EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EudraVigilance and Signal Detection

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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

National Competent Authorities (NCAs)

ICSRs within the EEA

Data-Processing Network
Secure e-reporting of Individual Case Safety Reports (ICSRs)

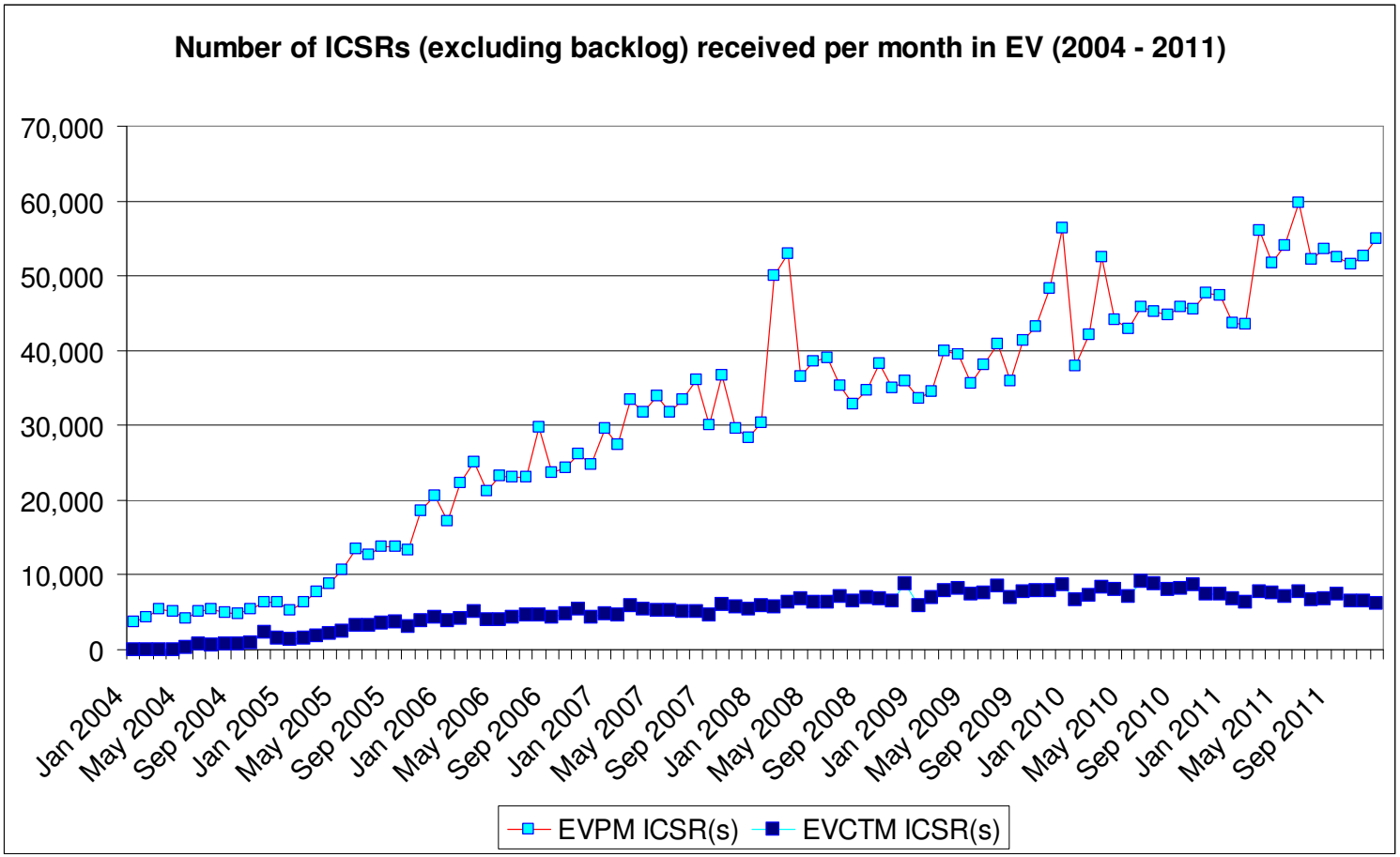
Signal Detection and Data Analysis for EMA/Member States (MSs)
ICSRs for all medicines authorised in the EEA

Marketing Authorisation Holders (MAHs)

ICSRs outside the EEA

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)

