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Pharmacy Faculty

Graduation Project Report

Graduation Project
Promotion of Pharmacovigilance among Patient Organizations in Europe - a Qualitative Study

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1. Abbreviations

Abbreviation	Meaning
ADR	Adverse Drug Reaction
DPR	Direct Patient Reporting
EMA	European Medicines Agency
EU	European Union
EUPATI	European Patients' Academy
EURORDIS	European Organization for Rare Diseases.
GTM	Grounded Theory Methodology
HCPs	Health Care Professionals
Lareb	Netherlands Pharmacovigilance Centre
NCAs	National Competent Authorities
PO(s)	Patient Organizations (s)
PV	Pharmacovigilance
QDCA	Qualitative Data Content Analysis
QUAL	Qualitative
QUAN	Quantitative
SCOPE	Strengthening Collaboration for Operating Pharmacovigilance Joint Initiative
WHO	Health World Organization

2. Problem of Study and Justification.

In most countries of the world, pharmacovigilance (PV) relies on an spontaneous system, this means when the patients experience a possible Adverse Drug Reaction (ADR), they communicate the symptoms to their Health Care Professionals (HCPs) who finally submit a report to the authorities. In many countries patients also have the possibility to report ADRs *directly* to their National Competent Authorities (NCAs), contributing to a safer use of drugs (van Grootheest & van de Berg, 2004).

Patient contribution to PV has been under question for long time (van Grootheest, de Graaf, de Jong-van de Berg, 2003; Hazell *et al.*, 2013, Inácio, Cavaco & Airaksinen, 2016; Rolfes *et al.* , 2017), nowadays it is accepted that patients can make high quality reports, patients provide detailed information about the impact of the ADRs on their life and they are more likely to report than HCPs (Rolfes et al, 2015; Rolfes et al, 2017). Their contribution to signal detection has also been validated (Hazell et al., 2013;) and the involvement of patients in pharmacovigilance is promoted as an important key to a balanced PV system (Smith & Benattia , 2016; van Hunsel, Harmark & Rolfes, 2019)

Despite the demonstrated value of reports submitted by patients, under reporting is a common problem in spontaneous reporting systems (Hazell & Shakir, 2006). To address the under reporting problem all stakeholders should be stimulated to actively participate in drug safety activities.

Patients and their representatives are important stakeholders in PV. It is common that patients suffering chronic conditions seek for support, advice and education to better understand their disease; often these needs are covered by becoming members of patient organization, including them in their support network (Hu, 2017).

To report, patients must be informed about pharmacovigilance, they must be aware of the possibility of reporting and the channels they can use to do so, they should understand the impact and importance of reporting, what can be reported and they must be persuaded to report (Lopez-Gonzalez, Herdeiro &Figueiras, 2009).

The infrastructure of patient organizations offers easy access to disseminate information to a specific group of consumers. Therefore, the role of patient organizations in the patient-centered approach is crucial and can be used to increase patient awareness of the importance of reporting ADRs and drug safety which could at the same time contribute reducing the under reporting of ADRs.

The situation of Patient Organizations (POs) in pharmacovigilance is somewhat unknown. The first study to analyse their role was published in 2018, Matos, Weits & van Hunsel found some organizations have few activities regarding pharmacovigilance and their collaboration with NCAs for PV matters is weak or inexistent.

The study was conducted through an online survey, this method allows to manage a big data base, but was inefficient at providing an in-depth perspective of the POs reality in PV and many features underlying the interaction with PV are still unknown.

Topics such as barriers at implementing PV activities, reasons why POs do not support PV activities, interaction with other PV stakeholders and strategies to stimulate POs as active promoters of PV had not been inquired properly and the results were not conclusive.

In addition, many of these organizations suggested they require support from NCAs to break down these barriers (Matos *et al.*, 2018), therefore, it is necessary to study all the components that describe the relationship of patient organizations in pharmacovigilance, to identify efficient mechanisms to strengthen patient organization within the pharmacovigilance system.

The purpose of this qualitative research is to conduct a follow-up study to understand POs perception towards PV, the barriers they face when implementing PV activities, their interaction with other stakeholders and suggest methods for the stimulation of POs as promoters of PV.

3. General Objective

Identify strategies National Competent Authorities in Pharmacovigilance can develop and implement to strengthen the participation of patient associations as active promoters of pharmacovigilance among its members.

4. Specific Objectives

- Qualitatively describe the role of patient organizations as promoters of pharmacovigilance.
- Identify the limitations presented by patient organizations in the promotion and encouragement of the report of adverse drug reactions.
- Determine opportunities for improvement in the communication process between patient organizations and pharmacovigilance centres.
- Develop a tool that stimulates patient organization participation in pharmacovigilance activities.

5. Theoretical Framework

Pharmacovigilance (PV) is defined by the Health World Organization (WHO) as the "science and activities related to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem" (WHO (a), n.d)

The safety of pharmaceutical products is monitored throughout all stages of the product life cycle. During the pre-marketing stages, there is a strong monitoring of the emerging ADRs; in this stages the availability of patients and screening tests are effective at identifying a series of Adverse drug reactions(ADRs) that usually are listed in the initial leaflets (Nourd & Plourde, 2019).

There are multiple reasons why not all adverse events and their real intensity are identified during screening tests, for example, the study population is too small to reach a significant incidence or is to homogeneous, some adverse events depend on the cultural or nutritional

environment in which the medication is used, some events go unnoticed during the trials because the detection technique is not included in the routine screenings and clinical trials have a limited duration which limits the possibility to determine long term use ADRs (Amery, 1999; Stricker & Psaty, 2004).

Post marketing the product is open for prescription and use in the general public; this means a bigger population with vast differences in cultural, environmental and genetic conditions are in contact with the product, which can enlarge the incidence of adverse reactions different from those discovered during pre-marketing stages. The product also becomes available for vulnerable groups like children, elderly and pregnant women who are commonly not included in clinical trials, therefore the safety profile has not been studied in detail for this groups, hence the importance of an effective monitoring system of ADRs as a continuous process for it's also known that ADRs can occur after long term use of a drug (Nourd & Plourde, 2019).

The safety evaluation has become more important and systematic because through time multiple events have evidenced the need of a monitoring system of ADRs, such as the contamination of diphtheria and smallpox vaccines with tetanus in the 19th century resulting in several deaths, and the sulphanilamide disaster in the USA in the 30's when an elixir formulated using diethylene glycol caused the death of over 100 people (AHMAD *et al.*, 2019; Banahan, 2011). Certainly one of the most significant events that shaped the current regulatory environment in PV is the congenital malformations associated to the use of thalidomide between the 50s and 60, it is estimated that over 10 000 children were born with anatomical abnormalities due to the use of this product by their mother during pregnancy (AHMAD *et al.*, 2019;Vargesson, 2015)

The World Health Organization (WHO) in the 21st World Health Assembly (1963), promoted PV at a country level by extending an invitation to all member countries to arrange for a systematic collection of information on serious ADR and so, the International Drug Monitoring System was launched (WHO, 1963; Uppsala Monitoring Centre, n.d).

Over time the PV system has improved and expanded to the point that currently 136 countries are members and submit reports of adverse drug reactions to the WHO global

database, VigiBase which at the same time feeds VigiAccess, the database that allows the general public to browse and view data of the ADR reports submitted worldwide.(WHO (b), n.d)

Pharmacovigilance is now established as a component of healthcare systems and it's final objective of safeguarding public health through the early detection of signals of new, rare or serious ADR continues to be the driven motivation behind all efforts.

The PV system in most countries relays in a passive or spontaneous reporting model, presenting the advantage of covering a large population and a wide range of drugs, apart from being relatively inexpensive yet, the main disadvantage of this type of system is that the reporting relies on the reporters motivation, being under reporting its biggest challenge at the moment. Under reporting affects likewise older drugs and not serious reactions as it affects newer drugs and serious reactions, to the point that it is estimated to range between 82% - 98% across multiple studies (Hazell& Shakir, 2006).

European regulations in the field of health increasingly revolve around a patient-centred approach. In 2001, all Member States were called on to taking "the appropriate measures to encourage patients, doctors, pharmacists and other healthcare professionals to report suspected adverse reactions to the national competent authority; for these tasks, organizations representing consumers, patients and healthcare professionals may be involved" (Directive No 2001/83/EC, 2001), and by 2010, members were demanded National Competent Authorities (each country PV agency)to enable channels for Direct Patient Reporting (DPR) of adverse reactions from the general public (Directive No 1235/201, 2010).

