Networking in drug and vaccine safety research

challenges, added value

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EC /EU Initiatives /projects to have Pan-European networks for drug safety research
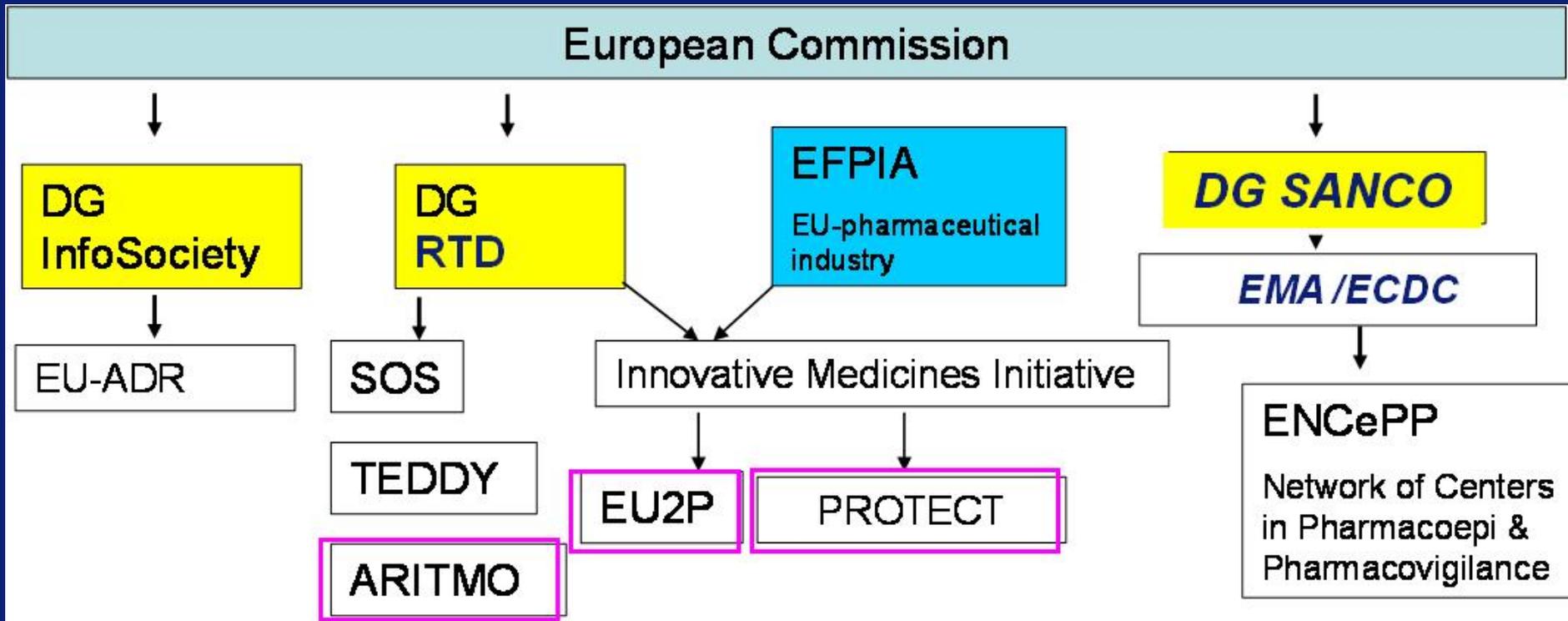
Many more coming up thanks to EMA

Objectives

- To <u>design</u>, <u>develop</u> and <u>validate</u> a computerized system that exploits data from electronic healthcare records and biomedical databases for the early detection of adverse drug reactions (18 partners)

- To assess and compare the risk of cardiovascular events and gastrointestinal events in users of any type of tNSAID or coxib. (12 partners)

- To analyse the arrhythmogenic potential of antipsychotics, antihistamines and anti-infectives and to identify genetic susceptibility (17 partners)

- Make available high quality and timely information on the safety of Pandemic Influenza Vaccine based on a concerted effort of European member states (ECDC funded)

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Where do these projects belong on the spectrum of drug safety research?

