



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EudraVigilance and Signal Detection

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An agency of the European Union





In this talk...

- Burden of Adverse Drug Reactions
- Spontaneous reporting systems/EudraVigilance
- Signal Detection and Evaluation
- Opportunities for improvement to support better health protection and promotion



Background – Need To Further Strengthen Pharmacovigilance

- 5% of all hospital admissions are for Adverse Drug Reactions (ADRs)
- 5% of all hospital patients suffer an ADR
- ADRs are the 5th most common cause of hospital death
- Estimated 197,000 deaths per year in EU from ADRs
- EU societal cost of ADRs amounts to Euro 79 Billion per year

Source: Annex 2 of the Report on the impact assessment of strengthening and rationalising EU Pharmacovigilance
COMMISSION OF THE EUROPEAN COMMUNITIES Sept 2008

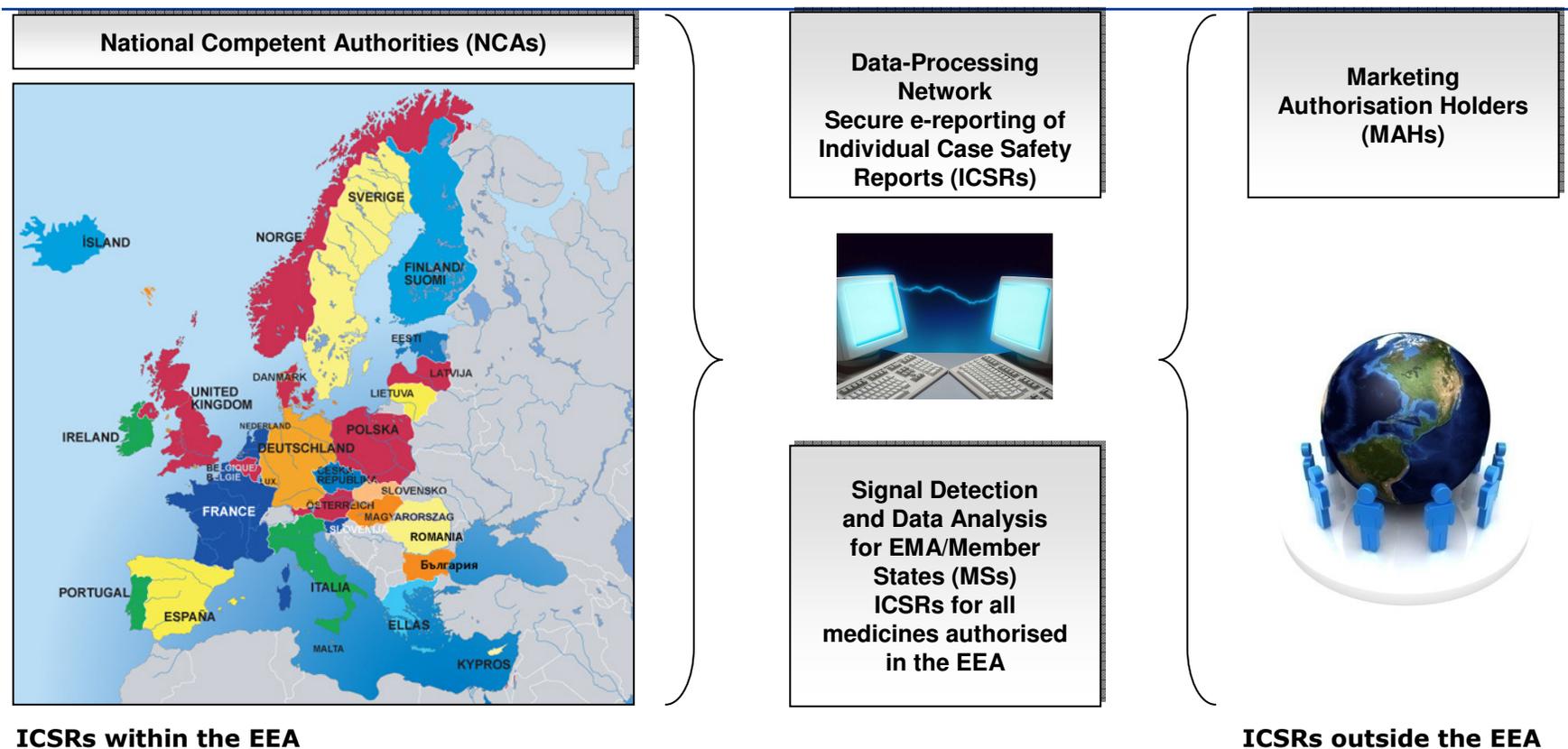


Post authorisation safety monitoring

- Pre-authorisation clinical trials are not of sufficient size to elucidate and characterize every adverse effect of a medicinal product
- Results cannot be assumed to be generalizable to patients who will use the product in a usual care setting
- Special populations such as elderly are underrepresented in preapproval clinical trails
- **Spontaneous reporting systems are an important source for safety monitoring in post authorisation “real-life” setting**



