20th November 2020

ENCePP in the time of COVID-19

Review of post-authorisation studies registered in the EU PAS register

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Introduction

- Several studies explored the EU PAS register to analyse **characteristics of post-authorisation studies (PASs) in Europe**;
- A part from two recently published papers investigating specifically studies that evaluated effectiveness of RMMs, the last publication exploring general characteristics of studies in the EU PAS register analyzed studies registered until **Oct 2016**;

British Journal of Clinical Pharmacology

Br J Clin Pharmacol (2017) **83** 884–893 884

DRUG SAFETY

Lessons learned on the design and the conduct review c

F1000Research

F1000Research 2017, 6:1447 Last updated: 20 NOV 2017

Check for updates

RESEARCH ARTICLE

REVISED An analysis of characteristics of post-authorisation studies registere referees: 2 appro

Robert Carroll[1], Sreera
Laura McDonald[2]

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DOI: 10.1002/pds.4434

REVIEW

WILEY

A review of studies evaluating the effectiveness of risk minimisation m electronic Regi

Pareen Vora[1] | Esth
Vineet Singh[4] | Alex A

British Journal of Clinical Pharmacology

Br J Clin Pharmacol (2019) **85** 476–491 476

REVIEW

Study design, process and outcome indicators of post-authorization studies aimed at evaluating the effectiveness of risk minimization measures in the EU PAS Register

Introduction

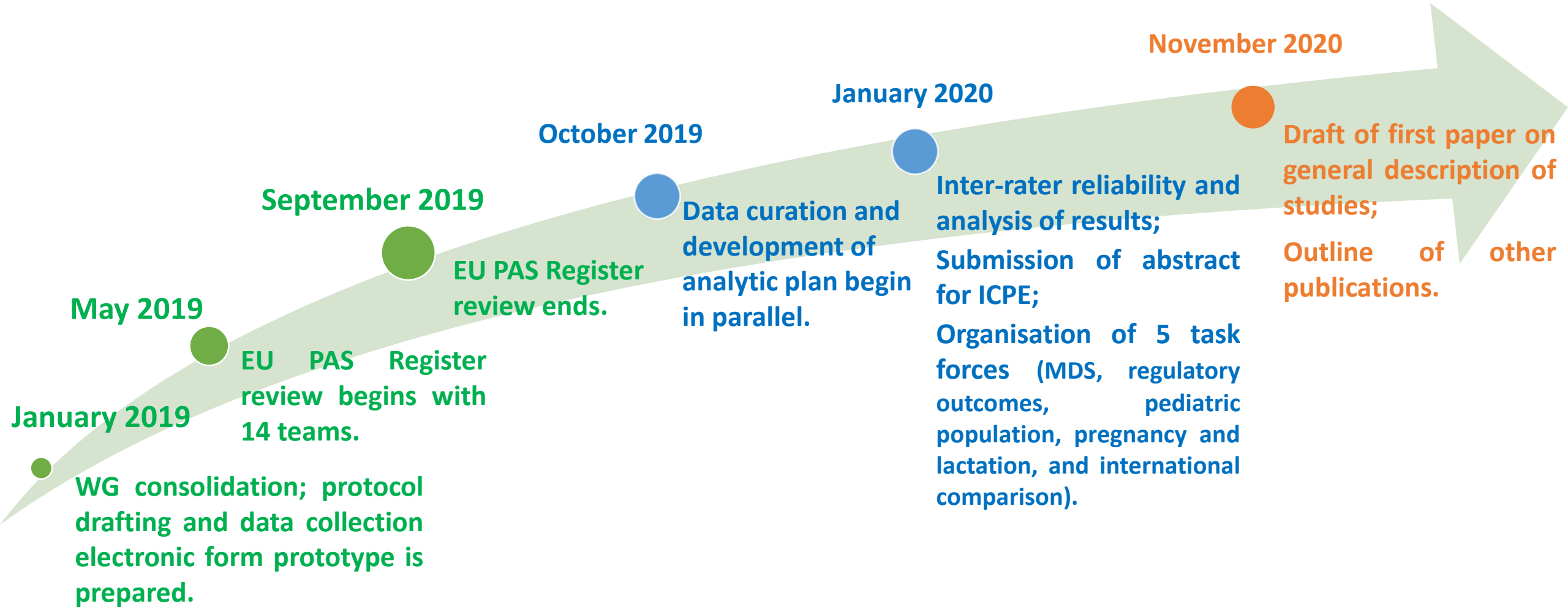
- Several studies explored the EU PAS register to analyse **characteristics of PASs in Europe**;
- A part from two recently published papers investigating specifically studies that evaluated effectiveness of RMMs, the last publication exploring general characteristics of studies in the EU PAS register analyzed studies registered untill **Oct 2016**;
- A large number of studies have been registered in the EU PAS register in the last three years;
- Aim of this work was to update the revision of the characteristics of PASs in the EU PAS register with special interest on **multiple database studies (MDSs).**

Agenda

- ✓ Methodological approach for EU PAS register review
- ✓Main results of descriptive analysis
- ✓Update on specific task force assessments:
  - a) Multiple database studies
  - b) Regulatory outcomes of registered PASs
  - c) Studies in pregnancy and lactation
  - d) Studies in paediatric populations
  - e) International comparison of studies

Methodological approach for EU PAS register review

The long journey of the review of EU PAS Register



Stepwise approach from data collection to analysis

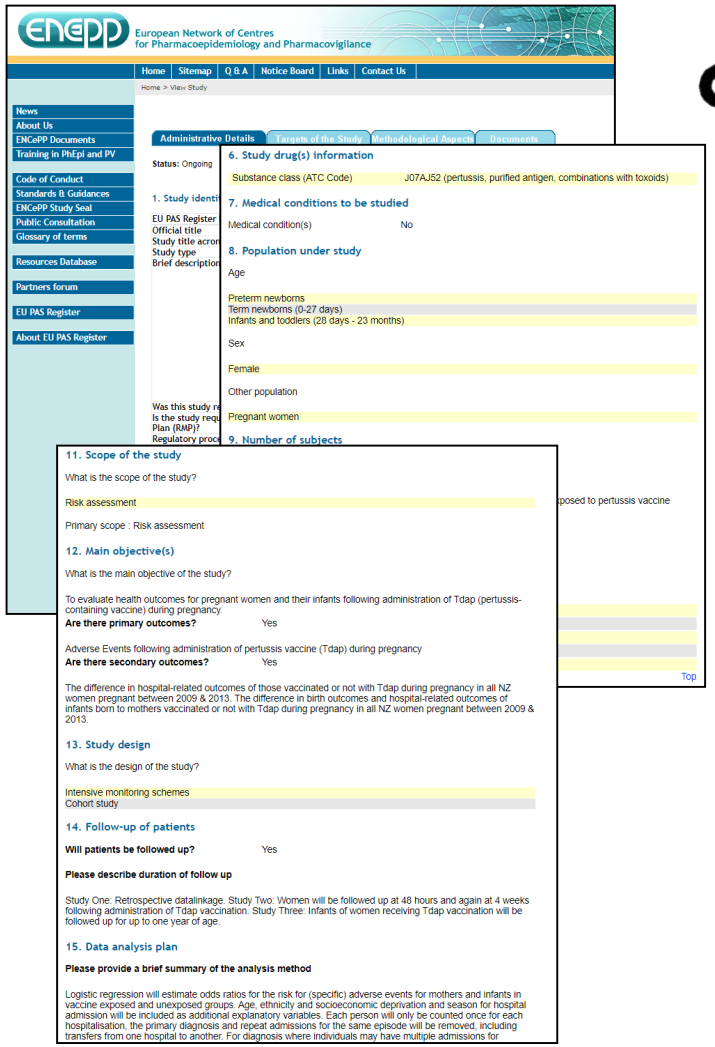
Development of data collection form for transferring key information from EU PAS register into the analytical dataset

