SCOPE Work Package 4
Survey Report

Topic 1 Audit of national reporting systems
Topic 1a Medication errors
Topic 2 Patient reporting
Topic 5 Review of IT systems and Special form of reports

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1 Introduction

The Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action spans over a 3 year time period (2013 - 2016) and has been created to support operations of pharmacovigilance in Europe following new requirements introduced by the European pharmacovigilance legislation which came into force in June 2012 (Regulation (EU) No 1235/2010). SCOPE gathers information and expertise on how regulators in Member States (MSs) run their national pharmacovigilance systems to develop and deliver guidance, training in key aspects of pharmacovigilance, and tools and templates to support best practice. SCOPE aims to support consistent approaches across the EU network for all pharmacovigilance system operations, which will benefit medicines safety monitoring and communications in the MS itself and the whole European market to safeguard public health.

SCOPE is divided into eight separate work packages, with five work packages focusing on pharmacovigilance topics to deliver specific and measureable objectives, ranging from improvements in Adverse Drug Reaction (ADR) reporting to assessment of quality management systems.

1.1 Document Revision History

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1.2 Definitions and abbreviations

Terminology	Description
ADR	Adverse Drug Reaction
AEFI	Adverse Events Following Immunization
App	Application
ATC	Anatomical Therapeutic Chemical
BI	Business Intelligence
CDPC	European Committee on Crime Problems
CHAFEA	Consumers, Health and Food Executive Agency
CT	Clinical Trials
CZ	Czech Republic
DB	Database
DHPC	Dear 'Healthcare professionals' Communications
EMA	European Medicines Agency
EU	European Union
EV	Eudravigilance
EVDAS	Eudravigilance Data Analysis System
FTE	Full Time Equivalent
FUP	Follow up
GP	General Practitioner
GVP	Good Pharmacovigilance Practices
HCP	Healthcare Professional
HER	Electronic Health Record
HL7	Health Level Seven
HR	Croatia
HU	Hungary
ICD	International Classification of Diseases
ICH E2B(R2)	International conference on harmonisation of technical requirements for registration of pharmaceuticals for human use- Data Elements for Transmission Of Individual Case Safety Reports E2B(R2)
ICSR	Individual Case Safety Report
IME	Important Medical Event Terms
IQR	Interquartile Range
IT	Information Technology
IT	Italy
LAB	Labelling
LAREB	Netherlands Pharmacovigilance Centre
LT	Lithuania
MAH	Marketing Authorisation Holder
MD	Medical Doctor
ME	Medication Errors
MedDRA	Medical Dictionary for Regulatory Activities
MP	Medicinal Product
MS	Member State

MS SQL DB	Microsoft SQL Database
N/A	Not applicable
NCA	National Competent Authority
NO	Norway
No	Number
PhV	Pharmacovigilance
PIL	Patient Information Leaflet
PSUR	Periodic Safety Update Report
PT	Portugal
Q	Question
Q&A	Questions & Answers
RMM	Risk Minimisation Measures
SCO	System Organ Class
SCOPE	Strengthening Collaboration for Operating Pharmacovigilance in Europe
SDR	Serious Drug Reaction
SNOMED-CT	Systematized Nomenclature of Medicine- Clinical Terms
SOP	Standard Operating Procedure
SPC	Summary of Product Characteristics
SPSS	Statistical Package for the Social Sciences
SUSAR	Suspected Unexpected Serious Adverse Reaction
T	Topic
UK	United Kingdom
UMC	Uppsala Monitoring Centre
WHO	World Health Organization
WP	Work Package
XLS	Excel Spreadsheet
XML	Extensible Mark-up Language
YCS	Yellow Card Scheme

1.3 Attachments

Ref No	Document name	Author(s)
1	Audit of national reporting systems survey- pdf version of final survey circulated to Member States	WP 4.1
2	Medication errors- pdf version of final survey circulated to Member States	WP 4.1a
3	Patient reporting- pdf version of final survey circulated to Member States	WP 4.2
4	Review of IT systems and special form of report- pdf version of final survey circulated to Member States	WP 4.5

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1.5 Executive summary

This report outlines the collection of information about EU National Competent Authorities (NCAs) for human medicines ADR reporting systems to provide pharmacovigilance information through four questionnaires completed by Member States (MSs). The term Member State (MS) was used instead of NCA because in some MSs Institutions who responded to our questionnaires are not formally NCAs, but they are part of the pharmacovigilance network in the particular MS.

The four surveys form the activity of the SCOPE Joint Action topics 1 (Audit of national reporting systems), 1a (Medication errors), 2 (Patient reporting) and 5 (Review of IT systems and special form of reports) and are part of WP4 led by HALMED (HR). Topics 3 (Awareness levels) and 4 (Reporting forms), which are also part of WP4, are not presented in this report, since they are led by MHRA (UK) and are going to be presented as separate documents. The results and findings from the survey will contribute towards recommendations for delivery of useful tools for improving MSs' ADR reporting systems in the framework of the new EU pharmacovigilance legislation.

Four (4) web-based questionnaires were developed by SCOPE WP4 topics 1, 1a, 2 and 5 led team in collaboration with contributing countries and collaborating partners. After launching the pilot survey in April 2014, collected responses were analysed and the questionnaires were finalized. Final questionnaires were distributed in June 2014 for completion to all EU countries, Norway, Iceland, and Lichtenstein. Responses from 28 MSs were collected and a detailed analysis was done.

1.5.1 Topic 1 Audit of national reporting systems

28 MSs provided answers to topic's questionnaire. Based on the quantitative and qualitative analyses of collected data a snapshot of the national reporting system was created.

First section of the questionnaire was devoted to describing the set-up of the national pharmacovigilance system such as:

- the characteristics of national ADR databases,
- institutions responsible for ADR reporting,
- legal obligation for HCPs to report ADRs,
- availability of channels for ADR reporting,
- means of accepting ADR reports from industry and
- availability of ADR reporting forms (paper end electronic).

The results showed that 75% of MSs have their ADR database for human medicines placed within the NCA. Almost all MSs have ICH E2B compatible databases which contain serious, non-serious and patient ADR reports. In all MSs ADRs are reported for medicinal

products and vaccines, while the number of MSs collecting ADR reports for food supplements, cosmetics and devices is a bit lower - 16, 17 and 24 respectively.

In 22 countries (79%) reporting of ADRs is mandatory for HCPs (defined by law), in 15 countries for both serious and non-serious and in 7 for serious ADRs only. The percentage of countries with mandatory reporting of ADRs for vaccines (Adverse Events Following Immunization - AEFI) are even higher (89% or in 26 countries (in 19 for serious and non-serious and in 6 for serious only). The highest percentage (38%) of all ADR reports is received via web-based application, even though the number of MSs having web based application as available reporting channel is lower than the number of MSs having mail reporting channel available, (21 vs. 28). All MSs who are responsible for accepting ADR reports from industry are compliant with new pharmacovigilance legislation and are receiving ADR reports through Eudravigilance Gateway/Webtrader. All MSs have ADR reporting forms available on their NCA's websites.

Second section of the questionnaire was dedicated to composition of ADRs (to medicinal products and vaccines/biologics) in NCA database. The aim of this section was to capture the total number of ADR reports in the 5 years period (2009-2013), stratification of ADRs by the type of reporter in 2013 in the whole database, and the percentage (%) of all spontaneous ADR reports by the type of healthcare professional (HCPs) in the observed 5 years period. Total number of ADRs received, as well as the total number of serious ADRs, is increasing in this period (2009-2013). In 2013 the majority of reports were received from the industry. Data on ADR reports categorized by patient age groups and gender were collected. Steadily most of the reports were reported for female patients in age group >18 years ≤ 69 years (adults). Data about ADR in most cases is provided to the public via cumulative reports on a website (i.e. annual reports or Drug Analysis Print).

Third section was dealing with Member States ADR processing capacity. This section starts with a free text question which is aimed to provide a general overview of ADR processing for different types of ADR reports (patient/industry/HCP) in each MS. It is also focussing on MS's specificities regarding ADR reports assessment and here MSs described in detail how the assessment is performed and which aspects are taken into consideration. The aim of this section is also to learn about time and resources available in each MS for ADR reporting processing.

Following sections were asking about performance indicators, performing duplicate detection and having duplicate detection system in place, percentages of follow up reports and what follow-up information is most often asked for. Indicators/metrics for assessing quality of reports were also provided. One section focused on how MSs identify ADR reports associated with drugs on additional monitoring list in their databases and if there is any difference in managing ADRs where suspect drugs are included in the EU additional monitoring list to those which are not included into this list. There was a section dedicated to traceability of biologics asking MSs have they implemented any useful methodology which improves the information collected on biologics. It was also focusing on brand and batch capturing for biologics and vaccines.

1.5.2 Topic 1a Medication Errors

28 MSs responded to this questionnaire. In 12 MSs HCPs are exempt from liability when reporting cases of medication errors (ME). 27 MSs reported that there are data privacy requirements at national level with regards to patient data, while 15 MSs have the same requirements regarding HCP data.
27 MSs stated that they are compliant with EU data protection laws.

With regards to coding of medication errors, 25 MSs perform it, if it is specified in ADR report and 20 MSs perform it during the assessment of ADR. In 24 MSs NCA is collecting data about medication errors. Fourteen (14) MSs exchange ADR reports of ME resulted in ADR with other institutions or organizations within their MS which are dealing with ME. Eight (8) MSs have an operational guideline (SOP) of ME to support coding, reporting, analysis and prevention in patient safety and pharmacovigilance systems. 26 out of 28 MSs handle patient reports of ME in the same way as HCP reports. 18 MSs provide feedback to the reporter of ME. Different countries take different approach in communicating risk-management strategies for ME, but some of the most popular methods are:

- Web sites (including dedicated web sites for patients)
- DHPC
- Changes in SPC/PIL/LAB

1.5.3 Topic 2 Patient reporting

The questionnaire focused on directed patient reporting of spontaneous ADRs to medicinal products including vaccines/biologics. Results and findings from the questionnaire were intended to provide a snapshot (from a period of 2009-2013) of national systems for direct patient reporting across MSs, and inform the recommendations for delivery of guidance on the operation of patient reporting systems in the EU.

26 of 27 member states indicated that patient ADR reporting has been introduced into their national legislation. All member states have legal specificities which are not different from provisions of the EU Directive (2010/85/EU) on patient reporting.

28 member states have patient reporting systems in place, with the majority introducing this in 2012/13, although the first member state to introduce this did so in 1968 and the second in 1996.

The total number of direct patient ADR reports increased significantly in 2013, as well as the number of serious ADRs.

24 member states confirmed that patients can report via mail, 21 that they can report via e-mail, 20 through fax and web-based forms, and 19 via telephone. 1 also specified mobile reporting, and 2 others that patients can report in person.

Patient reporting forms are made available through many sources; the most common source, aside from NCAs for human medicines, was regional ADR centres (8 member states), patient organisations (7), MAH (7) and healthcare (6) websites. In addition paper forms are made available at pharmacies for 7 member states.

Some MSs work with patient organisations to facilitate ADR reporting. The number of patient organisations involved per member state varied from 1 to 20. In some MSs there are individual patient organizations; in the others there is an overarching organization which covers more than one patient organisation in itself.

Most patient reports in 2013 were reported by consumer or patient (47%) themselves, followed by parents for children (23%) and children for parents (2%). There were some MSs with specific stratification by reporter. However, only 13 MSs provided responses for this question.

Most of the MSs (21/28) provided data on percentage (%) of patient ADRs in 2013 by gender. Patient ADRs are reported predominately for female patients (65%), this is in line with available literature.

24 MSs provide feedback to patients, 18 send acknowledgments, 15 provide individual case feedback, 4 respond with individual case feedback.

25 MSs confirmed that they follow up with the patient (consumer) reporters, while 3 MSs answered that they do not perform follow up. This might be due to national personal data protection policies. Also, 23 MSs ask patients for permission to contact their doctor.

25 NCAs consider reports valid without medical confirmation, while 3 MSs do not. 8 MS (30%) always seek medical confirmation, 16 MSs (59%) sometimes seek medical confirmation, while 3 MSs (11%) never seek medical confirmation for patient ADR reports, which might be due to national personal data protection policies.

14 MSs responded that patient ADR reports did not contribute to the detection of signals, 10 MSs responded that signals have been detected where patient ADR reports formed part of the evidence alongside reports from other sources, 3 MSs responded that signals have been detected based solely on patient ADR reports.

The majority (70%) of MSs agreed that patient reporting has made a positive contribution to PhV and patient safety.

20 MSs indicated future development plans for patient reporting and provided details about their plans. 7 are going to develop different educational activities aiming to raise awareness of ADR reporting among general public and/or patients, focusing primarily on general reporting scheme awareness campaigns and educational activities. 6 MSs indicated plans to develop the web-based forms for patients, and 5 are interested in mobile apps for ADR reporting. Also, 5 MSs informed on other improvement such as, education of staff, increase of staff, development of adequate IT support, further work with regional

centres, research into social media and making adjustments to the reporting system in order to make patient reporting easier.

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1.5.4 Topic 5 Review of IT systems and Special form of reports

Topic 5 received a survey response rate of 27 MSs.

First section of the questionnaire focused on national IT systems for ADR reporting. Information about different ADR systems and technologies used is collected, the purpose of ADR systems is reviewed and BI tools overview is provided.

Second section focused on electronic ADR reporting. Current state of electronic ADR reporting is evaluated, i.e. who is using it (patients/HCPs), how are the reports submitted and which standards are being used. The results showed that the vast majority of member states have implemented e-reporting and out of 4 MSs which haven't, 2 MSs were developing the application at the time of the questionnaire, one has lack of human resources and IT support and one is expecting a system developed by EMA.

Third section was specified for the evaluation of the state of implementation of electronic reporting and E2B (R2). Insights into technologies and databases used communication between systems and databases and transmission of ADR reports between respondent's institution and MAHs are provided.

Fourth section provided report on the current state of implementation of electronic health records in EU, integration with ADR reporting systems, registries and databases used as well as on identification of electronic systems and information sent between them. Only 4 MSs fully implemented electronic health record systems, while 12 MSs implemented it partially. Out of 6 MSs which haven't implemented it in 4 countries respondent's institution is not responsible for this activity. 5 MSs receive ADR reports from any system containing patient records or medical data.

Fifth section was devoted to traceability of biologics. Only one MSs stated that they use some IT system or a software tool for traceability of biologics. The tool is internal spreadsheet and it is not connected with any other system.

Sixth section was about possibilities of integration of mobile reporting with health records and health care systems, future perspectives and initiatives, as well as mobile and social network applications for ADR reporting. Two (2) MSs have mobile application available for ADR reporting. Both applications have the same fields as ones in their electronic forms and are unable to scan products license numbers and translate them to the product name. None MS has social network application available for ADR reporting.

1.6 Background

Work Package 4 focuses on national schemes for the spontaneous reporting of adverse drug reactions (ADRs) and aims to provide National Competent Authorities (NCAs) for human medicines with a full understanding of and best practice in systems for collecting adverse drug reactions. Information is gathered from European NCAs to understand their national pharmacovigilance IT system capabilities as well as implementation of patient reporting, types and reporting forms developed, and electronic reporting developments including those from clinical healthcare systems. This information will be used to create a media toolkit for raising awareness of ADR reporting systems, best practice guidelines, and performance indicators which will be supported through delivery of a training course for NCAs.

1.6.1 *Topics*

Within Work Package 4, there are six individual topics:

1. Audit of national reporting systems – lead: HALMED
1a. Medication errors- lead: HALMED
2. Patient reporting – lead: HALMED
3. Awareness levels – lead: MHRA
4. Review of reporting forms – lead: MHRA
5. Review of IT systems and Special form of reports – lead: HALMED

1.6.2 *Partners involved*

Contributing countries:

- AIFA (Italy)
- OGYEI (Hungary)
- INFARMED (Portugal)
- NOMA (Norway)
- SMCA (Lithuania)
- SUKL (Czech Republic)

Collaborative institutions:

- LAREB- Netherlands Pharmacovigilance Centre (The Netherlands)
- UMC- Uppsala Monitoring Centre (Sweden)
- The University of Nottingham (United Kingdom)

1.7 Context and scope of report:

Aim

To provide National Competent Authorities (NCAs) for human medicines with a full understanding of and best practice in systems for collecting and processing of adverse drug reactions. The results of this WP should provide a basis for development and management of ADR collection in MSs for a better EU Pharmacovigilance system in the scope of the Pharmacovigilance legislation which came into force in 2012.

Sponsors of SCOPE

The Consumers, Health and Food Executive Agency (CHAFEA) are an executive Agency of the European Commission who is responsible for initiating the SCOPE Joint Action and for providing the 70% of the funding. The remaining 30% of funding is provided by SCOPE partners.

Public interest

Collection and processing of ADRs is crucial to monitor the safety of all medicines for all members of the public. Having the correct information available in a timely manner will ensure that any safety issues can be identified and acted on promptly to protect public and individual patient health.

Audience

The audience for the survey are Member States' (MS) institutions. SCOPE Work Package Leaders conducted a short survey with all MSs prior to sending out WP4 questionnaires to all involved SCOPE MSs, to determine whether regional centres should be involved in responding to questionnaires. The majority of MSs replied that they would prefer the questionnaires to be completed by the institution that is the NCA only.

1.7.1 Main goal

This report aims to summarise results of the SCOPE surveys on topics:

- Audit of national reporting systems,
- Medication errors,
- Patient reporting and
- Review of IT systems and special form of reports.

The main goal is to provide snapshots of national pharmacovigilance systems to enable NCAs to improve their systems on the basis of existing practices in various MSs and to maximize efforts in their national spontaneous ADR reporting systems for human medicines and to direct next steps and recommendations.

1.7.2 Objectives

Results from the survey have been used to deliver snapshot of national pharmacovigilance systems, focusing specifically on ADR collection and processing, across EU member states and to direct next steps and recommendations. This is to support MSs to

meet requirements set out in the EU pharmacovigilance legislation, as well as to provide suggestions for MSs who wish to further improve their ADR reporting systems. Taking into account that some of the member states have already implemented certain measures from the new legislation, they are in a position to provide example, based on the own experience to other member states for an effective implementing of their activities.

1.7.3 Challenges

There are challenges posed from the potential interpretations of questions and terminology. This makes it difficult to generalise results and comparison of responses between respondents could be impacted by differences in interpretation. For recommendations themselves, there will always be the potential for challenges in national applicability with the significant range of contexts, stakeholders and factors relevant in different MSs. The size of the population of each MS and number of people employed within pharmacovigilance departments should also been taken into account when interpreting the results.

There were several challenges in the interpretation of results:

- Some technical difficulties occurred and question 4 in Medication errors questionnaire was not working properly. This question was followed up with each MS to better understand the responses.
- Some responses were contradictory, therefore in case we haven't received follow up answer from certain MS, their response on that question was excluded from the analyses.
- In some situations where there was expected to choose one of responses, some MSs choose multiple options and those answers were treated as invalid.
- There was confusion with "double negation", i.e. when answering to the option "Our institution is not responsible for this activity" with "no", some MSs considered it as double negation which in fact means confirmation. This issue was solved with targeted follow up.
- The questionnaires were designed to have "yes" and "no" option for each response offered. It was expected to select either one of them. Many MSs selected only options for which their answer was "yes". For matters of statistical analyses, all unselected options were considered as "no".

2 Methodology

2.1 Tool and survey method:

The platform chosen for the questionnaires was the Qualtrics Online Survey Service, which can be accessed at http://qualtrics.com/. It is an easy-to-use, full-featured, web-based tool for creating and conducting online surveys. A key feature of this service which

makes it more appealing is that supports all the question types used across the questionnaires.

Qualtrics allows export of the collected data to SPSS, Excel and other programmes and also has some statistical options within the platform, for which there is a possibility to do some statistics. The data held within Qualtrics is confidential with the capacity to complete all surveys and pilots.

The survey was developed by topics leader (HR) in collaboration with contributing countries in the WP4 (UK, NO, IT, HU, CZ, LT, PT) and collaborating institutions (LAREB, Uppsala Monitoring Centre (UMC) and The University of Nottingham).

A pilot survey was launched on 2nd April 2014. WP4 received responses to all surveys from eight contributing countries (CZ, HU, IT, LT, PT, NO, UK, HR) and one collaborating institution (LAREB) on the April, 18th 2014. Surveys were also sent to other collaborating institutions (UMC and Nottingham University) for review. The pilot aimed to gain peer review, maximise understanding and clarity of the questions posed, gain insight into the ease of retrieving the data and estimate time taken to complete the questionnaire to ensure the final pilot was as robust as possible. A face-to-face meeting was held on 29/30 May 2014 in London between topic leaders (HR and UK). Pilot analysis was performed and all suggestions and comments from respondents and collaborating institutions were taken into account when finalising the surveys. The WP4 lead, HR, used a psychologist and a statistician to help with pilot analysis and improvement.

WP4 launched the final version of its surveys on 11th June 2014 and sent to the SCOPE contact points in the MSs. This was the first survey launched in the SCOPE project. It was distributed for completion to all EU countries, Norway, Iceland, and Lichtenstein. The deadline for completing the survey was 11th July 2014. This deadline was extended individually for each MS to ensure that more responses were received.

Personalised follow up questions to MSs were sent out on 15th April 2015 with a deadline of 15th May 2015.

Reminders were sent, via email, to ensure that as many respondents as possible completed the pilot, final questionnaires and follow up responses respectively.

The final surveys were sent with detailed instructions for completion via an email link to all MSs' institutions responsible for ADR reporting, collection, processing, and data analysis on national level. Member States were asked to ensure that the survey was completed by a person who had an overview of all systems within the institution and not to provide his/her personal views.

The final surveys consisted off as follows:

1. Audit of national reporting systems- 84 questions

1a. Medication errors- 16 questions

2. Patient reporting – 69 questions

5. Review of IT systems and Special form of reports – 64 questions

It should be noted that introductory text or section headers appear as questions due to the functionality of Qualtrics although are not questions. Printable versions of the electronic surveys are included in Annexes.

2.2 Setting and participants:

WP4 surveys received an excellent response rate, with 28 partners completing all WP4 surveys, including several Member States (MSs) who are not officially part of the SCOPE consortium. It is important to note here that on two surveys regarding topic 4 Reporting forms and topic 5 Review of IT systems and special form of reports one member state (out of above mentioned 28 member states) did not respond, which means that those two surveys were completed by 27 member states in total.

Varying numbers of MSs responded to individual questions, and parts of questions, as these were not made mandatory to make completing the survey easier.

The fact that the response rate was considerably high should mean that results provide a good insight in present practices that can serve as a base for recommendations and toolsets.

2.3 Data analysis (quantitative and qualitative)

The questionnaires used a combination of multiple choice questions (both single and multiple questions allowed), drop-down menus, textboxes, and rating questions. For certain questions and subsequent follow up on questions, pre-set types of answers were mandated to ensure consistency in approach to facilitate coherent analysis. Free text comments have been reviewed to identify key words or topics and grouped together in order to identify themes and trends to inform the conclusions and recommendations.

Due to the nature of the questionnaire the analysis of data is mainly descriptive using graphical representations to outline key findings and trends.

3 Findings/Results

The results of each question in the survey are presented per topic in the following order:

1. Audit of national reporting systems
1a. Medication errors
2. Patient reporting
5. Review of IT systems and Special form of reports

3.1 Topic 1: Audit of national reporting systems

Question T1Q4:

Please describe in the form of short essay the set-up of the national pharmacovigilance system in your MS. In case there are regional pharmacovigilance centres in your MS, please make sure to all relevant information regarding their scope of work and interaction with NCA.

In the question 4 of Topic 1, a description of national pharmacovigilance system set-up in different MSs was given. Countries provided the information whether there is a division of responsibilities between two or more competent authorities with regard to ADR reporting. Furthermore, MSs provided information whether they use a national ADR database or a spread-sheet only, they specified the kind of database they use and provided the name of the manufacturer. In addition, MSs replied if there are regional or other local institutions and what are their responsibilities and relation with NCA. Finally, MSs described the flow of reports from the reporter to the national database and flow from regional centres (with the description of interaction with regional centres and their responsibilities), if existing. Member states provided their answers in the form of the short essay.

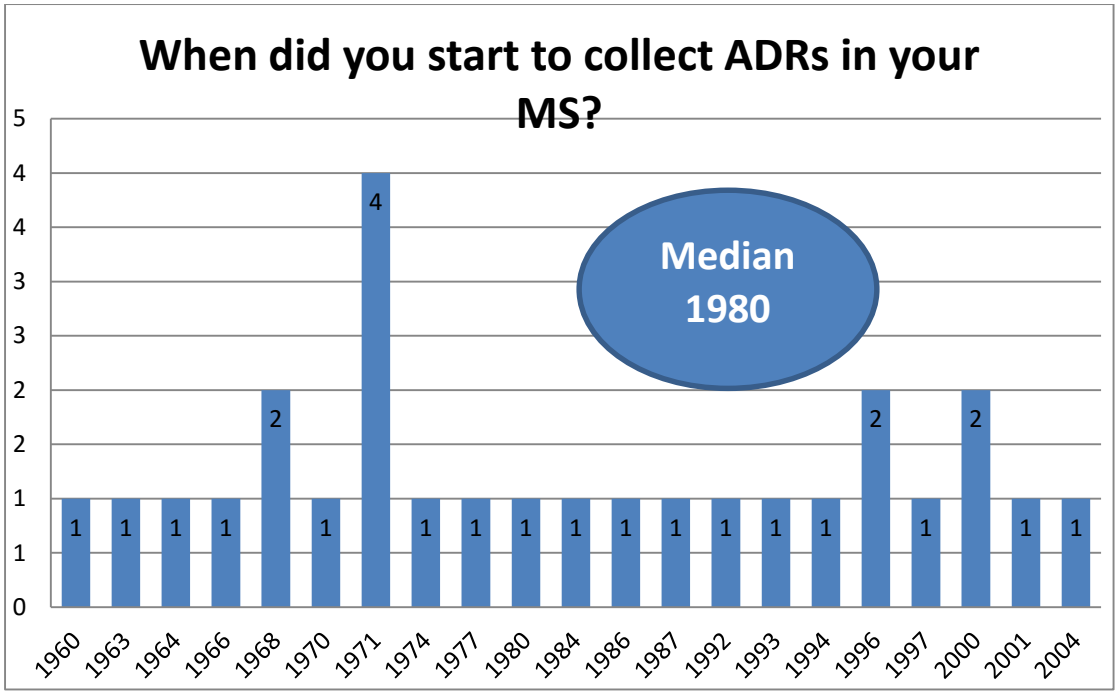
The answers obtained showed the **great diversity of national pharmacovigilance systems** which should be the basis of the SCOPE approach toward each individual country, respecting cultural differences and heterogeneity.

T1Q5 a) Reporting format

This set of questions is focussing on national ADR database in each MS, channels that are made available for receiving ADR reports and the way ADR reporting forms are made available to reporters.

Question T1Q6:

When did you start to collect ADRs in your MS?

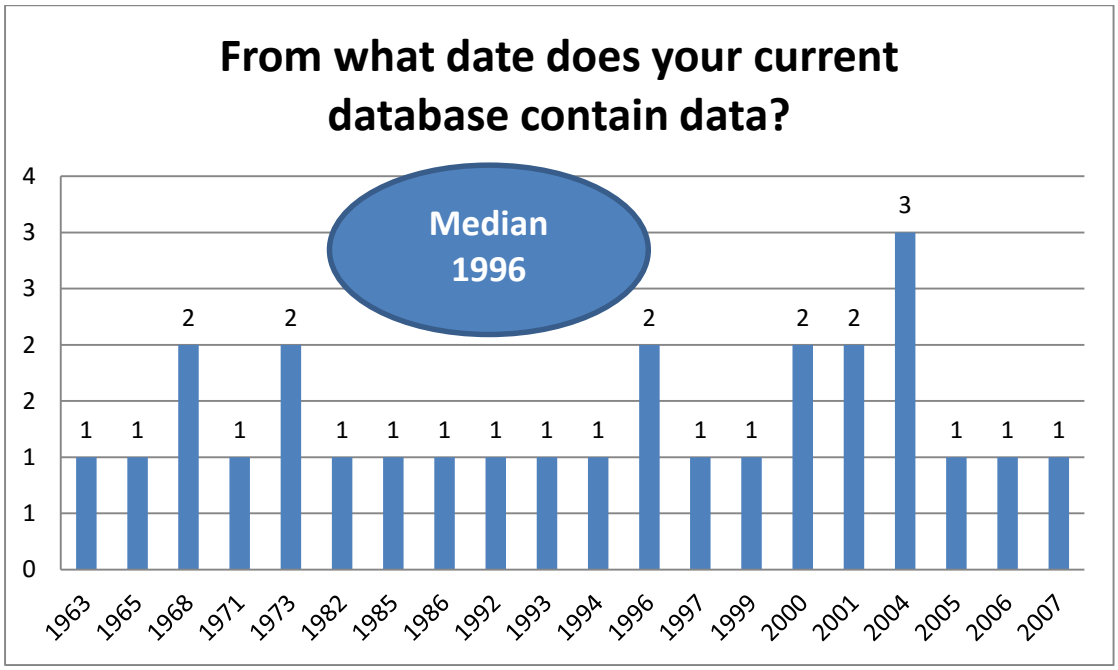


MODE: 1971

There is a wide period range of dates for starting the collection of ADRs across European countries, from 1960 until 2004, whereas more than 50% of MSs started by the year 1980.

Question T1Q7:

From what date does your current database contain data (YYYY)?

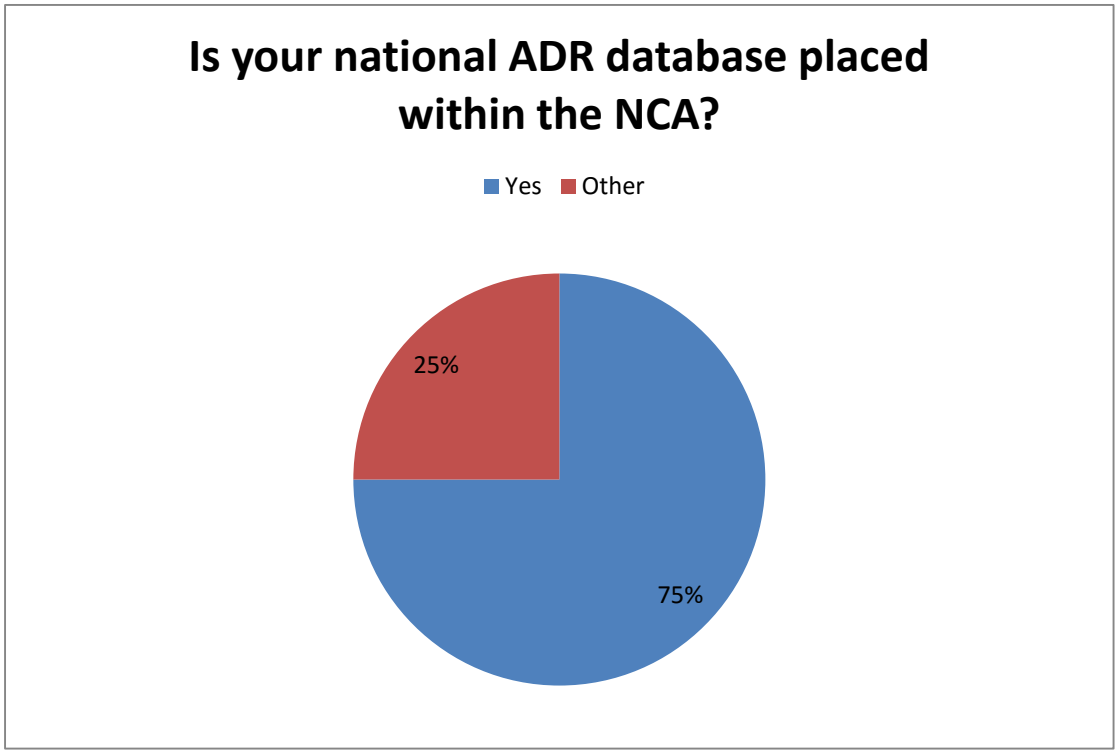


MODE: 2004

It is interesting to see that 14 countries have the database comprising all the ADRs since they have started to collect them. The "oldest" database is dating from 1963.

Question T1Q8:

Is your national ADR database placed within the NCA?

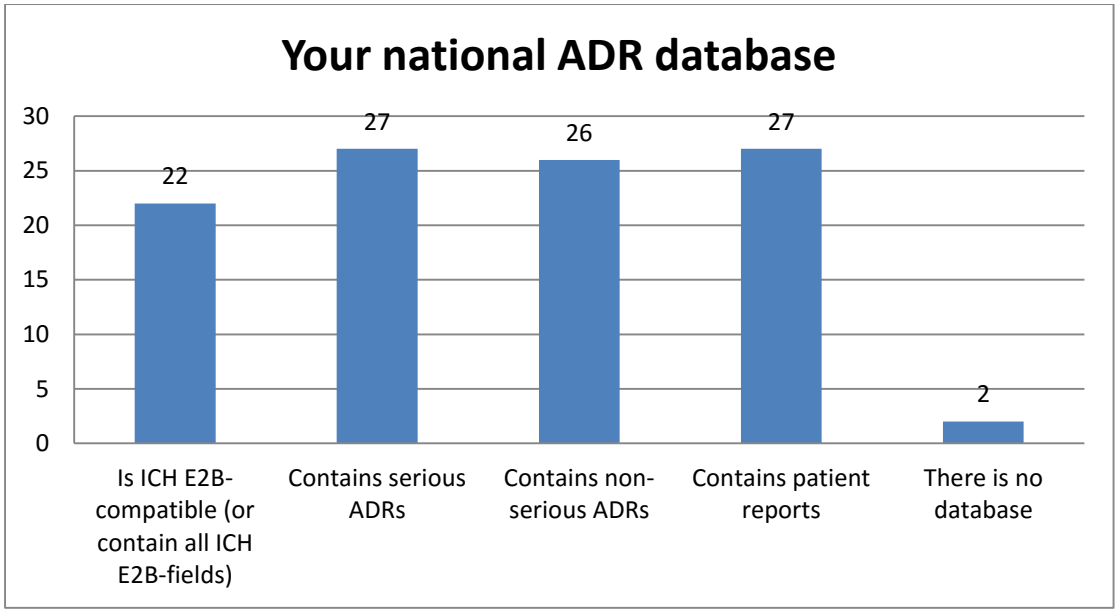


7 countries (25%) responded "other" to this question, out of which 4 countries are using the EudraVigilance as their national database and the remaining 3 are either not the NCA, have their database physically placed out of the NCA or not applicable.

Question T1Q9:

Your national ADR database:

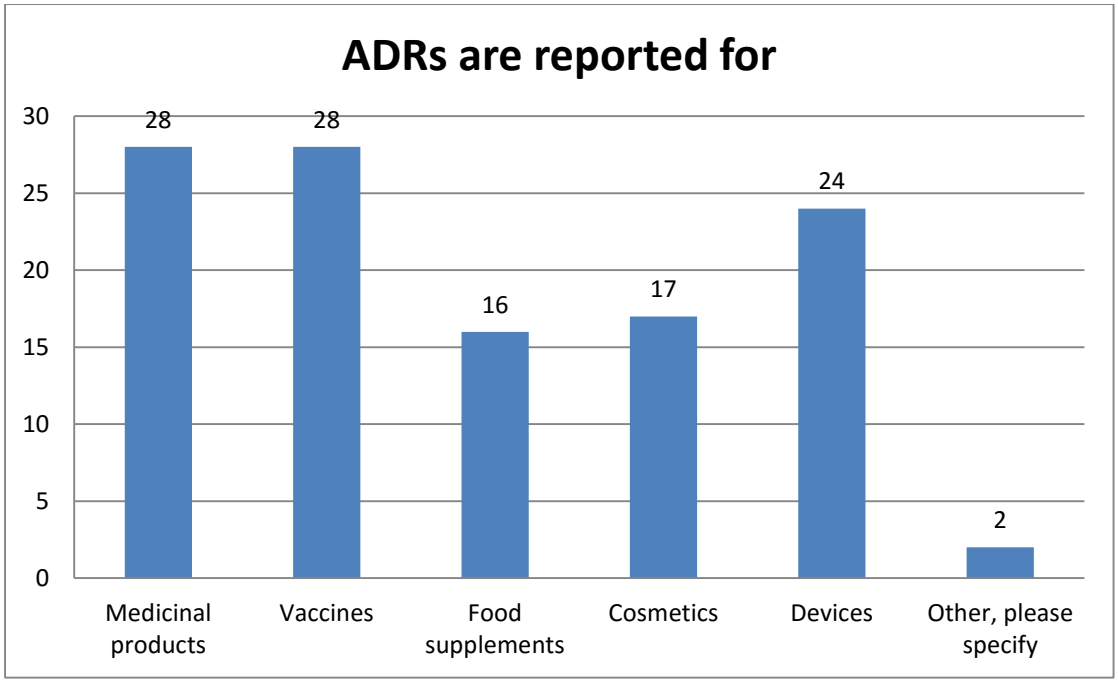
	Yes	No
Is ICH E2B-compatible (or contain all ICH E2B-fields)	❍	❍
Contains serious ADRs	❍	❍
Contains non-serious ADRs	❍	❍
Contains patient reports	❍	❍
N/A (there is no database)	❍	❍



The 2 countries are claiming that they do not have database. One of them actually uses Eudravigilance as their database. The other one described in the set-up of their national pharmacovigilance system their unique specificities.
Regarding the countries that answered that their national ADR database is not ICH E2B compatible, it should be noted that there are some inconsistencies in their answers provided (i.e. T1Q9 and T5Q13). Therefore, we presume that this was the misunderstanding.

Question T1Q10:
In your MS (any institution), adverse reactions are reported for:

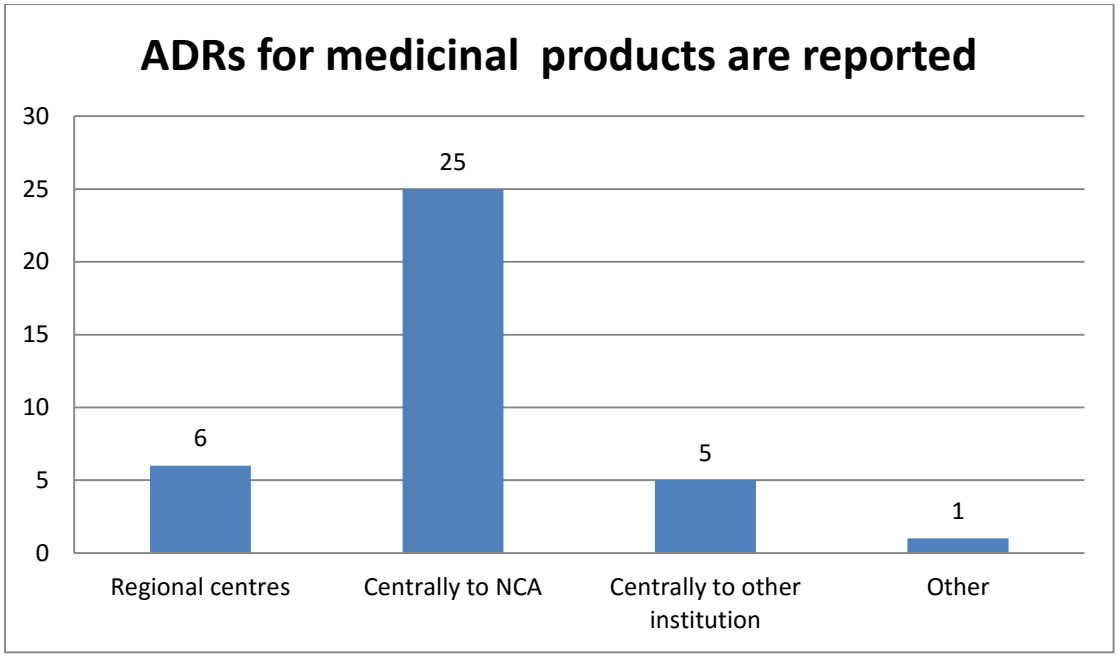
	Yes	No
Medicinal products	❍	❍
Vaccines	❍	❍
Food supplements	❍	❍
Cosmetics	❍	❍
Devices	❍	❍
Other, please specify	❍	❍



In all MSs ADRs are reported for medicinal products and vaccines, while the number of MSs collecting ADR reports for food supplements, cosmetics and devices is a bit lower - 16, 17 and 24 respectively.

Question T1Q11:
In your MS, ADRs for medicinal products are reported to:

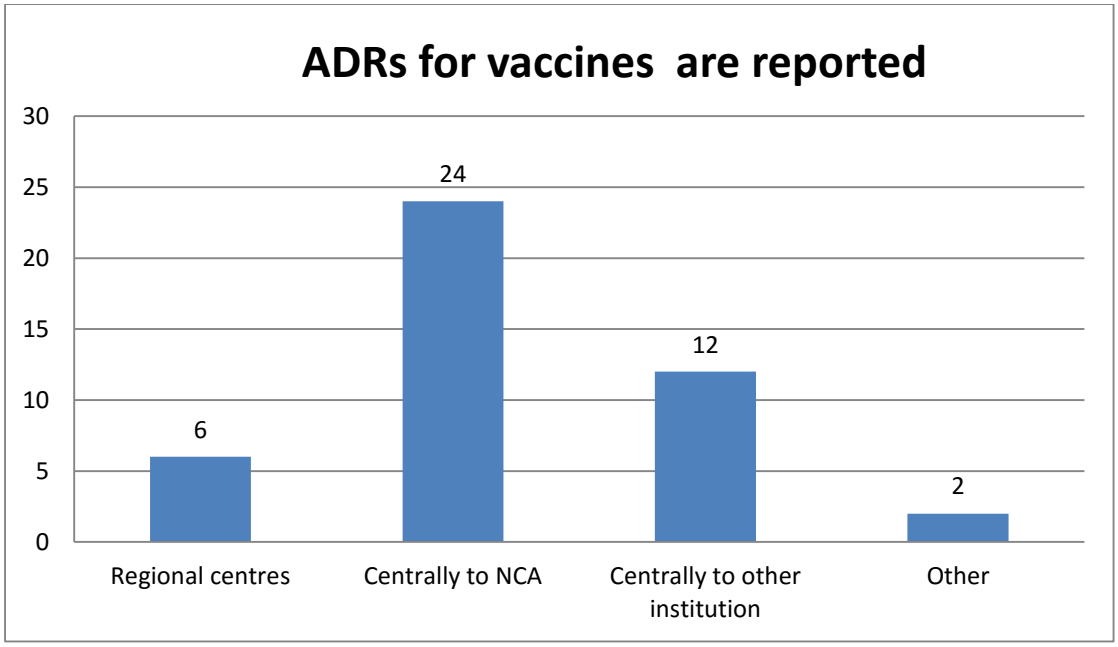
	Yes	No
Centrally to NCA	❍	❍
Regional centres (please specify the number of regional centres that ADRs for medicinal products are reported to)	❍	❍
Centrally to other institution, please specify	❍	❍
Other, please specify	❍	❍



Other mentioned institutions were mostly EMA and Institutes of Public Health for receiving vaccine reports.

Question T1Q12: In your MS, ADRs for vaccines are reported to:

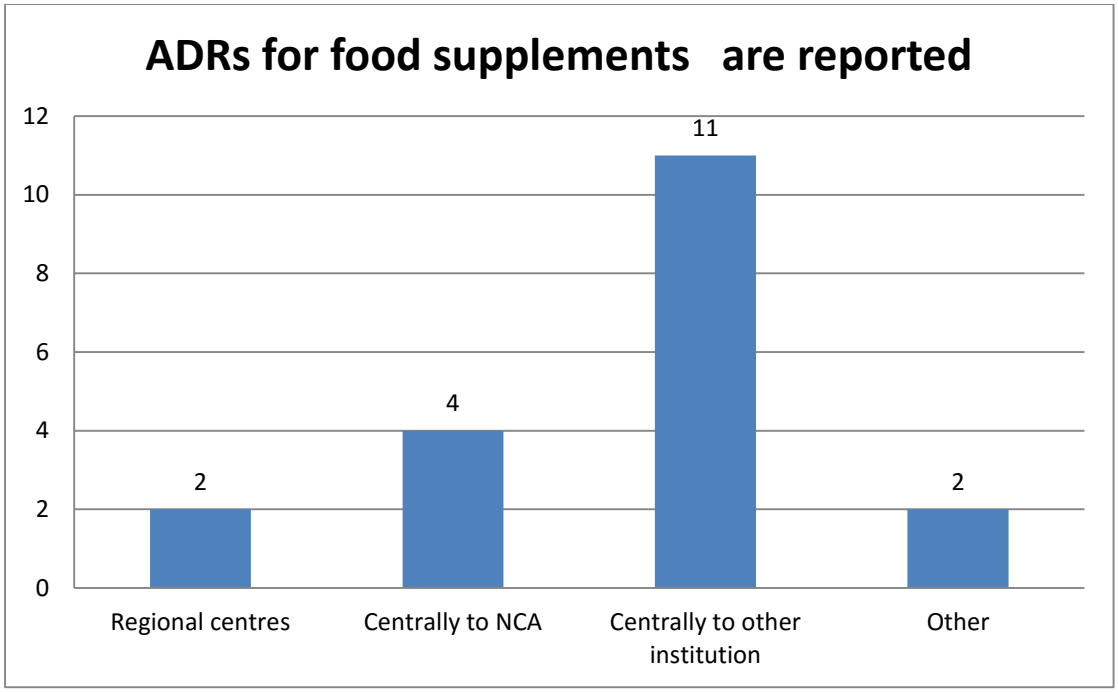
	Yes	No
Centrally to NCA	❍	❍
Regional centres (please specify the number of regional centres that ADRs for vaccines are reported to)	❍	❍
Centrally to other institution, please specify	❍	❍
Other, please specify	❍	❍



12 MSs answered that the AEFIs (adverse events following immunization) are reported also centrally to "other institutions", mostly to Public Health Institutions which are responsible for the immunization program in the MS. This is an important finding because a good collaboration should be defined between these Institutions to ensure keeping all reports in the EudraVigilance system. Important to define who between those institutions is responsible for sending the report from the HCP or patient to the EudraVigilance database.

Question T1Q13: In your MS, ADRs for food supplements are reported to:

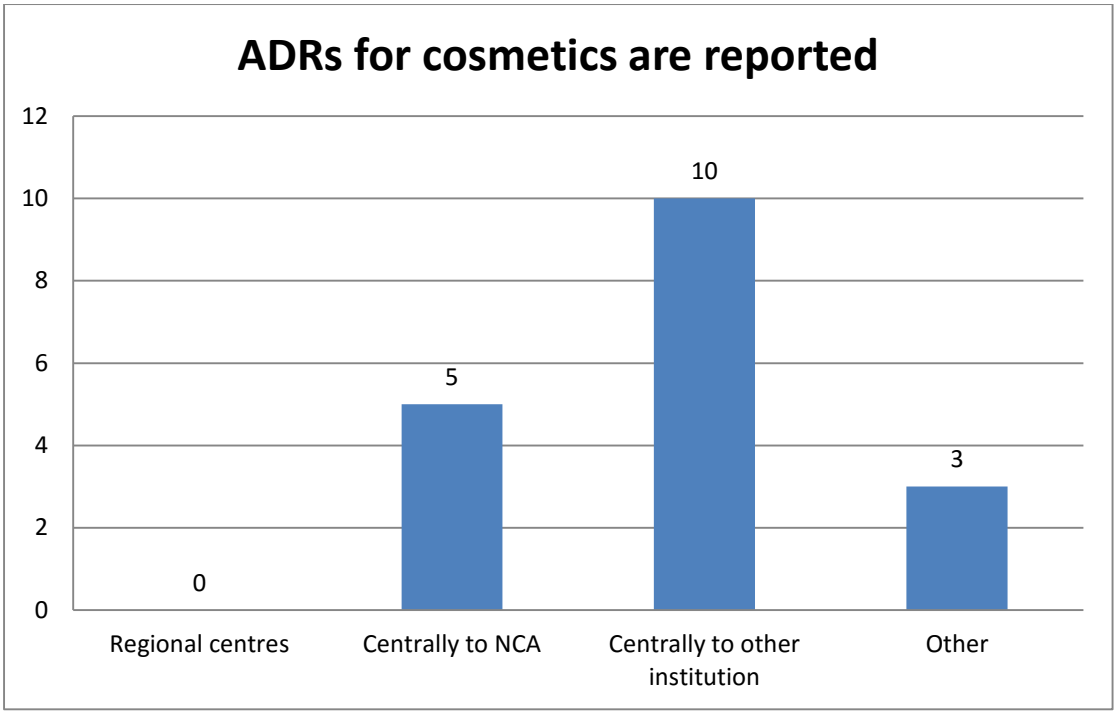
	Yes	No
Centrally to NCA	❍	❍
Regional centres (please specify the number of regional centres that ADRs for food supplements are reported to)	❍	❍
Centrally to other institution, please specify	❍	❍
Other, please specify	❍	❍



The scope of this WP is not reporting ADRs of food supplements, but the data show that 4 NCAs have integrated the reporting system into their NCA, which might be an example of good practice for other NCs. Most of the MSs answered that this kind of reporting is organized by another institution.

Question T1Q14: In your MS, ADRs for cosmetics are reported to:

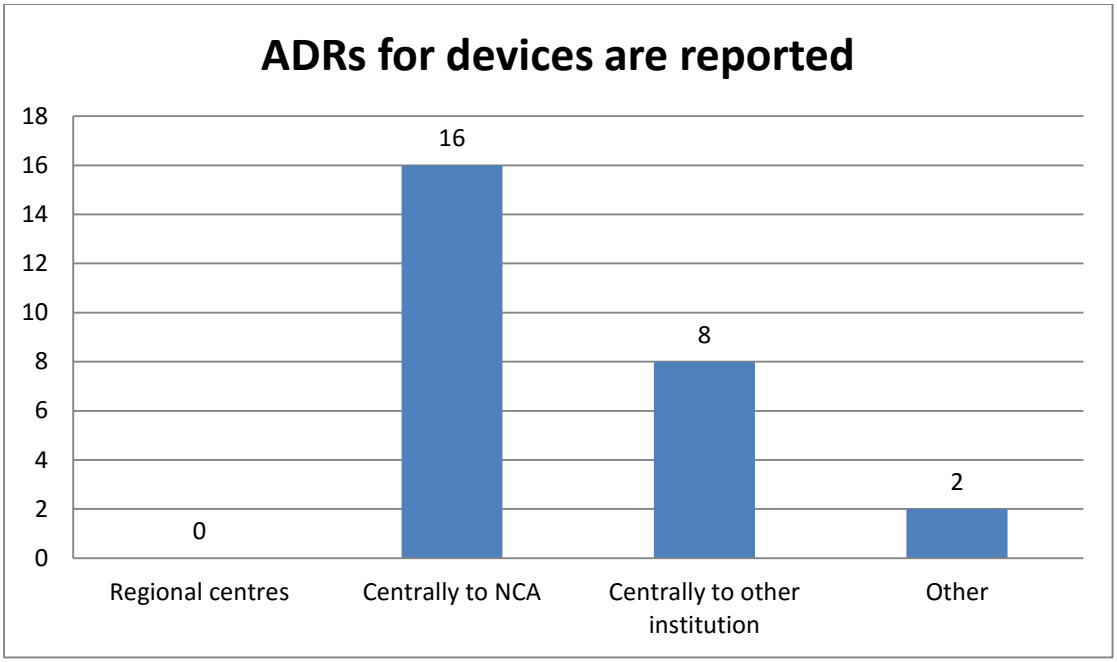
	Yes	No
Centrally to NCA	❍	❍
Regional centres (please specify the number of regional centres that ADRs for cosmetics are reported to)	❍	❍
Centrally to other institution, please specify	❍	❍
Other, please specify	❍	❍



In only 5 countries ADRs for cosmetics are reported centrally to NCA, but in the majority of countries these are reported to other institutions such as Ministries of Health, Institutes for Public Health, Chemical Agencies etc.

Question T1Q15: In your MS, ADRs for devices are reported to:

	Yes	No
Centrally to NCA	❍	❍
Regional centres (please specify the number of regional centres that ADRs for devices are reported to)	❍	❍
Centrally to other institution, please specify	❍	❍
Other, please specify	❍	❍

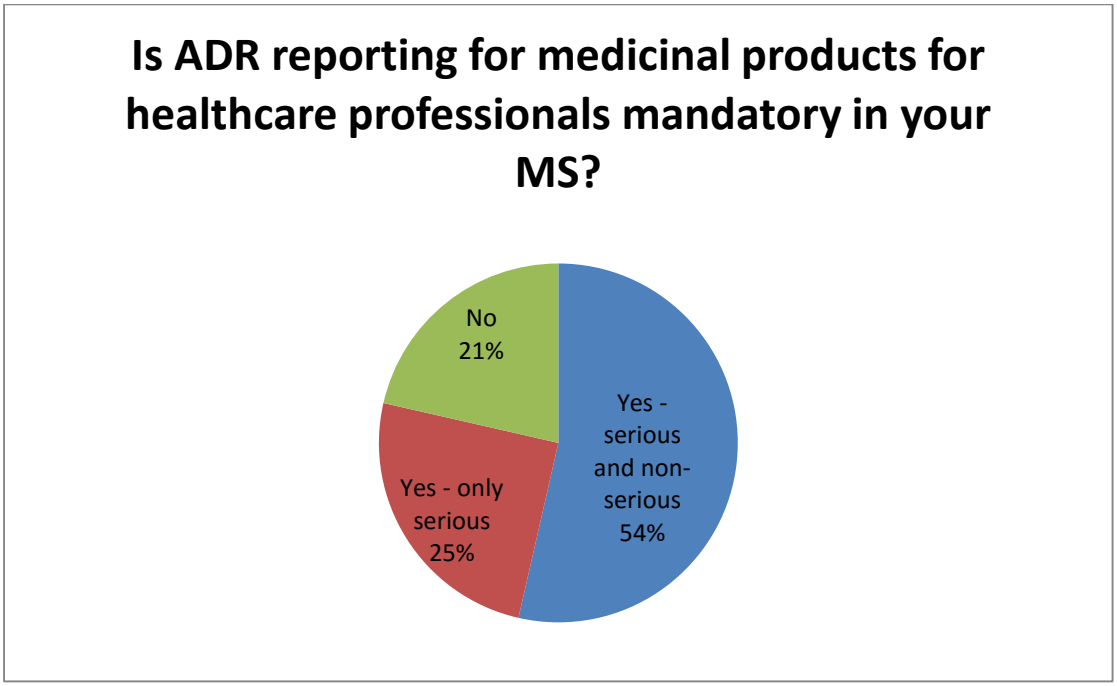


Most of the MSs answered that the reporting is made to the NCA while in other cases there is another institution which deals with ADRs reported for medical devices. The legislation how to report incidents in the area of medical devices and pharmacovigilance is a different one, but there are examples of combining of reporting in one division which is a challenge for the future development of medical device vigilance to come closer to pharmacovigilance.

Question T1Q16: ADRs for "OTHER" are reported

Only 1 response to this question was received. It concerned the “Toxicovigilance”, which is the occurrence of any toxic effect in humans following a single or repeated exposure to a mixture or substance, natural or synthetic, available on the market or in the environment and is reported to regional centres.

Question T1Q17: Is ADR reporting for medicinal products for healthcare professionals mandatory in your MS?

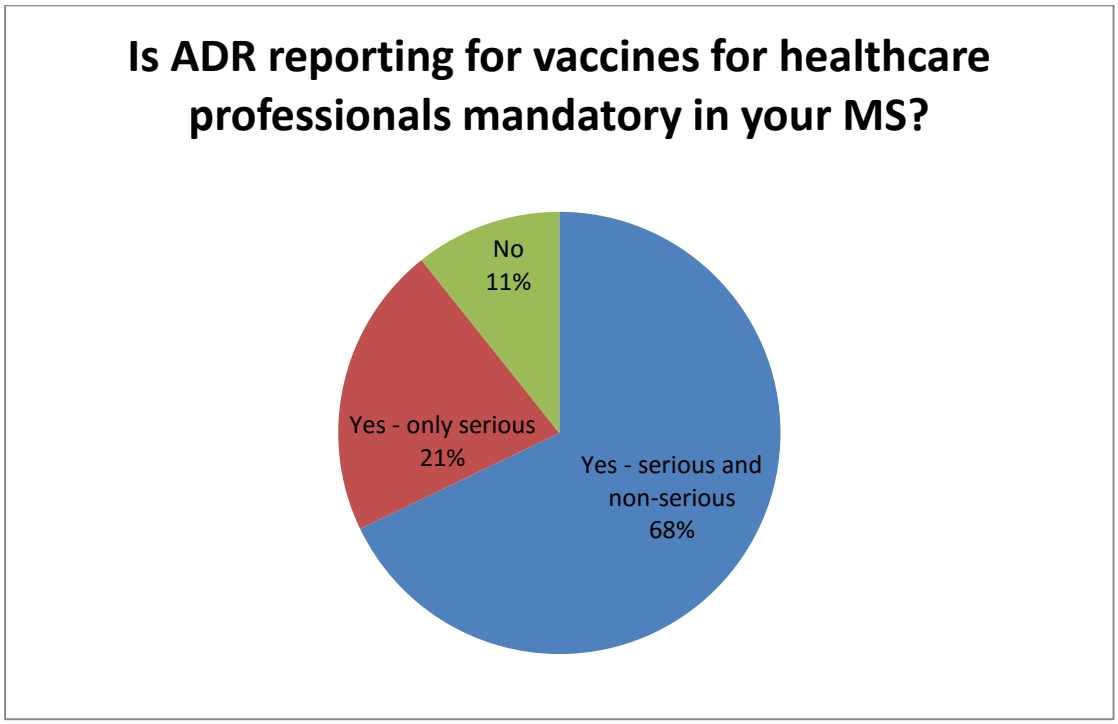


From 28 MSs which answered this question in 22 countries (79 %) in EU reporting of ADRs is mandatory for HCPs, in 15 countries (54%) for both serious and non-serious and in 7 (25%) for serious only.

Is ADR reporting for medicinal products for healthcare professionals mandatory in your MS?	Yes - serious and non-serious	**15**
	Yes - only serious	**7**
	No	**6**

Of the six countries that do not have mandatory reporting, four of them have the number of ADR reports /per million inhabitants above the European median number of reports (355.59/mil. in 2013).

Question T1Q18: Is ADR reporting for vaccines for healthcare professionals mandatory in your MS?

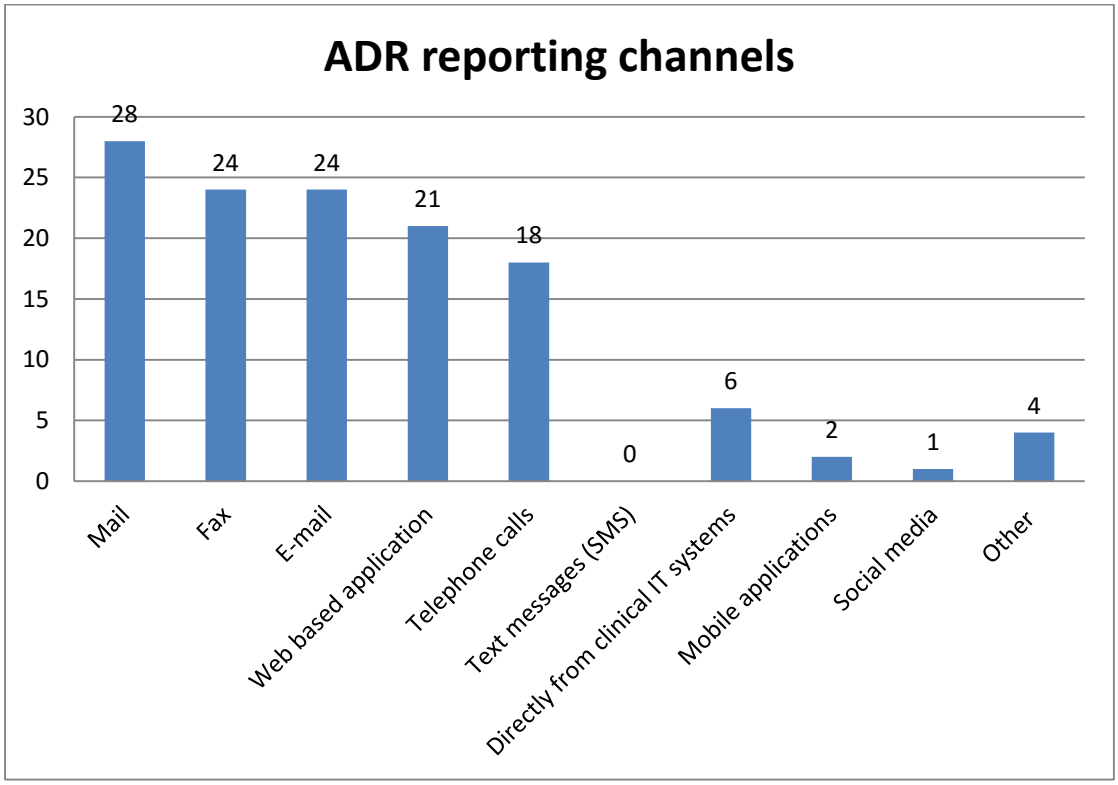


The percentage of countries where there is mandatory reporting of vaccine ADRs (AEFI) are even higher in comparison with the medicinal products - 89% or in 26 MSs (19 for serious and non-serious and 6 only for serious).

This can be explained by the fact that vaccines are given to healthy children or adults, and the safety surveillance for this kind of medicines is high. The mode of reporting to Public Health Institutions is additionally regulated at the national level and can be seen as an add-on to the pharmacovigilance legislation.

Question T1Q19: What channels for ADR reporting are made available by your institution for receiving ADR reports from HCPs?

		No
Mail	❍	❍
Fax	❍	❍
E-mail	❍	❍
Web based application	❍	❍
Telephone calls	❍	❍
Text messages (SMS)	❍	❍
Directly from clinical IT systems	❍	❍
Mobile applications	❍	❍
Social media, please specify	❍	❍
Other (sporadically-not through dedicated channels), please specify	❍	❍
Our institution is not responsible for this activity	❍	❍



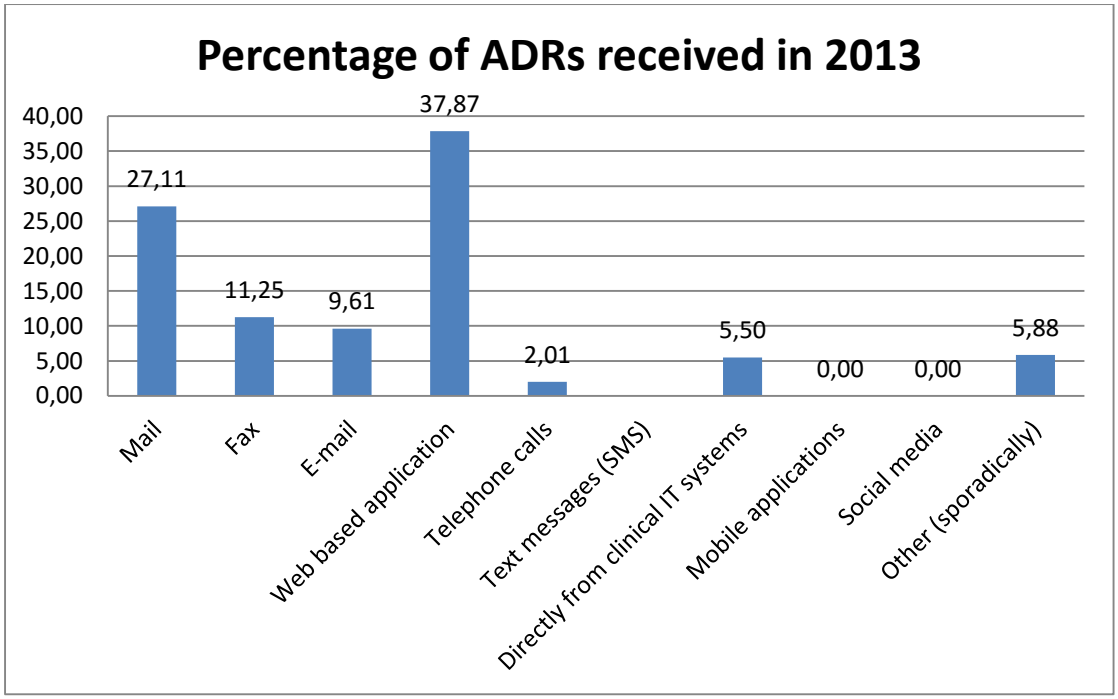
All MSs which have answered this question (28) have mail as an available reporting channel for receiving ADR reports from HCPs, while none of the MSs has text messages (SMS)

available, which is for example very much used in African countries. Two MSs have mobile applications and one MS has social media, precisely Facebook page, available. 18 MSs have telephone as an available report channel which is the most time consuming way of reporting for the centre.

6 MSs receive HCP ADR reports directly from clinical IT systems.

Question T1Q20: What percentage of ADRs is received using following methods in 2013?

Mail
Fax
E-mail
Web based application
Telephone calls
Text messages (SMS)
Directly from clinical IT systems
Mobile applications
Social media, please specify
Other (sporadically-not through dedicated channels), please specify
Our institution is not responsible for this activity



It is important to note that the highest percentage (37, 9%) of all ADR reports is received via web-based application, even though the number of MSs having web based application as available reporting channel is rather lower than the number of MSs having mail available, 21 versus 28 respectively. However, the proportion of ADRs received via mail is still high (27, 1 %).

It is interesting to note that in one MS, 100% of reports are received via mail. On the other hand, another MS receives the highest percentage of ADRs via web-based application (95%), which indicates the importance of understanding the national specific requirements for reporting.

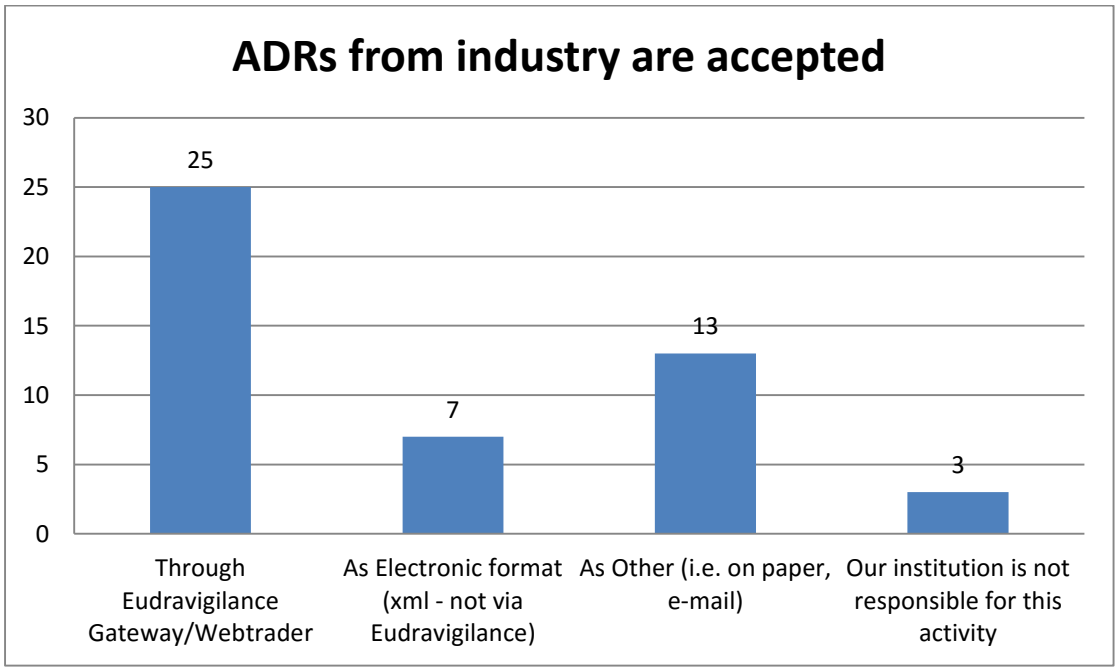
No ADR report was received via social media, mobile applications and text messages in 2013 in any MS. This kind of reporting is worth to explore for the future reporting ways with regard to the development of this kind of communication tools after 2013.

Question T1Q21: Please specify the reason(s) why you are unable to provide the requested percentages:

No response was received to this question.

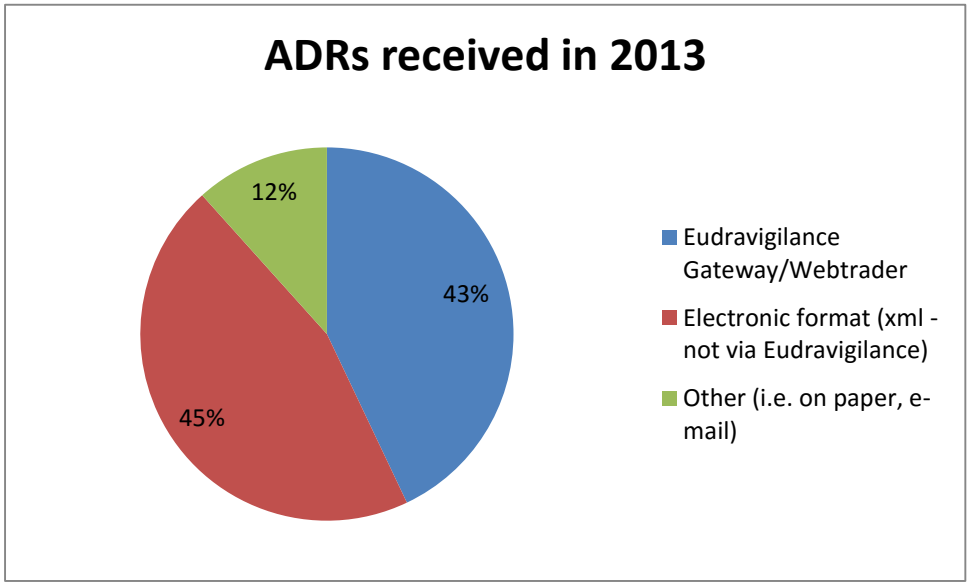
Question T1Q22: In which way does your institution accept ADR reports from industry and what percentage of ADRs is received using this method?