Signal detection

eu-adr

Signal strengthening

VAESCO

Hypothesis testing in a formal pharmacoepi study

SOS

Aritmo

Suspectibility/ personalized approaches

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SEVENTH FRAMEWORK PROGRAMME
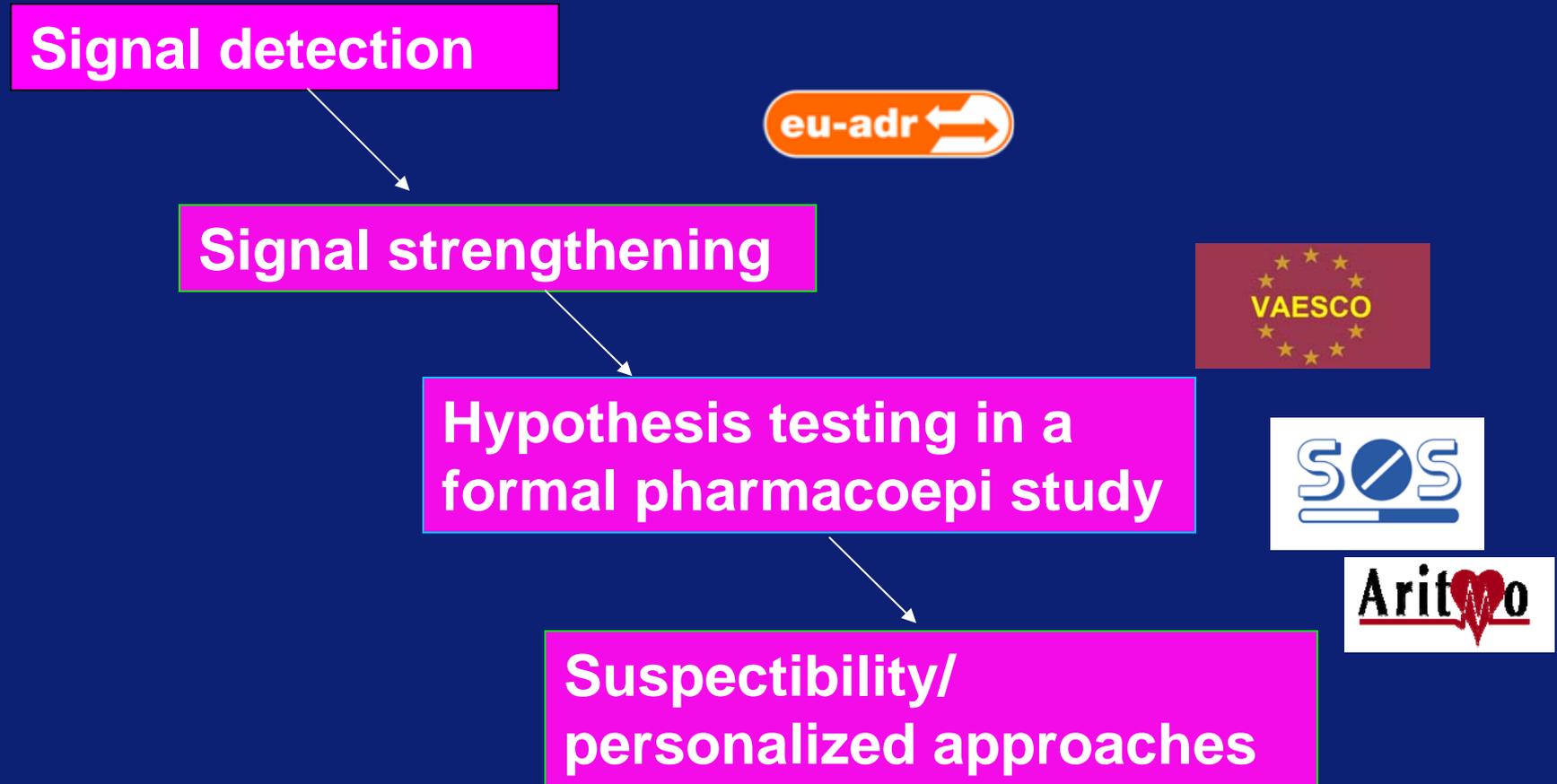
Challenges

Organisations
Differences in culture and experience between academia, public entities and private companies

People
Getting to know each other and the interests
Knowing your role and how to involve others
Speaking the same language
How to deal with IP and authorship