Distribution of studies across 14 centres for completion of data collection form with information from 1,426 studies from EU PAS register inception up to 31 December 2018

Quality check, re-evaluation and descriptive analysis of collected data

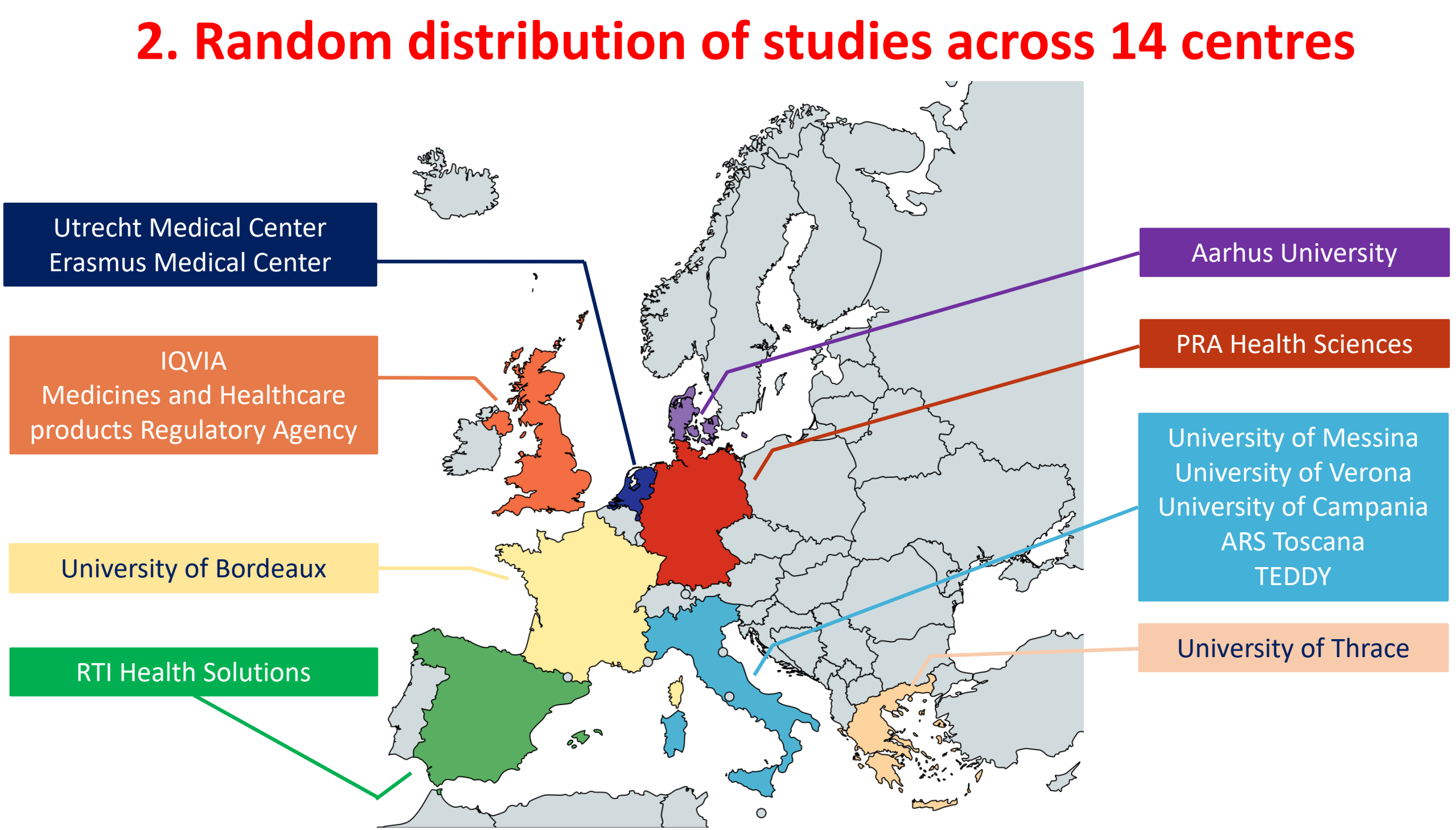
For key variables, independent validation of random sample of studies and inter-rater agreement analysis