	Accepted		ADRs received in 2013
	Yes	No	%
Eudravigilance Gateway/Webtrader	❍	❍	
Electronic format (xml - not via Eudravigilance)	❍	❍	
Other (i.e. on paper, e-mail), please specify	❍	❍	
Our institution is not responsible for this activity	❍	❍	



From 28 MSs which answered this question all MSs which are responsible for accepting ADR reports from industry are compliant with new pharmacovigilance legislation and are receiving ADR reports through Eudravigilance Gateway/Webtrader. However, if some technical issue occurs, some MSs have other possible ways for receiving ADR reports from industry (i.e. paper, fax etc.).
Three (3) MSs responded that they are not responsible for this activity.

In category “other”, MSs mostly referred to receiving reports from industry in case of some technical problems. Then the reports are accepted on paper and via e-mail.



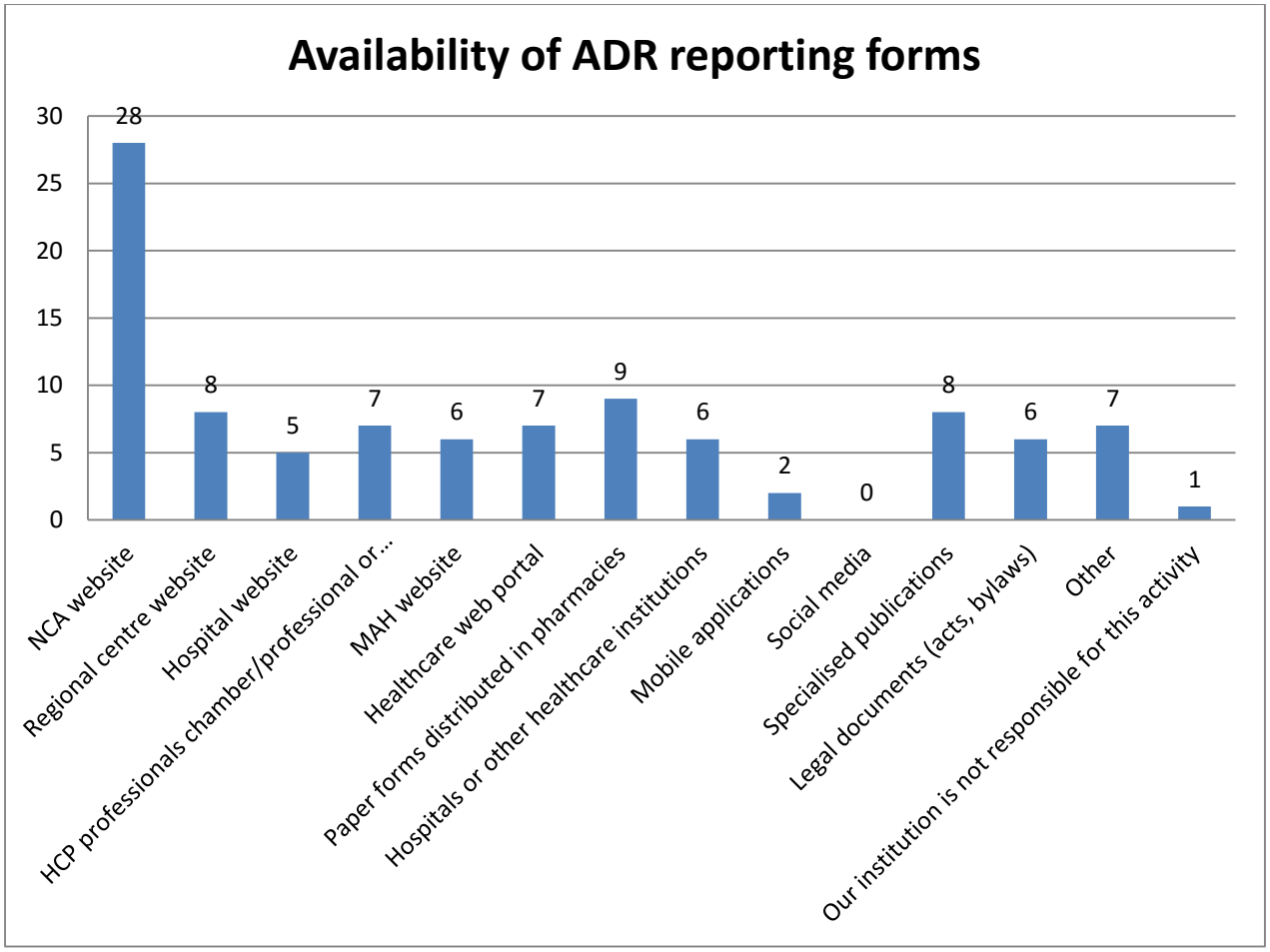
On the other hand, as shown above, a bit higher percentage of ADRs from industry is not received via Eudravigilance but some other channel: 57% versus 43%.

Question T1Q23: Please specify the means of accepting ADR reports from industry and/or any other specificity?

Thirteen (13) MSs specified the means of accepting ADR reports from industry. Eight (8) MSs receive reports from industry through Eudravigilance. Two (2) MSs have an E2B- compliant solution for receiving electronic ADR reports from industry. Out of specificities, receiving ADR reports on paper or via e-mail in case of technical problems were mentioned.

Question T1Q24: Please specify in which way ADR reporting forms are made available to reporters by your institution?

	Yes	No
NCA website	❍	❍
Regional centre website	❍	❍
Hospital website	❍	❍
HCP professionals' chamber/ professional or regulatory body website	❍	❍
MAH website	❍	❍
Healthcare web portal	❍	❍
Paper forms distributed in pharmacies	❍	❍
Hospitals or other healthcare institutions	❍	❍
Mobile applications	❍	❍
Social media, please specify	❍	❍
Specialised publications	❍	❍
Legal documents (acts, bylaws)	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍



All MSs which have answered this question (28) have ADR reporting forms available on their NCA's websites, and none MS has reporting forms available on social media. Two (2) MSs have their forms available on mobile applications.

Other:

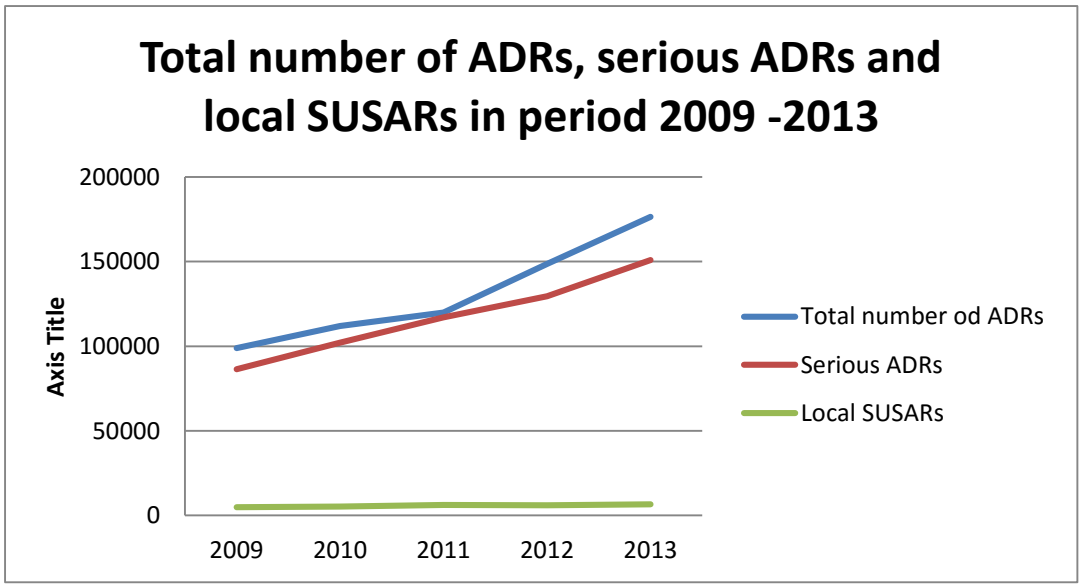
Bulletin Cito
EMA website
NIPH website (vaccines)
On paper, to the HCPs, attached to the letter of confirmation and thanking for ADR reporting
On request; professional meetings; together with bulletins
Paper form is available to anybody in a special shops
Patient organisation web site.
Pharmacies are obliged to assist patients in reporting ADRs.

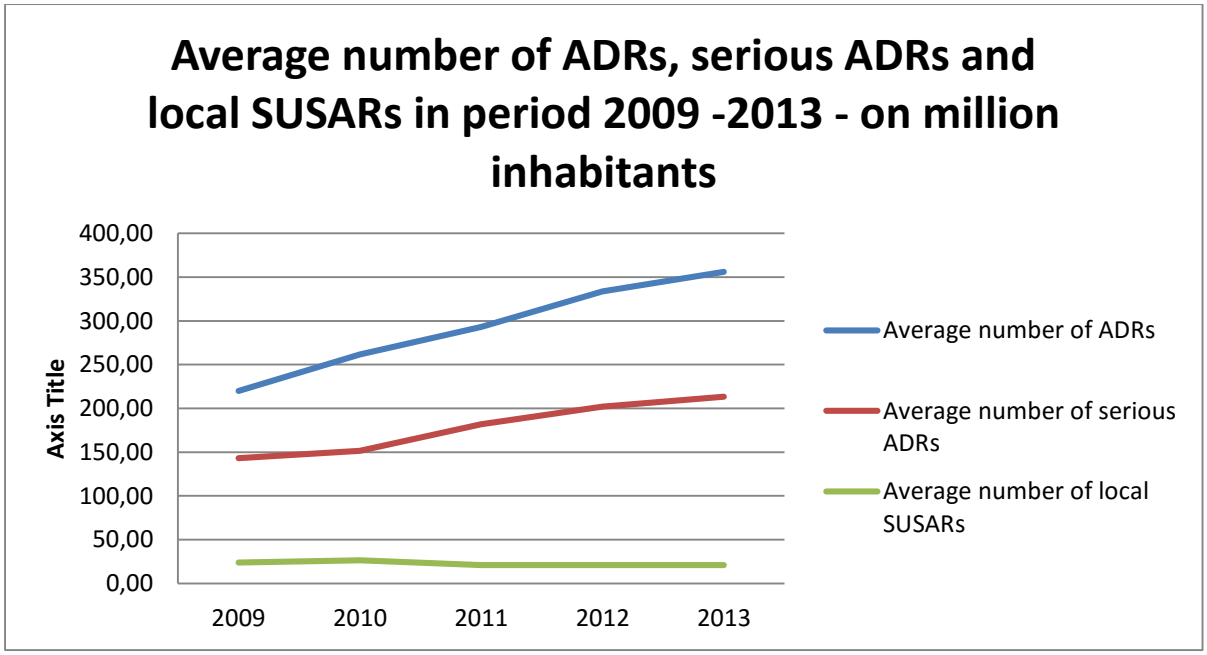
Question T1Q25: Composition of ADRs (to medicinal products and vaccines/biologics) in NCA database

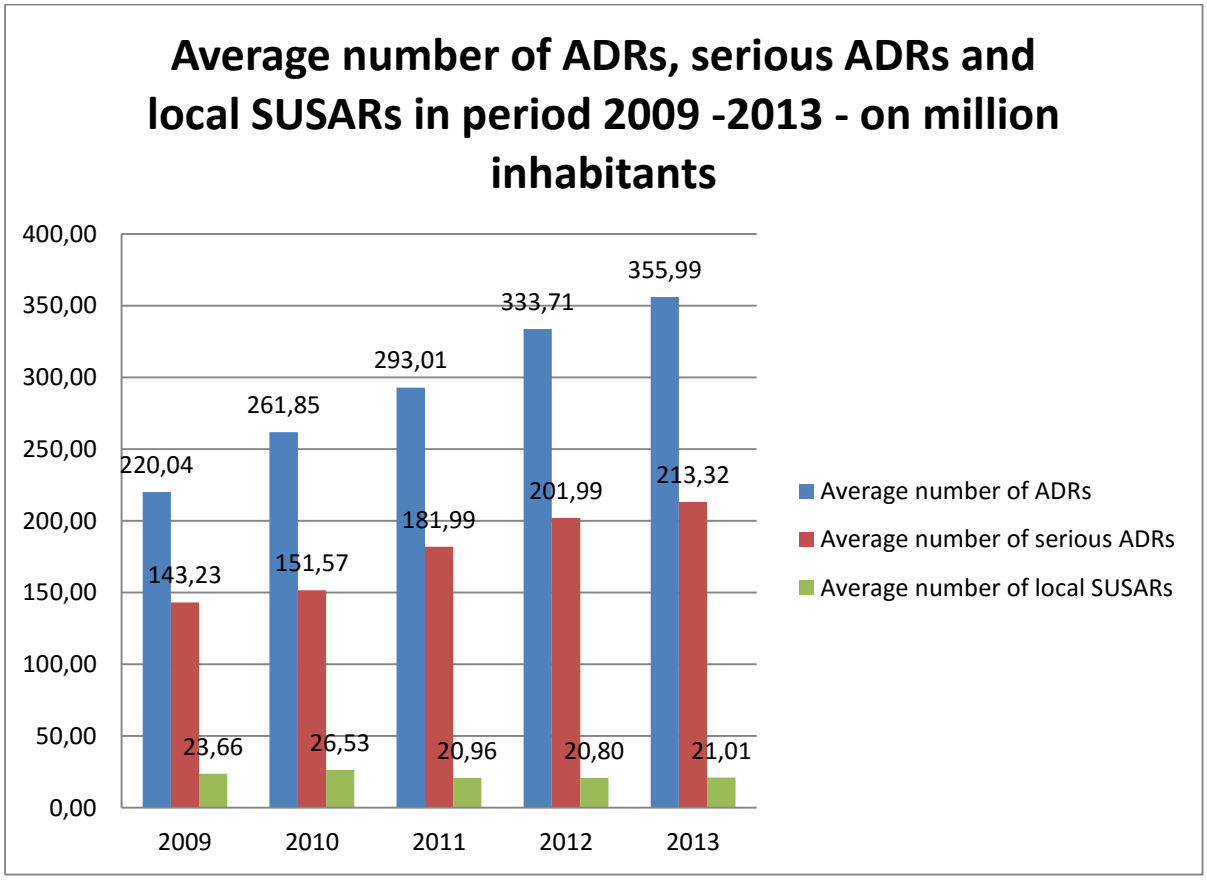
The aim of this section is to capture the total number of ADR reports in the last 5 years, stratification of ADRs by the type of reporter in 2013/whole database, and the % of all spontaneous ADR reports by the type of healthcare professional in the last 5 years.

T1Q26 How many ADR reports (from all sources: HCP/patient/industry/other) did you receive in:

	Total number of ADRs (spontaneous and solicited excluding clinical trials)	Total number of serious ADRs	Total number of local SUSARs	Our institution is not responsible for this activity
	Insert N/A if data is not available	Insert N/A if data is not available	Insert N/A if data is not available	Please tick if
2009				❑
2010				❑
2011				❑
2012				❑
2013				❑







Total number of ADRs received, as well as the total number of serious ADRs, is increasing in the observed period (2009-2013). The total number of local SUSARs is not growing, but is rather stable through this period of reporting.

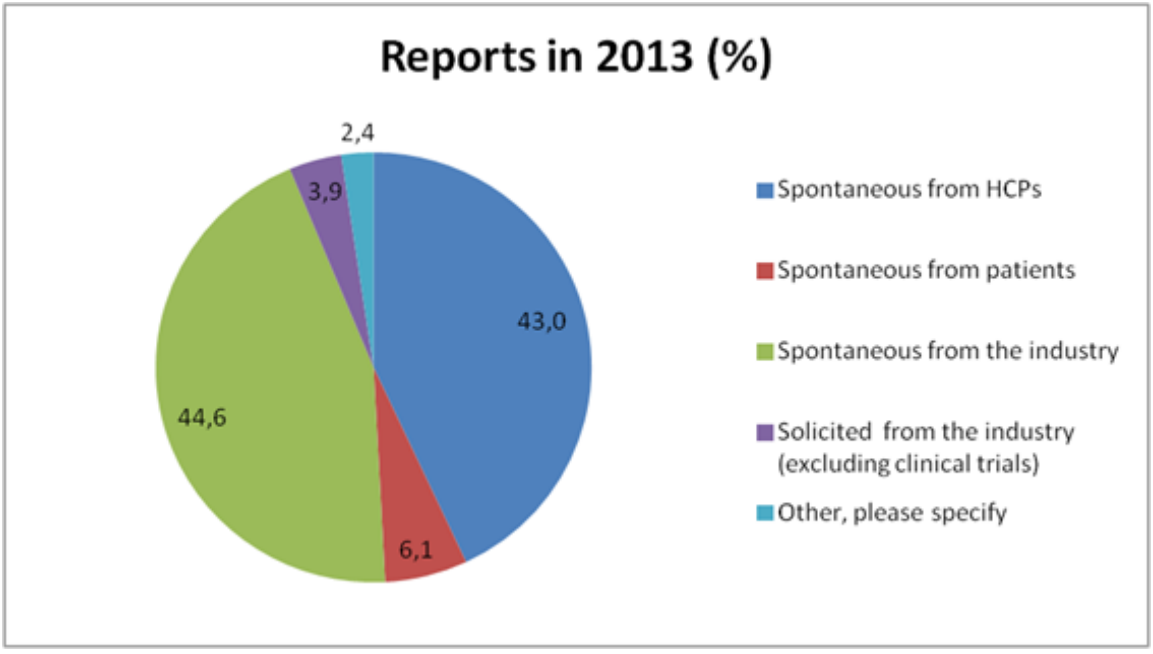
Statistically significant difference in increase of total number of ADRs is observed between years 2010/2011; 2011/2012 and 2012/2013. In following years the number of serious ADRs increased significantly as well (2011/2012; 2012/2013). The increase in the year 2012/13 can be explained by the new pharmacovigilance legislation which came into force in 2012 at the level of the EU.

Total number of all ADRs		
	Mean	Sig. (2-tailed)
2009 - 2010	-124,208	,640
2010 - 2011	-314,720	,015
2011 - 2012	-896,480	,017
2012 - 2013	-1366,160	,013

Number of serious ADRs		
	Mean	Sig. (2-tailed)
2009 - 2010	-507,182	,235
2010 - 2011	-548,565	,107
2011 - 2012	-527,609	,014
2012 - 2013	-1028,913	,045

Question T1Q27: What is the % of reports from your MS stratified by the type of reporter in 2013 / whole database? Please fill in the data either for 2013 or the whole database.

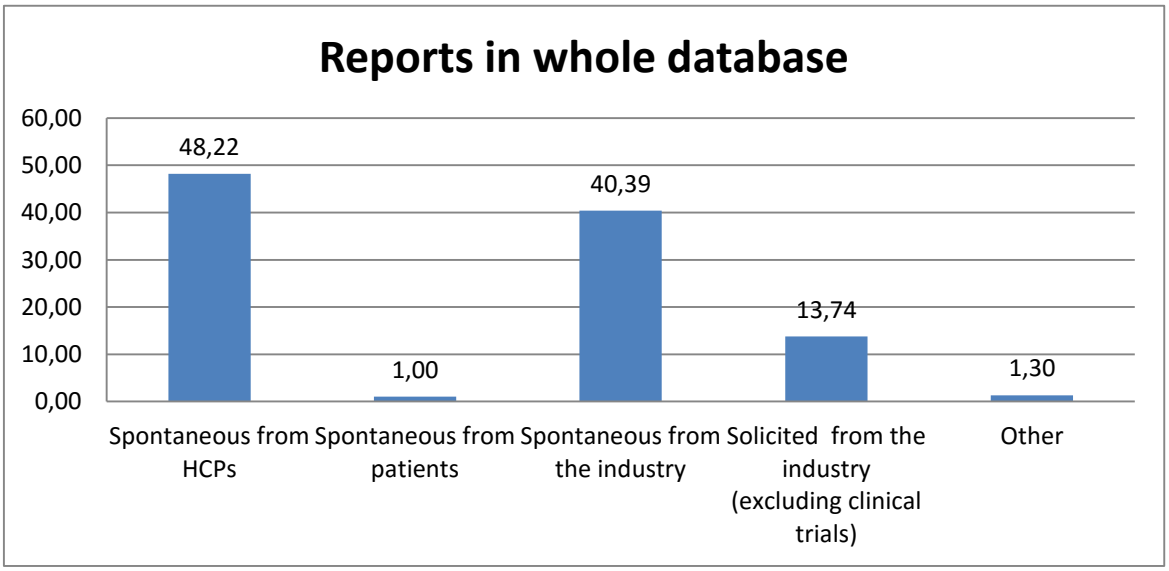
	2013	Whole database	Our institution is not responsible for this activity
	%	%	Please tick if applicable
Spontaneous reports directly from healthcare professionals			❑
Spontaneous reports directly from patients			❑
Spontaneous reports from the industry			❑
Solicited reports from the industry (excluding clinical trials)			❑
Other, please specify			❑



Twenty-six (26) MSs responded to this question, however responses from 2 MSs were not taken into consideration due to providing inconsistent percentages per given category. Therefore, based on the data provided by 24 MSs, it could be concluded, that majority of reports were received from the industry (44, 6 %) in 2013. However, direct reports from HCPs (43%) and direct patient reports (6, 1%) combined together add up to 49, 1%. This means that majority of reports represent direct reporting from the primary reporters.

Other:

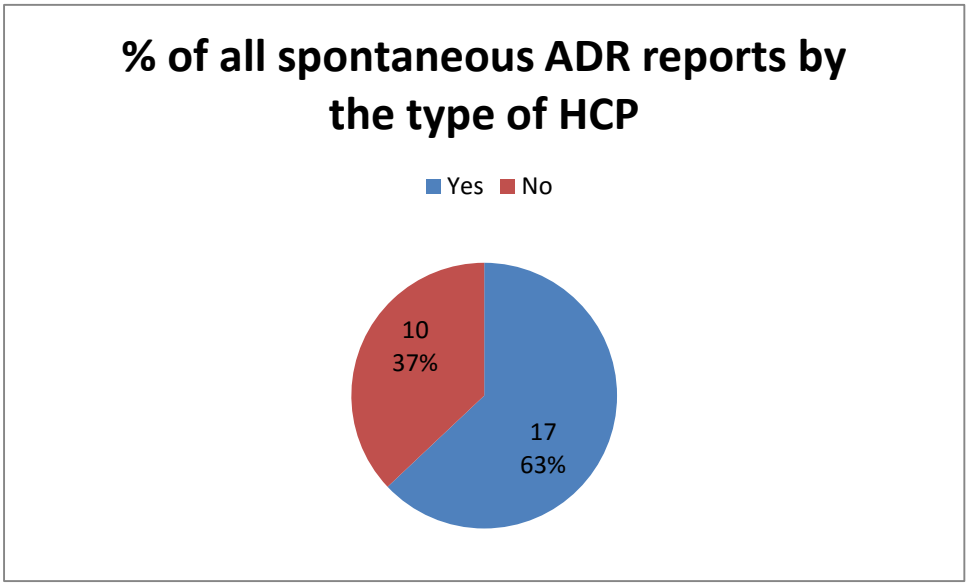
2 parents and 13 unknown
Due to several mergers in the database over previous years, searching the whole database would not be reliable without extensive validation checks.
Individual patient use
Literature
Literature reports
National Centre for Epidemiology
Pharmacist
Reports from CDPC and other regulatory institutions
Solicited reports from healthcare professionals



Only 5 MSs were able to provide the percentage of reports stratified by the type of reporter in the whole database. The data are a bit different when the whole database is compared to the data for only 2013. There are many possible reasons for that:

- Only 5 MSs were able to provide data for the whole database compared to 26 MSs for 2013
- Dates from which databases of those 5 MSs contain data are different (1965-2006)
- Patient reporting was introduced later as a consequence of the new pharmacovigilance legislation which came into force in 2012.

Question T1Q28: Does your national ADR database allow you to provide the % of all spontaneous ADR reports by the type of healthcare professional?



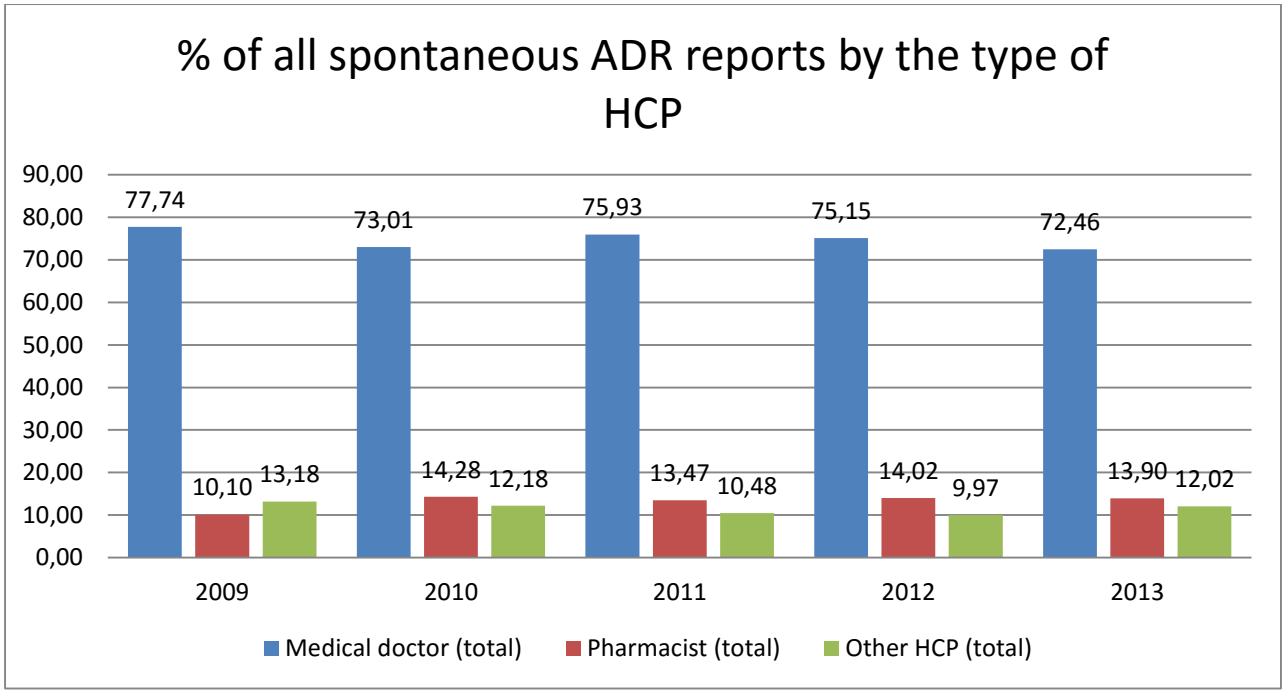
37% (N=10/27) of MSs are not able to provide data on the percentage of all spontaneous ADR reports by the type of HCP. The mentioned limitations of databases were:

All cases do not have the type of HCP reported
EudraVigilance (E2B field A.2.1.4.) has the following options for HCP qualifications: Physician, Pharmacist, Other HCP
Our database is no longer valid (no new entry), new one is under development
Our database only provides absolute numbers
We cannot provide information about the type of healthcare professional reporting adverse reaction without going through each case manually
We do not have a national database
We have difficulties on retrieving detailed information on the type of reporter either because the functionality for such queries in our database is yet to be developed or data is not available in the case itself. Import of data from paper based old cases into the new database is still ongoing. Data required is derived and compiled from two different sources: the old Excel spreadsheet, the new database.
We have to calculate it from excel rows

Question T1Q29: What is the % of all spontaneous ADR reports by the type of healthcare professional in the period from 2009 to 2013?

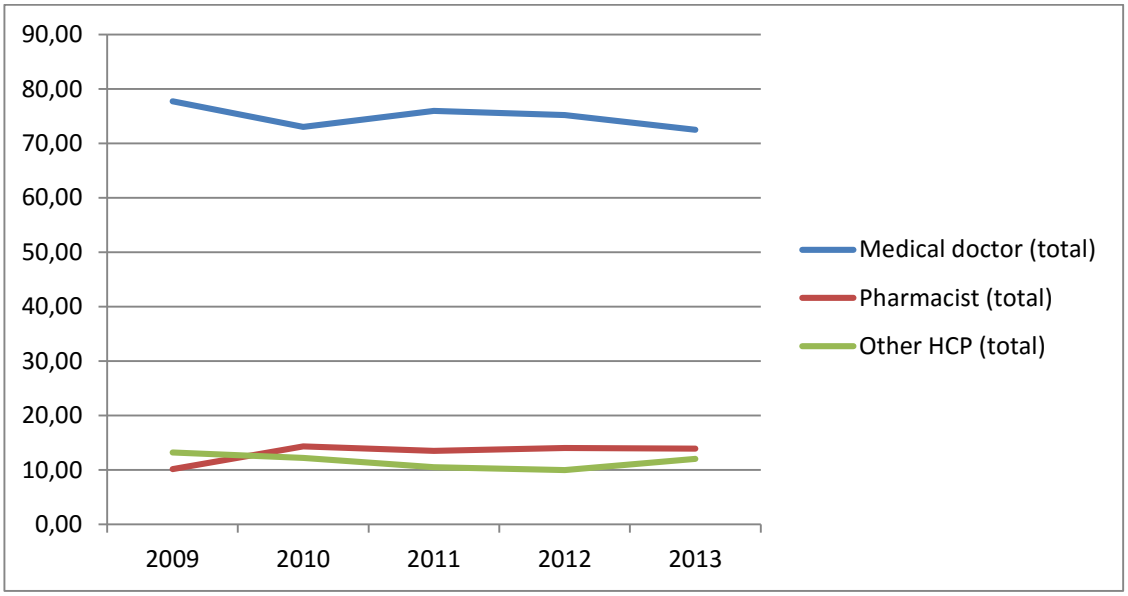
Please enter "N/A" as not applicable in boxes where you could provide required data, but at the moment you are unable due to some database limitations. Data for Medical doctor (total), Pharmacist (total) and Other HCP (total) are mandatory. Data for subgroups of above categories are optional.

	2009	2010	2011	2012	2013
Medical doctor (total)					
General practitioner					
Hospital doctor					
Other doctor/physician					
Pharmacist (total)					
Hospital pharmacist					
Community pharmacist					
Other pharmacist					
Other HCP (total)					
Veterinarian					
Dentist					
Medical biochemist					
Nurse					
Pharmaceutical technician					
Coroner					
Other, please specify					



In this question data for *"Medical doctor (total)"*, *"Pharmacist (total)"* and *"Other HCP (total)"* were mandatory. Data for subgroups of above categories were optional. Data for optional subgroups were excluded from the analysis due to low response rate and inconsistency in providing the data.

We can see that the percentages of ADRs reported by all medical doctors are slightly decreasing over the observed period likely due to the fact that the percentage of pharmacists and patients rises.



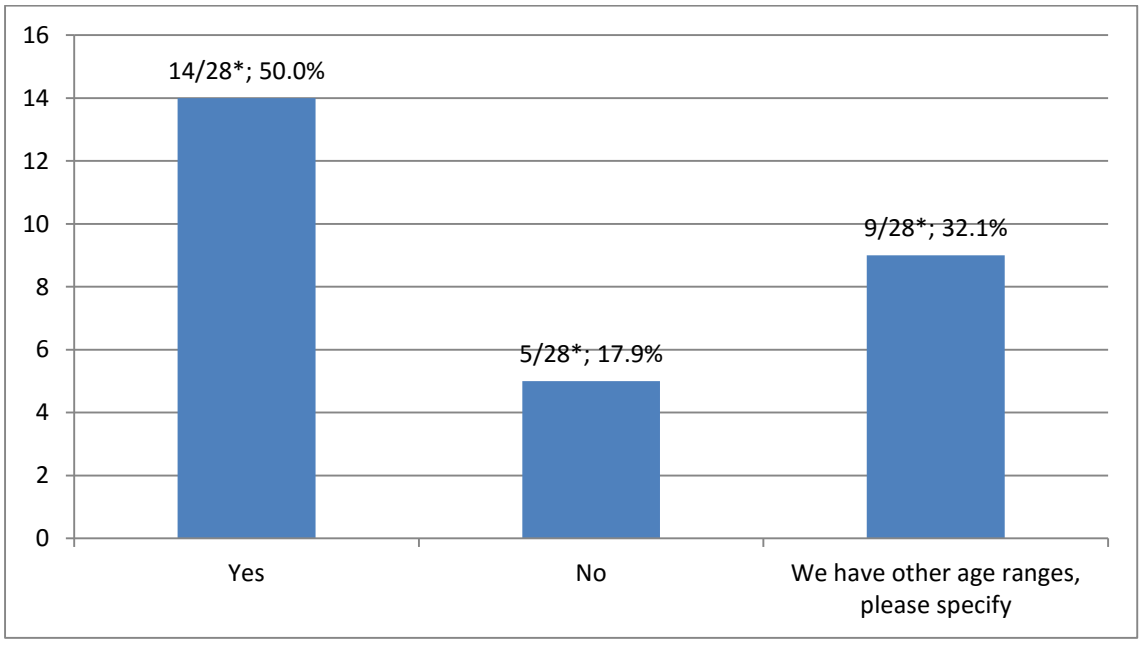
On individual basis, in 7 MSs decrease in total number of ADR reports reported by medical doctors is observed which should be addressed in the part of the awareness level of reporting.

Question T1Q30: c) Data on patient demographics

This set of questions is focussing on ADR reports' characteristics (by patient age groups and patient gender). In this section we would also like to learn if MS's provide access to ADR data to the public.

Question T1Q31: Are you able to provide data on ADR reports categorized by patient age groups as follows:
≤ 1 month;
>1 month≤ 4 years;
>4 years≤11 years;
>11 years<18 years;
>18 years≤ 69 years;
>69 years?

- ❍ Yes
- ❍ No
- ❍ We have other age ranges, please specify _____



*Number of respondents

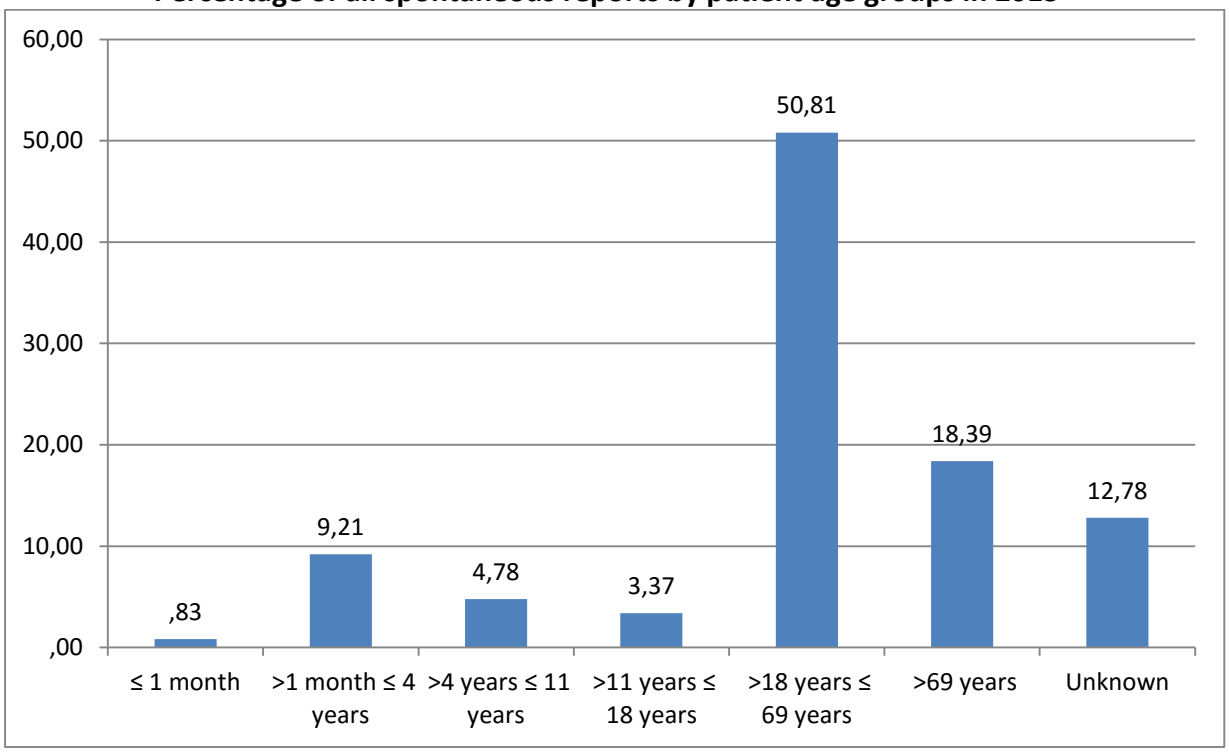
14 out of 28 MSs were able to provide data on ADR reports categorized by certain patient age groups, 5 MSs were not able to provide data and 9 MSs use different age ranges.

Question T1Q32: Please specify the % of all spontaneous reports in your ADR database by patient age groups in 2013:

Please enter whole numbers (i.e. decimals and symbol "%" should not be used).

_____ ≤ 1 month
_____ >1 month ≤ 4 years
_____ >4 years ≤ 11 years
_____ >11 years ≤ 18 years
_____ >18 years ≤ 69 years
_____ >69 years
_____ Unknown

Percentage of all spontaneous reports by patient age groups in 2013

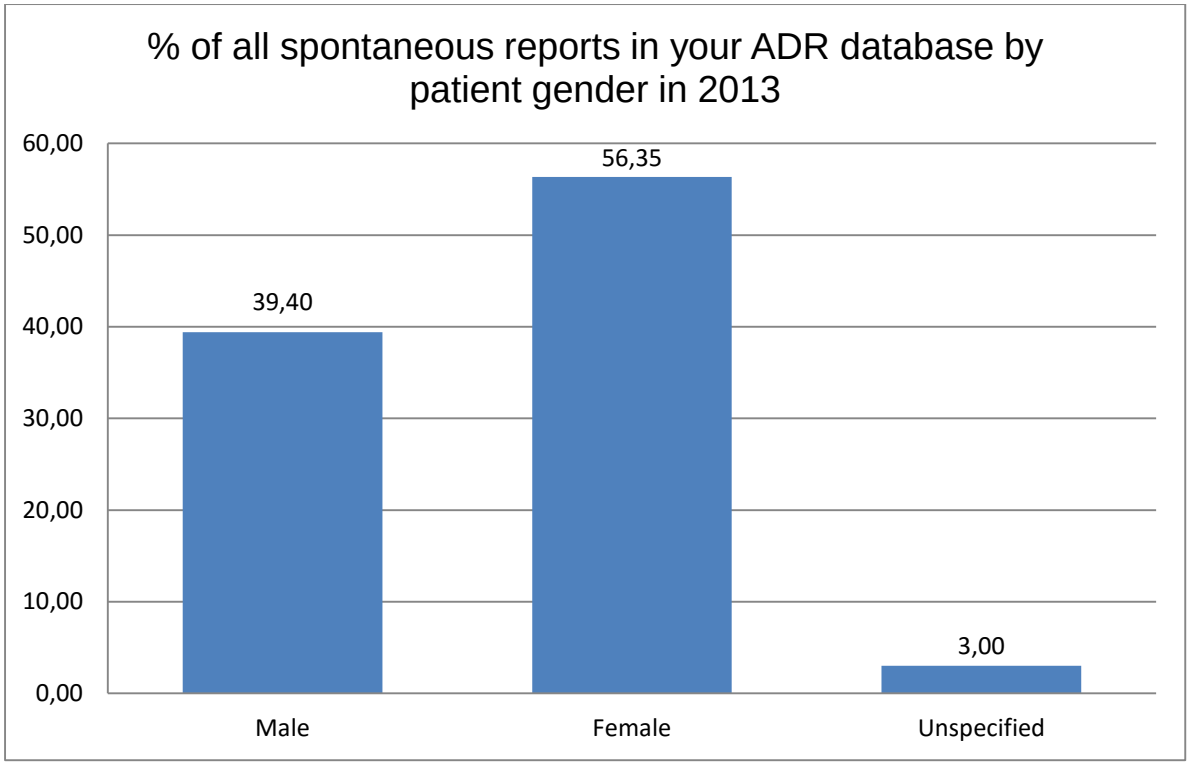


Response rate: n=14.

Most reports were reported for age group *>18 years ≤ 69 years* (adults), followed by age groups ***>** 69 years* and *>1 month ≤ 4 years*.

Question T1Q33: Please specify the % of all spontaneous reports in your ADR database by patient gender in 2013:

_____ Male
_____ Female
_____ Unspecified
_____ Data not available



Response rate: 28 countries but 4 MSs did not provide data.

In 56, 35% of reports (N=23) patients were female which is consistent with all literature data with regards to ADR reporting.

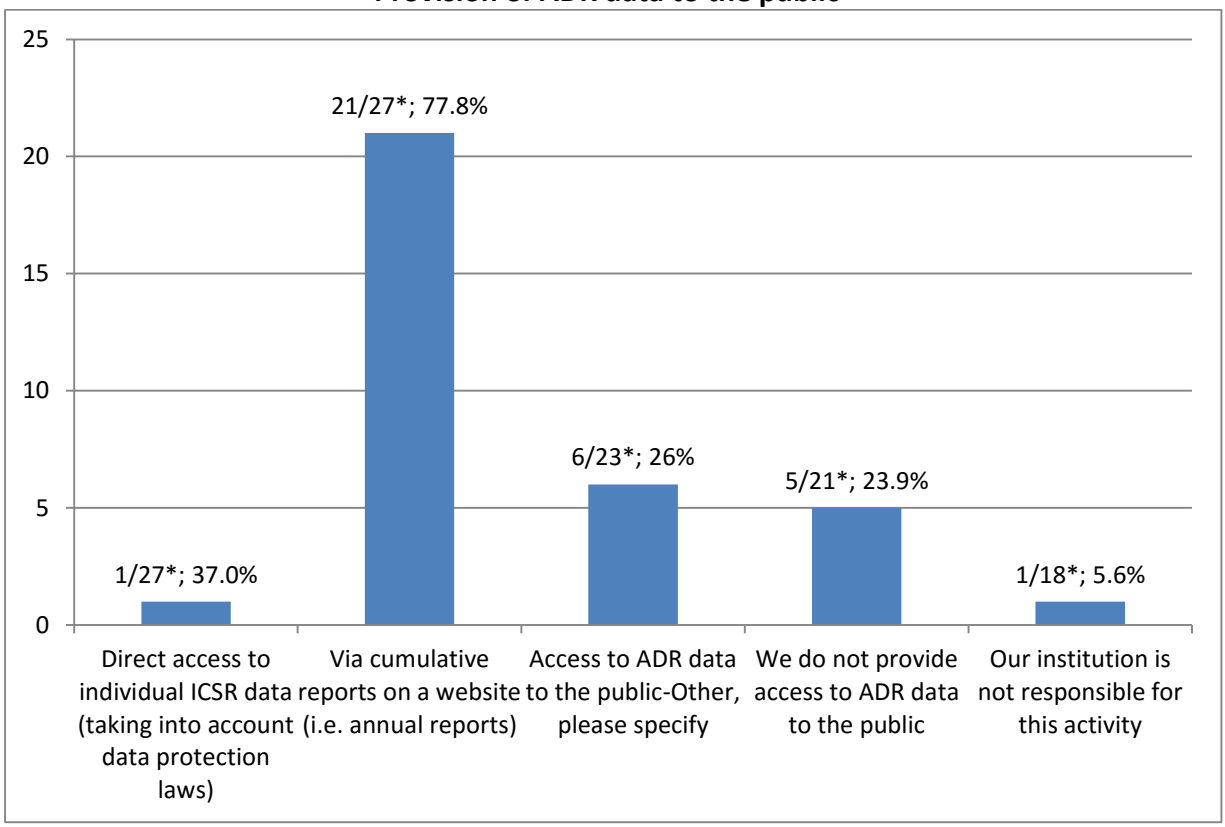
It is attention-grabbing to note that the percentage of category “data not available” is much higher for all reports than for patient’s reports.

On the MS level**,** in majority of reports patients were female except in 3 MSs. Two (2) MSs were excluded from the analysis in order to facilitate comparison with the data for patient reports due to the low number of patient reports in those two MSs. In one MS 100% of data is not available, but this MS was included in the analysis.

Question T1Q34: Do you provide access to ADR data to the public?

	Yes	No
Direct access to individual ICSR data (taking into account data protection laws)	❍	❍
Access via cumulative reports on a website (i.e. annual reports)	❍	❍
Other, please specify	❍	❍
We do not provide access to ADR data to the public	❍	❍
Our institution is not responsible for this activity	❍	❍

Provision of ADR data to the public



*number of respondents

Data about ADRs are in most cases provided to the public via cumulative reports on a website (i.e. annual reports or Drug Analysis Print). 6 countries provide abbreviated data on request.

Question T1Q35: Please provide database URL and date access started: -Date access started (MM/YYYY)

Two (2) MSs responded to this question, however, only one MS provided specific answer.

Question T1Q36: Please provide URL and date access started

Response rate: 28 countries responded and 12 countries provided their URL which means that they can be used in joined platform to share national data about ADRs.

All but one of responding countries started with giving access to PhV data from 2000 and just one country started prior 2000. This is now practice in more than half of MSs, which can be recommended to others in the light of transparency and sharing data.

Question T1Q37: d) Assessment of Member State ADR processing capacity

This section starts with a free text question which is aimed to provide a general overview of ADR processing for different types of ADR reports (patient/industry/HCP) in each MS. It is also focussing on MS's specificities regarding ADR reports assessment and it is expected here for MS to describe in detail how the assessment is performed and which aspects are taken into consideration. The provided bullet points serve as a reference only and do not represent an exhaustive list- MSs are encouraged to elaborate on their national specificities. The aim of this section is also to learn about time and resources available in each MS for ADR reporting processing.

Question T1Q38: Please provide a general overview of your ADR report processing for the different types of ADR reports. Please note any significant processing differences if existing depending on the report type (patient/industry/HCP) (free text – use following points as guidance, non-exhaustive list):

ADR report receipt
Prioritisation
Data entry
Validation
Assessment (please define each specific part of your assessment; e.g. completeness, seriousness, causality, expectedness, validity, etc.)
Further steps
Other, please specify

In question 38, a general overview of national ADR report processing for different types of ADR reports was given. Twenty seven (27) MSs provided their answer to this question. In the section regarding ADR report receipt, MSs mostly referred to different reporting formats (paper vs web based). Almost all MSs prioritise serious reports. Data entry depends on

reporting format; paper forms require manual data entry, while electronic forms have some level of automatic data capture. Four minimum criteria (identifiable reporter, identifiable patient, suspected drug, adverse reaction) are used for validation in most MSs. It should be noted that in some MSs validation is not an individual step in case processing, but it is done during data entry. Reports are mostly assessed for completeness, seriousness and causality. In section asking for further steps in case processing, most often mentioned actions were performing follow up, duplicate detection and signal detection.
In conclusion, there is no difference in processing of ADR reports from different reporter groups, the only difference is in data entry between on paper and electronically received reports.

Question T1Q39: Individual cases are assessed (please tick all criteria that apply):

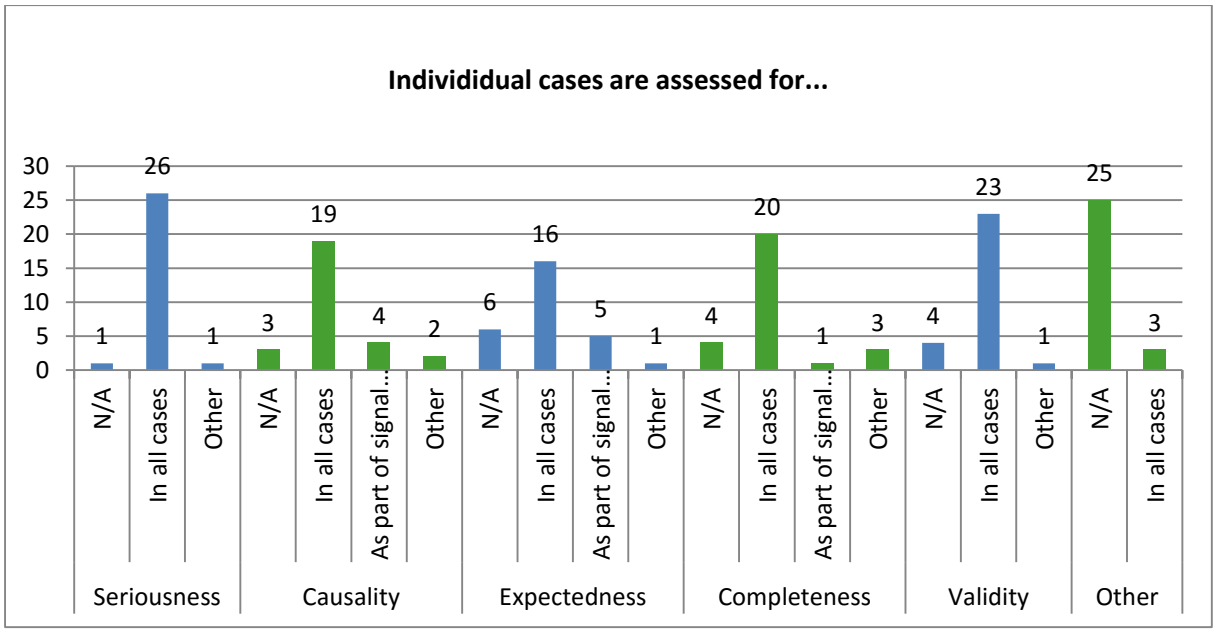
	Criteria						
	Seriousness	Causality	Expectedness	Completeness	Validity	Other	Our institution is not responsible for this activity
In all cases	❑	❑	❑	❑	❑	❑	❑
As part of signal assessment	❑	❑	❑	❑	❑	❑	❑
Other, please specify	❑	❑	❑	❑	❑	❑	❑

Question T1Q40: What are the other criteria in assessment of all cases (In all cases)?

Question T1Q41: What are the other criteria when assessment is done as part of signal assessment (As part of signal assessment)?

Question T1Q42: What are the other criteria used in assessment of "other"?

The aim of this group of questions was to collect information on what actually is considered "case assessment" within the network, presuming that not all MSs use the same convention when referring to case assessment. Second aim was to establish how the assessment criteria impacts the workload and the time required for processing of ICSRs by comparing responses to these questions with responses to question T1Q43.



Twenty eight (28) responses were received to this question.

- Seriousness
  - 26/28 MSs assess ICSRs for seriousness, while the response „Other“ from 1 MS also relates to the assessment of seriousness for all ICSRs performed upon receipt.
- Causality
  - 19 MSs perform causality assessment, while 4 MSs perform it as part of signal assessment and 3 MSs responded that performing causality assessment was not applicable to their processes.
  - It is worth noting that one MS responded that the assessment of causality, expectedness, completeness and validity does not fall within the scope of the current assessment as the new datasystem is being implemented, but it has been performed previously and is expected to be performed in the future again once the new datasystems are in place, meaning that actually 20 MSs perform also the causality assessment.
  - One MS did not directly respond that they perform causality assessment, but they provided a description of process which is basically a causality assessment (temporal association, review of medical history and concomitant medication considering the potential impact of either).
- Expectedness
  - 16/28 MSs responded they assessed cases for expectedness, and 6/28 respondents responded that assessing expectedness is not applicable to their processes. Five MSs responded they assess expectedness as part of signal assessment (4 of which are the same ones that perform causality assessment as part of the signal assessment).
  - Compared to other responses to this question (i.e. assessment of seriousness, causality etc.), it appears that assessment of expectedness is the least performed among MSs on a routine basis.
- Completeness and Validity

- 20/28 and 23/28 MSs responded they assessed cases for completeness and validity, respectively. In terms of completeness assessment, this result might be regarded as surprising, given that published articles list only one automated system for testing of the completeness of the ICSRs (i.e. the Completeness score by UMC). Validity in terms of 4 minimum criteria for a valid report might be expected as a unonimous criteria across MSs, however not all MSs assess the validity of the reports. It might also be assumed that the question was not phrased clearly enough for the respondents and that the high number of positive responses for the assessment of completeness are actually a consequence of misconception where completeness was sometimes regarded as validity.

Responses to questions 40, 41 and 42 clarified that:

- in some MSs case assessment is done at the regional centre level taking into account time to onset, de-challenge, re-challenge, alternative causes, previous knowledge, complementary exploration and other factors favouring causality;
- duplicate detection is regarded as an additional part of the assessment;
- additional contact is established with the reporter as a form of acknowledgement and a thank you note;
- in certain MSs where, presumably due to a very high number of reports, causality assessment is done only as part of signal assessment, cases are assessed according to a standard operating procedure to determine whether a request for further information is required. This is based upon the completeness of the case, expectedness and whether the case meets further criteria for follow-up; for example brand and batch details for biologics, a copy of the post mortem for fatal reports;
- concept wise, it is worth noting that in one MS the parts of the assessment process are divided between the national pharmacovigilance committee and the assessors, as follows: Seriousness assessed upon receipt, causality assessed by the Nat. PhV Committee, expectedness assessed by Scientific/Administrative personnel (as needed), completeness assessed upon receipt and by Nat. PhV Comm., validity assessed upon receipt and by scientific personnel.

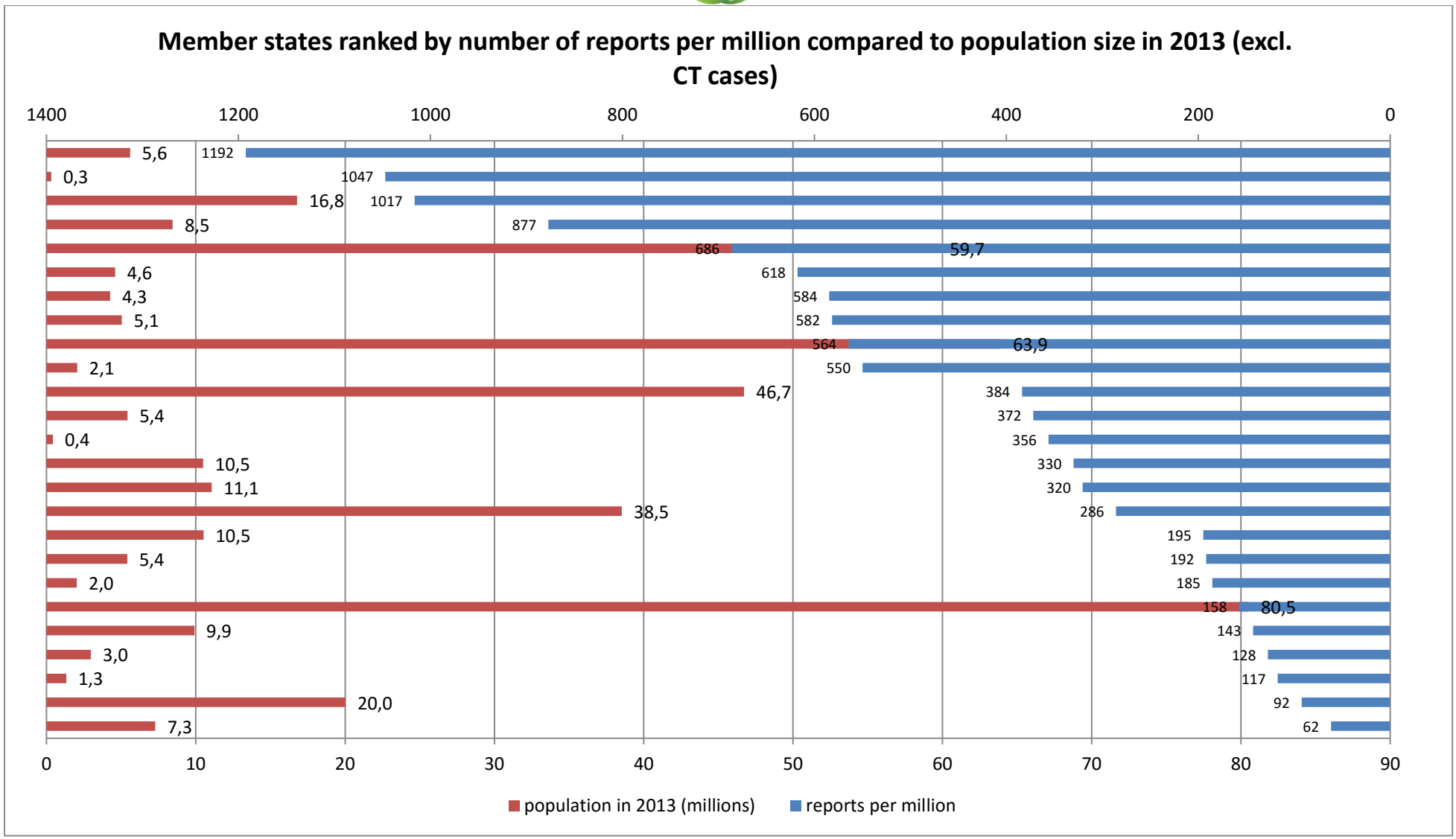
Overall, it can be concluded that great majority of MSs assess the causality, seriousness and validity of the reports when referring to case assessment, whereas the expectedness is assessed to a lesser degree. However, the approach with regards to the stage at which causality assessment (and other parts of the assessment, excluding seriousness) is performed is markedly different and two main concepts are noted. The first one encompasses assessment of *all the reports* and is undertaken by the majority of MSs. The alternative approach is performing the assessment during the signal assessment stage (4 MSs).

The 4 MSs performing causality assessment at signal assessment stage differ significantly by the number of reports per million inhabitants in 2013, ranging from 549 reports to 1192

reports (spontaneous and solicited excluding CT cases). This reporting rate is above EU average of 356 reports per million in 2013, hence an increased workload is the reasonable rationale for prioritisation, however there are other MSs with similar or higher numbers of reports that do not take this approach. For instance, one MS with 1016 reports per million in 2013 is in this regards similar to the one above mentioned with 1192 reports, however this MS assess *all* cases for seriousness, causality and expectedness. This MS is quite specific for having a dedicated institution for monitoring of the spontaneous reports which most likely enables the processing of the reports in above mentioned manner. The applicability of this approach to other MSs cannot be evaluated based on the data from this survey.
Member states at the higher end of the population-size scale also differ. One assesses cases at signal assessment stage. On the other hand, other assesses *all* cases owing to numerous regional centres. Although both countries receive a high number of reports per million inhabitants, procedure wise they utilize very much different processes.

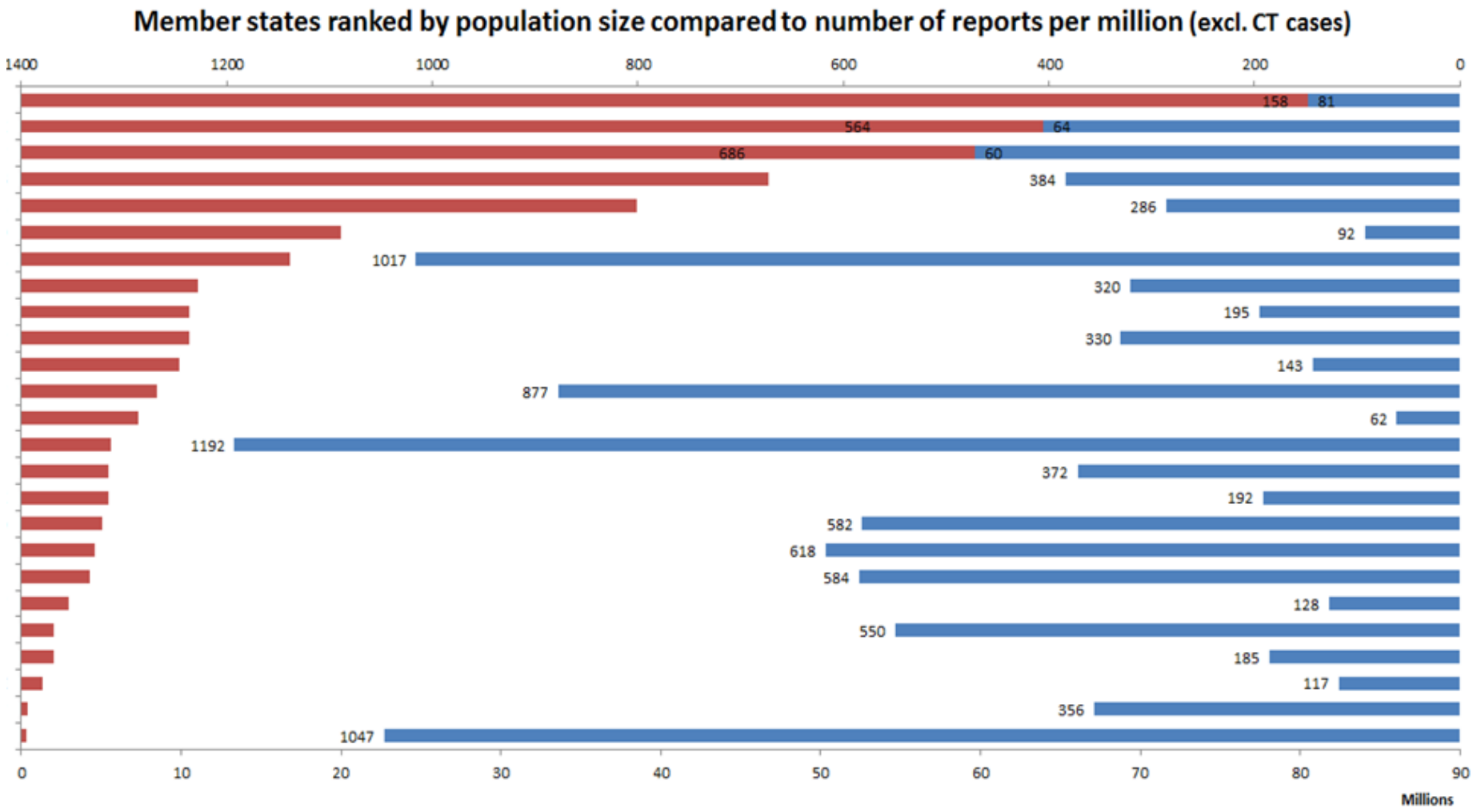
In conclusion, MSs assessment is largely uniform at a scientific level. However, one cannot use a common denominator when it comes to assessment processes and the population size does not seem to determine the approach taken.

A fact worth considering is that out of 10 MSs which receive above average number of reports (i.e. > 356 reports/million), 4 perform detailed assessment only at signal assessment stage and one has a unique pharmacovigilance institution dedicated to monitoring of spontaneous reports. Furthermore, the number of signals generated by 4 MSs (40) represents 67% (40/60) of all signals generated by Member States between July 2012 and December 2013 (Pacurariu et al, 2014).



(Please note that red bars for 3 MSs overlap with blue bars – larger font numbers to the right of red bars indicate the population size)

Of the top 10 MSs ranked by the number of reports per million, 7 are small MSs with population <10 million, 1 medium size MS with 16,8 million and 2 MSs with roughly population around 60 million.



Question T1Q43: Average time needed for ADR processing steps for an individual report:

	Average time/minutes	Our institution is not responsible for this activity
Manual data entry		❑
Manual validation		❑
Assessment		❑

This question was aimed at assessing the time needed for the whole case processing exercise, not only assessment. Assuming that reports from healthcare professionals are still often received on paper, it was considered useful to gain an insight into how much time is taken up by manual entry of data at the expense of assessment.

Average time needed (in minutes) for ADR processing steps		
	Mean	Median
Manual data entry	**55**	33
Manual validation	**20**	10
Assessment	**77**	50

- Manual data entry
  - In terms of manual data entry, there are 10 MSs that require ≥60 min to enter the case into the database. In 7 out of these 10 MSs, manual data entry is the most time-consuming part of the process, taking even more time than the assessment.
- Manual validation
  - Manual validation does not seem to be the time limiting part of the process. There are, however, MSs that require twice or three times more time for this step compared to the median. This should be interpreted with caution, as the definition of "manual validation" has not been provided.
- Assessment
  - In absolute numbers, 22/26 MSs assess a single case report in 2 hours or less. Mean time required for assessment is 77 minutes, whereas median is much lower – 50 minutes. The difference between mean and the median is due to the fact that 4 MSs reported much higher time needed for case assessment (i.e. 360 minutes).

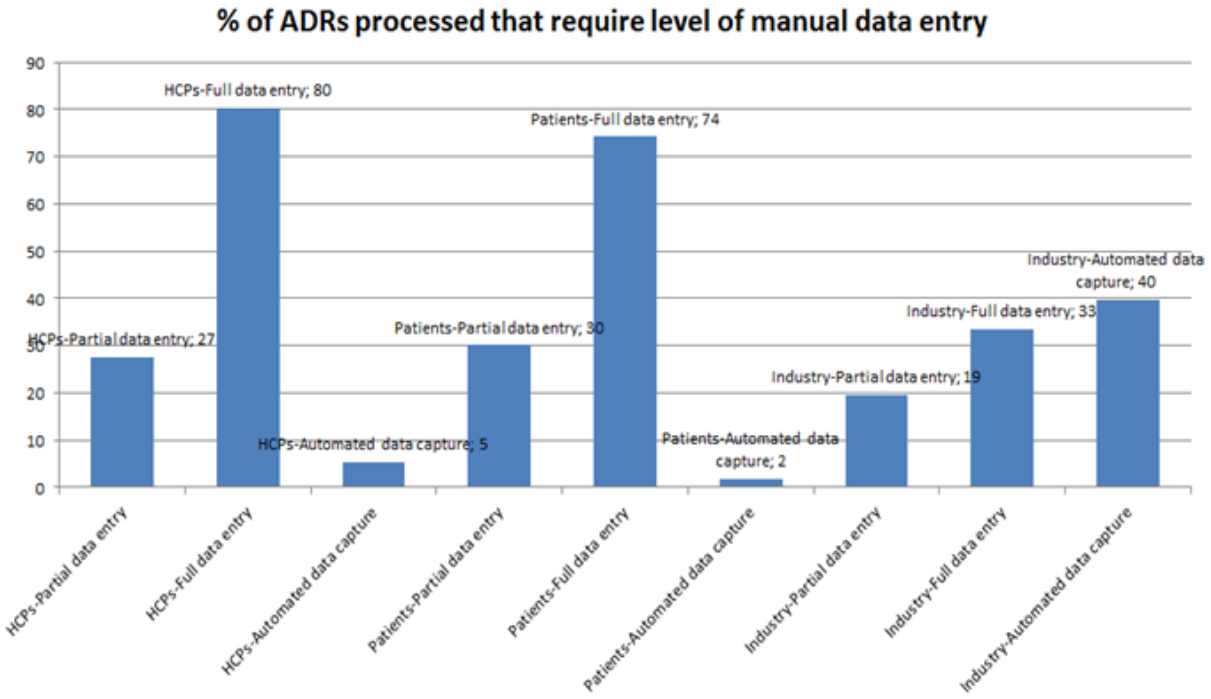
Average time needed for ADR processing steps- %		
	Mean	Median
Manual data entry	**36**	35
Manual validation	**13**	14
Assessment	**50**	54

On average, assessment takes up 50% of the time for the whole process, meaning that practically 50% of the time is spent on data entry and validation. As optimisation of data entry step results in more time for assessment, responses to this question should also be assessed in conjunction with database questionnaire responses to evaluate what (IT) solutions have been implemented by Mss reporting lowest time for data entry.

Question T1Q44: Please specify the percentage of ADRs processed that require level of manual data entry. Please enter whole numbers (i.e. decimals and symbol "%" should not be used).

	HCPs	Patients	Industry	Our institution is not responsible for this activity
Partial data entry Full data entry Automated data capture	Percentage of ADRs	Percentage of ADRs	Percentage of ADRs	Please tick if applicable ❑ ❑ ❑

Question T1Q45: Please explain all fully automated processes:



Average based on 27 responses.

Partial or full data entry refers to the level of manual input, whereas automated data capture refers to fully automated process.

- Entering data for Healthcare Professionals' and Patient reports
    - Responses indicate that 80% of HCPs reports and 74% of Patient reports are still entered fully manually into the MS's databases. The same pattern is visible for partial data entry where, on average, 27% of all HCP reports and 30% of all patient reports are entered manually. Portions of HCP and patient reports entered fully automatically into the databases is still very low 5% and 2% for HCP and patient reports, respectively.
    - These results are either not in line with responses to question 20, where the highest ranking channel for ADR reporting was Web-based application (38% of all reports in 2013), or Web-based applications still require a certain manual intervention (however, this would still not explain the very high percentage of fully manual data entry for HCP and Patient reports).

- Industry automated data capture
    - All respondents (5) to question 45 provided the same response, referring to EudraVigilance gateway for automated data capture. The all-respondents average for automated data capture is somewhat below expected indicating

that only 40% of all industry ICSRs are received directly through EV gateway. Alternatively, this low percentage might be the result of unclear predefined responses where "Industry – Automated data capture" might have been swapped for "Industry – Full data entry" as the clear instruction that the latter foresees purely manual input was lacking.

Question T1Q46: How many Full Time Equivalents (FTEs) are dedicated to ADR processing?

For example, a worker employed for 20 hours for ADR processing a week, where full-time work consists of 40 hours, is counted as 0.5 FTE; a worker employed for 10 hours for ADR processing a week, where full-time work consists of 40 hours, is counted as 0.25 FTE. Hence, in this case FTEs dedicated to ADR processing total 0.75.