Data
How to pool data
Ethical and privacy issues
Competitiveness and transparency
Overcoming differences in coding

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Partners in the FP-7 EU-ADR, SOS, ARITMO drug safety Consortia: mostly academic /SME

Consortium

Academic/ Pharepi centers

- SW :Brighton Collaboration
- IT : SIMG / Villa Sofia
- NL: Erasmus University MC
- ES: BIFAP
- SE : Karolinska Institutet
- UK: University of Bath

Public Health or Regulatory agencies

- **SE**: ECDC (funding agency)
- SE: Swedish Institute for Inf. Dis. Control
- DK:Staten's serum institute
- FI: National Public Health Institute
- NO: Norwegian Institute of Public Health,
- DE: Paul Ehrlich Institute
- NL: RIVM
- FR: AFSAPPS
- IT: AIFA
- ES: Agencia Española de Medicamentos y Productos Sanitarios

A different point of view is simply the view from a place where you are not

Yourpointofview.com

HSBC

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People: challenges and added value

Dealing with challenges

- Communication

- Frequent consortium meetings

- Good consortium agreement that deals with IP and authorship

Added value

- Getting to know each other: lowering thresholds and building trust

- Strenghtening of the pharmacoepidemiological community in the EU

- Broadening of horizon giving rise to innovations

- True discussions about pharmacoepidemiological methods

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Data challenges (pooling data across EU)

Dealing with challenges

- Distinguishing between 'perceived' and real issues

- Inventory of ethical and governance issues in each country regarding
  - Secondary use of pseudonimized data
  - Collection of biological samples (pharmacogenetics)

- Choosing model for datasharing

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Workmodels for combining data from various countries

Combining of raw data in <u>central</u> datawarehouse

Pooling of elaborated data (individual level)

Pooling of aggregated data (not individual level)

Common protocol studies and sharing of coefficients

Meta-analysis of individual studies

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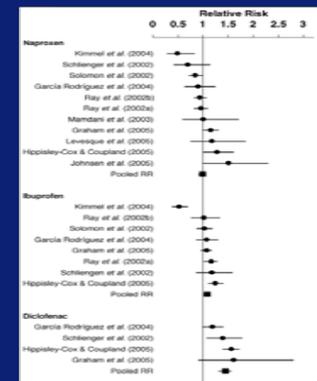
Common data model and local elaboration with standardized software
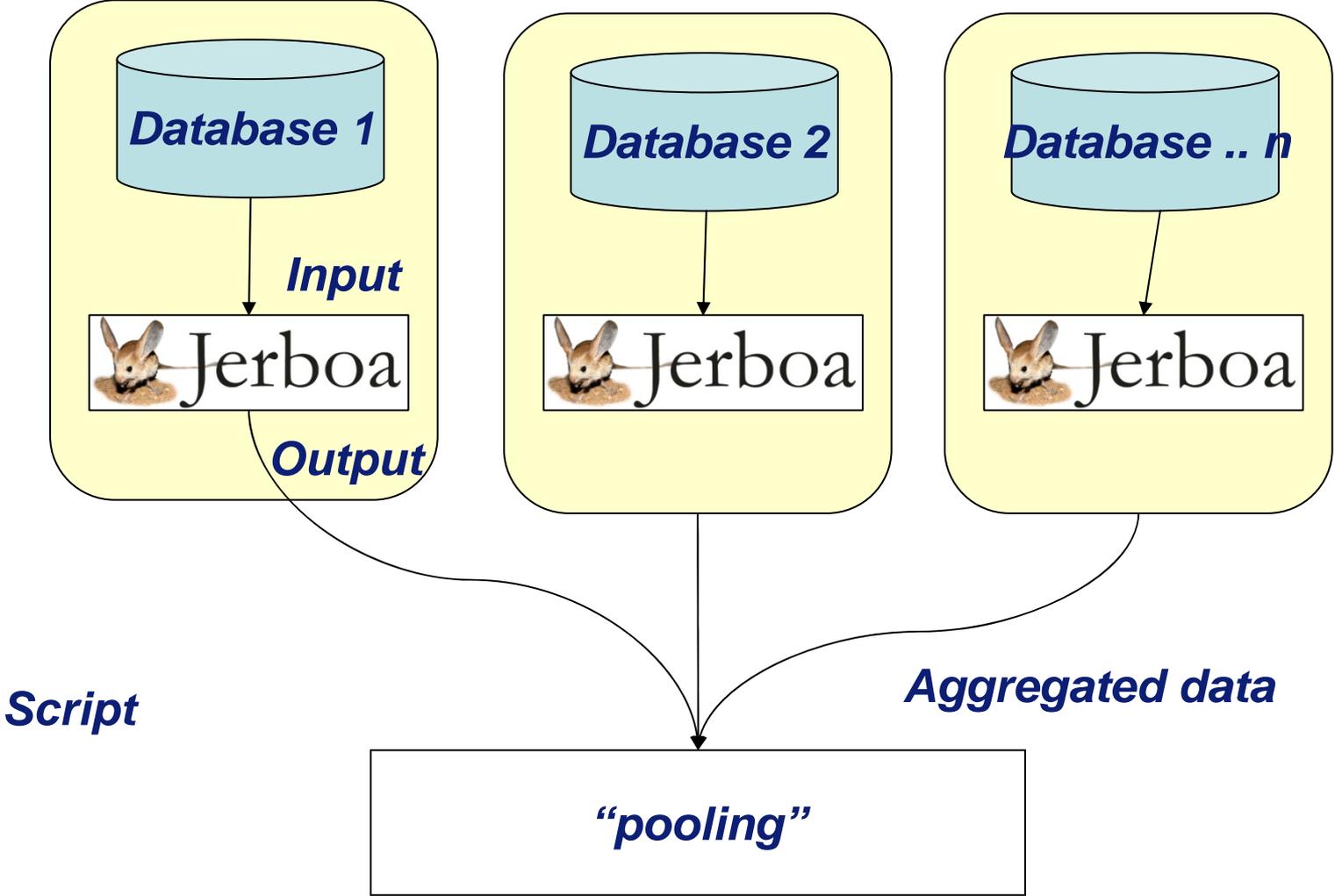
Output tables completely de-indentified (analytical datasets)