Even before the legislation was formally approved and started implementation in 2012, some countries in Europe had already many years of experience in this field. The Pharmacovigilance Centre of the Netherlands, Lareb, had enabled direct reporting since 2003 through a pilot plan that reaped encouraging results (Harmark, van Hunsel & Grundmark, 2015)

Ever since, there has been an increasing number of reports from patients in the Netherlands and the Centre has conducted multiple studies demonstrating that patient reports can contribute in a positive way by providing different information from that provided by Health Care Professionals (HCPs) and signal detection from reports made by patients is proportional to the amount of reports submitted by this same group (van Grootheest & van de Berg, 2004; van Hunsel *et al*, 2010(a); Rolfes et al, 2015). They have also studied the motivations that trigger patient reporting looking for a better understanding of patients role in PV.(van Hunsel et al, 2010-b). After 15 years of experience the Centre concludes that direct patient reporting contributes significantly to a reliable pharmacovigilance (van Hunsel, de Waals & Harmark, 2017).

Other studies are in line with these results, endorsing that patient reports provide a positive contribution to HCPs reports leading to an enhancement of the PV systems. (Hazell *et al.*, 2013) Patients are also more likely to report certain ADRs associated with genitourinary system and sex hormones, systemic hormonal preparations and sex hormone drugs (Banovac et al, 2017) and the possibility for patients to provide their experience through reporting in benefit of PV is by itself important for patients (Anderson et al, 2011)All of this studies support the need to involve patients in pharmacovigilance.

Patients sharing similar experiences and concerns group together into users and Patient Organizations (POs) providing emotional and moral support to one another (Hu, 2017). An important role of POs is representing the interest of their members, in the different activities they participate.

These organizations perform very important and varied functions in the patient support network, as example:

Education of the members and their families, emotionally strengthens its members by allowing them to share experiences related to their illness, raise public awareness, raise funds, provide consultancies, carry out activities to strengthen the group and teach them how to adapt to a style of life with their condition (WHO(c), n.d Hu, 2017).

The number of POs is rising in Europe, as well as the variety of interests they represent and the activities in which they operate, this increase stimulates the rising of alliances, coalitions, umbrellas and pan-European organizations, widening POs network but also increasing the complexity of the interactions making comparison between them hard to establish (Baggot & Foster, 2008).

Involvement of patients and their representatives following a patient-centred healthcare system, increases legitimacy, patient empowerment and better implementation of the chosen policies reason why POs have now a more active role in the development of new drugs (Perfetto et al, 2015;Ingelfinger & Drazen, 2016) collaboration in the development of guidelines, taking part in health technology assessment, reimbursement of treatments and participating in policy making (Barak &Nandi, 2011;Menon &Stafinski, 2011 ; Moreira, 2014 ; Picavet, Cassiman &Simoens , 2014).

POs also have a privileged position towards promoting PV and drug safety due to their close relation with their members and the network of interactions that allow them to easily share information and act as intermediates between patients and other stakeholders (de Lorenzo &Aspostolidis, 2019).

NCA joined to create the Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) initiative, with the purpose of helping PV NCAs operation across Europe following the new requirements of the legislation of 2012. Among the tools generated, the initiative highlights the importance of DPR and promotes the interaction with stakeholders, included Patient Organizations (the Strengthening Collaboration for Operating Pharmacovigilance in Europe, n.d).

However the SCOPE joint initiative found that 57% of NCAs do not work with any patient organization and when the collaboration exists it is most of the time reserved for umbrella or major patient organizations, which demonstrates there is still room to improve this interaction (SCOPE Work Package 4- ADR collection, n.d)

The sole measurement of enabling DPR is not enough to trigger report among patients, it is necessary to encourage involvement of the patients and their representatives in PV to

address the under reporting and obtain the benefits of patient centred approach (van Hunsel, Harmark & Rolfes, 2019).

5.1. The Role of Patient Organizations in Pharmacovigilance

Cristiano Matos *et al*, (2018) studied the role of European patient organizations in Pharmacovigilance, this publication is available on Apex 1. The data for the study was obtained through an online survey.

The survey inquired about POs perception on patient contribution to PV, their interaction with umbrella organizations on PV, the activities they perform towards drug safety, their interaction with PV NCAs, and explores some barriers patient organizations face when implementing PV activities.

The study is the first to evaluate POs involvement in PV providing a general panorama of the situation.

Nevertheless this study present important limitations such as: most of the questions were closed ended statements which limits the possibility to obtain respondents personal experiences and fully explore unknown aspects of their role, some aspects such as POs interaction with other PV stakeholders were not studied, the study does not look for possible solutions to the barriers POs present and the results published only present the quantitative data, the open text fields of the survey were not analysed.

These limitations make it important and necessary to complement the results with a qualitative analysis and provide a broad perspective of all the features that determine POs participation in PV.

The hereby presented study follows a mixed method design, where Matos *et al*, (2018) study present the quantitative (QUAN) phase and this manuscript presents the qualitative (QUAL) sequential phase which integrates both results findings.

The results from the QUAN phase and the analysis of the open text fields of the survey allow to select interesting participants to invite in an in-depth interview, develop a targeted interview guide and help in the quality assessment of this study by triangulation of results.

The purpose of this research is to conduct a qualitative follow-up study for the broad purpose of depth of understanding and corroboration about the perception, barriers, needs and PV preferences patient organizations present through a personal interview with their representatives.

Understanding in depth all of this aspects and taking POs opinion on how to improve the communication with NCA, could be the key towards the implementation of efficient strategies to stimulate POs as active promoters of drug safety.

6. Methodology

The purpose of conduction this qualitative explanatory research as a sequential study from Matos *et al*, (2018) is to provide complementarity and expansion of the role of patient organizations in pharmacovigilance. The qualitative research provides contextual understanding and improves the usefulness of the findings (Schoonenboom & Johnson, 2017).

This study was designed to cover similar topics than those from the quantitative phase such as: the activities they perform in PV the barriers they face towards the implementing of PV activities and the requirements from the NCA to stimulate their involvement, but without limiting the answers to a narrow list of selection; instead the participants are able to express their full perception of the phenomenon allowing to have an in depth perspective of it.

A very important aspect of mixed method study is the point of integration of the findings, Schoonenboom & Johnson, 2017); in this research the results from the quantitative phase will be integrated in the analysis of the hereby presented results. The findings from the

QUAN phase (available on Apex 1) will be generally compared with those discovered through this research.

Due to the characteristics of the materials studied and the data sources as well as the main questions for the analysis, different methodologies were adopted for the analysis of the survey open text fields and the interview.

The survey data were analyzed using Qualitative Data Content Analysis (QDCA) method. The reasons for using QDCA are: the main question for analysis was to describe the lineaments associated to the role of the POs in pharmacovigilance, the author was not involved in the process of sampling and data collection, the information provided in the open text fields is not enough to draw connection theories and the amount of data gathered from the survey is large.

QDCA is also used in this study for quota sampling a particular group of surveyors to refine the existing knowledge through the interview (Frey, 2018).

To achieve a holistic understanding of the phenomenon, Grounded Theory Methodology (GTM) was adopted for the interview study. Grounded Theory Methodology is a systematic method for constructing theoretical analysis from data; it provides rigorous yet flexible guidelines leading to the development of theory grounded in data (Charmaz & Belgrave, 2012) .

Despite the discussion about variations on the techniques, both methods are systematic, and performing both of them allows data and methodology triangulation. (Cho & Lee, 2014)

Qualitative Data Content Analysis as well as Grounded Theory Methodology were carried out using Dedoose.com.

Dedoose.com is a web based program which allows to organize and analyze data for qualitative and mixed method studies. The program facilitates the analysis of data, the development of tree coding structures and it also facilitates the identification of trends among the respondents (Dedoose, n.d.).

6.1 Survey Qualitative Data Content Analysis.

Qualitative Data Content Analysis (QDCA) is an analytical method used either in quantitative or qualitative research for the systemic reduction and interpretation of text, is commonly used for the analysis of open-ended survey questions as in this case (Frey, 2018)

In QDCA the raw data obtained from the open text fields are first treated for an easier management of the information (see 6.1.2 Survey Data Treatment section). The data are then analyzed by grouping quotations about similar topics under the same code or tag and at higher level codes attending to different features of the same aspect are grouped together into categories.

The results directly obtained from the codes and categories are sufficient for the purposes of this study; this stage sought to identify the lineaments present in the POs interaction with PV, select the participants for the interview and be of use for triangulation of results. The coding system consists only of codes and categories and is presented as part of the results under Figure 3.

The data treatment allows to give particular attention to aspects relating to the research question. This step is particularly useful due to the large amount of data available from the survey (Schreier, 2014).