	Validation	Data entry	Assessment	Our institution is not responsible for this activity
Medical Doctor				❑
Pharmacist				❑
Dentist				❑
Veterinarian				❑
Medical Biochemist				❑
Nurse				❑
Pharmaceutical technician				❑
Science graduate				❑
Administrative staff				❑
Students				❑
Other				❑

- Validation (19 responses)

Validation	
	FTEs*
Pharmacist	10,1
Medical Doctor	8,6
Science graduate	5,1
Administrative staff	3,3
Pharmaceutical technician	3,0
Students	0,8
Veterinarian	0,3

*if FTE<0,1, results not presented

Validation	
	FTEs
Mean	2,9
Median	0,75
Cumulative (all respondents)	31,1

- Data entry (21 responses)

Data entry	
	FTEs
Administrative staff	34,0
Pharmacist	12,6
Nurse	10,5
Other	10,3
Science graduate	6,2
Medical Doctor	2,0
Students	1,3
Veterinarian	0,5

Data entry	
	FTEs
Mean	7,0
Median	2,0
Cumulative (all respondents)	77,4

- Assessment (23 responses)

Assessment	
	FTEs
Pharmacist	54,4
Medical Doctor	41,4
Science graduate	5,1
Veterinarian	1,8
Medical Biochemist	0,4
Nurse	0,3

*if FTE<0,1, results not presented

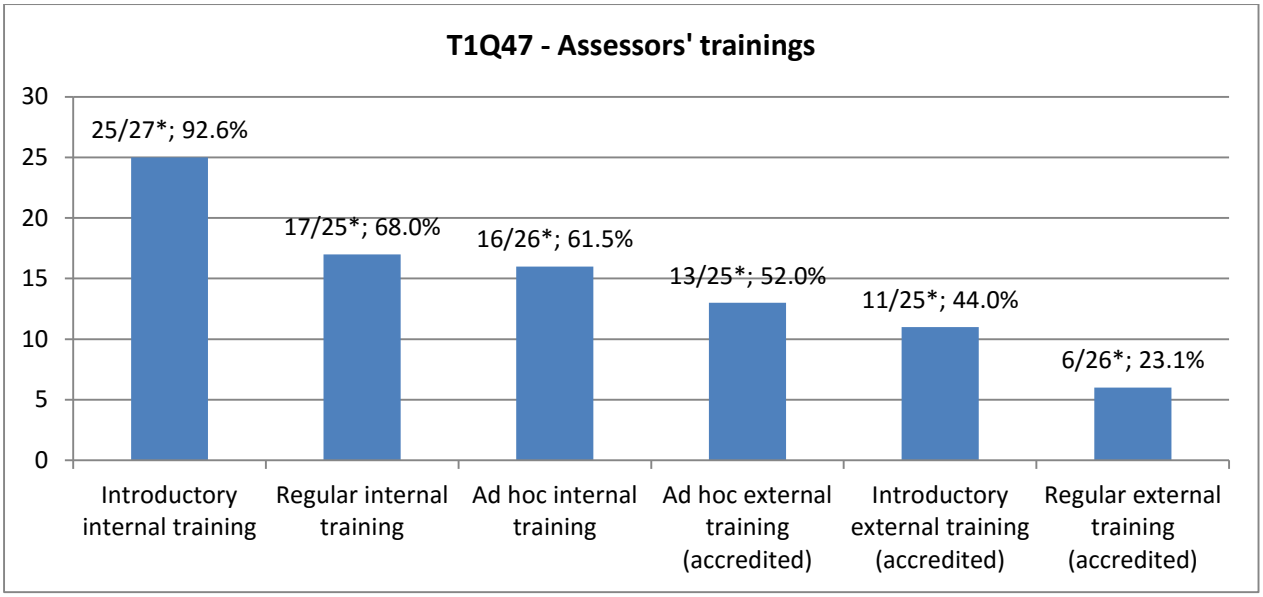
Assessment	
	FTEs
Mean	9,4
Median	0,3
Cumulative (all respondents)	103,4

Most FTEs for case processing are, expectedly, allocated to assessment (49%). This is in line with results presented in question 43, where we calculated that median relative proportion of assessment step within the whole case processing exercise is 54%. Overall the number of FTEs in the network dedicated to case processing adds up to 212, however this calculation is based on incomplete set of responses with some of the biggest MSs not providing the data.

Pharmacists are highest ranked by the number of FTEs (67), followed by medical doctors (54), administrative staff (37,3) and science graduates (16,4). Administrative staff is the most employed group for data entry (44%), and pharmacists and medical doctors together perform 60% of validation and 93% of assessments.

Question T1Q47: How are your assessors for ADR processing trained?

	Yes	No
Introductory internal training	❍	❍
Introductory external training (accredited)	❍	❍
Regular internal training	❍	❍
Regular external training (accredited)	❍	❍
Ad hoc internal training	❍	❍
Ad hoc external training (accredited)	❍	❍
No training	❍	❍
Our institution is not responsible for this activity	❍	❍

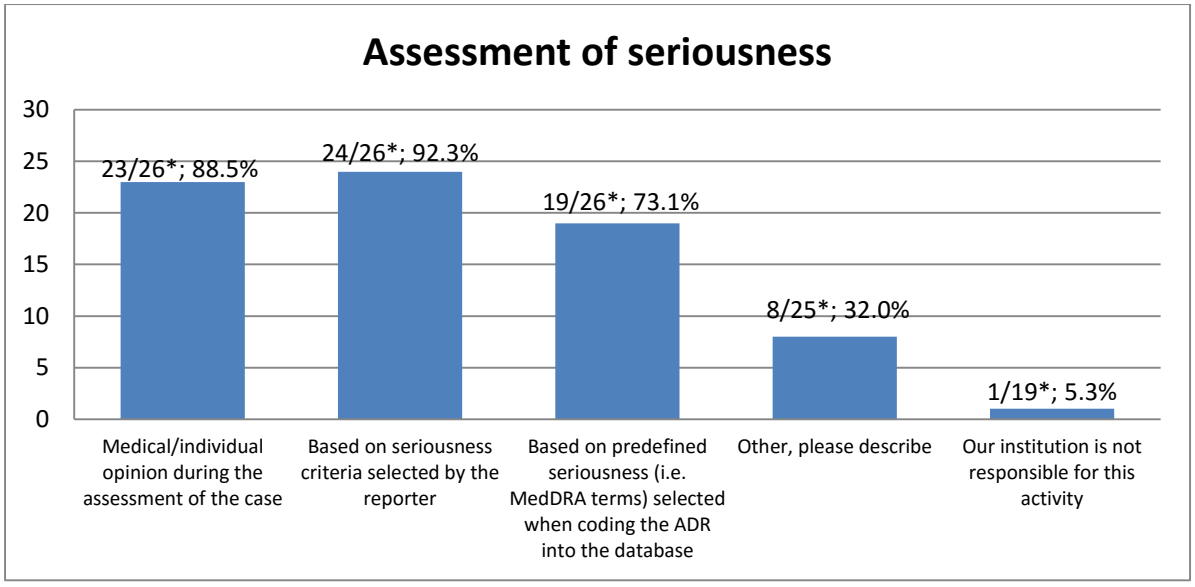


*number of respondents

Twenty five (25) out of 27 MSs internally train their assessors as an introductory session, and 17/25 MSs also provide internal trainings on a regular basis, while 16/26 MSs organize internal trainings on as-needed basis. External trainings are not as favoured as internal trainings and MSs will most often organize an external training when there is a special need for it (13/25), rather than providing external trainings on a regular basis (6/26). When a new member of staff is admitted, MSs favour organizing internal trainings (25/27) as opposed to external trainings (11/25), although some MSs will provide both external and internal trainings.
Two (2) MSs responded that their institution was not responsible for trainings.

Question T1Q48: How do you assess seriousness of ADR reports?

	Yes	No
Medical/individual opinion during the assessment of the case	❍	❍
Based on seriousness criteria selected by the reporter	❍	❍
Based on predefined seriousness (i.e. MedDRA terms) selected when coding the ADR into the database	❍	❍
Other, please describe	❍	❍
Our institution is not responsible for this activity	❍	❍



*number of respondents

MSs utilize several criteria for assessing seriousness. At least 2 seriousness criteria are used by 24 MSs and 17 MSs use 3 seriousness criteria. Four out of eight respondents referring to "Other" emphasized that IME list served as a criterion for assessing seriousness, which is in essence equal to option 3 ("Based on predefined seriousness…"), and remaining responses were equally distributed between WHO definition of seriousness and Directive 2001/83/EC definition of seriousness which are identical. Overall, there seems to be an alignment within the network regarding the assessment of seriousness.

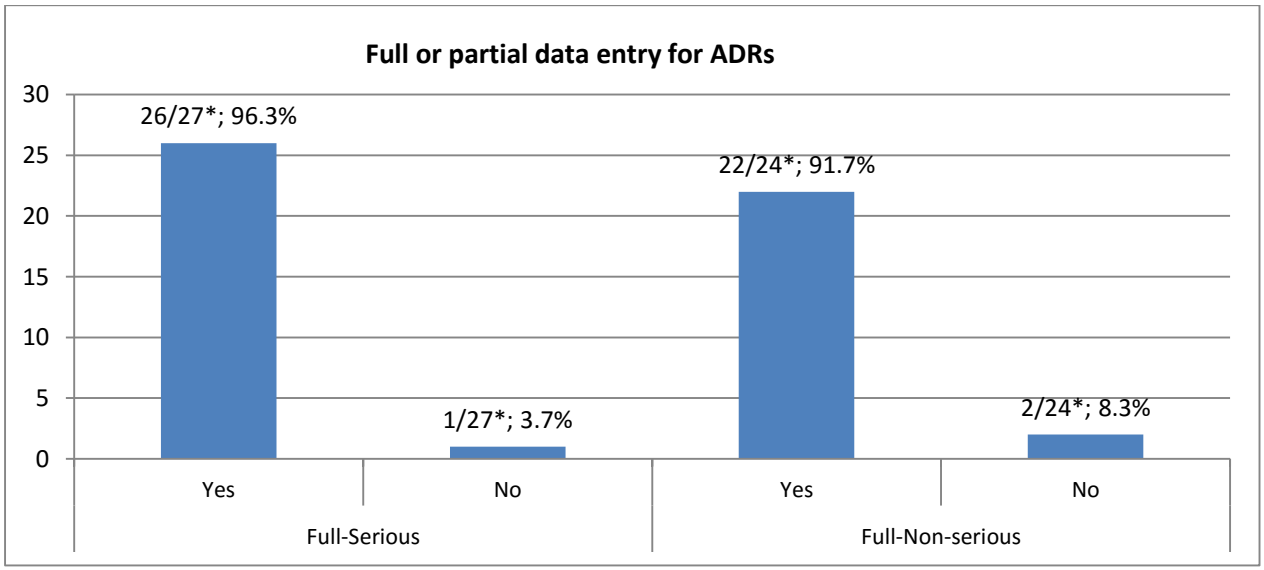
Question T1Q49: Please indicate whether you complete full or partial data entry for the following types of ADR reports?
("partial" could mean that only structured data is entered into the database - i.e. narrative from original report is omitted)

	Full		Partial		Our institution is not responsible for this activity
	Yes	No	Yes	No	Please tick if applicable
Serious	❍	❍	❍	❍	❑
Non-serious	❍	❍	❍	❍	❑
Other, please specify	❍	❍	❍	❍	❑

Question T1Q50: Please provide in one sentence what exactly is meant by 'partial' data entry in case of serious ADR reports.

Question T1Q51: Please provide in one sentence what exactly is meant by 'partial' data entry in case of non-serious ADR reports.

Question T1Q52: Please provide in one sentence what exactly is meant by 'partial' data entry.



*number of respondents

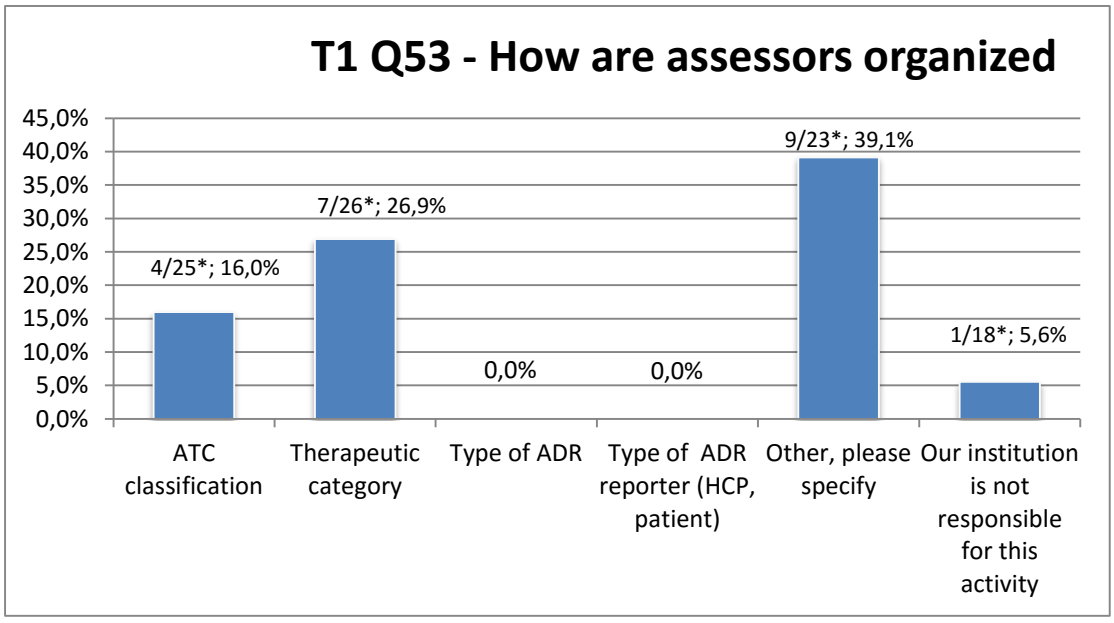
Complete serious cases are entered by 26 MSs. One MS responded they were not responsible for this activity and 1 stated they did not perform full data entry for serious cases.

Complete non-serious cases are entered by approximately ¾ of all MSs, while the rest perform partial data entry for non-serious cases and one MS is not responsible for this activity.
One MS responded to question 50 clarifying that narrative is omitted for partial entry of serious cases.
In terms of partial entry of non-serious cases, 2 MSs do not enter the case narrative and 1 does not fully handle non-serious reports stating that, nevertheless, data sufficient for signal detection should at least be entered i.e. ADR diagnoses and concerned drug.

One MS has a specific approach to non-serious reports in paper form (for electronic reports the information is already populated in the data fields) meaning that when a non-serious case is reported on a paper form partial data entry is carried out. This covers only coding of the suspect drug name (and batch number if reported), suspect reaction, patient details and reporter details.

T1Q53 In your institution, assessors are organized according to:

	Yes	No
ATC classification	❍	❍
Therapeutic category	❍	❍
Type of ADR	❍	❍
Type of ADR reporter (HCP, patient)	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍



* number of respondents

One quarter of MSs organizes assessors according to the therapeutic groups and in 16% MSs assessors are organized by ATC classification. It should be noted though that some MSs have their assessors organized in more than one way (i.e. by both therapeutic category and by ATC classification). However, 39% (12) of respondents chose to answer "Other". In general these responses can be subdivided into 2 categories:

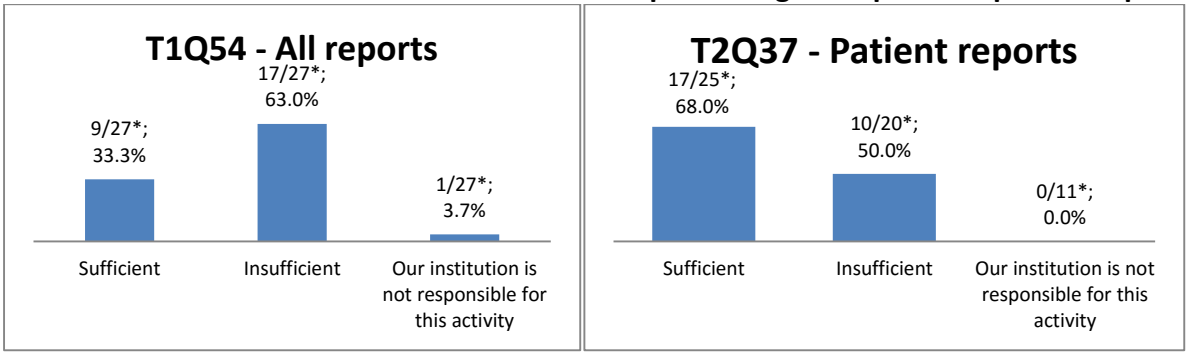
- no specific organization due to limited number of assessors;
- assessors organized according to experience/seniority and expertise.

One MS has a distinct system dependent upon whether a drug is on additional monitoring list or not. Only assessors reviewing ADR reports for additional monitoring products are organised according to therapeutic category. All assessors involved in case processing are organised into three teams no division by ADR type.

Question T1Q54: According to your estimations, the number of FTEs for ADR processing in your institution is:

- ❍ Sufficient
- ❍ Insufficient
- ❍ Our institution is not responsible for this activity

NCA's estimation of the number of FTEs for ADR processing: all reports vs. patient reports



*number of respondents

When asked whether the number of personnel for overall ADR processing is sufficient, almost 2/3 of respondents answered that they did not have a sufficient number of personnel at their disposal. However, the response was inverse when MSs were posed the same question but relating to processing of only patient reports (please see T2Q37). This is not unexpected given the relatively low numbers of patient reports in this moment compared to HCP reports.

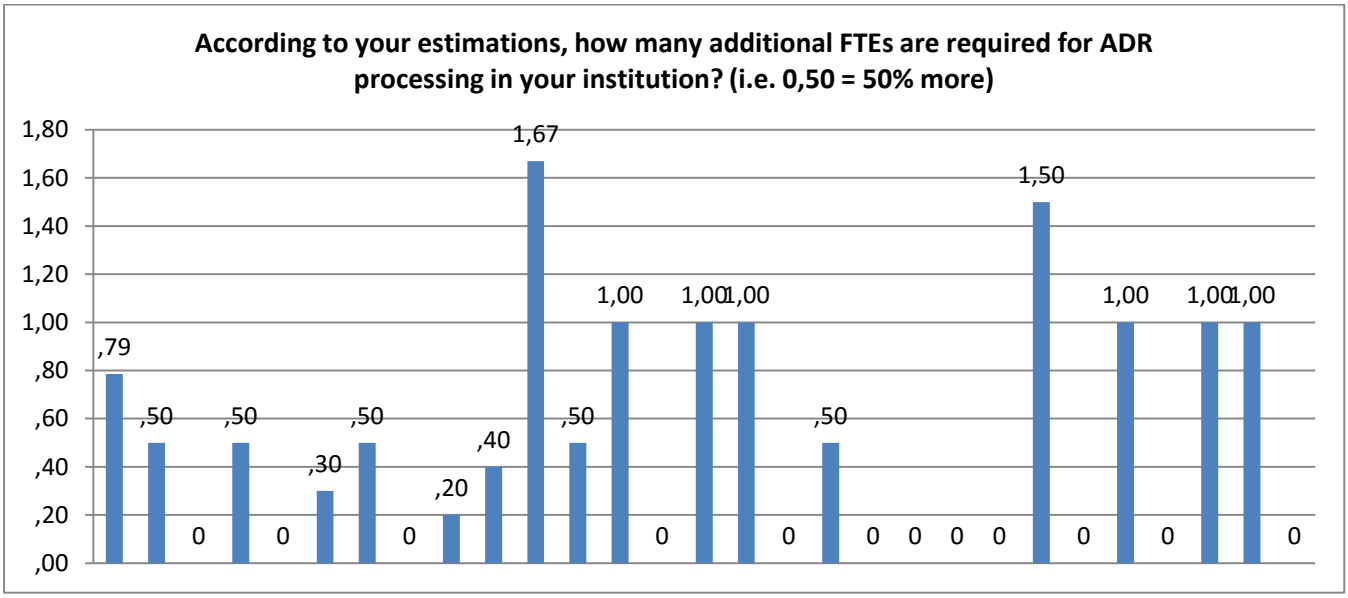
Reports per million	FTEs	Ratio (reports per million/10)/FTEs
158	9	1,76
581	15,7	3,70
564	9	6,27
618	8	7,73
62	0,8	7,75
1016	10,2	9,96
185	1,3	14,23
285	1,3	21,92
355	0,2	177,50

Sufficient No of FTEs

MSs that responded affirmatively to the question were very much different with regards the number of reports per million (from 62 to 1016) and the number of FTEs (from 0,2 to 15,7). Hence a single measure was introduced to assess whether the ratio of reports per million (divided by 10 for readability purposes) over the number of FTEs was similar. However, even in this regard, MSs were markedly different. Therefore, the ratio of workload and the number of personnel does not explain why certain MSs consider the number of FTEs for ADR processing sufficient or not.

Question T1Q55: According to your estimations, how many additional FTEs are required for ADR processing in your institution?

- ❍ 10%
- ❍ 20%
- ❍ 30%
- ❍ 40%
- ❍ 50%
- ❍ 60%
- ❍ 70%
- ❍ 80%
- ❍ 90%
- ❍ 100%
- ❍ >100 %, please specify_____



Based on 16 responses, MSs on average require almost 80% more FTEs for ADR processing.

Question T1Q56: What is the average amount of time required per assessor to assess a single HCP ADR report (in hours)?

- ❍ < 1 hrs
- ❍ 1-2 hrs
- ❍ 2-4 hrs
- ❍ 4-6 hrs
- ❍ 6-8 hrs
- ❍ >8 hrs
- ❍ Our institution is not responsible for this activity

		Count	col%
What is the average amount of time required per assessor to assess a single HCP ADR report (in hours)?	< 1 hrs	**5**	**18,5%**
	1-2 hrs	**13**	**48,1%**
	2-4 hrs	**8**	**29,6%**
	Our institution is not responsible for this activity	**1**	**3,7%**

Nearly half of all MSs assess a single ADR report in between 1-2 hours and almost 30% of MSs assess a single ADR report in between 2-4 hours (based on 27 responses).

Question T1Q57: If case processing in your institution is done by professionals other than medical doctors (MD), are ICSRs reviewed by MDs before submitting to the Eudravigilance?

- ❍ Yes, always
- ❍ Only in cases where assessor needs medical advice
- ❍ Case processing in our institution is done exclusively by medical doctors
- ❍ No
- ❍ Our institution is not responsible for this activity

		Count	col%
Review of ICSRs by MDs before submitting to the Eudravigilance	Yes, always	**6**	**22,2%**
	Only in cases where assessor needs medical advice	**12**	**44,4%**
	No	**5**	**18,5%**
	Case processing in our institution is done exclusively by medical doctors	**3**	**11,1%**
	Our institution is not responsible for this activity	**1**	**3,7%**

Six MSs have an additional check of the ICSR by a medical doctor and in 3 MSs case processing is done exclusively by medical doctors. These MSs account for 1/3 of all MSs (27 responses).

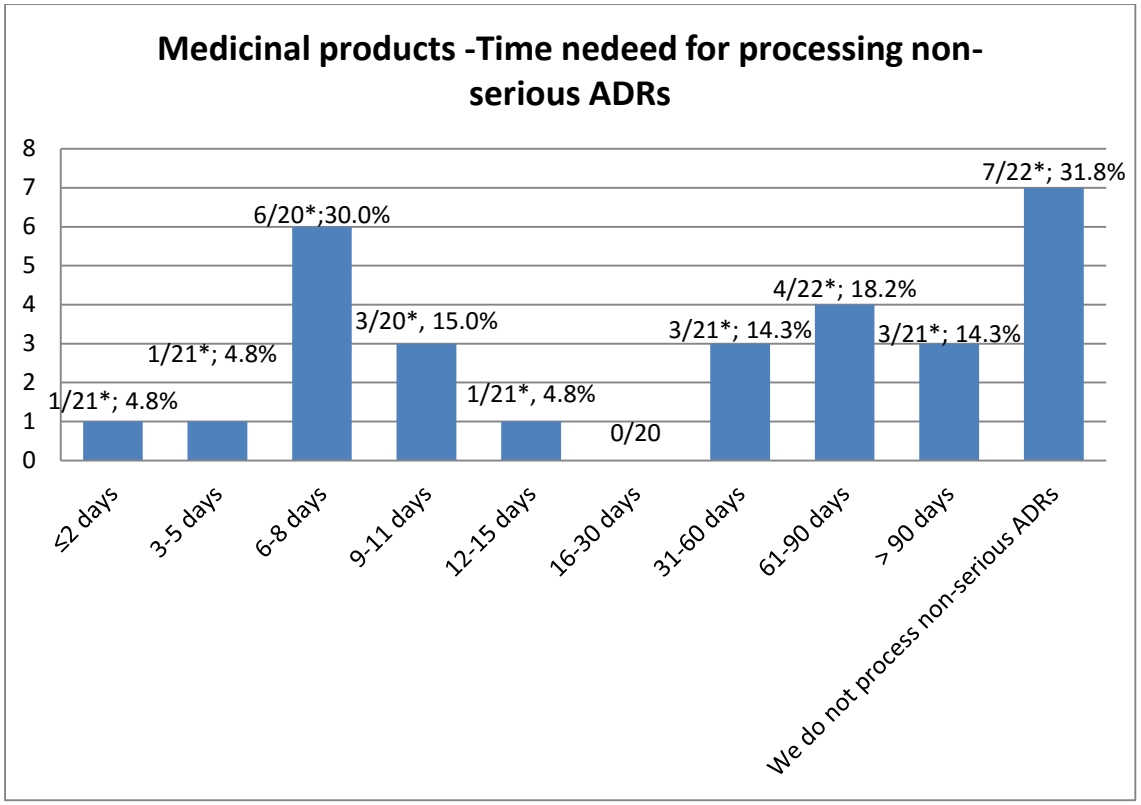
	Count	%	Count	Count	Count	Count	Count	Count
Yes, always	**6**	**22,2**	**1**	**1**	**1**	**1**	**1**	**1**
Time required for ICSR processing (hrs)			1-2	<1	2-4	<1	2-4	1-2

Based on the variability of responses by the 6 MSs where medical doctors review ICSRs before submission to the EudraVigilance, it appears that additional check by MDs does not affect the amount of time required to process a single report.

Question T1Q58: Performance indicators – processing timelines
The purpose of this section is to find out what is the average amount of time needed for the processing of a single non-serious and/or serious ADR report.

Question T1Q59: What is the average amount of time needed for the processing of a single NON-SERIOUS ADR report?
(start of the process is equal to the date of receipt of the ADR report into the database; end of process is equal to the date of sending of the ICSR to the Eudravigilance)

	Medicinal products		Vaccines/Biologics	
	Yes	No	Yes	No
≤2 days	❍	❍	❍	❍
3-5 days	❍	❍	❍	❍
6-8 days	❍	❍	❍	❍
9-11 days	❍	❍	❍	❍
12-15 days	❍	❍	❍	❍
16-30 days	❍	❍	❍	❍
31-60 days	❍	❍	❍	❍
61-90 days	❍	❍	❍	❍
> 90 days	❍	❍	❍	❍
We do not process non-serious ADRs	❍	❍	❍	❍
Our institution is not responsible for this activity	❍	❍	❍	❍



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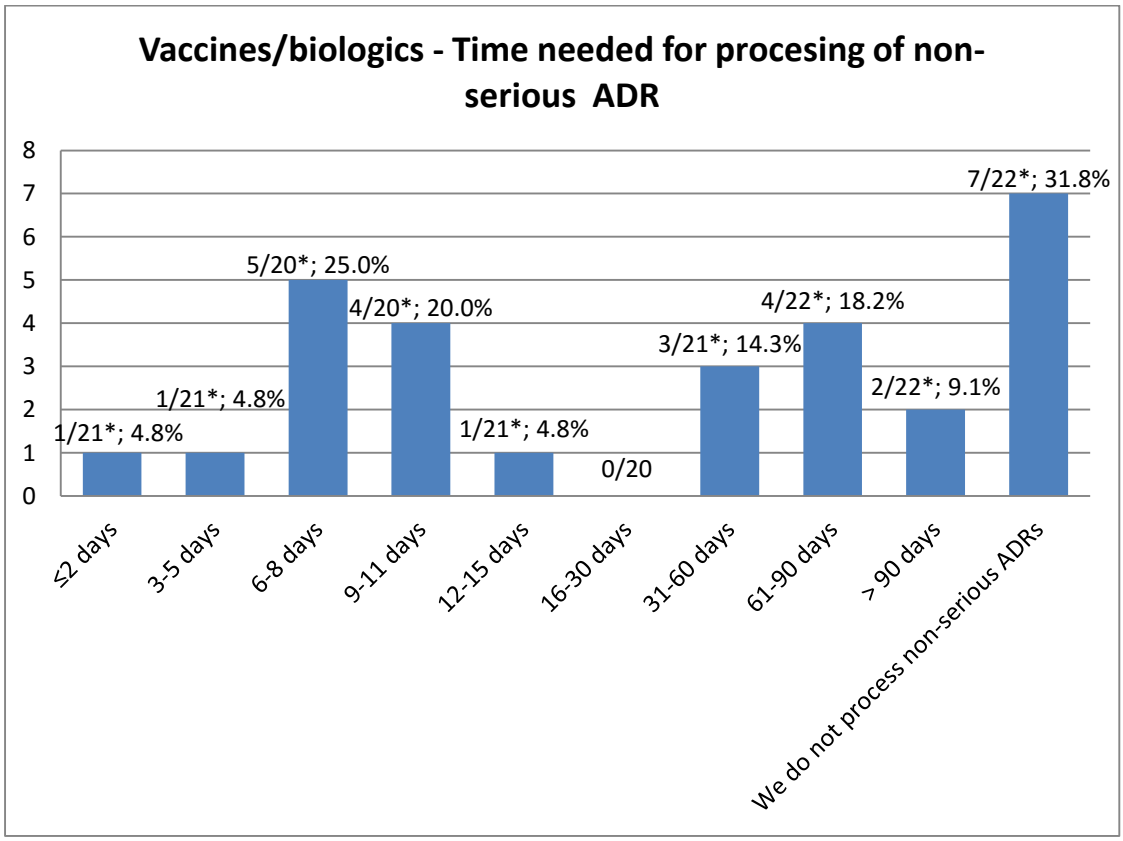

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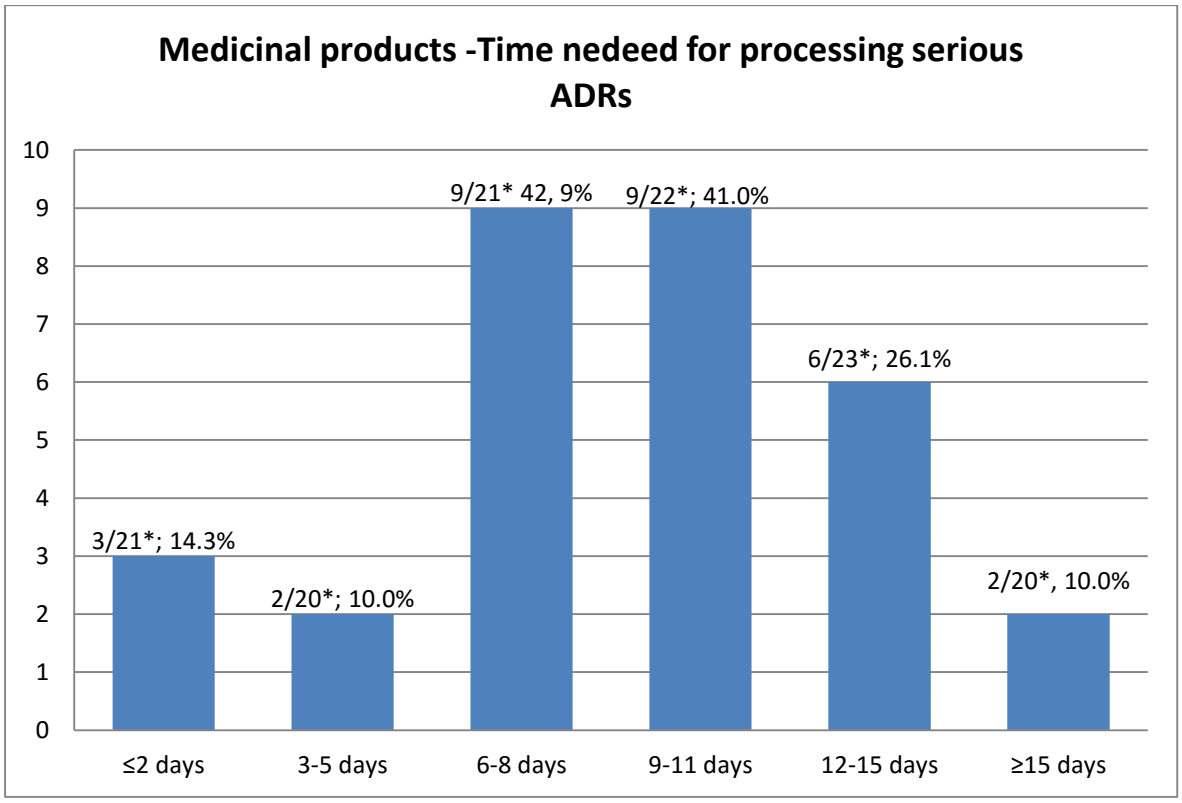
Question T1Q60: What is the average amount of time needed for the processing of a single SERIOUS ADR report?

(start of the process is equal to the date of receipt of the ADR report into the database; end of process is equal to the date of sending of the ICSR to the Eudravigilance)

	Medicinal products		Vaccines/Biologics	
	Yes	No	Yes	No
≤2 days	❍	❍	❍	❍
3-5 days	❍	❍	❍	❍
6-8 days	❍	❍	❍	❍
9-11 days	❍	❍	❍	❍
12-15 days	❍	❍	❍	❍
≥15 days	❍	❍	❍	❍
Our institution is not responsible for this activity	❍	❍	❍	❍



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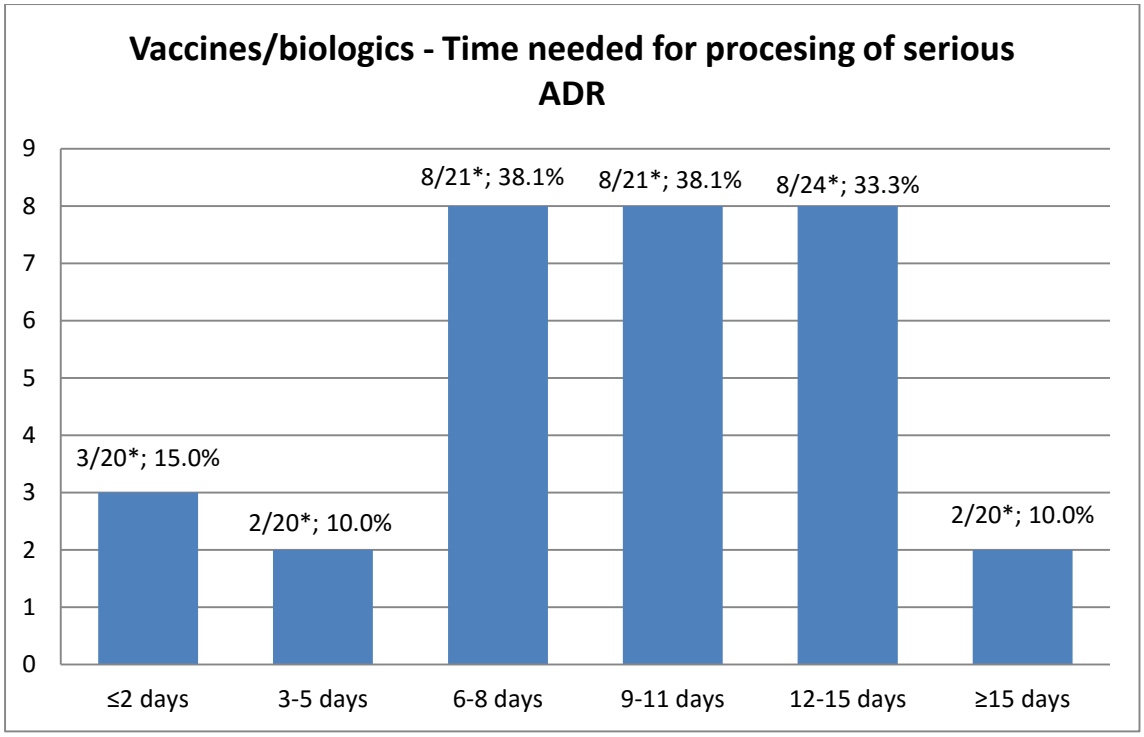


*number of respondents

All MSs (28) provided answers to this set of questions but not every MS provided Yes/No answer to all options given in the question (number of answers per option ranged from 20 to 24). Also, some countries offered more than one option within the question which was taken into account during the interpretation of results, since there can be only one average time for assessing ADRs.

Most MSs indicated that the average time for processing **non-serious ADRs** for medicinal products is **6-8 days** (6/20) and **61-90 days** (4/22).

Average time needed for processing **serious ADRs** for medicinal product is **6-8 days** (9/21) and **9-11 days** (9/22).

Analysis of the data for time processing of both serious and non-serious data for vaccines/biologicals follow the same pattern as the data for assessing ADRs for medicinal products except for one additional peak at **9-11 days** for non-serious ADRs (4/20). One additional peak was noticed also at **12-15** days for serious ADRs (8/24).

This additional peak might be statistical artefact due to small numbers, but it is indicative that it appeared both for serious and non-serious ADRs. Answers provided in different part of WP4 questionnaire related to traceability of biologics indicate that many MSs always follow-up for brand and batch data for vaccines/biologicals (please refer to T1Q79, T1Q80) which might explain longer time needed for processing.

Around 1/3 of the MSs (7/22) indicated that they **do not process non-serious ADRs**. We made further analysis to verify whether this statistics reflect true state of processing of non-serious ADRs among the states or some of the answers were ticked by mistake. In 2 cases more than one answer was ticked but in 5 cases MSs clearly stated they do not process all non-serious ADR reports. This raises question what is done with non-serious ADR reports at state level – how are they processed, how are they provided to MAHs for compiling PSURs

etc. One possible explanation is that MSs process non-serious ADRs but they don't send them to EV (*processing* as defined in question intro).

In some cases it was indicated that **processing time is longer then legally allowed** (>15 days for serious ADRs and >90 days for non-serious ADRs). Further analysis indicates that only in case of one MS it was clearly stated that timelines are exceeded. Probable reason for this MS's situation is lack of human resources which was indicated in their answer to T1Q54 and T1Q55.
In the case of other above mentioned countries more than one answer was ticked so this information cannot be considered relevant.

Question T1Q61: Duplicate detection
Responses to questions in this section give input if MSs perform duplicate detection and if they have a duplicate detection system in place.

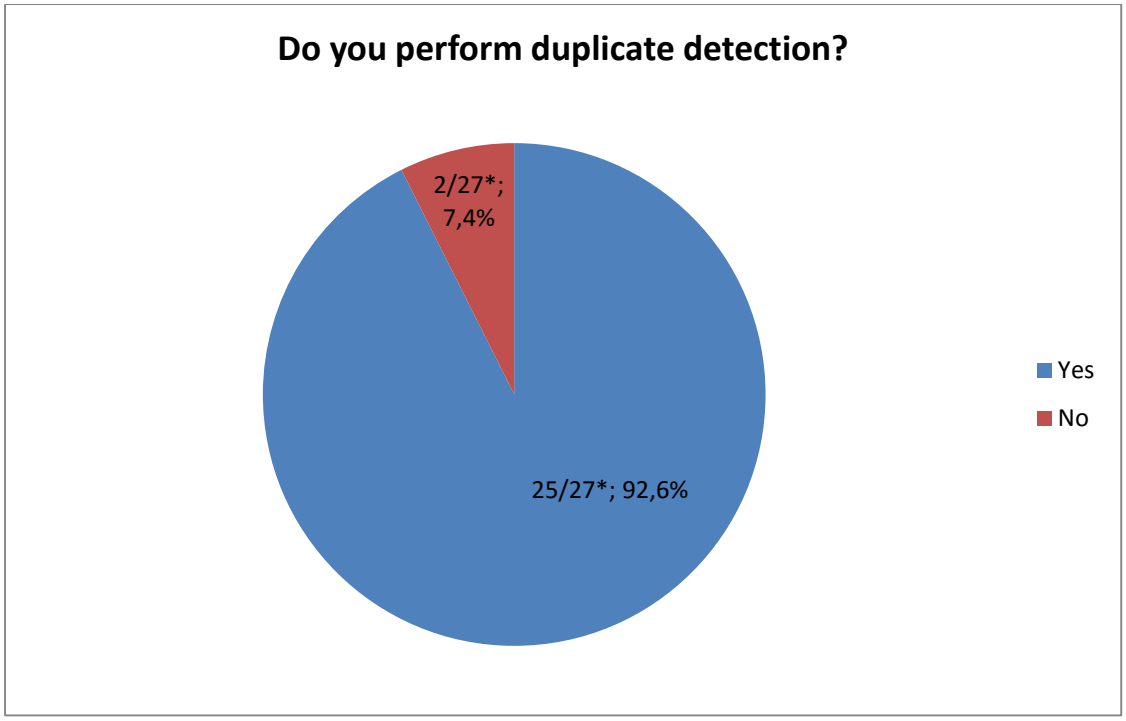
Question T1Q62: Do you perform duplicate detection?

	Yes	No
Yes, after sending to MAHs/EudraVigilance	❍	❍
Yes, before sending to MAHs/EudraVigilance	❍	❍
We do not perform duplicate detection	❍	❍
Our institution is not responsible for this activity	❍	❍

Question T1Q63: Do you have a duplicate detection system in place?

	Yes	No
Yes, we have an algorithm (SOP)	❍	❍
Yes, our database performs duplicate detection	❍	❍
We do not have duplicate detection system in place	❍	❍
Our institution is not responsible for this activity	❍	❍

28 MS provided answer to the T1Q62-63. One MS is not responsible for duplicate detection activity.



*number of respondents

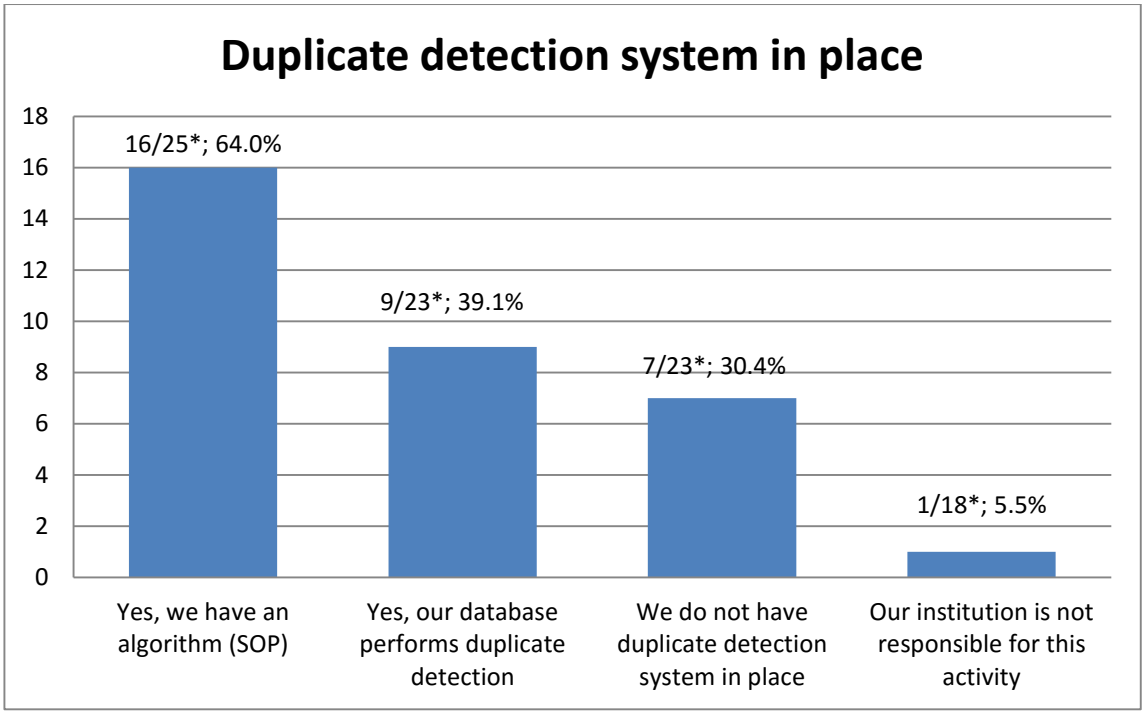
Our aim was to detect how many MSs perform duplicate detection regardless of whether they do it before or after sending ICSR to EV. For that reason first two answers are combined and considered as *Yes*.
93% of MSs do duplicate detection (25 MSs):

- before sending the ICSR to EV (17 MSs)
- after sending ICRSs to EV (8 MSs);
- both (5 MSs).

2 MSs do not perform duplicate detection. They use EV as their national database. However, there are 3 more MSs that use EV as their national database and still do duplicate detection.

The most popular method for duplicate detection is

- use of algorithm, SOP (16 MSs)
- performing a duplicate detection by the database (9 MSs)
- both (4 MSs)



*number of respondents

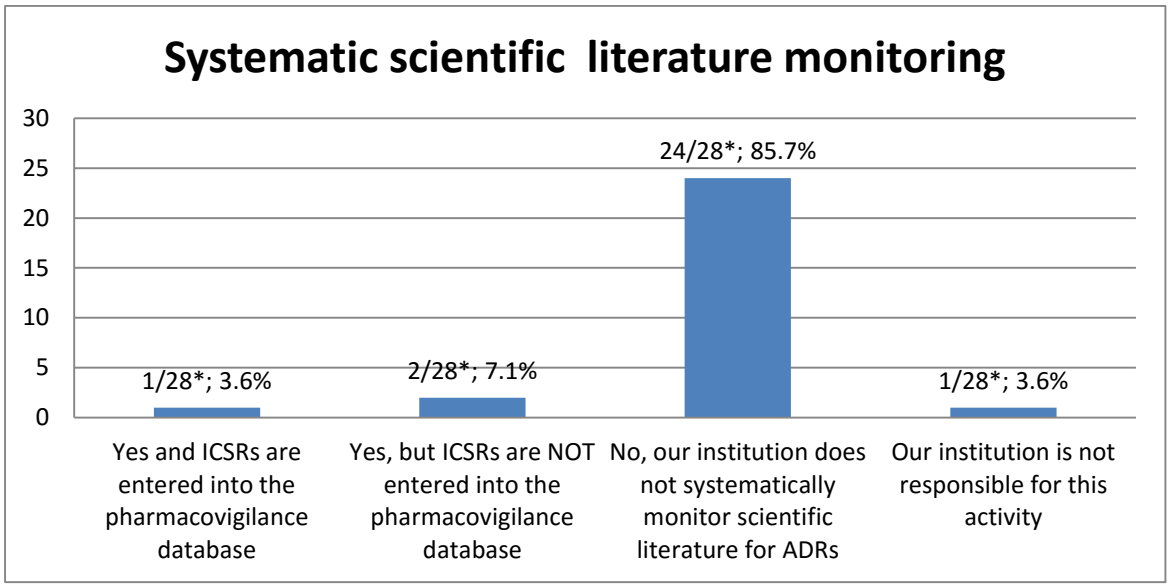
Few MSs (4) use more than one duplicate detection method.
5 MSs that stated they do duplicate detection have not implemented any duplicate detection methodology.

Question T1Q64: g) Literature reporting

Responses to questions in this short section should provide high-level information whether MS's perform systematic scientific literature monitoring.

Question T1Q65: Does your institution perform any systematic scientific literature monitoring?

- ❍ Yes and ICSRs are entered into the pharmacovigilance database
- ❍ Yes, but ICSRs are NOT entered into the pharmacovigilance database
- ❍ No, our institution does not systematically monitor scientific literature for ADRs
- ❍ Our institution is not responsible for this activity



*number of respondents

Twenty four (24) MSs **do not systematically monitor** scientific literature for ADRs and only one MS does it and enters ICSRs into the pharmacovigilance database.

Question T1Q66: Follow up

The purpose of this set of questions is to find out the percentage of follow up reports from direct HCP ADR reports in 2013 and what follow-up information is most often asked for.

Question T1Q67: What is the percentage of follow up reports from direct HCP ADR reports in 2013 if known? Blanks will be considered as unknown.

**success=any relevant information obtained in addition to the initial report*

Follow up definition according to GVP Module VI

	% followed up	% follow up success*	Our institution is not responsible for this activity
Serious			
Non-serious			
All ADRs (in case when there is only a possibility to get pooled data)			

Results:

	% followed up	% follow up success*
Mean - serious	34,9	53,4
Mean - non-serious	29,5	26,2
Mean - all ADRs (in case when there is only a possibility to get pooled data)	30,0	56,0

Fifteen (15) MSs provided at least a partial answer to this question.
Ten (10) MSs provided the percentage of follow up reports for serious cases, 8 MSs provided the percentage for non-serious cases and 1 MS provided the information for pooled data (serious and non-serious, since it was only possible to provide information for pooled data). The mean values for follow up reports were 34,9%, 29,5% and 30,0% for serious, non-serious and pooled data, respectively.
Ten (10) MSs provided the percentage of follow up success for serious cases, 9 MSs provided the percentage for non-serious cases and 2 MSs provided the information for pooled data (serious and non-serious, since there was only possible to provide information for pooled data). The mean values for follow up success were 53,4%, 26,2% and 56,0% for serious, non-serious and pooled data, respectively.
The presented mean values show that the rates of follow up reports are somewhat higher for serious cases. The rates of follow up success for serious cases are double the rates for non-serious cases, indicating that the reporters might be more willing to provide follow up information for serious cases. Higher follow up success for serious cases might also be a result of different approach of MSs to follow up of serious and non-serious cases (i.e. repeating the follow up request for serious cases).
In total, only 5 MSs provided both the percentage of follow up reports and the percentage of follow up success for both serious and non-serious cases or for pooled data (serious and non-serious, since there was only possible to provide information for pooled data). In contrast, a total of 13 MSs provided neither the percentage of follow up requests nor the percentage of follow up success. This might be due to the limitations of the IT systems used for follow up activities.

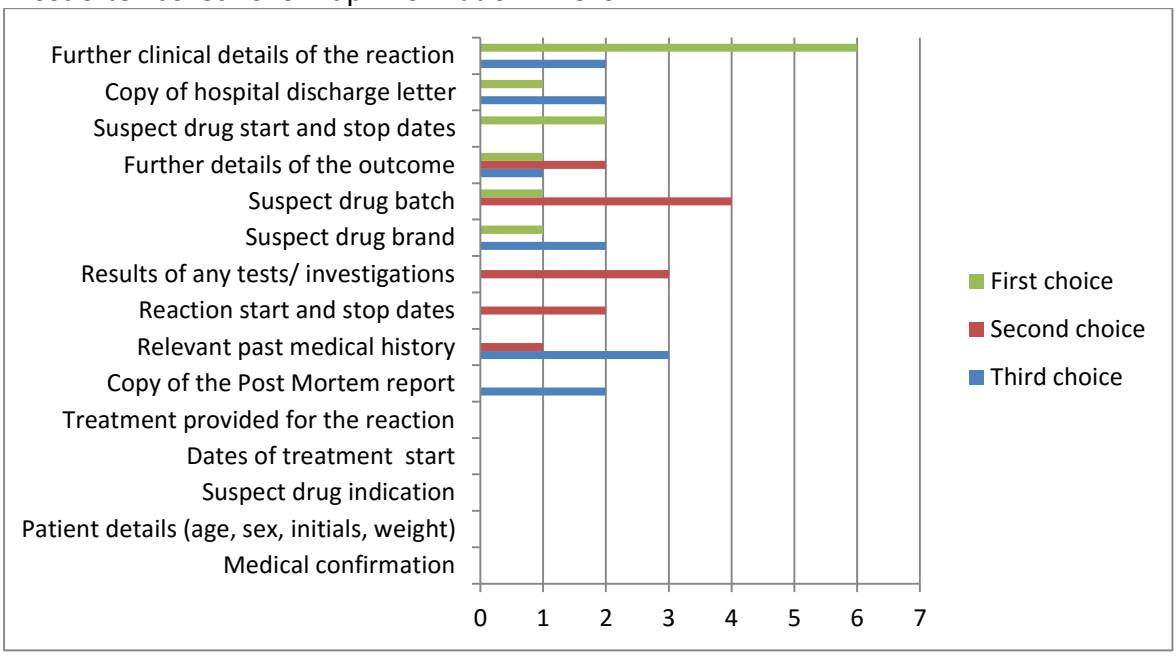
Question T1Q68: Tick follow-up information that you most often ask for (please select max 3 choices for each reporter group)?

	HCPs			Patients		
	1st choice	2nd choice	3rd choice	1st choice	2st choice	3rd choice
Medical confirmation (tick only for patient reports)						
Patient details (age, sex, initials, weight)						
Suspect drug brand						
Suspect drug batch						
Suspect drug indication						
Suspect drug start and stop dates						
Reaction start and stop dates						
Further clinical details of the reaction						
Results of any tests/ investigations						
Copy of hospital discharge letter						
Further details of the outcome						
Copy of the Post Mortem report						
Treatment provided for the reaction						
Dates of treatment start						
Relevant past medical history						
Other, please specify						

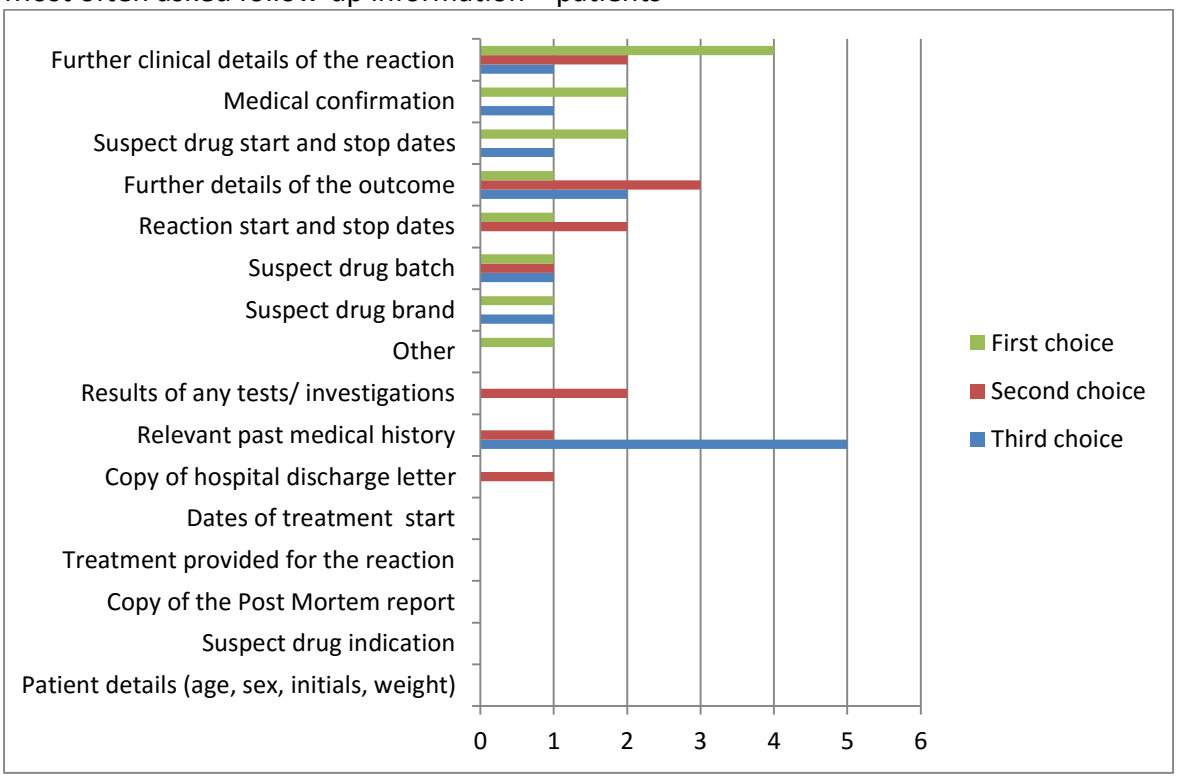
This question was exploring the type of follow up information which is most often requested for two specific reporter groups (HCPs and patients). 26 MSs provided information on the type of follow up information requested from HCPs and 24 MSs provided information for the patients.

Because of the difficulties with the interpretation of question, only MSs which provided data solely for three choices in the required order (1st, 2nd and 3rd choice) per reporter group were analysed: responses from 12 MSs for HCP reports and from 12 MSs for patient reports. The data are presented below.

Most often asked follow-up information - HCPs

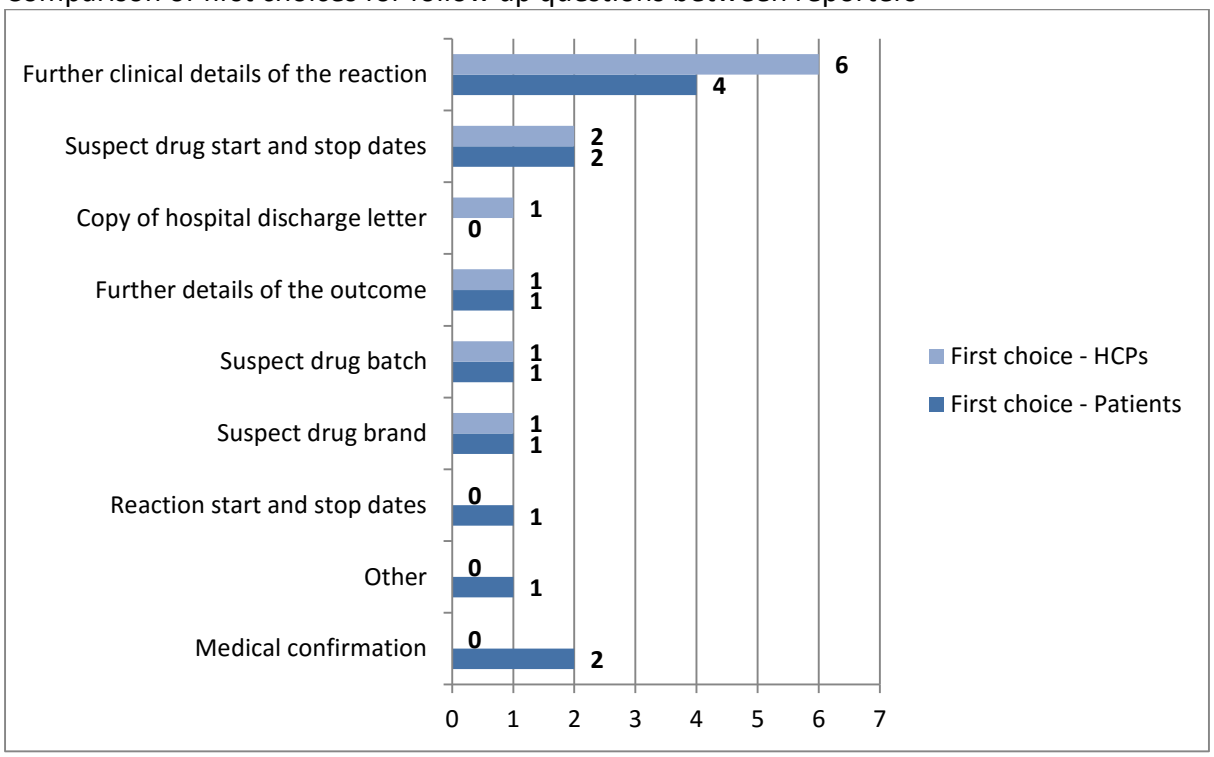


Most often asked follow-up information – patients



Although patient reports are complimentary to HCP reports and don't need additional medical confirmation, it is interesting to notice that one of the first choices chosen by MSs was "Medical confirmation".

Comparison of first choices for follow up questions between reporters



Question T1Q69: Benchmarking tools of assessing quality of the reports

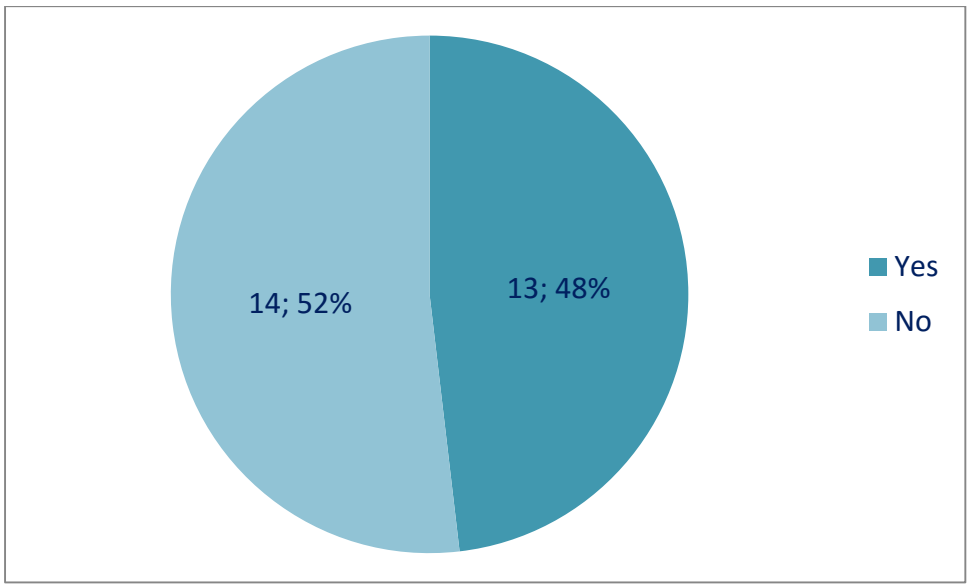
The purpose of this section is to find out what indicators/metrics for assessing quality of the reports are used.

Question T1Q70: Do you use any indicators/metrics for assessing quality of the reports?

- ❍ Yes
- ❍ No
- ❍ Our institution is not responsible for this activity

Twenty seven (27) MSs provided answers to this question. 13 MSs reported that they use indicators/metrics for assessing quality of reports, while 14 MSs does not use indicators/metrics.

Using indicators/metrics for assessing quality of the reports

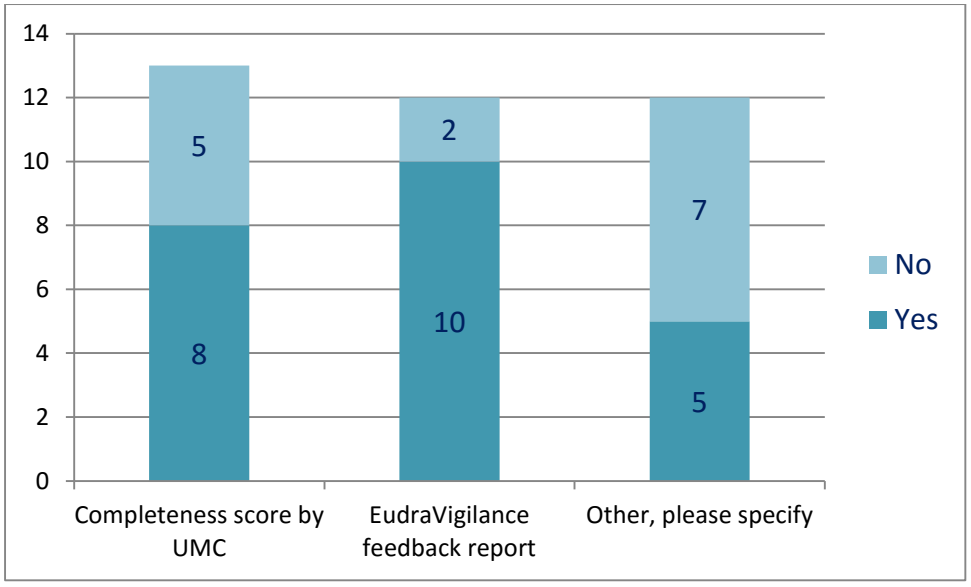


Question T1Q71: Please specify the indicators/metrics for assessing quality of the reports you use.

	Yes	No
Completeness score by Uppsala monitoring Centre (UMC)*		
EudraVigilance feedback report		
Other, please specify		
Our institution is not responsible for this activity		

(*Completeness is a quantitative measure describing the amount of information present in an ICSR. Uppsala Reports 54 (UR54, July 2011, available here)

Thirteen (13) MSs provided answer to this question. All 13 MSs provided the information about using UMC completeness score: 8 MSs use UMC completeness score, while 5 MSs do not use this indicator. 12 MSs provided the information about using EudraVigilance feedback report: 10 MSs use EV feedback report, while 2 MSs do not use this indicator. In total, 6 MSs use both UMC completeness score and EV feedback report as indicators/metrics for assessing quality of the reports. Additionally, 5 MSs reported that they use other indicators/metrics, while 7 MSs do not use additional indicators/metrics. Additional indicators/metrics used by the MS that provided this answer included internally identified indicators that are included in SOPs and regular compliance checks/quality audits.



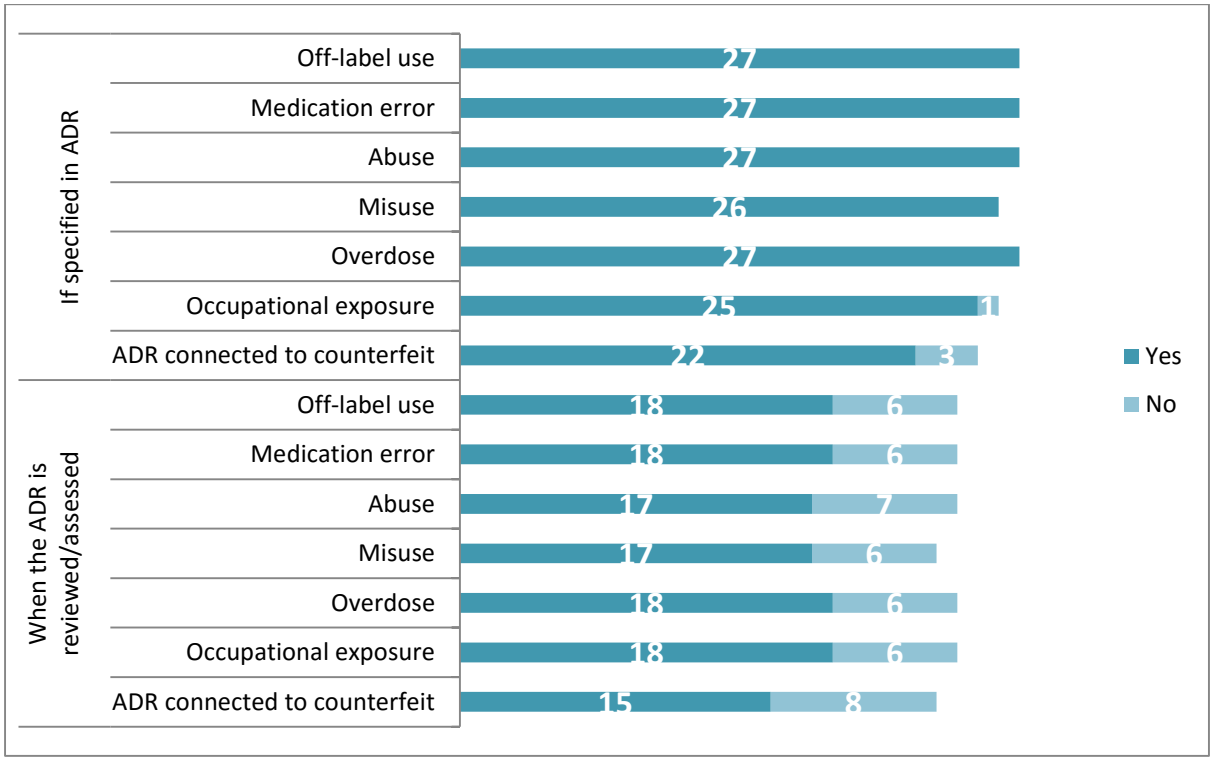
T1Q72 When do you code the following?

	If specified in ADR		When the ADR is reviewed/assessed	
	Yes	No	Yes	No
Off-label use				
Medication error				
Abuse				
Misuse				
Overdose				
Occupational exposure				
ADR connected to counterfeit				
Our institution is not responsible for this activity				

Twenty seven (27) MSs provided answers to the part of the question about the coding of special situations if specified in ADR report, while 24 MSs provided answers to the part of the question about the coding of special situations when the ADR is reviewed /assessed.
If specified in ADR report, all MSs who responded to this question code off-label use, medication errors, abuse, misuse (1 MS did not provide answer to this part of the question) and overdose. If specified in ADR report, 25 MSs (96,2%) code occupational exposure, while 1 MS (3,8%) does not (1 MS did not answer this part of the question). Somewhat lower rates are seen with coding of ADR connected to counterfeit, if specified in ADR: 22 MSs (88%) (are coding this special situation, while 3 MSs (12%) are not (2 MSs did not answer this part of the question).
When the ADR is reviewed, 18 MSs (75%) are coding off-label use, medication errors and overdose, while 6 MSs (25%) are not. Abuse is coded when the ADR report is reviewed in 17 MSs (70,8%), while in 7 MSs (29,2%) it is not coded. Misuse is coded when the ADR report is

reviewed in 17 MSs (73,9%), while in 6 MSs (26,1%) it is not coded; 1 MS did not answer this part of the question. 18 MSs (75%) are coding occupational exposure when the report is assessed, while 6 MSs (25%) are not. ADRs connected to counterfeit are being coded when the report is assessed in 15 MSs (65,2%), while in 8 MSs (34,8%) these special situations are not being coded; 1 MS did not provide answer to this part of the question.

MSs seem to be less inclined to code the above mentioned special situations when the ADR report is reviewed / assessed, compared to when these situations are specified in the report. Different approaches that MSs take with regards to this issue is probably in relation to the basic pharmacovigilance principle “do not infer an ADR” on one side and the striving to fulfil the requirements laid down by 2010 pharmacovigilance legislation with regards to these special situations on the other side. The observed differences in the approaches underpin the need for development of EU-wide guidelines for reporting and coding of ADRs arising from off-label use, medication errors, abuse, misuse, overdose, occupational exposure and for ADRs connected to counterfeit medicines.



Question T1Q73: Additional monitoring

This section is focusing on how MSs identify ADR reports associated with drugs on additional monitoring list in their databases and if there is any difference in managing ADRs where suspect drugs are included in the EU additional monitoring list to those which are not included into this list.

Question T1Q74: How do you identify ADR reports in your database which are subject to additional monitoring?

	Yes	No
Using a database flag at ADR report level	❍	❍
Using a database flag combined with reference data/drug dictionary level	❍	❍
Manually	❍	❍
Other, please specify	❍	❍
We do not identify ADR reports in our database which are subject to additional monitoring	❍	❍
Our institution is not responsible for this activity	❍	❍

Question T1Q75: Is there any difference in how ADRs are managed where suspect drugs are included on the EU additional monitoring list to those which are not included on the list?

❍ Yes, please specify _____

❍ No

❍ Our institution is not responsible for this activity

Question T1Q76: What % of ADR reports received in the period October-December 2013 included a drug on the additional monitoring list?