SCCS output for VAESCO

Individual	exposure	Interval length	Number of events
001xxxxx	1+15 +D1+D2	107	1
001xxxxx	1+15 +D1+D2+D3	21	0
001xxxxx	1+15 +D1+D2	54	0
001xxxxx	1+15 +D1+D2+exp1	42	0
001xxxxx	1+15 +D1+D2	141	1

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Lessons learned on data sharing

1. <u>Approach of distributed data network</u> is widely accepted, feasible and productive and it deals effectively with ethical and governance issues. It involves the DB holders and avoids political issues.

2. Jerboa has contributed widely to the success!

    Jerboa has been used in multiple projects now on more than 15 databases covering > 100 million persons.

    Jerboa was the basis for the successful generation of incidence rates of 12 events of special interest for the H1N1 vaccination safety monitoring by the European Medicines Agency (e.g. Guillain Barre)

Data challenges (overcoming coding and language differences)

Dealing with challenges

- Methods sought for mapping between terminologies
  - UMLS is a good starting method which was used in all projects
  - Laboursome

- Benchmarking and harmonization is important step
  - done on basis of standardized incidence rates

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Data challenges (overcoming coding and language differences)

eu-adr

Workflow of Terminology mapping

1. Event

2. Event Description Form

3. Search for UMLS concepts

Upper GIB

- Upper GIB
- Hematemesis / blood vomiting
- Oesophageal H
- Melaena
- GIH

Upper GIH

Hematemesis

Esophageal B

Melaena

GIH

www.euadr-project.org

From: Paul Avillach, Frantz Thiessard, Bordeaux
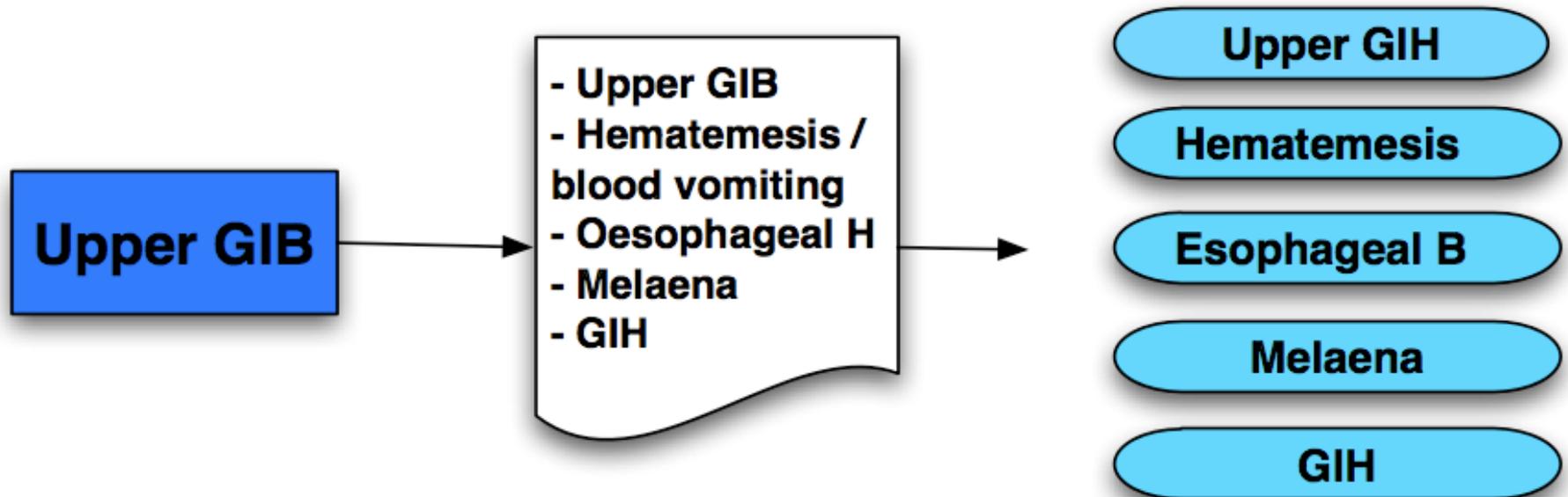
3. Search for UMLS concepts

- Upper GIH
- Hematemesis
- Esophageal B
- Melaena
- GIH

5. Conference calls for harmonisation issues

4. First Draft of Terminology mapping

	C0041909	Upper gastrointestinal hemorrhage	
RCD	X30Be	Upper gastrointest haemorrhage	ENG
RCD	X30Be	Upper gastrointestinal haemorrhage	ENG
RCD	X30Be	Upper GI - gastrointestinal haemorrhage	ENG
RCD	X30Be	Upper GI-gastrointes haemorrh	ENG
	C0018926	Hematemesis	
ICD10	K92.0	Haematemesis	ENG
ICD9CM	578.0	Hematemesis	ENG
ICPC	D14	Hematemesis/vomiting blood	ENG
ICPC2P	D14001	vomiting out blood	ENG
ICPC2P	D14001	Vomiting;blood	ENG
ICPC2P	D14003	Haematemesis	ENG
ICPC2P	D14003	Hematemesis	ENG
ICPCDUT	D14	Haematemesis/bloed braken	DUT
ICPCITA	D14	Ematemesi/vomito sanguinolento	ITA
RCD	J680.	Haematemesis	ENG
RCD	J680.	Vomiting blood	ENG
	C0239293	Esophageal bleeding	
ICD9CM	530.82	Esophageal hemorrhage	ENG
ICPC2ICD10DUT	MTHU011694	bloeding; oesofagus	DUT
ICPC2ICD10DUT	MTHU054119	oesofagus; bloeding	DUT
RCD	J10y0	Haemorrhage of oesophagus	ENG
RCD	J10y0	Oesophageal haemorrhage	ENG
RCD	Xa7TU	Oesophageal bleeding	ENG

[...]