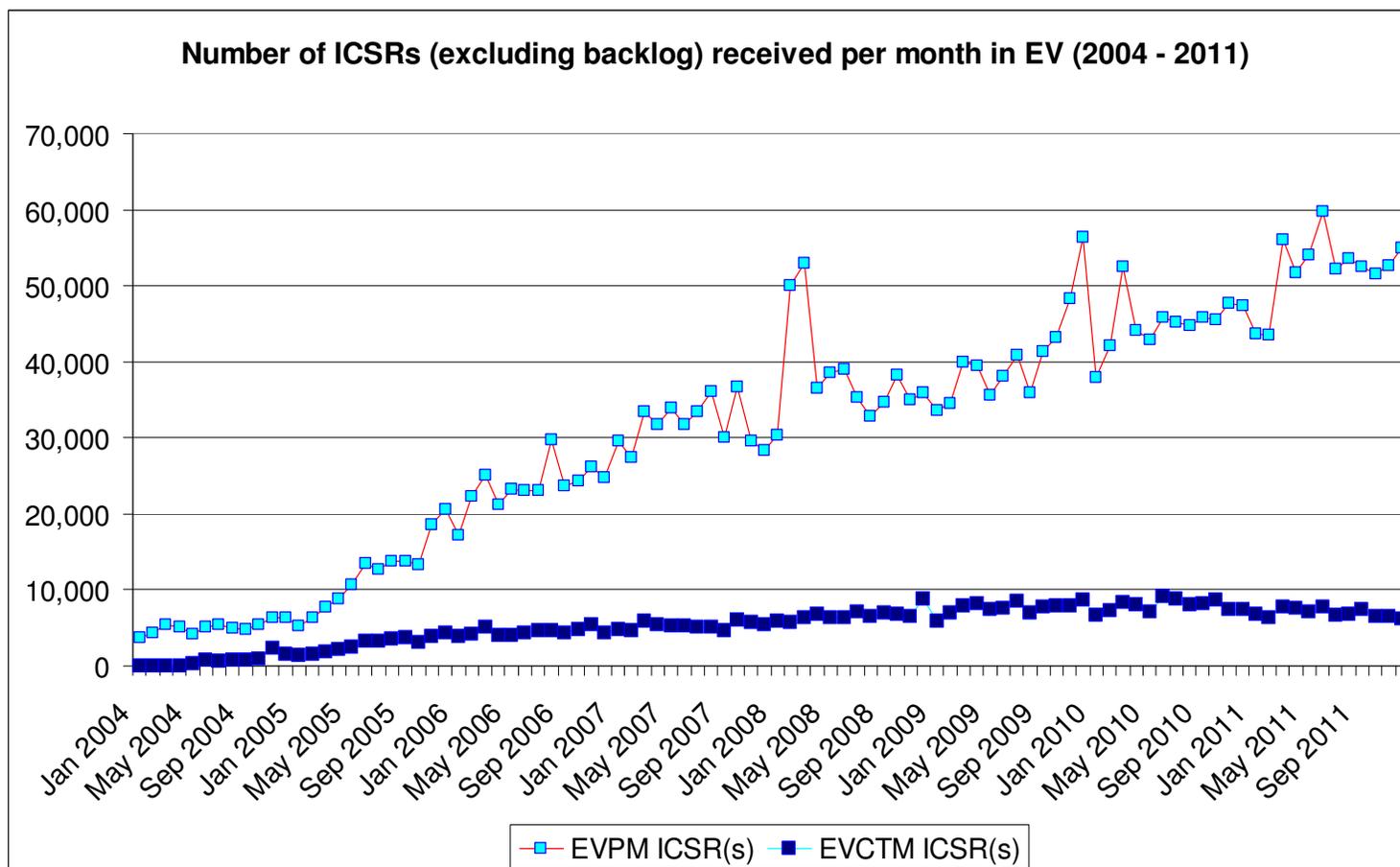
EudraVigilance



Facilitates mandatory e-reporting of adverse reactions in the EU



EudraVigilance Reports per month





EudraVigilance

Total number of cases = over 3 million (over 5 million ICSRs)

- **Post-Authorisation Module (EVPM)**