❍ % _____

❍ Data not available

❍ Not implemented yet

❍ Our institution is not responsible for this activity

Question T1Q77: Please provide information on % of ADR reports which included drug on the additional monitoring list in other/longer period, if available (optional).

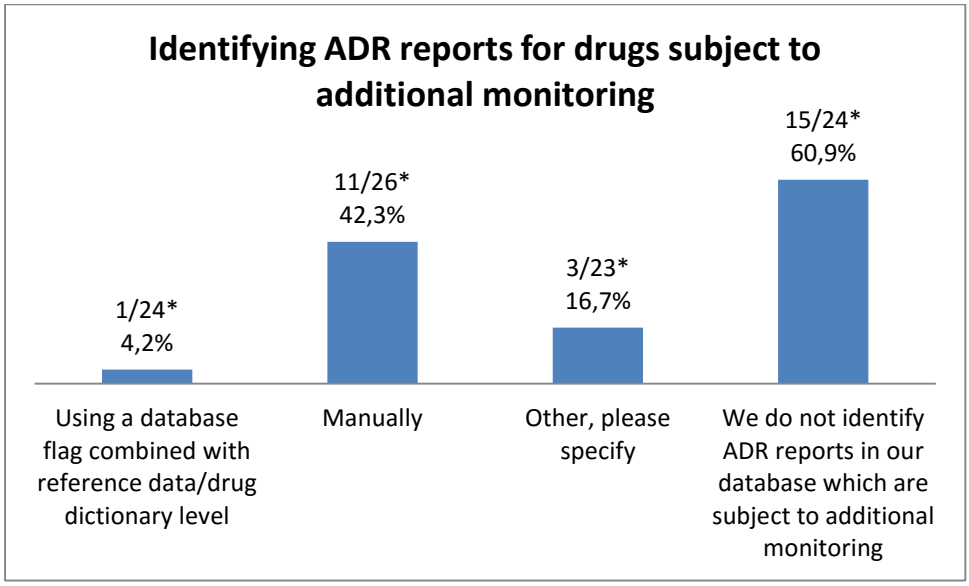
- ❑ Period (MM/YYYY-MM/YYYY) _____
- ❑ % of ADR reports including drug on the additional monitoring list _____
- ❑ Data not available
- ❑ Our institution is not responsible for this activity

Almost 60% (15/26) of the MSs **do not identify** ADR reports for drugs **subject to additional** monitoring in their databases.
The ones that do it, usually do it manually (11/26). None of the MSs is identifying ADR reports by using a database flag at ADR report level (response rate 24 MSs) and only one MS is able to identify ADR reports subject to additional monitoring by using a database flag combined with reference data/drug dictionary level.

4 MSs chose "other" as an answer to the question on the practice regarding identification of ADRs for drugs on additional monitoring. The answers were following:

- check from the registry
- internal additional monitoring for national suspected ADR issues
- we do not specify ADR reports in our database which are subject to additional monitoring– during the analysis reclassified as positive answer *"We do not identify ADR reports in our database which are subject to additional monitoring"*
- with our drug database

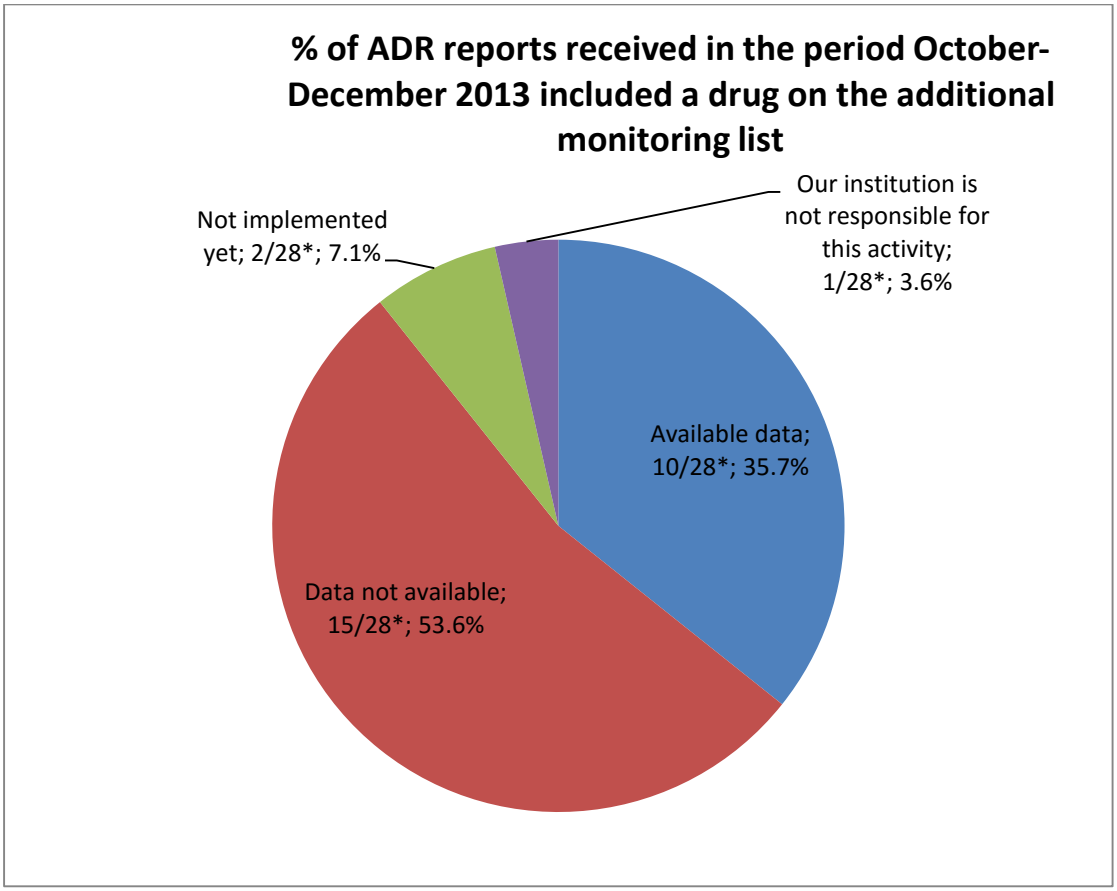
but they don't change the overall impression that throughout the EU **there is few or no MSs** which implemented technical solutions for tracking drugs subject to additional monitoring.



*number of respondents

This is probably the reason why more than 50% (15/28) of MSs were not able to provide answer to T1Q76 on % of ADR reports which include drugs on the additional monitoring list

received in the period October-December 2013. The ones that were able to provide the answer to this question indicated that between 0.5 and 13 % of the ADRs received in period October-December 2013 accounted for the drugs on additional monitoring.

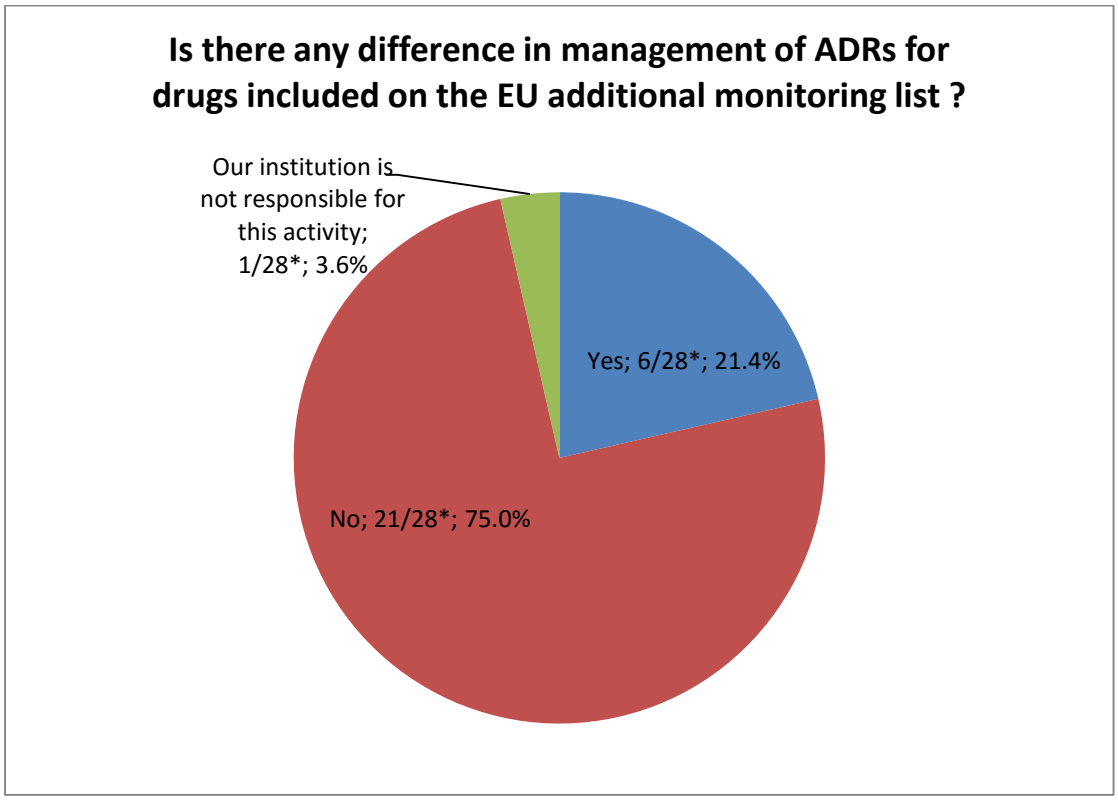


*number of respondents

Even less MSs (6/28) were able to provide information on ADR reports which included drugs on the additional monitoring list in other/longer period than October-December 2013.
6 MSs provided data on % of ADRs for drugs on additional monitoring for time period other that October-December 2013. They all provided data on period longer than 3 months (from 6 months up to 6 years) with the % of ADRs for drug on additional monitoring list ranging from 0 to 17 %.

Time period	% of ADRs for drugs which are subject to additional monitoring	Method for identifying ADR reports which are subject to additional monitoring
01/2008-12/2013	4%	Manually
01/2013-09/2013	2,6 %	?
01/2013-12/2013	1,6 %	Manually
01/2014-06/2014	Data not provided	„With our drug database“
01/2014-06/2014	17%	Manually
10/2013-06/2014	11%	Manually

Regarding the difference in ADR management where suspect drugs are included on the EU additional monitoring list, 75% MSs doesn't make difference between management of ADRs for drugs on additional monitoring list and ADRs for drugs that are not. This difference reflects in different prioritisation of ADRs for drugs on additional monitoring list, or assigning the cases to the more experienced assessors.



*number of respondents

Question T1Q78: Traceability of biologics

The aim of this section is to learn if MSs have implemented any useful methodology which improves the information collected on biologics. It is also focusing on brand and batch capturing for biologics and vaccines.

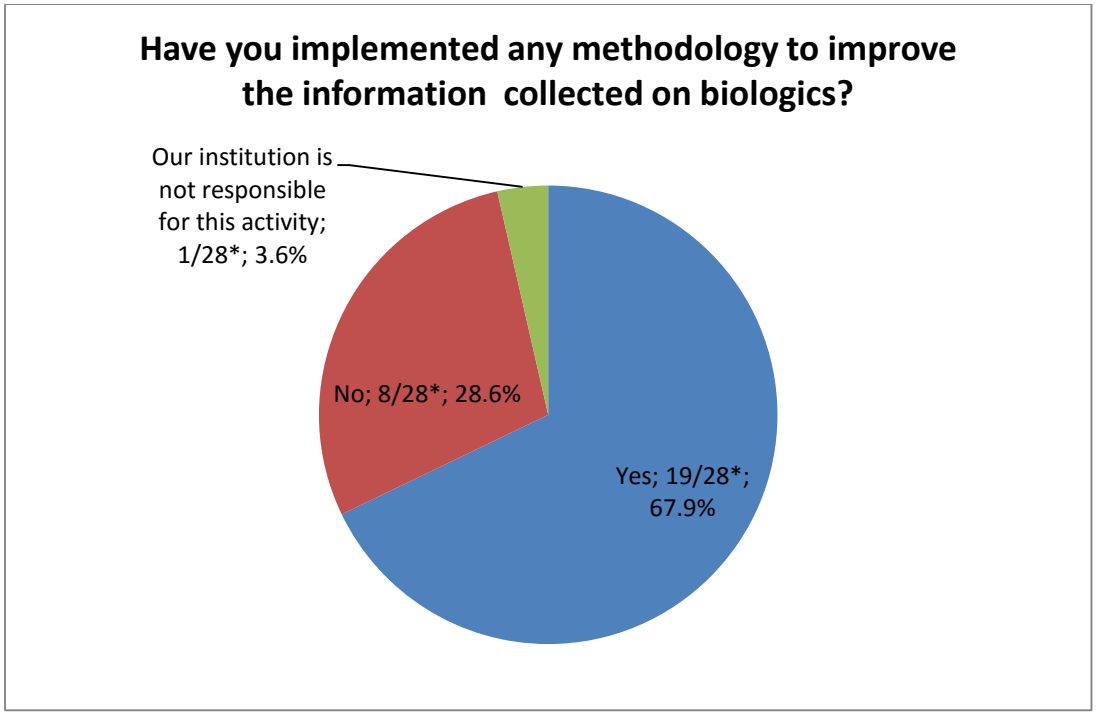
Question T1Q79: Have you implemented any methodology to improve the information collected on biologics?

- ❍ Yes, please describe: _____
- ❍ No
- ❍ Our institution is not responsible for this activity

Question T1Q80: Do you systematically capture brand and batch for biologics and vaccines?

	Biologics - batch		Biologics - brand		Vaccines - batch		Vaccines - brand		Our institution is not responsible for this activity
	Yes	No	Yes	No	Yes	No	Yes	No	Please tick if applicable
Only when provided in a report	❍	❍	❍	❍	❍	❍	❍	❍	❑
If missing from the form, always followed up	❍	❍	❍	❍	❍	❍	❍	❍	❑
If missing from the form, sometimes followed up, based on the assessment	❍	❍	❍	❍	❍	❍	❍	❍	❑
We do not systematically capture	❍	❍	❍	❍	❍	❍	❍	❍	❑
Other, please specify	❍	❍	❍	❍	❍	❍	❍	❍	❑

Twenty eight (28) MSs provided answer to this question – One (1) MS is not responsible for handling biologics.



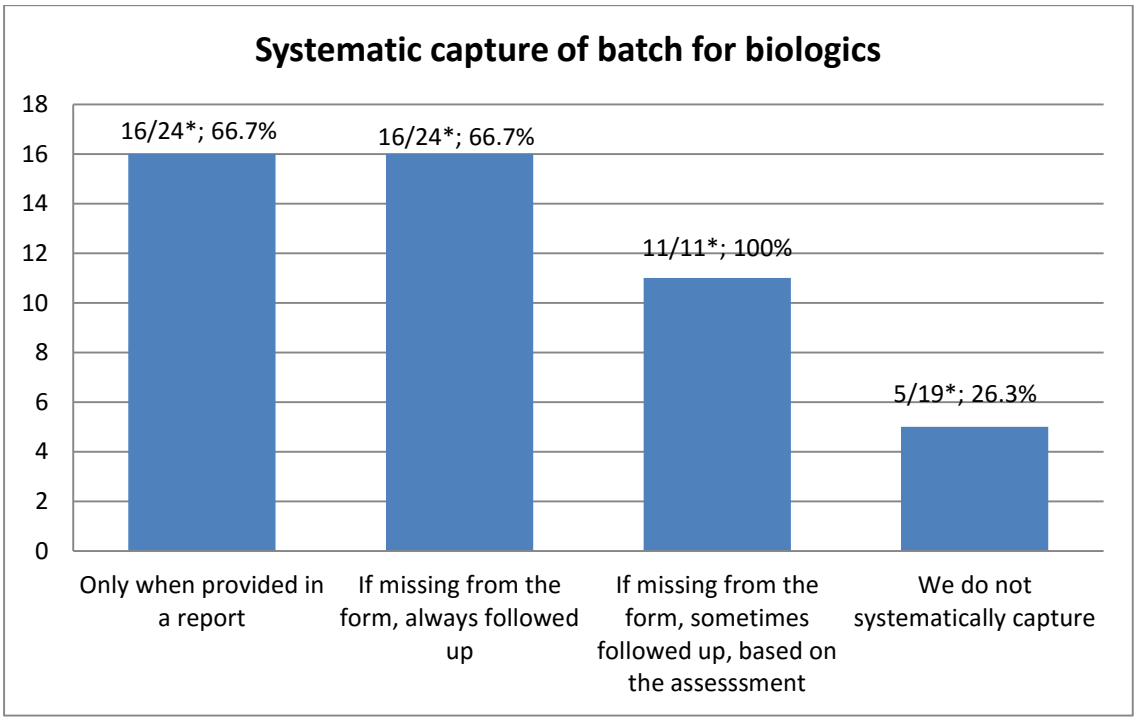
*number of respondents

Nineteen (19) MSs stated that they have implemented methodology for improving the information collected on biologics. Answers can broadly be attributed in three categories:

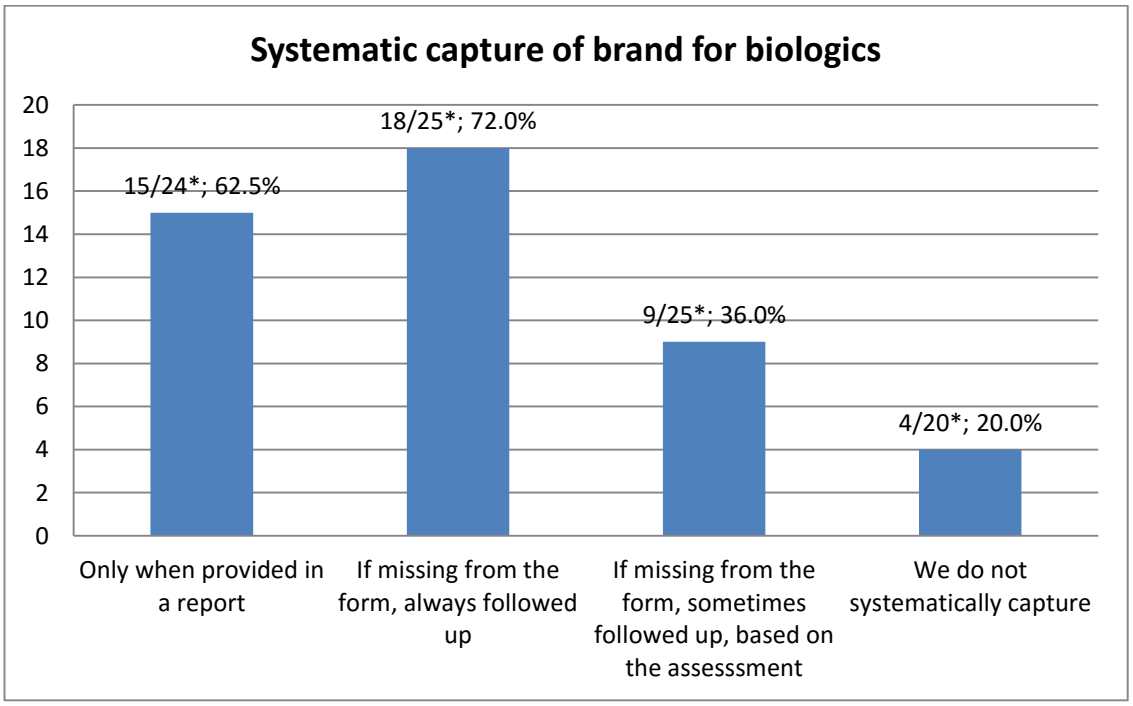
- Provision of brand/batch specific field in ADR reporting form
- Defined procedure for follow-up request in case brand and batch data are not provided
- Technical solution for prompting for brand/batch number in case ADR for vaccine/biologic is being reported

Regarding the systematic capturing brand and batch for vaccines and biologics the results are following:

- Biologics:

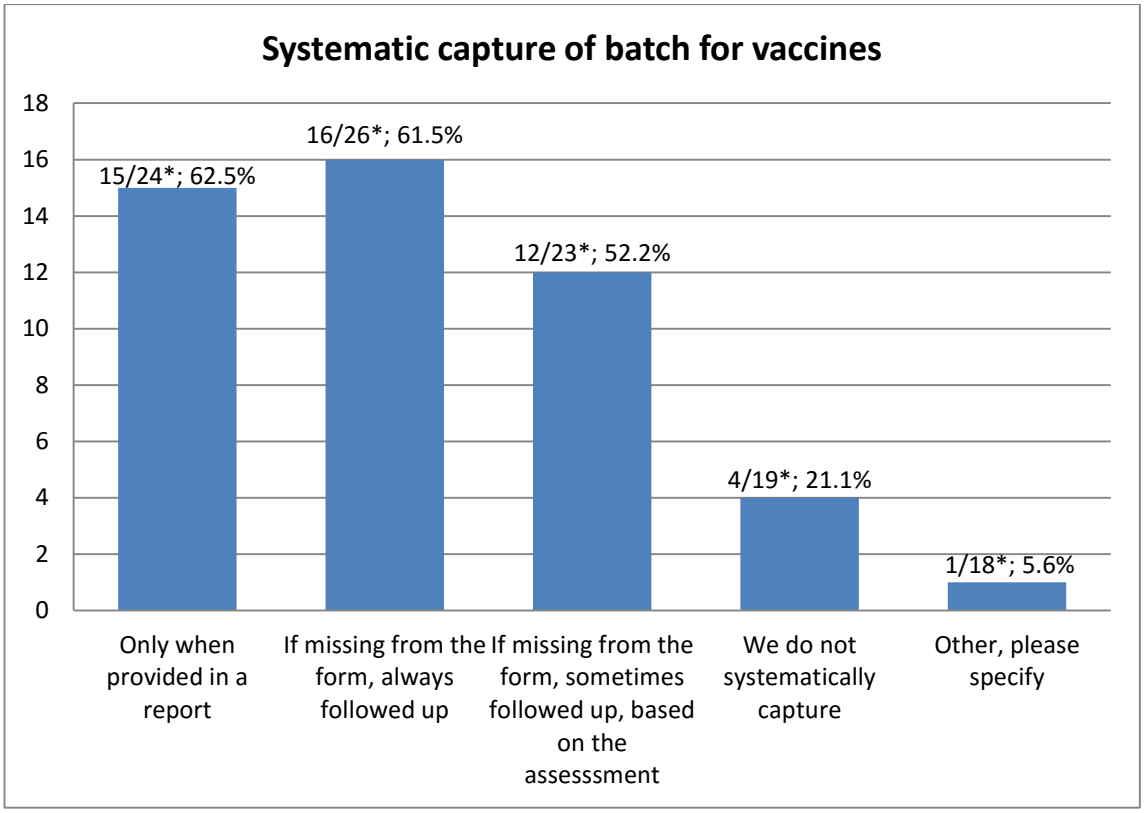


*number of respondents

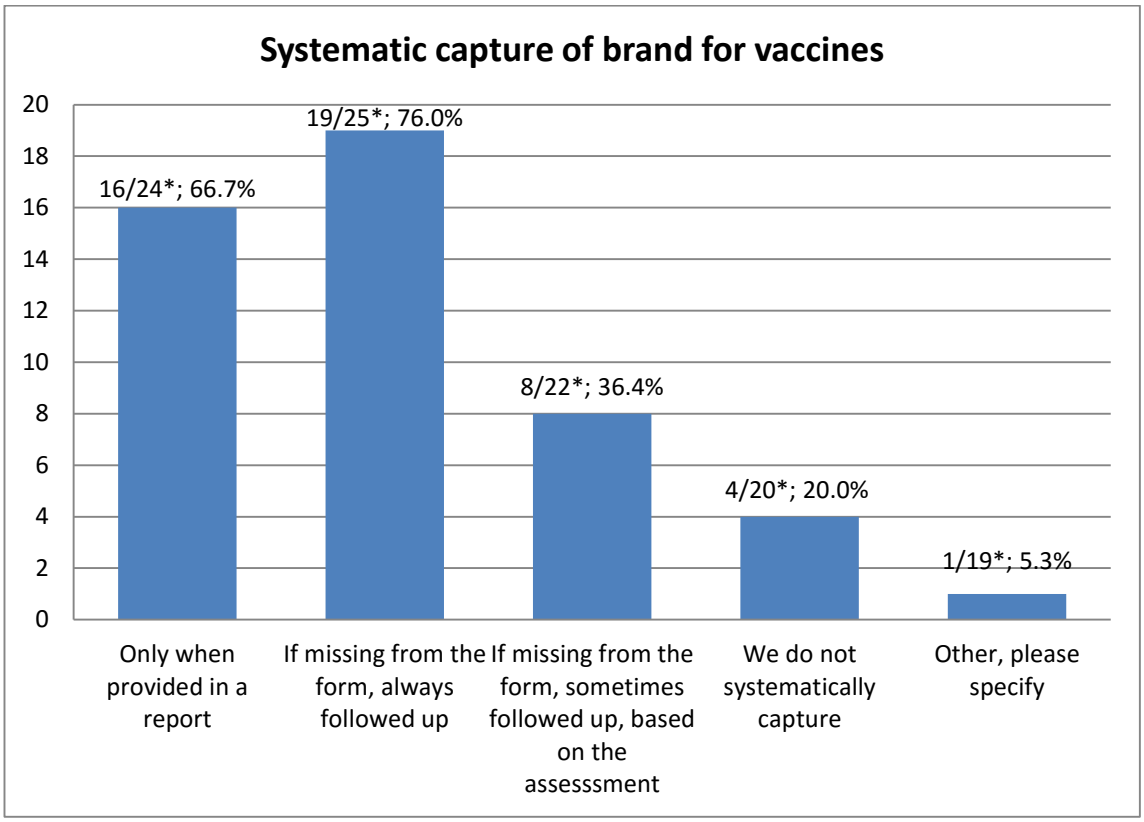


*number of respondents

- Vaccines:



*number of respondents



*number of respondents

Analysis of the results showed that around 20% (5/19 for biologics batch, 4/20 for biologics brand, 4/19 for vaccine batch, 4/20 for vaccines brand) of MSs answered that they do not systematically collect data on brand and batch of the biologics and vaccines. This is not in line with legal requirement in EU so it should be cleared what are the reasons for this results.

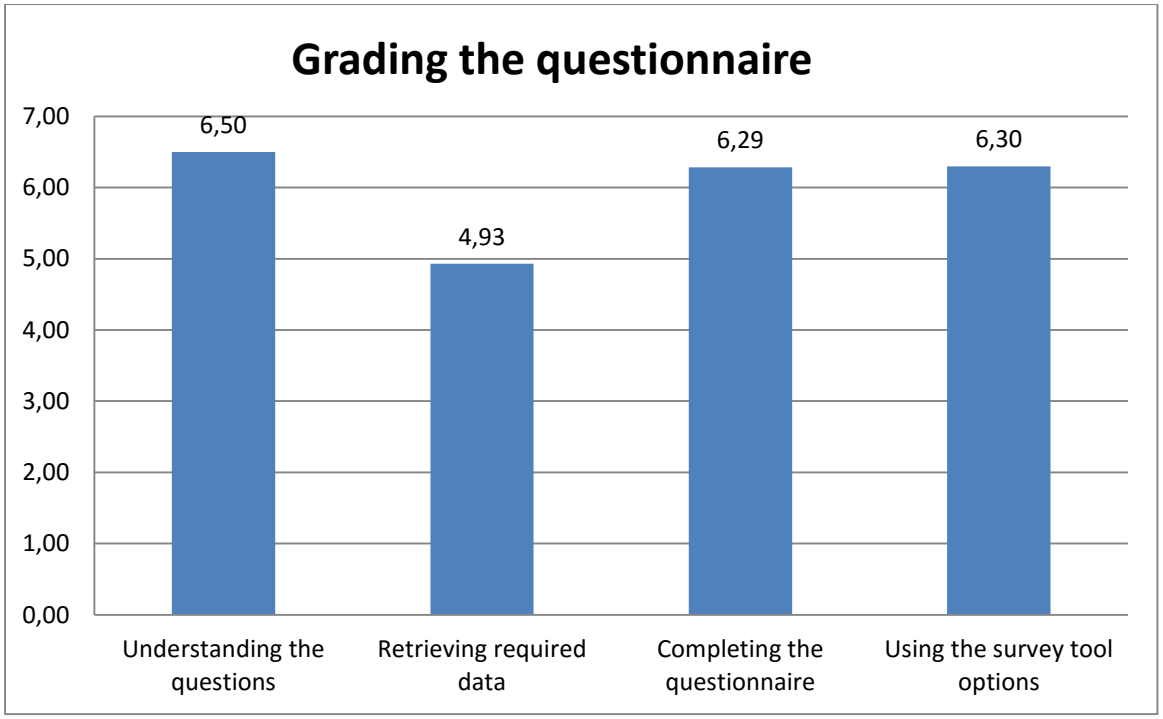
Only one MS chose answer "*Other, please specify*", both for systematic capture of batch and brand for vaccines providing an explanation that they can see vaccines batch number through the vaccine registry. This should be considered in interpretation of their previous answer on collecting data on brand and batch of the vaccines.
Over 60% of the MSs answered that they collect data of brand and batch for vaccines and biologicals **only** when it is provided in the report. However, rather large percentage of countries (between 61 and 76%) indicated that they always follow up brand and batch data if missing from the report. This discrepancy in data maybe can be attributed to somewhat ambiguous phrasing of questions – we believe most MSs collect brand and batch data if it is provided in the report and then different percentage of MSs follow-up **all cases** and some of the countries follow up cases **based on the assessment**.
Regarding the patterns between vaccines and biologics no significant differences have been noted other that somewhat higher percent of MSs always follow-up for brand name for vaccines than biologics (72 vs. 76 %).

T1Q81: l) Summing up

Question T1Q82: Please write down any additional comments you would like to share with regard to your national reporting system.

Twelve (12) MSs provided some additional comments regarding their national reporting system. Some of the comments provided additional information related to specific question and were very helpful for interpretation of the specific answer. Some comments referred to the survey itself stating that it would be great to have an option to save (pdf) and print completed questionnaire before sending- for checking and for filing. Furthermore, it was mentioned that comment boxes after each question would be useful.

Question T1Q83: Finally, we would like to kindly ask you to grade this questionnaire.
_____ Understanding the questions
_____ Retrieving required data
_____ Using the survey tool options
_____ Completing the questionnaire



The questionnaire was graded with a mean of six out of ten for understanding the questions, retrieving required data, completing the questionnaire and using the survey tool options.

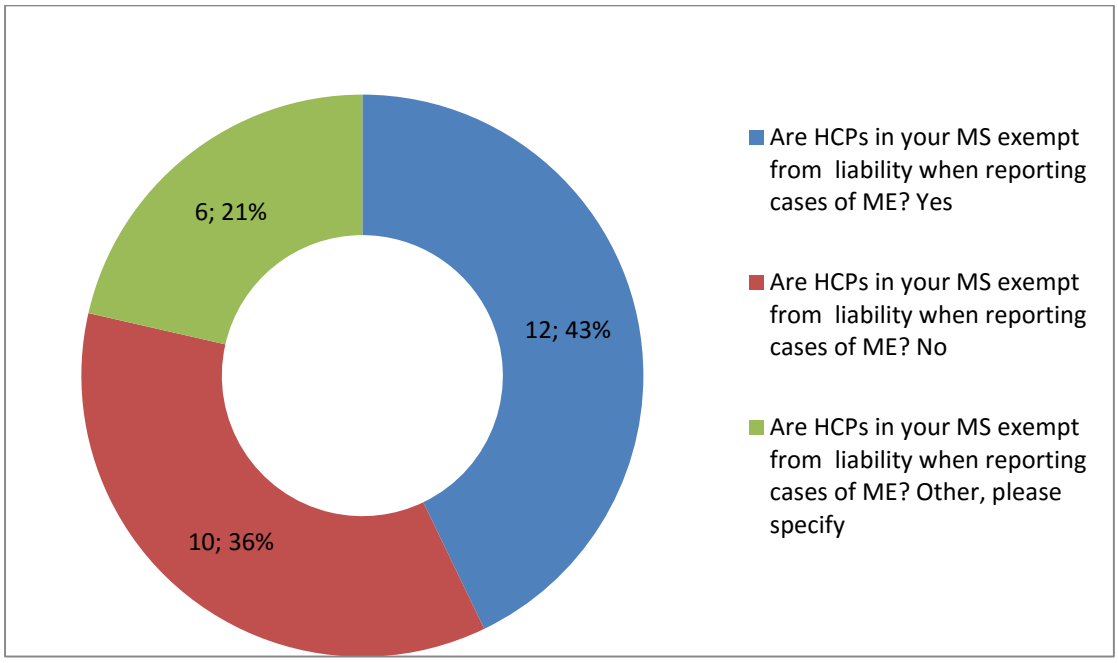
T1Q84 Please check if you have answered all questions. You can use "back button" to go through the survey and make sure everything is filled in before submitting.
Please note that choosing "next button" is going to automatically submit the questionnaire. Thank you!

Question 84 was not a question but thanked respondents for completing the questionnaire and allowed the questionnaire to be submitted.

3.2 Topic 1a: Medication errors

Question T1aQ3 Are HCPs in your MS exempt from liability when reporting cases of ME?

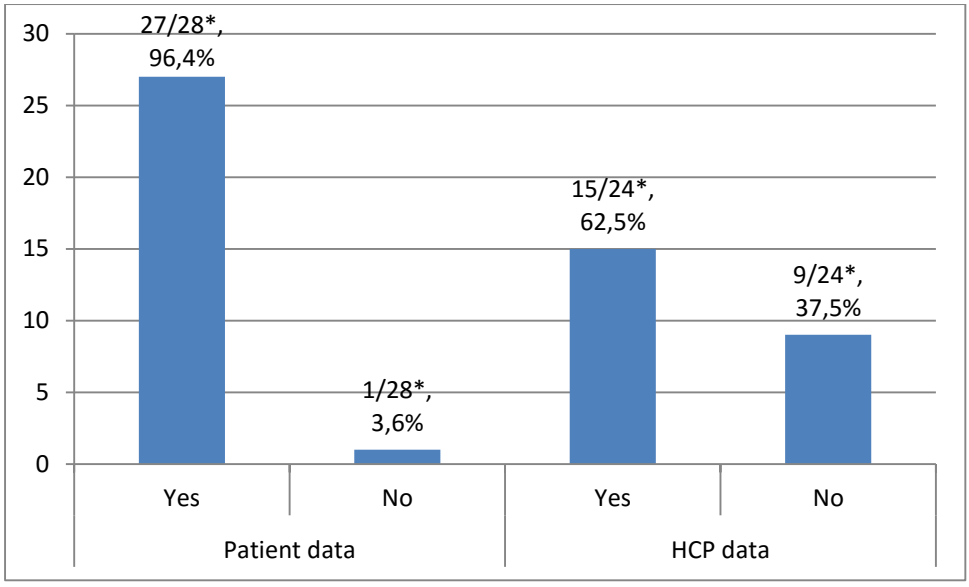
- ❍ Yes
- ❍ No
- ❍ Other, please specify _____



28 MSs responded to this question. 12 MSs reported that they have system in place which makes exemption from liability for HCPs when reporting cases of ME, 10 MSs don't make any exemption from liability for HCPs and 6 MSs provided more detailed answer which indicates that question itself wasn't clear enough.

Question T1aQ4 Are there data privacy requirements at national level in your MS?

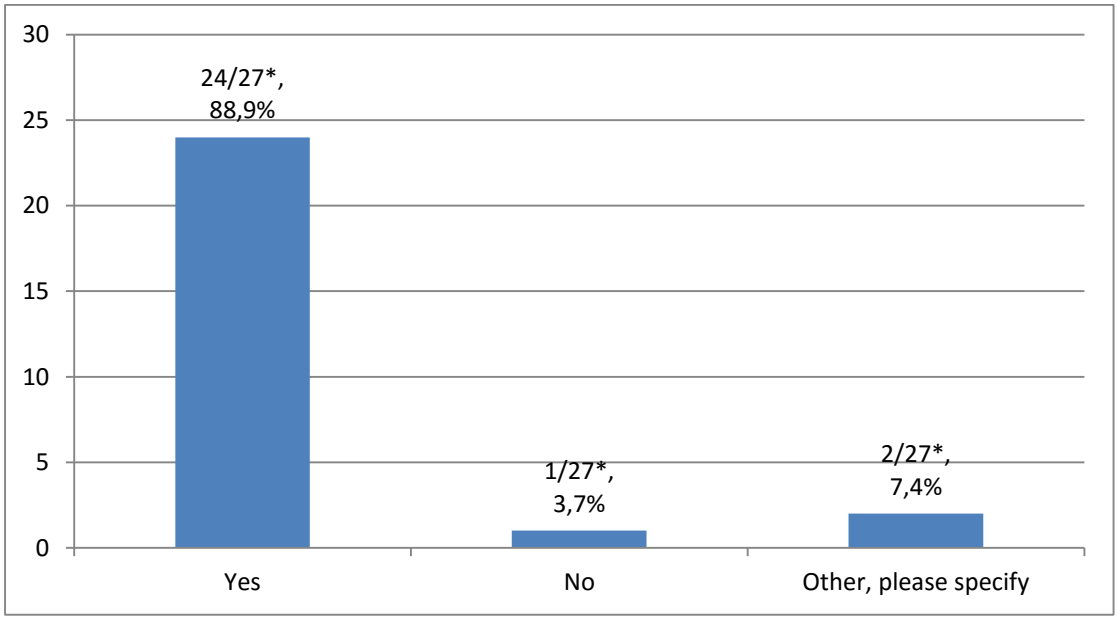
	Patient data	HCP data
Yes	❍	❍
No	❍	❍



27 MSs reported that there are data privacy requirements with regard to patient data and just one MS indicated that there are no such requirements on national level. In regard to HCP data, 24 MSs provided their response: 15 indicated that there are data privacy requirements at national level and 9 that there are no such requirements at national level.

Question T1aQ5 Are those requirements compliant with EU data protection laws in reporting systems?

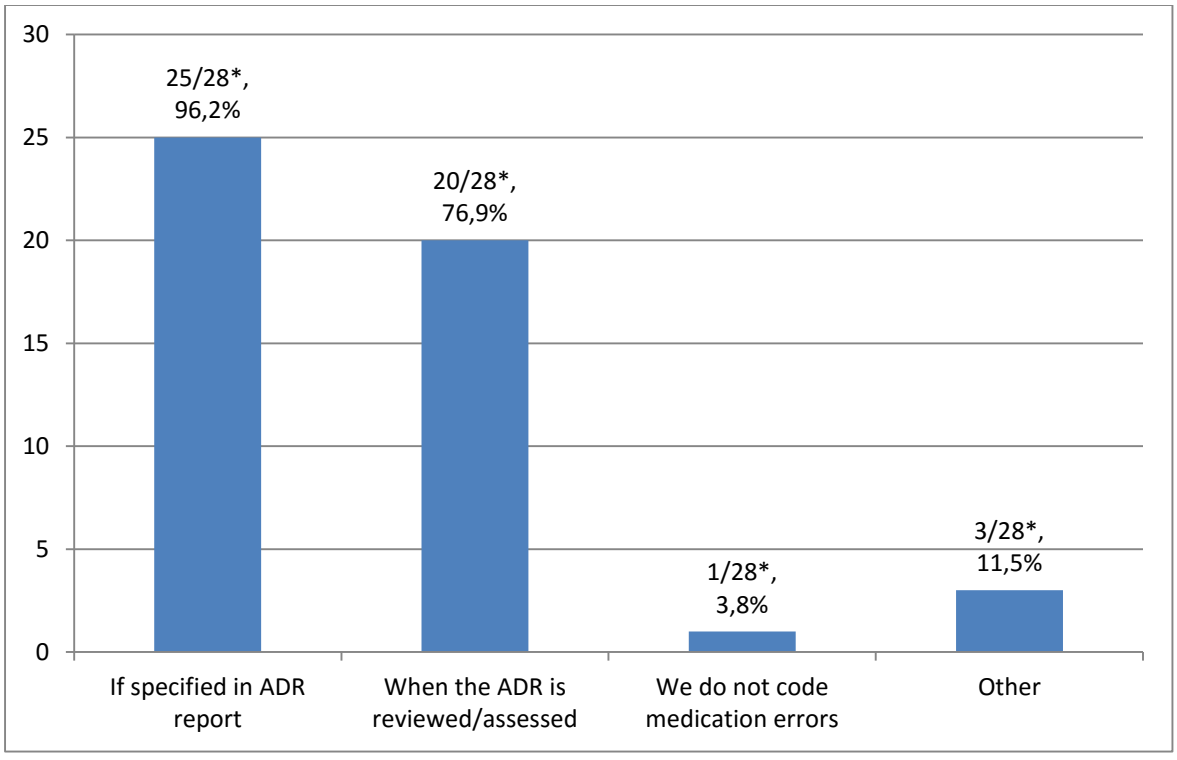
- ❍ Yes
- ❍ No
- ❍ Other, please specify _____



Out of 27 responses received to this question, most of them indicated that national legislation is compliant with EU data protection laws and just one MS indicated that their national data privacy requirements are not compliant with EU data protection laws.

Question T1aQ6 When do you code medication errors?

	Yes	No
If specified in ADR report	❍	❍
When the ADR is reviewed/assessed	❍	❍
We do not code medication errors	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

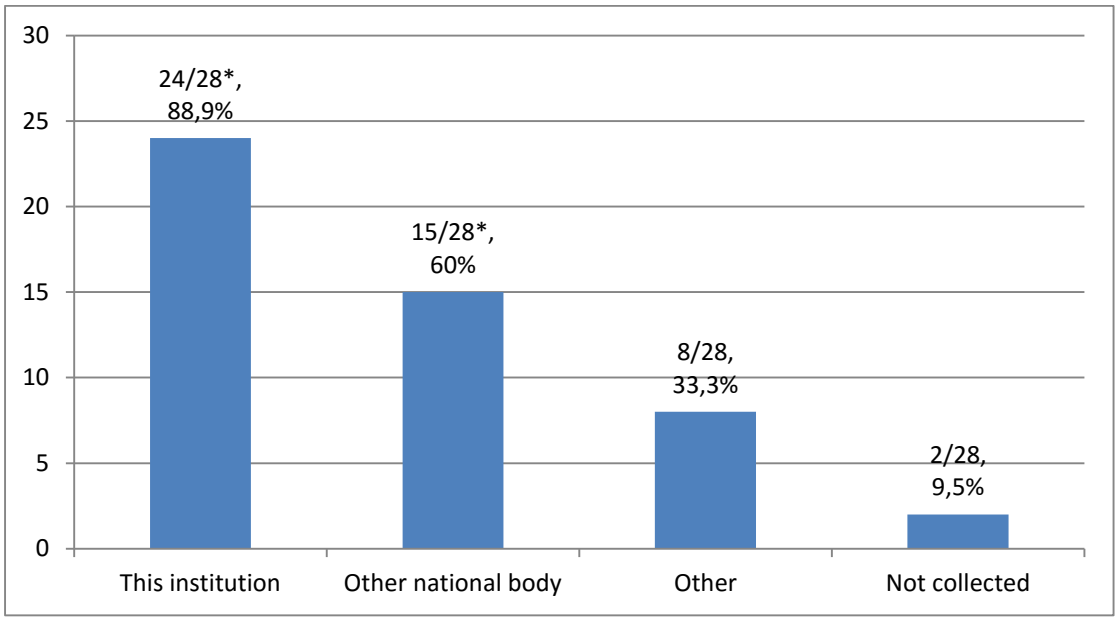


28 MSs responded to this question. MSs could give a positive answer to more than one option. 18 MSs indicated that they are both coding medication errors if specified in ADR report and when the ADR is reviewed/assessed. In addition 2 MSs stated that they are just coding when the ADR is reviewed/assessed (20 in total) and 7 MSs stated they are just

coding when ADR is specified in the report (25 in total). One MS stated that they don't code medication errors and 3 MSs provided some other answer.

Question T1aQ7 Who collects data about medication errors in you MS?

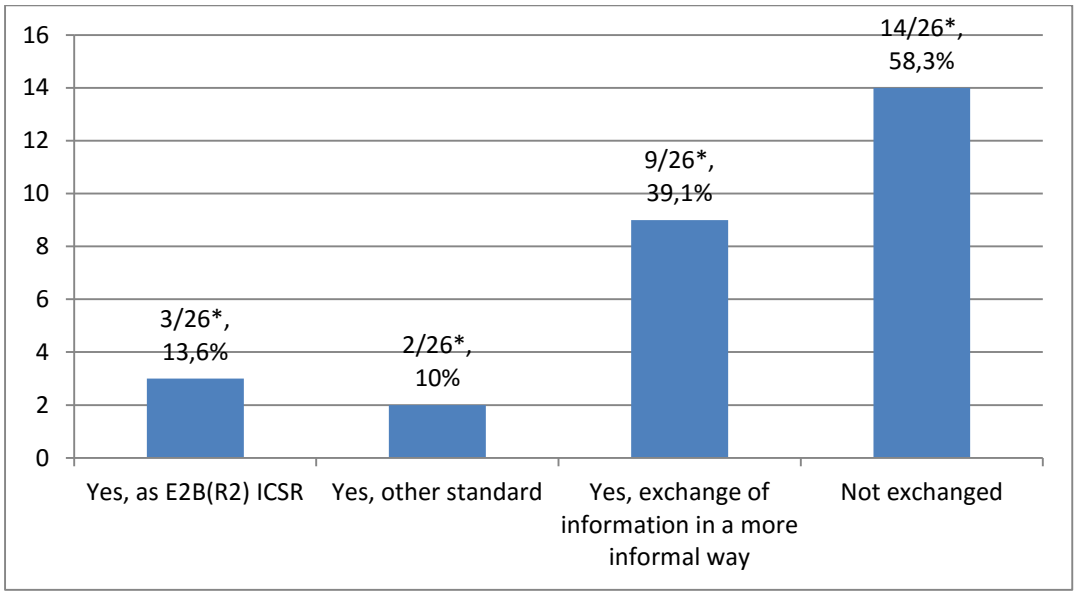
	Yes	No
This institution	❍	❍
Other national body, please specify	❍	❍
Other, please specify	❍	❍
Not collected	❍	❍



All 28 MSs selected at least one option in this question. In 24 MSs, institution which populated this survey (NCA in most MSs) is responsible for collection of medication errors, in 15 MSs there is some other institution responsible for collection of medication errors besides NCA. In 8 MSs some other organisation is responsible for collection of ME (a professional organisations, Health General Directorate, Regional programmes, Physicians Chamber, Pharmaceutical Chamber, Nurses Chamber, Poisoning Centres, regional pharmacovigilance centres, Regional Health Agencies, some hospitals may do this in relation to quality improvement work although rarely systematically).

Question T1aQ8 If resulted in ADR, do you exchange following ADR reports with other institutions or organizations in your MS?

	Yes	No
Yes, as E2B(R2) ICSR	❍	❍
Yes, other standard, please specify	❍	❍
Yes, exchange of information in a more informal way	❍	❍
Not exchanged	❍	❍
Our institution is not responsible for this activity	❍	❍

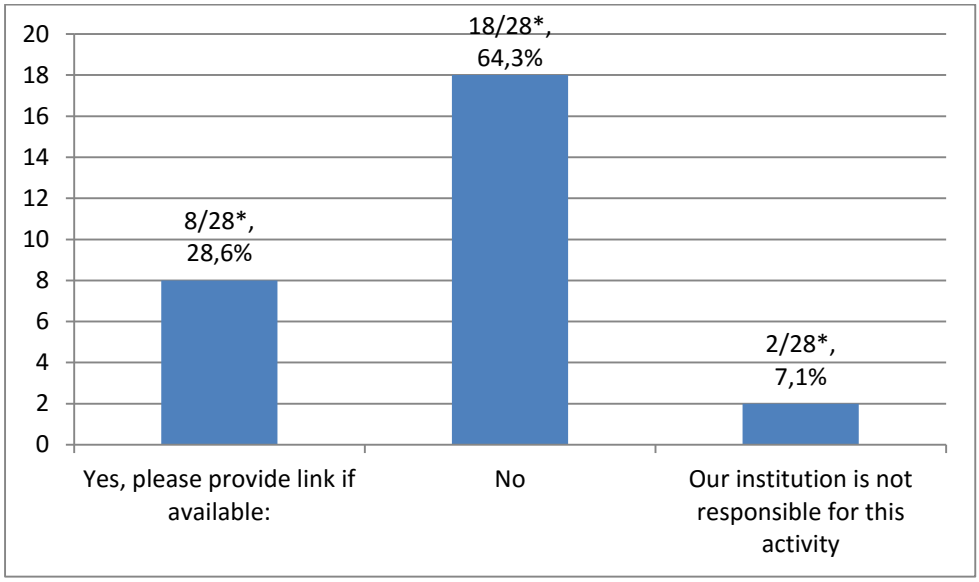


26 MSs provided answer to this question. Only 3 MSs stated that they exchange information of ADRs resulted from ME with other responsible institutions or organisations as E2B (R2) ICSR, 2 MSs as some other standard and 9 MSs exchange information in more informal way.

Unfortunately, 14 MSs do not exchange information with other national institutions about ADR resulting from medication errors. Responses form MSs show clearly that there is a large room for improvement.

Question T1aQ9 Does MS have an operational guideline (SOP) of medication errors to support coding, reporting, analysis and prevention in patient safety (if existing) and pharmacovigilance systems?

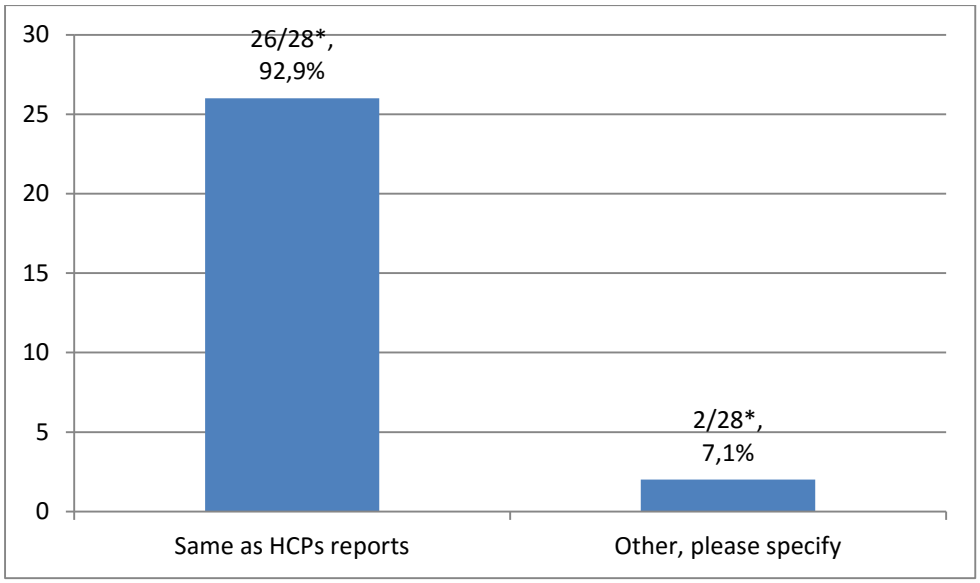
- ❍ Yes, please provide link if available: _____
- ❍ No
- ❍ Our institution is not responsible for this activity



Response rate for this question was 28. 8 MSs stated that they have SOP of medication errors to support coding, reporting, analysis and prevention in patient safety and pharmacovigilance systems, 18 MSs stated that they don't have such SOP and in 2 MSs institution which responded to this survey is not responsible for collecting reports of ME.
Further analysis of responses from MSs who have SOPs, showed that 2 respondents made reference to GVP VI as their SOP and other responses were about internal SOPs.
In general, recommendation could be made for organisations handling reports of ME to develop operational guideline (SOP) of medication errors to support coding, reporting, analysis and prevention in patient safety and pharmacovigilance systems.

Question T1aQ10 How are patient/consumer reports of medication errors handled?

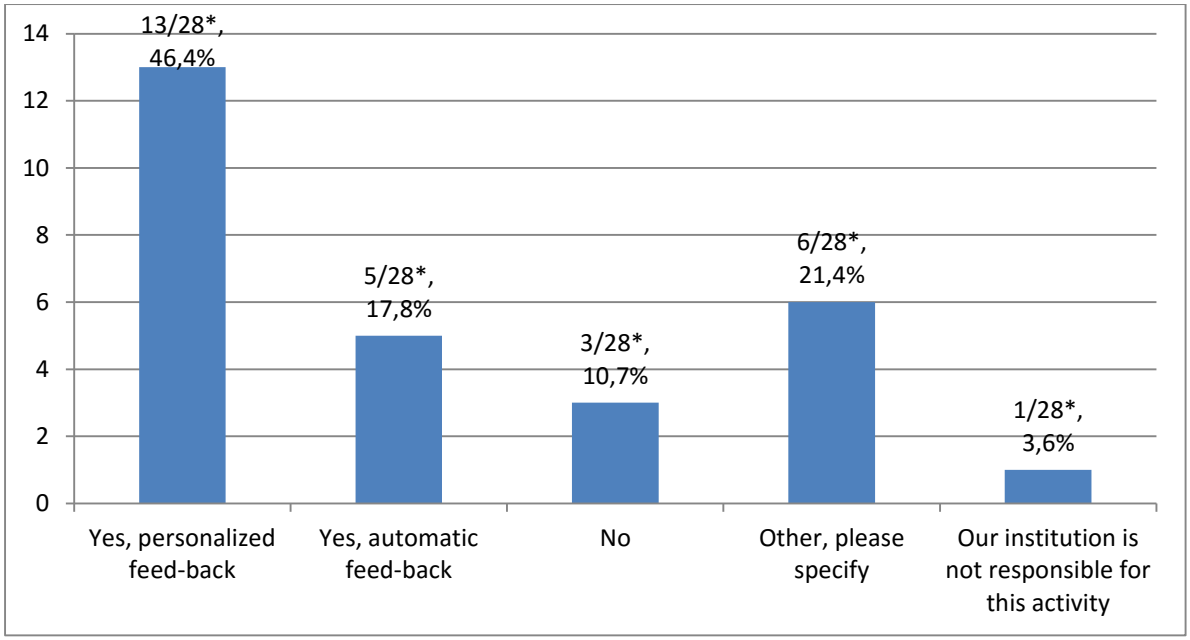
- ❍ Same as HCPs reports
- ❍ Not applicable
- ❍ Other, please specify _____
- ❍ Our institution is not responsible for this activity



All 28 MSs responded to this question. Almost unanimously, responding countries stated that they are handling patient reports of ME same as HCP reports. Just two MSs are handling these reports in different way.

Question T1aQ11 Do MS feed-back to the reporter of ME (encouraging reporting and building trust)?

- ❍ Yes, personalized feed-back
- ❍ Yes, automatic feed-back
- ❍ No
- ❍ Other, please specify _____
- ❍ Our institution is not responsible for this activity



Response rate for this question was 28. Most of respondents (18) stated that they provide some kind of feed-back to reporters of ME, predominantly personalized one (13 out of 18, 5 MSs have automated feed-back). 3 respondents stated that they don't give any feed-back to reporters and 1 stated that their institution is not responsible for collecting reports of ME. Additionally, 6 MSs indicated that they communicate with reporters of ME in some other way.

Question T1aQ12 How do MS communicate risk-management strategies for ME to healthcare providers, patients and caregivers? In your description please include all bodies mentioned in Q6.

Different countries take different approach in communicating risk-management strategies for ME, but some of the most popular methods are:

- Web sites (including dedicated web sites for patients)
- DHPC
- Changes in SPC/PIL/LAB
- Educational materials
- RMMs
- Newsletters/Bulletins
- Alerts/Drug Safety updates/Patient Safety Alerts
- Workshops/congresses/conferences for HCPs
- E-mail notifications
- Through SMS
- Press/Media
- Publications in professional journals

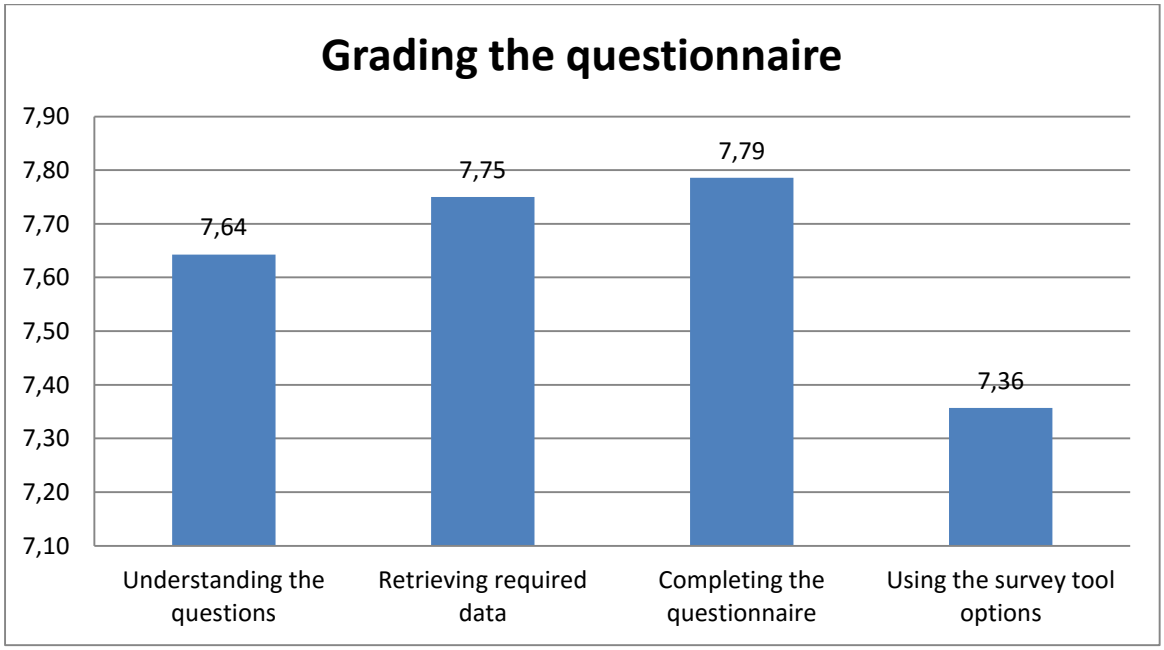
- Through communication with patient safety organisations
- Through communication with professional associations
- Guidelines
- As part of formal education for HCPs

T1aQ13 Summing up

Question T1aQ14 Please write down any additional comments you would like to share with regard to medication errors processing:

19 MSs provided some additional comments with regard to medication errors processing. Most of additional comments referred to collaboration with other institutions responsible for collection of medication errors. Lot of valuable data was provided here, and many problems were stressed out.
Technical problem occurred with question 4 asking are there data privacy requirements at national level. Namely, it was impossible to answer "yes" for both patient and HCP data. 10 MSs provided correct answer to this question here in additional comments box.

Question T1aQ15 Finally, we would like to kindly ask you to grade this questionnaire.
_____ Understanding the questions
_____ Retrieving required data
_____ Using the survey tool options
_____ Completing the questionnaire



The questionnaire was graded with a mean of 7,63 out of ten for understanding the questions, retrieving required data, completing the questionnaire and using the survey tool options.

Question T1aQ16 Please check if you have answered all questions. You can use "back button" to go through the survey and make sure everything is filled in before submitting. Please note that choosing "next button" is going to automatically submit the questionnaire. Thank you!

Question 16 was not a question but thanked respondents for completing the questionnaire and allowed the questionnaire to be submitted.

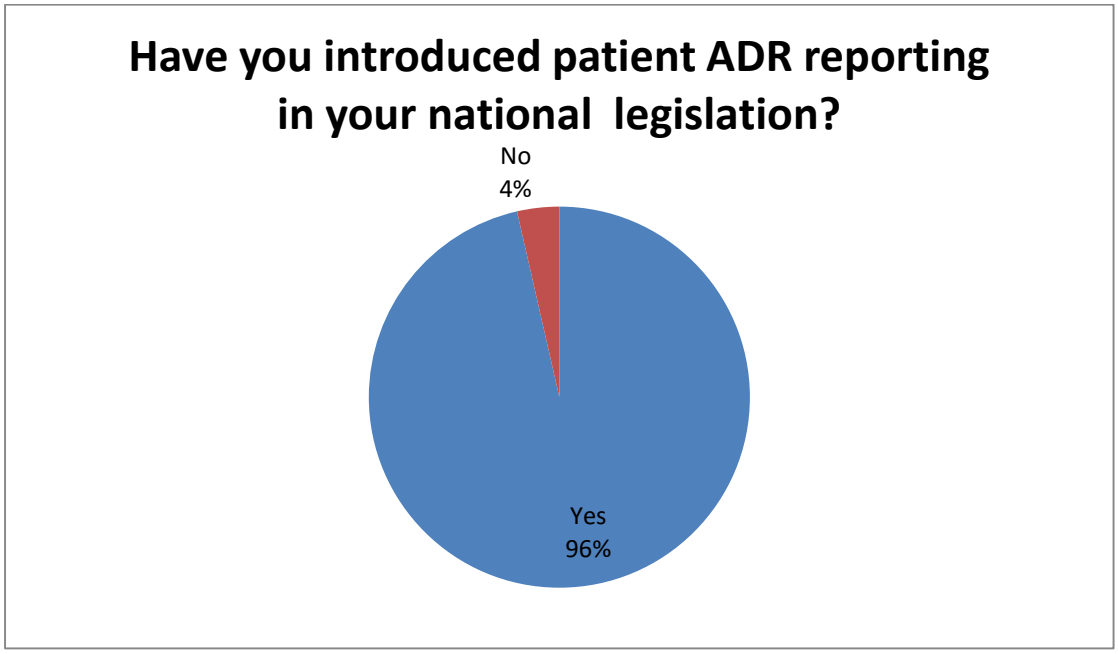
3.3 Topic 2: Patient reporting

T2Q4 This questionnaire refers to spontaneous direct patient adverse drug reaction reports only.

T2Q5 a) General overview

This set of questions is focussing on patient reporting system in each MS, specific legislation status and resources needed for patient reports processing.

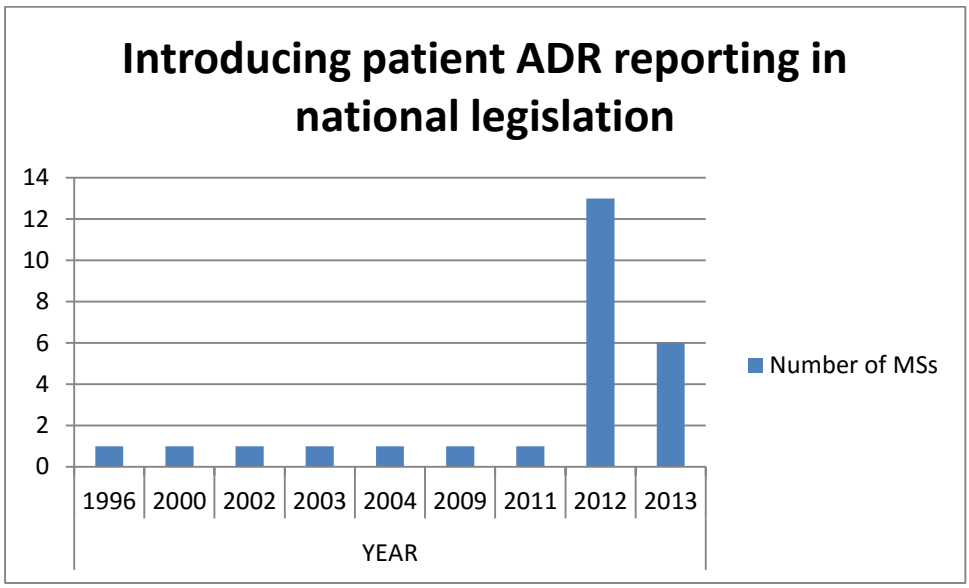
Question T2Q6: Have you introduced patient ADR reporting in your national legislation?



Question T2Q7: If NO, why not?

Only one (1) MS stated that they have not introduced patient ADR reporting in their national legislation with an explanation that it was not considered necessary to describe patient reporting specifically, as it is a part of ADR reporting in general.

Question T2Q8: If YES, when? MM/YYYY



MODE = 2012

Question T2Q9: Do you have legal specificities which are different from provisions of EU Directive on patient reporting (Directive 2010/84/EU)?

		Count	%
Do you have legal specificities which are different from provisions of EU Directive regarding patient reporting (Directive 2010/84/EU)?	No	27	100,0%

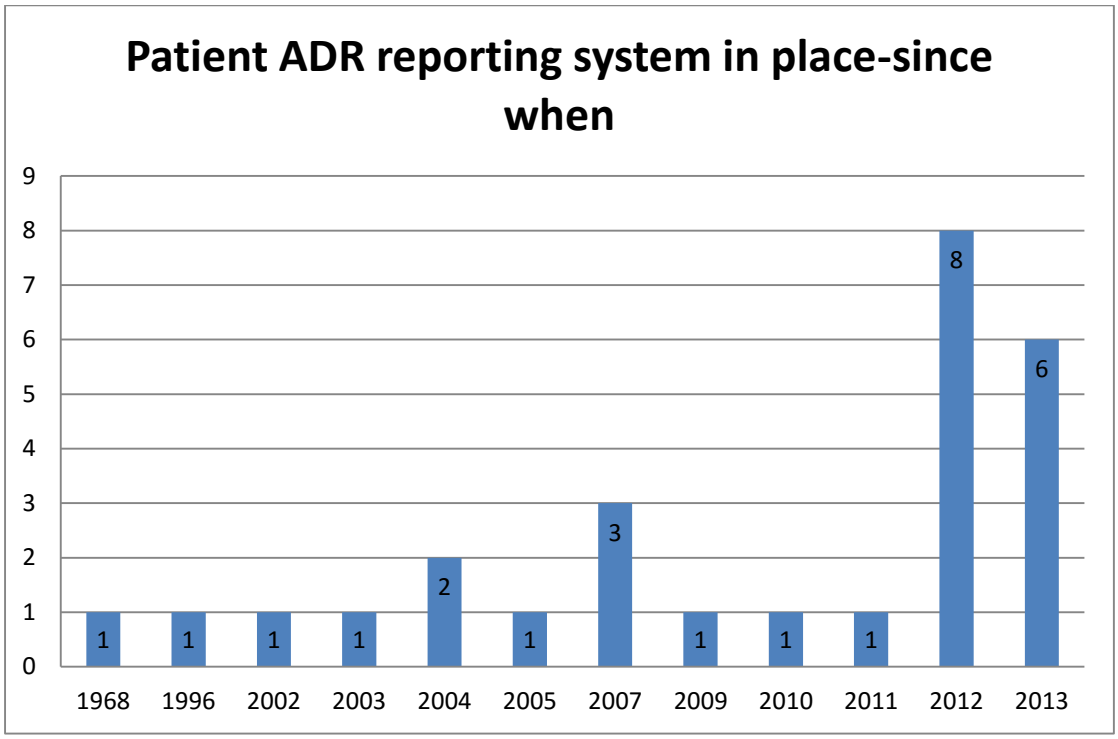
Question T2Q10: If YES, please describe:

No response was received to this question.

Question T2Q11: Is patient ADR reporting system in place in your country?

		Count	col%
Is patient ADR reporting system in place in your country?	Yes	28	100,0%

Question T2Q12: If YES, since when, please specify (YYYY):



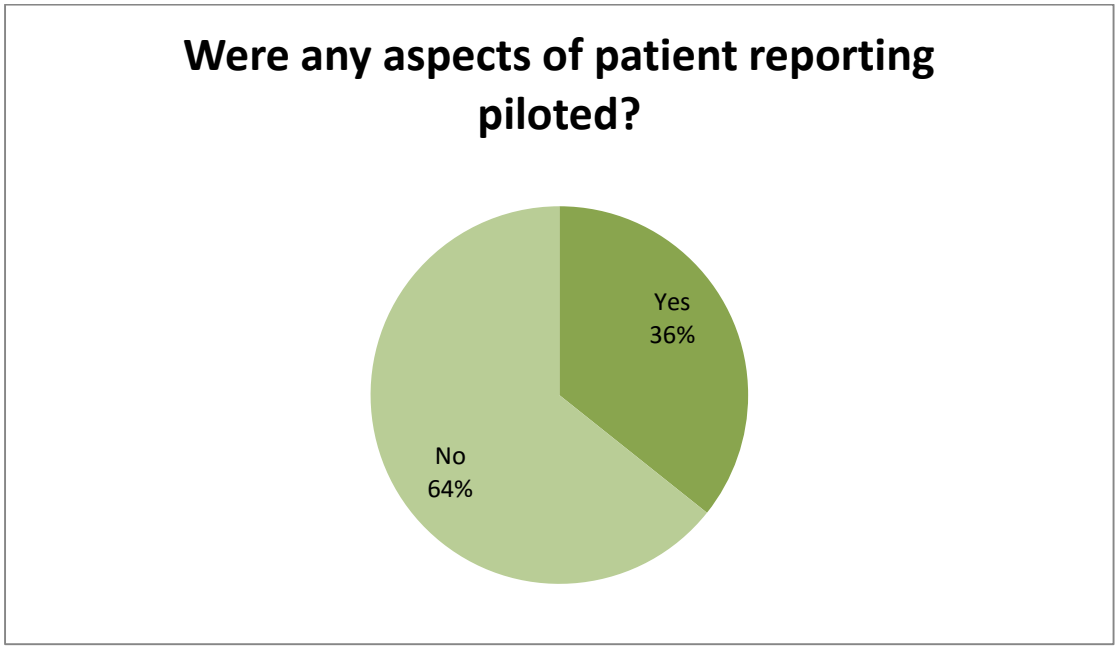
MODE: 2012

In majority of countries ADR patient reporting system exists from 2012 -2013, following the Pharmacovigilance requirements which had a tremendous impact on introducing patient reporting. However, there are number of countries that introduced patient reporting much earlier, in one MS starting even back in 1968.

Question T2Q13: If NO, why not?

No response was received to this question.

Question T2Q14: Were any aspects of patient reporting piloted?



