

**Erasmus MC**

University Medical Center Rotterdam

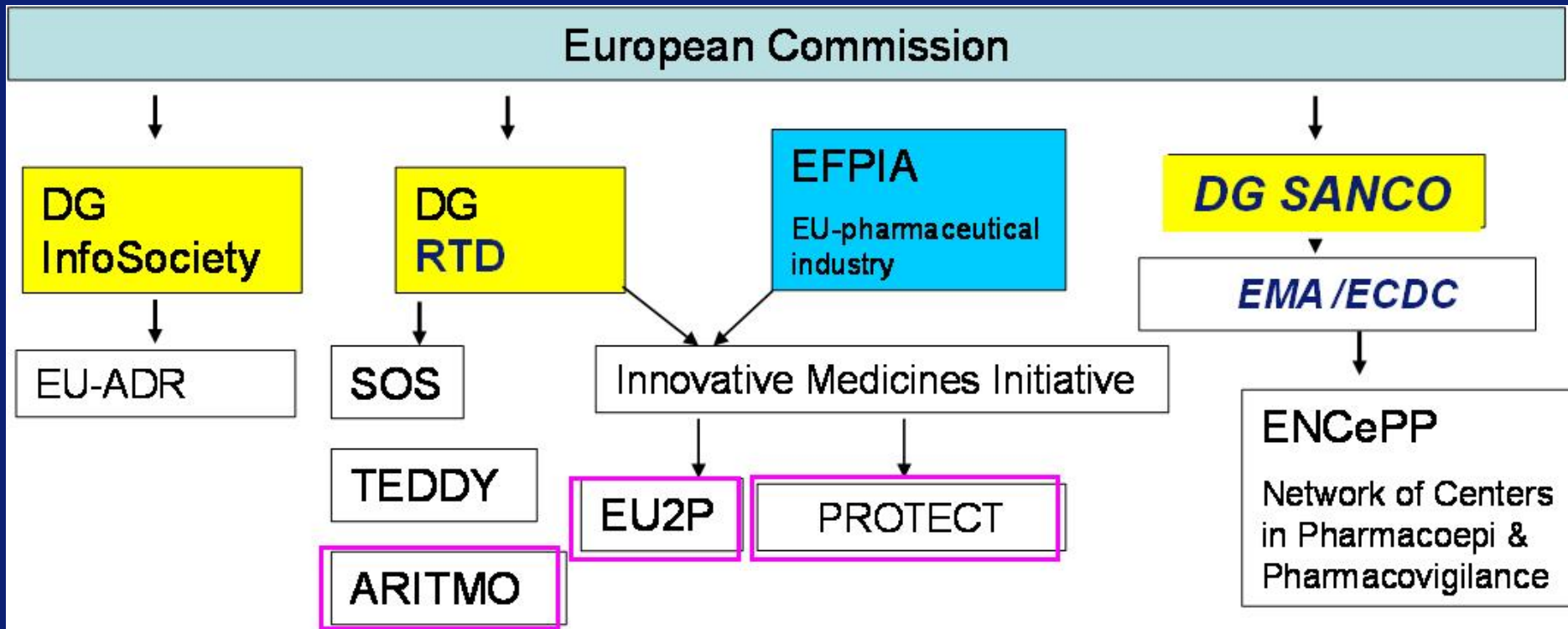


# Networking in drug and vaccine safety research

**challenges, added value**

**Prof. Miriam CJM Sturkenboom**

# EC /EU Initiatives /projects to have Pan-European networks for drug safety research



*Many more coming up  
thanks to EMA*



# Objectives



- To design, develop and validate 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)