The coding and categorization is an interactive process since there is a constant comparison among excerpts and codes to modify the coding frame in the process (Schreier, 2014).

Qualitative data content analysis has two different approaches for the coding frame elaboration; deductive and inductive approach, the difference between both centers on how initial codes and categories are developed (Cho & Lee, 2014).

When prior knowledge about the phenomenon under study is limited, the codes are drawn directly from the data and this is known as inductive approach. Inductive approach challenges the research focus or takes it on a different direction as it is open to discover new ideas or fresh insight (O'Reilly, 2009).

Contrarily, deductive approach starts with preconceived codes or categories emerging from the study of prior research or literature (Cho & Lee, 2014).

It's important to clarify that in this study the categories generated proceed from both deductive and inductive methods. The categories Positive about DPR, Negative about DPR, Doubtful about DPR and Reasons for not supporting PV, were created deductively, or theoretically based, prior to the data analysis. The rest of the categories emerged from the data through its analysis following an inductive methodology.

QDCA is a useful technique for description of the data, but it cannot be used to draw cause and effect conclusion. Nonetheless, combined with other methods, it is possible to make causal claims, hence the importance of triangulation of results (Allen, 2017)

The steps to content analysis include the selection of the data, the condensation and the elaboration of a coding system and will be explained in detail bellow.

6.1.1 Selecting the Material

The survey (Matos *et al.* 2018) is the source of data for this analysis. It consisted in 27 questions, from which, the following open-ended were chosen for study:

Table 1.

Survey questions analyzed through Qualitative Data Content Analysis.

Number in Survey	Question
8	In general how much focus does your organization have on drug safety issues?
15	Please give your general opinion on the value of direct patient reporting in pharmacovigilance?
16	What are the initiatives in your organization to support pharmacovigilance?
17	If a patient contacts your organization to share a reaction suffered related to their medication, what do you do?
18	Do you have any goal for your activities in Pharmacovigilance?
19	Do you collaborate with your National Competent Authorities regarding Pharmacovigilance?
20	Have your activities regarding pharmacovigilance changed since the new EU legislation in 2012, which makes it mandatory in the EU for countries to enable patient reporting?
22	If you have the intention to support pharmacovigilance activities or to be involved in pharmacovigilance, what are the barriers found?
23	What would you need from the pharmacovigilance centre/community to achieve this?
24	What other information you need/or could be useful to spread among patients about pharmacovigilance and patient reporting?
25	If you don't see a role in supporting pharmacovigilance, why not?

Retrieved from "*The Role of European Patient Organizations*", Matos, Weits & van Hunsel, 2018.

Although not all of these questions seem to be useful in answering the objectives of this research, after reading the data for the first time to familiarize, it is evident that many of the answers received do not seem to strictly answer the questions. Surveyors express themselves in matters different from the ones directly asked. This is why none of these questions were neglected.

In addition, analyzing all this data may lead to the identification of unknown codes directly related with questions under study.

6.1.2 Survey Data Treatment

At this point, the analysis extended to 11 questions from 337 surveys answered. The meaning condensation process was then carried out in order to simplify the analysis and start identifying trends for possible codes.

Meaning condensation is the process of analyzing individually each sentence and compress it into a brief statement that keeps the main sense of what was said. This process is time consuming and must be done with constant reflexivity, so that the real essence of the sentence is maintained (Kvale, 2007) . Figure 1 shows an example of the condensation process as carried out in this study.

The condensation process was done using excel, but the data was converted into word format, for an easier management in Dedoose.com.

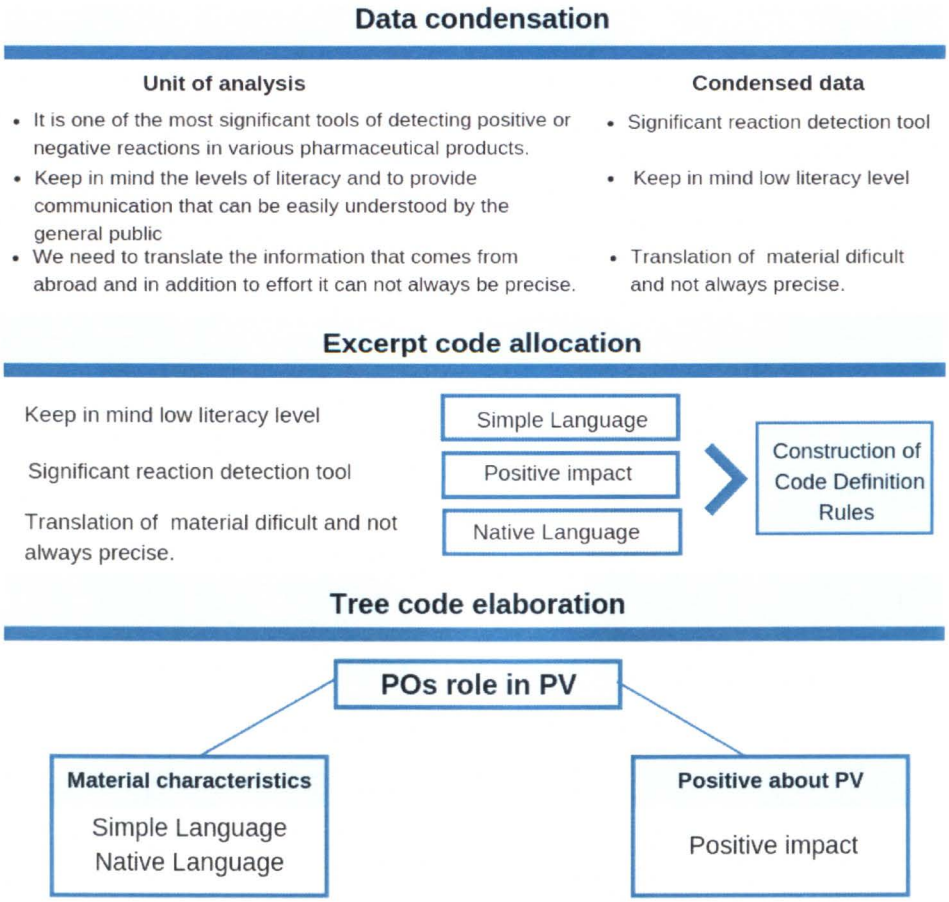

Figure 1. Qualitative Data Content Analysis; data condensation and code allocation example.

Self-elaboration.

6.1.3 Coding System Development

The coding system is the systematic description of data through coding. Writers in qualitative analysis use a variety of terms to talk about coding. For the purpose of this study, the terms used are codes and categories. Codes are short labels to which excepts can be related to; categories on the other hand refer to a higher hierarchy label, they describe the association between codes.

The coding structure from this analysis is part of the results, and is thus available on Figure 3 of the results section, the light blue boxes are categories and the white boxes are codes, only 4 categories were created deductively (Positive about DPR, Negative about DPR, Doubtful about DPR and Reasons for not supporting PV) the rest emerged from the data as inductive coding. Figure 1 shows an example of how the coding system was created in this study.

To render transparency, reproducibility and account for the quality of this methodology, Code Definition Rules were created simultaneously during the coding and categorization process for guidance and reflexivity on the coding application. Code definitions consist of five parts: a code name, a description of what is meant by that name, defining units of analysis, positive examples, and decision rules (Schreier, 2014). The coding rules for this analysis are available on Apex 2.

Defining units of analysis is the process of selecting the smallest unit to be analysed and coded. The unit can be a letter, a word, a sentence or even a bigger section of the material; if the unit of analysis is too small it can result in fragmentation and if it's too big it may be difficult to manage; the unit of analysis in this study is defined per code in the Code Definition Rules (Schilling, 2006)

After all excerpts were coded, a final check of the allocation of codes vs the code definition rules was undertaken.

The units of analysis per code area available on Apex 3.

6.2 Interviews

6.2.1 Grounded Theory Methodology

Grounded Theory Method (GTM) is the systematic inductive, comparative and interactive method for constructing a theoretical analysis from data. In GTM there are explicit analytical strategies and implicit guidelines for data collection, however, none of this steps

can be standardize; the research adapts to the general principles of the methodology, there is no specific form of working (Charmaz & Belgrave, 2012)

GTM refers specifically to the method used for the systematically development of theories or results obtained from the data, where sampling, data collection method and tools are paramount in the development of a theory that observes a wide perspective of the problem under study.

This particular study follows some of the strategies introduced by K. Charmaz (Bryant & Charmaz, 2007); the data is not condensed to avoid fragmentation and capture the participant full intention. And the coding process can be explained as focus coding and theoretical coding.