The following details related to piloting patient reporting were provided from different MSs:

1. A nationwide pilot was launched in January 2005 with a paper reporting form and access via the Yellow Card website.

2. In 2012-2013 when we piloted our new form with ADR and medication error (ME) reporting. We wanted to test the form and obtain feedback on difficulty and complexity, time to fill in and ways to improve the form. Four cases containing a mix of ADRs and MEs were compiled together with a feedback form containing 7 open-ended questions. A summary of the cases is as follows; Case 1: ME and ADR; confusion between drug A and drug B causing hypertension and headache in the patient. Case 2: ME and ADR; decrease in the absorption of drug C due to concomitant administration of a drug D Case 3: ADR on a reaction suspected to be related to a new treatment. Case 4: Several ADRs reported by an investigator of a clinical trial. Cases 1 and 2 were written from a patient's perspective while the other 2 cases studies were from a HCP angle. One of the four test cases together with the feedback form and the report form were randomly distributed to 17 Medicines Authority personnel including 5 participants who had no scientific background. After one week, a reminder was sent to those who had not returned the form. All cases and forms were collected within 3 weeks of initial distribution. Following the first round of comments received, the report form (amended to address the comments) and feedback form were circulated a second time to assess whether issues identified were adequately resolved.

3. In May 2007, one NCA ran a pilot project, i.e. accepting patient/consumer ADR reports. Little was done to promote the project and only 5 reports were received. Subsequently, this NCA decided to accept patient/consumer ADR reports, starting on January 1st, 2008.

4. It was tested if patients could provide enough information in the report in order to ensure a proper causality assessment.

5. Paper reporting was not piloted. Patient online reporting was piloted in collaboration with WHO/UMC in 2012.

6. Pilot testing in a closed user group.

7. Regional pilot 2007.

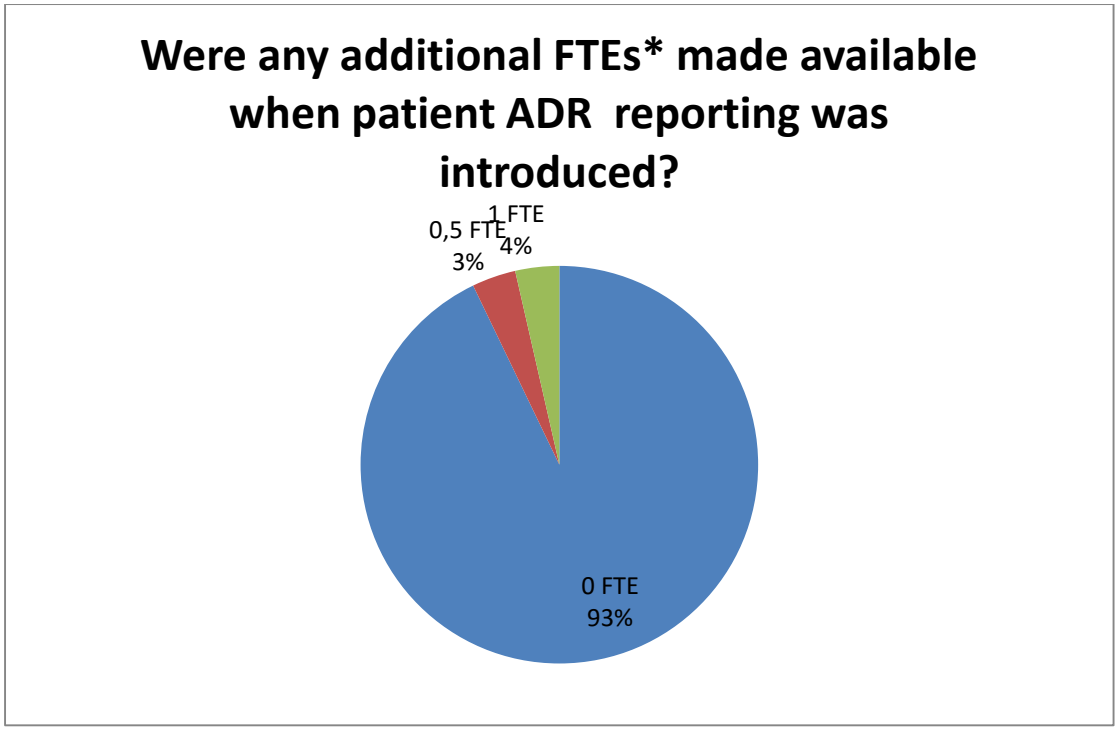
8. The website has been updated with relevant information. A campaign regarding safe use of medicines was additional launched in May 2013.

9. A first pilot was funded by the NCA and carried out by Consumers and Users Organization. Once developed our electronic form, a second pilot with general public took place.

Question T2Q15: Were any additional FTEs* made available when patient ADR reporting was introduced (please enter the number of FTEs):

**FTE= Full Time Equivalent (For example, a worker employed for 20 hours for ADR processing a week, where full-time work consists of 40 hours, is counted as 0.5 FTE; a worker employed for 10 hours for ADR processing a week, where full-time work consists of 40 hours, is counted as 0.25 FTE. Hence, in this case FTEs dedicated to ADR processing are 0.75)*

_____ Additional FTEs



Although, majority of countries stated that patient reporting has made significant impact on their reporting system and resources, almost none of the EU countries increased the number of FTEs to follow the introduction of the patient reporting into their PhV system. Only 2 countries increased the number of FTEs as the result of introducing patient reporting by 0,5 and 1 FTEs, respectively.

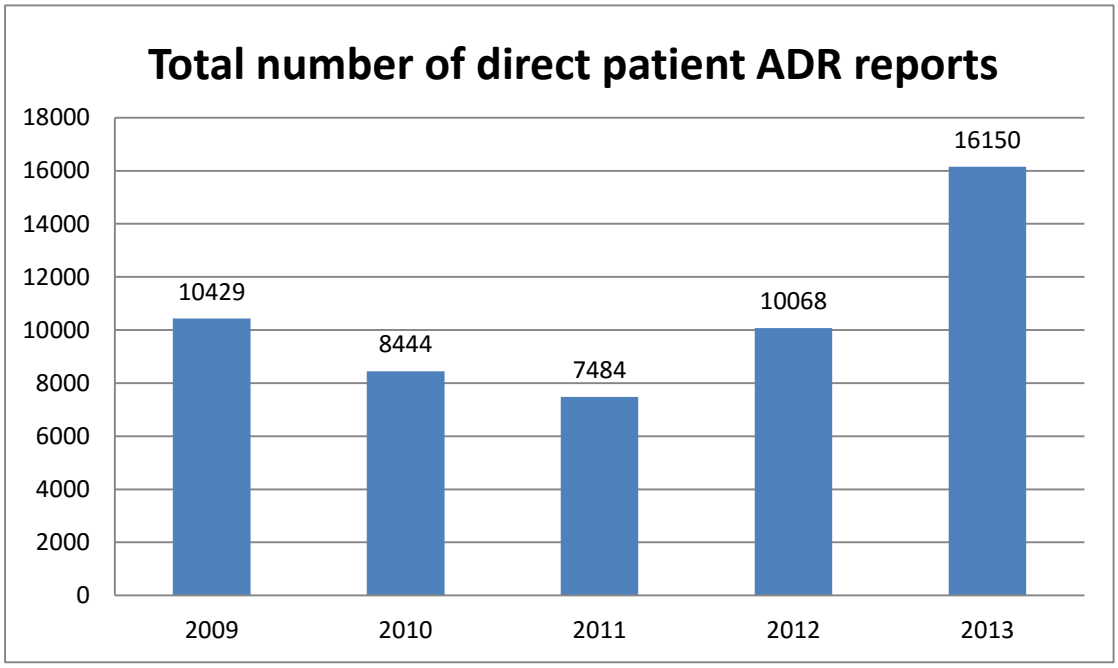
T2Q16 b) Making patient reporting forms available

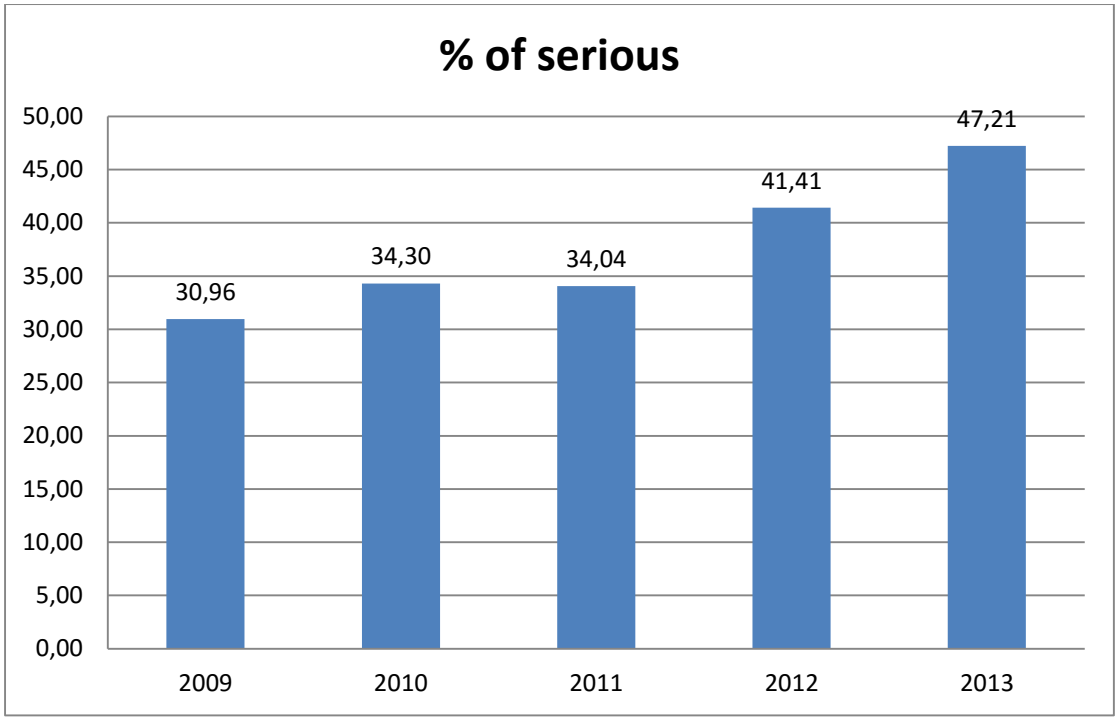
The aim of this section is to capture the total number of patient ADR reports in the last 5 years, what the available channels for patient reporting are and how visible they are. This section is also focusing on collaboration and communication with patient organizations.

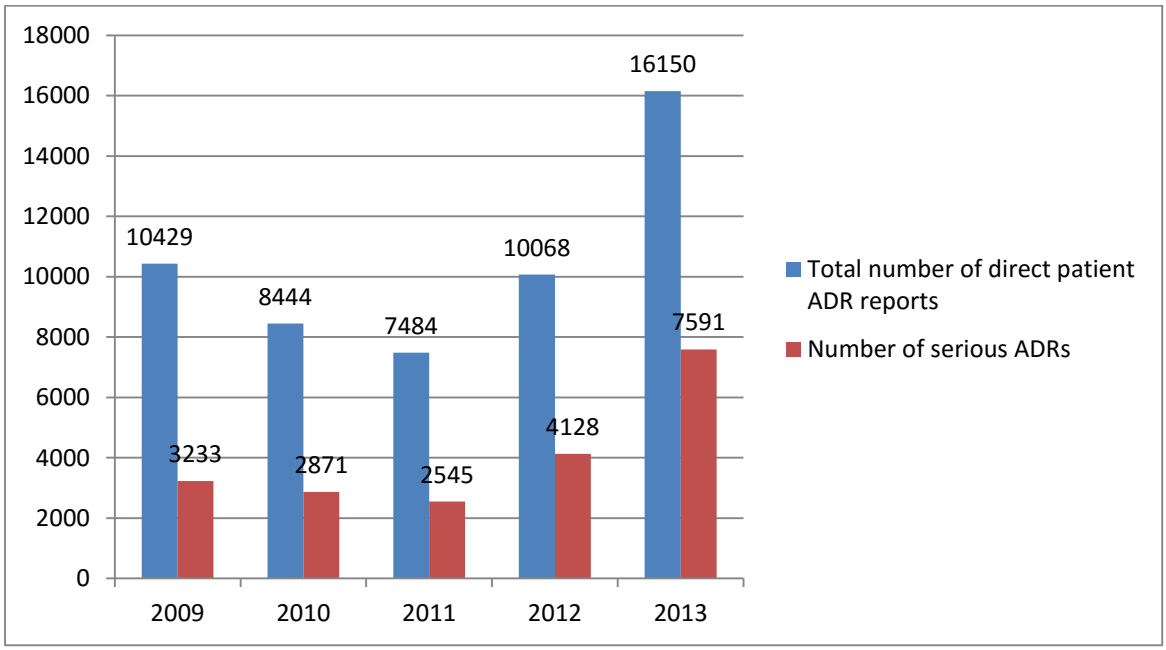
Question T2Q17: How many direct patient ADR reports in total did you receive in following years and what percentage of them was serious?

*Seriousness according to NCA

	TOTAL	Serious* %	Our institution is not responsible for this activity
2009			❑
2010			❑
2011			❑
2012			❑
			❑

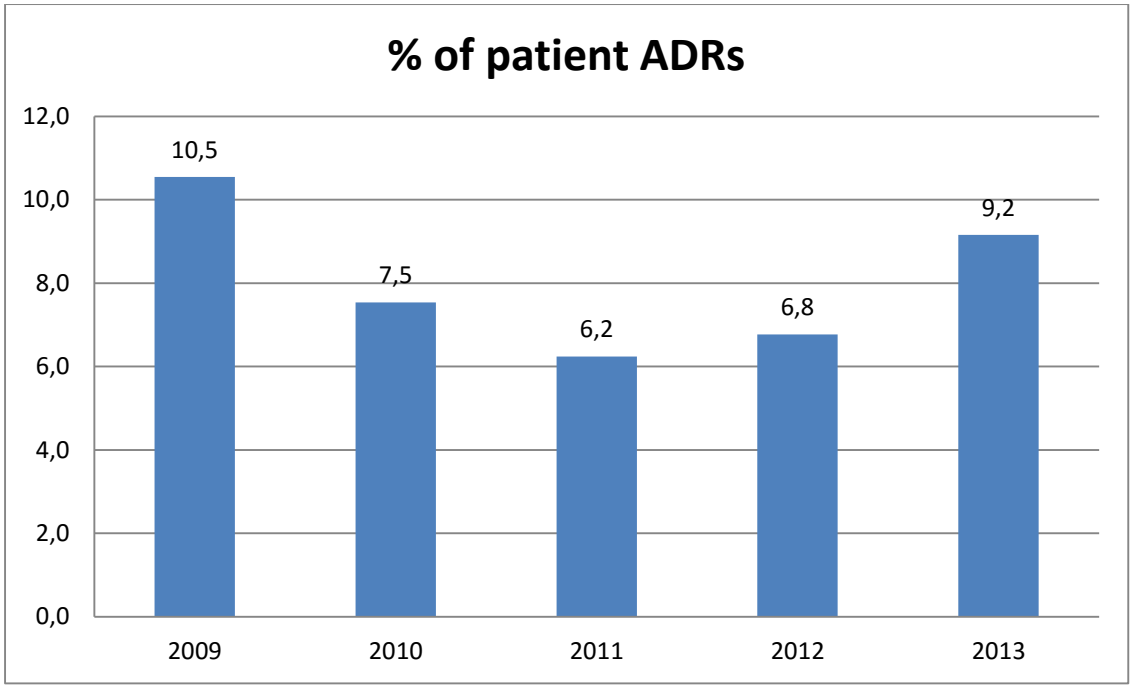




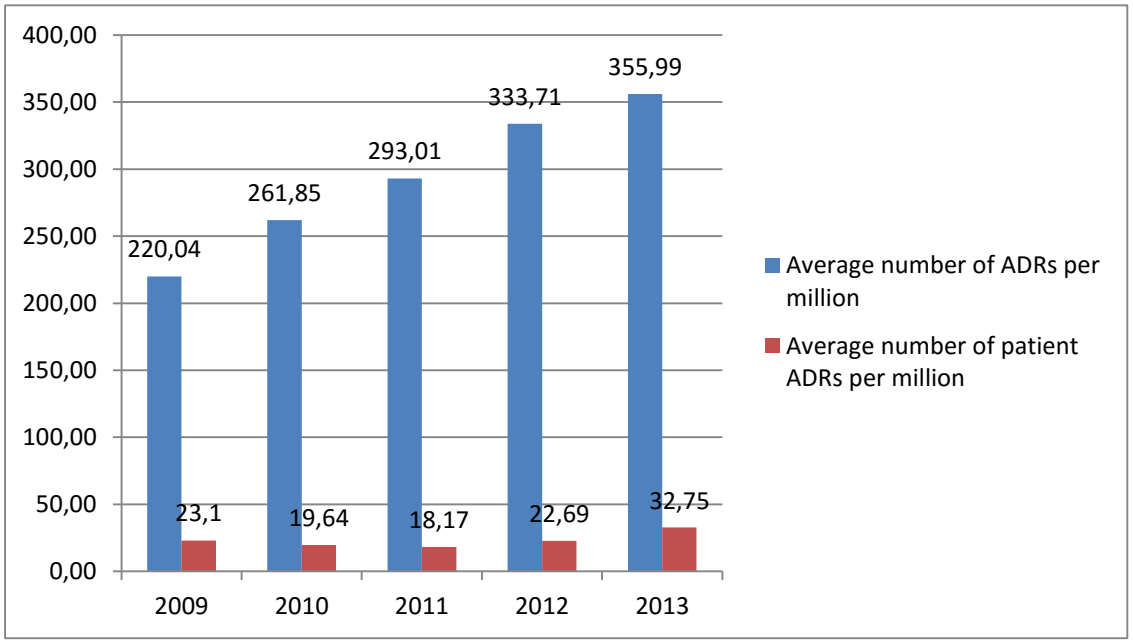


The total number of direct patient ADR reports increased significantly in 2013, as well as the number of serious ADRs. This result corresponds with findings in T2Q12 where it was shown that in majority of countries (14) ADR patient reporting system exists from 2012 -2013, following the Pharmacovigilance requirements.

The following graph shows the percentage of total number of direct patient ADR reports in total number of ADRs (please see T1Q26).



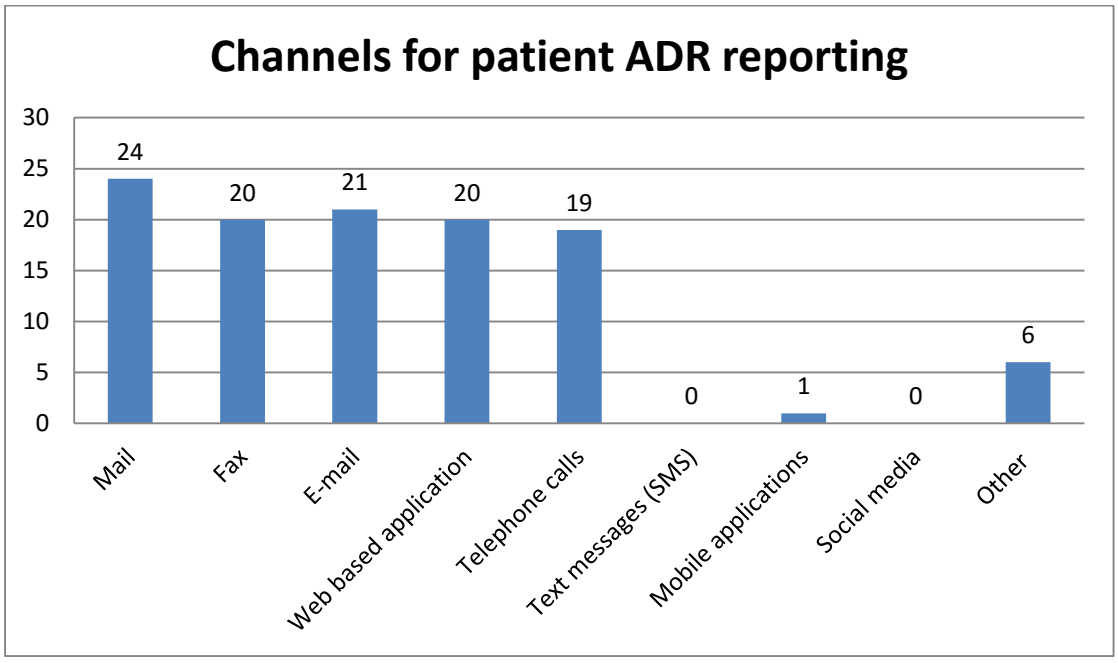
The average percentage of direct patient ADRs is lower than 10% across MSs.
2 MSs have not provided answer to this question (N=26).



Twelve (12) MSs have less than 1% of direct patient reports in total in observed period, while two MSs have much higher median of direct patient reports- around 30% and around 20%.
In total, 21 out of 26 MSs are below the median, which means that only 5 MSs are above the median of 7,5 %.

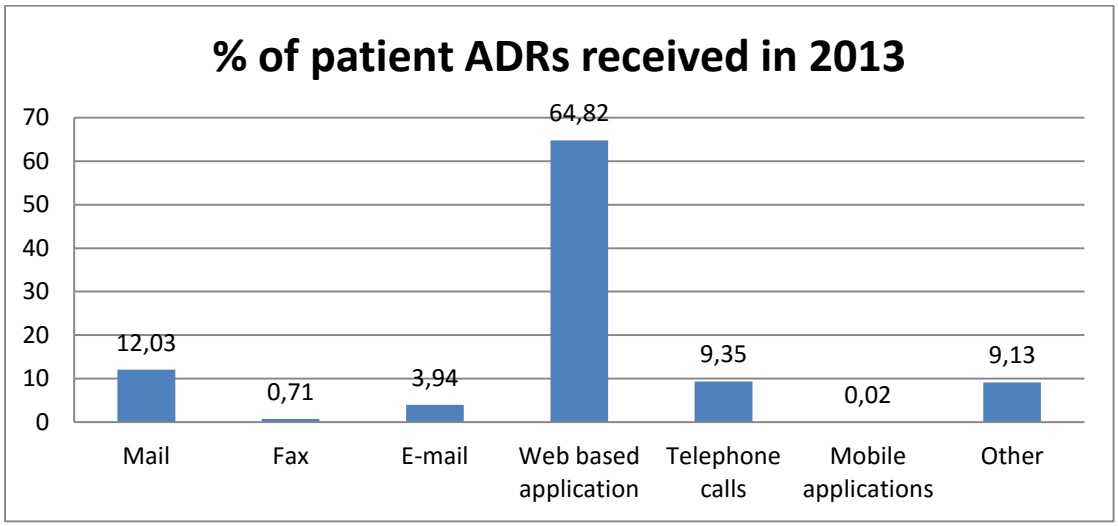
Question T2Q18: What are the existing channels for patient ADR reporting in your country and how many patient ADRs are received via these methods in 2013?

			No. of reports	Our institution is not responsible for this activity
	Yes	No	(please enter the number)	(please tick if applicable)
Mail	❍	❍		❑
Fax	❍	❍		❑
E-mail	❍	❍		❑
Web based application	❍	❍		❑
Telephone calls	❍	❍		❑
SMS	❍	❍		❑
Mobile applications	❍	❍		❑
Social media, please specify	❍	❍		❑
Other, please specify	❍	❍		❑



Only one MS has mobile application available for direct patient reports.

6 MSs stated that they have some "other" available channel, including reporting in person, patient-doctor Q&A, other web portals linking to the NCA's website etc.

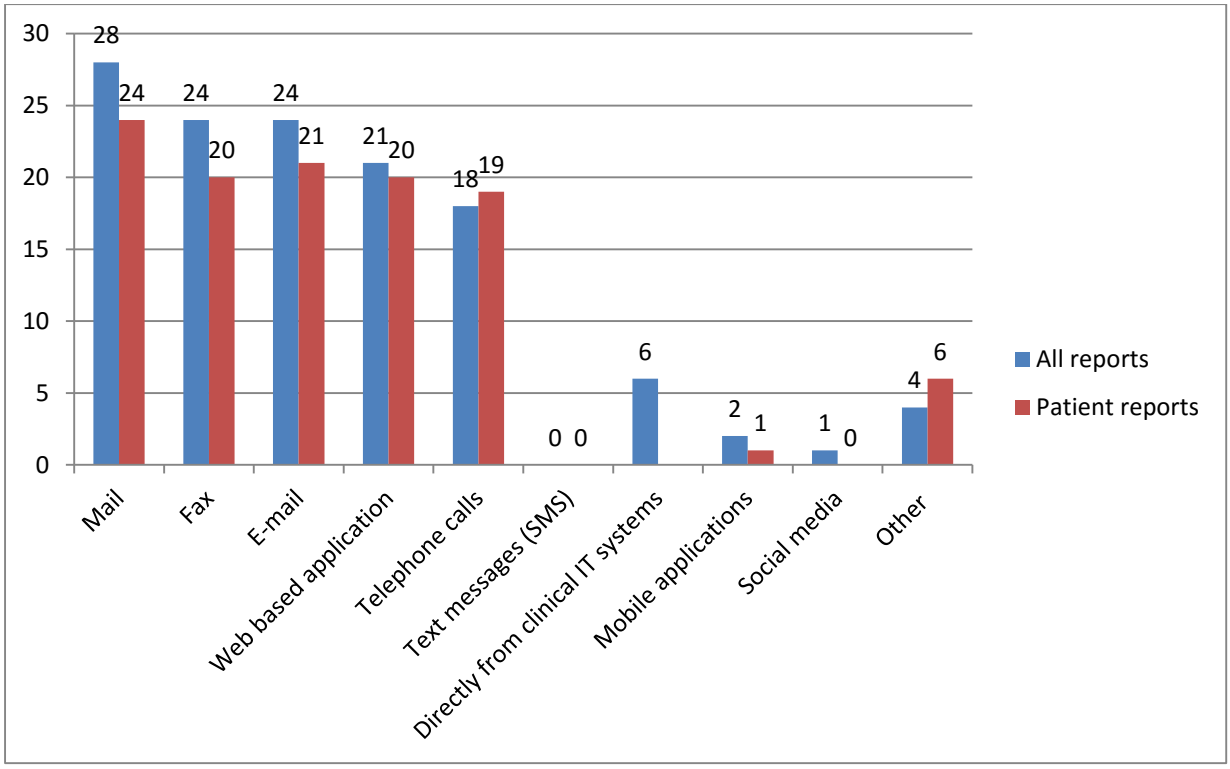


The percentage of ADR reports received via web-based application is rather high (64,82%).

In one MS 100% of patient ADR reports is received via web-based application.

In 2 MSs most of direct patient ADR reports are received via telephone (38,00% and 74,51% respectively), this being the reporting tool which needs additional resources.

The following graph shows comparison of results for available channels for ADR reporting for all reports (please see T1Q19) and specifically for patient reports.



Mail is available reporting channel for ADR reports from HCPs in all MSs, while 3 MSs do not have this channel available for patient ADRs. One MS did not respond to the question regarding reporting channels for patient ADRs (T2Q18).

In 85,7% MSs fax and e-mail are available for HCP reports, while those percentages are a bit lower for patient ADRs, 74,1% and 77,8 % respectively.

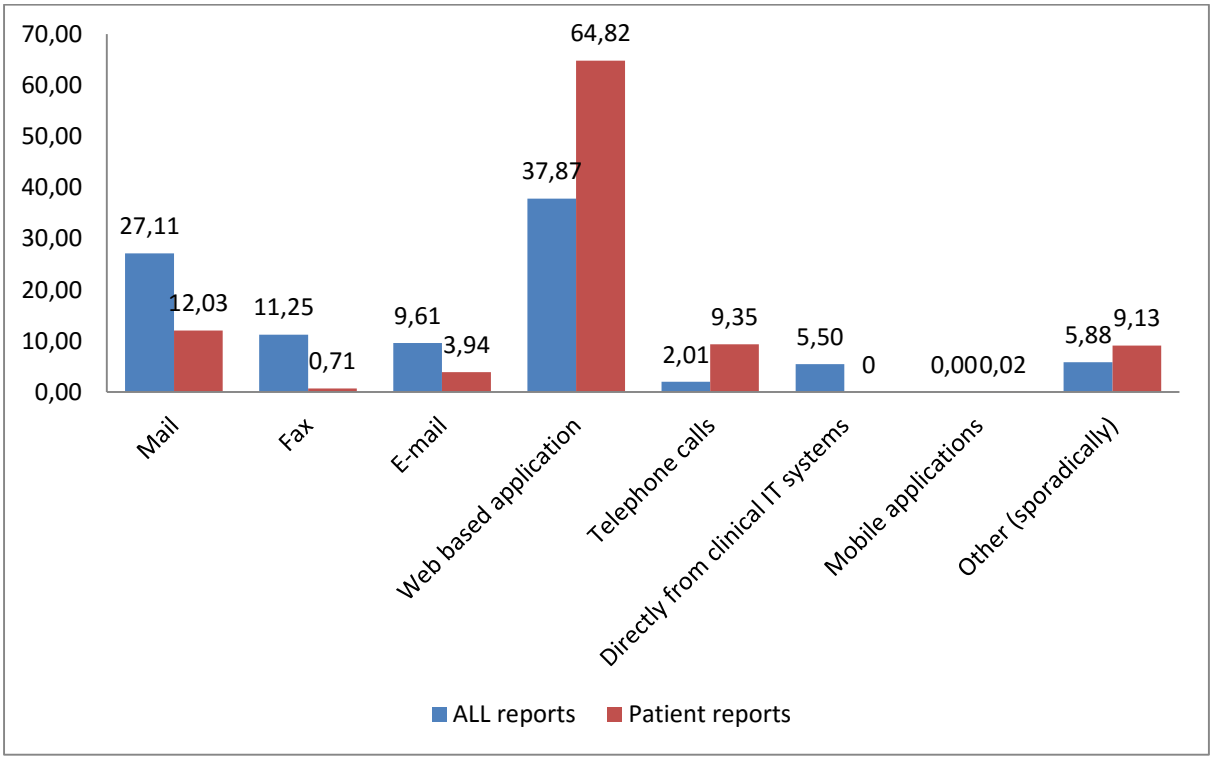
The number of MSs which have web based application for receiving HCP and patient ADR reports is similar. The same MSs do not have web application for HCPs and patients, with two exceptions- one MS has web based application for HCPs, but not for patients, and another one has web based application only for patients.

None of the MSs have text messages as available reporting channel, neither for HCPs nor patients.

Mobile applications are available in 2 MSs for HCP reports and in 1 MS for patient reports.

Following graph shows comparison of results between percentages of ADRs received in 2013 for all reports (please see T1Q20) and patient reports.

Percentage of ADR reports received through different channels among all reports and patient reports in 2013



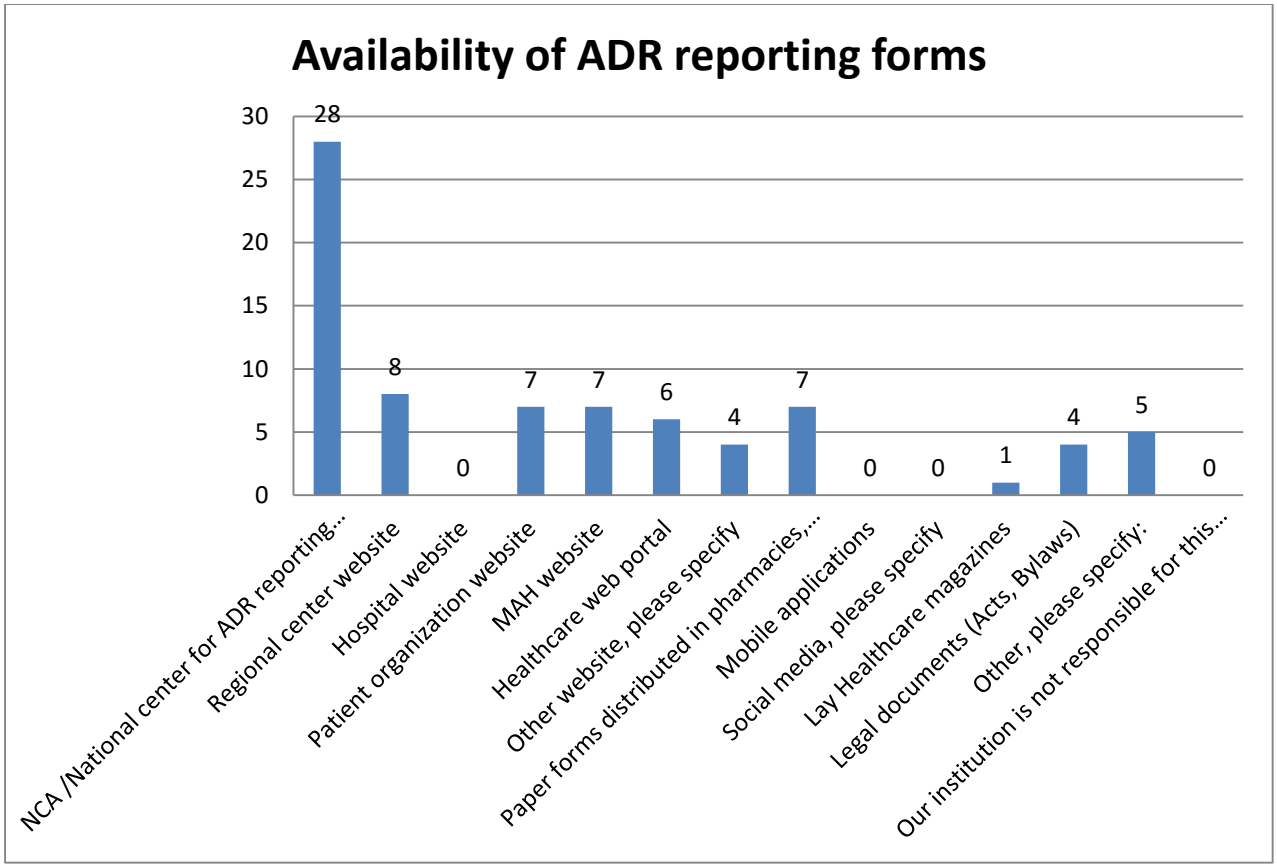
The percentage of ADRs received through web-based application is much higher among patient population. Mail is still the channel through which significant number of ADRs is received, however much more from HCPs27,11%) than from patients (12,03%).

Patients use telephone calls more often than other reporters, while fax and e-mail are used with much lower frequency.

In one MS only 2 patient ADR reports were received in 2013 through mobile application.

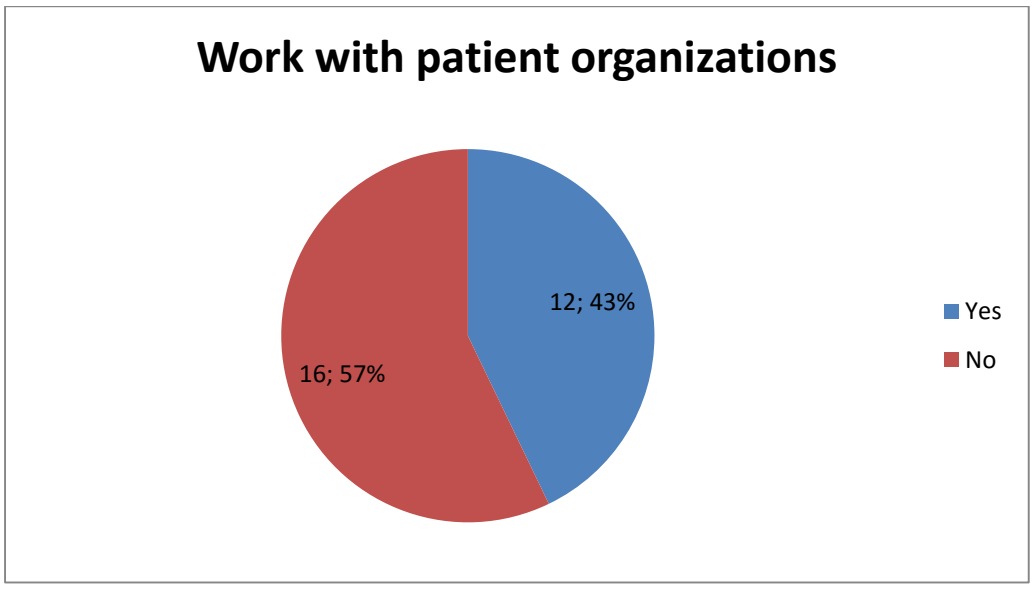
Question T2Q19: Please specify in what way ADR reporting forms are made available for patient reporting?

	Yes	No
NCA /National centre for ADR reporting website	❍	❍
Regional centre website	❍	❍
Hospital website	❍	❍
Patient organization website	❍	❍
MAH website	❍	❍
Healthcare web portal	❍	❍
Other website, please specify	❍	❍
Paper forms distributed in pharmacies, hospitals or other healthcare institution	❍	❍
Mobile applications	❍	❍
Social media, please specify	❍	❍
Lay Healthcare magazines	❍	❍
Legal documents (Acts, Bylaws)	❍	❍
Other, please specify:	❍	❍
Our institution is not responsible for this activity	❍	❍



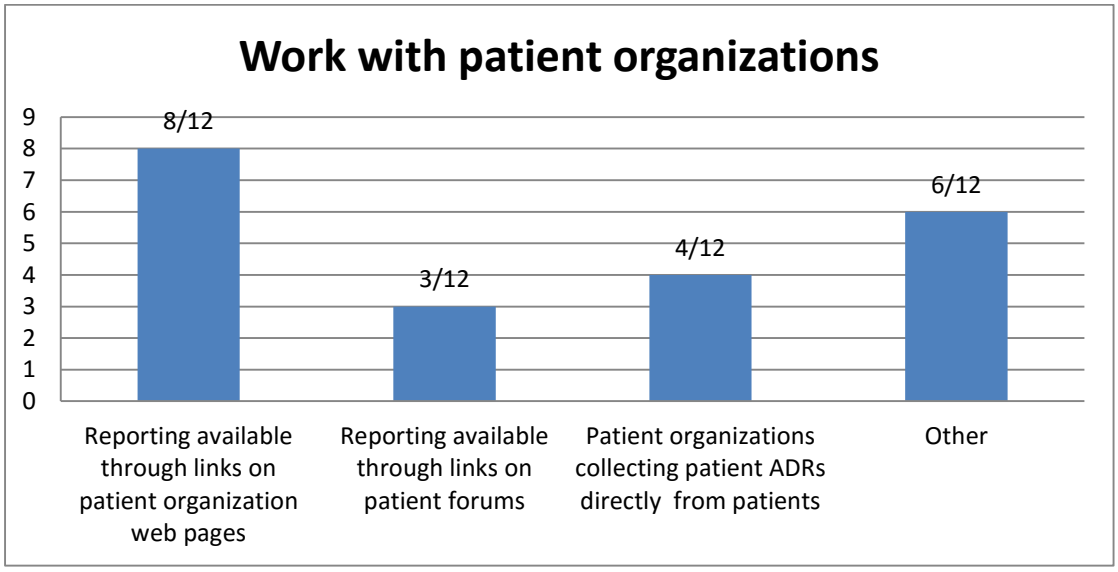
All MSs which have responded to this question (N=28) **have** ADR reporting forms available for patient reporting on NCA's website, while none of them has forms available on hospital website, mobile applications or social media.

Question T2Q20: Do you work with any patient organizations to promote or support patient ADR reporting?



Question T2Q21: If YES, please specify:

	Yes	No
Reporting available through links on patient organization web pages	❍	❍
Reporting available through links on patient forums	❍	❍
Patient organizations collecting patient ADRs directly from patients	❍	❍
Other, please specify	❍	❍



Question T2Q22: Please specify how many specific patient organizations you work with on patient ADR reporting:

9 MSs provided their answer to this question. Number of specific patient organizations they work with varied from one to 20. It is important to note that some MSs stated that they collaborate with all major patient organizations within their country, or with one "umbrella" patient organization which is representing all patient organizations.

Question T2Q23: Please list their scope of work based on underlying disease (e.g. rare diseases, multiple sclerosis, DM, etc.):

Most often mentioned diseases were:

1. Cancer (4 times)

2. Diabetes mellitus (3 times)

3. Multiple sclerosis (3 times)

4. Haematological diseases (3 times)

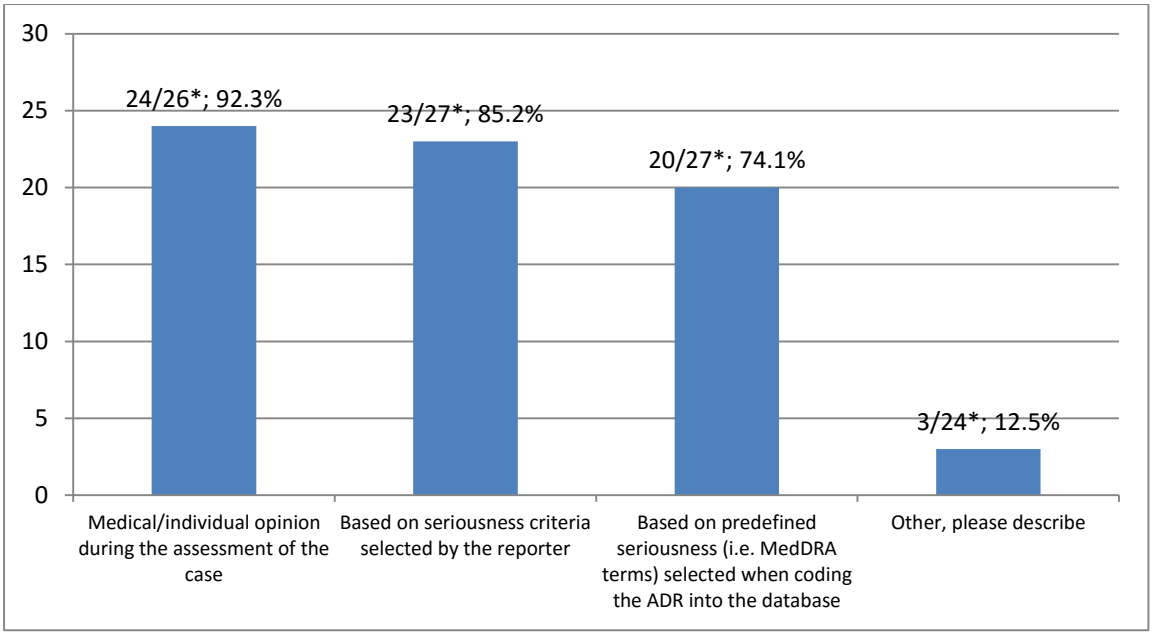
T2Q24 Characteristics of patient ADR reports

The purpose of this set of questions is to learn about patient ADR reports; characteristics (i.e. Seriousness assessment, age groups, gender, the type of product and also the type of reporter).

Question T2Q25: How do you assess seriousness of ADR reports?

	Yes	No
Medical/individual opinion during the assessment of the case	❍	❍
Based on seriousness criteria selected by the reporter	❍	❍
Based on predefined seriousness (i.e. MedDRA terms) selected when coding the ADR into the database	❍	❍
Other, please describe	❍	❍
Our institution is not responsible for this activity	❍	❍

Response rate: 27 MSs



*number of respondents

Most MSs use medical/individual opinion during the assessment of the case as the main criteria for assessing seriousness of patient ADRs. MSs generally use more than one criterion to assess seriousness of patient ADR reports, however there are some MSs that use only one criterion.

Some MSs indicated that they use different criteria than specified in the question ie. 2 MSs use EMA Medical Events List as per GVP which could also be considered as predefined criteria.

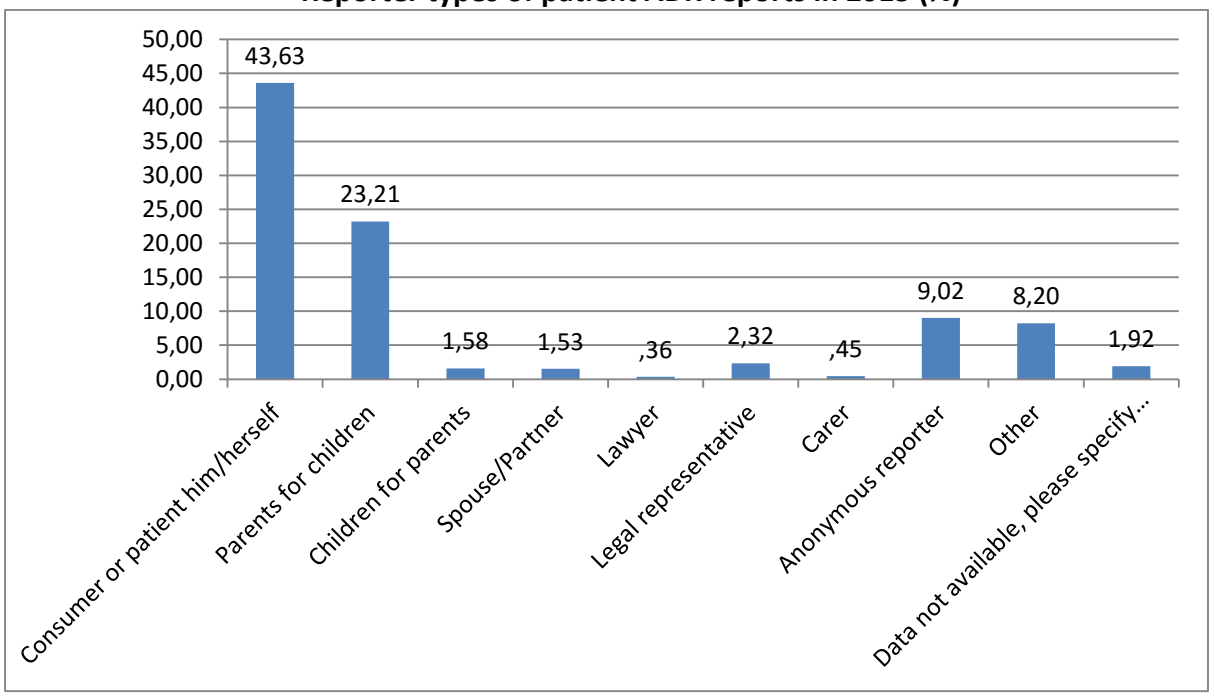
One MS uses National Pharmacovigilance Committee for assessing seriousness of patient ADR (low number of patient ADR has to be taken into account).

Question T2Q26: Please specify % of the reporter of patient ADR reports in 2013:

	%	Our institution is not responsible for this activity
Consumer or patient him/herself		❑
Parents for children		❑
Children for parents		❑
Spouse/Partner		❑
Lawyer		❑
Legal representative		❑
Carer		❑
Anonymous reporter		❑
Other, please specify		❑
Data not available, please specify reason		❑

Only 13 MSs were able to provide answer to this question. 9 MSs don't have available data on reporter and the mentioned reasons were limitations of databases, incomplete data entry, this information is not captured etc.

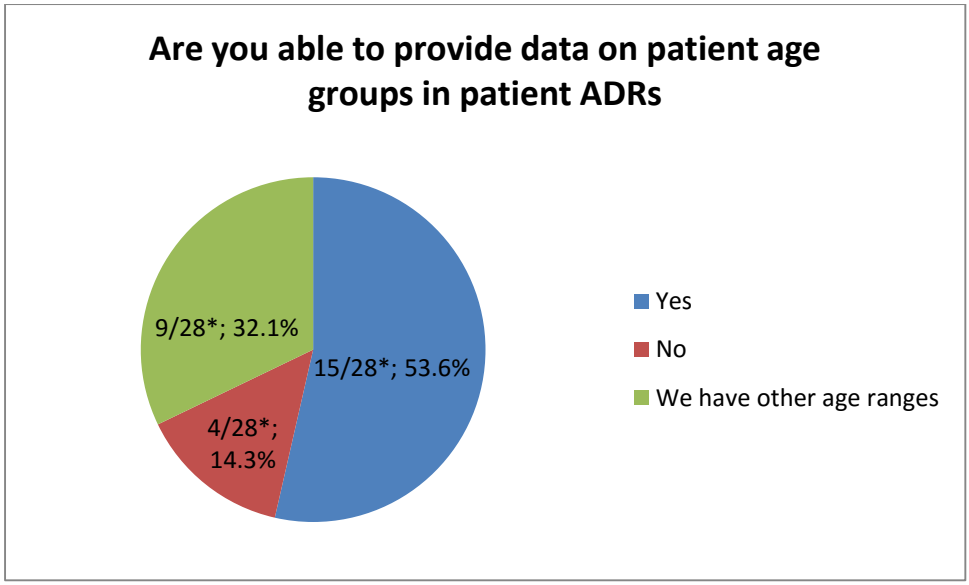
Reporter types of patient ADR reports in 2013 (%)



Most patient reports were reported by consumer or patient (46,63%) themselves, followed by parents for children (23,21%) and children for parents (1,58%). There were some MSs with specific stratification by reporter. For example, one MS received all reports from parents in 2013, however, they have small number of patient ADRs. Another MS receives all reports from anonymous reporter, because of specific legal requirements regarding privacy of reporter of patient reports.

Question T2Q27: Are you able to provide data on ADR reports categorized by patient age groups as follows: ≤ 1 month > 1 month ≤ 4 years > 4 years ≤ 11 years > 11 years ≤ 18 years > 18 years ≤ 69 years > 69 years ?

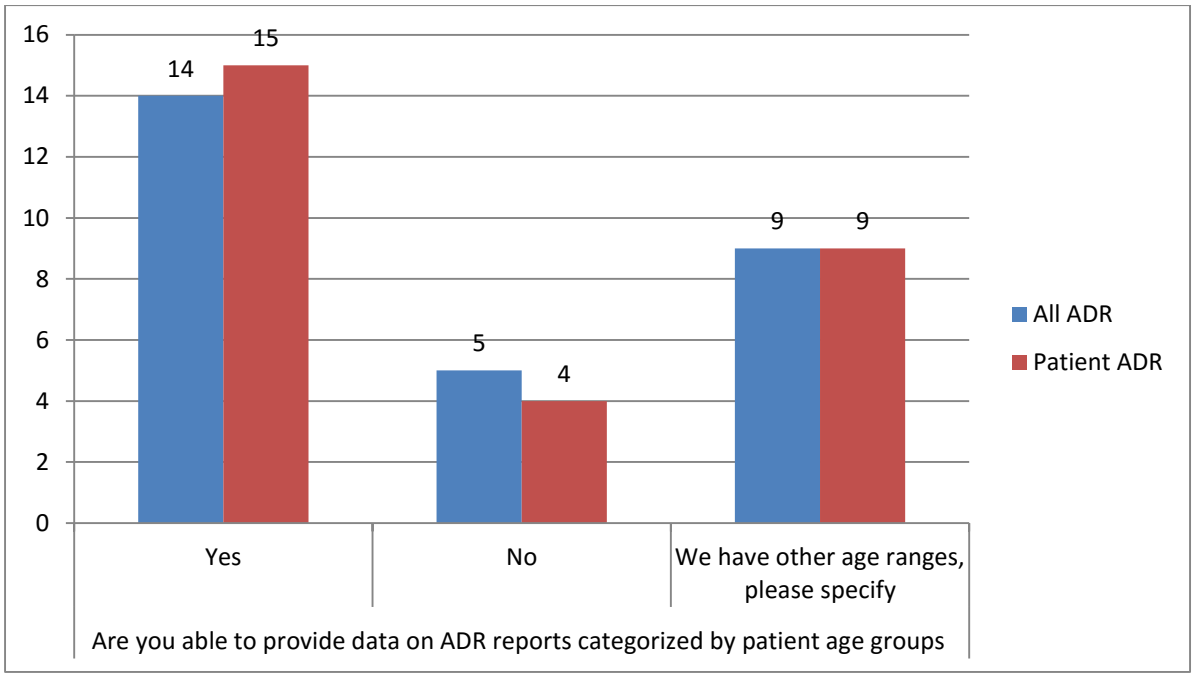
- ❍ Yes
- ❍ No
- ❍ We have other age ranges, please specify _____
- ❍ Our institution is not responsible for this activity



*number of respondents

Around 50% of MSs (54%, 15/28) were able to provide data on patient ADR reports categorized by patient age groups.
4 MSs are not able to provide data according to requested age range and those MSs are not the same ones as those who are not able to provide data on reporter of patient ADR (T2Q26).
It is interesting to notice that 9 MSs use different age ranges than the proposed age ranges in the question.

The following graph shows comparison of results received for data on ADR reports categorized by patient age groups between all reports (please see T1Q31) and patient reports. We can see that results are pretty similar.



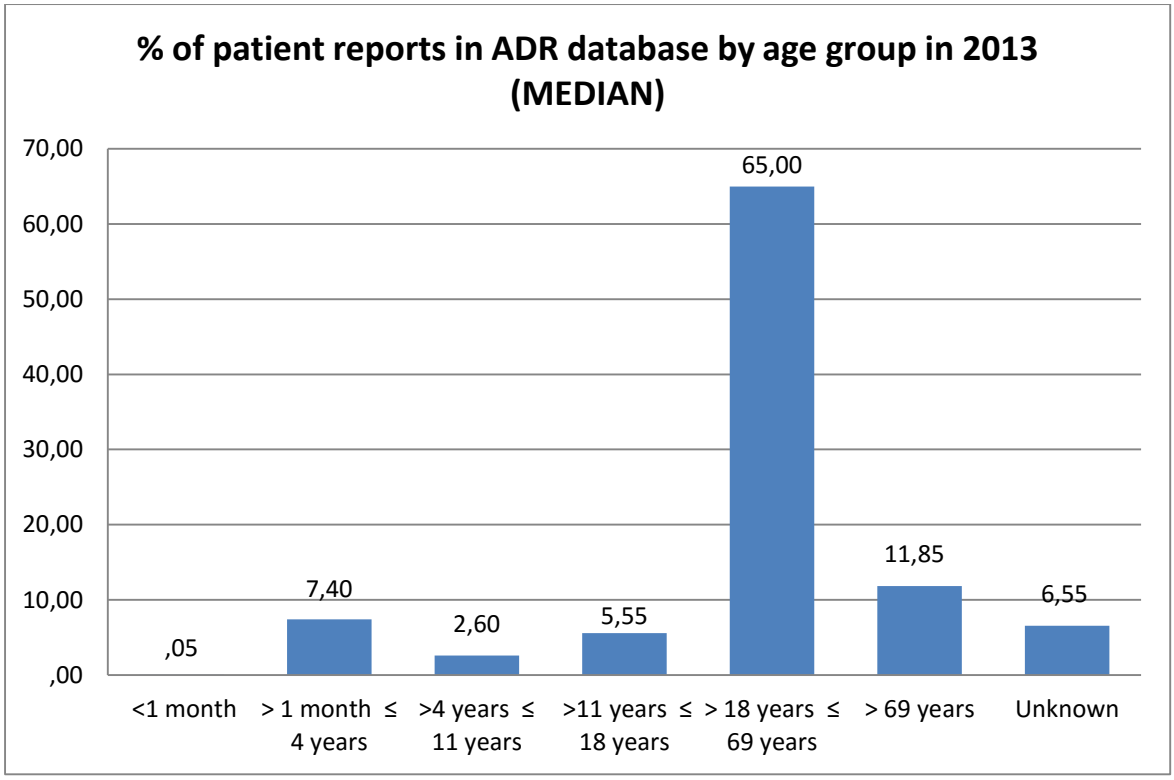
*28 MSs answered to both questions

Question T2Q28: Please specify the % of patient reports in your ADR database by patient age groups in 2013:

Please enter whole numbers (i.e. decimals and symbol "%" should not be used).

_____ ≤ 1 month
_____ > 1 month ≤ 4 years
_____ > 4 years ≤ 11 years
_____ > 11 years ≤ 18 years
_____ > 18 years ≤ 69 years
_____ > 69 years
_____ Unknown

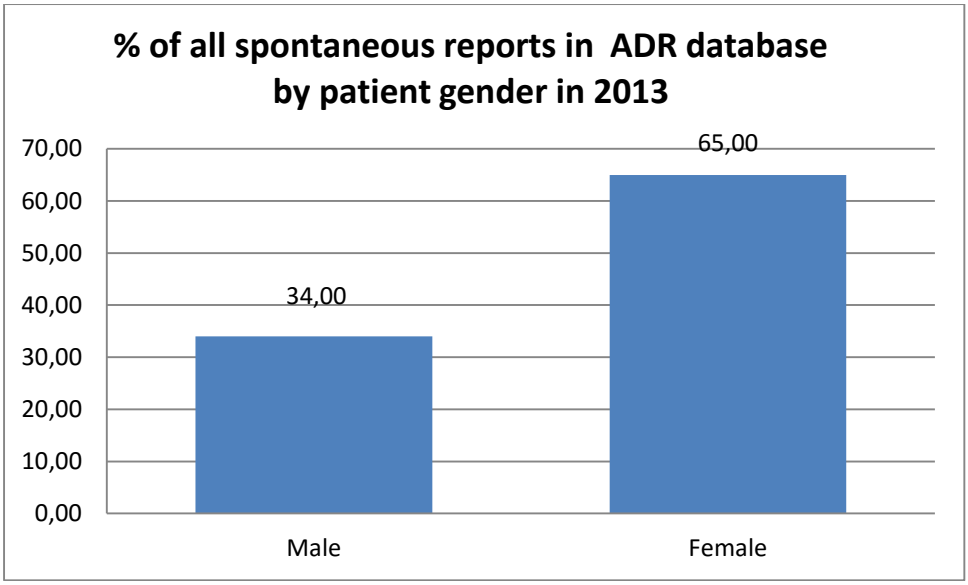
Response rate: 14 MSs



Most patient reports were reported for age group *> 18 years ≤ 69 years* (adults) and *> 69 years*, followed by age group *>1 month ≤ 4 years*. This is understandable since age group *>18 years ≤ 69 years* has the biggest range (51 years) and patients in age group *> 69 years* usually use more medicines, therefore higher number of reported ADRs can be expected.
It should be noted that results are shown without 2 MSs, since they are outliers due to the small number of patient ADRs (median was calculated to make results more statistically representative).

Question T2Q29: Please specify the % of patient reports in your ADR database by patient gender in 2013:

_____ Male
_____ Female
_____ Unspecified
_____ Data not available, please specify reason



Most of MSs (21/28) provided data on % of patient ADRs by gender.
Some of respondents had different reasons for not providing data:

- it would be possible but what is the meaning
- old database, old dataset
- no ADR reports from patients in 2013
- transition of database currently – data retrieval difficult

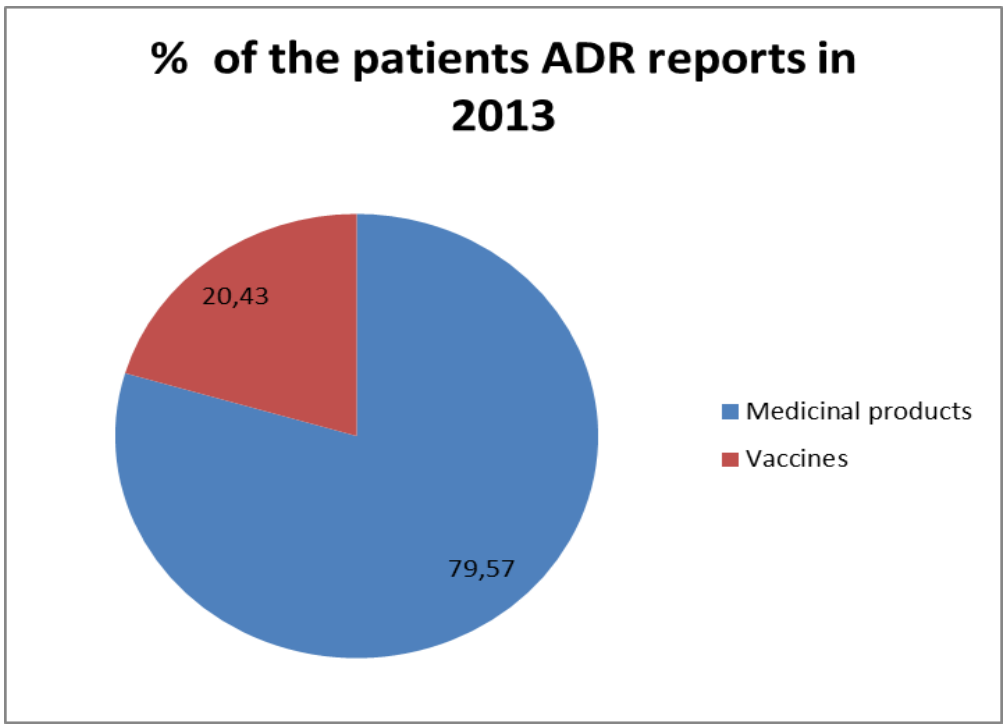
Patient ADRs are reported predominately for female patients, which is supported in with currently available literature. 2 MSs were excluded from the analysis due to the fact that they are outliers (small number of patient ADRs).

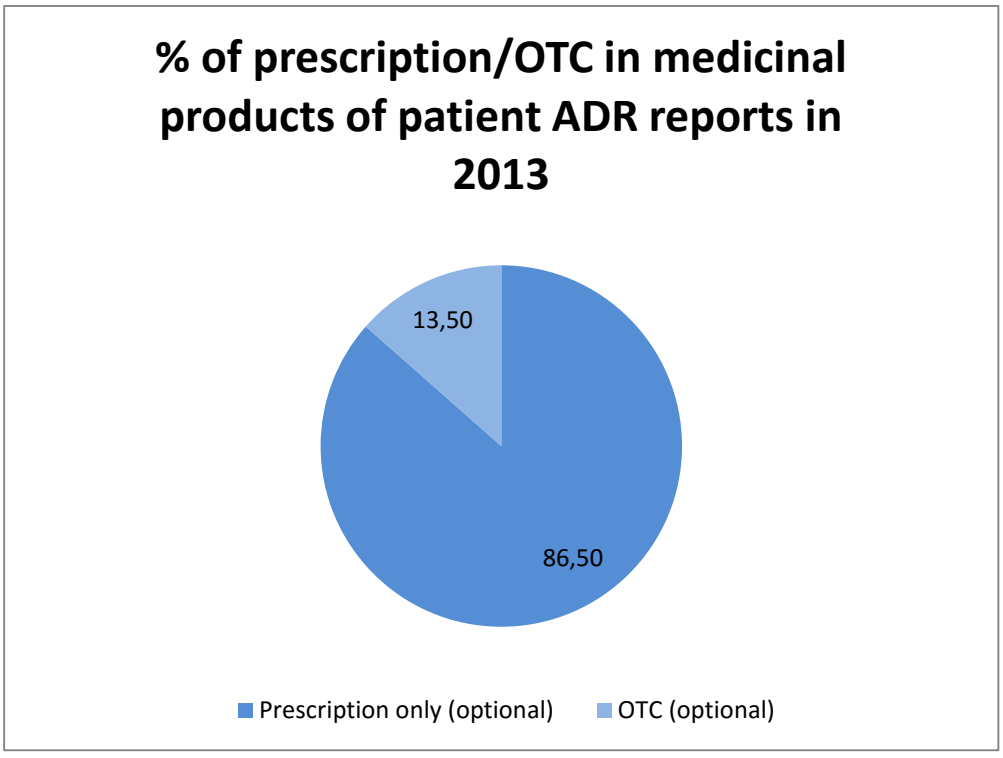
Analysis according to specific country revealed that only in one MS more patients were male but also that MS has high proportion of unspecified reports that could influence the results.

Question T2Q30: Please specify the % of patient ADR reports in 2013, where applicable:

	%	Our institution is not responsible for this activity
Medicinal products		❑
Prescription only (optional)		❑
OTC (optional)		❑
Vaccines		❑
Cosmetics		❑
Food supplements		❑
Other, please specify		❑

Response rate: 20 MSs





Most reports are related to medicinal products (79,57%), among which 86,50 % of reports refer to prescription only medicines.

From the 22 responding MSs, answers from 20 MSs were analysed in this question, since two countries provided inconsistent answers.
Between 20 analysed countries, only one provided the percentage of reports for category food supplements (1, 47%), therefore it was not possible to calculate the EU mean for food supplements. Consequently, a category food supplement was excluded from the total analysis and the percentages for the remaining categories in this MS (medicinal products and vaccines) were weighted to make 100 percent in total. Moreover, only one MS provided the percentage of reports for category cosmetics, however the remaining answers for other categories from that MS were inconsistent and therefore responses from that MS were excluded from the further analysis.

T2Q31 d) Review of Member State ADR processing capacity
This section is dedicated to learn about time and resources available in each MS for patient reporting processing. It is also focussing on MS's specificities regarding patient ADR reports assessment and it is expected here for MS to describe in detail how is the assessment performed and which aspects are taken into consideration. Finally, in this section we would like to learn if there are differences between HCP and patient ADR reports processing and what those are.

Question T2Q32: When assessing an ADR what aspects do you consider (i.e. completeness, seriousness, causality, expectedness, validity...)? Please describe:

Based on responses from 28 MSs, consumer/patient ADR reports are assessed in the same way as medically confirmed reports. In addition to assessment of completeness, seriousness, validity, causality and expectedness, respondents often stress the need for a follow up with the reporter. Some MSs try to obtain the patient's GP's contact details in case this was not reported on the form (i.e. patient ADR reporting form in one MS has a field for GP's details), and even assess the seriousness after consulting with the GP. However, there are certain differences in the approach with regards to the whole patient report processing and prioritisation (please see responses to T2Q35).

Question T2Q33: If patient ADR reports are processed manually in your Institution, what is the most time-consuming part of the process?

	Average number of minutes needed per report for the part of the process	Our institution is not responsible for this activity	ADR reports are not processed manually
Manual data entry		❑	❑
Manual validation		❑	❑
Assessment		❑	❑

Average ad median time for patient report processing is very similar compared to HCP reports (please see T1Q43). There is consistency in responses and MSs that require the longest amount of time to process HCP reports are the same ones that require the most time to process patient reports, especially in terms of time needed for assessment.

	MEAN	MEDIAN
Manual data entry (minutes)	**50**	**33**
Manual validation (minutes)	**22**	**25**
Assessment (minutes)	**72**	**53**

Median time for assessment across 25 MSs is 53 minutes, which is approximately 50% of time required for the median time for the whole patient report process. In 2 MSs patient reports are not processed manually at all.

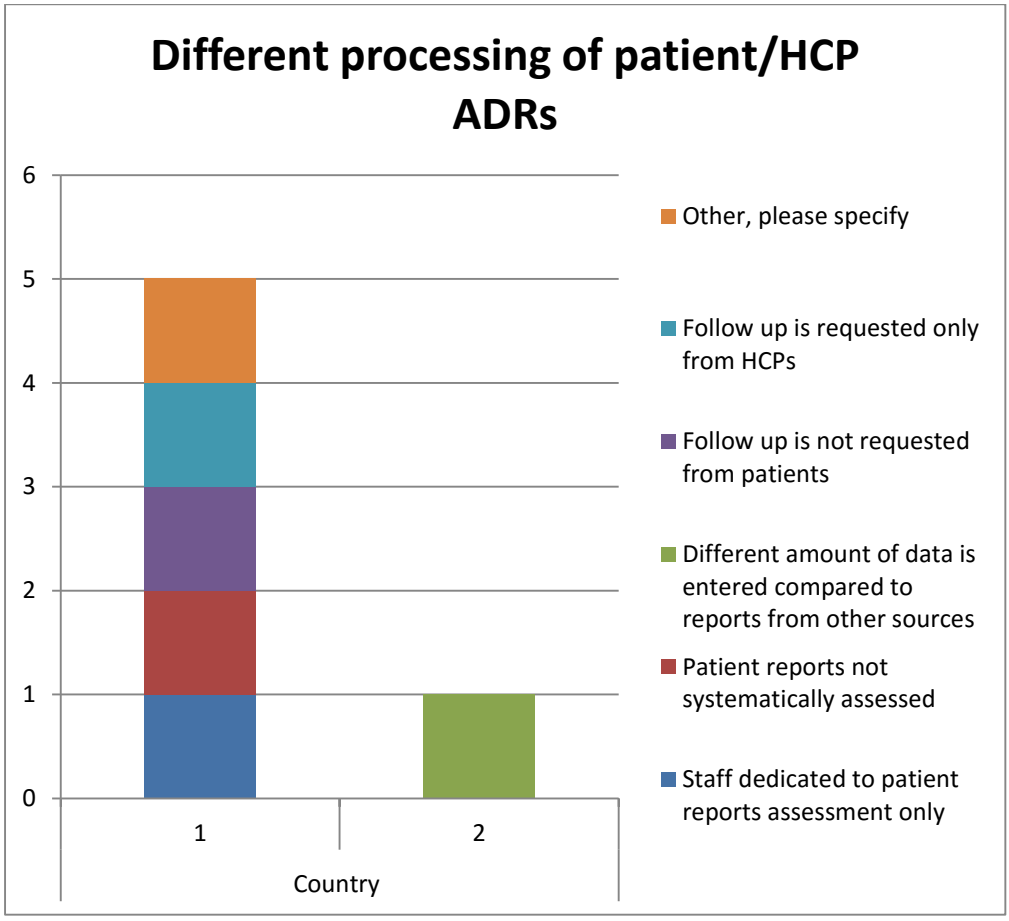
Question T2Q34. Are patient ADR reports processed differently than ADR reports from HCPs?

