Improving data collection as part of pregnancy safety studies: Towards standardization of data elements in pregnancy reports from public and private partners –A contribution from the ConcePTION Project

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INTRODUCTION

- Pregnant women are often excluded from clinical trials related to drug safety.
- Evidence from post-marketing observational studies is often heterogeneous due to varying definition of key elements.
- A reference framework of **Core Data Elements (CDE)** to study drug use during pregnancy has been developed as part of the ConcepTION project.
- AIM: Assess **the adherence to the CDE items** of **data collected by different stakeholders** (public and private institutions) researching drug safety in multiple sclerosis treatment.

METHODS

- Data Access providers (DAPs) were **A) Pregnancy registries**, **B) Enhanced pharmacovigilance programs (PRIM)** and **C) Teratology information services (TIS)**

A. Gilenya Novartis	B. Gilenya PRIM Novartis	C. TIS from ENTIS
Aubagio Sanofi	MAPLE-MS Merck KgaA	- Swiss TIS
Aubagio OTIS Sanofi		- Israel TIS (Zerifin & Jerusalem)
The Dutch Pregnancy Drug Register (Lareb)		- UK TIS

- Data collection: **DAPs were asked to answer Yes/No questions for each CDE item**
  - Can the CDE item be taken directly from the database ? → if Yes = **DIRECTLY TAKEN**
  - Can the CDE item be derived by combining data from the database ? → if Yes = **DERIVED**
  - Does the DAP collect data which is similar but divergent from the CDE item → If Yes = **DIVERGENT**
  - Is the CDE item missing from the database ? → if Yes = **MISSING**

CDE items	TOTAL DAPs n Directly taken	Derived	Divergent	Missing	TOTAL DAPs % Directly taken	Derived	Divergent	Missing
Database Administrative Details								
Mother case identifier	7	0	0	0	100%	0%	0%	0%
Baby case identifier	7	0	0	0	100%	0%	0%	0%
Mother-Baby case identifier/link	6	1	0	0	86%	14%	0%	0%
Primary reporter type	7	0	0	0	100%	0%	0%	0%
Primary reporter contact details	7	0	0	0	100%	0%	0%	0%
Initial report date	7	0	0	0	100%	0%	0%	0%
Prospective status	7	0	0	0	100%	0%	0%	0%
Maternal Details								
Mother's date of birth	6	0	1	0	86%	0%	14%	0%
Mother's age at LMP	4	2	1	0	57%	29%	14%	0%
Maternal BMI pre-pregnancy	3	2	1	1	43%	29%	14%	14%
Pregnancy Details								
Date of LMP	7	0	0	0	100%	0%	0%	0%
EDD	6	1	0	0	86%	14%	0%	0%
Source of directly-reported EDD	5	2	0	0	71%	29%	0%	0%
Plurality	6	1	0	0	86%	14%	0%	0%
Prenatal test(s)	7	0	0	0	100%	0%	0%	0%
Maternal Medical History								
Maternal pre-pregnancy medical conditions (history)	7	0	0	0	100%	0%	0%	0%
Medication Exposure Details								
Drug name(s)	7	0	0	0	100%	0%	0%	0%
Drug start date	5	2	0	0	71%	29%	0%	0%
Drug stop date	5	2	0	0	71%	29%	0%	0%
Drug indication(s)	6	1	0	0	86%	14%	0%	0%
Peri-LMP exposure	5	2	0	0	71%	29%	0%	0%
Trimester 1 exposure	5	2	0	0	71%	29%	0%	0%
Trimester 2 exposure	5	2	0	0	71%	29%	0%	0%
Trimester 3 exposure	5	2	0	0	71%	29%	0%	0%
Route of exposure	6	0	0	1	86%	0%	0%	14%
Dose per use	6	1	0	0	86%	14%	0%	0%
Frequency of use	5	1	0	1	71%	14%	0%	14%
Maternal Outcome Details								
Maternal medical conditions arising in pregnancy	7	0	0	0	100%	0%	0%	0%
Maternal death	6	0	0	1	86%	0%	0%	14%
Pregnancy Outcome Details								
Pregnancy outcome collection status	6	1	0	0	86%	14%	0%	0%
Date of end of pregnancy	6	1	0	0	86%	14%	0%	0%
Gestational age at end of pregnancy	6	1	0	0	86%	14%	0%	0%
Induced termination	7	0	0	0	100%	0%	0%	0%
Ectopic pregnancy	6	1	0	0	86%	14%	0%	0%
Stillbirth	6	1	0	0	86%	14%	0%	0%
Spontaneous abortion	7	0	0	0	100%	0%	0%	0%
Molar pregnancy	6	0	0	1	86%	0%	0%	14%
Blighted ovum	6	0	0	1	86%	0%	0%	14%
Live birth	7	0	0	0	100%	0%	0%	0%
Live Stillborn Outcome Details								
Gestational timing of live/stillborn offspring	6	1	0	0	86%	14%	0%	0%
Infant birth weight	7	0	0	0	100%	0%	0%	0%
Infant sex	7	0	0	0	100%	0%	0%	0%
Infant head circumference	5	1	0	1	71%	14%	0%	14%
Infant birth length	7	0	0	0	100%	0%	0%	0%
Small for Gestational Age at delivery	4	3	0	0	57%	43%	0%	0%
Large for Gestational Age at Delivery	4	3	0	0	57%	43%	0%	0%
Neonatal Infant Outcome Details								
Complications in the first year of life	7	0	0	0	100%	0%	0%	0%
Postnatal death of live born infant	7	0	0	0	100%	0%	0%	0%
Malformation Details								
Congenital anomaly	7	0	0	0	100%	0%	0%	0%
Details of all congenital anomaly(ies)	6	1	0	0	86%	14%	0%	0%
Infant malformation case classification	3	4	0	0	43%	57%	0%	0%