The analytical process of GTM can be described by the systematic allocation of interesting segments of the data into codes and the elaboration of theory that describes the possible relationships between those codes.

The focus coding is the elaboration of short tags that closely describe the data but at the same time remain open to all possibilities, allowing the modification of the tag, creation of a more specific tag and re allocation of excerpts at any time. Theoretical coding has a higher level of abstraction; for the emerging of theoretical coding it is necessary to compare focus codes to create a new code that captures a number of focus codes (Belgrave &Seide, 2019).

Following K Charmaz (Bryant & Charmaz, 2007) constructivist approach the codes are elaborated by what we see as significant in the data therefore the researcher needs to reflectively and constantly ask what is the data suggesting, what is the point of view and what other theoretical categories the datum fits?

An important characteristic of GTM is the simultaneous development of methodology procedures; such as data collection and data analysis. (Bryant & Charmaz, 2007); It allows to acquire a sense of the direction of the analysis in the process. It provides the advantage of directing the subsequent interviews with more targeted questions coming from the

analysis of previous interviews and the theory generated is constantly molded with every interview.

The coding structure is developed as part of an intellectual process for the construction of relationships and rules explaining the connections between the different codes; such connections will be explained under the Discussion section.

The specific processes of GTM followed in this study will be explained in detail bellow.

6.2.2 Sampling Method and Size

Quota sampling and referral sampling were used in this study; both trends are non-probability sampling methods. Non probability sampling is the process of selection that assigns some participants higher chances to be included in the study than others. (Daniel, 2012)

Using 2 sampling methods is possible to include interviewees with very diverse perspectives in the study; considering the heterogeneity and maximum variation attributed to this sampling methodology, the size of the sample is determined by the saturation point.

Saturation is reached when the data obtained through new interviews is not throwing new results or is repetitive or redundant. Saturation is recognized when neither new categories nor codes emerge from the analysis of new interviews (Fusch & Ness, 2015)

6.2.2.1 Quota Sampling

Quota Sampling is a sampling procedure in which participants are divided into mutually exclusive subcategories with the help of quota controls; the interviewer solicits participation from all different subcategories. This procedure combines availability sampling, since the participants had to agree to be interviewed and purposive sampling by targeting members with specific characteristics Daniel, 2012.

The POs who answered the survey from Matos *et al.* (2018) study (n=337) were the source for quota sampling. To be recruited for the interview, these contacts agreed to participate in a future study and they had to have an "interesting opinion" identified through the QDCA.

In question 27 of the survey, the surveyors were asked if they wanted to participate in an in depth interview regarding the role of PO in PV. Out of the 337 surveys received, 98 organizations agreed to participate in the interview and were suitable for selection.

Through QDCA, some organizations were tagged to have "interesting opinions" which is defined as an energetically negative or positive answer to one or more of the questions of the survey. Not all answers provided by the subject need to have the same trend, the "interesting opinion" is assigned when there is a highlight in one of the answers.

From the 98 organizations that agreed to participate, total of 27 organizations were also tagged as "interesting opinion" and were included in the sample list.

Quota sampling controls were carried in order to separate the POs in mutually exclusive categories; a triage was carried out using the sampling controls of Table 2.

This categorization is necessary to ensure variability among participants; the "interesting opinion" was designated by the impression caused by a single answer but the general panorama could be different and had to be evaluated.

Table 2.

Triage quota controls applied to patient organizations tagged as "interest opinion"

Green	Yellow	Red
POs that have • Positive perception of PV, • Have initiatives on PV • Interact with NCA and/or other stakeholders • Have future projections in PV.	Patient organization that have mixed answers. It means, they have items of the green and red classification. Also used when the data provided is not enough for classification.	POs that have • Negative opinion about PV • Have no activities on PV of their own, • Do not interact with NCA nor other stakeholders • Do not have any goal or future projections on this matter.

*Code green and red require at least 3 items present.

Self-elaboration

The quota sampling added 27 organizations to the list (6 red, 15 yellow and 6 green)

6.2.2.2 Referral Sampling

It is a procedure of selection based on suggestions; it was included in this study by adding contacts suggested by PhD. Florence van Hunsel, MSc, Cristiano Matos and Gerda Weits (Lareb POs contact person) to the sample list. These contacts, all members or former members of a POs, were added to the list due to their wide experience in the topic.

Referral sampling added 7 contacts to the list.

Both sources made up a list of 34 contacts from 18 countries in Europe.

A total of 16 interviews were conducted from which 12 were from quota sampling (red=4, yellow=3 and green =5) and 4 contacts were from referral. The sampling procedure is explained in Figure 2.

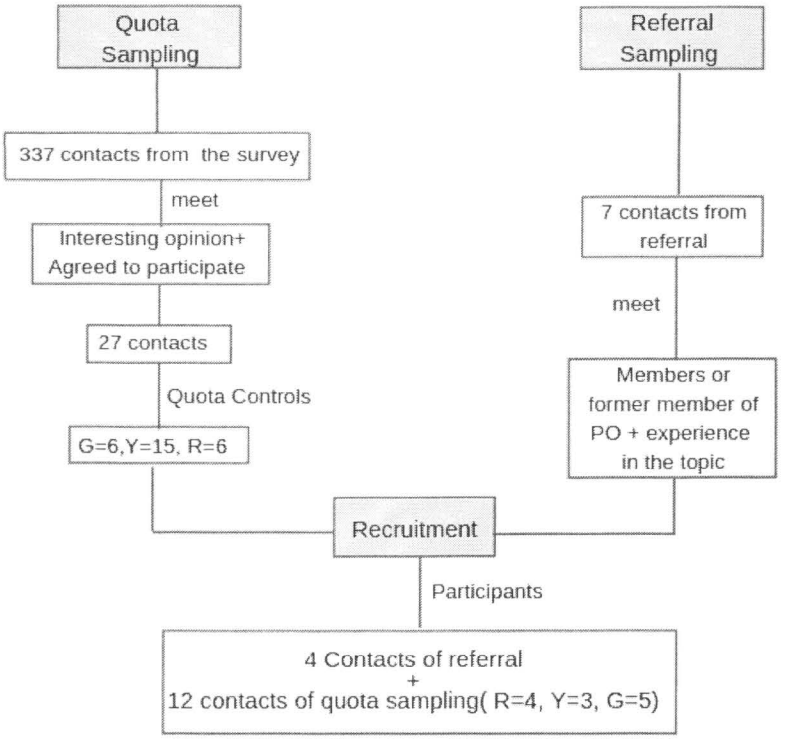

Figure 2. Interview sampling method.

R=red, Y=yellow, G=green
Self-elaboration

6.2.2.3 Sample Description

The differences among POs recruited are so wide that it becomes important to provide other indicators to describe the variability of their perspectives.

This study gathers interviewees located in 11 countries of the European Union distributed as shown below:

Table 3.

Patient organization interviewed per country.

Country	Number of POs	Country	Number of POs
Croatia	2	Netherlands	2
England	2	Portugal	2
France	1	Spain	1
Germany	1	Sweden	2
Ireland	1	Switzerland	1
Luxemburg	1		

Self-elaboration.

It is quite common that POs build their existence around a cause; most of the time their cause is the disease or condition they advocate for. The condition was not a parameter considered when the organizations were invited to participate, but drug safety panorama also differs by disease.

Table 4 shows causes participant POs support. Some of the interviewees had a very active participation in the PO field, being members of more than one organization; the table shows the cause they were linked to in their survey answers. Two interviewees were former members of a PO, the table also shows the cause they used to advocate for, this information was obtained from the interview.

Table 4.

Advocating causes among interviewees.

Cause	Number of POs
Diabetes Mellitus	1
Epilepsy	1
Hearing Problems	1
Hypophysis Conditions	1
Melanoma	1
Men cancer (Prostate and Testicles)	1
Mental Conditions	1
Myeloma	2
Multiple Diseases	4
Multiple Rare Diseases	1
Rheumatic Diseases	1
Spinal Muscular Atrophy	1

Self-elaboration

6.2.3 Recruitment Process and Confidentiality

The recruitment was done by email. The email included a brief explanation of the study as a follow up from the survey analysis (Stage 1 or quantitative phase of this mixed method study) and an attachment with confidentiality details regarding the interview. An example of the email is available on Apex 4 and the confidentiality details attachment on Apex 5.

Lareb's Privacy Specialist confirmed that confidentiality details observed the General Data Protection Regulations of the European Union (Regulation 2016/679, 2016)

Each email was sent with the contact or the PO name for a more personal connection.