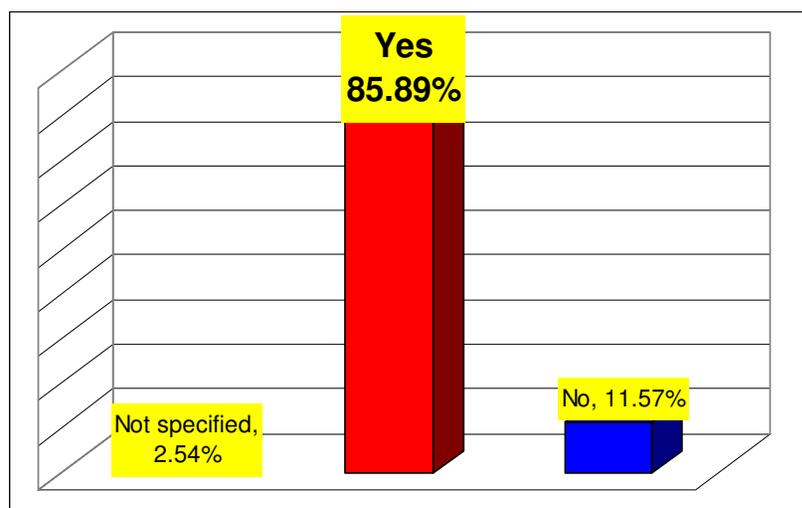
elderly - **25%** of all EVPM reports

EVPM	%
0 - 17 Years	8%
18 - 64 Years	43%
65 - 74 Years	13%
75 - 84 Years	9%
>= 85 Years	3%
DQI	25%

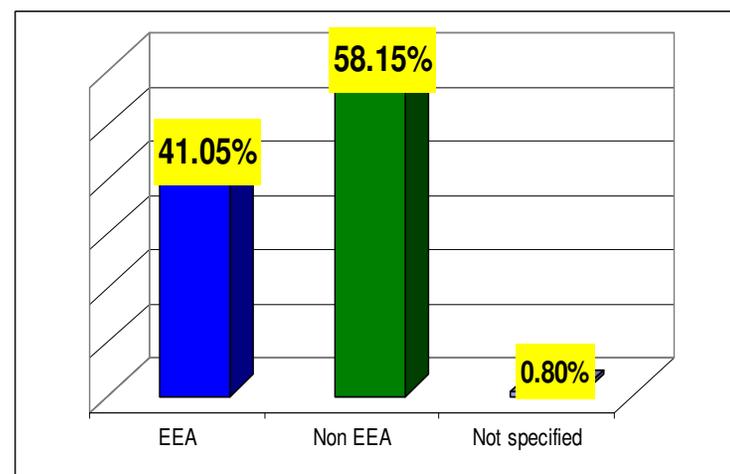


Spontaneous reports for elderly in EV by seriousness criteria

Serious?



