Improving teratogen surveillance in the UK

An exploratory linkage and disproportionality analysis of national congenital anomaly and primary care dispensing data

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UK teratogen surveillance capabilities are limited:

- Existing bespoke systems rely on active reporting and mainly focus on structural anomalies
- No routine monitoring of all medication
- No focussed monitoring of newly authorised medication
- No co-ordination of academic centres
- No single data system with national coverage
- Limited capabilities to detect emerging teratogens or determine teratogen exposure in the pregnant population

Bespoke systems:
- *UKTIS*
- *MHRA YCS*

Academic research centres:
- *Primary care datasets*
- *Not routinely interrogated*

EUROMEDICAT centres:
- *Anomalies only*
- *Not UK specific*

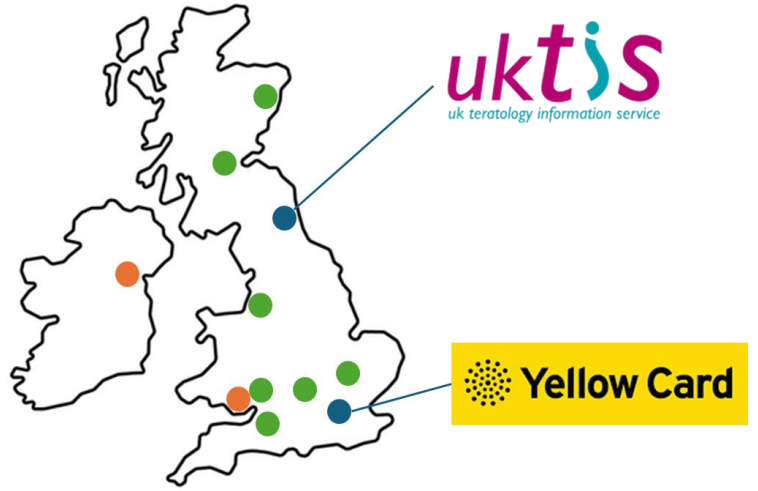

Figure 1: *Current teratogen monitoring efforts in the UK*

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Exploratory linkage and disproportionality analysis

What are the project and sub-study aims?

PROJECT AIM: Explore the use of national e-health record datasets to identify statistical signals which can focus denominator-based comparative cohort studies

SUB-STUDY AIMS: (1) Link English congenital anomaly and primary care medication dispensing data; (2) Case-control analysis of each exposure-anomaly pair

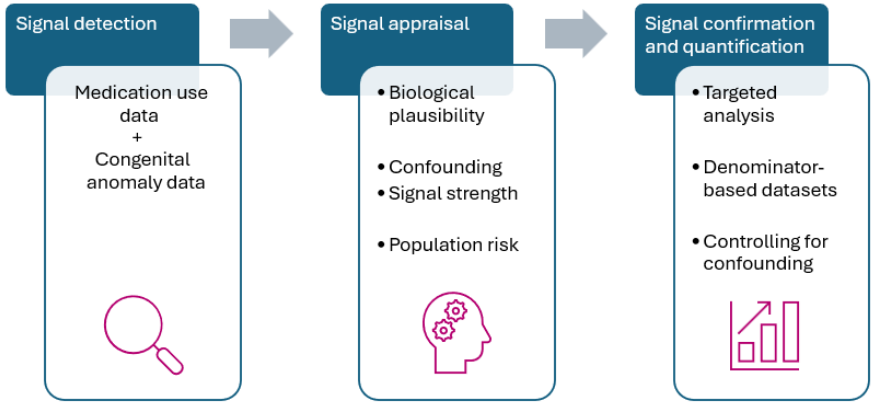

Figure 2: *Schematic of the proposed teratogen surveillance system*

NDRS
NATIONAL DISEASE REGISTRATION SERVICE

National (England) Congenital Anomaly Registry

CA Dataset

- Data from England
- Several data streams
- Collected national data since 2018
- Covers ~600k pregnancies/year
- Collects ~13k anomalies/year (~2.35%)
- Includes data on genetic anomalies/diagnoses
- Includes some maternal demographic data