Prior to the interview, participants were asked for their participation consent and any confidentiality questions were cleared.

Participants willing to undergo the interview had to respond via email and confirm the best date and time and communication mean. Interviews were conducted using Zoom meeting or regular phone call and one interview was face to face.

Zoom meeting program allows scheduling virtual meetings with visual and sound interaction. The participant can access the meeting by clicking on a link sent after agreement of date and time. (Zoom. us, n.d.)

The invitation to participate in the interview was sent in rounds; 3 to 9 interview invitations were sent per round.

The first round, with 3 invitations, had the exploratory aim of enhancing the interview guide. It allowed to modify the questions, their structure or composition and to include better "Help text".

The purpose of sending invitations in rounds is to have a better management of time for the interview, transcription, analysis and to apply modifications to the interview guide as all stages were happening simultaneously in accordance with GTM.

6.2.4 Interview Guide

New questions with the purpose of understanding the role of patient organizations in PV, their strengths and limitations arose from the survey QDCA. These questions were modeled and included in the interview guide.

The interview guide was actively improved during the research. The simultaneous data analysis allows to drive the interview questions into new emerging topics.

This approach to create more targeted questions based on the analysis of previous answers is known as Funnel questions (Peterson, 2000).

As the saturation point was reached for some questions first than for others, the Funnel Question approach grants the possibility of targeting the question to the topics that were not saturated yet.

Samples of the 3 interview guides used in this study are available on Apex 6.

6.2.5 Interview Data Treatment

After verbal authorization, each interview was audio recorded using a Samsung Galaxy J7 mobile phone and transcribed verbatim.

The transcription was done manually using oTranscribe.com a web based program that allows to manage text and audio in the same screen, it includes tools to slow the speed of the interview and make time marks in the text to reduce the time of transcription (Bently, n.d) .

A word file was created per interview recorded and uploaded to Dedoose.com for its analysis.

Data were stored at Lareb in accordance with European Union Data Protection Regulation and was only used for the scientific purpose of the results presentation at University of Costa Rica or further publication of the results.

6.2.6 Interview Data Analysis.

As previously emphasized data collection process is held simultaneously with the data analysis; the steps recruitment, interview, transcription and analysis were happening in parallel.

In GTM time is an essential tool in the development of a focus and ongoing hypotheses, pursuing hunches and following leads, and constructing the ongoing analysis (O'Reilly, K , 2009) .

After recording and transcribing every interview, the data was uploaded to Dedoose.com for its analysis.

Excerpts from the first 2 rounds of interviews were focus coded; by the end of these rounds it was possible to start drawing theory or connections between some of the existing codes.

With the codes emerging from later interviews, the data had to be constantly question, to determine if the excerpt could be associated to an existing code or if it was necessary to create a new focus code for it. Excerpts could be allocated under more than one code.

By the 13th interview, it was possible to establish up to 4 levels of abstraction and interconnection between codes, developing a tree coding structure with the components of the problem.

At this point saturation was reached in fields such as Activities in PV, Barriers, Breaking the Barriers, Interaction with NCA, Other POs and Interaction with professionals. The last 3 interviews were used to focus on Arguments for not having a role, Patient involvement and Industry (stakeholder) allowing to proceed faster with the last interviews and confirm saturation where it was specifically needed.

The tree code structure generated and the code allocation was also assessed by Dr. Matos and Dr. van Hunsel; this procedure is important for the triangulation and will be further explained on section 9. Strengths and Limitations of the study.

A total of 541 excerpts from all 16 interviews were analyzed and coded, the list of excerpts per code is available on Apex 7 .

6.2.7. Triangulation

The triangulation of results is an important method to assess quality in qualitative research (May & Pope, 2000). Triangulation is the process of comparing perspectives and results obtain through different data sources. The objective of triangulation is to diminish researcher bias in the data and the likelihood of misinterpretation (Cho, Lee, 2014).

Triangulation of data collection methods was carried out by comparing the data obtained from the survey and from the interviews.

Comparing methods of analysis is another type of triangulation; in this case QDCA is compared to GTM.

The last type of triangulation considered in this study is researcher triangulation, PhD. Florence van Hunsel and MSc. Cristiano Matos together with the author of this sript assessed the code allocation and shared their points of view. Comparing all perspectives about code allocation particularly permit to diminish misinterpretation.

6.3. Tool to Stimulate Patient Organizations Participation in Pharmacovigilance

Based on the findings of this research, this project aims to develop a tool that can stimulate the participation of patient organization in PV, the results point at a vast list of tools for this purpose.

POs consider that research creates awareness and they want real life examples; they want to see how other countries and other organizations are doing in this field, this could give them ideas to follow in their own organizations.

Following the findings of these 2 codes, the tool developed consists of a document that explains the activities POs are carrying out in PV and the strategies to overcome the barriers. The tool is presented as Apex 8.

Although it seems most of the strategies are to be implemented by NCAs, Industry and other stakeholders, it is important for POs to know about them so that they can push together in the same direction.

7. Results

7.1. Survey Qualitative Data Content Analysis Results.

Figure 3 presents all the categories and code extracted from the survey data analysis, the units of analysis per code and category that feed these results are available on Apex 3.

Each box includes one category and the codes that explain that category. However the categories are presented independently from one another because the data collection method does not provide enough insight to be able to understand the connection between them.

The most important categories found through the QDCA are those explaining all possible perspectives POs have towards PV- Positive about DPR, Doubtful about DPR and Negative about DPR- Activities in PV, POs Needs in PV, Material Characteristics and Reasons for not Supporting PV.

These categories are helpful to understand POs situation in PV and are of practical use to develop solutions to the problems they face.

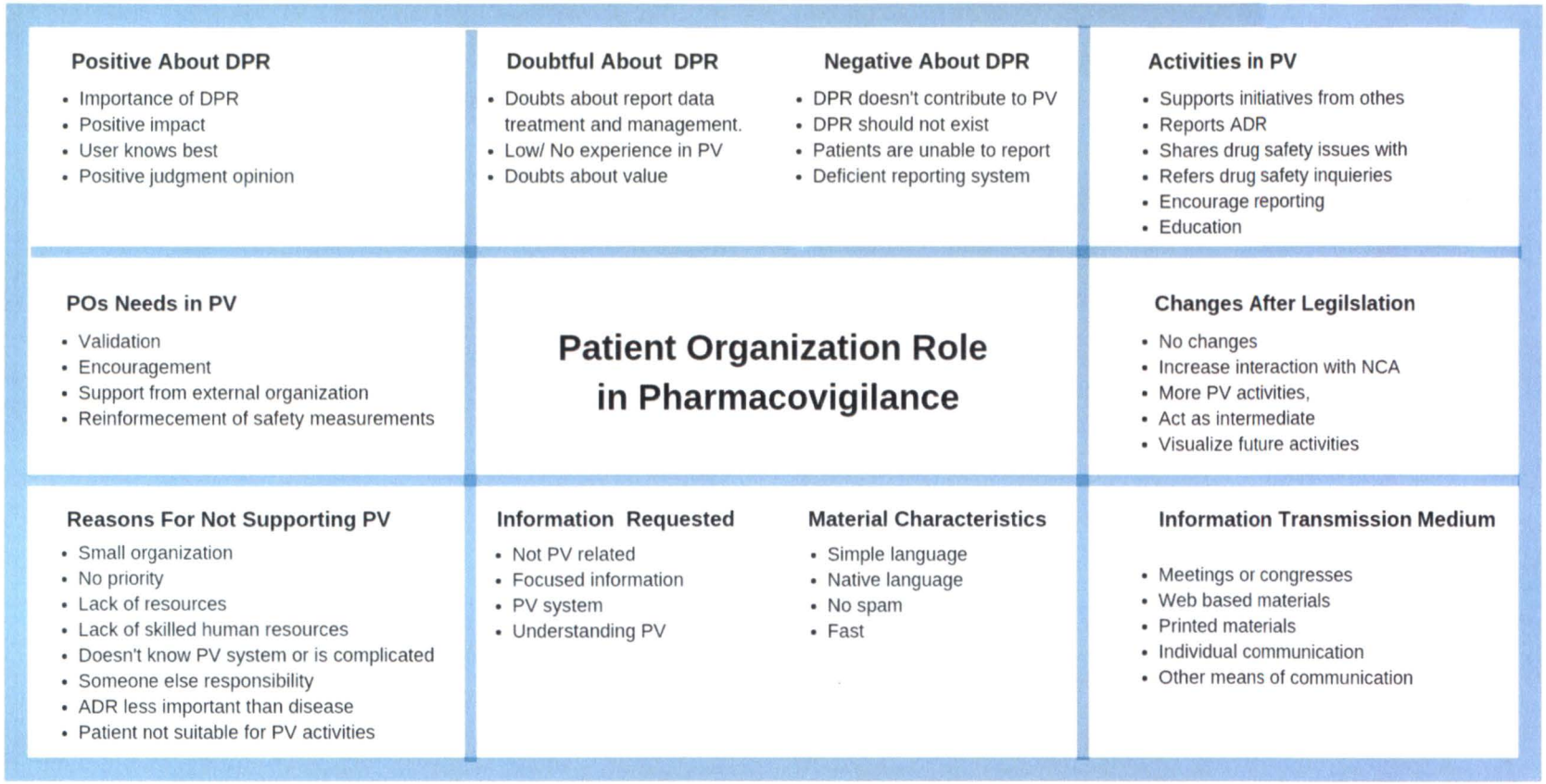

Figure 3. Survey qualitative data content analysis codes and category

Self -elaboration

7.2. Interview Grounded Theory Methodology Results

Figure 4 presents the tree coding structure obtained from the interview analysis using GTM, the excerpts feeding the codes are available on Apex 7.