1. Development of data collection form

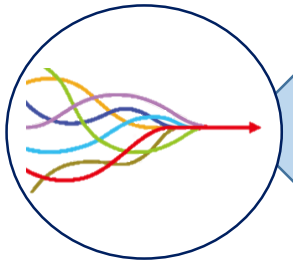


Title	Status_of_Study	Funding_source	Data_collection	Secondary_data	Multiple_database_study	Study_type_new_classification
Current raltegravir use: clinical practice in UK centres	ONGOING	Funded by pharmaceutical company	Mixed	More than 1	Yes	Observational study
Post-market clinical follow-up study – Retrospective evaluation o	FINALISED	Funded by pharmaceutical company	Secondary	EHR	Yes	Observational study
Validation of a US Health Care Claims Database for the Study of	FINALISED	Funded by pharmaceutical company	Secondary	More than 1	Yes	Observational study
Organization of Teratology Information Specialists (OTIS) Vedol	ONGOING	Funded by pharmaceutical company	Mixed	More than 1	Yes	Observational study
Forteo/Forsteo post-approval osteosarcoma surveillance study	FINALISED	Funded by pharmaceutical company	Secondary	More than 1	Yes	Observational Study
Outpatient care with long-acting bronchodilators:	ONGOING	Funded by pharmaceutical company	Mixed	Existing registry	Yes	Observational study
Non-interventional Cohort Study to Investigate Sertindole Prescri	FINALISED	Funded by pharmaceutical company	Secondary	Chart abstraction	Yes	Observational study
MULTICENTER PROSPECTIVE OBSERVATIONAL STUDY OI	FINALISED	Funded by pharmaceutical company	Primary	Not applicable	No	Clinical trial
CONTOUR Australia: Condition of Submental Fullness and Trea	ONGOING	Funded by pharmaceutical company	Primary	Not applicable	No	Observational study
An Observational Post-Authorisation Safety Specialist Cohort M	FINALISED	Funded by pharmaceutical company	Primary	Not applicable	No	Observational study
An observational multicenter study on antibiotic resistance of He	ONGOING	Funded by pharmaceutical company	Primary	Not applicable	No	Observational study
A Prospective, Observational Study of Individuals Who Serocon	ONGOING	Funded by pharmaceutical company	Primary	Not applicable	No	Observational study
Multi-centre study of the in vitro activity of ceftolozane/tazobactar	ONGOING	Funded by pharmaceutical company	Primary	Not applicable	No	Other
A Cross-sectional Survey of Patients and Caregivers (20150228)	ONGOING	Funded by pharmaceutical company	Primary	Not applicable	No	Survey
Post-marketing study of ropinirole prolonged release tablets in F	FINALISED	Funded by pharmaceutical company	Mixed	More than 1	Yes	Observational Study
Evaluation of the effectiveness of the abatacept (ORENCIA®) int	FINALISED	Funded by pharmaceutical company	Mixed	Chart abstraction	Yes	Observational Study
Mabthera Drug Utilisation Study and Patient Alert Card Evaluatic	FINALISED	Funded by pharmaceutical company	Mixed	Chart abstraction	No	Other
An observational, multi-center study to evaluate the safety of def	ONGOING	Funded by pharmaceutical company	Secondary	More than 1	Yes	Observational Study
EUROmediCAT: Safety of Medication Use in Pregnancy in Relat	ONGOING	More than one	Mixed	More than 1	Yes	Observational Study
Isotretinoin and the effectiveness of the pregnancy prevention pr	FINALISED	Funded by national/international drug agency	Mixed	More than 1	Yes	Observational study
Comparative effectiveness of insulines vs analogues to prevent	FINALISED	More than one	Secondary	More than 1	No	Other
A/H1N1 pandemic vaccines and pregnancy outcomes	FINALISED	Funded by national/international drug agency	Secondary	EHR	No	Other
Pertussis in Pregnancy Safety (PIPS) Study	ONGOING	More than one	Mixed	More than 1	Yes	Observational Study
Assessment of the safety of LABAs in asthma in routine care by	FINALISED	More than one	Mixed	More than 1	Yes	Observational Study
A prediction model for future exacerbation risk in children	PLANNED	Self-funded	Secondary	More than 1	Yes	Observational Study
205639 - Meta-analysis of the risk of autoimmune thyroiditis dise	FINALISED	Funded by pharmaceutical company	Mixed	Not applicable	No	Review or meta-analysis
ADVANCE POC I Risk pillar - Testing new approaches to monitc	FINALISED	Funded by public entities, excluding drug agencies	Secondary	More than 1	Yes	Observational study
ADVANCE POC I Benefit-Risk pillar – testing new approaches tc	FINALISED	Funded by public entities, excluding drug agencies	Secondary	More than 1	Yes	Observational study
Prospective non-interventional cohort study to assess safety anc	FINALISED	Funded by pharmaceutical company	Secondary	More than 1	Yes	Observational Study
A prospective observational registry study to characterise norma	FINALISED	Funded by pharmaceutical company	Primary	Not applicable	No	Observational Study
Descriptive Study of the Incidence of Malignancy in Patients wit	PLANNED	Funded by pharmaceutical company	Mixed	Existing registry	Yes	Observational Study
Post-authorisation safety study to assess the risk of urinary tract	ONGOING	Funded by pharmaceutical company	Secondary	More than 1	Yes	Observational Study
A non-interventional post-authorisation safety study (PASS) of v	ONGOING	Funded by pharmaceutical company	Secondary	More than 1	Yes	Observational Study
Retrospective Cohort Study of Certolizumab Pegol (Cimzia®) ar	ONGOING	Funded by pharmaceutical company	Secondary	Chart abstraction	Yes	Observational Study
A description of the UK NHS hospital resource use and patient q	ONGOING	Funded by pharmaceutical company	Mixed	EHR	Yes	Observational Study
Multi-component assessment systems and predicting future risk	PLANNED	More than one	Mixed	EHR	Yes	Observational Study
Can social listening data be used to provide meaningful insights	FINALISED	Funded by pharmaceutical company	Secondary	Unknown	No	Observational Study
Post-Marketing Observational Cohort Study of Patients with Infla	ONGOING	Funded by pharmaceutical company	Mixed	EHR	Yes	Observational Study
Characterising the risk of major bleeding in patients with Non-Va	FINALISED	Funded by national/international drug agency	Mixed	More than 1	Yes	Observational Study
Risk of lactic acidosis associated with metformin use in patients	ONGOING	Funded by public entities, excluding drug agencies	Mixed	More than 1	Yes	Observational Study
Post Authorisation Safety Study (PASS): an European observati	ONGOING	Funded by pharmaceutical company	Mixed	Not applicable	No	Survey
Evaluation of the potential for and clinical impact of increased Al	ONGOING	Funded by pharmaceutical company	Mixed	More than 1	No	Observational Study
A Retrospective Evaluation of PD-L1 expression on primary non-	PLANNED	Funded by pharmaceutical company	Mixed	Existing registry	No	Observational Study
Observational Study of the Effectiveness of Vedolizumab on Tre	ONGOING	Funded by pharmaceutical company	Primary	Not applicable	No	Observational Study
A multi-centre observational study to describe the impact of vedo	ONGOING	Funded by pharmaceutical company	Mixed	EHR	Yes	Observational Study
A 5-year enhanced Pharmacovigilance surveillance initiative to s	ONGOING	Funded by pharmaceutical company	Primary	Not applicable	No	Survey
Prospective observational study to describe routine use of XGEV	PLANNED	Funded by pharmaceutical company	Primary	Not applicable	No	Observational Study
PRJ2282 / 201491: CHESS: CPRD-COPD Hawthorne Effect Study	FINALISED	Funded by pharmaceutical company	Mixed	Existing registry	Yes	Observational Study
Assessment of physical functioning and handling of Spiolto® R	ONGOING	Funded by pharmaceutical company	Primary	Not applicable	No	Observational Study

2. Random distribution of studies across 14 centres



3. Quality check, re-evaluation and descriptive analysis of collected data

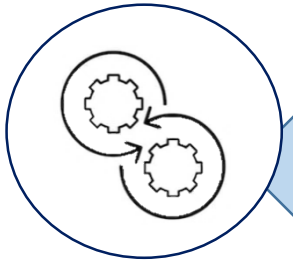


A. Harmonisation of terminology used to classify recorded information

All classifications were harmonised in terms of spelling, case (upper or lower) or any other differences that were identified in free text information

B. Missing data analysis

Two expert reviewers went through the EU PAS website to collect and record the missing information in the dataset according to the instructions



C. Data consistency check

A number of checks on the coherence of information reported for correlated variables for individual studies were performed

Data consistency check for multi-database studies

	MDS N=319 (%)	Check conducted	Rationale
Data collection			
Primary*	24 (7.6%)	Yes	A study based on primary data collection cannot be MDB study according to the definition
Secondary use of DBs**	293 (91.8%)	No	-
Unknown	2 (0.6%)	Yes	If we do not know the source of the data we cannot say it is a MDB study

*Newly-collected data for the research question that has been addressed by the study
**Use of data that have been already collected, irrespective of the research question (e.g. claims data, EHR)