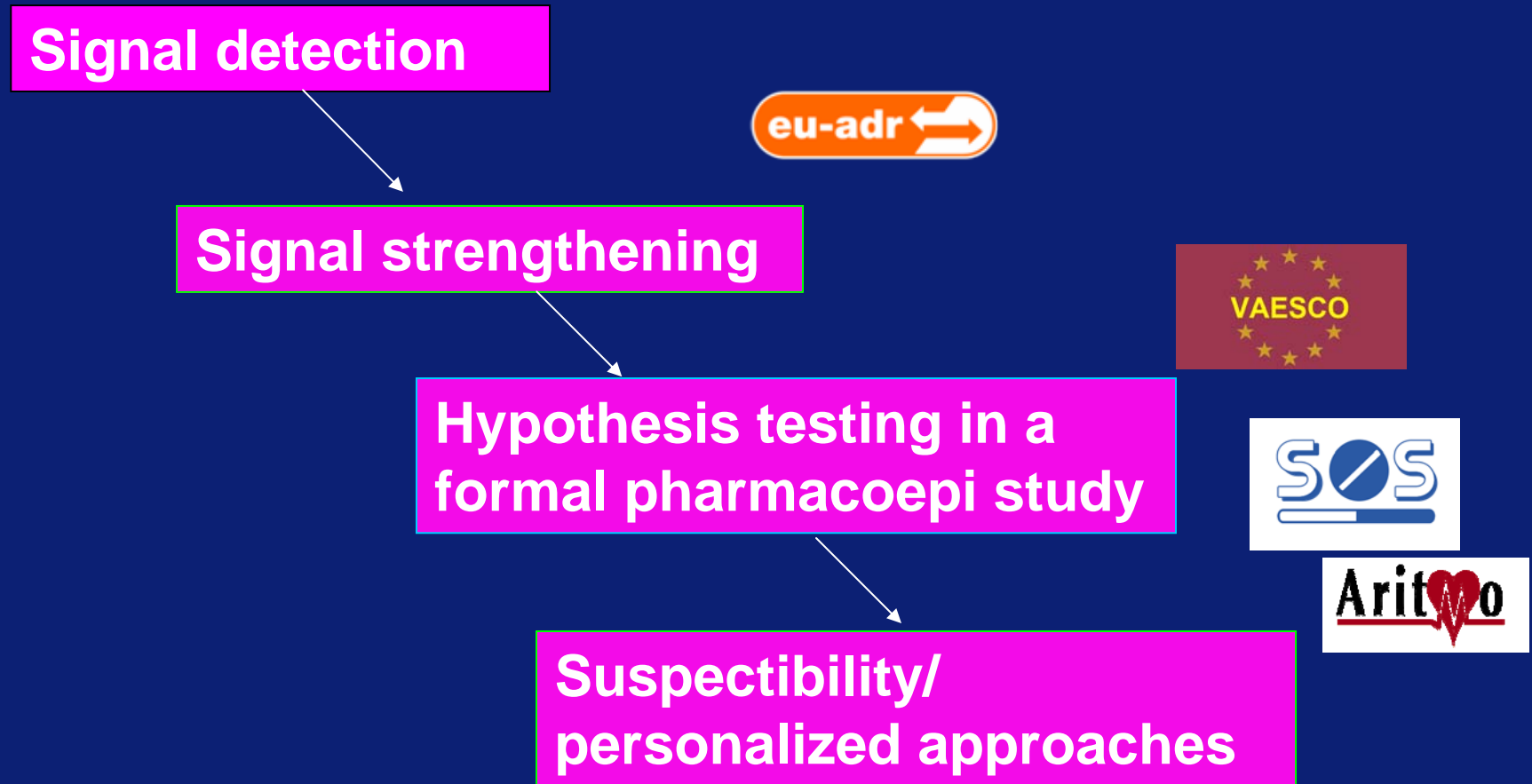


- To analyse the arrhythmogenic potential of antipsychotics, antihistamines and anti-infectives and to identify genetic susceptibility (17 partners)



- 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)

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



# 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

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



TAU (Tel-Aviv) 

# 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*



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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
- Strengthening of the pharmacoepidemiological community in the EU
- Broadening of horizon giving rise to innovations
- True discussions about pharmacoepidemiological methods

# 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

# Workmodels for combining data from various countries

*Combining of raw data in central datawarehouse*

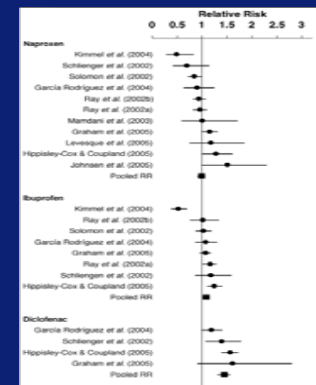
*Pooling of elaborated data  
(individual level)*