The interview is a data collection method which permits to obtain a deep insight of all features explaining POs connection with PV, including the way these underlying features are linked with each other, this explains why it is possible to present the results as a tree structure.

The Patient Involvement category is of particular interest to explain why patients and POs should be part of PV, what their contribution to PV is and what benefits they obtain from it. Being aware of drug safety allows them to make informed decisions about their own health care, participate in drug development and drive public changes based on drug safety risks.

The Arguments for not Having a Role are ideological limitations, the most important being Benefit not visible, most of patients expect to find a solution when reporting but the process is more complex than that.

All activities found are of great importance to understand how POs approach to drug safety; these activities can be an example to many organizations that are starting their path in PV.

It is important to remember POs are only one of the stakeholders concerned in drug safety, there are good and poor examples of interaction with other stakeholders, but it is of particular interest the complaints regarding their interaction with NCAs.

The barriers POs face can be classified as external and internal, Miscommunication with PV Community is the most important among the externals and the barriers concerning staff the most important among the internals. With more staff, more people could follow education and attend other patient's needs such as PV.

The Strategies to Overcome the barriers are mainly more education, improvements in the PV system and more awareness for drug safety. However the most important premise is

without a doubt that patients want to be involved in the development of every strategy concerning their integration to PV.

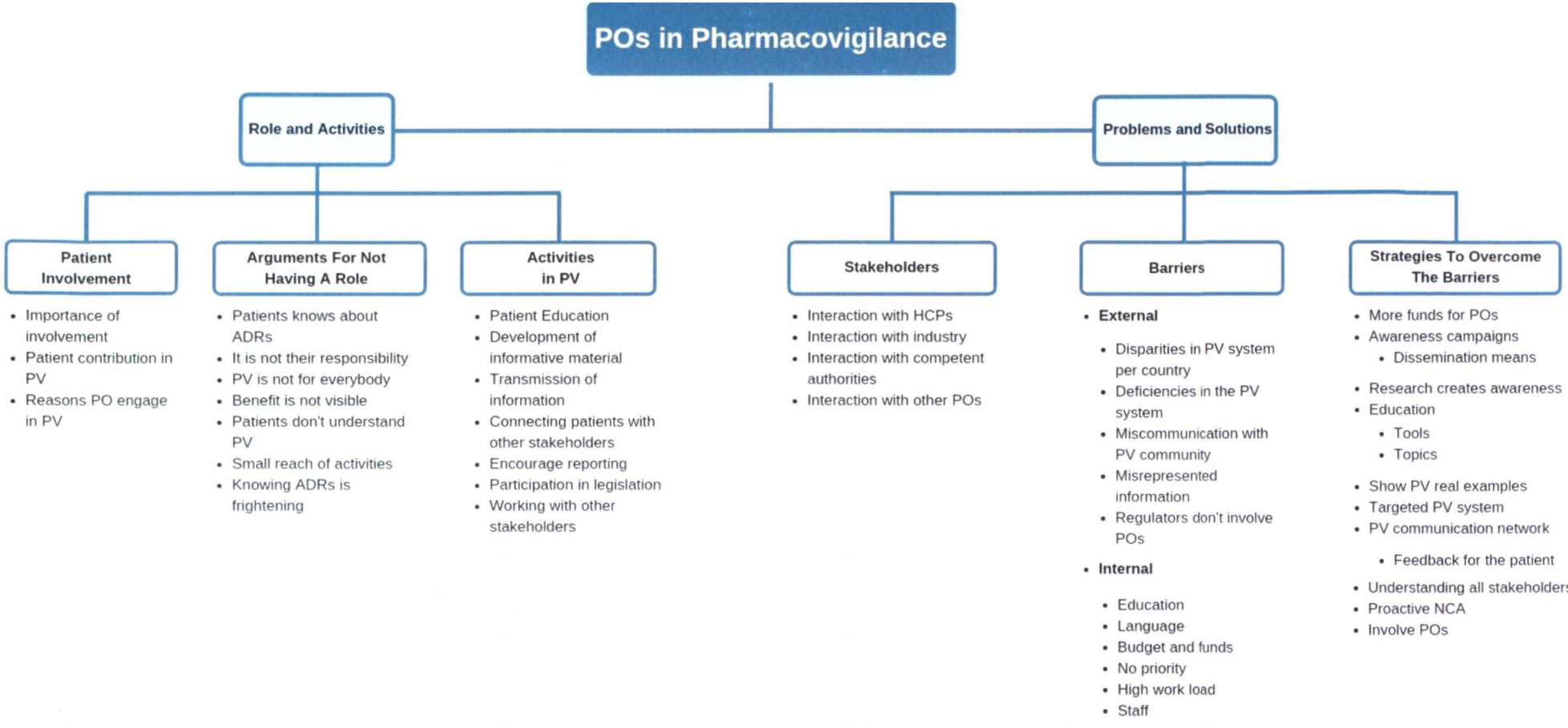

Figure 4. Tree coding structure: Patient organizations in PV, their role, barriers and strategies to stimulate them in the PV system Self-elaboration

7.3. Important Excerpts

Excerpts explaining some of the shared ideas among interviewees were selected to provide the reader with a broad comprehension of some of the most important codes of this research. These excerpts are presented on Table 5.

Table 5.

Excerpts extracted from the interviews analyzed through GTM.

Interview	Excerpt	Code
Int.9.1.	"In the end the side effect happens in the patient and what matters happens in the patient, so the patient is the primary data source, we've been advocating for collecting information from the primary data source and basically cutting up a middle man or woman who would introduce some bias onto the situation"	Importance of Involvement
Int.4.1.	"The patient is taking the drug and is impacted by it, so I think they need to be very well informed about what are normally expected side effects and what might be potential issues and concerns that they should report. So I think it's absolutely critical for ongoing safety monitoring and future drug development"	Importance of Involvement
Int.3.1.	"At the moment there was a trial question at EMA we tried to find out who could work in the benefit risk at the beginning. So there was this question and half of the people were patients themselves and half of the people were people representing patients and health care professionals and the question was "you get a new medicine and the medicine promises you will die until 15 months without progression of the tumor, but there is a risk of sudden death, what would you do? And what you could see is that most of the representatives said "yes... but sudden death... hmm I should not use it", but all patients said .. "yeah you speak about the risk but I should see it as a benefit, I know that I'm dying within a couple of years in a terrible way because of a tumor, so sudden death is not an important risk for me. I want to know, does it help me the next 15 months to keep my daily activities better than I could do before?", so that was a very good expression in the differences in looking to it"	Patient Contribution in PV

