant use during pregnancy and reports of a rare heart and lung condition in newborn babies

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Safety Announcement
Additional Information for Patients
Additional Information for Healthcare Professionals
Data Summary

Safety Announcement

[12-14-2011] The U.S. Food and Drug Administration (FDA) is updating the public on the use of selective serotonin reuptake inhibitor (SSRI) antidepressants by women during pregnancy and the potential risk of a rare heart and lung condition known as persistent pulmonary hypertension of the newborn (PPHN). The initial Public Health Advisory in July 2006 on this potential risk was based on a single published study. Since then, there have been conflicting findings from new studies evaluating this potential risk, making it unclear whether use of SSRIs during pregnancy can cause PPHN.

Discussion & Next Steps

Paediatric and Perinatal Epidemiology
Affiliated to the Society for Pediatric and Perinatal Epidemiologic Research

doi: 10.1111/ppe.12004

Trends in the Use of Antiepileptic Drugs among Pregnant Women in the US, 2001–2007: A Medication Exposure in Pregnancy Risk Evaluation Program Study

Conclusions: AED use during pregnancy increased between 2001 and 2007, driven by a fivefold increase in the use of newer AEDs. Nearly one in eight AED-exposed deliveries involved the concomitant use of more than one AED. Additional investigations of the reproductive safety of newer AEDs may be needed.

RESEARCH

the bmj | *BMJ* 2015;350:h1035 | doi: 10.1136/bmj.h1035

Statins and congenital malformations: cohort study

Conclusions Our analysis did not find a significant teratogenic effect from maternal use of statins in the first trimester. However, these findings need to be replicated in other large studies, and the long term effects of in utero exposure to statins needs to be assessed, before use of statins in pregnancy can be considered safe.

Pregabalin use early in pregnancy and the risk of major congenital malformations

Neurology. 2017 May 23;88(21):2020-2025. doi: 10.1212/WNL.0000000000003959. Epub 2017 Apr 26.

CONCLUSIONS: Findings did not confirm the suggested teratogenic effects of pregabalin, although they cannot rule out the possibility of a small effect.

Discussion & Next Steps

June 2, 2015

Antidepressant Use Late in Pregnancy and Risk of Persistent Pulmonary Hypertension of the Newborn

Krista F. Huybrechts, MS, PhD[1,2]; Brian T. Bateman, MD, MSc[1,2,3]; Kristin Palmsten, ScD[4]; et al

» Author Affiliations | Article Information

JAMA. 2015;313(21):2142-2151. doi:10.1001/jama.2015.5605

Conclusions and Relevance Evidence from this large study of publicly insured pregnant women may be consistent with a potential increased risk of PPHN associated with maternal use of SSRIs in late pregnancy. However, the absolute risk was small, and the risk increase appears more modest than suggested in previous studies.