*Pooling of aggregated data  
(not individual level)*

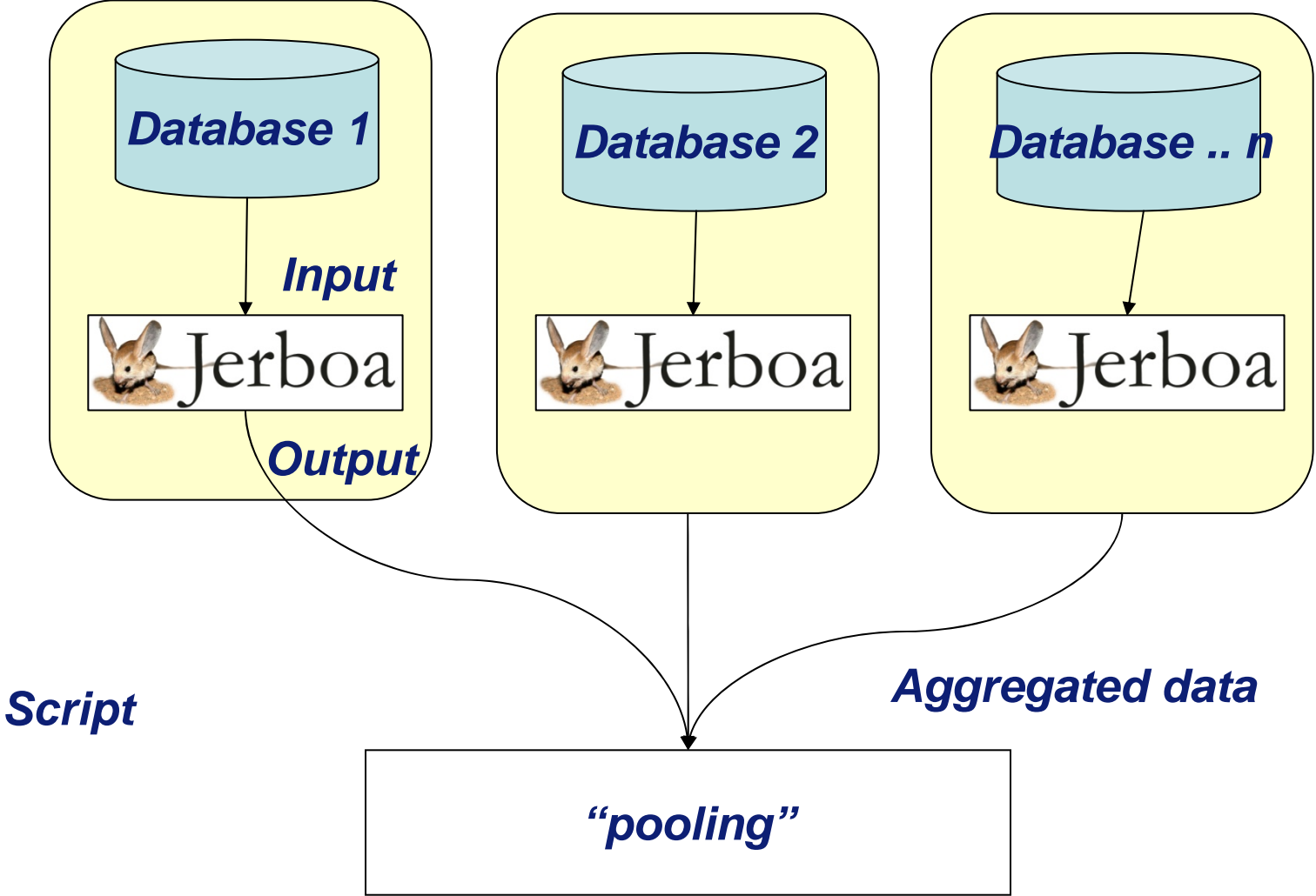
*Common protocol studies and sharing  
of coefficients*