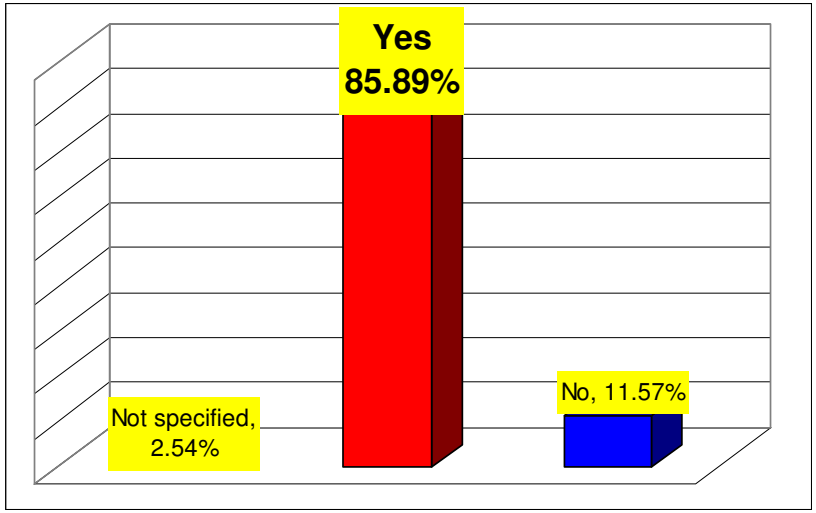
- **Post-Authorisation Module (EVPM)**

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

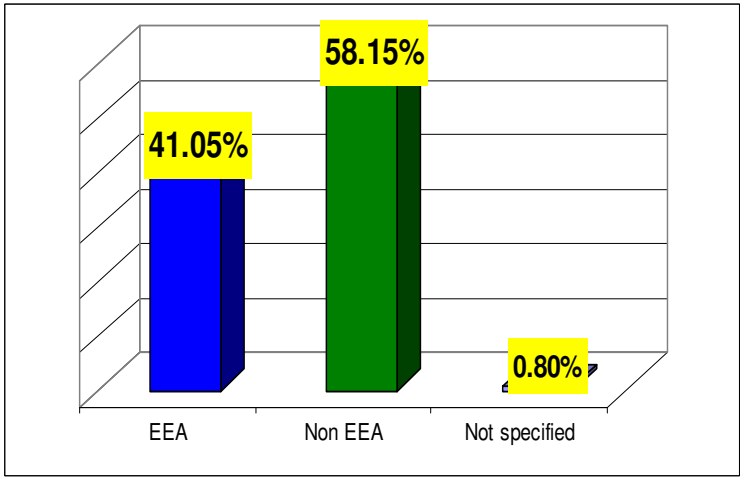
EVPM	%
0 - 17 Years	8%
18 - 64 Years	43%
65 - 74 Years	13%
75 - 84 Years	9%
>= 85 Years	3%
DQI	25%

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)

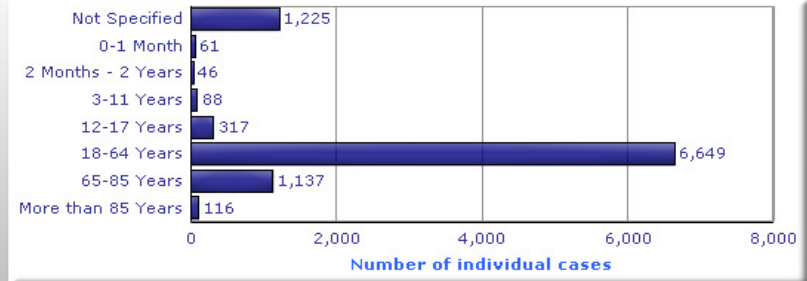
Inform healthcare professionals and the general public by publishing collated adverse reaction data related to spontaneous reports for authorised medicines via web reports (website)

EudraVigilance Access Policy Implementation (2)