Origin



Seriousness	Death	Life threat	Hospital	Disabling	Congenital	Other
Not specified	24%	27%	17%	29%	29%	24%
Yes	14%	9%	45%	4%	0%	32%
No	62%	64%	38%	67%	71%	44%



Spontaneous reports for elderly by ATC code of a suspected medication

Anatomical Therapeutic Chemical (ATC) code	%
Antineoplastic and immunomodulating agents	14.2%
Nervous system	12.3%
Cardiovascular system	11.6%
Blood and blood forming organs	11.2%
Antiinfectives for systemic use	8.9%
Musculo-skeletal system	7.0%
Alimentary tract and metabolism	6.5%
Genito-urinary system and sex hormones	2.3%
Systemic hormonal preparations, excluding sex hormones and insulins	2.0%
Respiratory system	1.6%
Sensory organs	1.1%
Dermatologicals	0.7%
Antiparasitic products, insecticides and repellents	0.2%
Various	1.9%
Not specified (for non recoded products)	33.3%



Most commonly reported Preferred Terms (PT) in elderly spontaneous cases

Top PT - EEA
Nausea
Dyspnoea
Vomiting
Diarrhoea
Thrombocytopenia
Pyrexia
Pruritus
Dizziness
Confusional state
Rash



Opportunities for improvement in Data collection and Transparency

- Emphasise the importance of spontaneous reporting through targeted campaigns
- Products under additional monitoring (new PhV legislation)
- Reporting of overdose, abuse, misuse, medication error (new PhV legislation)
- Improved data quality (general, encourage reporting of age)
- Facilitaion of patient reporting (new PhV legislation)
- Increase transparency and provide better information on medicines





EudraVigilance Access Policy Implementation (1)

Inform healthcare professionals and the general public by publishing collated adverse reaction data related to spontaneous reports for authorised medicines via web reports (website)

European database of suspected adverse drug reaction reports

Contacts | FAQ | Glossary

English (en)

Home About Understanding reports Search Medicine safety

Online access to suspected side-effect reports



On this website you can view data on **suspected side-effects** also known as suspected adverse drug reactions for authorised medicines in the European Economic Area (EEA).

This data is presented in a format called a **web report**. Currently the data only relates to medicines approved through the **centralised authorisation procedure**.



Search for a report

Search here for suspected adverse drug reaction reports

News

01/12/2011	xxxx
01/12/2011	xxxx

[More news...](#)



How to report a side-effect

Key information

- ▶ The information on this website relates to **suspected side effects**, i.e. medical events that have been observed following the use of a medicine, but which are **not necessarily related to or caused by the medicine**.
- ▶ Information on suspected side effects **should not be interpreted** as meaning that the medicine or the active substance causes the observed effect or is **unsafe to use**. Only a detailed evaluation and scientific assessment of all available data allows for robust conclusions to be drawn on the benefits and risks of a medicine.
- ▶ The European Medicines Agency publishes this data so that its stakeholders, including the general public, can access information that European regulatory authorities use to review the safety of a medicine or active substance. **Transparency** is a key guiding principle of the Agency.



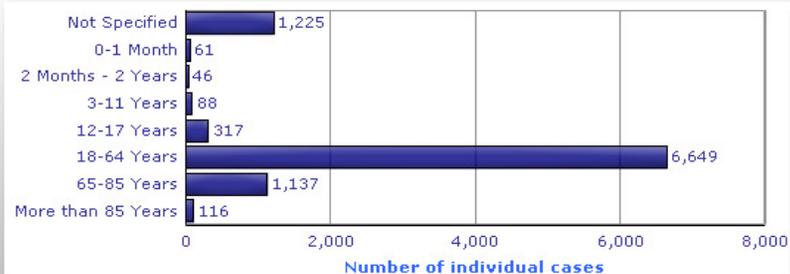


EudraVigilance Access Policy Implementation (2)