Discussion & Next Steps

- R package deployment to OHDSI GitHub

Contact

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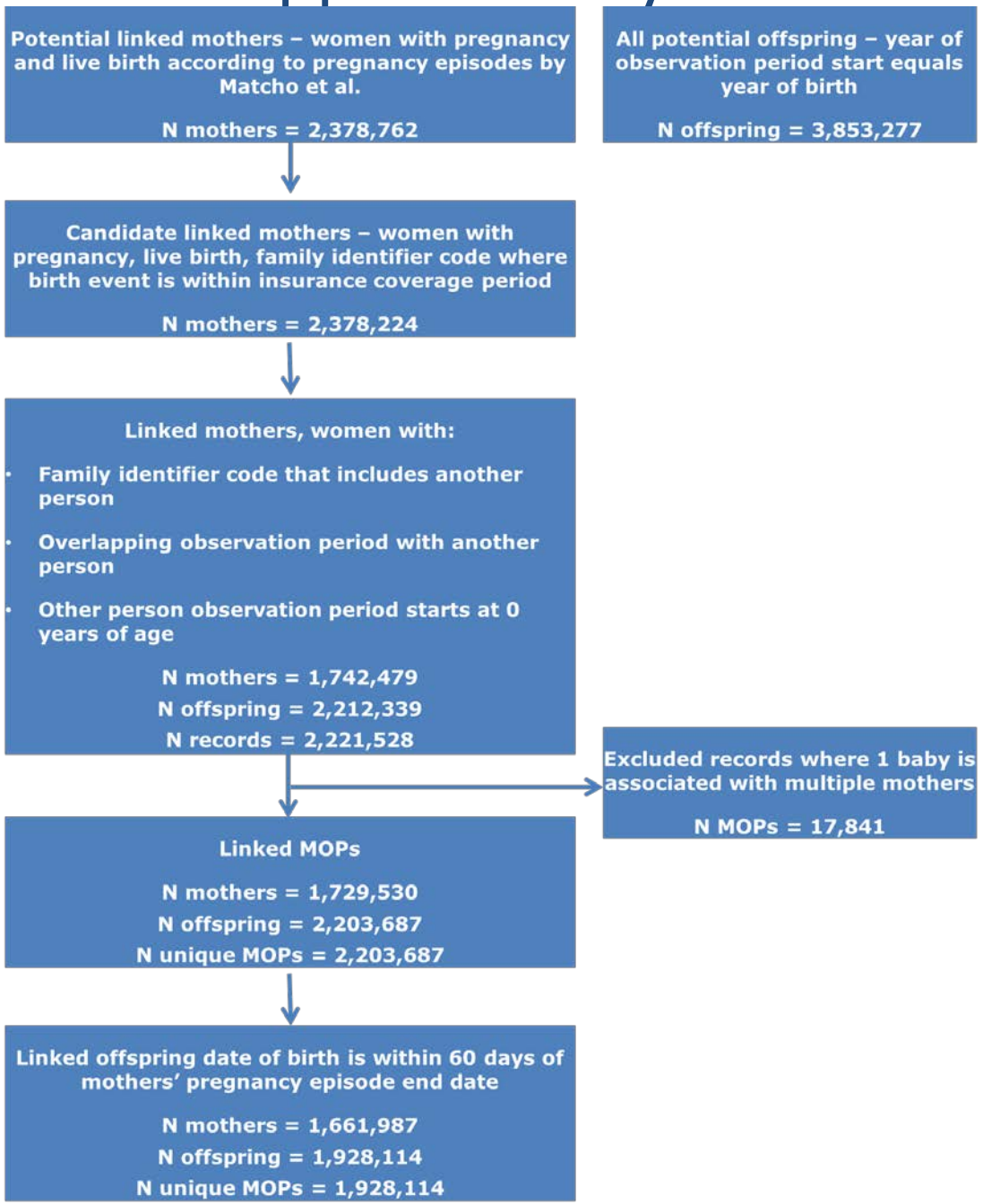
Supplementary



Supplementary

- Three cohorts were constructed and characterized
  - MOP cohort: composed of the mother and linked-offspring pairs
  - All-mothers cohort
  - All-offspring cohort
- A mother can be linked to one or more offspring and each offspring can be linked to one mother
- Mothers can have one or more pregnancy events
- MOP mothers
    i. Matcho et al. [14] algorithm identifies pregnancy episodes; limited to live births
    ii. Initial pool of women limited to those whose birth event was during insurance coverage period
    iii. Restricted to those who share a family identifier code and overlapping observation time with another person who is 0 years of age at database entry

  II. MOP offspring
    a. People associated with mothers in I.iii. are candidate offspring
    b. Restricted to those whose insurance coverage start date is within 60 days of linked mothers pregnancy end date

  III. All-mothers: mothers identified using the pregnancy episode identification algorithm [14] who have had a live birth outcome

  IV. All-offspring: people 0 years of age at database entry
- index date in the linked-mothers, linked-offspring, and all-mothers cohorts is the pregnancy episode end date; index date in the all-offspring cohort is date of birth