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

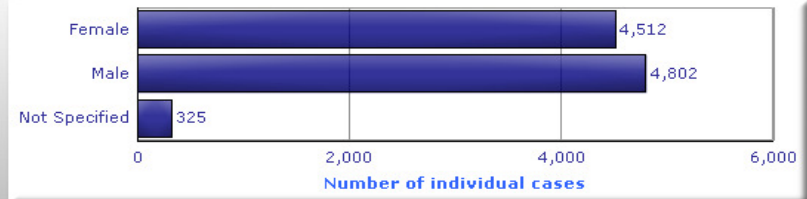
Number of individual cases by Age Group

	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**



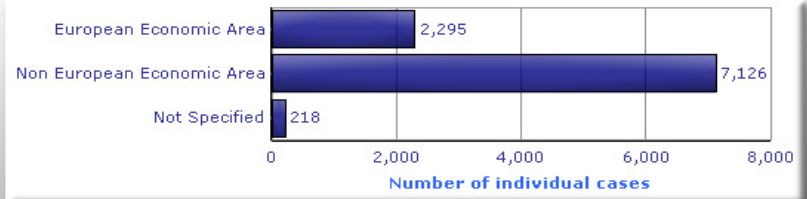
Number of individual cases by Sex

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

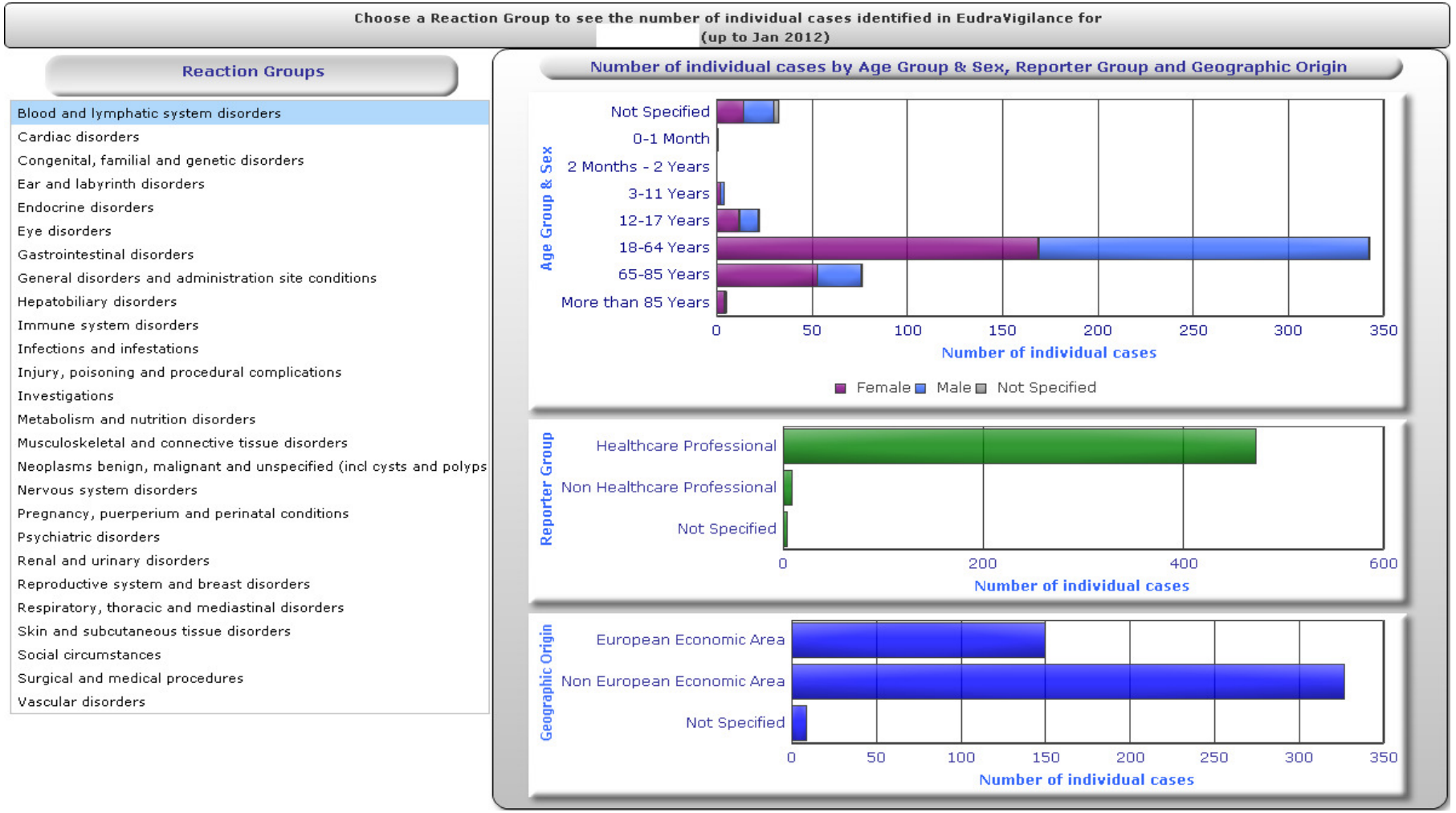


Number of individual cases by Geographic Origin (EEA/Non-EEA)

