

Algorithms to identify major congenital malformations in routinely collected healthcare data: A systematic review

Drug Safety

Melanie H. Jacobson^{1*}, Meritxell Sabidó², Ana Sofia Afonso³, Adebola Ajao⁴, Eman A. Alghamdi⁵, Susan E Andrade⁶, Dimitri Bennett⁷, Vineetkumar Kharat⁸, Marie-Laure Kürzinger⁹, Maryline Le Noan-Lainé¹⁰, Ditte Mølgaard-Nielsen¹¹, Gayle Murray¹, Elena Rivero-Ferrer¹², Sandra Lopez-Leon^{8,13}

¹ Global Epidemiology, Johnson & Johnson, Titusville, NJ, USA

² Patient Focused Real World Evidence, Merck Healthcare KGaA, Darmstadt, Germany

³ Global Patient Safety, Eli Lilly BV, Utrecht, the Netherlands

⁴ United States Food and Drug Administration, MD, USA

⁵ Saudi Food and Drug Authority, Riyadh, Saudi Arabia

⁶ Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA, USA

⁷ Global Evidence and Outcomes, Takeda Development Center Americas, Inc. Cambridge, MA, USA

⁸ Global Drug Development, Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA

⁹ Global Epidemiology and Benefit Risk, Patient Safety & Pharmacovigilance, Sanofi, Gentilly, France.

¹⁰ Global Patient Safety, Eli Lilly, Cork, Ireland

¹¹ Global Safety, Novo Nordisk, Søborg, Denmark

¹² Pharmacoepidemiology and Risk Management, RTI Health Solutions, Barcelona, Spain

¹³ Rutgers Center for Pharmacoepidemiology and Treatment Science, Rutgers University, New Brunswick, New Jersey, USA

*Corresponding author: mjacob17@its.jnj.com

Supplemental Material. Search terms and rationale for selection

1. Terms to identify MCM
Congenital Abnormalities[Mesh:NoExp] OR congenital abnormalit*[tiab] OR congenital deformit*[tiab] OR congenital defect*[tiab] OR birth defect*[tiab] OR congenital anomal*[tiab] OR congenital malformation*[tiab] OR Teratogens[Mesh]
2. Terms to identify electronic healthcare data
"Premier"[tiab] OR "Solucient"[tiab] OR "Cerner"[tiab] OR "Ingenix"[tiab] OR "LabRx"[tiab] OR "IHCIS"[tiab] OR "marketscan"[tiab] OR "market scan"[tiab] OR Truven[tiab] OR IBM Watson[tiab] OR Merative[tiab] OR Optum[tiab] OR "Medstat"[tiab] OR "Thomson"[tiab] OR "pharmetrics"[tiab] OR "healthcore"[tiab] OR "HealthCore Integrated Research database"[tiab] OR HIRD[tiab] OR "united healthcare"[tiab] OR "UnitedHealthcare"[tiab] OR "UHC"[tiab] OR "GPRD"[tiab] OR "general practice research database"[Text Word] OR "Clinical Practice Research Datalink"[Text Word] OR "Research Database"[All] OR "Group Health"[tiab] OR "HCUP"[tiab] OR ("Healthcare Cost"[tiab] AND "Utilization Project"[tiab]) OR ("Health Care Cost"[tiab] AND "Utilization Project"[tiab]) OR "MEPS"[tiab] OR "Medical Expenditure Panel Survey"[tiab] OR "NAMCS"[tiab] OR "National Hospital Ambulatory Medical Care Survey"[tiab] OR "National Ambulatory Medical Care Survey"[tiab] OR "NHIS"[tiab] OR "National Health Interview Survey"[tiab] OR "Kaiser"[tiab] OR "Health Maintenance Organization"[tiab] OR "HMO"[tiab] OR "Cleveland Clinic"[tiab] OR "Lovelace"[tiab] OR "Department of Defense"[tiab] OR "Henry Ford"[tiab] OR "i3 Drug Safety"[tiab] OR "i3"[tiab] OR "Aetna"[tiab] OR