*Meta-analysis of individual studies*



# Common data model and local elaboration with standardized software

**LOCAL**



# Output tables completely de-identified (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

# Lessons learned on data sharing

1. Approach of distributed data network 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

# Data challenges (overcoming coding and language differences)

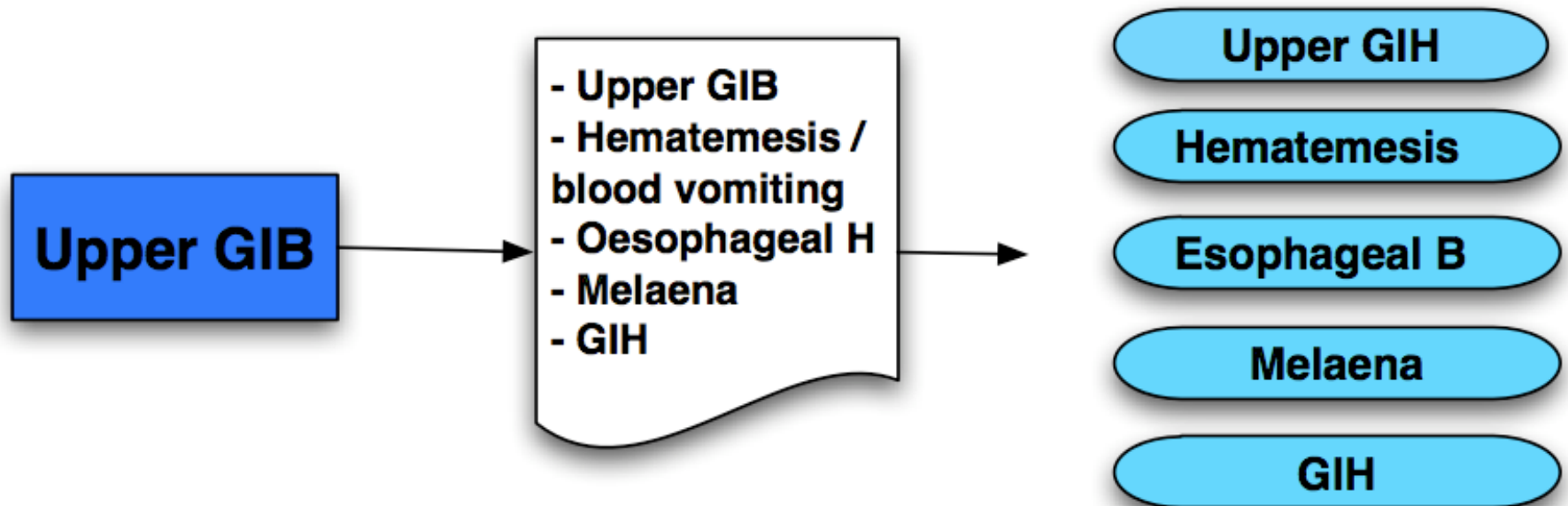


## Workflow of Terminology mapping

1. Event

2. Event  
Description Form

3. Search  
for UMLS  
concepts





### 3. Search for UMLS concepts

Upper GIH

Hematemesis

Esophageal B

Melaena

GIH

### 5. Conference calls for harmonisation issues

### 4. First Draft of Terminology mapping

<b>C0041909</b>		<b>Upper gastrointestinal hemorrhage</b>	
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
<b>C0018926</b>		<b>Hematemesis</b>	
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/loed braken	DUT
ICPCITA	D14	Ematemesi/vomito sanguinolento	ITA
RCD	J680.	Haematemesis	ENG
RCD	J680.	Vomiting blood	ENG
<b>C0239293</b>		<b>Esophageal bleeding</b>	
ICD9CM	530.82	Esophageal hemorrhage	ENG
ICPC2ICD10DUT	MTHU011694	bloeding; oesofagus	DUT
ICPC2ICD10DUT	MTHU054119	oesofagus; bleeding	DUT
RCD	J10y0	Haemorrhage of oesophagus	ENG
RCD	J10y0	Oesophageal haemorrhage	ENG
RCD	Xa7TU	Oesophageal bleeding	ENG

[...]