4. Inter-rater agreement analysis

Substantial agreement (k= 0.61-0.80)

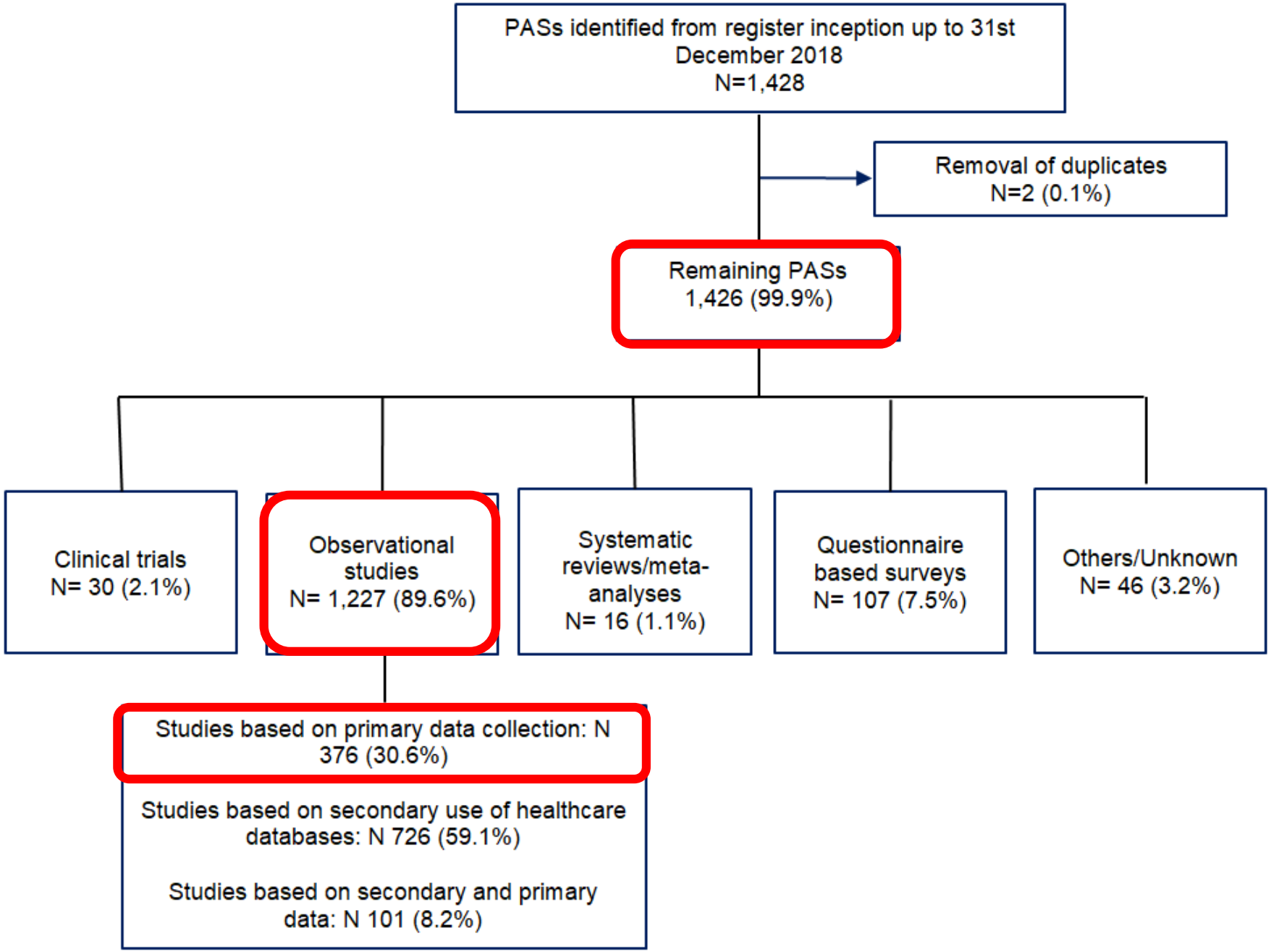
Moderate agreement (k= 0.41-0.60)

Fair agreement (k= 0.21-0.40)

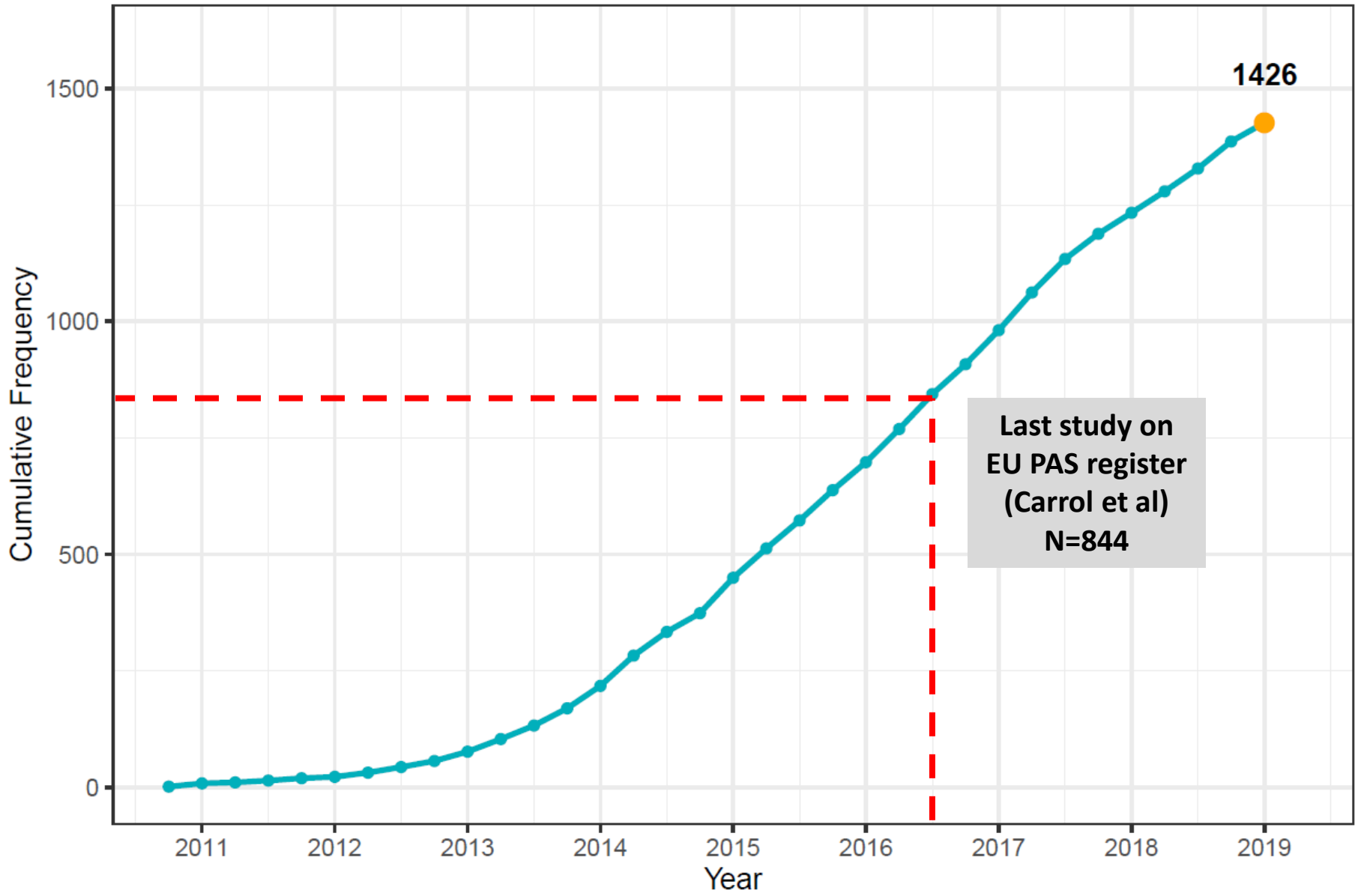
Variables	Categories	Kappa coefficient*	Agreement N 214 (%)	Total kappa coefficient*
Study type	Clinical trials	0.795	200 (93.5)	**0.769**
	Observational studies	0.758		
	Systematic reviews/ Meta-analyses	1.000		
	Questionnaire-based surveys	0.769		
	Others	0.795		
	Unknown	-		
Data Collection	Primary	0.717	171 (79.9)	**0.649**
	Secondary	0.666		
	Primary and secondary (mixed)	0.562		
	Unknown	-		
Drug type	Non-biologic	0.685	176 (82.2)	**0.646**
	Biologic	0.827		
	Both biologic and non-biologic	-		
	None	0.497		
	Unknown	-		
Use of reference drug for formal comparison	Yes	0.659	171 (79.9)	**0.587**
	No	0.621		
	Unknown	0.127		
Setting	Routine	0.493	193 (90.2)	**0.509**
	Experimental	0.829		
	Unknown	-		
	Not applicable	0.509		
Secondary data	Chart abstraction	0.481	145 (67.8)	**0.496**
	Claims database	0.131		
	EHR	0.457		
	Existing registry	0.505		
	Not applicable/ not secondary data	0.728		
	More than 1	0.579		
	Unknown	0.314		
Multiple database study	Yes	0.503	176 (77.6)	**0.479**
	No	0.478		
	Unknown	0.274		
Orphan drug	Yes	0.478	179 (83.6)	**0.382**
	No	0.422		
	Unknown	-		