From: Paul Avillach, Frantz Thiessard, Bordeaux

Added value of data sharing in EU

Added value of sharing data in EU

Transparency about quality of data and structured approach to mapping of codes coding

Enlarging the scale on which we can rapidly do investigations (e.g. H1N1v)

Taking advantage of the heterogeneity in exposure

Keeping in pace with US: putting EU on the map

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Persontime contribution for background incidence estimation of events of special interest
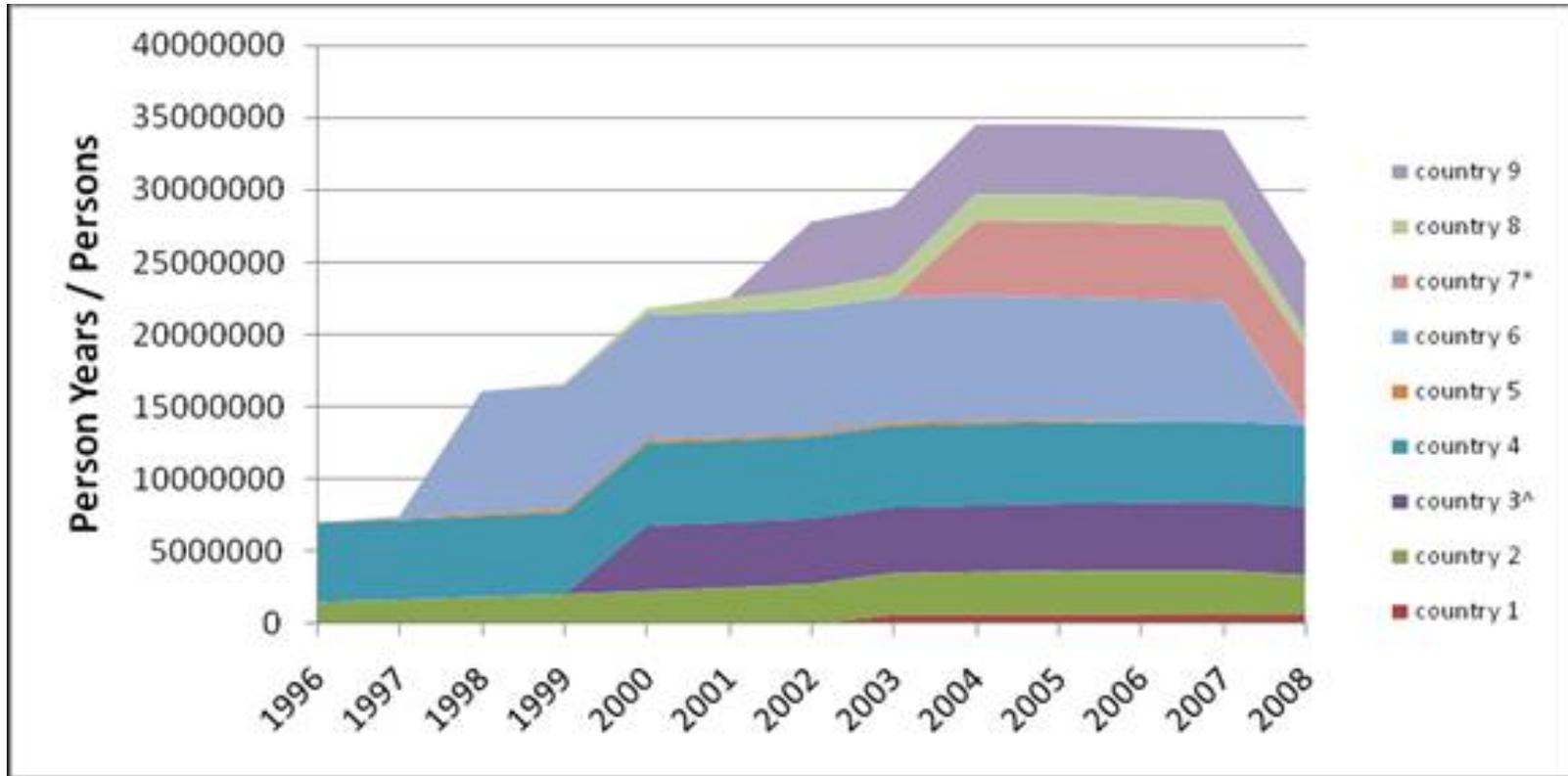
More than 260 million PY

Conclusions

EC funded drug safety research is effectively making many (ENCePP) centers work together

Issues in ethics/governance for data sharing can be overcome

Differences in languages and coding in databases in various can be addressed

These networks are boosting the collaborations and accessibility of data in the EU and may rapidly change the landscape for this type of research.

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