- ❍ Yes
- ❍ No
- ❍ Our institution is not responsible for this activity

Question T2Q35: If YES, indicate how:

	Yes	No
Staff dedicated to patient reports assessment only	❍	❍
Patient reports not systematically assessed (if this option is chosen, please tick all sub options below that apply)	❍	❍
Only serious patient reports are assessed	❍	❍
Only fatal patient reports are assessed	❍	❍
Not assessed at all	❍	❍
Patient reports are systematically excluded from overall signal detection	❍	❍
Different amount of data is entered compared to reports from other sources	❍	❍
Follow up is not requested from patients	❍	❍
Follow up is requested only from HCPs	❍	❍
Other, please specify	❍	❍

Two MSs responded that they process patient ADR reports differently than ADR reports from HCPs. The following table provides more detail:

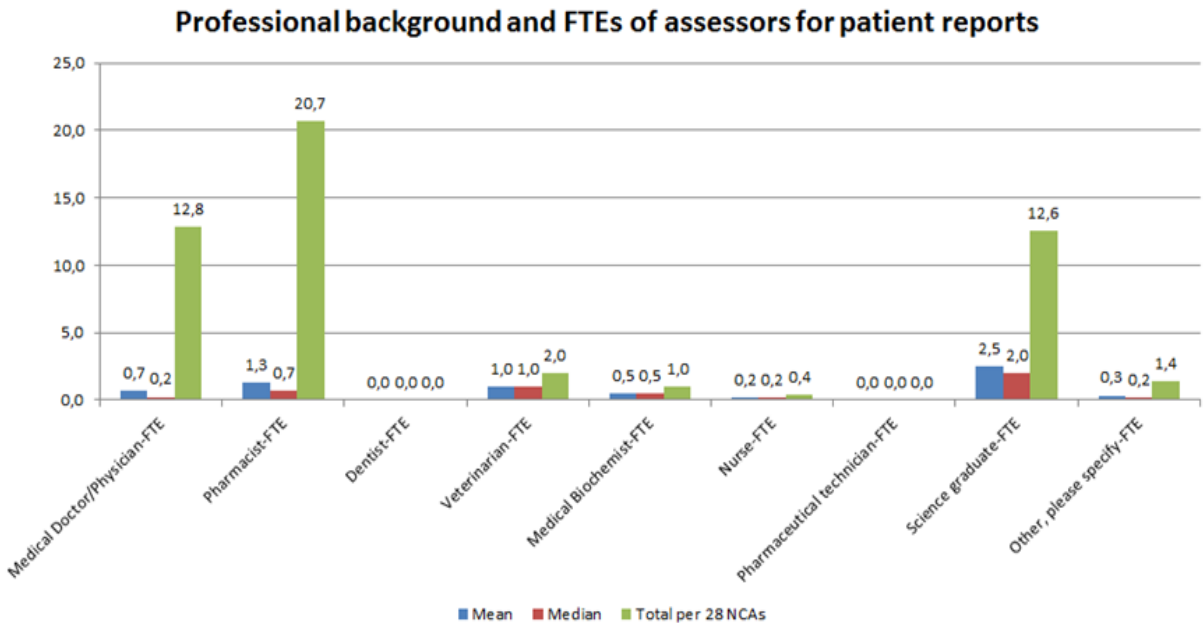


One MS chose 5 categories in which patient ADRs processing differs from HCP ADRs processing. For the category "Other" this MS provided further details: HPC reports are only paper based and handled by regional centres, patient reports are only sent electronically and handled by NCA. HPCs are given feedback, while feedback is not given to patents (not possible, anonymous reports).

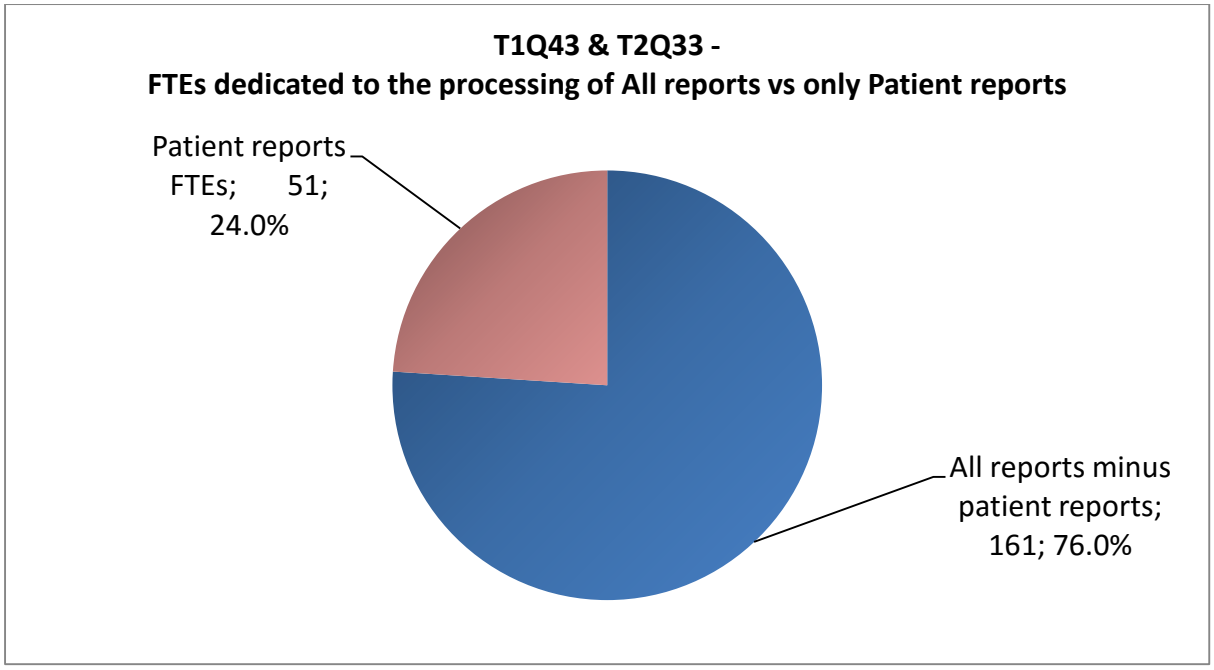
Question T2Q36: Please specify the professional background and Full Time Equivalents (FTEs)* of your assessors for patient ADR assessment:

**FTE= Full Time Equivalent (For example, a worker employed for 20 hours for ADR assessment a week, where full-time work consists of 40 hours, is counted as 0.5 FTE; a worker employed for 10 hours for ADR assessment a week, where full-time work consists of 40 hours, is counted as 0.25 FTE. Hence, in this case FTEs dedicated to ADR assessment are 0.75)*

	FTE
Medical Doctor/Physician	
Pharmacist	
Dentist	
Veterinarian	
Medical Biochemist	
Nurse	
Pharmaceutical technician	
Science graduate	
Other, please specify	



Professional background of assessors is the same irrespective of the type of the report (please see T1Q46). Green bars in the chart represent the total number of FTEs in the network based on responses from 24 MSs. One NCA responded that assessors' professional background was no different from HCP reports without further specifying. Apart from the pre-defined answers, respondents listed an assistant/administrative staff, a biologist and a molecular biologist/health management professional under the "Other" category.



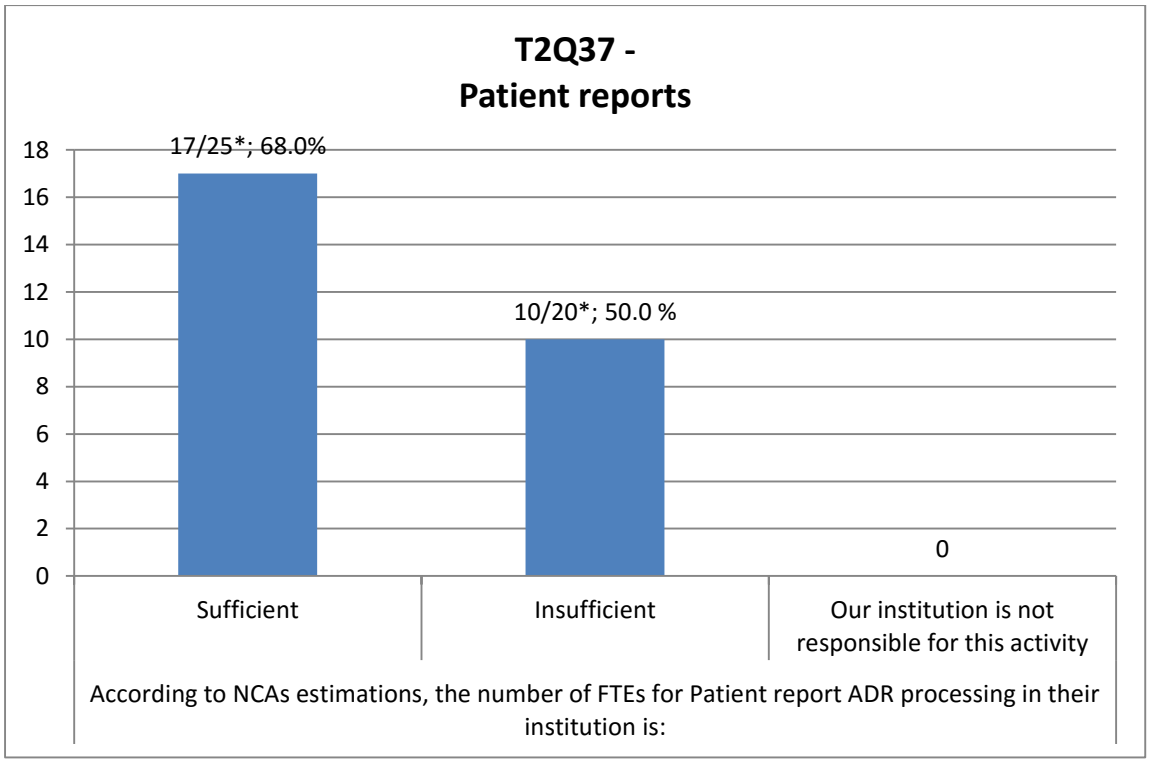
Processing of patient ADR reports takes up around one quarter of human resources in the network (24 respondents).

Question T2Q37: According to your estimations, the number of FTEs dedicated for patient ADR processing in your Institution is:

	Yes	No
Sufficient	❍	❍
Insufficient	❍	❍
Our institution is not responsible for this activity	❍	❍

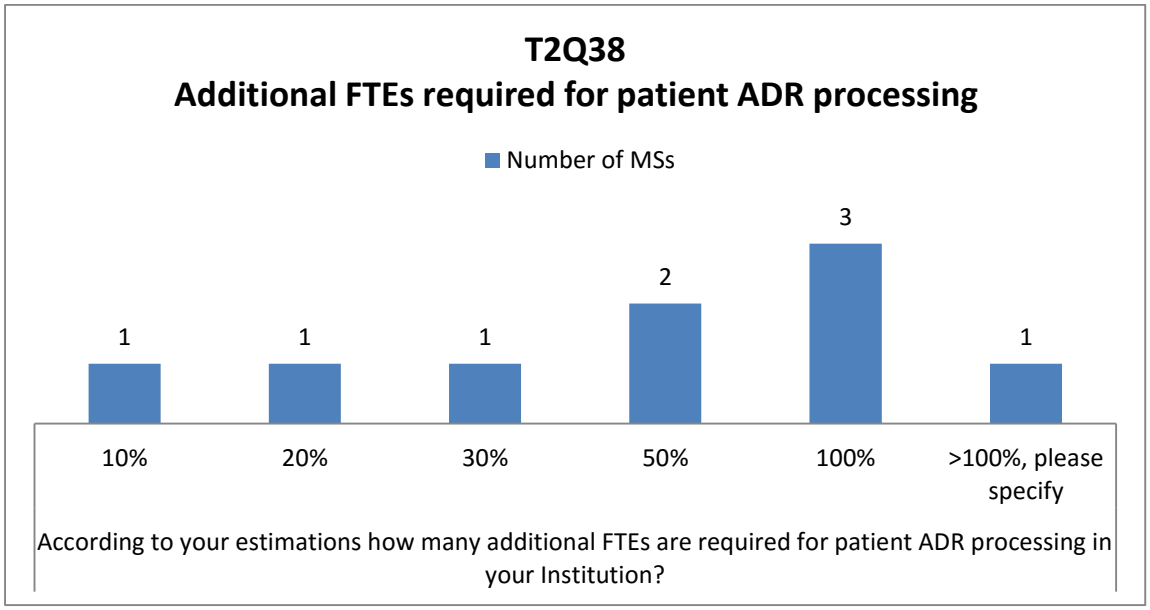
Question T2Q38: According to your estimations how many additional FTEs are required for patient ADR processing in your Institution?

- ❍ 10%
- ❍ 20%
- ❍ 30%
- ❍ 40%
- ❍ 50%
- ❍ 60%
- ❍ 70%
- ❍ 80%
- ❍ 90%
- ❍ 100%
- ❍ >100%, please specify: _____



Please see T1Q54

Of the 10 respondents that responded they required more personnel for processing of patient ADR reports, 9 also specified exactly how much more personnel they required.



Question T2Q39: What is the average amount of time required per assessor to assess a single patient ADR report (in hours)?

- ❍ < 1 hrs
- ❍ 1-2 hrs
- ❍ 2-4 hrs
- ❍ 4-6 hrs
- ❍ 6-8 hrs
- ❍ >8 hrs
- ❍ Our institution is not responsible for this activity

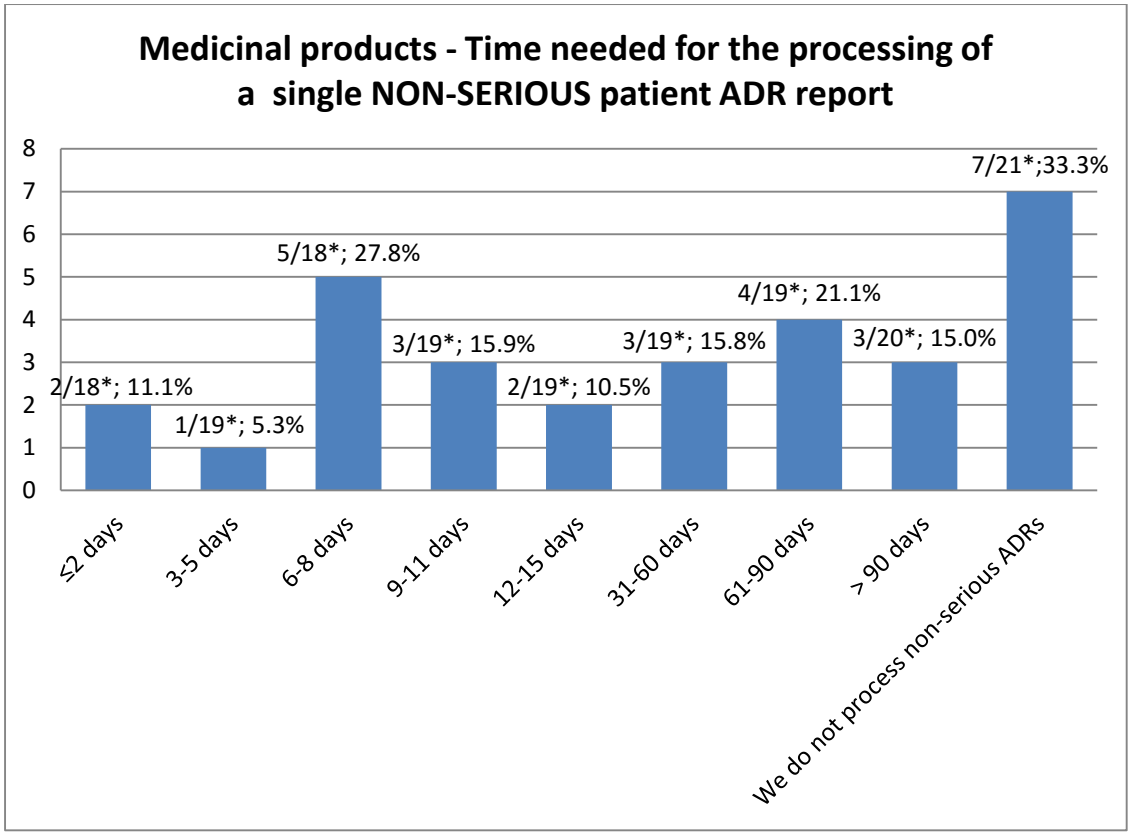
A comparison of the amount of time required to assess a single patient and HCP report

		Patient report		HCP report	
		Count	%	Count	%
Average amount of time required per assessor to assess a single ADR report	<1 hrs	**9**	**32,1%**	**5**	**18,5%**
	1-2 hrs	**10**	**35,7%**	**13**	**48,1%**
	2-4 hrs	**5**	**17,9%**	**8**	**29,6%**
	4-6 hrs	**2**	**7,1%**	**1**	**3,7%**

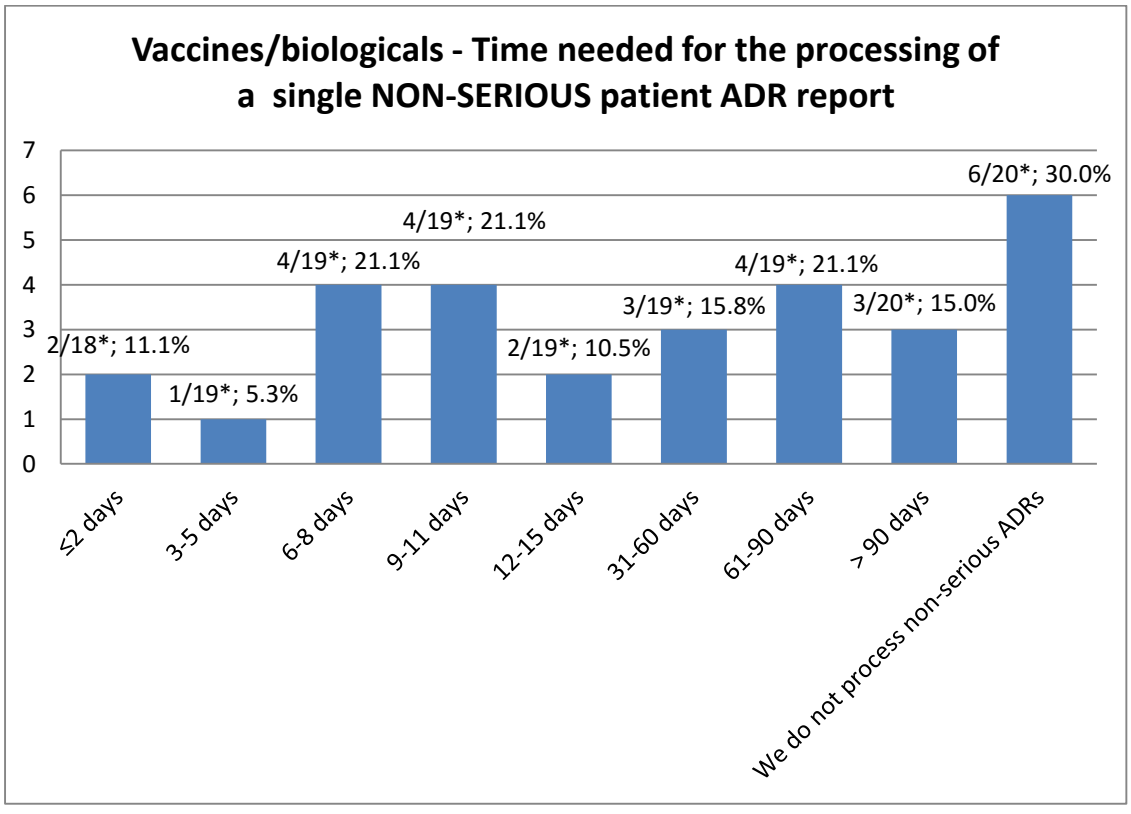
Thirty-six (36) % of respondents responded that patient reports were assessed within 1 to 2 hours followed by 32% responding that patient reports are assessed in less than 1 hour. Almost half of all the respondents estimate that it takes 1 to 2 hours to assess HCP reports followed by nearly 30% estimating it takes 2 to 4 hours to assess a single HCP report.

Question T2Q40: What is the average amount of time needed for the processing of a single NON-SERIOUS patient ADR report?
(start of the process is equal to the date of receipt of the ADR report into the database; end of process is equal to the date of sending of the ICSR to the Eudravigilance)

	Medicinal products		Vaccines/Biologics	
	Yes	No	Yes	No
≤2 days	❍	❍	❍	❍
3-5 days	❍	❍	❍	❍
6-8 days	❍	❍	❍	❍
9-11 days	❍	❍	❍	❍
12-15 days	❍	❍	❍	❍
16-30 days	❍	❍	❍	❍
31-60 days	❍	❍	❍	❍
61-90 days	❍	❍	❍	❍
> 90 days	❍	❍	❍	❍
We do not process non-serious ADRs	❍	❍	❍	❍
Our institution is not responsible for this activity	❍	❍	❍	❍



*number of respondents

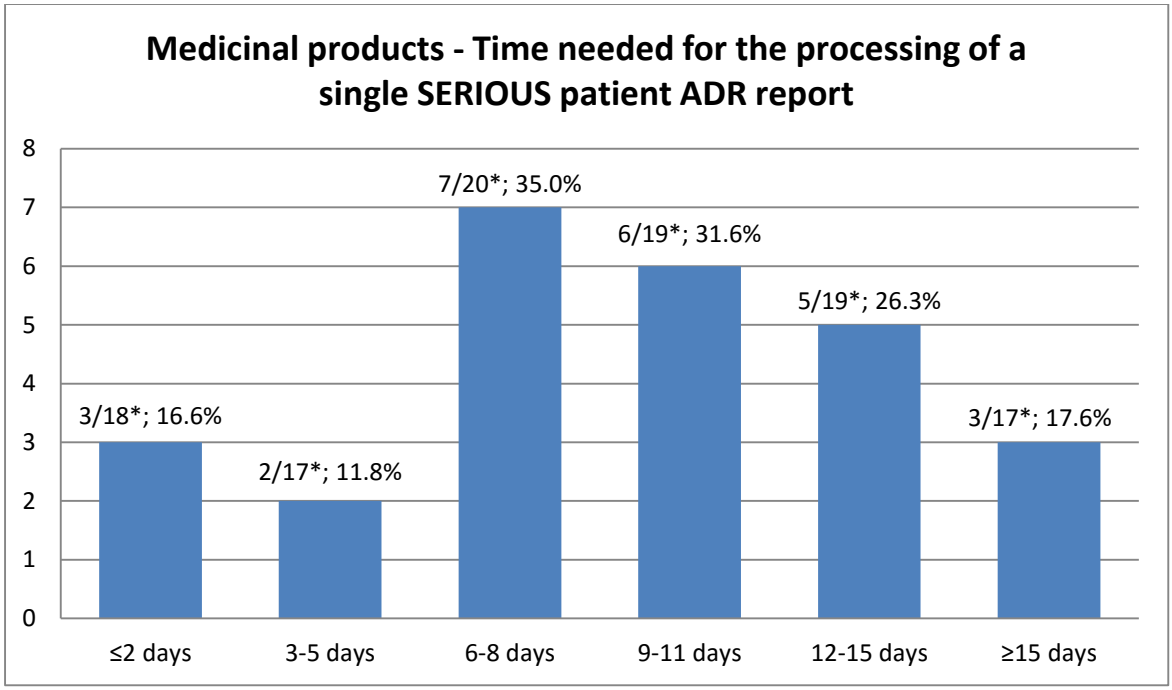


*number of respondents

Question T2Q41: What is the average amount of time needed for the processing of a single SERIOUS patient ADR report?

(start of the process is equal to the date of receipt of the ADR report into the database; end of process is equal to the date of sending of the ICSR to the Eudravigilance)

	Medicinal products		Vaccines/Biologics	
	Yes	No	Yes	No
≤2 days	❍	❍	❍	❍
3-5 days	❍	❍	❍	❍
6-8 days	❍	❍	❍	❍
9-11 days	❍	❍	❍	❍
12-15 days	❍	❍	❍	❍
≥15 days	❍	❍	❍	❍
Our institution is not responsible for this activity	❍	❍	❍	❍



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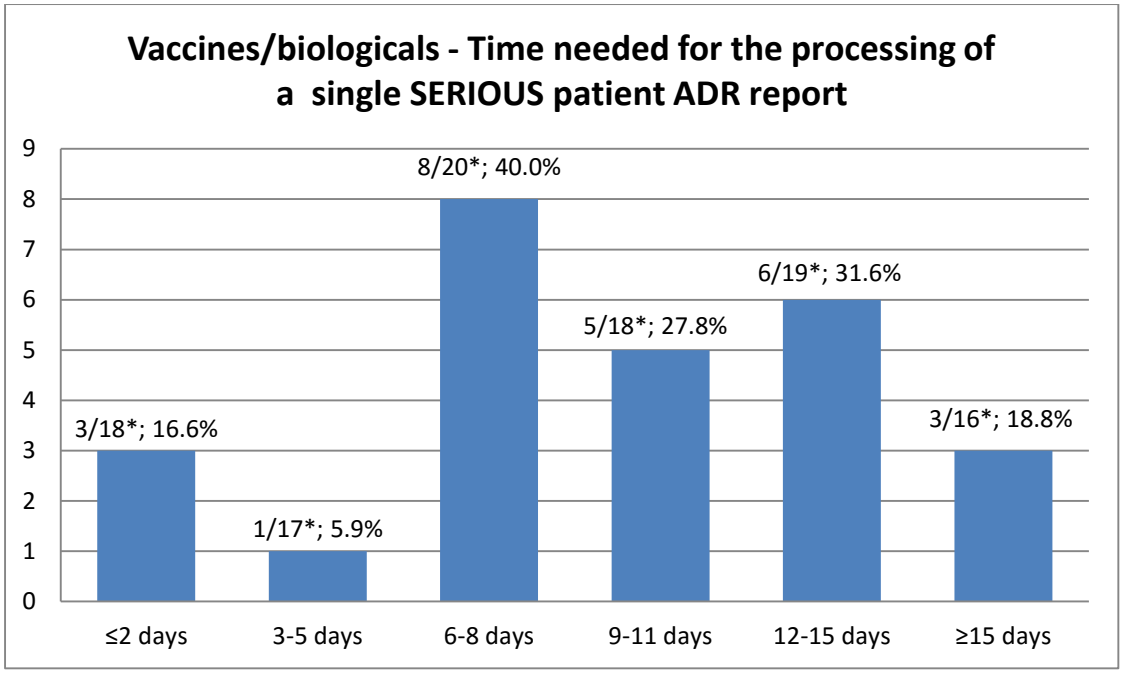


*number of respondents

All countries provided answers to this set of 4 questions but not every MS provided Yes/No answer to all options given in the question (number of answers per option ranged from 16 to 21). Also, some countries offered more than one option within the question which was taken into account during the interpretation of results since there can be only one average time for assessing ADRs.
Most MSs indicated that the average time for processing non-serious ADRs for medicinal products is 6-8 days (5/18) and 61-90 days (4/19).
Average time needed for processing serious ADRs for medicinal product is 6-8 days (7/20) and 9-11 days (6/19).

Analysis of the data for time processing of both serious and non-serious data for vaccines/biologics follow the same pattern as the data for assessing ADRs for medicinal products except for one additional peak at 9-11 days for non-serious ADRs (4/19). One additional peak was noticed also at 12-15 days for serious ADRs (6/19).
This additional peak might be statistical artefact due to small numbers, but it is indicative that it appeared both for serious and non-serious ADRs. Answers provided in different parts of WP4 questionnaires related to traceability of biologics indicate that many MSs always follow-up for brand and batch data for vaccines/biologicals (please refer to T1Q79 and T1Q80) which might explain longer time needed for processing.

Around 1/3 of the MSs (7/21) indicated that they do not process non-serious ADRs.

Analysis of the data showed little or no difference in timelines needed for processing patient ADR related to all ADRs.

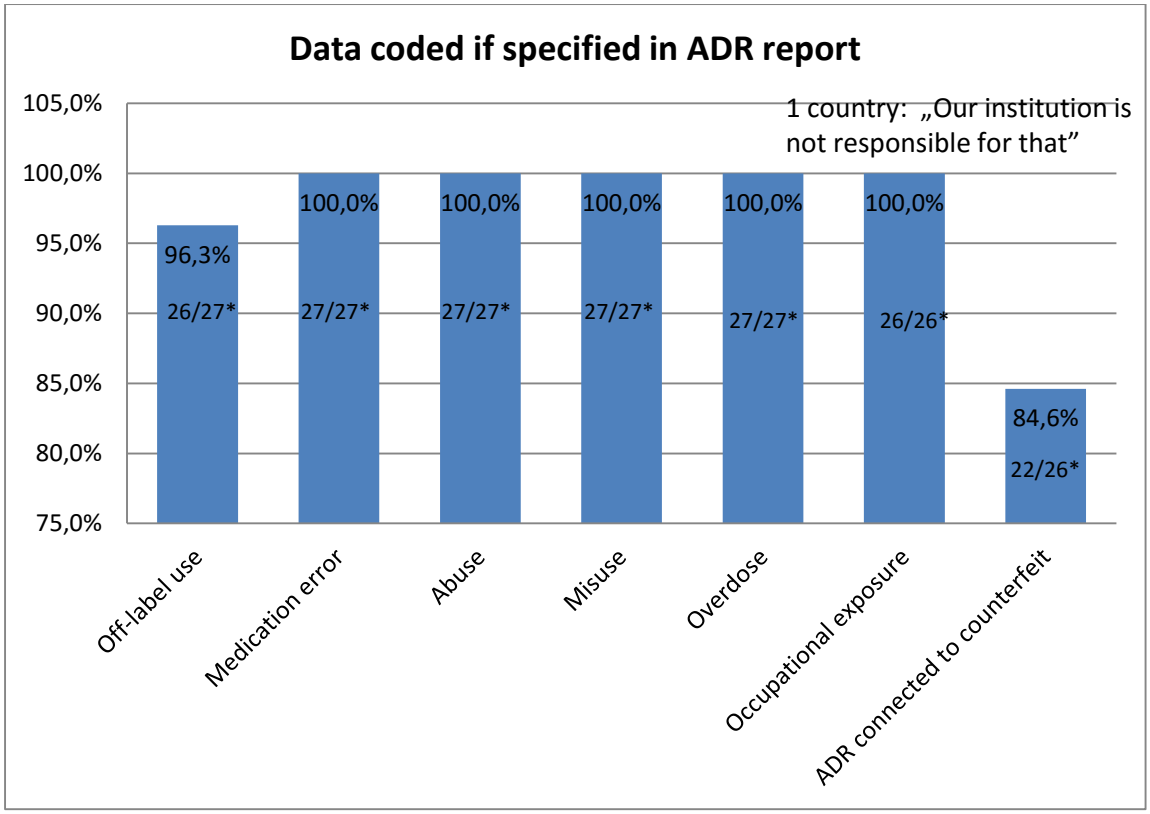
A comparison was made to find out whether there is a difference in processing of a single non-serious and/or serious ADR report between all (please see T1Q59 and T1Q60) and patient ADRs (please see T2Q40 and T2Q41).
Analysis of the data showed little or no difference in timelines needed for processing patient ADR related to all ADRs. Most MSs indicated that the average time for processing **non-serious ADRs** for medicinal products (both for all and patient ADRs) is **6-8 days** (6/20 all, 5/18 patient) and **61-90 days**. (4/22 all, 4/19 patients).
Average time needed for processing **serious ADRs** for medicinal product is **6-8 days** (9/21 all, 7/20 patient) and **9-11 days**. (9/22 all, 6/19 patients).
Analysis of the data for time processing of both serious and non-serious data for vaccines/biologicals follow the same pattern as the data for assessing ADRs for medicinal products except for one additional peak at **9-11 days** for non-serious ADRs (4/20 all, 4/19 patients). One additional peak was noticed also at **12-15** days for serious ADRs (8/24 all, 6/19 patients).

In addition, around 1/3 of the MSs (7/22 all, 7/21 patient reports) indicated that they **do not process non-serious ADRs** with similar pattern between all and patient ADRs.

Coding practice for off-label use, medication error, abuse, misuse, overdose, occupational exposure, ADRs connected to counterfeit in patient ADRs

Question T2Q42: When do you code the following in patient ADRs:

	If specified in ADR report		When the ADR is reviewed/assessed		We do not routinely code for this	
	Yes	No	Yes	No	Yes	No
Off-label use	❍	❍	❍	❍	❍	❍
Medication error	❍	❍	❍	❍	❍	❍
Abuse	❍	❍	❍	❍	❍	❍
Misuse	❍	❍	❍	❍	❍	❍
Overdose	❍	❍	❍	❍	❍	❍
Occupational exposure	❍	❍	❍	❍	❍	❍
ADR connected to counterfeit	❍	❍	❍	❍	❍	❍
Our institution is not responsible for this activity	❍	❍	❍	❍	❍	❍



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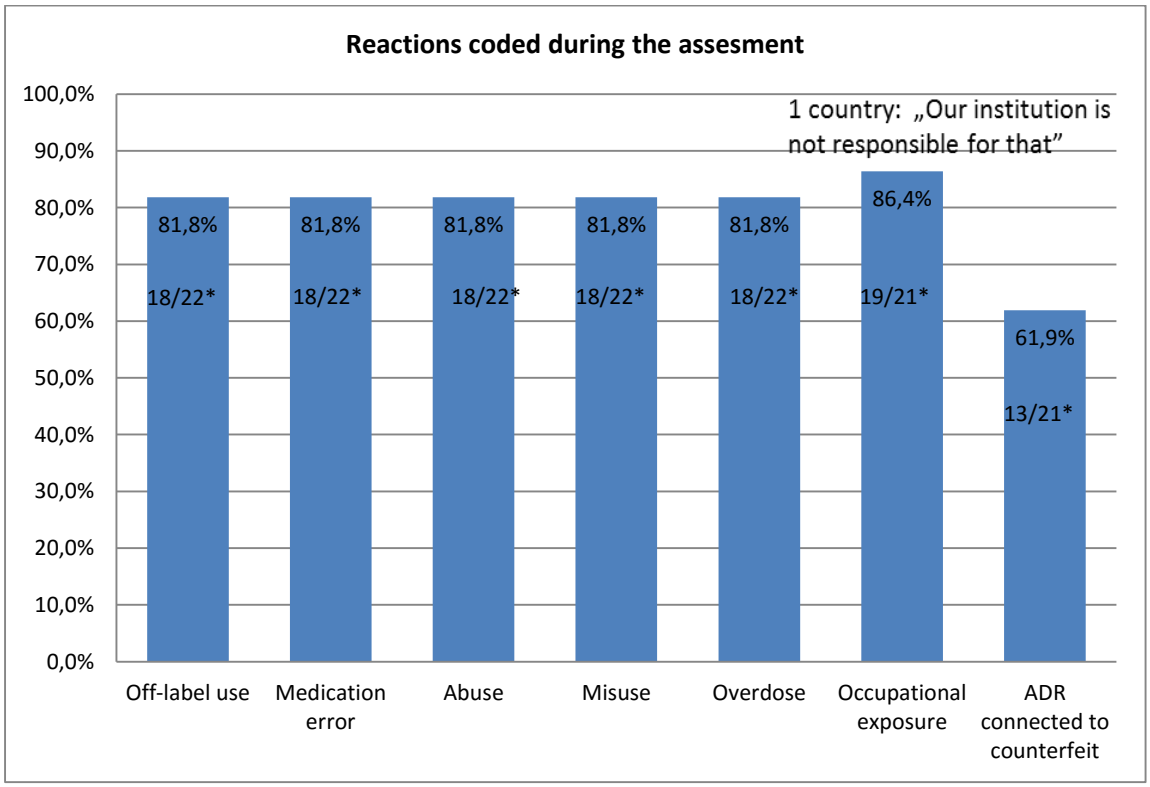


*Number of respondents

Different number of MSs answered to different subset of questions:

- on average 27 MSs provided answer to question whether they code special kind of reactions (off-label use, medication error…) if already reported in ADR
- on average 22 MSs per option provided answers on question about coding during assessment
- on average 13 answers in total per option for question on not routinely coding off-label use, medication error, abuse, misuse, overdose, occupational exposure…

The exception was always number of answers for option- our institution is not responsible for this activity with lower response rate.

Difference in number of responses makes the analysis more difficult but the general conclusion is that almost all MSs code for specific reactions (off-label use, medication error, abuse….) if it is stated in report which was expected and in line with new definition of ADR introduced with new PhV legislation. Only one MS stated they do not code off-label use if specifically stated in patient ADR report.

In around 80 % of MSs (average number of answers 22 MSs per option) reactions are coded during the assessment of the case. From the question it cannot be concluded which percent of cases are additionally coded during the assessment. This kind of assessment requires more time for assessment as well as assessors expertise.

We compared results received for this question (T2Q42) to the ones received fot T1Q72. The aim of these two questions were to see coding practices of MSs related to coding for off-label use, medication error, abuse, misuse, overdose, occupational exposure, ADRs connected to counterfeit.
Similar pattern was seen between the MSs in coding strategies with regards to the HCPs and patient ADRs.
Difference in number of responses makes the analysis more difficult but the general conclusion is that almost all MSs code for specific reactions (off-label use, medication error, abuse….) if it is stated in report which was expected regardless of the fact if it is a case of patient report and in line with new definition of ADR introduced with new PhV legislation. Only one MS stated they do not code off-label use if specifically stated in patient ADR report and not in HCP reports.

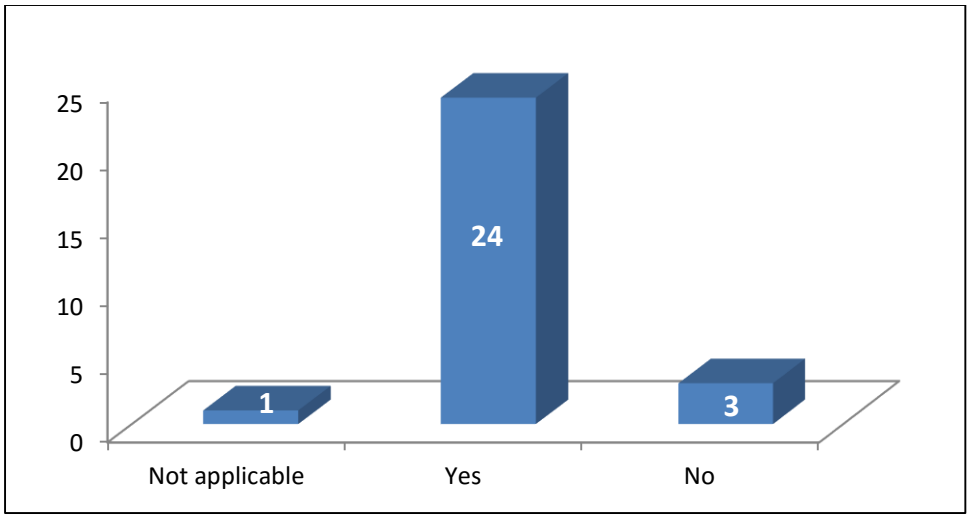
T2Q43 Feedback and follow-up

The purpose of this section is to find out if feedback is provided to patient reporters, if the patient reports are followed up and how is it done. Moreover, information on medical confirmation is collected – whether actively sought, when it is done and what is the percentage of medically confirmed reports (definition according to GVP Module VI is provided within this set of questions).

Question T2Q44: Do you give feedback to patients?

- ❍ Yes
- ❍ No
- ❍ Not applicable, please specify reason _____
- ❍ Our institution is not responsible for this activity

28 MSs provided answer to this question. 24 MSs provide feedback to patients; 1 MS responded "not applicable", since feedback to patients is provided at the level of regional centres; 3 MSs responded "no" to this question, which might be due to national personal data protection policies.



Question T2Q45: What feedback do you give to patients?

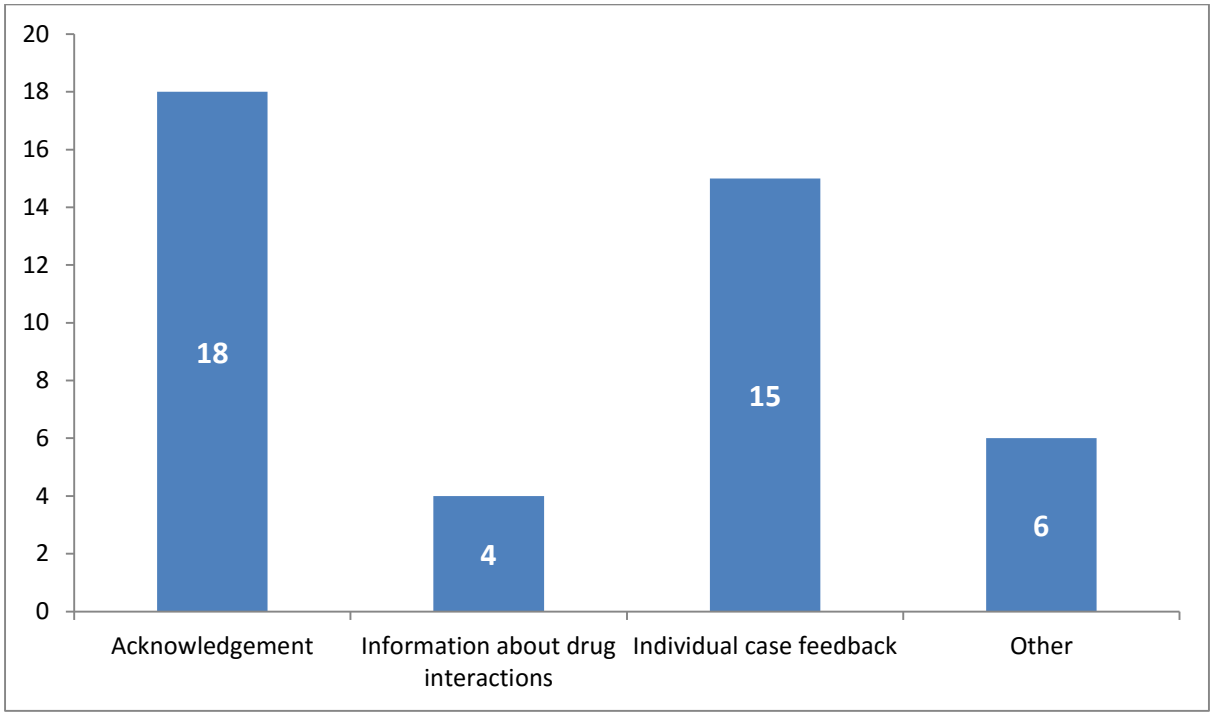
	Yes	No
Acknowledgement only		
Information about drug interactions		
Individual case feedback		
Other, please specify		
Our institution is not responsible for this activity		

Twenty-three (23) MSs provided answer to this question. 18 MSs provide acknowledgements, out of which 7 MSs chose "Acknowledgement only" as the only option in this question. 15 MSs provide individual case feedback, 4 MSs provide information about drug interactions and 6 MSs answered "other" and provided further information about the feedback, which is either provided if requested or assessed as needed, or includes information not offered in this question (feedback provided in case of suspected quality problem and ADR and feedback which includes SPC information, i.e. indications, dosage, warnings, pregnancy/lactation, reactions etc.).

The type and amount of data included in automated acknowledgements were not investigated in this question. For these acknowledgements it can however be considered to

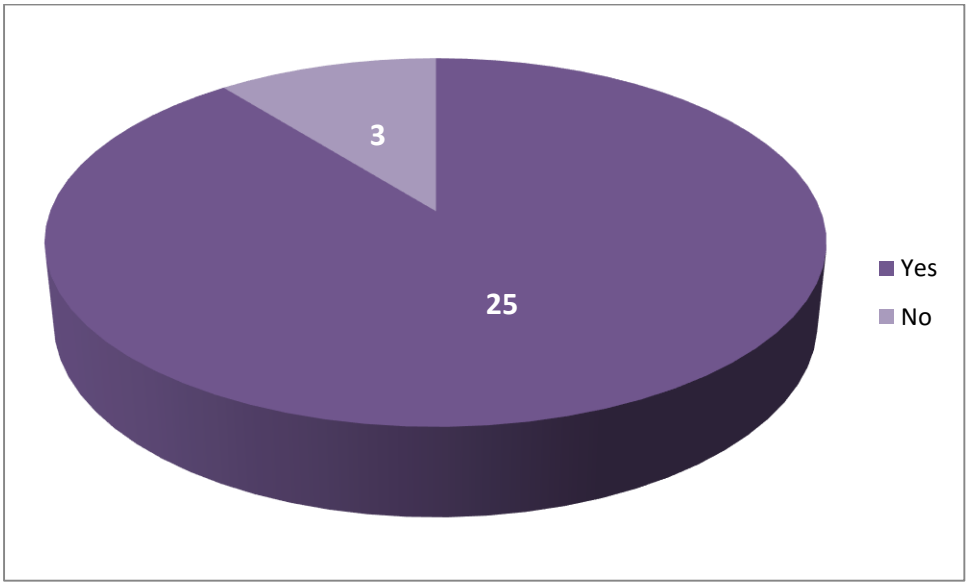
include as many relevant information as needed in order for the acknowledgements to be as informative as possible.

The type of feedback provided to patients is presented below.



Question T2Q46: Do you perform follow up?

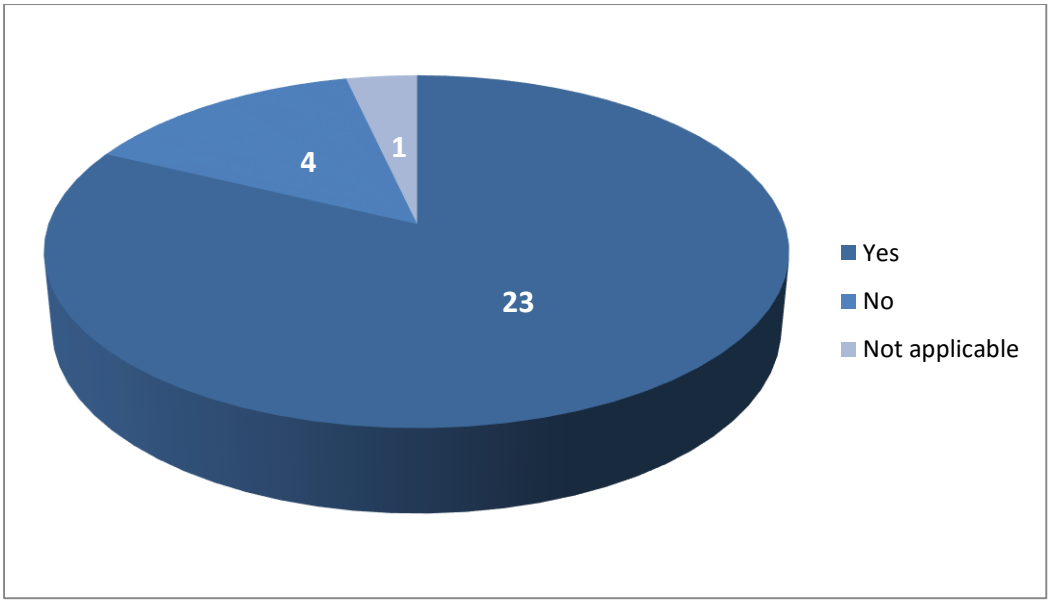
- ❍ Yes
- ❍ No
- ❍ Not applicable, please specify reason _____
- ❍ Our institution is not responsible for this activity



Twenty-eight (28) MSs provided answer to this question, out of which 25 MSs confirmed that they perform follow up, while 3 MSs answered that they do not perform follow up. This might be due to national personal data protection policies.

Question T2Q47: Do you ask patients to contact their doctor?

- ❍ Yes
- ❍ No
- ❍ Not applicable, please specify reason _____
- ❍ Our institution is not responsible for this activity



Twenty-eight (28) MSs provided answer to this question. Twenty-three (23) MSs answered "yes"; 4 MSs answered "no", which might be due to national personal data protection policies and 1 MS answered "not applicable", providing the clarification that it rarely in special circumstances asks patients to contact their doctor.

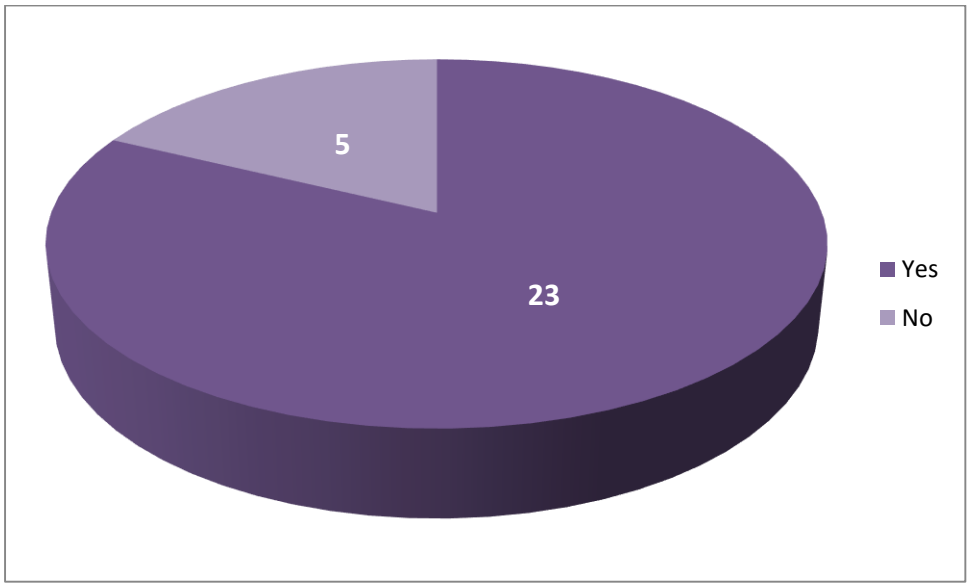
Question T2Q48: Do you just contact patients' doctor without asking for permission?

- ❍ Yes
- ❍ No
- ❍ Not applicable, please specify reason _____
- ❍ Our institution is not responsible for this activity

This question was presented to 5 MSs which did not answer "yes" to T2Q47. Four (4) MSs responded "no" and 1 MS, in which contact details of patients' doctor are mandatory field for patients' reports, responded "yes".

Question T2Q49: Do you follow up directly with patients?

- ❍ Yes
- ❍ No
- ❍ Not applicable, please specify reason _____
- ❍ Our institution is not responsible for this activity



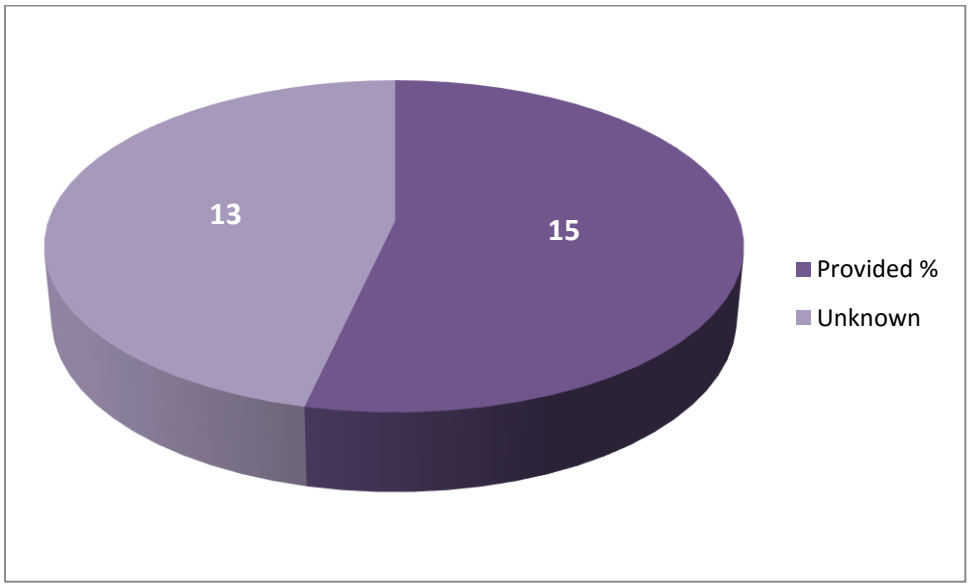
Twenty-eight (28) MSs provided answer to this question. 23 MSs (82,1%) follow up directly with patients, while 5 MSs (17,9%) do not follow up directly with patients. This might be due to national personal data protection policies or if follow up with patients is done at the level of regional centres.

Question T2Q50: What is the % of medically confirmed patient ADR reports?

In accordance with the ICH-E2D guideline (Module VI, EMA/873138/2011).
**a healthcare professional is defined as a medically-qualified person such as a physician, dentist, pharmacist, nurse, coroner or as otherwise specified by local regulations;*
**a consumer is defined as a person who is not a healthcare professional such as a patient, lawyer, friend, relative of a patient or carer.*
Medical documentation (e.g. laboratory or other test data) provided by a consumer that support the occurrence of the suspected adverse reaction, or which indicate that an identifiable healthcare professional suspects a reasonable possibility of causal relationship between a medicinal product and the reported adverse event, are sufficient to consider the spontaneous report as confirmed by a healthcare professional.
If a consumer initially reports more than one reaction and at least one receives medical confirmation, the whole report should be documented as a spontaneous report confirmed by a healthcare professional and be reported accordingly.

*Similarly, if a report is submitted by a medically qualified patient, friend, relative of the patient or carer, the case should also be considered as spontaneous report confirmed by a healthcare professional***.**

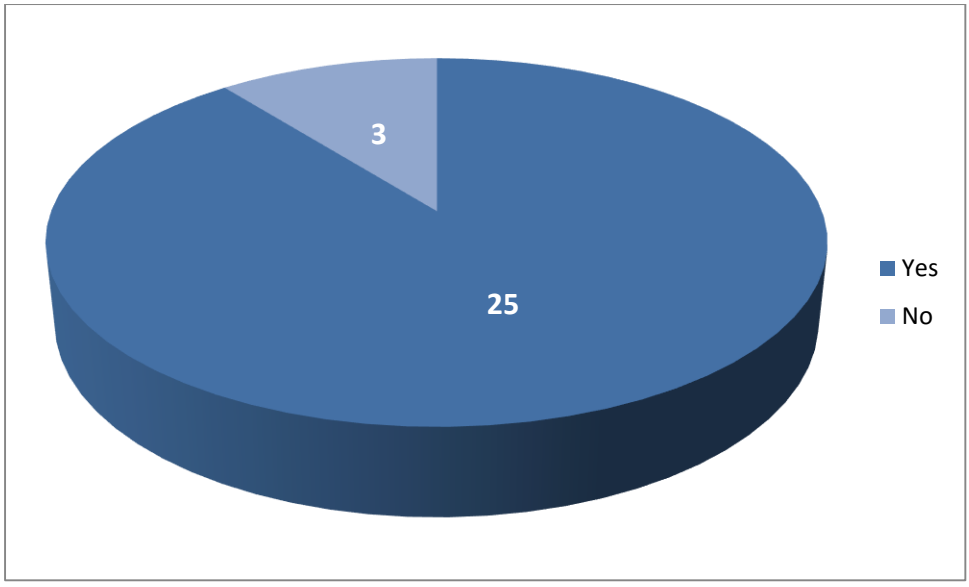
- ❍ % _____
- ❍ Unknown
- ❍ Our institution is not responsible for this activity



Twenty-eight (28) MSs provided answer to this question. 15 MSs (53,6%) provided the percentage of medically confirmed patient ADR reports, while 13 MSs (46,4%) did not provide this information, which might be due to national ADR database limitations.
The mean percentage of medically confirmed patient ADR reports is 39%, based on the data provided by 15 MSs. It should, however, be noted that absolute numbers of patient reports are quite low for some MSs who have high rates of medically confirmed patient ADR reports.

Question T2Q51: Do you consider reports valid without medical confirmation?

- ❍ Yes
- ❍ No
- ❍ Our institution is not responsible for this activity

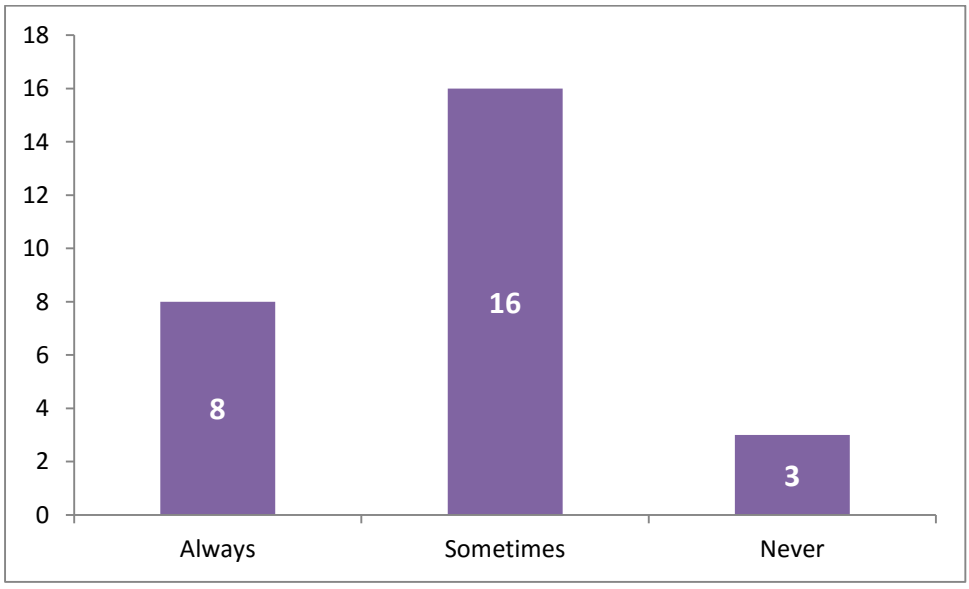


Twenty-eight (28) MSs provided answer to this question. 25 MSs (89,3%) consider reports valid without medical confirmation, while 3 MSs (10,7%) do not.

Question T2Q52: Is medical confirmation actively sought for patient ADR reports?

- ❍ Always
- ❍ Sometimes
- ❍ Never
- ❍ Our institution is not responsible for this activity

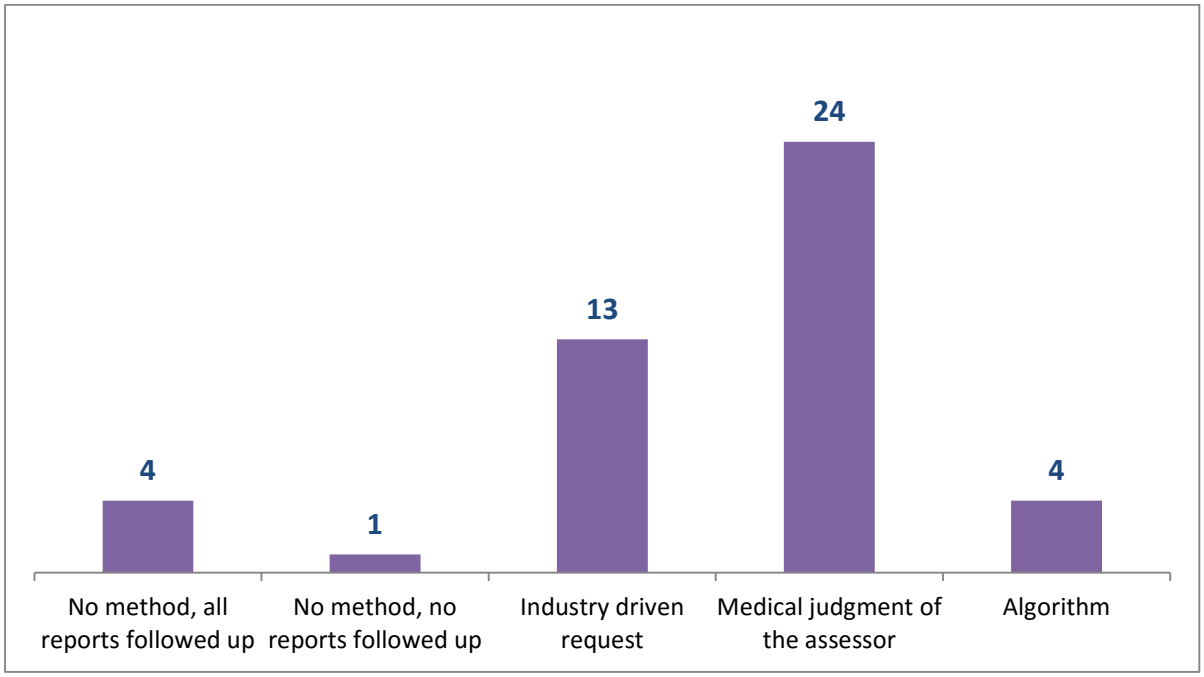
Twenty-seven (27) MSs provided answer to this question. 8 MSs (29,6%) always seek medical confirmation, 16 MSs (59,3%) sometimes seek medical confirmation, while 3 MSs (11,1%) never seek medical confirmation for patient ADR reports, which might be due to national personal data protection policies.



Question T2Q53: What method do you use to determine which reports are followed up for further?

**follow up defined according to GVP Module VI*

	Yes	No
No method, all reports followed up		
No method, no reports followed up. Please specify why		
Industry driven request		
Medical judgment of the assessor		
Algorithm, please specify if available		
Our institution is not responsible for this activity		



Twenty-seven (27) MSs provided answer to this question. Twenty-four (24) MSs (96,0%) responded that the medical judgment of the assessor is used to determine which reports are followed up further, 13 MSs (61,9%) responded that follow up is determined by industry driven requests, 4 MSs (16,7%) responded that algorithm is used to determine which reports to follow up, 4 MSs (16,7%) responded that all reports are followed up while 1 MS (4,8%) responded that no reports are followed up since it is not possible because the reports are anonymous.

Out of 4 MSs which responded that algorithm is used, 1 MS stated that there is SOP in place to follow, 1 MS stated that biological medicinal product are followed up when information about brand and batch number is not included, 1 MS responded that medical confirmation is sought for serious reports and 1 MS responded that serious reports are followed up if not medically clear. Request for follow up information (about exploring the possibility to provide the SOP) was sent to 1 MS. No responses have so far been received.

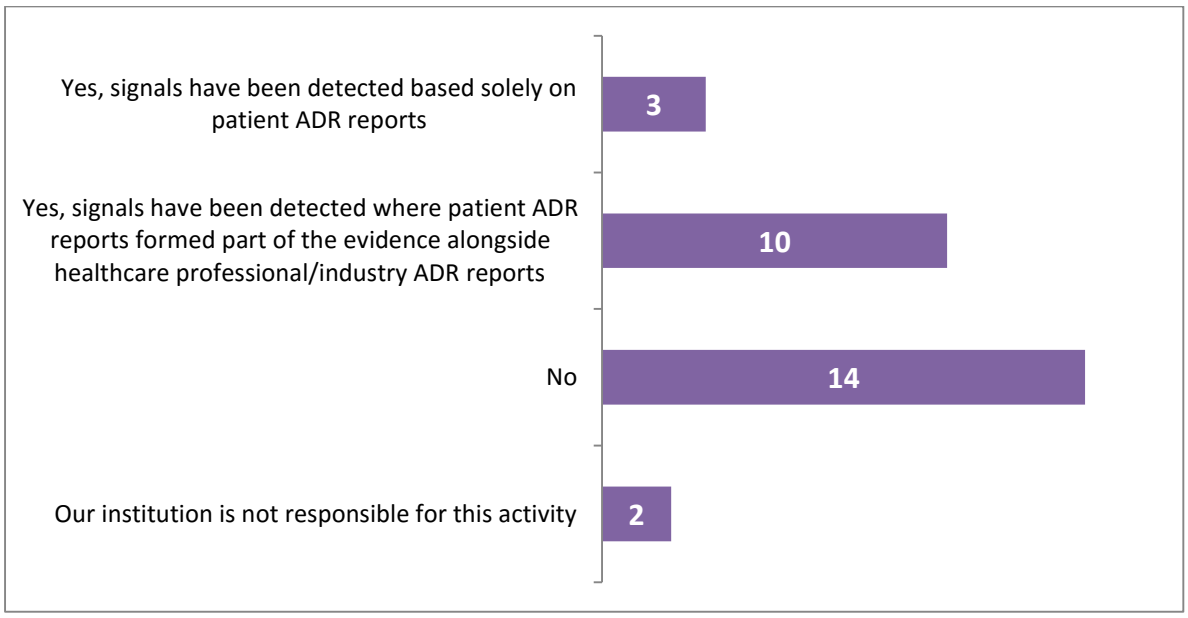
T2Q54 Signals

This set of questions is focusing on signals from patient ADR reports – number of signals in the certain period of time. Free text field is provided to specify which the related safety issues were.

Question T2Q55: Have patient ADR reports contributed to detection of any signals (multiple choices possible)?

- ❑ Yes, signals have been detected based solely on patient ADR reports
- ❑ Yes, signals have been detected where patient ADR reports formed part of the evidence alongside healthcare professional/industry ADR reports
- ❑ No
- ❑ Our institution is not responsible for this activity

Twenty-eight (28) MSs provided answer to this question. Fourteen (14) MSs responded that patient ADR reports did not contribute to detection of signals, 10 MSs responded that signals have been detected where patient ADR reports formed part of the evidence alongside reports from other sources, 3 MSs responded that signals have been detected based solely on patient ADR reports and 2 MSs responded that their institution is not responsible for this activity. It is important to note, in line with Guideline on good pharmacovigilance practices (GVP) Module IX – Signal management that signal detection is the first step in signal management, followed by signal validation, analysis and prioritisation, assessment and subsequent recommendation for action. Additionally, with regards to operation of the EU regulatory network, it is important to note that signals discussed at the PRAC represent only a subset of all signals discussed in the regulatory framework, as discussed by A. C. Pacurariu et al. in *A Description of Signals During the First 18 Months of the EMA Pharmacovigilance Risk Assessment Committee* (Drug Saf (2014) 37:1059–1066, DOI).



Question T2Q56: If YES, please specify the number of signals detected:

Question T2Q57: If YES, please specify the time period these signals were detected over:

Question T2Q58: If YES, please provide more details of the ADRs safety issues:

The answers to the questions 56-58 were grouped in a table below. Eleven (11) MSs (provided answer to this question. Four (4) MSs did not provide the number of signals detected, the time period the signals were detected over and the details of the safety issues.

Country	Number of signals	Time period	Source of signals	Details on signals
X	2	2013	Solely from patient reports	Not provided
X	1	2012	Solely from patient reports	Infanrix and extensive swelling of vaccinated limb
X	1	2014	Solely from patient reports	Pseudoephedrine and misuse
X	34	2010-2013	Involving patient reports	Examples include varenicline and epilepsy, finasteride and memory impairment, leuporelin and injection site reactions and oxybutynin and mouth ulceration
X	at least 8*	2005-2008	Involving patient reports	Pergolide and pathologic gambling, latanoprost and dizziness, topical tacrolimus and malignancies,valproic acid and pubertas praecox, fluorescein and anaphylactic reactions, paroxetine and restless legs, tramadol and flushes, venous thromboembolism and Yasmin
X	at least 3	Not specified	Not specified	Elthroxin and symptoms of hypo-/hyper-dose, Pandemrix, HPV vaccine and POTS
X	1	2013	Involving patient reports	Not provided

* as identified from F. van Hunsel et al: The proportion of patient reports of suspected ADRs to signal detection in the Netherlands: case–control study (Pharmacoepidemiology and Drug Safety 2011; 20: 286–291)

T2Q59 Comparison to ADR reports from healthcare professionals

Question T2Q60: Have you performed any comparison of patient ADR reports to healthcare professional reports?

- ❑ Completeness, please describe your findings _____
- ❑ Seriousness, please describe your findings _____
- ❑ Other, please describe _____
- ❑ No, we have not performed any comparison
- ❑ Our institution is not responsible for this activity

Eight (8) MSs provided information about completeness comparisons, 7 MSs provided information about seriousness comparisons and 6 MSs provided information about other performed comparisons.
Six (6) MSs provided general comments regarding the completeness of patient vs. HCP reports. Four (4) MSs commented that patient reports contain more details, are informative and provide more information on the impact on quality of life, while 2 MSs commented that the completeness of structured data is lower in patient reports.
Four (4) MSs provided general comments regarding the seriousness of patient vs. HCP reports. One (1) MS commented that the proportion of non-serious reports is lower in patient reports than in overall reports from all reporters, while another MS commented that HCPs report serious reports more frequently than patients. One (1) MS commented that there is no difference in seriousness between patient and physician reports, but that patients report serious ADRs more frequently than pharmacists. One (1) MS commented that the perception of seriousness is different for patients and perhaps not always in line with what the definition of serious ADR is.
Four (4) MSs provided general comments on other comparisons, which included proportion of total reports, gender, age, time lag between suspect adverse drug reaction and reporting, number of ADRs, SOCs, ADR-terms, drugs, drug-ADR combination, causality, categories of seriousness and outcomes. No specific data were provided.

Three (3) MSs included references to relevant scientific articles:

1. Effect of Pharmacist Involvement on Patient Reporting of Adverse Drug Reactions: First Italian Study by R. Leone et al (Drug Safety 2013; 36(4):267–276);
2. Adverse Drug Reaction Reporting by Patients in the Netherlands – Three Years of Experience by J. de Langen et al (Drug Safety 2008; 31(6):515-524);
3. Evaluation of patient reporting of adverse drug reactions to the UK 'Yellow Card Scheme': literature review, descriptive and qualitative analyses, and questionnaire surveys (Health Technology Assessment 2011 May; 15(20):1-234).

Ad 1. This study investigated the potential impact of an intervention to promote patient reporting in community pharmacies in the Veneto region of Italy and compared the characteristics of patients' and general practitioners' (GPs) reports of ADRs collected over a 1 year-period (April 2010–March 2011). No specific completeness indicators were used; the authors did discuss that the reports sent by patients were mostly adequate, since about 80 % of reports contained all the information needed for their evaluation. Regarding the seriousness (according to WHO criteria), patients in this study reported a higher percentage

of known and non-serious reactions than did GPs, with serious reports comprising only 5.1% (95% CI 4.1-6.1) of all patient reports, while 20.8% (95% CI 15.1-26.1) of GP reports were serious. Other comparisons performed in this study include:

- causality (according to Naranjo algorithm score) – 87.1% (95 % CI 85.6–88.7) of patient reports were classified as possible, while 87.6% (95 % CI 83.3–91.9) of reports by GPs were classified as probable;
- sex and age distribution – in both groups more reports were made by women than men, and by those aged 18–65 years compared with older people; this difference was greater in patient than in GP reports;
- type of reaction (according to the WHO-ART system organ classes) – patients more frequently reported gastrointestinal reactions (particularly abdominal pain, nausea and diarrhoea), whereas GPs more frequently reported systemic problems (headache, fever) and skin reactions (urticaria, pruritus and erythematous rash); the most evident differences between the two groups of reports were observed for reports of gastrointestinal, skin, application site, haematological and liver reactions;
- suspected drugs (according to first level ATC classification) – drugs belonging to ATC groups M (musculoskeletal system) and N (nervous system) were more frequently reported by patients than by GPs, whereas those belonging to groups J (anti-infective drugs for systemic use), L (antineoplastic and immunomodulating agents) and V (various) were more frequently reported by GPs than patients.