Main results of descriptive analysis

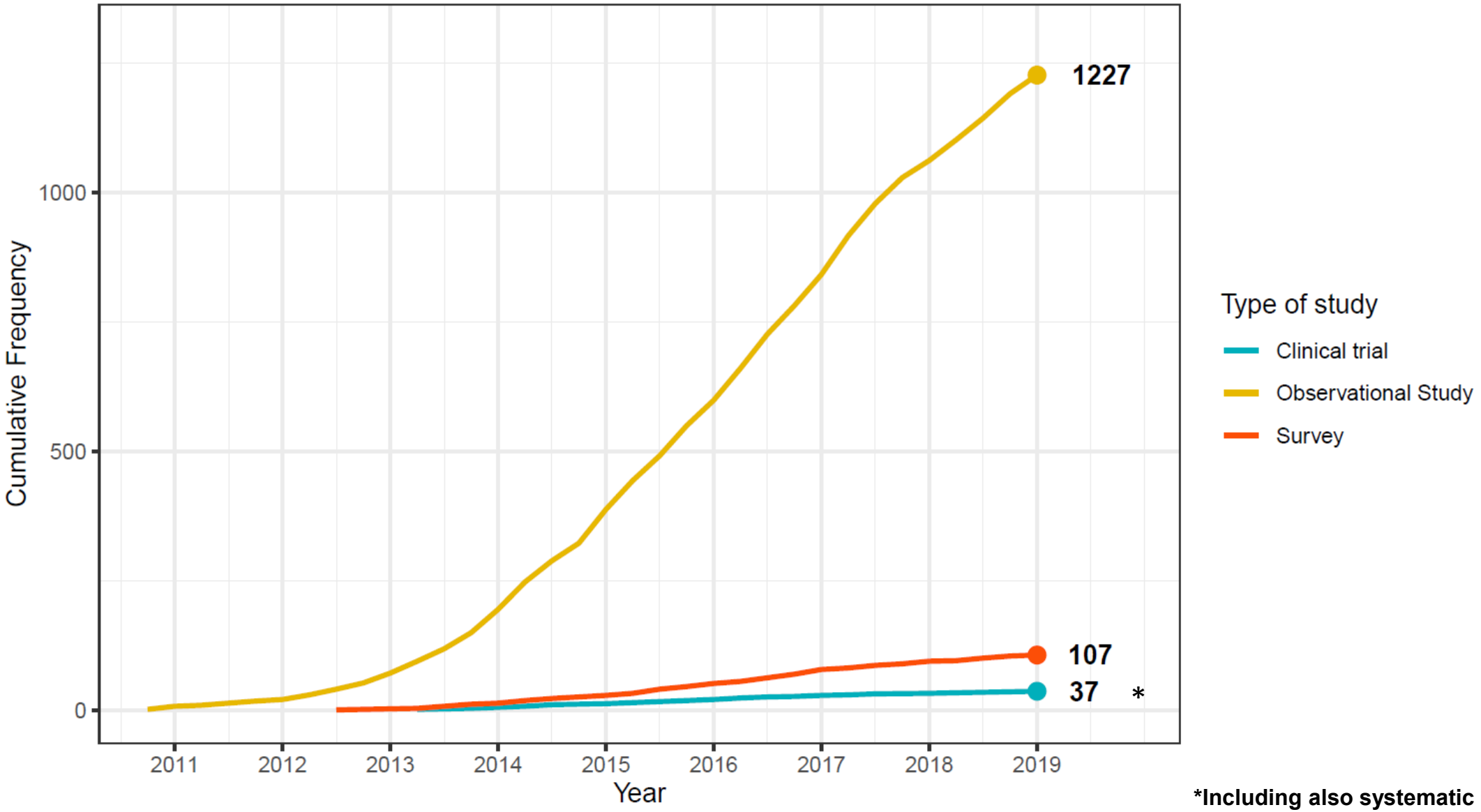
Flowchart of studies registered in the EU PAS register till Dec 2018



Cumulative frequency of studies registered in the EU PAS register from its inception to 31 Dec 2018