"Humana"[tiab] OR "Wellpoint"[tiab] OR "IMS"[tiab] OR "Intercontinental Marketing Services"[tiab] OR "IMS Health"[tiab] OR "Geisinger"[tiab] OR "GE Healthcare"[tiab] OR "MQIC"[tiab] OR "PHARMO"[tiab] OR PPRN[tiab] OR Perinet[tiab] OR "Perinatal Research Network"[tiab] OR "Pilgrim"[tiab] OR "Puget Sound"[tiab] OR "Regenstrief"[tiab] OR "Saskatchewan"[tiab] OR "Tayside"[tiab] OR "MEMO"[tiab] OR "Veterans Affairs"[tiab] OR "Partners Healthcare"[tiab] OR "Mayo Clinic"[tiab] OR "Rochester Epidemiology"[tiab] OR "Indiana Health Information Exchange"[tiab] OR "Indiana Health"[tiab] OR "Intermountain"[tiab] OR "THIN"[tiab] OR "The health improvement network"[Text Word] OR "blue cross"[tiab] OR "health partners"[tiab] OR "health plan"[tiab] OR "health services"[All] OR "Nationwide Inpatient Sample"[tiab] OR "National Inpatient Sample"[tiab] OR "medicaid"[tiab] OR "medicare"[tiab] OR "Outcome Assessment"[tiab] OR "insurance database"[tiab] OR "Data Warehouse"[tiab] OR "ICD-9"[All] OR "international statistical classification"[All] OR "international classification of diseases"[All] OR "ICD-10"[All] OR "Database Management Systems"[Mesh] OR "Medical Records Systems, Computerized"[Mesh] OR "CPT"[All] OR "Current procedural terminology"[All] OR "drug surveillance"[tiab] OR ("claims"[tw] AND "administrative"[tw]) OR ("claims"[tw] AND "insurance"[tw]) OR ("data"[tw] AND "administrative"[tw]) OR ("claims"[tw] AND "database"[tw]) OR ("claims"[tw] AND "data"[tw]) OR "Databases, Factual"[Mesh] OR "Databases as topic"[Mesh] OR "Medical Record Linkage"[Mesh] OR "ICD-9-CM"[All Fields] OR "ICD-10-CM"[All Fields] OR "READ code"[All Fields] OR "ICPC code"[All Fields] OR ("TennCare" [tiab]) OR ("RAMQ" [tiab]) OR ("Cigna" [tiab]) OR ("HealthVerity" [tiab]) OR "HCA" [tiab] OR "TriNetX"[tiab] OR "PCORnet"[tiab] OR "National Patient-Centered Clinical Research Network"[tiab] OR

((british columbia[tiab]) AND ((health[tiab]) OR (data[tiab]) OR (database[tiab]) OR (population[tiab])))

OR ("CIHI"[tiab]) OR

((manitoba[tiab]) AND ((center for health policy[all fields]) OR (population[tiab]) OR (health insurance[tiab]))) OR

((ontario[tiab]) AND ((population[tiab]) OR (OHIP[tiab]) OR (registered persons database[tiab]) OR (health insurance [tiab]) OR (ICES[All Fields]) OR (Institute for Clinical Evaluative Sciences[All Fields])))

OR ((Alberta[tiab]) AND ((health[tiab]) OR (data[tiab]) OR (database[tiab]) OR (population[tiab]) OR (Alberta Health and Wellness[All Fields])))

OR (electronic medical record*[Text Word]) OR "health insurance database"[Text Word] OR (electronic health record*[Text Word]) OR "GePARD"[tiab] OR "EUROmediCAT"[tiab] OR "EUROCAT"[All] OR "Danish"[tiab] OR "Denmark"[tiab] OR "Valencian"[tiab] OR "Finnish"[tiab] OR "Finland"[tiab] OR "EFEMERIS"[tiab] OR "SNIIRAM"[tiab] OR "SNDS"[tiab] OR "Emilia"[tiab] OR "Tuscany"[tiab] OR "Caserta"[tiab] OR "Catalunya"[tiab] OR "SIDIAP"[tiab] OR "FISABIO"[tiab] OR "IPCI"[tiab] OR "Mondriaan"[tiab] OR "Norwegian"[tiab] OR "Norway"[tiab] OR "Scotland"[tiab] OR "SAIL"[tiab] OR "Malta"[tiab] OR "Swedish"[tiab] OR "Sweden"[tiab] OR "regional registers"[tiab:~5] OR "linked registers"[tiab:~5] OR "national registers"[tiab:~5] OR "Metropolitan Atlanta"[tiab] OR ("registry"[tiab] AND ("birth defects"[tiab] OR "congenital"[tiab])) OR "National Birth Defects Prevention Network"[tiab]