The number of individual cases identified in EudraVigilance for is 9,639 (up to Jan 2012)

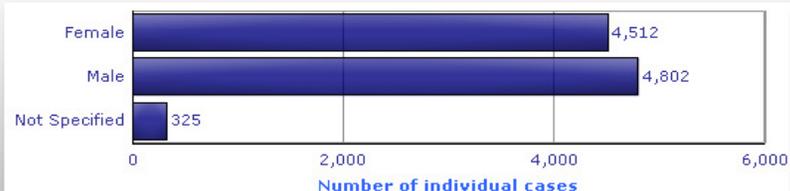
Number of individual cases by Age Group

	Cases	%
Not Specified	1,225	12.7
0-1 Month	61	0.6
2 Months - 2 Years	46	0.5
3-11 Years	88	0.9
12-17 Years	317	3.3
18-64 Years	6,649	69.0
65-85 Years	1,137	11.8
More than 85 Years	116	1.2
Total	9,639	100.0



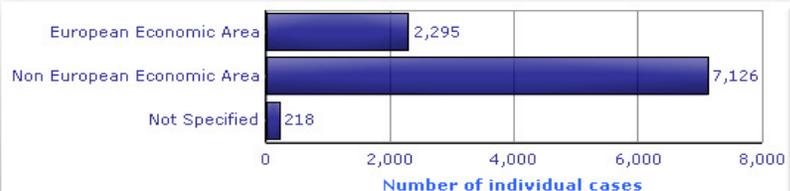
Number of individual cases by Sex

	Cases	%
Female	4,512	46.8
Male	4,802	49.8
Not Specified	325	3.4
Total	9,639	100.0



Number of individual cases by Geographic Origin (EEA/Non-EEA)

	Cases	%
European Economic Area	2,295	23.8
Non European Economic Area	7,126	73.9
Not Specified	218	2.3
Total	9,639	100.0





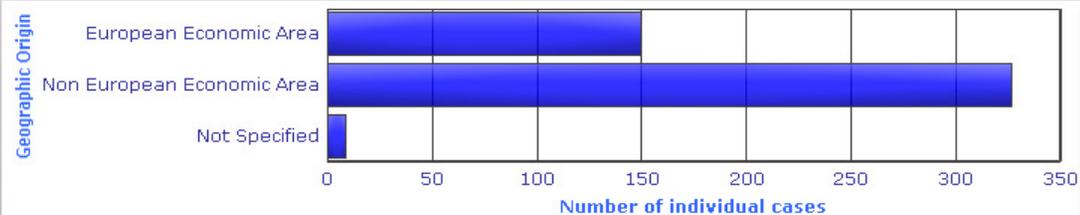
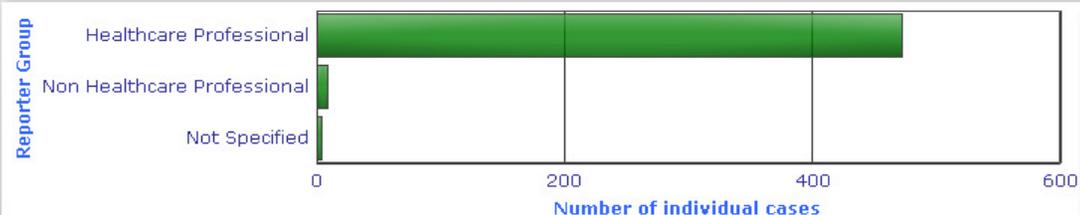
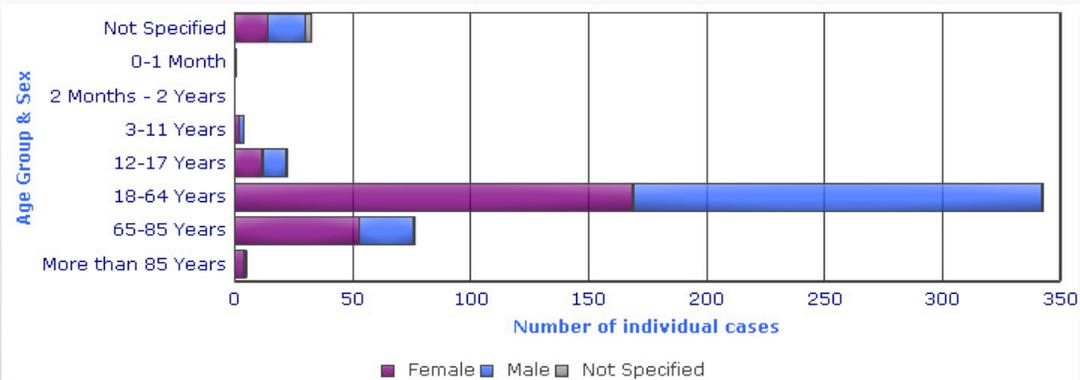
EudraVigilance Access Policy Implementation (3)