Ad 2. To the knowledge of the authors, this was the first study to describe long-term experiences with patient reporting as part of a spontaneous reporting system. In this study, the number of reports received, age and sex of the patients, characteristics of the most frequently reported drugs and characteristics of the ADRs (most frequently reported ADRs, seriousness, outcome) reported to LAREB in a 3-year period (April 2004–April 2007) were compared between patient reports and reports from healthcare professionals (general practitioners, specialist doctors and pharmacists). No specific completeness indicators were used; the authors however discuss that only electronic reporting, which facilitates the completeness of information, is available to patients and that only if all mandatory fields are filled in the report can be submitted to the centre; another general comment on patient reports usually containing sufficient medical information to be useful to pharmacovigilance was made. The seriousness (according to CIOMS criteria) of the reports was not significantly different between reports from patients (19.5%) and from healthcare professionals (21%). However, patients reported a significantly higher number of life-threatening ADRs (5.2% vs 2.7%) and disability (2.3% vs 0.4%) than healthcare professionals. Other comparisons performed in this study include:

- sex and age - of the reports from patients, 63% of the patients were female compared with 61% in the reports from healthcare professionals; the mean age of patients in the reports from patients was also similar (48 years) to that in the reports from healthcare professionals (49 years);
- suspected drugs (according to first three levels of the ATC classification) - the five drug categories most frequently reported by patients were successively HMG Co-A reductase inhibitors (‘statins’), selective serotonin reuptake inhibitors, β-adrenoceptor antagonists (‘β-blockers’), anticoagulants and proton

pump inhibitors; the top five drugs reported by the different groups of healthcare professionals showed great similarity with that of patients;

- most frequently reported ADRs (according to MedDRA) and outcome – nervous system disorders, psychiatric disorders, gastrointestinal disorders, musculoskeletal disorders and general disorders/administration-site conditions were the five most involved organ systems for patients and general practitioners, there were strong similarities between reports received form patients and reports from other healthcare professionals; regarding the outcome – there was a significant difference between patient reports and reports from healthcare professionals in the proportion of reports that included mention of the outcome of the ADR (87% vs 68%; $\chi 2$ test: $p < 0.01$), patients reported non-recovery (35.4%) from the ADR significantly more often than healthcare professionals (16.7%).

Ad 3. The objectives of this publication were to evaluate the pharmacovigilance impact of patient reporting of ADRs by analysing reports of suspected ADRs from the UK Yellow Card Scheme (YCS) and comparing reports from patients and HCPs and to elicit the views and experiences of patients and the public about patient reporting of ADRs. The objectives and research questions relate to:

- a review of the literature
    - Study 1: Review of the world literature describing and comparing patient and HCP reporting of ADRs
- studies based on the analysis of Yellow Card data for patients and health professionals evaluating the pharmacovigilance impact of patient reporting of suspected ADRs
    - Study 2: Description of the characteristics of reports from patients and HCPs
    - Study 3: Assessment of the pharmacovigilance impact of reports from patients and HCPs using signal generation analysis and clinical assessment of reports.
    - Study 4: Qualitative analysis of reports from patients and HCPs
- studies considering the views and experiences of patients and members of the public regarding patient reporting
    - Study 5: Questionnaire survey to capture the views and experiences of patients who have made reports
    - Study 6: Telephone interviews to explore further the views and experiences of patients who have made reports
    - Study 7: Focus groups and usability testing with members of the public regarding patient reporting
    - Study 8: Omnibus survey to assess public awareness of the YCS.
-

Ad Study 2. The objectives were to: identify the characteristics of patients reporting to the YCS; identify the types of drug, types of suspected adverse reaction and seriousness of suspected reactions reported by patients; determine whether there are differences in the time lag between ADR occurrence and reporting for patients and health professionals; investigate the factors associated with patient reports compared with those made by health professionals. No specific completeness indicators were used in this study. Regarding the seriousness, similar proportions of reports contained at least one reaction term that was

classified as 'serious' by the MHRA (58.3% for patients vs 58.8% for HCPs; p = 0.58). The following were recorded more commonly in HCP reports than in patient reports: 'caused hospitalisation' (18.8% vs 12.9%, respectively); 'life-threatening' (11.1% vs 6.2%, respectively); and 'caused death' (2.6% vs 0.7% respectively) (p < 0.001 for each comparison). Other comparisons performed in this study include:

- age and sex of patients: significantly more Yellow Card reports were made for female patients, whether reported by the patient or via HCPs (both p < 0.001); the median age of patients, as reported by either patients or HCPs, was similar (p = 0.06);
- method of reporting: the most frequent method used to report an ADR was the paper Yellow Card form for both reporter groups (79.0% of patients and 87.7% of HCPs); the internet was the next most frequent method (17.6% of patients and 12.3% of HCPs), followed by the telephone (3.5% of patients and 0.03% of HCPs);
- reactions: patient reports contained a significantly higher number of suspected ADRs per report than did HCP reports [median (IQR) of 3 (2 to 5) vs 2 (1 to 3), respectively; p < 0.001]; almost one-half (45.2%) of HCP Yellow Card reports contained only one ADR compared with 21.6% of patient Yellow Card reports; only 3.3% of HCPs reported over five reactions per report compared with 21.8% of patient reports (p < 0.001 overall); more patient reports had mention of a nervous system disorder problem (41.5%) than those of another organ system; this was followed by problems categorised as 'general disorders and administration site conditions' (39.8%), problems that were also the second most common organ system affected according to the HCP reports (23.1%); the most common category in the HCP reports was skin and subcutaneous tissue disorders (23.2%); the median (IQR) word count (excluding reports with zero word counts) used to describe the suspected reaction was significantly higher for patient reports than for HCP reports [45.0 (22.0 to 74.0) vs 15.0 (9.0 to 26.0), respectively; p < 0.001];
- suspected drugs: a higher proportion of patient reports than of HCP reports contained more than one suspect drug (16.1% vs 9% respectively; p < 0.001); the most frequent category of drug suspected of being linked to an ADR was for the nervous system, for both patient (33.2%) and HCP (26.2%) reports; this was followed by cardiovascular system drugs from patient reports (21.8%) and anti-infectives for systemic use from HCP reports (19.4%); a statistically significant difference in the percentage of type of suspect drug between reporters was shown for drugs of the nervous system; cardiovascular system; systemic hormonal preparations, excluding sex hormones and insulin; antiparasitic products, insecticides and repellents; herbals/complementary medicine (which all had higher proportions in the patient than HCP reports); anti-infectives for systemic use; antineoplastic and immunomodulating agents; blood and blood-forming organs; and, 'various' (all of which had higher proportions in the HCP than the patient reports);
- time lag between suspect adverse drug reaction and reporting: patient reporters took a significantly longer median (IQR) time than HCPs to report their reaction to the MHRA [104 (27 to 463) vs 28 (13 to 75) days, respectively; p < 0.001]; however, there was a higher percentage of missing data for the variable 'time

from reaction to report' among patient reports (61.0% of such reports) than among HCP reports (33.2%);

- reaction outcome: a significantly higher proportion of HCPs than patient representatives reported fatal outcomes to the reaction (2.6% vs 0.7%; $p < 0.001$); a significantly higher proportion of HCPs than patient representatives reported that the patient was recovering or that the ADR was resolving (28.4% vs 16.8%; $p < 0.001$); more patients than HCPs reported that they had not recovered or that the reaction had not resolved (36.4% vs 22.2%; $p < 0.001$);

Ad Study 3. For the purpose of this report only the full summary of this study is presented here as follows:

"Using the anonymised data provided by the MHRA for all patient and HCP reports received by the YCS between 1 October 2005 and 30 September 2007, signal generation analysis was undertaken on the whole database of patient and HCP reports.

We identified SDRs, which are 'statistical signals' when the reporting rate for a suspected ADR in association with a particular medicine is disproportionate to that of other products in the database. We then investigated the effects (on SDRs) of including and excluding patient reports from the HCP database. We also did clinical causality assessments on selected drug–ADR pairs from patients and HCPs.

For the signal generation analysis there were 16,566 drug–reaction pairs from patient reports and 28,775 from HCPs, with only 4340 (10.6%) pairs common to both groups. The HCP data set generated a significantly higher proportion of SDRs from the different drug–reaction pairs reported [1939 SDRs (6.7%) vs 649 (3.9%) respectively; difference in proportions 2.8%, 95% CI 2.4% to 3.2%]. Also, a higher proportion of HCP SDRs were for reactions classified as 'serious' by the MHRA compared with patient SDRs (48% vs 28.5% respectively; difference in proportions 19.5%, 95% CI 15.4% to 23.6%) or for drugs undergoing intensive surveillance (black triangle drugs) (30.7% vs 10.9% respectively; difference in proportions 19.8%, 95% CI 16.6% to 23.0%). A similar proportion of SDRs in both groups (15%) was assessed as not being listed on the product's SPC and therefore potentially providing new information.

After combining the patient and the HCP data sets, an additional 508 SDRs were generated that were not produced by either data set alone, whereas 186 SDRs generated by the HCP data set alone were no longer present. The combined data set identified 47 SDRs for reactions classified as serious by MHRA which had not previously recorded on SPCs, whereas eight generated by the HCP data set alone were no longer present. Among the sample of individual reports assessed for causality, most were assessed as having a 'possible' causal association, regardless of reporter group.

Overall, patients appeared to have the potential to make a positive contribution to signal generation by:

- reporting different drug–ADR pairs and generating different SDRs from HCPs
- generating SDRs that may be considered important in the context of pharmacovigilance
- generating additional SDRs when combined with data from HCP reports
- providing information that may be valuable when assessing the likelihood of a causal association between a particular drug and reaction."

Ad Study 4. For the purpose of this report only the full summary of this study is presented here as follows:

"We undertook a qualitative analysis of reports from patients and HCPs and purposively selected a wide range of different types of report. Focusing on the free text describing the ADRs we undertook a content analysis to describe the characteristics of 230 patient and 179 HCP reports, followed by a more detailed inductive qualitative analysis of the free text (which included 40 additional patient reports of drugs purchased OTC and complementary therapies).

The content analysis of text describing suspected reactions showed that patient reports were more likely than those from HCPs to include information about symptoms (93% vs 78%) and to stress the extreme nature of these (47% vs 17% of reports). They were also more likely to highlight the impact of the reaction on the patient (47% vs 12%), particularly the emotional impact (34% vs 7%) or social impact (27% vs 7%). Patients commonly reported on temporal associations, with 61% stating that the suspected ADR had followed the administration of the drug; 26% that it had improved on stopping the drug, 22% that it had occurred on withdrawal of the drug, and 7% that it had recurred on restarting the drug.
The in-depth qualitative analysis demonstrated the richness of accounts from patients and provided numerous detailed and elaborate descriptions of suspected reactions. Patient Yellow Card reports also contained information on reasons for drugs being prescribed, reasons for reporting, how patients identified the ADR, and responses from HCPs. Particularly striking were reports, often in relation to central nervous system drugs, which were extremely distressing, and sometimes frightening, describing confusion, agitation, panic symptoms, mood swings, suicidal thoughts and electric shock sensations. Patient reports vividly described the effects of suspected ADRs on patients' lives, illustrating impact in terms of serious disruption to social and occupational functioning and marked emotional effects. By contrast, where HCPs did comment on the effects of suspected ADRs on patients' lives, the accounts were usually brief and rarely illustrated the profound impact recorded in patient reports."

T2Q61 Lay press monitoring

Question T2Q62: Does your institution perform any systematic lay press monitoring?

- ❍ Yes and ICSRs are entered into the pharmacovigilance database
- ❍ Yes, but ICSRs are NOT entered into the pharmacovigilance database
- ❍ No, our institution does not systematically monitor lay press for ADRs
- ❍ Our institution is not responsible for this activity

Twenty-seven (27) MSs provided answer to this question. 20 MSs (74,1%) responded that their institution does not systematically monitor lay press for ADRs. 3 MSs (11,1%) responded that they perform systematic lay press monitoring and that ICSRs are entered into the pharmacovigilance database. Another 3 MSs (11,1%) responded that they perform systematic lay press monitoring and that ICSRs are not entered into the pharmacovigilance database, while 1 MS (3,7%) responded that their institution is not responsible for this activity.
Request for follow up information ("Please provide details/method - frequency, key words") was sent to 6 MSs. Responses have been received from 4 MSs. The results showed that in 3 out of 4 MSs lay press is monitored on daily bases. In all 4 MSs provider is external

(subscription/contract). Key words mostly include NCA name, terms like medicine, medical device etc., other keywords relating to high profile topics are included as needed.

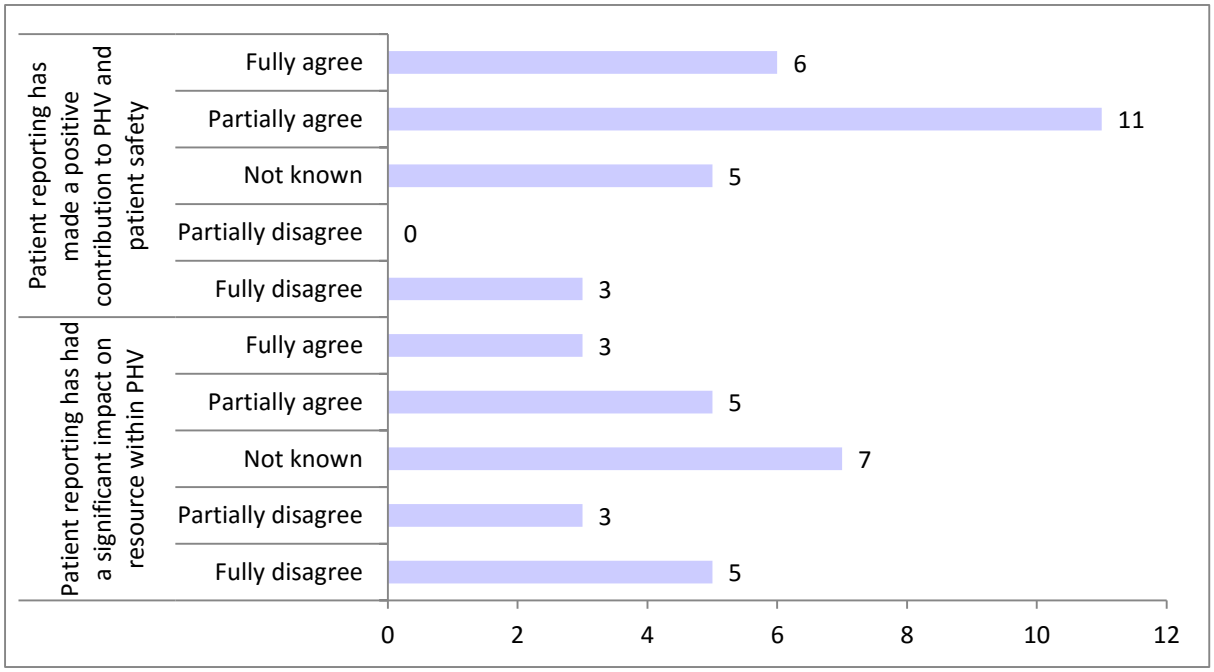
T2Q63 Impact of patient reporting to pharmacovigilance in MS and future plans

This section is looking at impact on resource in PHV and on signals and patient safety. The other question is left open for MS to elaborate on their experience (positive and/or negative) with patient reporting and the future plans with patient reporting.

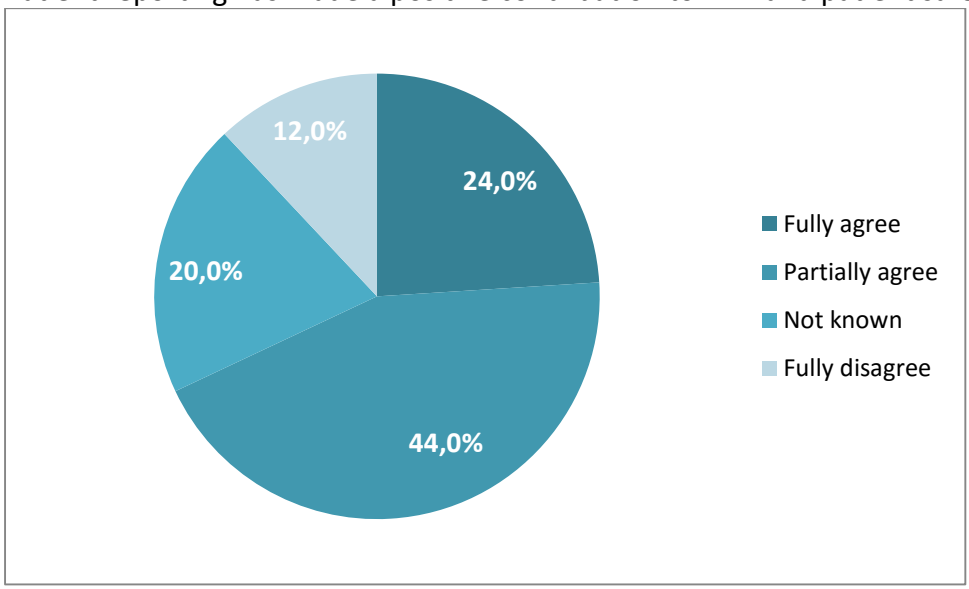
Question T2Q64: Please grade the impact of patient reporting on pharmacovigilance in your MS.

_____ Patient reporting has had a significant impact on resource within PHV
_____ Patient reporting has made a positive contribution to PHV and patient safety

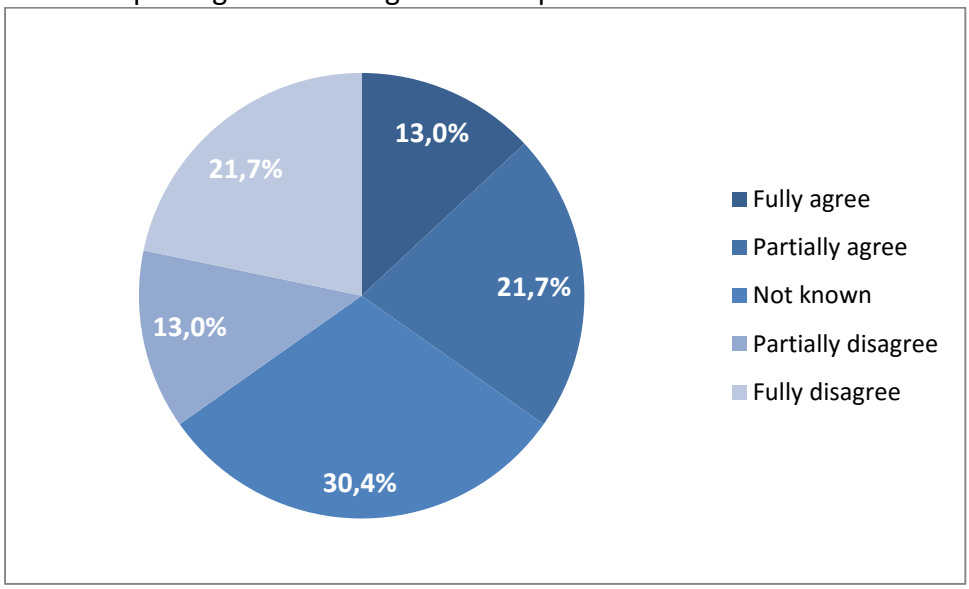
Twenty-six (26) MSs provided answer to this question.
Majority of MSs agreed that patient reporting has made a positive contribution to PHV and patient safety: 6 MSs (24,0%) agreed fully, while 11 MSs (44,0%) agreed partially.
The impact of patient reporting has had on resource within PHV differs among MSs: 8 MSs agreed (either fully or partially) that patient reporting has had a significant impact on resource; 8 MSs disagreed (either fully or partially) and 7 MSs neither agreed nor disagreed with that statement.



Patient reporting has made a positive contribution to PHV and patient safety:



Patient reporting has had a significant impact on resource within PHV:



Question T2Q65: Please describe based on your experience what are your future plans with patient reporting.

Twenty (20) MSs provided answer to this question.
Seven (7) MSs are planning different educational and other activities aiming at raising awareness and promotion of ADR reporting among general public and/or patients, focusing primarily on general reporting scheme awareness campaigns and educational activities. 6 MSs reported that they plan more active engagement and communication with patient organisations in order to increase reports received from this reporter group. 5 MSs are planning or already are in the process of developing the web-based form for patient reporting, while 5 MSs reported that they are planning or developing the mobile app for

ADR reporting. 5 MSs reported other planned improvements such as education of staff, increase of staff, development of adequate IT support, further work with regional centres, research into social media and making adjustments to the reporting system in order to make patient reporting more easy. The remaining two MSs reported that at the moment there are no specific future plans regarding patient reporting.

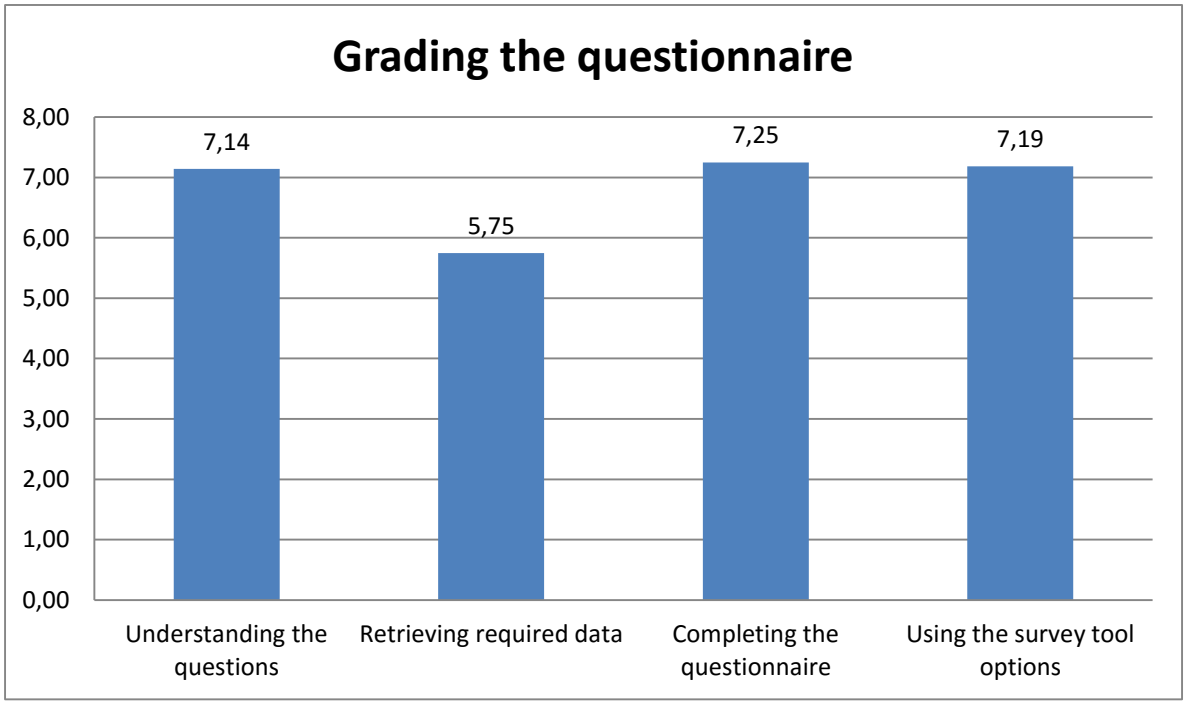
T2Q66 j) Summing up

Question T2Q67: Please write down any additional comments you would like to share with regard to your patient reporting system:

Sixteen (16) MSs provided additional comments with regard to their patient reporting system. Six (6) MSs stated that it was impossible for them to calculate additional FTEs required specifically for processing of direct patient ADR reports.

Question T2Q68: Finally, we would like to kindly ask you to grade this questionnaire.

_____ Understanding the questions
_____ Retrieving required data
_____ Using the survey tool options
_____ Completing the questionnaire



The questionnaire was graded with a mean of 6,83 out of ten for understanding the questions, retrieving required data, completing the questionnaire and using the survey tool options.

T2Q69 Please check if you have answered all questions. You can use "back button" to go through the survey and make sure everything is filled in before submitting.
Please note that choosing "next button" is going to automatically submit the questionnaire. Thank you!

Question 69 was not a question but showing appreciation to respondents for completing the questionnaire and allowed the questionnaire to be submitted.

3.4 Topic 5: Review of IT systems and special forms of reports

A questionnaire was divided into several sections depending on the section topic. The results will be interpreted in similar sections as in the survey.

Q5-Q9: Report on national IT systems for ADR reports processing

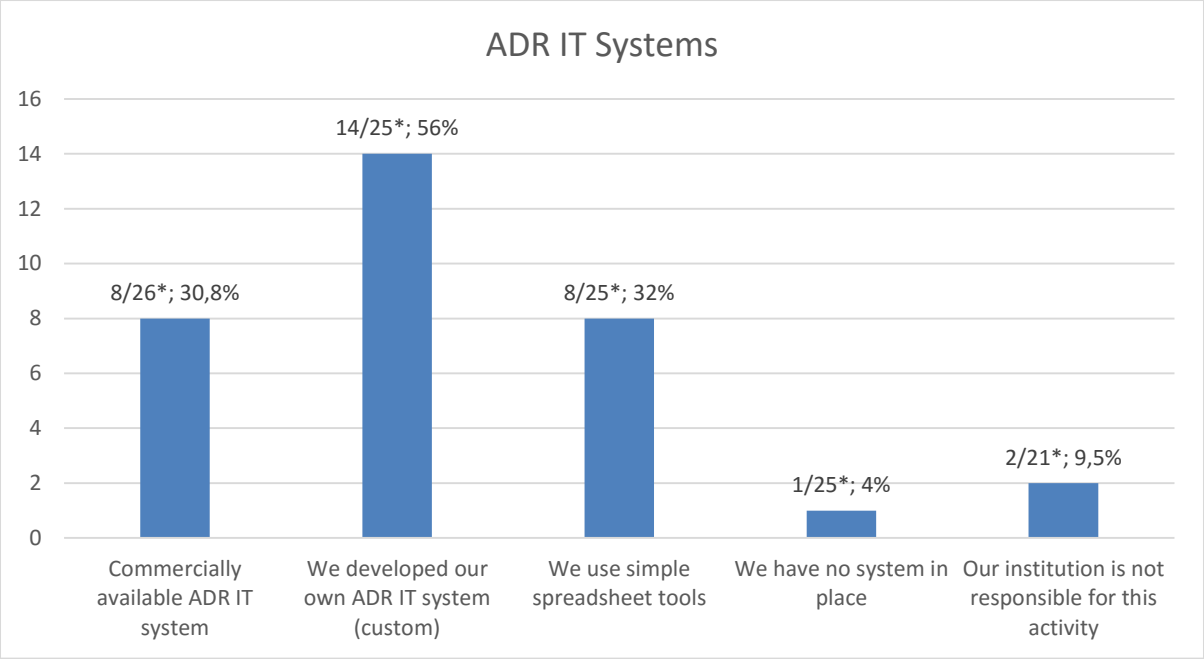
Summary points

- Section is focused on national IT systems for ADR reporting
- Information about different ADR systems and technologies used is collected
- Purpose of ADR systems is reviewed
- BI tools overview

Question T5Q5: Your institution uses:

	Yes	No
Commercially available ADR IT system, please specify	❍	❍
We developed our own ADR IT system (custom)	❍	❍
We use simple spreadsheet tools	❍	❍
We have no system in place	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

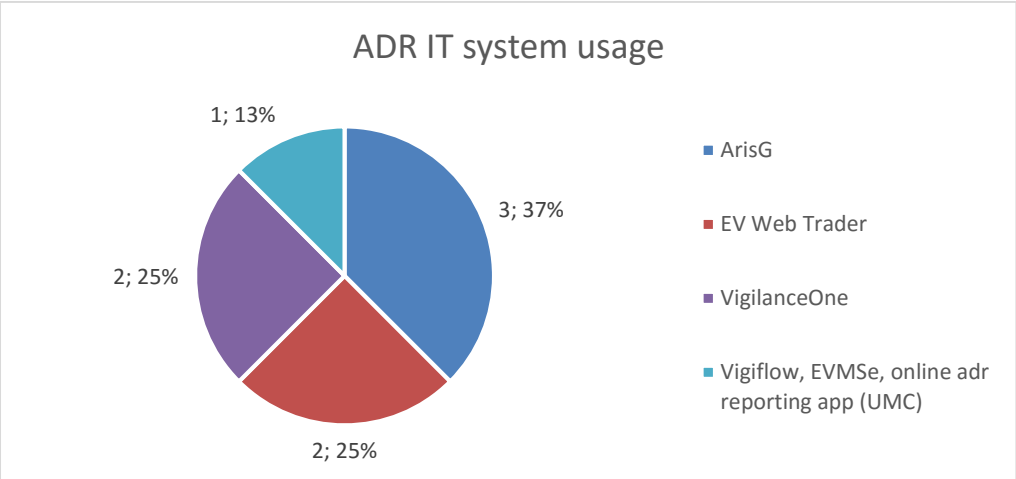
This question was intended to give the overview of how many countries developed their own system and how many countries are using commercially available system or have no system at all. The following charts are representing answers collected.



*Number of respondents

One MS answered "Other, please specify" and the answer was "EudraVigilance is used as our national database". We can consider this as commercially available system since this country is EU member state and has legal obligation of using EV. Therefore, this answer is added to "Eudravigilance EVWEB" answer that was also made by one other MS. This change influenced the answers on T5Q5 and the chart was modified due to changes made.

Summary view per commercially available ADR IT system:



Commercially available ADR IT systems used:

ArisG	3 MSs	
Eudravigilance EVWEB	2 MSs	Corrections made for two MSs based on previous answer
VigilanceOne	2 MSs	
Vigiflow, EVMSe, online adr reporting app (UMC)	1 MS	

Two countries answered that they don't have any system developed. When deeper analysis was made into individual survey answers it was clear that only one of the above mentioned countries doesn't have any system developed and that the other one has custom developed system (MS SQL DB) but also uses Eudravigilance as national database. We can consider that this answer was clicked here by mistake.

Some of the respondents (3 MSs) are using both commercially available and custom developed system in combination with simple spreadsheet tools. These multiple answers gave us larger number of respondents than there really were.

There are also four respondents that are using only simple spreadsheets as their national databases.

After analysis is made, we can see that most of the countries are using custom developed systems. Others are using commercially available system and that ArisG is the mostly used system. EV Web and Vigilance One have the same number of users.

The recommendation for countries that don't use any system except simple spreadsheets is to start using systems developed by EMA as they are available to all MSs. Issues that could be raised here are double data entry, especially if it is manual as well as the possible loss of historic data if all of the received ADRs were not entered into EV.

We compared results received for this question (T5Q5) to the ones received for T1Q55 (Estimation of additional FTEs required for ADR processing).

- Premise:
  - If simple spreadsheets are used > more FTEs are needed

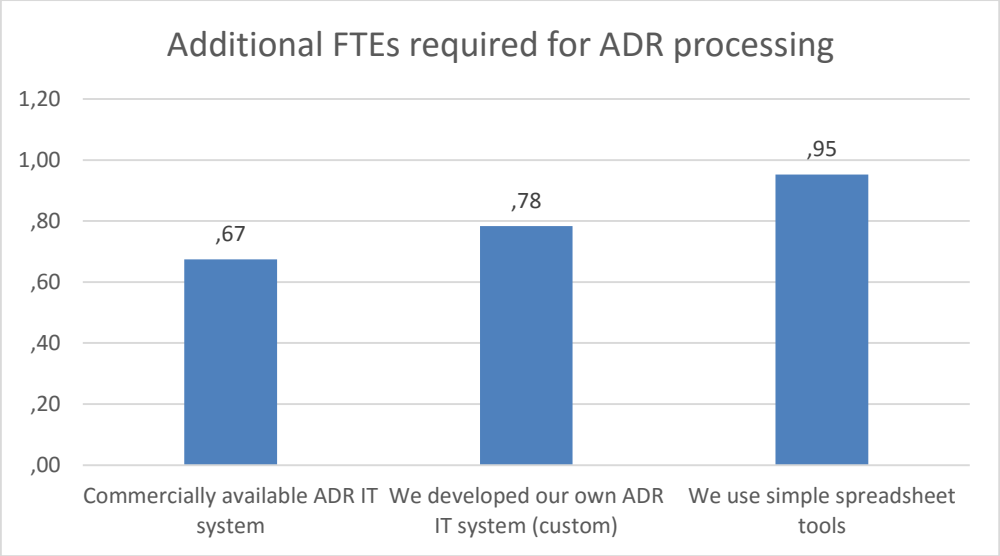


Chart above shows that number of FTEs needed is in dependence with ADR system used. If simple spreadsheets are used and there's no IT system in place, additional FTEs are needed. We can conclude that if more advanced system is used, there's a lesser need for additional FTE's.

Question T5Q6: If your ADR IT system is custom developed which technologies are used?

Data base:
Programming technology/language:
Operating system:

We received responses from 14 respondents what corresponds with the number of countries that answered "Yes" on the T5Q5, option "We developed our own ADR IT system (custom)".

When analysing textual answers we have noticed that an error was made. In the 5th row the database answer was ArisG which is an application. The database answer is stated under "Programming technology/language" column and the value is Oracle. We are missing programming technology answer here. We must consider that ArisG is the name of commercially available software and probably some customization has been made to make it more appropriate for this MS's IT system and specific needs.

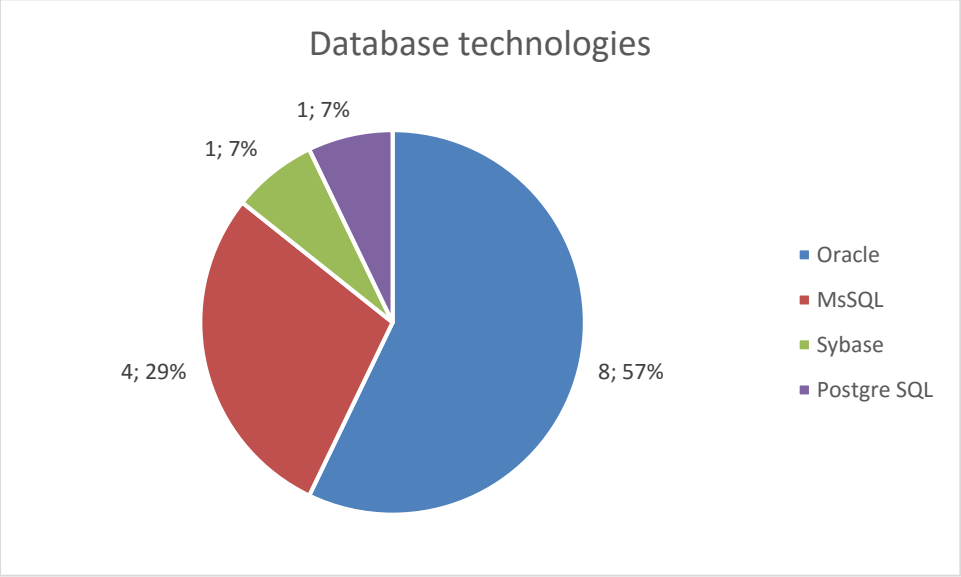
In 9th row, answer is My SQL (MySQL - Open Source SQL database management system, is developed, distributed, and supported by Oracle Corporation) and it can be considered as an Oracle database and it will be considered like one when making analysis.

Another correction is made in the 12th row. Application X (privacy protection) is also application name. From the column "Programming technology/language" we can conclude that this MS is using MsSQL database. The table below shows all answers and corrections.

Original answers:

Row. No.	Data base:	Programming technology/language:	Operating system:
1	Oracle	Java	Unix/Windows
2	MsSQL	C#, .NET Framework	Microsoft Windows Server 2008 R2 Standard
3	PostgreSQL 8.4.9	Java 1.6.0_29	Centos Server, Apache Tomcat 6.0.33
4	ORACLE 10G	vb .NET	Windows server 2003
5	ARISg	Oracle	Windows XP SP2
6	ORACLE 8I	client server/forms and reports 6I	Windows
7	Oracle	dot net	using a webbrowser
8	Oracle	Java/ / ASP	Microsoft Server 2003
9	My SQL	PHP	Linux
10	Sybase	Visual Basic	Windows
11	Oracle	Java	Linux
12	Application X	Microsoft/ASP 3.0 y Visual Basic 6/ SQL Server 2008	Windows
13	MS SQL Server 2005	Java/J2EE/JBoss, Enterprise Java Beans (EJB) Business logic layer	Linux Redhat Enterprise 5, Windows Server 2003 Standard
14	MS SQL	MS Dyamics CRM, SQL, J-script	Win server

Following pie chart shows corrected results:



When analysing "Programming technology/language" and "Operating systems" columns, it was obvious that the question wasn't fully understandable. It was seen through the different answers received even with wrong values. Nevertheless, the conclusion we made

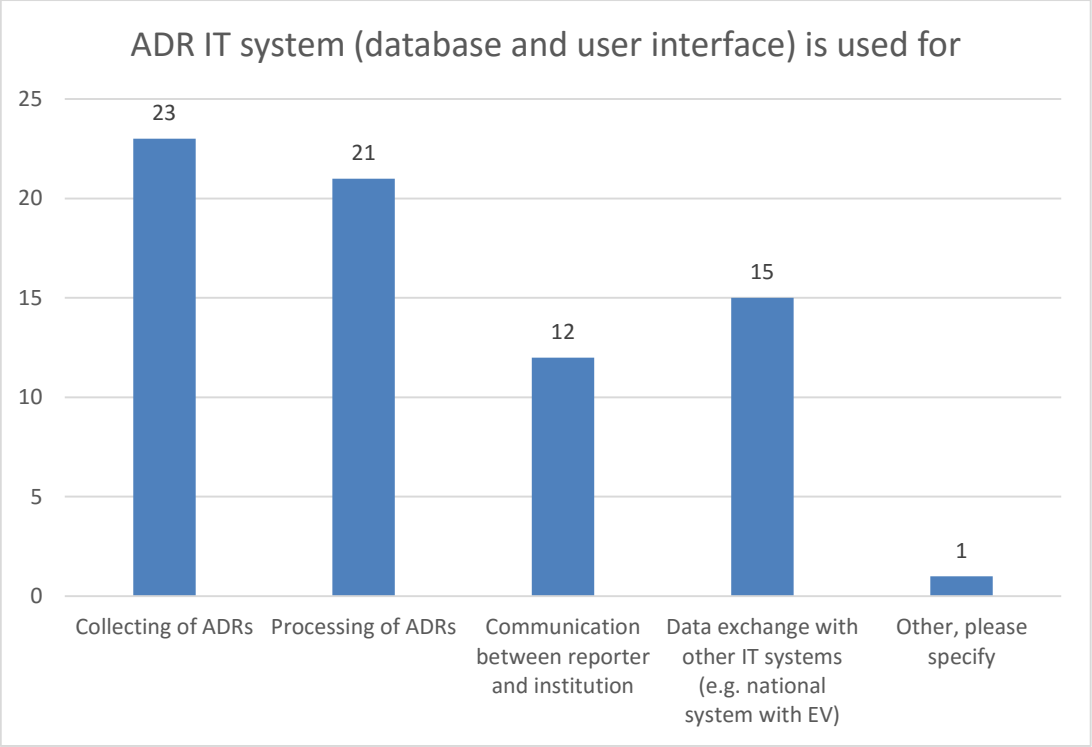
is that majority of countries are using Microsoft Windows as operating system and the second one is Linux. When looking at "Programming technology/language" answers, we see that standard technologies/ programming languages (java, .NET, VB, c#, etc.) are used.

Question T5Q7: Your ADR IT system (database and user interface) is used for:

	Yes	No
Collecting of ADRs	❍	❍
Processing of ADRs	❍	❍
Communication between reporter and institution	❍	❍
Data exchange with other IT systems (e.g. national system with EV)	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

Responses showed that there are significant differences between countries. Some of the countries use their system for all of the mentioned activities like collecting, processing, communication and data exchange with other systems. We can consider these systems as best practice or as the most advanced systems that include all activities regarding ADR reporting.

Summary results are the following:



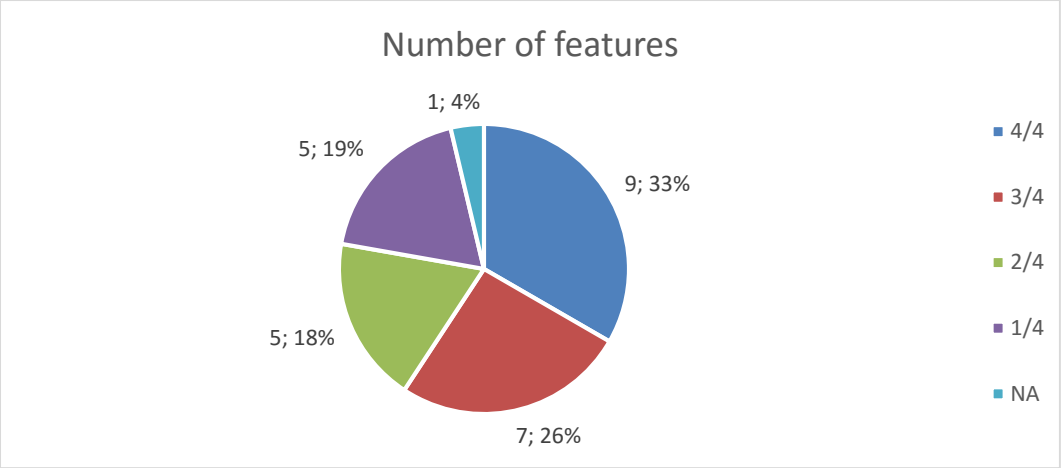
26 respondents answered this question.

One (1) country answered "Other, please specify" and the answer was "Is used for transposing of ADR into ICSR and then transmission of ICSR to company and EMA".

The following chart is showing us features that certain system includes:

- Collecting of ADRs
- Processing of ADRs
- Communication between reporter and institution
- Data exchange with other IT systems

The results are showing the number of respondents which are using system with certain number of features.

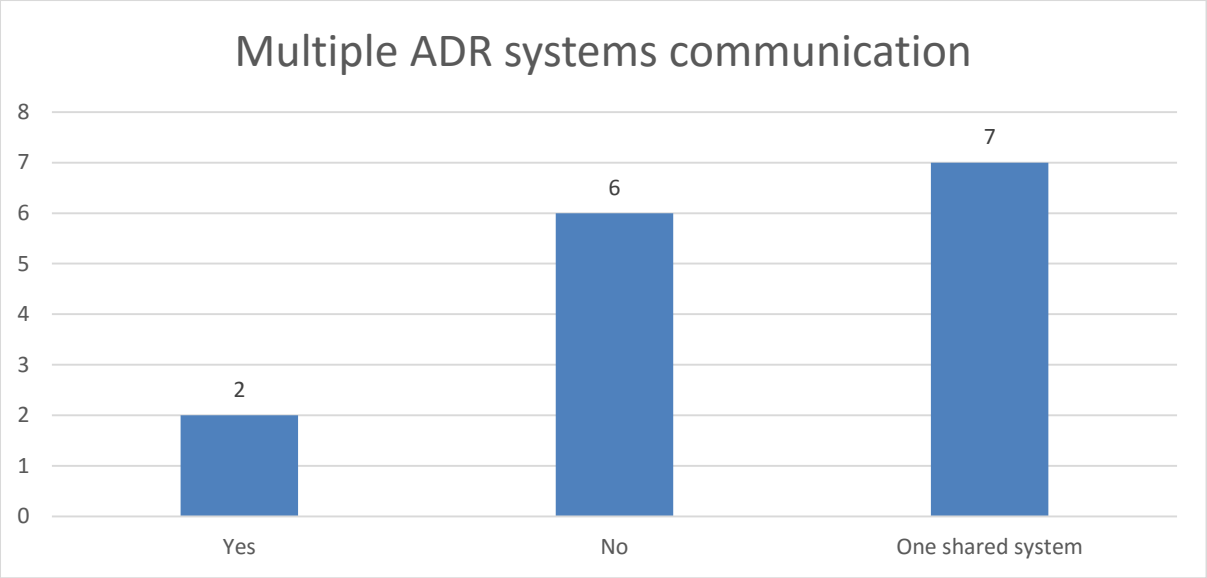


From the overview presented above, it can be seen that most of the respondents (9 MSs) are using their system for all four features (collecting, processing, communication and data exchange). Respondents, which have implemented all of the system features, can be considered as the most advanced users.

12 MSs have implemented two or more features and after the deliverables and guidelines are finished, suggestions could be made how to improve their systems.

Question T5Q8: If more than one ADR IT system exists in your MS, (for example regional centres), do they communicate with each other:

	Communication between ADR databases within the NCA/regional centres
Yes	❍
No	❍
One shared system	❍
Not applicable	❍
Our institution is not responsible for this activity	❍



27 respondents answered this question.

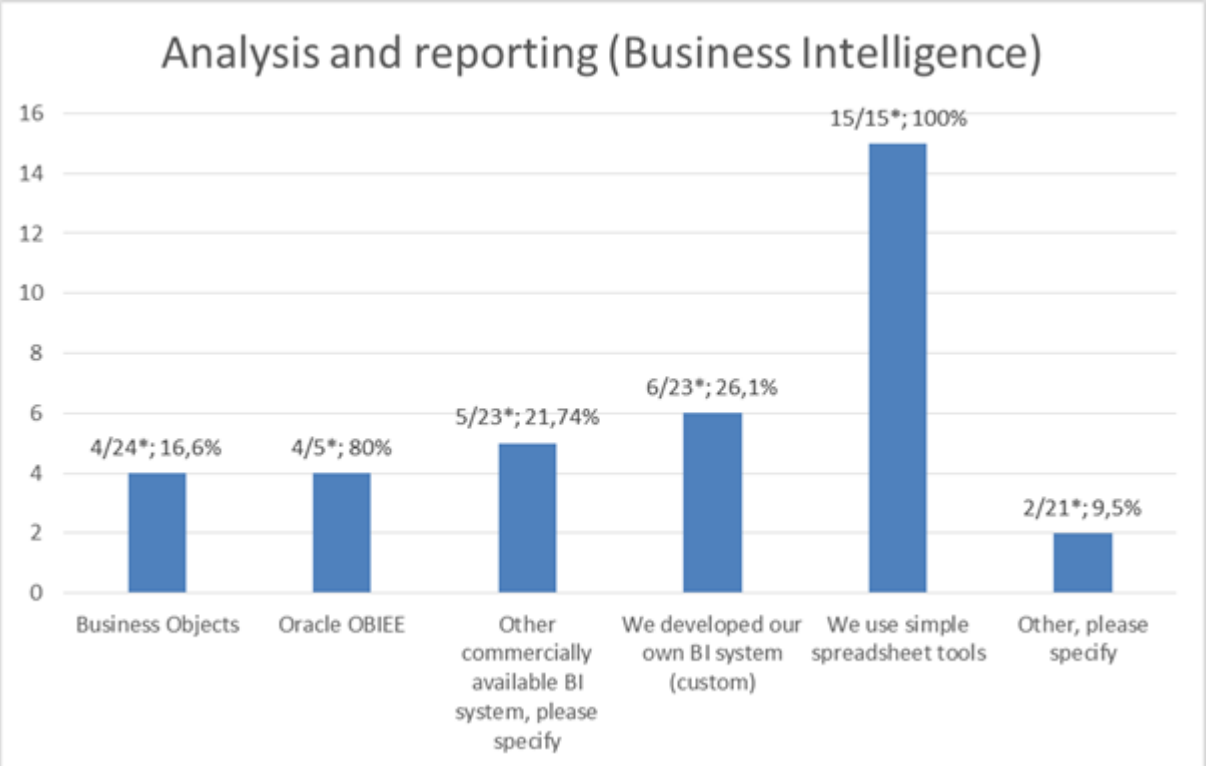
In question T5Q8, some corrections of answers received were needed. Three (3) MSs had to be additionally checked and followed up with T1 and individual survey answers. Namely, one MS provided two answers ("Not applicable" & "Our institution is not responsible for this activity"), however this was considered valid. The answer from second MS was corrected to "No", as they don't have shared or multiple systems, after follow up. Third MS answered both "Yes" and "No" to this question, therefore that answer was excluded from analysis.

One MS has one shared system in place but the system isn't used at the moment. This is a technical possibility which can be activated when needed.
One MS has implemented multiple ADR systems communication and 6 MSs have one shared system in place.
"Not applicable" and "Our institution is not responsible for this activity" answers are not shown in the chart.

Question T5Q9: For analysis and reporting (Business Intelligence) what do you use?

	Yes	No
Business Objects	❍	❍
Microstrategy	❍	❍
Oracle OBIEE	❍	❍
Other commercially available BI system, please specify	❍	❍
We developed our own BI system (custom)	❍	❍
We use simple spreadsheet tools	❍	❍
We have no system in place	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

This question shows which tools are used for reporting and business intelligence. Most of the countries still use simple spreadsheet tools like Excel and some use solutions developed by EMA, custom developed or commercially available software with specific adjustments and requests.



*Number of respondents

Corrections are made for the following answers.

Other commercially available BI system:

One MS answered they are using Excel. This answer was transferred to the answer "We use simple spreadsheet tools".
Another MS answered they are using EV-DAS (Eudravigilance Data Analysis System) which is the name of Oracle OBIEE developed by EMA, so it can be considered they answered Oracle OBIEE.

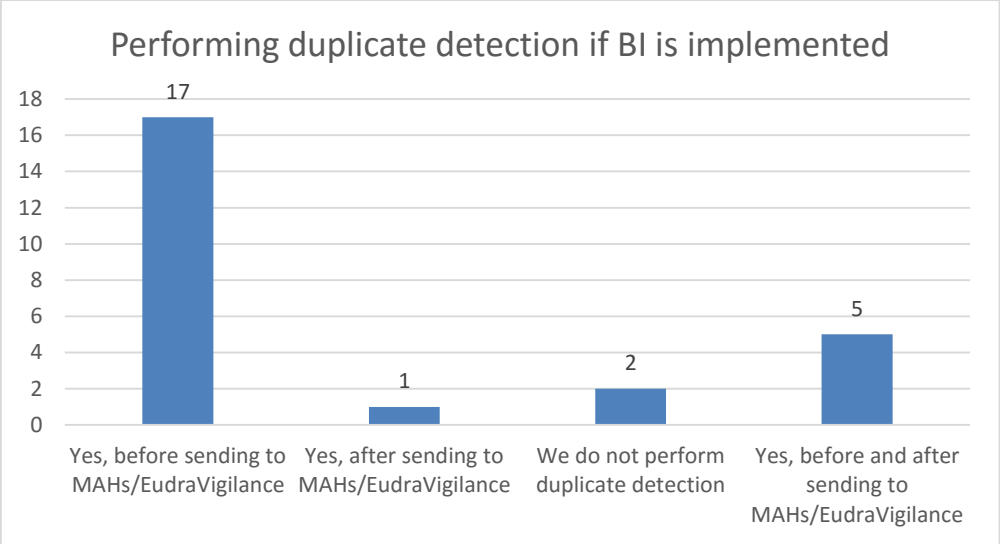
Other, please specify:

One MS's answer was transferred to Oracle OBIEE as they are using EVDAS as BI tool. Another MS answered they are using EV WEB, so the answers were interpreted as one answer/choice and was transferred to "Other, commercially available system". Furthermore, one MS is using Pentaho which is commercially available software and it was transferred under answer "Other commercially available BI system"
One MS answered they are using QBE in ArisG which can also be considered as commercially available BI system but this answer will be considered as different, specific solution, because data sources can be customized and system can differ depending on the specific customer requests.

We compared results received for this question (T5Q9) to the ones received for T1Q62 (Performing duplicate detection).

- Premise: If BI system is implemented, performing duplicate detection is easier
  - 17 countries perform duplicate detection before sending ADRs to MAH/EV
  - 1 country performs duplicate detection after sending ADRs to MAH/EV
  - 5 countries perform duplicate detection before and after sending to MAHs/EudraVigilance
  - 2 countries don't perform duplicate detection even though they have implemented BI > this is possible if EV is used as national DB

Following chart is graphical representation of statistical results.


Performing duplicate detection if BI is implemented
18
16
14
12
10
8
6
4
2
0
17
1
2
5
Yes, before sending to MAHs/EudraVigilance
Yes, after sending to MAHs/EudraVigilance
We do not perform duplicate detection
Yes, before and after sending to MAHs/EudraVigilance

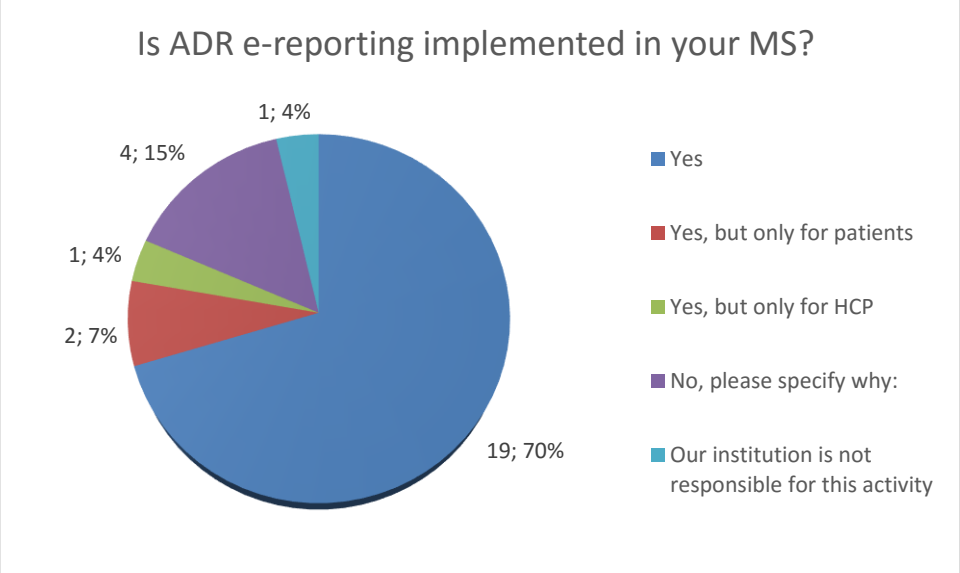
Q11-Q14: Electronic ADR reporting

Summary

- Evaluation of current state of electronic ADR reporting, i.e. who is using it (patients, HCP's), how the reports are being submitted and which standards are being used

Question T5Q11: Is ADR e-reporting implemented in your MS?

- ❍ Yes
- ❍ Yes, but only for patients
- ❍ Yes, but only for HCP
- ❍ No, please specify why: _____
- ❍ Our institution is not responsible for this activity



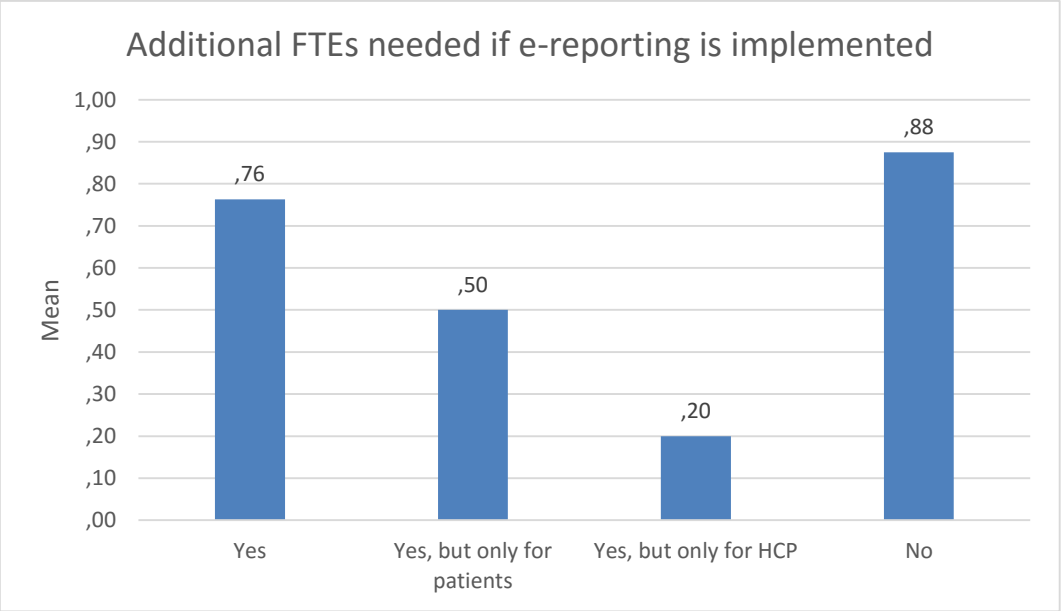
The answers showed that majority of the countries have implemented ADR e-reporting. Some of them have developed e-reporting just for patients, some for HCPs, and 4 countries don't have e-reporting implemented. Three main reasons mentioned by 4 MSs explaining why they don't have system in place are:

- currently under development
- lack of human resources and IT support
- expecting a system developed by EMA

One country is not responsible for this kind of activity.

We compared results received for this question (T5Q11) to the ones received for T1Q55 (Estimation of additional FTEs required for ADR processing).

- Premise: If e-reporting isn't implemented > Additional FTEs are needed
  - If e-reporting isn't implemented, we can assume that manual data entry is more frequent which requires larger number of additional FTEs and more time to process ADRs. Also, we can assume that if e-reporting is implemented, larger number of ADRs received is expected

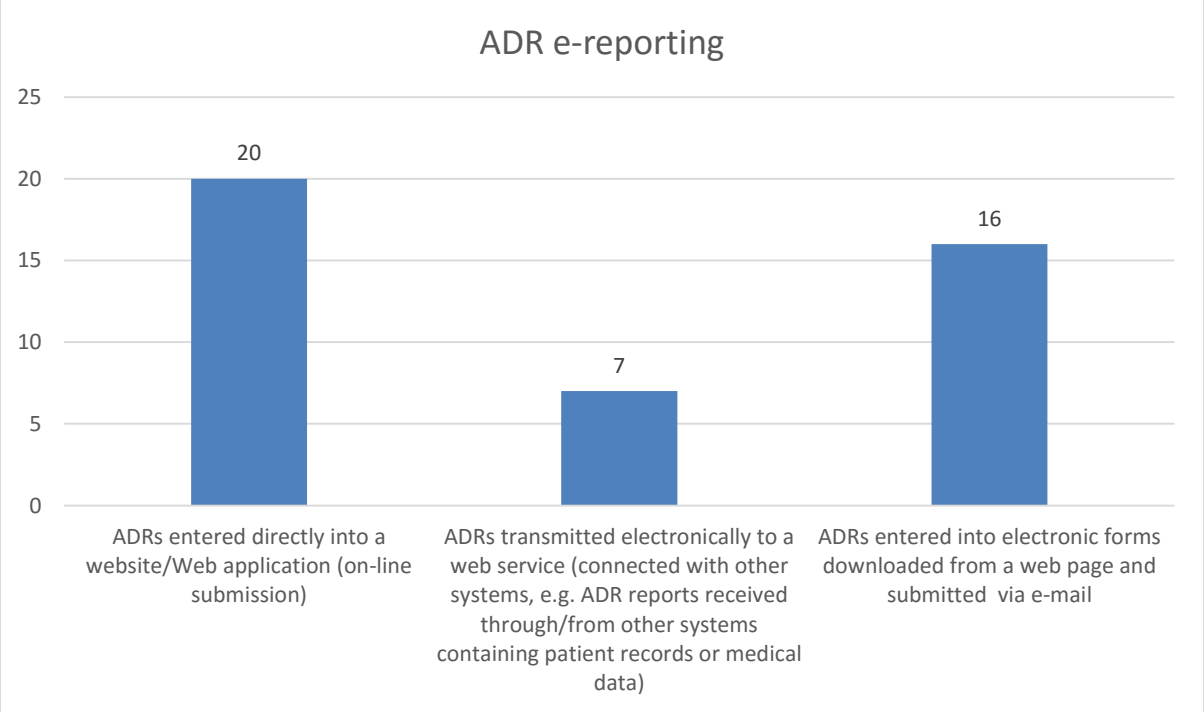


The chart above shows that additional FTEs are needed in two cases. First, if e-reporting is implemented and second, if e-reporting isn't implemented. In the first case, it is the higher quantity / number of ADRs received if e-reporting is implemented and in the second case it is the amount of manual work if paper ADR reports are received.

Question T5Q12: For ADR e-reporting the following is used:

	Yes	No
ADRs entered directly into a website/Web application (on-line submission)	❍	❍
ADRs transmitted electronically to a web service (connected with other systems, e.g. ADR reports received through/from other systems containing patient records or medical data)	❍	❍
ADRs entered into electronic forms downloaded from a web page and submitted via e-mail	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

This question shows what is used for ADR e-reporting. We can see that there are three most common ways how electronic ADR can be reported. Please notice that number of answers is larger than number of respondents, because some of the MSs gave more than one answer. Twety-six (26) respondents answered this question.



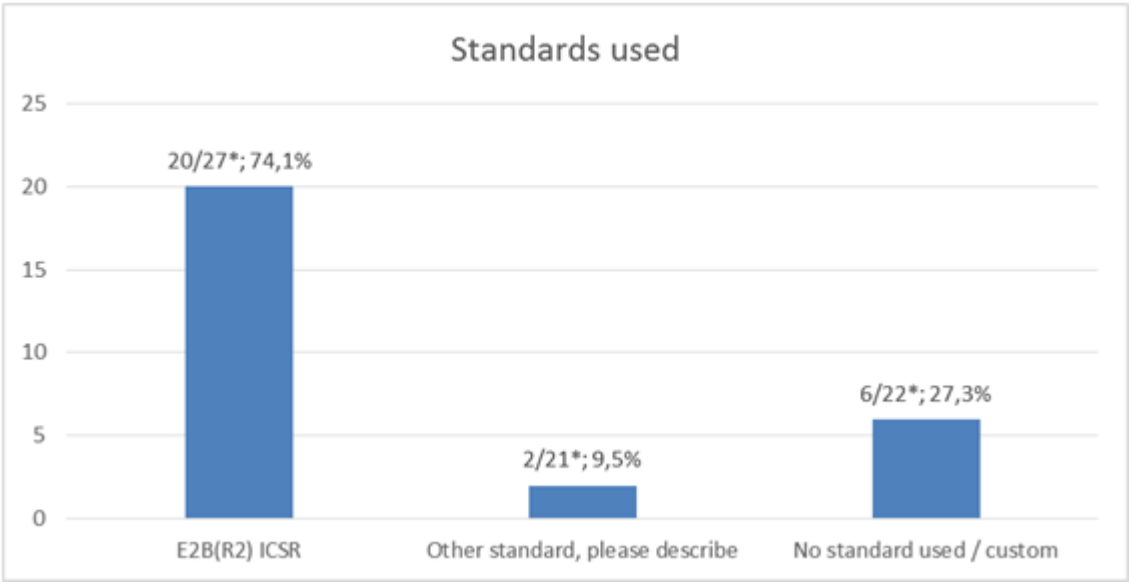
We received three answers under category “Other, please specify”. One was paper, fax; second one was “N/A”; and the third one was EV WebTrader only for MAHs.

Corrections have been made and text answer “EV WebTrader only for MAHs” is categorized as “ADRs entered directly into a website/Web application (on-line submission)”.

Question T5Q13: If ADR report is submitted as an electronic message, which standard is used?

	Yes	No
E2B(R2) ICSR	❍	❍
E2B(R3) ICSR	❍	❍
Other standard, please describe	❍	❍
No standard used / custom	❍	❍
Our institution is not responsible for this activity	❍	❍

When ADR report is submitted as an electronic message, the majority of respondents are using currently valid E2B (R2) ICSR standard. It should be noticed that, at the time this survey was launched, no MS had implemented E2B (R3) ICSR standard which would become mandatory in 2016.



*Number of respondents

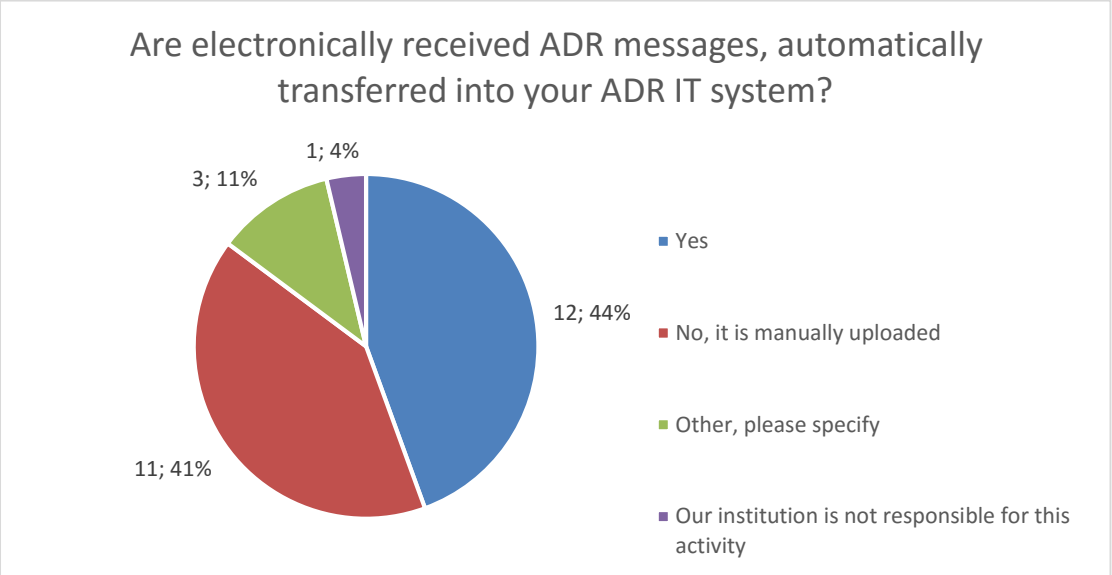
One MS chose the option “Other, please specify” and stated that they are using E2B(R2) standard but they have some additional fields added. Another MS’s answer was “we receive

the information as a text file (.txt), we then transcribe it into Eudravigilance using the inbuilt E2B standard" which cannot be considered as valid answer since the question was about the electronic message.

When the survey was carried out, no one was using E2B(R3) standard.

Question T5Q14: Are electronically received ADR messages, automatically transferred into your ADR IT system?

- ❍ Yes
- ❍ No, it is manually uploaded _____
- ❍ Other, please specify _____
- ❍ Our institution is not responsible for this activity



27 MSs answered

Two (2) MSs have partially automatic or partially manual transfer of electronically received messages into their ADR IT systems. One of those MSs has automatic transfer of ADR entered directly into website/web application and the other one is receiving xml from the WebPages ("the WebPages sends an XML document from the report by email, we copy these XML document to the suitable folder, from where a web service processes the report").

Q16-Q23: State of implementation of electronic reporting and E2B(R2) in you institution

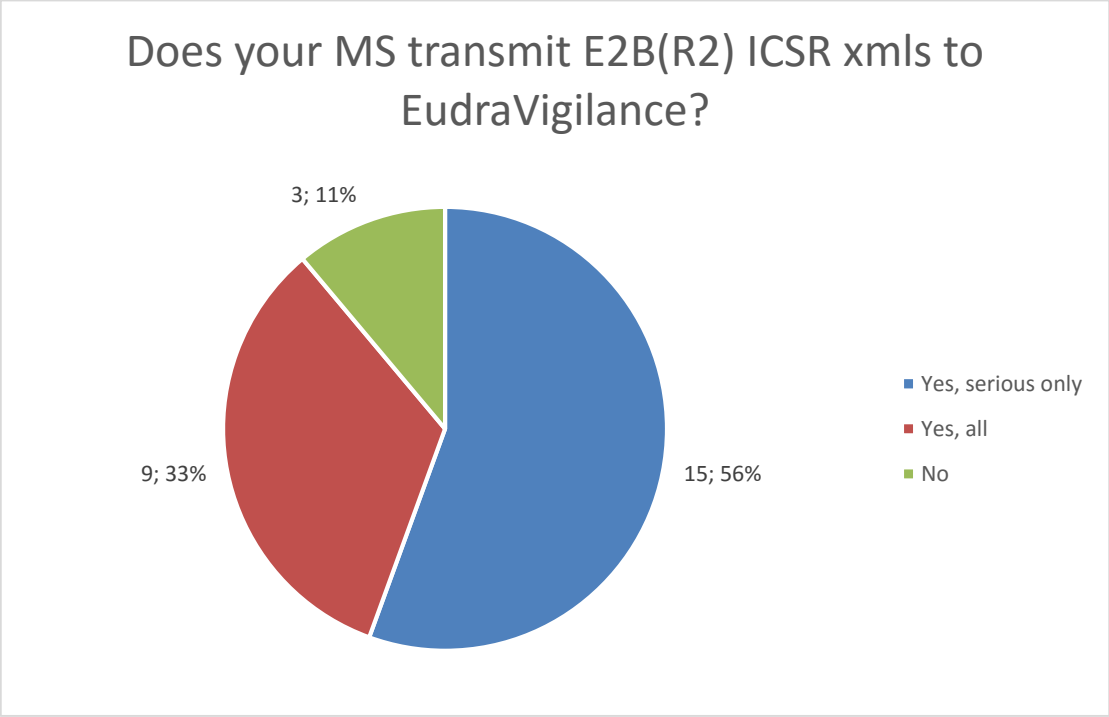
Summary

- State of implementation of electronic reporting
- Insight into technologies and databases used
- Communication between systems and databases
- Transmission of ADR reports between your institution and MAHs

Question T5Q16: Does your MS transmit E2B(R2) ICSR xmls to EudraVigilance?

- ❍ Yes, serious only
- ❍ Yes, all
- ❍ Yes, other. Please specify: _____
- ❍ No
- ❍ Our institution is not responsible for this activity

Purpose of this question was to see the current state of transmission of ADR reports into Eudravigilance DB per country. 27 countries answered this question and there was a slight difference in which type of ADR they are transmitting to EV.



It was interesting to see that three countries answered they are not transmitting ADRs into Eudravigilance. For one of those MSs, this isn't an issue since they don't

have their own Pharmacovigilance system. The other MS is using Eudravigilance as their national database and all ADRs received are initially registered in an MS SQL database and then registered into Eudravigilance. The third country didn't provide explanation why they are not transmitting ADRs into EV.

Two (2) MSs provided textual answers. One answered that they are transmitting all serious and non-serious ADRs with expedited reporting criteria to EV and the other one answered they are transmitting serious, downgraded and nullified reports to EV. We have transferred this answer to "Yes, serious only" selection as some of the countries have stated that in compliance with GVP module "serious ADRs" cover downgraded and nullified reports also.