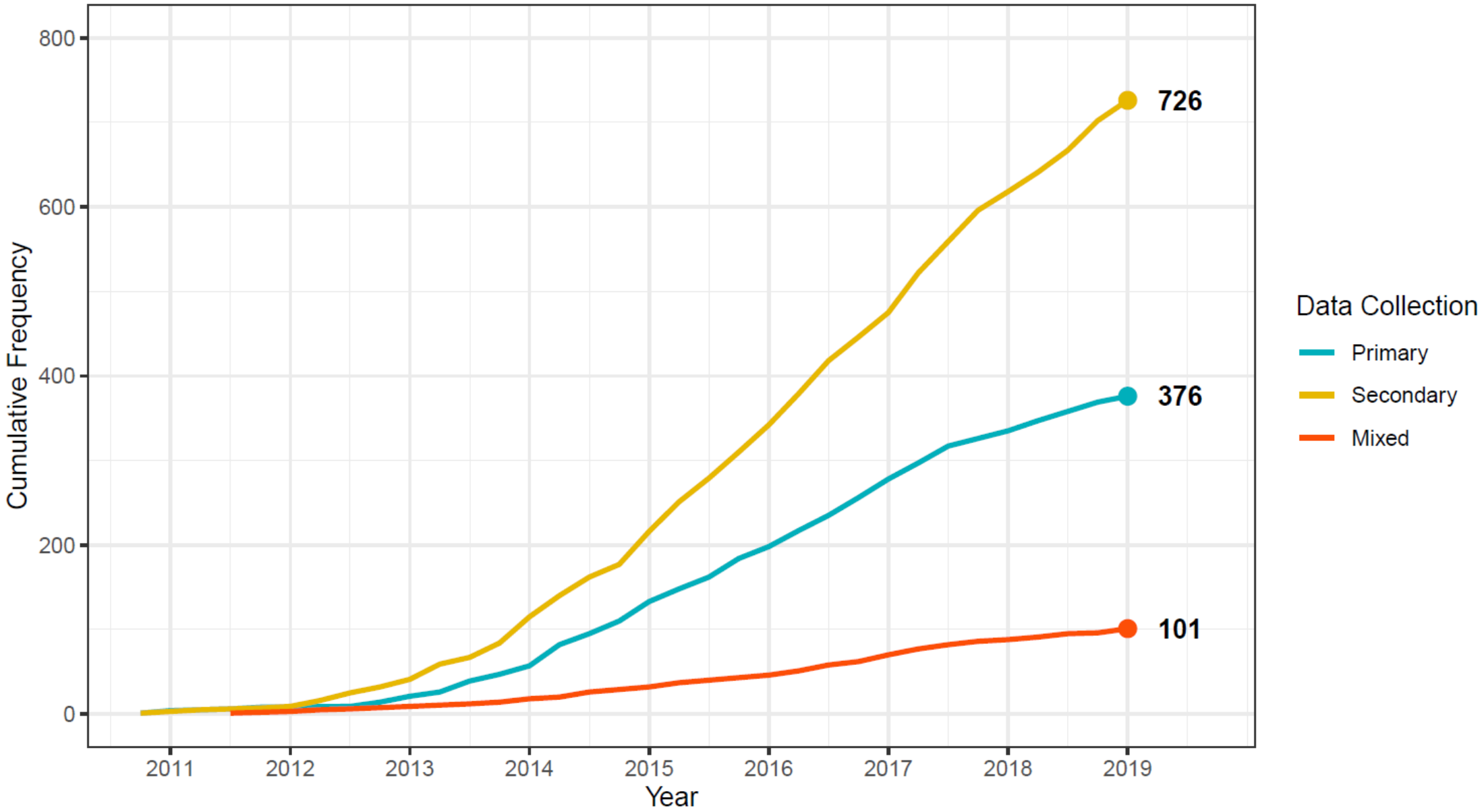


Cumulative frequency of studies in the EU PAS register: study type

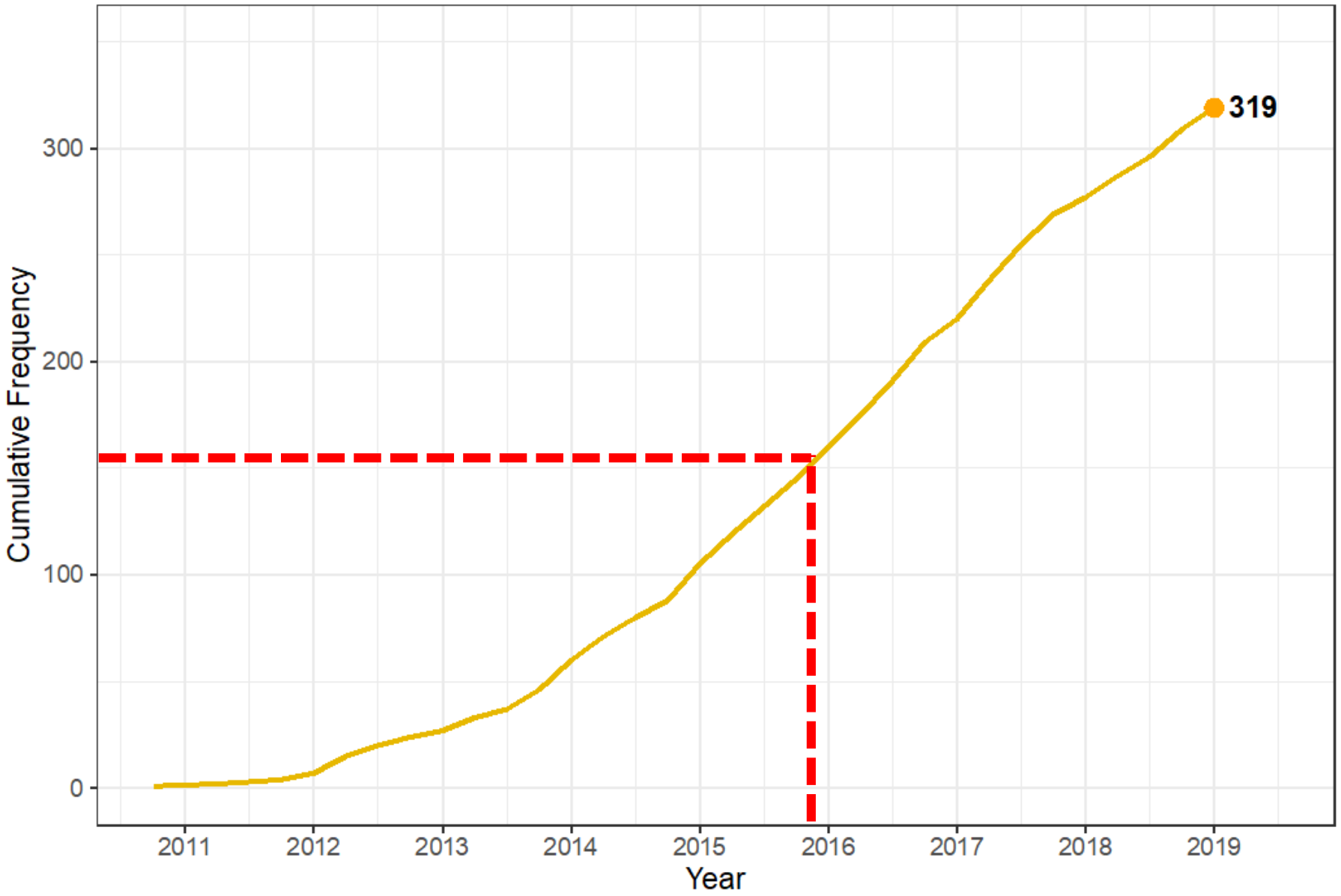


*Including also systematic reviews of clinical trials

Cumulative frequency of observational studies in the EU PAS register: data collection



