Exposure to SSRI/SNRI and depression in pregnancy and long-term childhood outcomes: the effect of modifying factors

First published: 04/10/2021

Last updated: 23/04/2024

Study Ongoing

Administrative details

EU PAS number

EUPAS43416

Study ID

43417

DARWIN EU® study

No

Study countries

- ☐ Belgium
- ☐ Croatia
- ☐ Denmark
- ☐ Finland

- [ ] France
- [ ] Germany
- [ ] Ireland
- [ ] Italy
- [ ] Malta
- [ ] Netherlands
- [ ] Poland
- [ ] Réunion
- [ ] Spain
- [ ] Sweden
- [ ] Switzerland
- [ ] Ukraine
- [ ] United Kingdom

Study description

Approximately, 10-20% of pregnant women suffer from depression and 4-10% use selective serotonin reuptake inhibitor (SSRI) antidepressants at some stage during pregnancy. There is conflicting evidence regarding the risk of congenital anomalies and long-term neurodevelopmental outcomes such as autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) associated with in utero exposure to SSRI and serotonin and norepinephrine reuptake inhibitors (SNRI). Existing studies in the literature often lack the power to assess the effect of time varying confounders such as variation in maternal disease status, breastfeeding, and transient or chronic interactions with other medications on risk of adverse outcomes, and few examine other aspects of neurodevelopment. This study will help create evidence-based clinical guidelines on risks and benefits of antidepressant treatment in pregnancy. The objectives of this study are: 1) to develop algorithms to identify and validate maternal depression, neurodevelopmental outcomes and breastfeeding in healthcare data sources. 2) to describe patterns of SSRI/ SNRI antidepressant

use before, during, and after pregnancy and during lactation. This includes describing co-medication patterns, predictors of discontinuation, switching patterns, and trajectories of use over time. 3) to assess the association between in utero exposure to SSRI / SNRIs and neurodevelopmental outcomes. It will examine the potential additional impact of maternal depression, breastfeeding and concomitant exposure to P-glycoprotein (P-gp) or breast cancer resistance protein (BCRP) transporter inhibitors/substrates on neurodevelopmental outcomes in children. A second objective is to perform a EUROmediCAT safety study to assess the risk of major congenital anomalies associated with exposure to SSRI / SNRIs in the first trimester of pregnancy, and to evaluate the impact of co-medication with P-gp or BCRP transporter substrates on risk.

Study status

Ongoing

Research institutions and networks

Institutions

Centre for Maternal, Fetal and Infant Research (MFIR), Ulster University

United Kingdom (Northern Ireland)

First published: 31/01/2023

Last updated: 20/03/2024

Institution | Educational Institution | ENCePP partner

Leibniz Institute for Prevention Research and Epidemiology - BIPS

Germany

First published: 29/03/2010

Last updated: 26/02/2024

Institution | Not-for-profit | ENCePP partner

Swansea University Medical School

United Kingdom

First published: 01/02/2024

Last updated: 01/02/2024

Institution | Educational Institution | Hospital/Clinic/Other health care facility

Ulster University

United Kingdom (Northern Ireland)

First published: 01/02/2024

Last updated: 20/03/2024

Institution | Educational Institution

The Foundation for the Promotion of Health and Biomedical Research of Valencia Region (FISABIO)

Spain

First published: 01/02/2024

Last updated: 05/11/2024

Institution

University of Oslo

First published: 01/02/2024

Last updated: 01/02/2024

Institution

NIHW, Finland, CHUT France, University of Ferrara Italy, CNR-IFC, Tuscany Italy, University of Oslo Norway, FISABIO Spain, SAIL Wales UK, EUROmediCAT UK

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Maria Loane

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 06/05/2019

Study start date
Planned: 04/01/2021

Actual: 08/05/2021

Data analysis start date
Planned: 01/03/2022

Date of interim report, if expected
Planned: 31/03/2023

Date of final study report
Planned: 31/12/2024

Sources of funding

- EU institutional research programme

More details on funding

Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 821520.

Study protocol

Protocol for DP 1.2 v01-10-2021.pdf(2.1 MB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Safety study (incl. comparative)

Main study objective:

To assess the association between in utero exposure to SSRI / SNRIs and neurodevelopmental outcomes and major congenital anomalies

Study Design

Non-interventional study design

Case-control

Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code

(N06A) ANTIDEPRESSANTS

ANTIDEPRESSANTS

Medical condition to be studied

Depression

Population studied

Age groups

Preterm newborn infants (0 – 27 days)

Term newborn infants (0 – 27 days)

Infants and toddlers (28 days – 23 months)

Children (2 to < 12 years)

Adolescents (12 to < 18 years)

Special population of interest

Pregnant women

Estimated number of subjects

6000000

Study design details

Outcomes

Children with neurodevelopmental outcomes, Children with congenital anomalies

Data analysis plan

Each partner contributing to the study will run centrally produced analysis scripts on their own data, and upload aggregated results or effect estimates to the ConcePTION platform for meta-analyses by the postdoc researcher. Descriptive analysis: categorical variables will be summarized by frequencies and proportions of each modality, including the proportion of missing data. Mean, standard deviation and error, median and interquartile range will be provided for continuous variables. 95% Confidence intervals (CI) will be estimated using Normal approximation for quantitative relevant parameters. Cells with small numbers will be collapsed. We will conduct univariate and multivariate logistic, poisson, or linear regression and Cox proportional hazards regression on the data sources, based on an agreed SAP.

Data management

Data sources

Data source(s)

EFEMERIS

German Pharmacoepidemiological Research Database

ARS Toscana

EUROmediCAT central database

SAIL Databank

Data source(s), other

NorPD, Emilia Romagna GPs drug prescription, Drugs and Pregnancy Finland

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Data sources (types)

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

Other

Data sources (types), other

Case-control surveillance database

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Unknown

Check completeness

Unknown

Check stability

Unknown

Check logical consistency

Unknown

Data characterisation

Data characterisation conducted

No