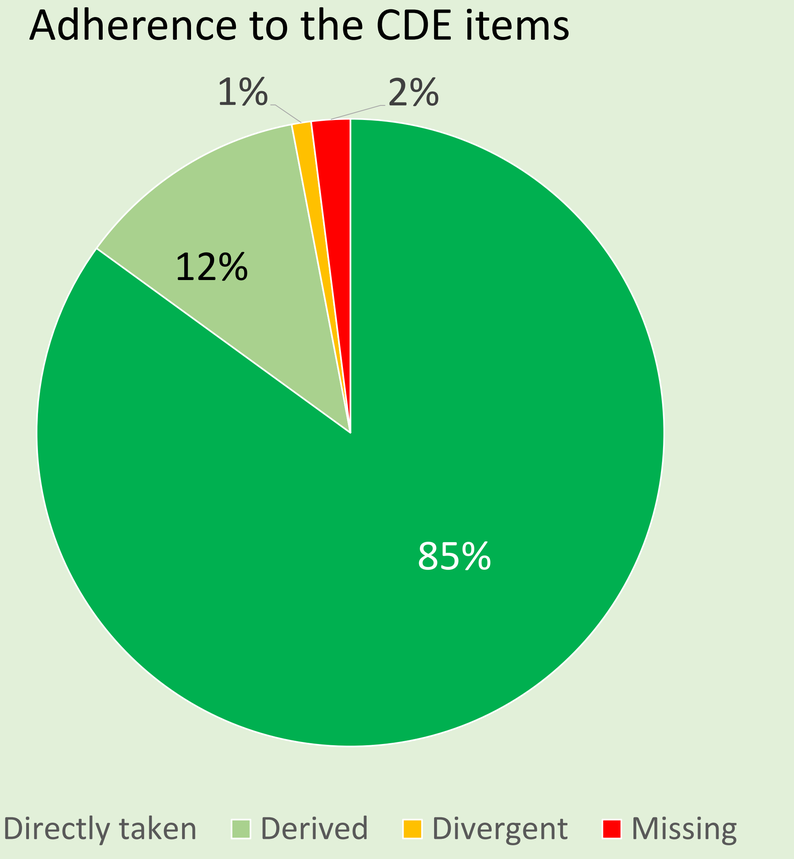
RESULTS

CDE = 51 specific items

- 305/357 (85%) CDE items were directly taken
- 42/357 (12%) CDE items were derived
- 3/357 (1%) CDE items were divergent
- 7/357 /2%) CDE items were missing

Divergent items:
- Mother date of birth
- Mother's age at last menstrual period
- Maternal BMI pre-pregnancy

Missing items
- Maternal BMI pre-pregnancy
- Route of exposure
- Frequency of use
- Maternal death outcome
- Molar pregnancy outcome
- Blighted ovum outcome
- Infant head circumference outcome

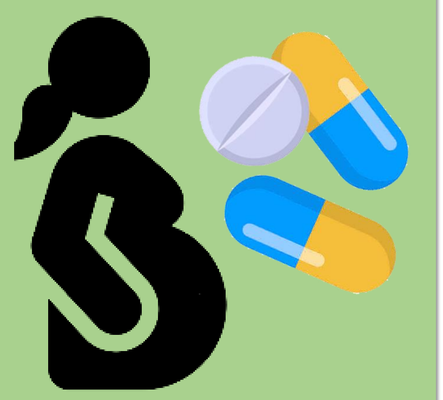


CONCLUSION

DAPs were able to match a very high proportion of the CDE items, indicating that alignment of dataset content and clinical definitions by diverse stakeholders is feasible, an important prerequisite for harmonization and exchange of data analysis.

This indicates that previously collected data from different data collection methods could be exploitable as such.

The low proportion of missing or divergent items and the possibility to adapt these variables to finally match current standards give the perspective of qualitative pharmacovigilance data collection in the future.



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