Choose a Reaction Group to see the number of individual cases identified in EudraVigilance for (up to Jan 2012)

Reaction Groups

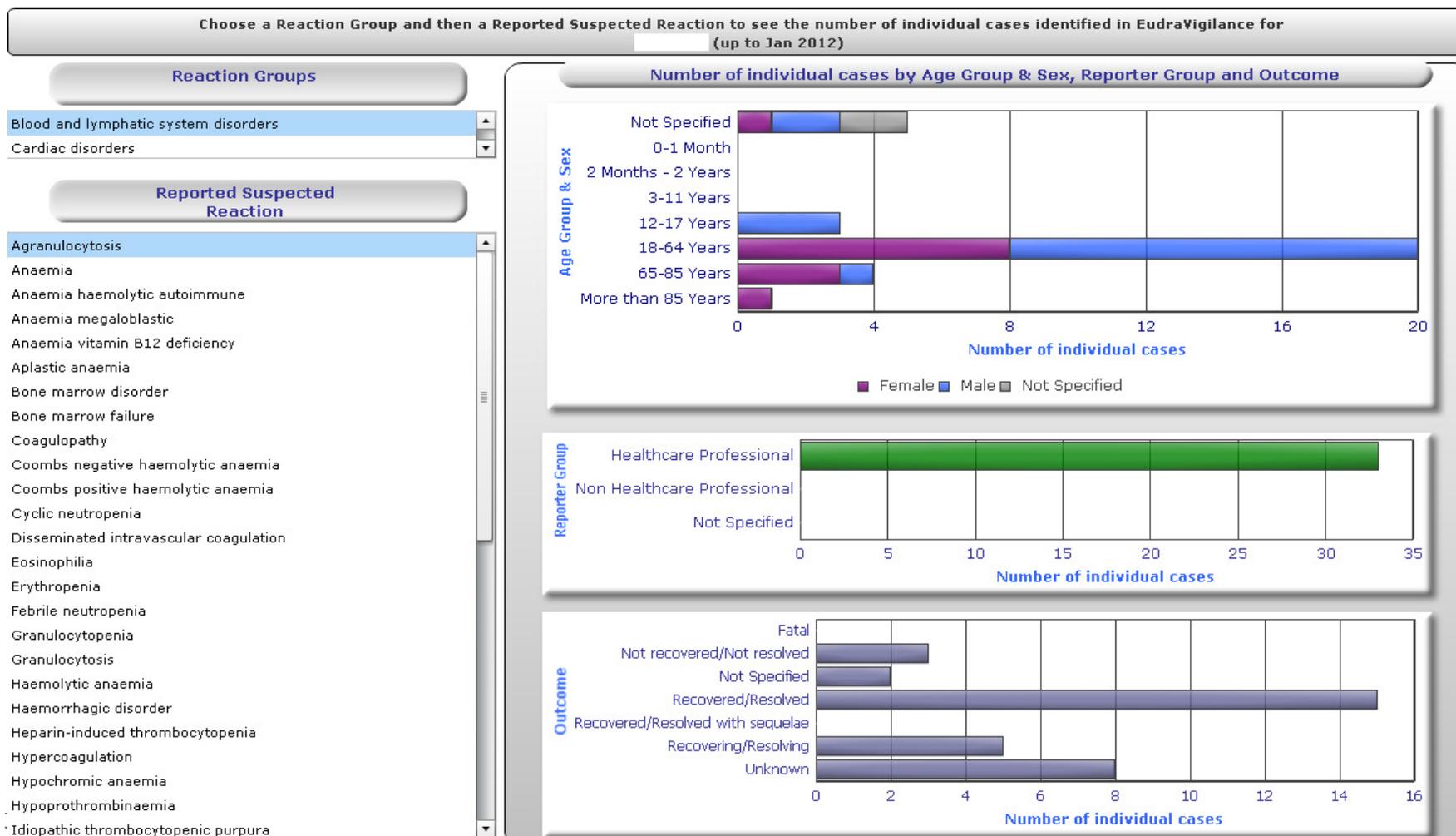
- Blood and lymphatic system disorders
- Cardiac disorders
- Congenital, familial and genetic disorders
- Ear and labyrinth disorders
- Endocrine disorders
- Eye disorders
- Gastrointestinal disorders
- General disorders and administration site conditions
- Hepatobiliary disorders
- Immune system disorders
- Infections and infestations
- Injury, poisoning and procedural complications
- Investigations
- Metabolism and nutrition disorders
- Musculoskeletal and connective tissue disorders
- Neoplasms benign, malignant and unspecified (incl cysts and polyps)
- Nervous system disorders
- Pregnancy, puerperium and perinatal conditions
- Psychiatric disorders
- Renal and urinary disorders
- Reproductive system and breast disorders
- Respiratory, thoracic and mediastinal disorders
- Skin and subcutaneous tissue disorders
- Social circumstances
- Surgical and medical procedures
- Vascular disorders