*From: Paul Avillach, Frantz Thiessard, Bordeaux*

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# Added value of data sharing in EU

# Added value of sharing data in EU

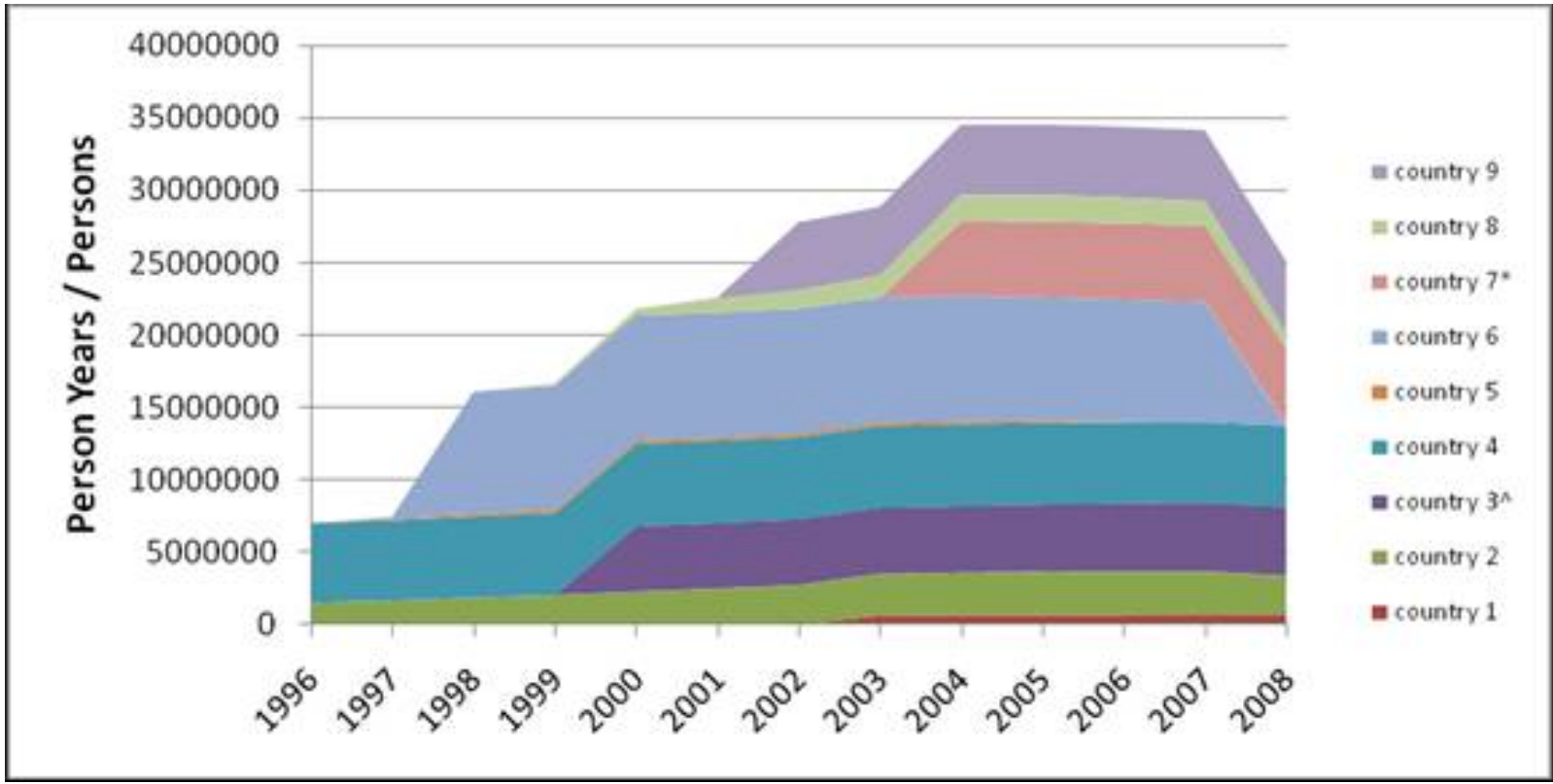
Transparency about quality of data and structured approach to mapping of codes coding

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

# 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.