Cumulative frequency of MDS registered in the EU PAS register



	Clinical trials N=30 (%)	Observational studies N=1227 (%)	Systematic reviews/ Meta-analyses N=16 (%)	Questionnaire-based surveys N=107 (%)
	N (%)	N (%)	N (%)	N (%)
Requested by a regulator				
Yes	10 (33.3)	571 (46.5)	5 (31.3)	68 (63.6)
No	18 (60.0)	637 (51.9)	11 (68.8)	39 (36.4)
Unknown	2 (6.7)	19 (1.5)	0 (0.0)	0 (0.0)
Source of funding				
Pharmaceutical company	20 (66.7)	1005 (81.9)	10 (62.5)	97 (90.7)
National/international drug agency	0 (0.0)	53 (4.3)	3 (18.7)	1 (0.9)
Public entities excluding drug agencies	8 (26.7)	65 (5.3)	2 (12.5)	5 (4.7)
Self-funded	1 (3.3)	23 (1.9)	1 (6.2)	0 (0.0)
More than one source	0 (0.0)	62 (5.1)	0 (0.0)	4 (3.7)
Unknown	1 (3.3)	19 (1.5)	0 (0.0)	0 (0.0)
Secondary data				
Chart abstraction	0 (0.0)	55 (4.5)	0 (0.0)	1 (0.9)
Claims database	0 (0.0)	165 (13.4)	0 (0.0)	0 (0.0)
EHR	1 (3.3)	182 (14.8)	0 (0.0)	1 (0.9)
Existing registry	3 (10.0)	136 (11.1)	0 (0.0)	1 (0.9)
Not applicable-not secondary data	25 (83.3)	376 (30.6)	16 (100)	104 (97.2)
More than 1	0 (0.0)	286 (23.3)	0 (0.0)	0 (0.0)
Unknown	1 (3.3)	27 (2.2)	0 (0.0)	0 (0.0)

	Clinical trials N=30 (%)	Observational studies N=1227 (%)	Systematic reviews/ Meta-analyses N=16 (%)	Questionnaire-based surveys N=107 (%)
	N (%)	N (%)	N (%)	N (%)
Use of reference drug for formal comparison				
Yes	7 (23.3)	336 (27.4)	4 (25.0)	5 (4.7)
No	22 (73.4)	844 (68.8)	10 (62.5)	100 (93.5)
Unknown	1 (3.3)	47 (3.8)	2 (12.5)	2 (1.9)
Scope of the study *				
Disease epidemiology	4 (13.3)	212 (17.3)	2 (12.5)	8 (7.5)
Risk assessment	13 (43.3)	696 (56.7)	11 (68.8)	36 (33.6)
Drug utilisation	4 (13.3)	444 (36.2)	1 (6.3)	23 (21.5)
Effectiveness evaluation	17 (56.7)	855 (69.7)	15 (93.8)	77 (72.0)
Other	14 (46.7)	246 (20.0)	3 (18.8)	40 (37.4)
Population of interest – age*				
Children	5 (16.7)	442 (36.0)	7 (43.8)	25 (23.4)
Adults	27 (90.0)	1103 (89.9)	15 (93.8)	105 (98.1)
Elderly persons	19 (63.3)	1008 (82.2)	13 (81.3)	98 (91.6)
Pregnant women	2 (6.7)	132 (10.8)	2 (12.5)	3 (2.8)
Breast-feeding women	0 (0.0)	13 (1.1)	0 (0.0)	0 (0.0)

* Multiple options are possible

Characteristics of studies based on secondary use of existing healthcare data (± primary data collection)

	Chart abstraction N=60 (%)	Claims database N=169 (%)	EHRs N=186 (%)	Existing registry N=144 (%)	More than one type of data N=290 (%)
	N (%)	N (%)	N (%)	N (%)	N (%)
Protocol deposited					
Yes	34 (56.7)	82 (48.5)	123 (66.1)	87 (60.4)	209 (72.1)
No	26 (43.3)	87 (51.5)	63 (33.9)	57 (39.6)	81 (27.9)
Scope of the study					
Disease epidemiology	5 (8.3)	26 (15.4)	34 (18.3)	38 (26.4)	49 (16.9)
Risk assessment	17 (28.3)	30 (17.8)	29 (15.6)	28 (19.4)	53 (18.3)
Drug utilisation	28 (46.7)	57 (33.7)	72 (38.7)	45 (31.3)	117 (40.3)
Effectiveness evaluation	24 (40.0)	37 (21.9)	52 (28.0)	32 (22.2)	54 (18.6)
Other*	17 (28.3)	30 (17.8)	29 (15.6)	28 (19.4)	53 (18.3)
Drug of interest					
Biologic	24 (40.0)	32 (18.9)	32 (17.2)	34 (23.6)	57 (19.7)
Both biologic and non-biologic	2 (3.3)	3 (1.8)	1 (0.5)	6 (4.2)	5 (1.7)
Orphan drugs	8 (13.3)	14 (8.3)	16 (8.6)	24 (16.7)	20 (6.9)
Publication available					
Yes	18 (30.0)	62 (36.7)	73 (39.2)	40 (27.8)	94 (32.4)
No	42 (70.0)	107 (63.3)	113 (60.8)	104 (72.2)	196 (67.6)

Factors associated to the registration of MDSs vs non-MDSs among observational studies based on secondary use of already existing healthcare data

	Multiple Database Studies
	OR [95% CI]
Protocol deposited	2.012 [1.461 - 2.768]
ENCePP seal	3.004 [1.696 - 5.308]
Requested by a regulator	2.883 [2.117 - 3.918]
RMP status*	
EU RMP 1	2.609 [1.414 - 4.804]
EU RMP 2	1.127 [0.354 - 3.580]
EU RMP 3	2.086 [1.506 - 2.887]
Non-EU RMP only	0.581 [0.285 - 1.181]
Not applicable	0.508 [1.414 - 4.804]
Missing - no info at all	0.477 [0.354 - 3.580]
Population of interest – (Age)	
Children	2.522 [1.846 - 3.444]
Adults	1.048 [0.639 - 1.717]
Elderly persons	1.157 [0.764 - 1.748]
Unknown	1.581 [0.316 - 7.878]

*** EU RMP 1: EU risk management plan 1 (imposed as condition of marketing authorisation); EU RMP 2: EU risk management plan 2 (specific obligation of marketing authorisation); EU RMP 3: EU risk management plan 3 (required)**

Update on specific assessments

Reviev
Out

Introduction

- Description of 'main' study: E
- MDS and strategies, reference

Methods

- Brief reference to results of th
- Refined definition of MDS
- Methods to estimate sensitivi
  define the final list of studies
- Data extraction
- Data analysis

Regulatory
pharmacoepidemiolo
studies requeste

BACKGROUND:

One of the goals of the new Pharmacovigi
increase transparency of the regulatory proc
PRAC oversight, specific procedures and tim
of the monthly meeting minutes and the endo
database for PASS registration represent maj
This was a response to previous concerns
Risk Management activities such as protocols
A review of publicly available information on
new Pharmacovigilance legislation, highlight
had been achieved but there were still some
partial availability of information (limited info
limited registration of studies in the EU PA
different sources (different study type inform
limited use of study identification elements
across the EU PAS Registrants.(3)

According to the EMA website "Non-inte
answers": *Protocols and public abstracts of*
are publicly available in the EU PAS Regis
Pharmacoepidemiology and Pharmacovigila
imposed non-interventional PASS final study
found only in centrally authorised medicines
European public assessment report (EPA
medicinal products included in 'mixed' proc
were also involved can be found on the Co
publishes the outcomes of final study re
authorisation safety studies (PASS) for NAPs

The aim of this study is to understand the re
multidatabase studies performed in Europe.