Interview	Excerpt	Code
Int.12.1	"In 1997, there were online communities and discussion lists both in the US and Europe, men who had been treated for long periods with the new highly active antiretroviral treatments were reporting body shape changes and side effects that nobody had seen before, they were gaining 20kg of weight in several weeks, in a short time [...] that was in fact how the lipodystrophy syndrome was detected, by spontaneous discussions of patients online, trying to understand what it was [...] When we analyze what the patients were saying first, the description of what they had was extremely precise by using lay language you could read what they said and visualize immediately what they had without a photo".	Patient Contribution in PV
Int.9.2	"It's a little bit frustrating because everyone wants the data, no one wants to give anything back to the patient who reports, which is the driver for the reporting."	Benefit not Visible
Int.11.1	"At education events we always talk about drug safety[...] When we talk to our patients, if there are sort of unusual side effects of things, we encourage them to report it . At our education meetings we always have the leaflet from HALMED that talks about it. They have a little sort of leaflet which we give away to patients and say you can report any unusual side effect."	Patient Education
Int.2.1.	"First of all, we have to inform and train the patient organizations that are part of our coalition so they, in turn, urge patients to report any adverse effects they may have."	Patient Education/ Interaction with Other POs.
Int.13.1	"When EURORDIS is making a policy for Europe on how to develop ERNs and how to implement them in the different member states of Europe, you see for instance in Italy and Spain and also France, the national alliance and that is the umbrella organization takes the lead, in the Netherlands we are the ones siting at the desk of the ministry talking about our needs".	Interaction with Other POs/ Underestanding all Stakeholders.
Int.5.1.	"But it's multi-level responsibility, in other words we can't just dump it on one party, we can't leave it on the regulators, we can't leave it on the pharmaceutical companies, we have to rely on each other, it's a shared responsibility"	Stakeholders
Int.11.2.	"The specialists and whoever sees the patient at the time, they don't report it, they just note it in their... you know it doesn't get through the agency that deals with it and I am sure that is the case"	Interaction with Health Care Professionals

Interview	Excerpt	Code
Int.1.1	"I spoke to some nurse she does anesthetics and audiological work in a hospital, when people need to have something operated in their nose, throat or ears, so she does the anesthetics and she didn't know that anesthetics could hurt the hearing, she was working in this kind of work and she didn't know"	Interaction with Health Care Professionals
Int.11.3.	"At the moment I think there is lots of Lip service to patient involvement and patient centered and this and that, and that lip service the more you go to central Europe, southern Europe, this little countries are really not doing anything truly, unless you find an individual Dr who is really serious and takes serious what he does but as a system, I don't think it exists."	Disparities in the PV System per Country
Int.5.2.	"Social media, it can sometimes exasperate something; someone sitting in Finland who has a normal indication, he or she happens to have an opinion and goes online in the middle of the night and says something and then this is picked up by a patient having the same pharmaceutical drug in China who says "hey look have you seen this" and you know there is no screening [...] Suddenly this things go viral and there is panic for no reason. I mean this is the case of the Doctor who associated MMR vaccine to autism."	Misrepresented Information
Int.14.1	"For instance for chemical drugs we have one system and then you also have another issue that for instance natural products, herbal products, supplement, a lot of people do that and most of the people think they don't have any interaction or adverse effect, so first they are not aware of this and then they don't know they can report and who to report this effects, it's not to the national authority of medicines but to the ministry of agriculture, a different department."	Deficiencies in the PV System
Int.7.1.	" The regulatory agencies they come with us because they are somehow obliged because in some cases involvement of PO it's just ticking the box, and that is not quite helpful, so from our side from the PO side, based on our contribution we must or we should somehow prove that our involvement is absolutely essential in order to deal when it comes to PV, for instance to build a more robust system"	NCAs do not Involve Pos.
Int.13.2.	"A problem of course is funding, compared to other countries in Europe, the Dutch situation, we are rather rich, but we also have a lot of obligations, we have to print 4 times a year 2,5 thousand times a magazine, we have to have a website and we have to organize hospital meetings and symposiums, it's very expensive."	Funds and

Interview	Excerpt	Code
Int.12.2.	"There are other organizations that know the problem but they are not with a state of mind to make constructive proposal, they complain basically, they want to see everybody to the court and etc etc. But when we ask them, what can we do? What would you suggest to improve? they don't know, they haven't thought of it, they haven't discussed with PV experts, they are not ready to respond"	State of mind barrier
Int.6.1.	"They were asking me if the leaflet is understandable for patients, it was about side effect in young children [...] I felt if I had a seriously ill baby of 3 or 6 months, maybe crying a lot and also babies who are not sick cry a lot, how can I check if he's crying because he has a headache from the medication as side effect? one of the serious side effect was loss of vision, how could I check to my baby that this is on the way?"	Targeted
Int.5.3.	"It is a cultural change that leads to a national pv police, they need to work with the patient groups and build up that cultural cooperation and trust because that is essential".	PV Communication Network
Int.12.3.	"When there are safety alerts, sent out by NCA, often they don't know who to send it to, the case was when there were various Avastin which were contaminated and some were used to be injected in the eyes of patients with macular degeneration, but only the organization for breast cancer received first the information of some contaminated vials, because the Avastin was by that time was an off label use, you don't know as a regulator which are all the organizations that could receipt your communication but contrary if you would send out the same information to each organization, they would decide."	PV Communication Network
Int.1.2.	"But then again, we need to inform what we know by now and we also need to inform that we need more research we need more studies into different kind of medical treatments because some of the things may be able to be changed when they do some more research and test and try out things so this is also for us to raise that this is needed."	Research Creates Awareness
Int.3.2.	"You can't understand PV if you do not understand what the problems are from the side of the regulators, what the problems are from the side in the clinical practice, from the side of the other stakeholders for instance, otherwise you can make solutions that are not workable."	Understand all Stakeholders

Self-elaboration

8. Discussion

This study, together with Matos et al (2018) are innovative for they account for the patient organizations' perspective on pharmacovigilance, there is available literature on some of the discussed categories of this study, however for the categories activities in pharmacovigilance, arguments for not having a role and barriers, this study limits to compare results obtained from both QUAN and QUAL phase of the mixed method research and introduce innovative information in the field.

8.1. Role and Activities

8.1.1. Patient Involvement

The perspective about patient involvement is explained by 3 different codes, the importance of involvement, patient contribution in PV and the reasons why POs engage in PV activities.

POs consider involvement in PV important since the patient is the one who knows what really happens in their body and the impact adverse reactions have in their quality of life, reporting through HCPs only adds a filter to the process (see Int.9.1, Table 5). Furthermore, involvement is important activity for self-care and allows patients to make informed decisions by having risk/benefit information about their treatments (see excerpt Int4.1., table 5).

Patient organizations consider patient perspective is different from that of HCPs, regulators and other stakeholders, which makes their participation indispensable (See excerpt Int.3.1., table 5).

The QUAN analysis only studied patient contribution to PV, nevertheless, the statements "Patient describes information based on their experience with medicines" (n=205) and

"Patients give more information on the impact of ADRs in their quality of life" (n=204) (Table 5, Apex 1) are congruent with the importance of involvement category of the QUAL phase.

These codes are also observed on the QDCA of the survey open text fields, where the Positive about DPR category presents similar findings (Figure 3).

POs consider patient contribution in pharmacovigilance broad and has a big impact. Some statements of the QUAN phase are also present in the QUAL phase: "Patient can contribute to the detection of new adverse drug reactions" (n=200) "Patients can be useful describing the severity of reported reactions" (n=185) and "Patients can report information that is useful even without medical confirmation" (n=157). The real implications of these 3 statements can be illustrated with excerpt Int.12.1 (Table 5).

These findings are congruent with multiple studies validating patient input in pharmacovigilance (Inácio, Cavaco & Airaksinen, 2017).

Other important components of patient input to PV discovered through QUAL analysis include, ADR reports from patients keep the drug leaflets updated, their involvement in PV improves drug safety, patient voice can drive changes and they build for future generations.

The reasons why POs engage in PV are very diverse, some participants engage because they had suffered an adverse reaction that changed their lives, some engage because they got to meet their PV NCAs and establish connections with them, others have seen their member needs evolve as there are more treatments available to manage their disease, which changes their group focus from increasing survival and life time to improvement of the quality of life and some organizations consider they would only engage if there is a problem among their members.

8.1.2. Arguments for not Having a Role.

Only one of the 16 organizations interviewed appears to have no activities at all in pharmacovigilance; however many organizations explained some arguments for not getting

involved. The category is not allocated under Problems and Solutions as these are ideological limitations. This findings were only obtained through the QUAL phase, and represent the most difficult limitation of POs involvement as driving ideological changes is difficult.

The code "Benefit not visible" is of particular interest since this idea is quite frequent among POs, they consider when reporting there is not a visible benefit for the patient, the side effect does not disappear and the patient does not get much of a useful feedback. (see Int.9.2., table 5)

A strategy to tackle this problem is also presented by patients under the code "PV communication network" which will be explained later. Most of these arguments can be overcome with education, setting proper expectations of reporting among POs, and involving them in any related activities so a sense of commitment and belonging is developed.

The QUAL analysis of the survey open text field also present some arguments for not having a role under the category "Negative about DPR" for example "patients are unable to report ADRs" and under the category "Reasons for not supporting PV" the code "Someone else responsibility".