3. Terms to identify studies likely to contain algorithms

Retrospective cohort[Text Word] OR (epidemiology [MeSH Terms]) OR (Epidemiologic Methods[MeSH Terms]) OR (phenotype[Text Word]) OR (Validation Study[Publication Type]) OR (positive predictive value[Text Word]) OR (Validation Studies as Topic[MeSH]) OR (Sensitivity and Specificity[MeSH]) OR (Diseases Category/epidemiology[MeSH]) OR (Predictive Value of Tests[MeSH]) OR (Reproducibility of Results[MeSH]) OR (Predictive Value[Text Word]) OR (Algorithm) OR (Algorithm[Mesh]) OR ("Database study"[tiab])
4. Terms to identify study population "Pregnant Women"[Mesh] OR "Maternal-Fetal Relations"[Mesh] OR "Pregnancy"[Mesh] OR "Fetal Development"[Mesh] OR "Infant"[Mesh] OR "Maternal Exposure"[Mesh]
5. Terms to exclude studies not likely to utilize administrative and claims data ("Editorial" [pt] OR "Letter" [pt] OR "Meta-Analysis" [pt] OR "Randomized Controlled Trial" [pt] OR "Clinical Trial"[pt] OR "Clinical Trial, Phase I" [pt] OR "Clinical Trial, Phase II" [pt] OR "Clinical Trial, Phase III" [pt] OR "Comment" [pt] OR "Controlled Clinical Trial" [pt] OR "case reports" [pt] OR "Clinical Trials as Topic" [Mesh] OR "double-blind" [All] OR "placebo-controlled" [All] OR "pilot study" [All] OR "pilot projects" [Mesh] OR "Review" [pt] OR "Systematic Review"[pt] OR "Prospective Studies" [Mesh]) OR biomarker[Title/Abstract] OR "Practice Guideline" [Publication Type]
6. Combining Searches 1 2, 3, 4 excluding Search 5 Filters: English only, from January 1, 2010 – April 11, 2025 N=2,242

The general search strategy was developed based on prior work by Mini-Sentinel and the Observational Medical Outcomes Partnership (OMOP) [1, 2]. It involved a combination of the following components: (1) keywords and Medical Subject Heading (MeSH) terms to identify records of MCMs; (2) terms designed to capture studies utilizing routinely collected healthcare data; (3) terms aimed at identifying epidemiologic studies likely to contain algorithms; (4) terms to identify the study population of interest (i.e., pregnant women and offspring); and (5) exclusion terms. The detailed search terms are available in the Supplemental Material.

Regarding the terms in component (2), which aimed to identify studies based on routinely collected healthcare data, we included those specified by Mini-Sentinel/OMOP and additionally included terms for other known electronic healthcare databases [3]. To build the terms related to MCMs in component (1), we first identified terms used in published meta-analyses [4-6]. Once a preliminary list was formed, topic experts and an expert librarian gave input in the search terms. As recommended by the Mini-Sentinel authors, MeSH terms were generally preferred as search terms due to their likely specificity.

References

1. Carnahan RM. Mini-Sentinel's systematic reviews of validated methods for identifying health outcomes using administrative data: summary of findings and suggestions for future research. *Pharmacoepidemiol Drug Saf.* 2012 Jan;21 Suppl 1:90-9.
2. Carnahan RM, Moores KG. Mini-Sentinel's systematic reviews of validated methods for identifying health outcomes using administrative and claims data: methods and lessons learned. *Pharmacoepidemiol Drug Saf.* 2012 Jan;21 Suppl 1:82-9.
3. Thurin NH, Pajouheshnia R, Roberto G, Dodd C, Hyeraci G, Bartolini C, et al. From Inception to ConcePTION: Genesis of a Network to Support Better Monitoring and Communication of Medication Safety During Pregnancy and Breastfeeding. *Clinical Pharmacology & Therapeutics.* 2022 2022/01/01;111(1):321-31.
4. Sun L, Xi Y, Wen X, Zou W. Use of metoclopramide in the first trimester and risk of major congenital malformations: A systematic review and meta-analysis. *PLoS One.* 2021;16(9):e0257584.
5. Lassen D, Ennis ZN, Damkier P. First-Trimester Pregnancy Exposure to Venlafaxine or Duloxetine and Risk of Major Congenital Malformations: A Systematic Review. *Basic Clin Pharmacol Toxicol.* 2016 Jan;118(1):32-6.
6. Kaplan YC, Richardson JL, Keskin-Arslan E, Erol-Coskun H, Kennedy D. Use of ondansetron during pregnancy and the risk of major congenital malformations: A systematic review and meta-analysis. *Reprod Toxicol.* 2019 Jun;86:1-13.