Number of individual cases by Age Group & Sex, Reporter Group and Geographic Origin





EudraVigilance Access Policy Implementation (4)





Signal Management (SM) definition and steps

SM – set of activities to determine based on various data sources* whether there are new risks associated medicinal products or whether risks have changed

Steps:

- **signal detection**
- signal validation and confirmation
- prioritisation, analysis and assessment
- recommendation for action

* ICSRs (EudraVigilance, national databases, company specific), data from active surveillance systems or studies, literature and other available



Statistical outputs for Signal Detection in elderly

Implemented recently



Reaction PT	PRR (-)	PRR	PRR (+)	New	New EEA	New Non EEA	New Fatal	Total	EEA	Non EEA	New elderly	Total elderly
Arrhythmia	0.44	1.17	3.12	4	1	3	3	4	1	3	2	2
Bradycardia	1.14	1.66	2.43	27	13	14	2	27	13	14	1	2

EudraVigilance safety monitoring:

- baseline **once monthly**
- **twice monthly week frequency** for products subject to additional monitoring
- more frequent than above only in specific situations





Opportunities to strengthen Signal Detection

- Focused SD in elderly: Targeted Medical Events, drug-drug interactions, medication errors
- Statistical signals of disproportionate reporting in sub-groups (IMI-PROTECT WP3)
- Consider possibilities for development of signal detection algorithm for drug/drug and drug/disease interactions
- Characterise/understand better patterns of ADR reporting in elderly
- Create Standardised MedDRA queries for defined areas of interest in elderly
- Identify and maintain list of drugs of interest in elderly



Conclusions

- ADRs are big burden to patients and society
- Signal Detection using spontaneous reporting systems is an important source for safety monitoring in post authorisation “real-life” setting, especially in populations underrepresented in preapproval clinical trails such as the elderly
- The main objective of the new pharmacovigilance legislations is to promote and protect public health by reducing burden of ADRs and optimising the use of medicines
- There are opportunities for improved data collection and enhanced signal detection that should be considered carefully in order to further strengthen pharmacovigilance in the older population



Thank you!