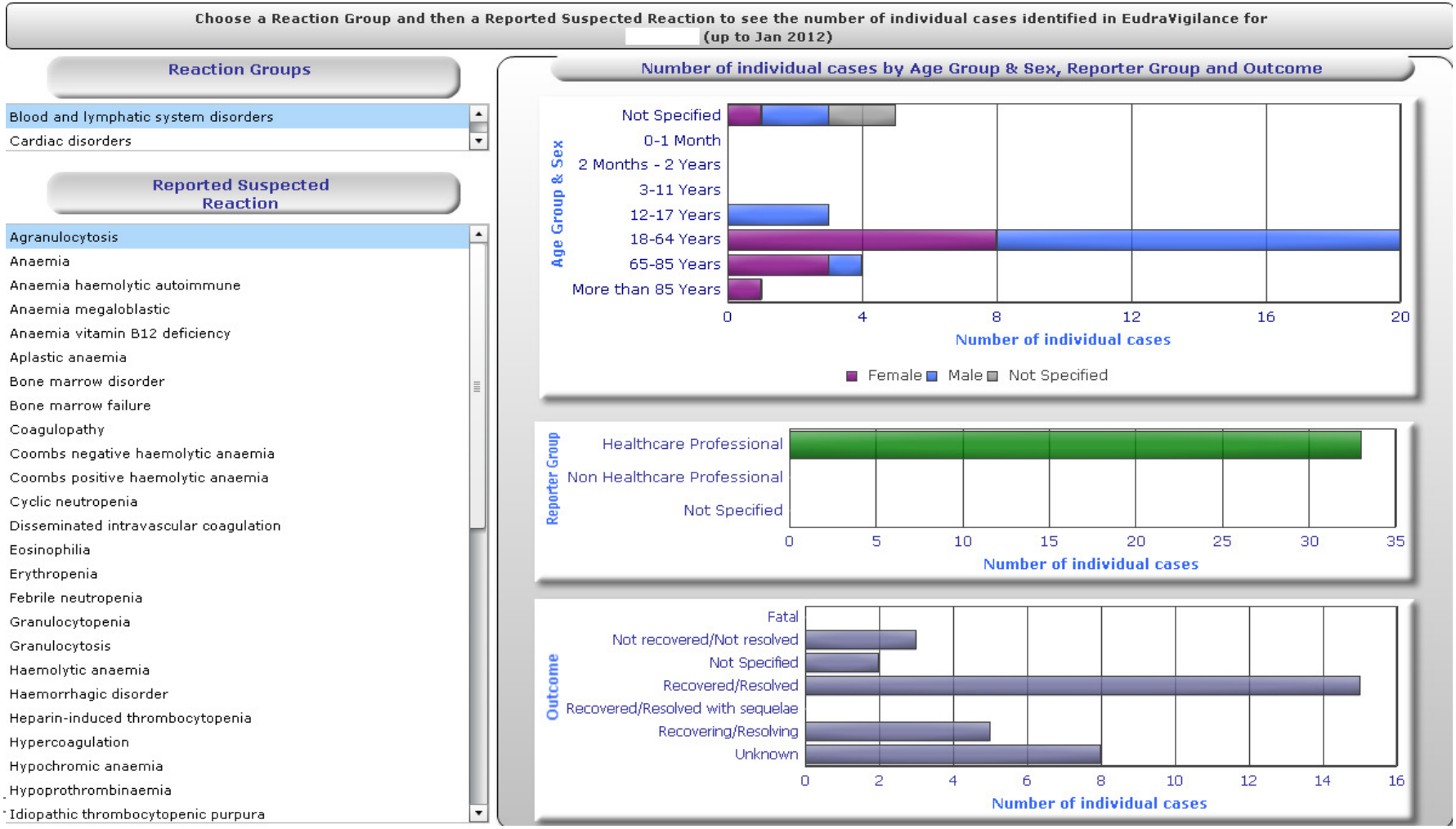
	Cases	%
European Economic Area	2,295	23.8
Non European Economic Area	7,126	73.9
Not Specified	218	2.3
Total	**9,639**	**100.0**



EudraVigilance Access Policy Implementation (3)



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 weather 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!