NHS Business Services Authority

Primary care medication dispensing dataset

Medicines Dataset

- Captures ~1.2b events/year
- Main purpose is NHS medicines spending analysis
- Limited Rx data up to Apr-20
- From Apr-20 (e-prescribing)
- Now captures date of dispensing
- Still missing Rx dose/frequency

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Linkage of congenital anomaly and dispensing datasets

Which datasets were combined, and analysis technique

1. Dataset exclusions

CA cases:

- *No EDD*
- *Teratogen induced*
- *Genetic/cytogenetic aetiology*

2. Exposure classification

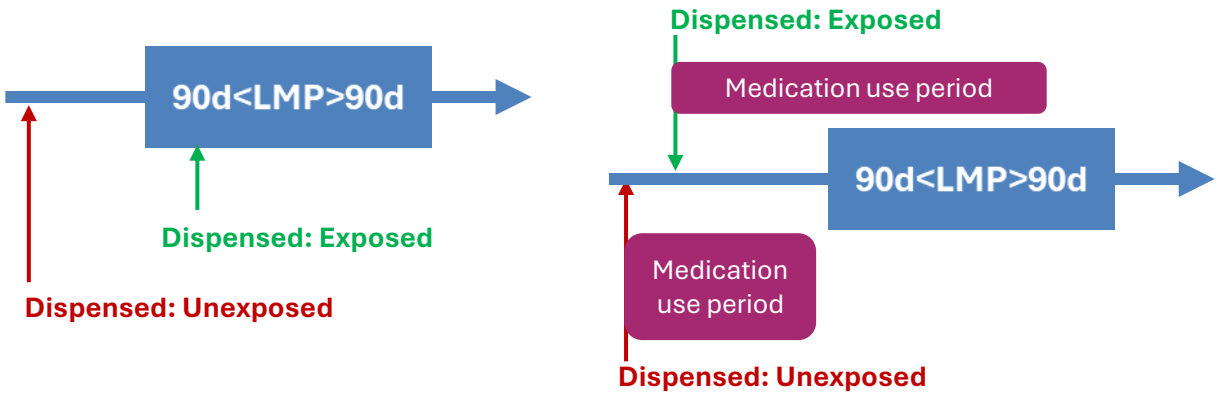

Figure 3: *Exposure classification algorithm*

3. Analysis methods

- Case-malformed control analysis - First trimester exposure incidence compared between those with a specific anomaly and all other anomaly cases in the analysis dataset (repeated for each exposure-anomaly pair)
- Calculation of reporting odds ratio (ROR) with 95% confidence interval and Yates' chi-squared statistic
- Sensitivity analysis - Bonferroni correction for multiple testing

4. Signal detection criteria

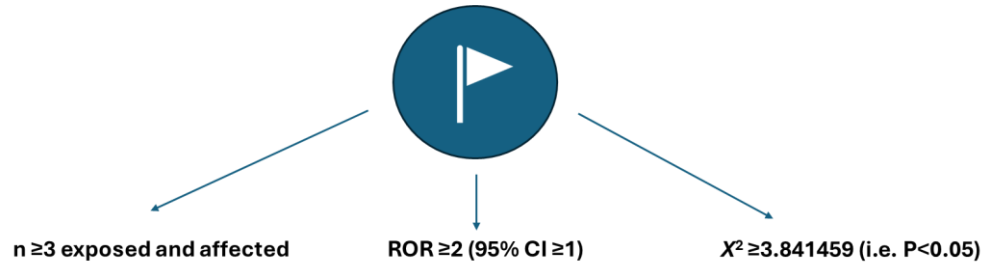

Figure 4: *Signal detection criteria for each case-control analysis*