Post-Authorisation Studies in Paediatric population: data from the EU-PAS registry

Name	Institution

Pregnancy and lactation

Lead: Leonardo Pereira

One of the objectives in ConcePTION, an IMI-funded international study, is to provide important innovations to move beyond product-specific pregnancy registries and/or related observation studies to enhance our understanding of medica
strategy: an assessment
Post-Authorisation Studies
observational studies focu
registries studies publishe
data from highest level to
the summary of product
studies led to update the r

population in order to:

- assess the possible i
  research in this popu
- describe the epidem
  different class of age
  them;
- evaluate the impact
  drug (in terms of mar

Assessment of the utilization of secondary data in European countries based on the EU PAS Register

Step 1: Data collection

Apart from the data that is already collected regarding the studies of the EU PAS Register, we need to document in which countries each study was conducted. This can happen using the appropriate search field on the EU PAS Register website. A series of columns will be added, titled by each country's name and a drop-down choice of "Yes" or "No" will be available to point out if the study was or not conducted in this country. This is considered necessary, since there are studies conducted in multiple countries.

Step 2: Inclusion criteria

Only studies conducted in European countries will be included, since Europe is the region with the most admissions in EU PAS Register and comparisons could be more relevant. (This criterion will be set during the data collection, implementing the search in European countries only.) Furthermore, only observational studies will be included, since both clinical trials and surveys naturally use primary data and reviews/meta-analyses are not relevant for this research question.

REVIEW

Clin Pharmacol Ther. 2020;108:228-235

Different Strategies to Execute Multi-Database Studies for Medicines Surveillance in Real-World Setting: A Reflection on the European Model

Rona Gini[1,*], Miriam C. J. Sturkenboom[2], Janet Sultana[3], Alison Cave[4], Annalisa Landi[5,6], Alexandra Pacurariu[4], Giuseppe Roberto[1], Tania Schink[7], Gianmario Candore[4], Jim Slattery[4], and Gianluca Trifirò[8] on behalf of the Working Group 3 of ENCePP (Inventory of EU data sources and methodological approaches for multisource studies)

MDS if:

A. Studies conducted using more than one source of secondary data not linked at patient level **AND**

B. With a common protocol applied in parallel to two or more data sources (meta-analyses of observational studies conducted at different time points and without common protocol **ARE NOT MDS)**

Additional elements to consider:

- MDS may concern either the same country or different countries;
- If two or more DBs can be *theoretically* linked at patient level (e.g. related to the same catchment area) but have not been linked, they should be considered components of a MDS;
- MDS may concern different types of secondary data (e.g. Dutch claims and Dutch EMRs) or the same type of secondary data (e.g. Italian EMRs and UK EMRs).

WG subgroups – Multiple Database Studies

Members

Vera Ehrenstein (Aarhus University), Daniel Dedman (MHRA), Rosa Gini and Giuseppe Roberto (ARS Toscana), Gianluca Trifirò and Janet Sultana (UniVR, UniMe);

Objective

To characterize MDS and explore their regulatory impact in relation to the methodological approach used

Work done so far

- A protocol for more detailed data collection (e.g. strategy) on MDS was developed
- Each study initially flagged by MDS has been validated by two experts. A random sample of non-MDSs has been validated as well.

WG subgroups – Regulatory outcomes

Members

Mariana Almas (IQVIA – lead), Bettina Rillmann (PRA Solutions), Lisette Hoogendoorn (IQVIA), Janet Sultana (UniMe), Thomas Goedecke (EMA).

Objective

To evaluate regulatory outcomes of studies that have been finalized

Work done so far

- Developed a detail protocol for data collection using publically available data sources, such as documents available on the EMA website

WG subgroups – Paediatrics

Members

Carmen Ferrajolo, Annalisa Capuano and Concita Rafaniello (Uni. of Campania), Annalisa Landi, Maddalena Toma, Elisabetta Volpe, Simona Ravera, Mariagrazia Felisi, Yuliya Matsiyas, Antonella Didio and Fedele Bonifazi (TEDDY)

Objective

1. Assess	**the possible impact of the recent regulatory initiatives in promoting the clinical research in this population**	✓ Study promoted by pharmaceutical company, regulatory drug agency, academy ✓ Imposed condition of marketing authorization or on voluntary basis by the marketing holder
2. Describe	**epidemiological research framework in paediatrics, considering the different class of ages and identifying the still uncovered therapeutic areas for each of them**	✓ Age-category according ICH ✓ Disease under study ✓ Study medicine
3. Evaluate	**the impact of the finalised PASs on the regulatory actions taken on the specific drug (e.g. SmPC changes)**	✓ Changes in the regulatory actions ✓ Evidence in paediatric population

WG subgroups – Pregnancy and lactation

Members

Leonardo Pereira, Caitlin Dodd and Miriam Sturkenboom (Uni. Of Utrecht), Katia Verhamme (Erasmus University Medical Center, Rotterdam)

Objective

- Landscape analysis of **clinical and observational studies focusing on pregnancy and lactation in EU PAS register and clinicaltrial.gov** from highest level to more detailed data;
- Only studies with primary or secondary outcomes related to pregnancy outcomes or lactation effects and exposure to medications will be included;
- assessment on SPC to investigate whether the congenital anomalies findings of these studies led to update of the respective label.

WG subgroups – International comparison of PASs

Members

Christos Kontogiorgis (Lead), Georgios Poulentzas, Panagiotis Nikolaos Lalagkas (Democritus University Of Thrace)

Objective

To identify potential differences (and the reasons behind them) in the type of data (primary/secondary) used in studies carried out across different countries.

Conclusions

- Assessing the studies registered in the EU PAS register requires multidisciplinary and advanced expertise;
- Availability of protocols is essential for correct interpretation of the studies and rapidly sharing methodological approaches (e.g. COVID-19);
- A large number of studies are based on primary data collection, without any comparator and just descriptive;
- In general, pharmaceutical companies are the main sponsor, irrespective of whether the studies are imposed by regulatory agencies;
- Number of MDSs is increasing and assessing their impact in relation to the adopted methodological strategies may inform regulatory agencies as well as scientifc community.

Thank you for the attention

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