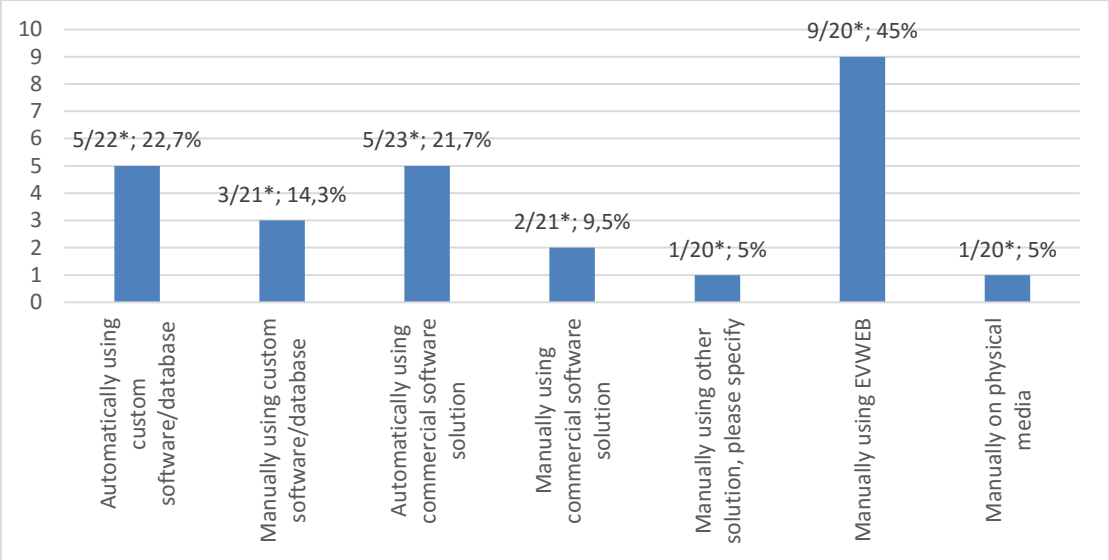
Question T5Q17: How do you transmit these to EV?

	Yes	No
Automatically using custom software/database	❍	❍
Manually using custom software/database	❍	❍
Automatically using commercial software solution	❍	❍
Manually using commercial software solution	❍	❍
Automatically using other solution, please specify	❍	❍
Manually using other solution, please specify	❍	❍
Manually using EVWEB	❍	❍
Manually on physical media	❍	❍
Not applicable	❍	❍
Our institution is not responsible for this activity	❍	❍

In the chart below it can be seen that most of the respondents are still transmitting ADRs manually into EV DB which means that progress can be made in this particular area.

In the case of manual transmission, the majority of the respondents answered they are using EVWEB for ADR transmission. The second most common answer was custom software/database solution.

In the case of automatic transmission we have received the same number of answers (5) for both of the given/offered answers.



*Number of respondents

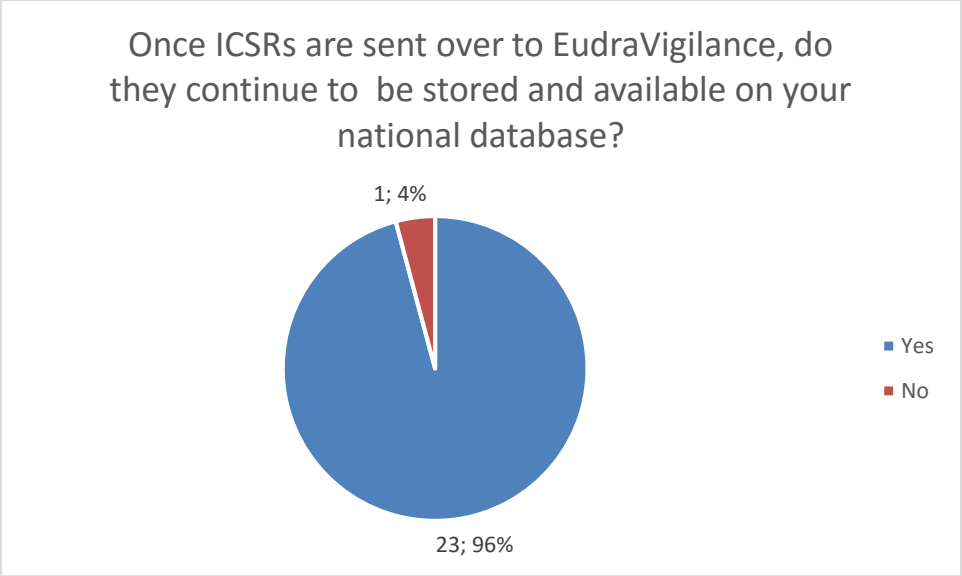
From the answers received, it is visible that only 10 countries are using automatic transmission into EV. Five (5) of them are using commercial software solution and the other 5 are using custom software or database for automatic transmission.

One of the benefits of the automatic transmission is time saving, i.e. less time is spent for sending cases into Eudravigilance. The other benefit of automatic transmission is that there is no possibility of human mistake of not sending or forgetting to send an ADR into EV. The risk appears if there are no controls and measures in place to reduce the risk of system malfunction or if there are no SOPs providing alternative measures if ADRs can't be sent automatically to EV. Respondents which have automatic transmission in place can be considered as the ones with the good practice.

Question T5Q18: Once ICSRs are sent over to EudraVigilance, do they continue to be stored and available on your nationals´ database?

- ❍ Yes
- ❍ No
- ❍ Our institution is not responsible for this activity

Twenty four (24) responses were received for this question. Only one country answered they don't continue to store ICSRs in their national's database. The reason for that is they are using Eudravigilance as their national database and the question wasn't interpreted correctly.



*This pie-chart shows the status before correction

The corrections have been made for this MS's and their answer was transferred to "Yes" option, since ADRs continue to be stored in Eudravigilance which is considered to be their national database. We can see that all respondents have plans to continue to store ICSRs in their national databases after they are sent to Eudravigilance.

Question T5Q19: If yes, please specify for how long:

This question is in relation with T5Q18. It is connected with answer "Yes", when MSs continue to store ICSRs in their national databases after sending them to Eudravigilance.

When looking at text answers received for this question, we can say that most of the respondents are storing ICSRs for unlimited time. There are differences in case of different legal obligations. In one MS, ICSRs received form HCPs need to be stored for 75 years but the ICSRs received from patients are kept forever. In another MS there is a minimum legal requirement that cases need to be kept for 20 years but at the moment they are kept permanently. We've added "Forever" column into table to be clear what the answers were.

Text Response	Forever
30 years	No
All sent reports are saved on the computer and are available at all times.	Yes
always as spread-sheet + xml file saved	Yes
for an indefinite time	Yes
forever	Yes
for ever	Yes
Forever	Yes
forever	Yes
ICSR sent to EudraVigilance are stored in our national database forever.	Yes
indefinite	Yes
Indefinitely	Yes
Indefinitely	Yes
Infinitely	Yes
Not limited. Stored and available through VigiFlow database.	Yes
Permanently	Yes
Since 2004 year all reports have been stored in our ADR database, we don't think over for how long, at the moment we have all of them. Only minimum time period for archiving of reports is stated in our law (20 years)	Yes
since 2008, for unlimited time	Yes
The ICSRs from HCP are stored in the national archive for 75 years, the ICSRs from patients are stored in the national archive forever	Combined
time for storage of case reports is unlimited	Yes
Undated	Yes
unlimited	Yes
unlimited period	Yes
Unlimited time	Yes

If we conclude that two above mentioned MSs also store/keep ICSRs received for unlimited time we have just one exception which is keeping ICSRs for 30 years.

Question T5Q20: If no, please specify why not:

This question is in relation with T518. It is connected to answer "No", when MSs don't continue to store ICSRs in their national databases after sending them to Eudravigilance.

One MS answered here that they don't have national ADR database and the reason is they are using Eudravigilance as their national database. We can see that question wasn't interpreted correctly.

Here is the quotation from WP4 T1Q4 where they are confirming conclusion we've made: "In 2008, the Medicines Authority migrated all data from a local IT database (used from 2004-2008) to Eudravigilance. The national Adverse Reactions Database is Eudravigilance and it is compliant with ICH M2 for E2B transmissions (B2)."

Since we've made corrections to this answer, and since the ICSR's sent to Eudravigilance are kept forever, we can say that this MS is also keeping ICSRs for unlimited time.

Question T5Q21: Do you intend to:

	Yes	No
Continue to have your own database (either in house or outsourced)	❍	❍
Use EudraVigilance only within the next 1 year	❍	❍
Use EudraVigilance only within the next 3 years	❍	❍
Use EudraVigilance only within the next 5 years	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

In this question we have received answers for just three out of six choices we've offered.

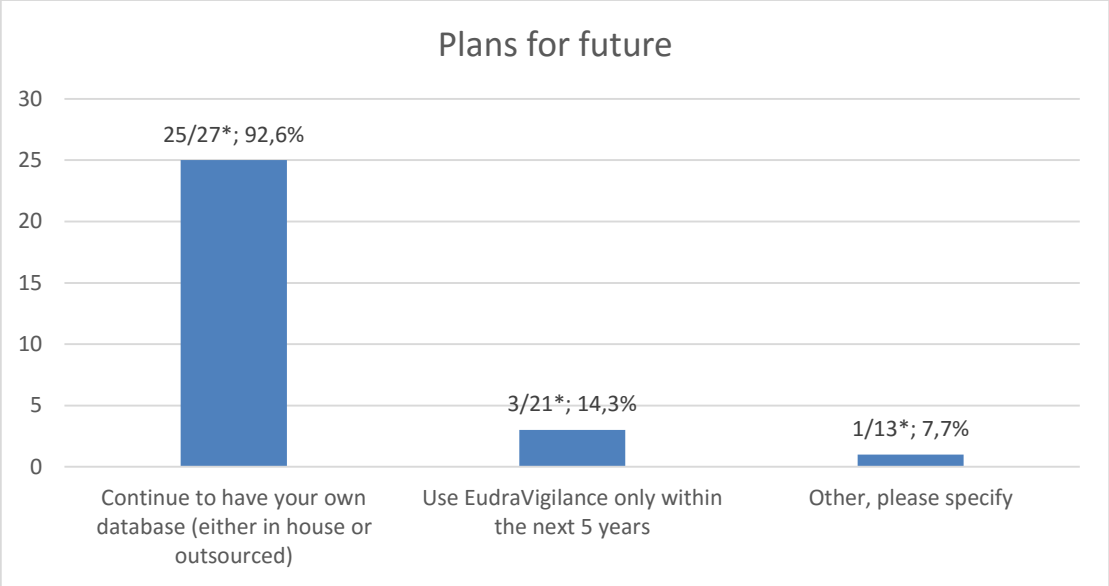
When „Other, please specify“ answers were analysed, we have noticed there are corrections that needed to be made to those answers. The answers we've received for this option are shown below.

“Other, please specify” answers per country:

- Not considered for the time being.
- We use EV also for statistics, signal detection *> correction - goes to continue to have your own database (either in house or outsourced) answer*
- We do not plan to change current condition: Combination of local tracking tool (xls) with EV as national database *> correction - goes to continue to have your own database (either in house or outsourced) answer*
- We will continue to use our database in national language and translate/transfer data to EV *> correction - goes to continue to have your own database (either in house or outsourced) answer*
- We are currently in the process of gaining national database *> correction - goes to continue to have your own database (either in house or outsourced) answer*

The chart below shows results after we have corrected the answers. It can be seen that most of respondents have plans to continue to use/have their own database

irresepective of Eudravigilance. Please note that number of answers is higher than number of respondents because some of the MSs provided more than one answer.

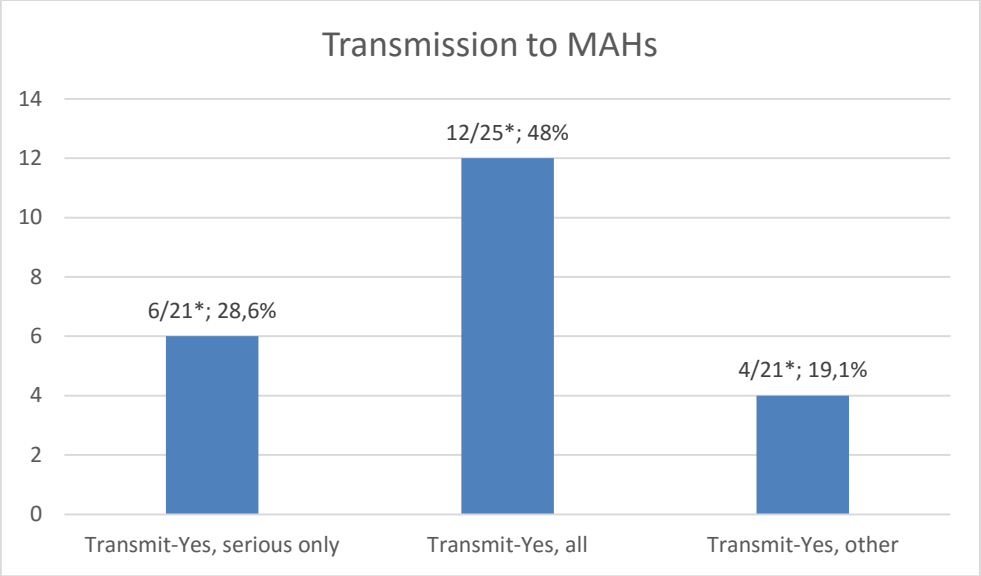


*Number of respondents

Question T5Q22: Does your institution transmit/allow access E2B(R2) ICSR xmls to MAHs?

	Transmit		Access	
	Yes	No	Yes	No
Yes, serious only	❍	❍	❍	❍
Yes, all	❍	❍	❍	❍
Yes, other. Please specify:	❍	❍	❍	❍
No, we do not	❍	❍	❍	❍
Our institution is not responsible for this activity	❍	❍	❍	❍

This question gives an insight how institutions share ADRs with MAHs. The question was divided in two statements - transmission and allowing access.



*Number of respondents

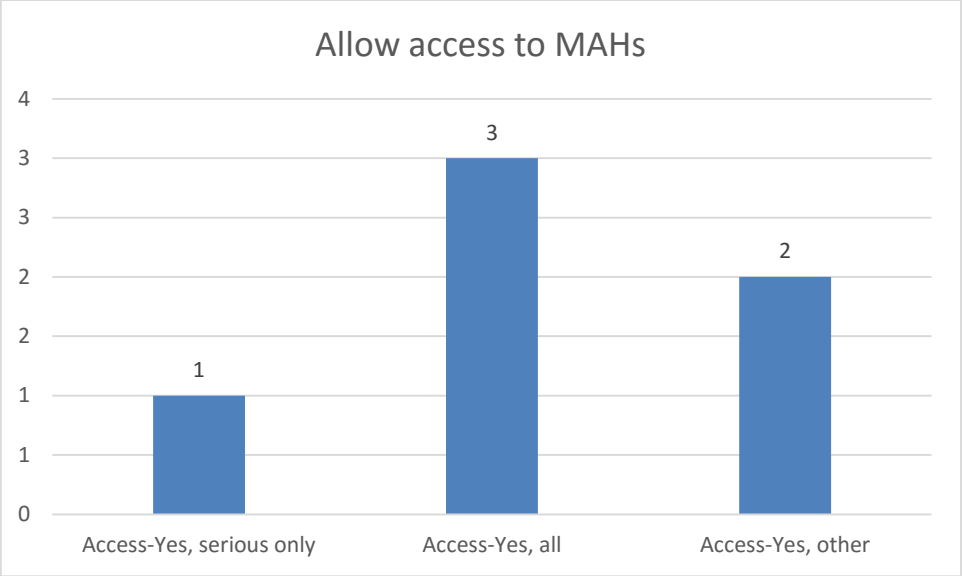
It can be concluded from the chart that majority of respondents transmit all ADRs to MAHs and a smaller number sends just the serious ones. There were also four "Yes, other" answers. Comments are added to certain country answer.

"Yes, other" answers:

- MS 1- Serious expedited and non-serious by request > *ADRs are transmitted to MAH on request*
- MS 2 - Serious, downgraded and nullified > *can be transferred to serious according to Q16.*
- MS 3 - Quarterly > *ADRs are transmitted periodically, not all the time*
- MS 4 - Only for their products > *ADRs are transmitted to MAHs just for their products*

6 MSs transmit just the serious ADRs to MAHs.

When analysing second part of a question, we noticed that lower number of countries allows access to MAHs into their DB.



*23 respondents answered this question

In this question we also had "Yes, other" answers. Two respondents provided this option. Comments to this question are added to certain country answer.

"Yes, other" answers:

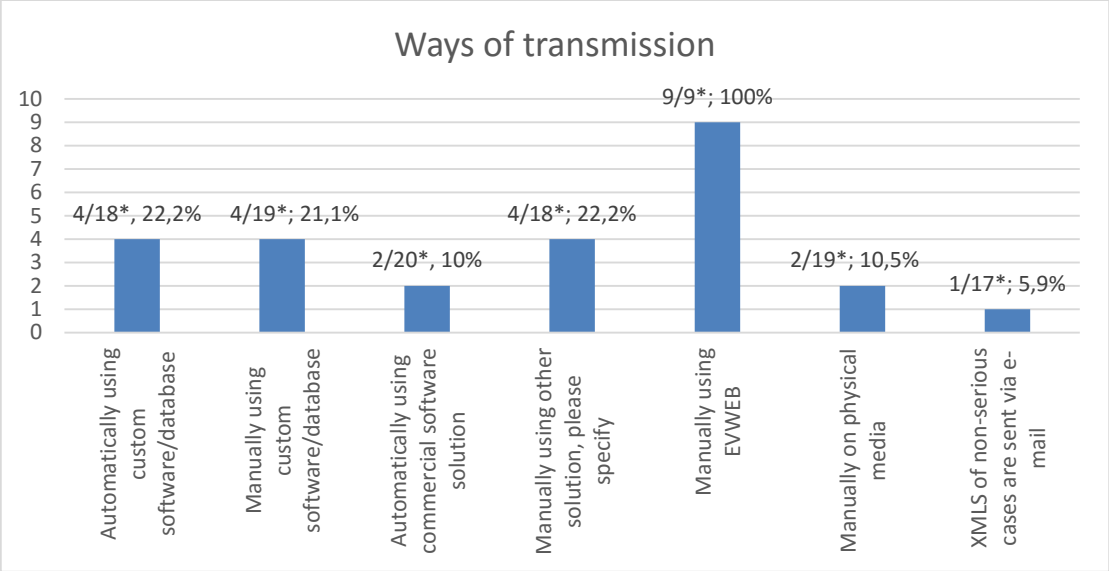
- MS 1 - ICSRs (serious and non-serious) related to MAH's MPs could be provided to MAH on his request - as printout from our ADR db, there is no direct access > *there's no "on-line" access available, just physical (paper printouts)*
- MS 2 - Only for their products> *MAHs are allowed access just for their products*

Question T5Q23: How do you transmit these to MAHs?

	Yes	No
Automatically using custom software/database	❍	❍
Manually using custom software/database	❍	❍
Automatically using commercial software solution	❍	❍
Manually using commercial software solution	❍	❍
Automatically using other solution, please specify	❍	❍
Manually using other solution, please specify	❍	❍
Manually using EVWEB	❍	❍
Manually on physical media	❍	❍
XMLS of non-serious cases are sent via e-mail	❍	❍
Not applicable	❍	❍
Our institution is not responsible for this activity	❍	❍

When transmission of ADRs is performed, it can be done in two ways, manual and automatically.

This question provided an overview of different ways of transmission. It can be seen (chart below) that most of the countries have manual transmission, and that the most common way of transmission is by using EVWEB.



*Number of respondents

From the received answers, it is visible that only six respondents use automatic transmission software. Two of them are using commercial software solution and four of them are using custom software for transmission. These MSs are potentially good practice examples.

We had text answers when “Manually, using other solution, please specify” answer was chosen. Comments to this question are added to certain country answer.

Text answers per respondent were:

- MS 1 - EV Gateway
- MS 2 - If MAH cannot receive E2B we sent a paper form > *MS answered they are automatically sending ADRs using custom software, so this is an alternative*
- MS 3 - Mail > *this is also an alternative, they are using EVWEB*
- MS 4 - Non-serious reports are only sent as pdf line-listings twice a year
- MS 5 - Secure e-mail exchange
- MS 6 - XMLs or database printouts of serious cases are sent via e-mail to particular MAH which are not able to receive our ADR reports in E2B R format due to special marks in alphabet, there is only small number of such MAHs - about 10

One of the benefits of the automatic transmission is time saving, i.e. less time is spent for sending cases to MAHs. The other benefit of an automatic transmission is that there is no possibility of human mistake of not sending or forgetting to send an ADR. The risk appears if there are no controls and measures in place to reduce the risk of system malfunction or if there are no SOPs providing alternative measures if ADRs can't be sent automatically to MAHs.

Q25-Q44: Report on the current state of implementation of electronic health records in EU

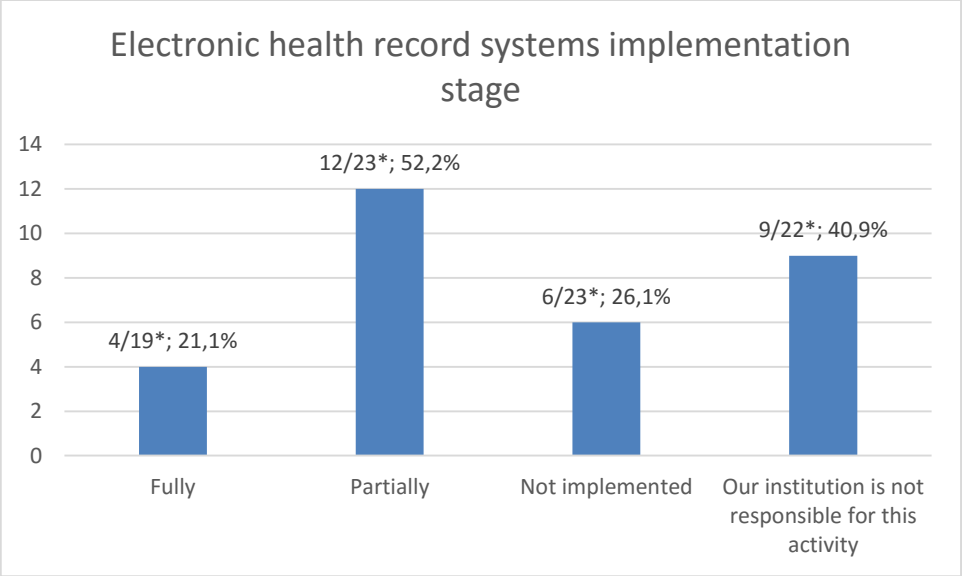
Summary

- Current state of implementation of electronic health records
- Integration with ADR reporting systems
- Registries and databases used
- Identification of electronic systems and information sent between them

Question T5Q25: Are electronic health records used by the healthcare system in your member state?

	Yes	No
Fully	❍	❍
Partially	❍	❍
Not implemented	❍	❍
Our institution is not responsible for this activity	❍	❍

This question provides information about electronic health record systems implementation stages and responsibilities.



*Number of respondents

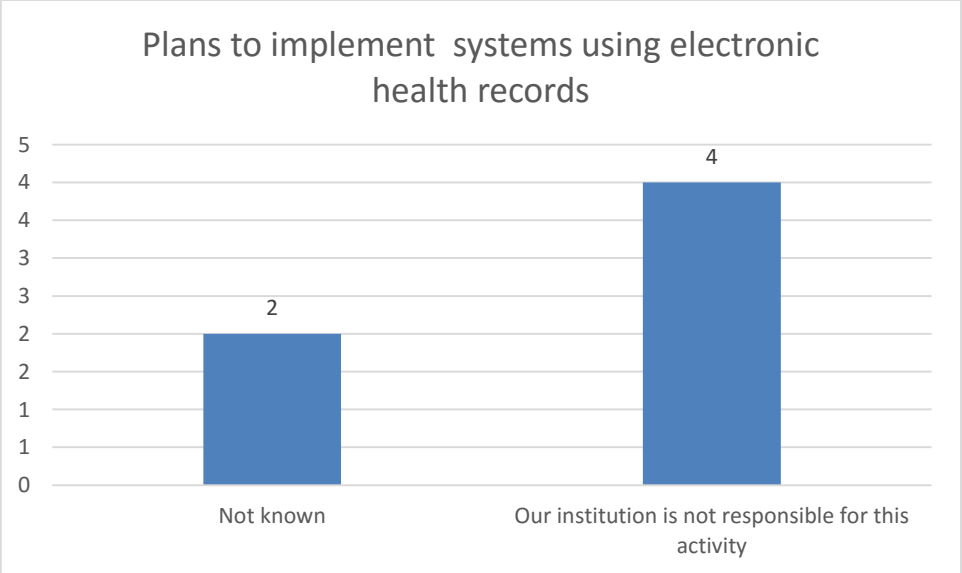
Some respondents answered both "Our institution is not responsible for this activity" and some other answer in case they have information that this kind of a system is being developed or exists in their MS. We have excluded answers from 2 MSs as they were in conflict / contradictory: one MS's answers were "Not implemented" and "Fully implemented" and the other one's answers were "Partially implemented", "Not implemented" and "Our institution is not responsible for this activity".

Question T5Q26: If not implemented, do you know if there are plans to implement systems using electronic health records within:

- ❍ < 1 year
- ❍ 2-3 years
- ❍ > 3 years
- ❍ Not planned
- ❍ Not known
- ❍ Our institution is not responsible for this activity

This question is connected to T5Q25 – "Are electronic health records used by the healthcare system in your member state?" and it was displayed to the respondent only if "Not implemented" answer was chosen in T5Q25.

Six countries answered to this question. Two of them answered that they didn't know if there were future plans to implement systems using electronic health records and four countries answered that their institution was not responsible for this activity.



Question T5Q27: How many electronic health record systems exist in your MS:

Number of systems: (Please enter numerical value)

Please specify names of the systems:

Here we can see text answers received for this question with 13 respondents answering:

Number of systems: (Please enter numerical value)	Please specify names of the systems:
20	5 regional hospital EHR systems and approx. 15 different GP EHR systems
Unknown	Primary care; EMIS, SystmOne, Vision, iSOFT, Microtest, plus many other secondary care
unknown	DIPS, Winmed, Infodoc, System X, Gerica, Winmed2/Forskrivningsmodulen, Visma, Curit, Hove, CGM, Metavision, Doculive (This is probably not all)
2	System1, System2*
UNK	N/A
many different	
N/A	N/A
17 (to date only 17 out of 21 *blinded* Regions have an EHR implemented or under implementation in a pilot stage)	EHR, to be understood as a systematic collection of electronic health information about an individual patient, is the common name used for those systems in all regions
3	E-prescription, National System for Adverse Events Reporting (for hospital care only), IZIP (electronic healthcare booklet)
Unknown	Unknown
unknown but approx. 50	
	several but not exactly known
	discharge summaries, admissions and discharge records, requests for medical tests, access to test results

*system names were anonymised

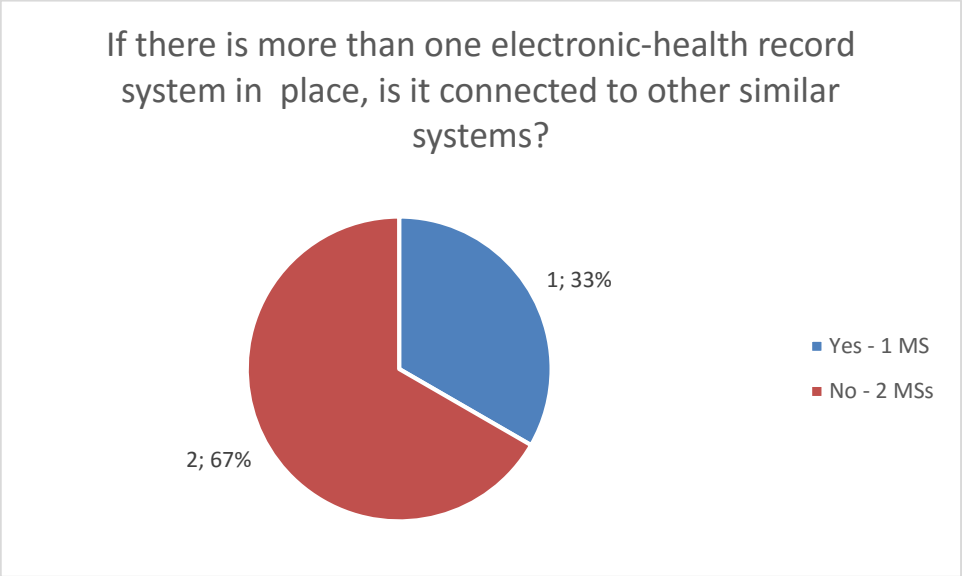
What can be seen from the upper table is that some MSs have more than one EHR system in place, and some don't have information if there are EHR systems in place.

One MS stated they have 2 EHR systems in place. We needed to correct this answer as System1 is main EHR system, and hospitals have their own hospital information systems (System2).
Hospital information systems are provided by different manufacturers but they are all connected with System1. If we consider them as EHR systems we can say that this MS has more than 2 EHR systems in place.

Question T5Q28: If there is more than one electronic-health record system in place, is it connected to other similar systems?

- ❍ Yes
- ❍ No
- ❍ Our institution is not responsible for this activity

For the countries which answered that they have more than one electronic health record system in place, this question was displayed. From positive responses to previous question (13), just three MSs answered this one. One MS answered they have EHR connected with other similar systems and 2 MSs answers were negative.



Question T5Q29: If YES, is there at least one electronic-health record system connected with other health systems, please indicate which of the following listed below:

	Yes	No
Patient registry	❍	❍
Electronic prescription	❍	❍
Electronic referral	❍	❍
Spontaneous ADR reporting system	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

This question is connected to previous question (T5Q28). Since only one MS answered positively to previous question, just one answer to this question was received.

Electronic health record system in this MS is connected with two other systems- Patient registry and Electronic prescription system.

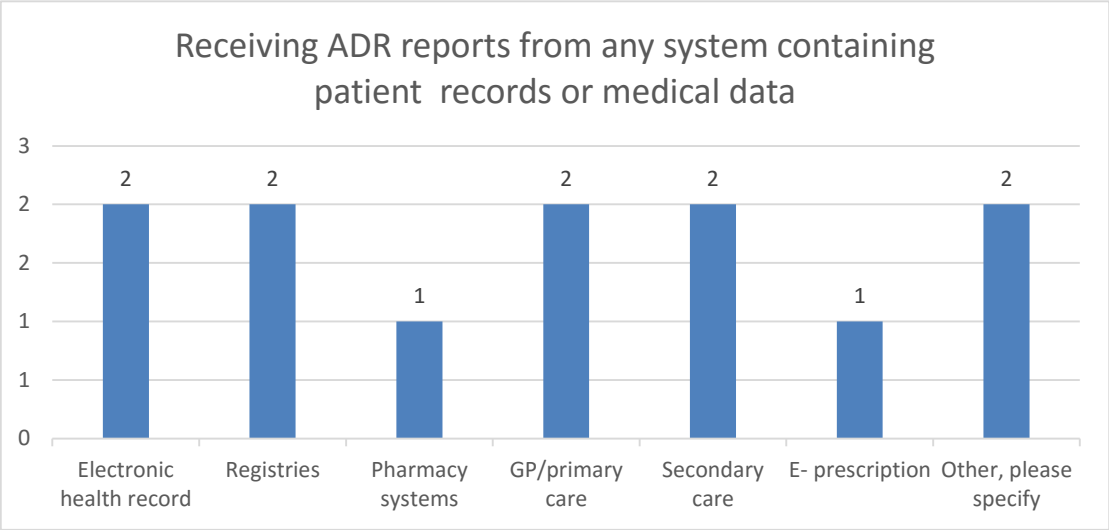
Question T5Q30: Do you receive ADR reports from any systems containing patient records or medical data?

	Yes	No
Electronic health record	❍	❍
Registries	❍	❍
Pharmacy systems	❍	❍
GP/primary care	❍	❍
Secondary care	❍	❍
E- prescription	❍	❍
Other, please specify	❍	❍
No, we do not receive	❍	❍
Our institution is not responsible for this activity	❍	❍

The aim of this question was to see if there are MSs that are receiving ADRs from other systems, containing patient records or medical data. This could potentially have influence on a number of ADRs received and could be considered as good practice.

Five (5) respondents answered to this question and from the chart we can see that some of them have established connections with more than one system from which they can receive ADRs.

18 respondents answered this question.



From the answers received, it is visible that one MS has connections with four systems (EHR, Pharmacy systems, GP/primary care and Secondary care). ADRs received from other systems improve quality of data received because data in those systems are checked and consistent.

Another MS also receives ADRs from more than one system and we can consider those two MSs as good practices examples.

Two respondents answered “Other, please specify”. Text answers from both of them showed that they are currently not receiving ADRs from mentioned systems. Both countries have plans and are currently working on development of these systems to be able to receive ADR from connected systems, containing patient records or medical data.

This type of system connections ensures data quality, consistency and data accuracy.

Question T5Q31: If you receive ADR reports from Registries, please specify type:

	Yes	No
Patient registry	❍	❍
Disease registry	❍	❍
Drug registry	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

This question is connected to T5Q30. MSs which responded that they receive ADRs from registries were to answer this question.

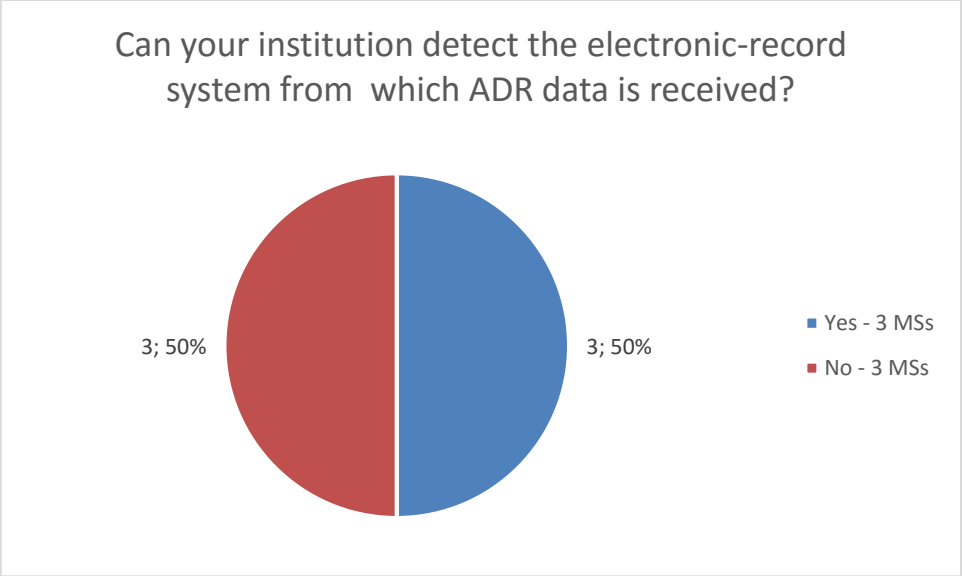
In total, two countires answered this question. The first one receives ADRs from Disease registry and the other one answered „Other, please specify". This MS is receiving data from other competent authority within the same country and collaboration is based on a protocol signed between them.

Question T5Q32: Can your institution detect the electronic-record system from which ADR data is received?

❍ Yes
❍ No
❍ Our institution is not responsible for this activity

The intention of this question was to see if an ADR is received from another EHR system, is it possible to detect which system it was received from. It might be useful information to know the source of the data received into one's system. In case EHR system contains important data, it can be used as formal basis for user authentication or for data analysis.

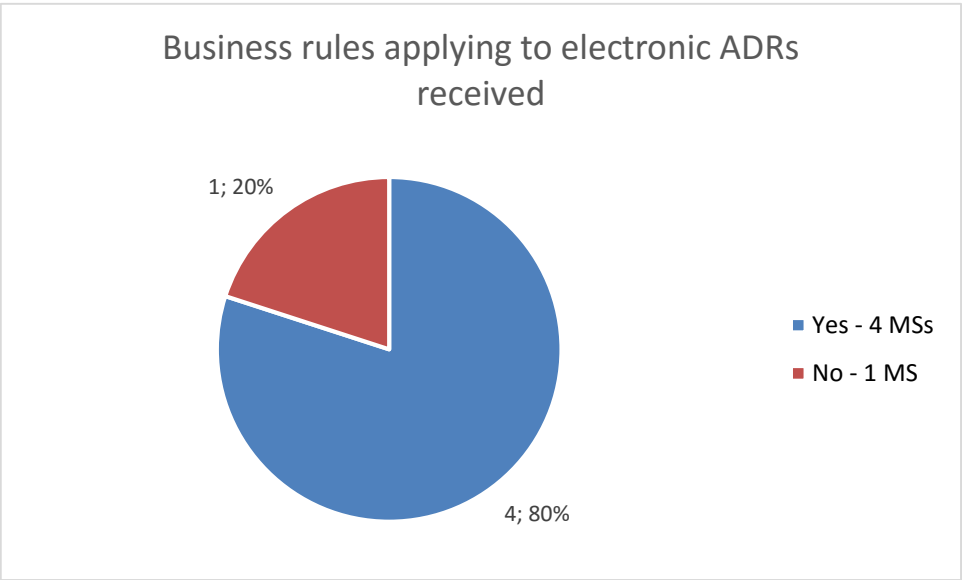
Three (3) MSs are able to detect EHR system from which is the ADR received.



Question T5Q33: Are there business rules applied to electronic ADR message received (deriving from health records) to ensure ADR messages are valid?

- ❍ Yes
- ❍ No
- ❍ Our institution is not responsible for this activity

When electronic ADRs are received, the data received need to be checked and business rules must be applied to ensure right data has entered the system. 4 MSs have business rules embedded into their systems to be sure correct data are received.



Applying business rules to data received from other systems is considered good practice. It is less time consuming as this can be regarded as the first filter or validity check. If electronic ADR message doesn't comply with business rules, it won't be received into the system and there is no need for someone to check each message for the mistakes.

Question T5Q34: Type of communication between your institution and the ADR reporter (in case ADR reports are received from electronic health record system) is:

	Yes	No
One-way (ADR report received as incoming message)	❍	❍
Two-way (exchange of incoming and outgoing messages)	❍	❍
Our institution is not responsible for this activity	❍	❍

Intention of this question was to find out what kind of communication is established between reporter and the institution when receiving electronic ADR reports from electronic health record system. Usually it is one-way, inbound communication, when the electronic ADR report comes as an incoming message. The emphasis was on the two-way communication and from the results it can be seen that only one MS has that kind of a communication established. Three other MSs which answered to this question have only one way communication.

Our additional questions to MS, which has two way communications in place, were to provide us with details regarding ways of communication, how communication is carried out, whether there are there any notifications in the system and how MAHs are registered for communication.

The answer was that communication is performed through gateway and MAHs have their post-boxes where they receive documentation sent to them. To be able to receive documentation, MAHs need to be registered within NCA. There are no notifications implemented, although MAHs have to check their post-box daily.

Question T5Q35: Is it possible for an ADR reporter to be registered in more than one system which has implemented the electronic-health record?

- ❍ Yes
- ❍ No
- ❍ Our institution is not responsible for this activity

Four (4) respondents answered "Yes" to this question, which means that reporter can be registered in more than one system with implemented EHR. Only one country/respondent answered that reporter can be registered in one system only.

Question T5Q36: If YES, is there a way to uniquely identify the ADR reporter?

- ❍ Yes
- ❍ No
- ❍ Our institution is not responsible for this activity

This question is connected to T5Q35 about the possibility for an ADR reporter to be registered in more than one system which has implemented the electronic-health record.

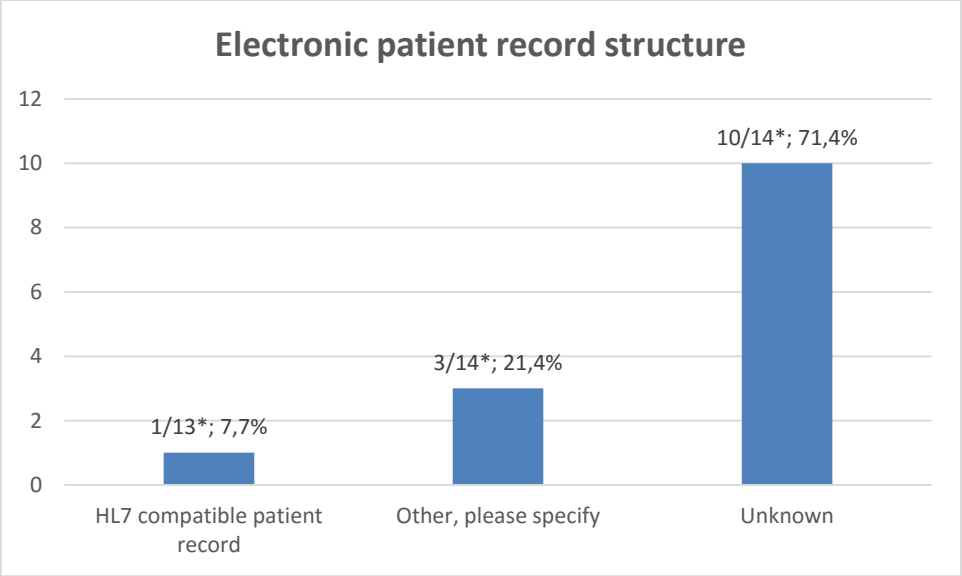
One respondent answered that it was possible to identify ADR reporter uniquely.

Unique identifier of reporter is important in case we want to know which reporter sent a certain ADR and how. Also, it is useful for evaluation and rewarding of reporters since a clear list of ADRs reported can be obtained.

Question T5Q37: Electronic patient record is structured as:

	Yes	No
HL7 compatible patient record	❍	❍
Other, please specify	❍	❍
Data is not structured	❍	❍
Unknown	❍	❍
Our institution is not responsible for this activity	❍	❍

In the following chart we can see the electronic patient record structure. The aim of this question was to see if all MSs use the same standard or different standards are used. Most of the respondents don't have information which standard is used and one respondent answered that they are using HL7 (Health Level Seven) compatible patient record.



*Number of respondents

There were three "Other, please specify" answers:

- ICD 10
- No specific standard
- E2B format

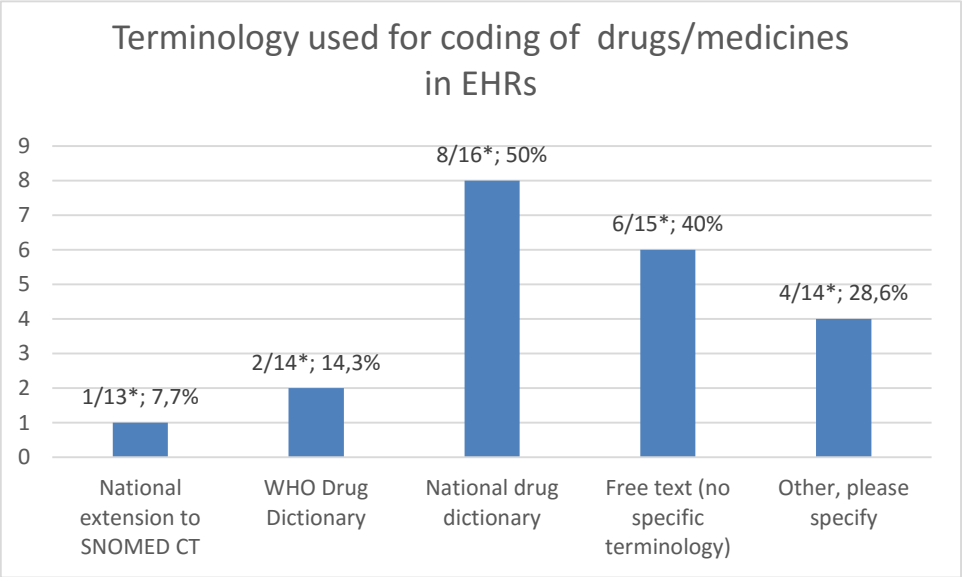
From the answers received, we can conclude that respondents haven't fully understood the question.

Question T5Q38: What terminology is used for coding of drugs/medicines in electronic health records in your member state?

	Yes	No
National extension to SNOMED CT	❍	❍
WHO Drug Dictionary	❍	❍
National drug dictionary	❍	❍
Free text (no specific terminology)	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

This question shows which terminology is used for **coding of drugs/medicines in the electronic health records** of the member states.

The chart below shows that there are many different terminologies used for coding of drugs/medicines, depending on a respondent. We can see that the following are used: national extensions to SNOMED CT (1 respondent), WHO drug dictionary (2 respondents), National drug dictionaries (8 respondents), 6 respondents use no specific terminology and 4 respondents provided additional text answers.



*Number of respondents

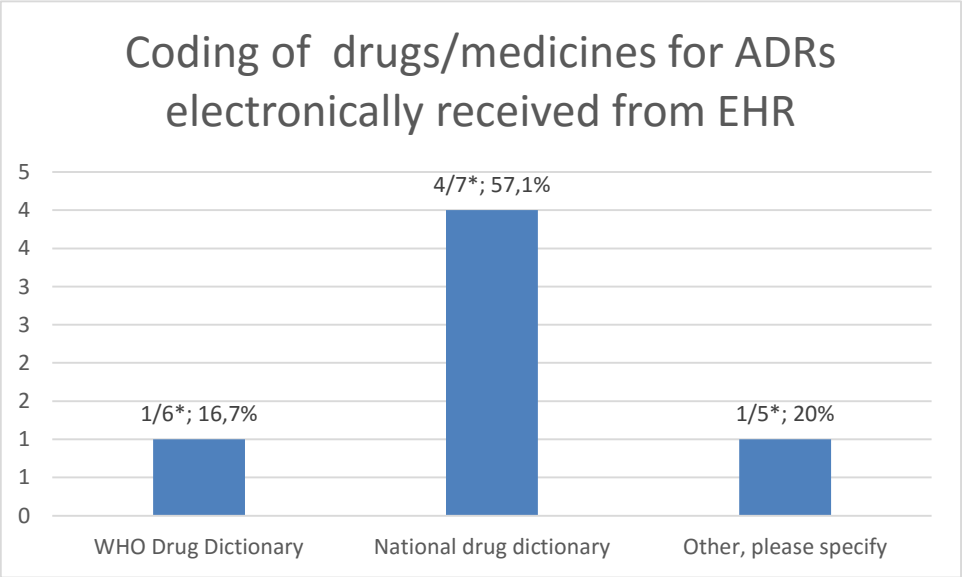
“Other, please specify” answers were:

- AIS / ATC
- No ADRs are received from EHR
- Unknown, with the comment that one MS uses several different EHRs

Question T5Q39: If you receive ADRs electronically from electronic health records, what terminology is used for coding of drugs/medicines in your institution?

	Yes	No
National extension to SNOMED CT	❍	❍
WHO Drug Dictionary	❍	❍
National drug dictionary	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

The intention of this question was to find out what terminology is used for coding of drugs/medicines in the institution when ADRs are received electronically from electronic health records. Answers from 6 respondents were received: 1 respondent is using WHO drug dictionary, 4 respondents are using national drug dictionaries and 1 respondent is using a different technique.



*Number of respondents

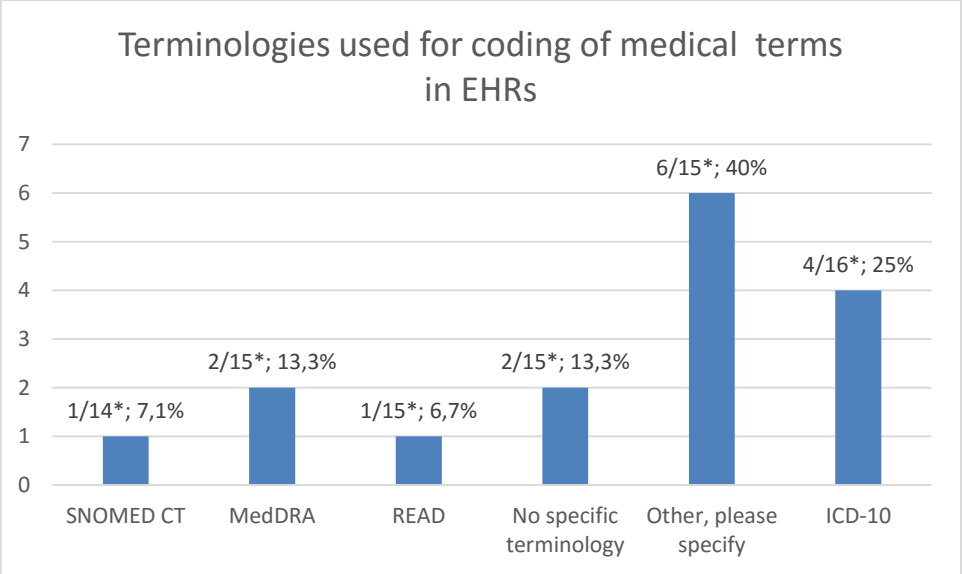
One MS provided "Other, please specify" answer specifying that they are using "Dictionary based on licensing data".

Question T5Q40: What terminologies are used for coding of medical terms in electronic health records in your member state?

	Yes	No
SNOMED CT	❍	❍
MedDRA	❍	❍
READ	❍	❍
WHO-ART	❍	❍
ICD-10	❍	❍
No specific terminology	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

This question shows what terminologies are used for **coding of medical terms in electronic health records** in member states. 13 respondents answered this question. Some of the respondents gave multiple answers as shown in the chart below.

The ICD-10 terminology is used by the most of respondents.



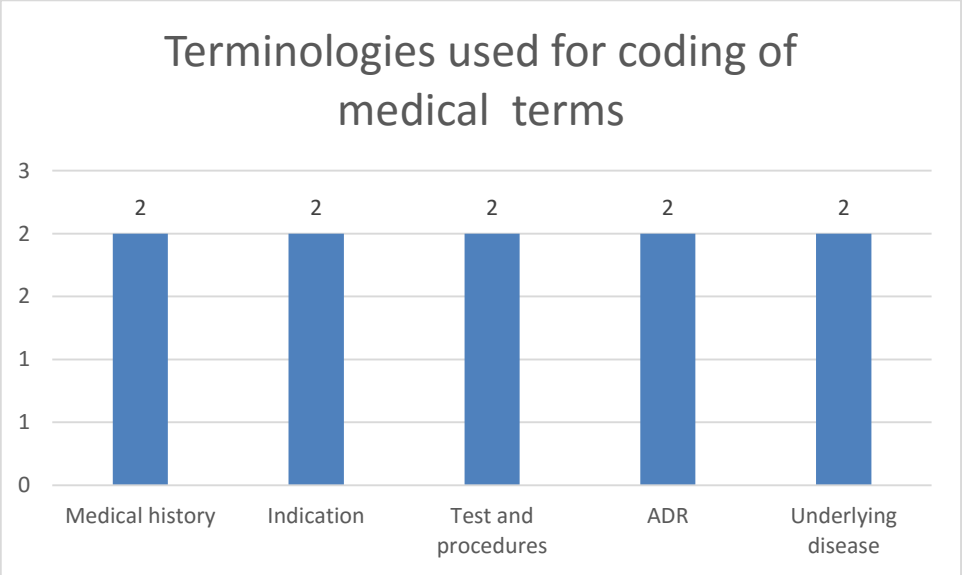
*Number of respondents

When "Other, please specify" text answers were analysed, it was found that respondents also use ICD-10 for diagnosis and ICD-9-CM, ICPC and ICD-10 for disease classification. Other respondents did not have this information or they were not sure which terminology was used for coding of medical terms in EHR.

Question T5Q41: What do you code in MedDRA?

	Yes	No
Medical history	❍	❍
Indication	❍	❍
Test and procedures	❍	❍
ADR	❍	❍
Underlying disease	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

Only 2 respondents answered this question. Both respondents use MedDRA for coding of Medical history, Indication, Test and procedures, ADRs and Underlying diseases.



Question T5Q42: If you receive ADRs electronically from electronic health records, what terminology is used for coding of medical terms in your institution?

	Yes	No
SNOMED CT	❍	❍
MedDRA	❍	❍
READ	❍	❍
WHO-ART	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

The intention of this question was to see what terminology is used for coding of medical terms when ADRs are received electronically from electronic health records.

We recieved answer from 7 respondents . All 7 are using MedDRA for coding of medical terms when ADRs are received electronically from electronic health records and in the textual answer they also stated that they don't receive any ADRs from EHR systems.

Question T5Q43: What do you code in MedDRA?

	Yes	No
Medical history	❍	❍
Indication	❍	❍
Test and procedures	❍	❍
ADR	❍	❍
Underlying disease	❍	❍
Other, please specify	❍	❍
Our institution is not responsible for this activity	❍	❍

Seven (7) respondents answered they are using MedDRA for coding of Underlying diseases, ADRs, Test and procedures, Indication and Medical History. All except one MS, code Medical history using MedDRA.

Question T5Q44: If not MedDRA, how do you map these terms to MedDRA for populating your database and transmitting to EudraVigilance?

	Yes	No
Manually on a case by case basis	❍	❍
Automatically using software based mapping	❍	❍
Automatically based on a mapping previously created between terminologies	❍	❍
Our institution is not responsible for this activity	❍	❍

This question shows how terms are mapped to MedDRA when respondents are populating their own databases and transmitting ADRs into Eudravigilance. From the answers received it is visible that all three respondents do it manually on a case by case basis. 2 MSs are also using automatic mapping previously created between terminologies. Preparation and initial mapping is also manually done and it is prerequisite for this way of mapping. One MS is also performing automatic, software based mapping.

Both above mentioned MSs, which are using automatic mapping software or previously created mappings, can be considered as good practice examples.

Q46-Q48: Traceability of biologics

Summary
- Software tool and methodologies applicable for traceability of biologics
- Short overview what is currently in use

Question T5Q46: Do you use some IT system or a software tool for traceability of biologics?

❍ Yes
❍ No
❍ Our institution is not responsible for this activity

One respondent answered "Yes" to this question.

Question T5Q47: If yes, please provide the name and manufacturer of the system/tool implemented

Name:
Manufacturer:

This question is connected with previous question (T5Q46). From text answer this MS provided it was found that they are using internal spreadsheets tool for traceability of biologics.

Question T5Q48: Is the system/tool integrated with other health systems (drug registry, patient registry …)?

❍ Yes
❍ No
❍ Our institution is not responsible for this activity

The answer from above mentioned MS to this question was "No" as internal spreadsheets are not connected with any other system.

Q50-Q60: Integration with mobile reporting

Summary
- Possibilities of integration of mobile reporting with health records and health care systems
- Future perspectives and initiatives
- Mobile and social network applications for ADR reporting

Question T5Q50: Have you implemented mobile or social network application for ADR reporting?

	Yes	No
Mobile app	❍	❍
Social network app	❍	❍
Our institution is not responsible for this activity	❍	❍

Two respondents answered "Yes", that they are using Mobile app for ADR reporting.

We have received no response for Social network app usage.

We have followed up this question with one MS because we received different information in WP4 Topic 4 questionnaire "Reporting forms".

The answer was that this MS is using already developed mobile application for ADR reporting. It is the http://www.evedrug.eu/myereport.php application which is available in different countries and it allows sending reports from all types of mobile devices.

Question T5Q51: If you collect ADR reports via the following, when was it implemented?

	HCP - Since month/year (MM/YYYY)	Patients - Since month/year (MM/YYYY)
Mobile applications		
Social network app		

MS 1- App was implemented in 10/2009 for HCPs and in 10/2012 for patients.

MS 2- App was implemented in 10/2012 for HCPs and it was still not implemented for patients at the time of the survey.

Question T5Q52: Please provide details and URL of any app, and mobile app platforms used

MS 1- https://verbraucher-uaw.pei.de/fmi/iwp/cgi?-db=Verbraucher-UAW&-loadframes

MS 2- https://itunes.apple.com/it/app/adr-fimmg-aifa/id564273942?mt=8

Question T5Q53. Does your mobile app contain different fields to your electronic forms?

- ❍ Yes
- ❍ No
- ❍ Our institution is not responsible for this activity

From answers received, we can conclude that there is no difference in fields used for electronic forms and for mobile app.

QuestionT5Q54: If Yes, please provide the details:

No answers received. This question is connected to answer "Yes" in T5Q53.

Question T5Q55: Is your mobile app able to scan product license numbers and translate this to product name?

- ❍ Yes
- ❍ No
- ❍ Our institution is not responsible for this activity

Both apps are unable to scan products' license numbers and translate them into the product name.

Question T5Q56: If Yes, please provide details:

No answers received. This question is connected to answer "Yes" in T5Q55.

Question T5Q57: Is your mobile app able to detect products from the additional monitoring list to prompt the reporter for additional data?

- ❍ Yes
- ❍ No
- ❍ Our institution is not responsible for this activity

Both apps are unable to detect products from the additional monitoring list in order to prompt the reporter for additional data.

QuestionT5Q58: If Yes, please provide the details:

No answers received. This question is connected with answer "Yes" in T5Q57.

Question T5Q59: If not already implemented, do you plan to implement mobile app in:

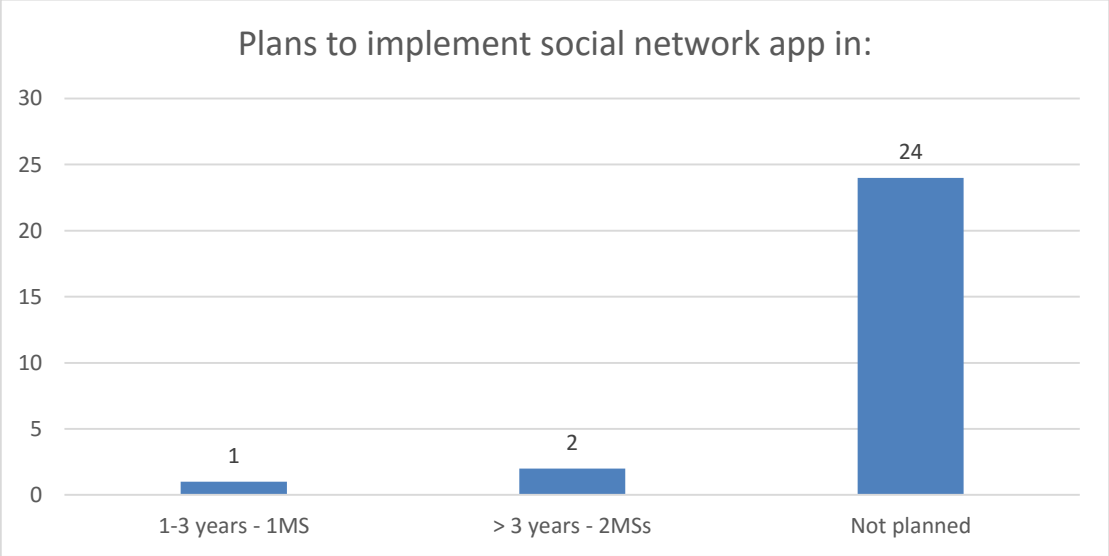
- ❍ < 1 year
- ❍ 1-3 years
- ❍ > 3 years
- ❍ Not planned
- ❍ Our institution is not responsible for this activity

From responses we have received we can see that there are plans to implement mobile app for ADR reporting. There are 5 MSs that have plans to develop and/or implement mobile app for ADR reporting. 2 MSs plan to do that in less than a year, 3 MS in period from 1 - 3 years and one in more than 3 years from the time this survey was taken.

Question T5Q60: If not already implemented, do you plan to implement social network app in:

- ❍ < 1 year
- ❍ 1-3 years
- ❍ > 3 years
- ❍ Not planned
- ❍ Our institution is not responsible for this activity

From responses received we can see that there are plans to implement social network ADR reporting. There are 3 MSs that have plans for implementing social network app for ADR reporting. 1 MS has plans to do this in period form 1- 3 years, and the other 2 MSs have plans to do this in period greater than 3 years.



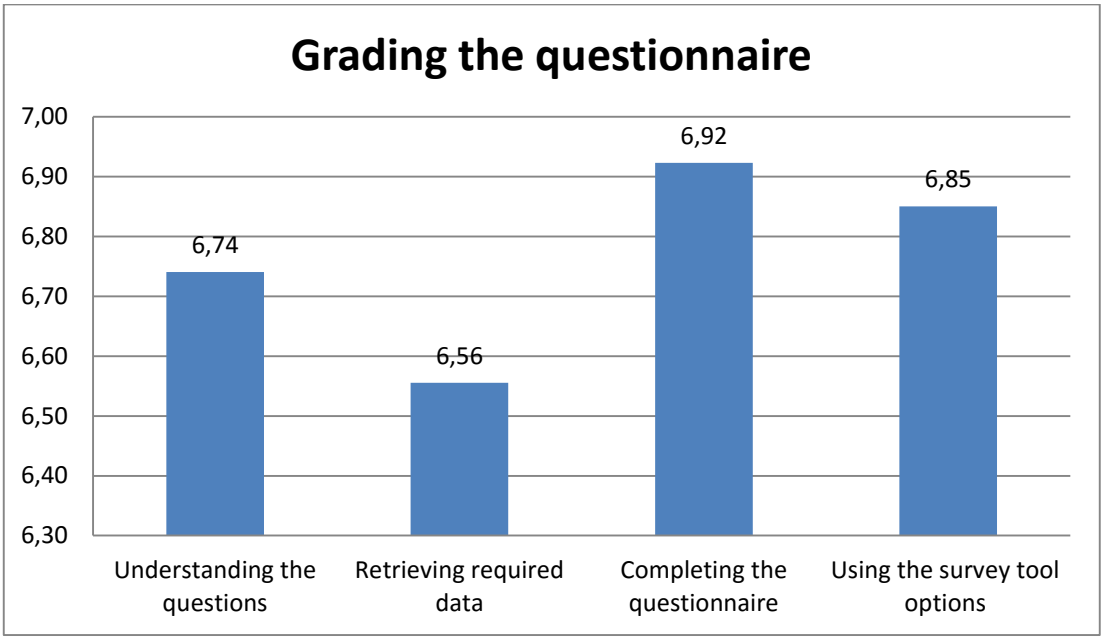
T5Q61 g) Summing up

Question T5Q62: Please write down any additional comments you would like to share with regard to your national IT system for ADR reporting:

Fifteen (15) MSs provided some additional comments regarding their national ADR reporting systems. Some of the comments provided additional information related to specific questions and were very helpful for interpretation of the specific answer. Some of the comments were about future plans for implementing new or upgrading existing ADR reporting systems. There were also comments regarding wrong answers to certain questions and corrections that were needed to be done.

Question T5Q63: Finally, we would like to kindly ask you to grade this questionnaire.

_____ Understanding the questions
_____ Retrieving required data
_____ Using the survey tool options
_____ Completing the questionnaire



The questionnaire was graded with a mean of 6, 77 out of ten for understanding the questions, retrieving required data, completing the questionnaire and using the survey tool options.

T5Q64 Please check if you have answered all questions. You can use "back button" to go through the survey and make sure everything is filled in before submitting. Please note that choosing "next button" is going to automatically submit the questionnaire. Thank you!

Question 64 was not a question but expressing gratitude to respondents for completing the questionnaire and allowing the questionnaire to be submitted.

4 Conclusion

A good response rate was obtained for the surveys sent out (28/31 for Topic 1 Audit of national reporting systems; 28/31 for Topic 1a Medication errors; 28/31 for Topic 2 Patient reporting and27/31 for Topic 5 Review of IT systems and special form of reports). Those results indicate a real interest in this area and a high ambition for improvement among MSs. Responses also show significant **diversity** of practices in different MSs. Different MSs have different systems for ADR processing, some legal specificities in addition to the EU legal requirements, different number of employees in pharmacovigilance departments, different budgets, different IT systems etc. Therefore, it is impossible to give unique recommendation which would fit all MSs. We will try to give recommendations through the deliverables from this Work Package on different levels (low, medium and high level), so every MS could take something from the recommendations and tailor it to their national, specific needs. We found plenty of good practice examples and are of the opinion that sharing those examples and experiences would have great impact. It is important to stress out once again that when interpreting the results and giving recommendations, we should bear in mind the great variety in the way how the work in PhV is performed among MSs.

5 Recommendations and toolkit suggestions

The following set of recommendations is based on findings from the surveys. For each recommendation proposed, the main advantages and disadvantages are set out.

5.1 Topic 1 Audit of national reporting systems

<table>
<tr><td colspan="2">Snapshot and analysis of national reporting systems
Review paper on national pharmacovigilance systems in MSs until 2013</td></tr>
<tr><td>Advantages:
Special SCOPE issue of Drug Safety
Overview and highlights of survey findings
Target audience - wider scientific community
Sustainable means of communication for SCOPE results</td><td>Disadvantages:
Challenges with timelines for publishing the paper</td></tr>
</table>

Transition to E2B-R3 • The position paper with recommendations for NCAs about the transition process to E2B-R3 and with outstanding issues toward EMA • Specifying MS' needs related to introduction of E2B-R3 reporting within their system (findings to implement)	
Advantages: • EMA interested in results of SCOPE. This topic might be a good example of highlighting MS' specific and common challenges in this transition period. • To provide the current state of progress made • MSs would like to have more clear guidance regarding timelines and how to introduce R3 system into the MS	**Disadvantages:** • As this topic is covered by EMA, duplication of work should be avoided

Duplicate detection • Provision of guideline to interested MSs indicating criteria for duplicate detection (e.g. defining EV fields that should be checked during duplicate detection process) • Providing case studies (good practices) to interested MSs indicating criteria for duplicate detection • Providing data (specification) for upgrade of the ADR DB functionality by introducing duplicate detection algorithm which could find a list of potential duplicates	
Advantages: • Optimization of duplicate detection process • Lower number of duplicates in MS' database	**Disadvantages:** • Implementation of the process requires resources • Benefit - cost ratio questionable in case of upgrading DB functionalities with algorithm for MSs with low number of duplicates

Additional monitoring • Guidance (Good practice) for identification, management and increase of number of ADR reports for drugs subject to additional monitoring • Introducing technical solution for identifying ADR reports subject to additional monitoring by using a database flag or database flag combined with reference data/drug dictionary	
Advantages: • Ability to capture and track ADRs for drugs on additional monitoring list • Higher quality of reports resulting in better signal detection	**Disadvantages:** • Implementation of the process requires resources • Challenge to maintain and keep list of drugs on additional monitoring up-to-date

Benchmarking tools- quality of ICSR • Guidance document with recommendations to use more than/at least one source /set of indicators/ metrics for assessment of quality of reports	
Advantages • Ability to identify strengths and weaknesses • Ability to use the indicators to define the strategic goals/future development more precisely	**Disadvantages** • Need for development of relevant indicators

Active approach to comparison of ADR reports from different reporter groups • Guidance document with case studies	
Advantages • Provides insight into the pharmacovigilance impact of these reports • These insights might feed into other pharmacovigilance activities (e.g. signal management)	**Disadvantages** • Possibly time consuming

5.2 Topic 1a Medication errors

<table>
<tr><td colspan="2">Joint Position paper covering 3 topics:

1. Exemption from liability for HCPs when reporting cases of ME
2. Coding of medication errors
3. Collaboration with other institutions which deal with medication errors

• Position paper with:
○ recommendation for exemption from liability for HCPs when reporting ADR cases related to ME
○ recommendations for best practice for coding of ME
○ description of best practices in EU related to collaboration with other institutions which deal with ME</td></tr>
<tr><td>Advantages:
• Encouraging HCPs to report these important cases
• More information about handling of medicines in real life
• Harmonized approach to coding of cases of medication errors
• Better tracking of cases of medication errors
• Improving duplicate detection of ME cases</td><td>Disadvantages:
• Legal issues
• Time consuming</td></tr>
</table>

5.3 Topic 2 Patient reporting

Snapshot and analysis of national reporting systems • Review paper on national patient reporting systems in MSs until 2013	
Advantages: • Specific SCOPE publication • Overview and highlights of survey findings • Target audience - wider scientific community • Sustainable means of communication for SCOPE results	**Disadvantages:** • Challenges with timelines for publishing the paper

Collaboration with patient organizations to promote and support patient ADR reporting • Guidance document with case studies	
Advantages: • Receiving more direct patient ADR reports • Increasing patients awareness level of NCA existence • Empowerment of patients	**Disadvantages:** • Time consuming • Lack of resources • Challenges in prioritization towards approaching patient organizations

Feedback to patients • Document focusing on information that can be included into the feedback to patients • Check-list and already generic formatted text for MSs to use and adapt according to national needs • Automatic, semi-automatic and individual feedback	
Advantages • Patients are more knowledgeable of availability of relevant sources of information and also of aims of pharmacovigilance activities	**Disadvantages** • In some circumstances patients may misunderstand that the NCA can give individual health advice

5.4 Topic 5 Review of IT systems and special form of reports

<table>
<tr><td colspan="2">E-reporting, automatic transmission of ADRs and communication between various systems
Guidance document providing Information, instructions & tips for implementing and improving ADR IT systems
Representation where we are & where we want to be
Divided into three different levels based on MSs ADR IT system maturity
Level 1 – basic, low level, usually no system in place
Level 2 – operating level, analysis of the systems in place
Level 3 – advanced level, analysis of the advanced functionalities
Providing case studies on functionalities</td></tr>
<tr><td>Advantages:
• Increasing efficiency
Less administrative time
More time for professional assessment
Quick communication between systems
• Better data quality
Validated, checked and accurate data
Faster and easier data collecting
Common data dictionaries and registries
Predefined data inputs
• Error prevention
Human error prevention
System error prevention
Business rules
• Reducing risk
Error prevention
SOPs in place</td><td>Disadvantages:
Historic data migration
Existing DB data accuracy and integrity
Costs of implementation
No SOPs in place for business continuity in case of system failure
Insufficient human resources</td></tr>
</table>

6 Annexes

Annex 1: Topic 1 Audit of national reporting system survey questions

Audit of national reporting systems.pdf

Annex 2: Topic 1a Medication errors survey questions

Medication errors.pdf

Annex 3: Topic 2 Patient reporting survey questions

Patient reporting.pdf

Annex 4: Topic 5 Review of IT systems and special form of reports survey questions

Review of IT systems and special form of reports.pdf