8.1.3. Activities in Pharmacovigilance

The "Activities in PV" were studied both in the QUAN and QUAL phase. The statement "Encourage them to talk to their doctors/pharmacists about ADRs suffered." (n= 247) is grouped under "Connecting patients with other stakeholders" in the QUAL phase, this code also groups connecting patients with hospitals, industry and in the case of umbrellas, they direct member organizations with the corresponding authorities in each country.

The QUAN phase statement "We help him to report the ADRs suffered to the PV system." (n= 96) is parented with "Encourage reporting" code, they consider the reporting system is not user friendly and therefore teach the patient how to report. This activity was also found through QDCA.

Both phases confirm organizations usually encourage reporting by posting the NCAs link for reporting on their website (n=20) .

The statement "We communicate the information to the national competent authority" (n=20) was also found in the QDCA, patient organizations do not only communicate drug safety issues to NCAs, they also transfer this information to the industry, HCPs, EMA and according with the QUAN phase, the information is also shared with patients within the organizations (n=119) to warn them of any possible drug safety problems.

The QUAL phase also sheds light to more activities POs perform, they participate in decision making at a legislative level, they work together with other stakeholders whether it is for material development or as guests in their conferences or meetings and even when the resources are limited within the organization some have managed to support PV activities by acting as a conduit of information, however the strongest activity POs perform in PV is that of educating their members.(see Int.11.1, Table 5)

POs are aware that PV is a mean to achieve a safe drug environment and the education in this field covers much more than the reporting on side effects, in fact they stimulate a self-care culture among members; they warn them not to obtain medicines from uncertain sources, monitor any changes within their bodies to identify ADRs, take their treatment as indicated by their physicians and keep them updated with information about their medication for the patient to make informed decisions.

Umbrella and coalition organizations recognize their position and take their role seriously by educating in cascade, they hope the information they give to national organization can be finally passed on to patients. (See Int.2.1., Table 5)

Only 86 organizations in the survey agreed with the statement "We organize activities (seminars, campaigns, workshops, courses) to help patients to be aware of drug safety" in the QUAN phase, but the QUAL phase confirms education is the strongest activity POs perform as a PV stakeholders.

Finding POs carry so many activities related to drug safety is very promising, however, many of this activities are on a reactive response; they take actions only when their members or they personally have been affected by a drug safety issue.
It is necessary to encourage their participation in a more systematic way.

8.2. Problems and Solutions

8.2.1. Stakeholders

Patient organizations are only one of the stakeholders to whom PV concerns. Their interaction with industry, competent authorities, health care professionals and other patient organizations are part of the problem and part of the solutions, all actors should work together to obtain better results, problems in their integration could affect PV development.

The European Patient Academy (EUPATI) initiative is a multi-stakeholder consortium from pharmaceutical industry, academia and patient organizations. EUPATI education program forms patient experts in multiple topics, including PV (EUPATI, n.d.).
Another leading initiative is the EURODIS Summer School, the training focuses on providing participants with knowledge and skills to become experts in medicines research and development, pharmacovigilance is also available as an online training module (EURORDIS Open Academy, nd).

Both initiatives are well known among POs, many interviewees recognize attending these courses helped them understand PV.

Umbrella organizations perform the same activities than national organizations therefore the statements from the QUAN phase: "We spread information on safety issues to our member organizations" (n=22), "We send guidelines for member organizations with positions regarding drug safety issues" (n= 13) and "We encourage member organizations to collaborate with the National Competent Authorities"(n=28) are observed under Education (Role and Activities) .

The difference between national and umbrella organizations relies on the position they have in the hierarchical structure of the POs network.

Umbrellas interact and receive information from competent authorities and transfer it to national organizations, while the national organizations interact with umbrella, adapt the information to the national context and deliver to patients.
This interaction is not the rule; the level of involvement in legislative activities varies between countries (See Int.13.1., Table 5)

In many cases POs interact with each other without necessarily forming coalitions or umbrellas, when they have a common problem they sum efforts to achieve the same goal.
This explains why interactions between umbrellas, coalitions and national organizations cannot be clearly differentiated.

The QUAN phase only analyses the interaction with Umbrellas, the GTM in QUAL phase allows illustrating POs interaction with other PV stakeholders. PV responsibilities cannot be dropped exclusively on one stakeholder (See Int.5.1., Table 5)

There are some good experiences in the interaction with HCPs: they are invited as speakers in POs meetings or conferences and POs count on HCPs organizations as reliable sources of information. Despite these good interactions, many interviewees consider HCPs are not doing enough, they should do more awareness and education on drug safety and encourage patients to report known and rare ADRs. It is also important for HCPs to build popular trust by reporting ADRs.(See Int.11.2., Table 5).

Patient perception of under reporting from HCPs is actually accurate and multiple studies confirm HCPs do not report ADRs. The under reporting is associated to ignorance of the reporting process, lack of time or are unsure about the causality of the ADR, in some cases HCPs also find the reporting mechanisms complicated (Gahr *et al.*, 2016; Gupta, Apoorva & Malhotra, 2018; Hohl *et al.*, 2018)

Some anecdotes make POs think HCPs also need constant education on ADRs and PV, in the case of general practitioner; they should accept and validate the patient experience of ADRs.(See Int.1.1., Table 5).

The QUAN phase showed that only a small number of organizations collaborate with NCA (n=88). The results of the QUAL phase confirm this interaction needs to be improved.
EMA initiatives are highlighted and applause among POs, who wish this initiatives were reproduced at national levels. NCAs improvement in engaging with POs is recognized, yet miscommunication continues to be the biggest problem; some POs do not know their NCAs.

The interaction with Industry is quite similar; there are really good cooperation examples and a general thinking that they should do more.

The QDCA also demonstrates under the code Support from external organization" that POs need other stakeholders to work together and help them improve their development in PV.

8.2.2. Barriers

There are many other barriers presented by patients apart from those associated to their interaction with stakeholders. These barriers can be classified as external or internal, depending whether they have the control of finding a solution inside the organization.

The external barriers are mostly associated to the PV system. PV systems are different among EU member countries, some countries have a more structured PV system than others and this becomes a problem particularly for umbrella and pan-european organizations (See Int.11.3), they have to deal with the PV systems of all different countries where they are present.

An interesting barrier is that one of misrepresented information to the public, fake and pseudoscience lead patients in the wrong directions, it is not a barrier directly linked to PV, but wrong information can make patients follow their treatment in an appropriate way or stop it suddenly causing serious consequences. At the same time POs are limited to present information freely to the public, fearing this could cause fear among their patients. (See Int.5.2., Table 5).

A big category of this study is that one of deficiencies in the PV system. There are common experiences such as : the reporting system is not user friendly or patients think it is complicated, the language used is not understandable for the lay person, some PV reporting forms do not provide enough open text for the patient to articulate their whole experience, they consider this happens because the system was not user tested, real patients were not involved in the development process.
The information does not have an appealing format and is difficult to find, the patient first needs to know where to report, otherwise is not easy to access. On top of that, in some countries PV of natural and chemical products are managed by different NCAs. (See Int.14.1., Table 5) and there is a common feeling that NCAs do not involve POs (See Int.7.1., Table 5).

Internal barriers such as the low budget were analyzed also in the QUAN phase where 135 organizations agreed to be affected by this barrier. Budget is limited and it gets more difficult to distribute when POs have to comply with a series of activities to be recognized as Patient Organizations. (See Int.13.2., Table 5).

The staff working at POs is mostly working on a volunteer basis, most of this staff are also patients, their health conditions limits their active participation at the organization, together with having a high work load due to their own life activities, explain the "Lack of resources to be involved in PV activities" (n=130) from the QUAN phase.

Patient advocates have different backgrounds, their education is not necessarily associated to health, the staff needs to receive education in PV to be able to pass their knowledge down to patients, this is congruent with the statement "We don't know what to communicate to improve patients involvement in PV" (n=53).

Another big barrier is not having the priority to get involved in PV activities; which may be due to not having a pharmacological treatment for their disease as found through the QDCA or their patients do not complain from ADRs frequently or because they are not in the state of mind for participating in a constructive way to improve the PV system. (See Int.12.2., Table 5).

Interviewees consider it takes time for people to be ready to understand the information, which may indicate involvement in PV goes progressively as more POs reach this understanding.

8.2.3. Strategies to Overcome the Barriers.

Interviewees suggest a series of strategies to facilitate POs involvement in PV. The strategies focus on changes to the PV system, education in PV, POs involvement and more awareness of PV.

The QUAN phase assumed POs only needed more information from the PV community, however the QUAL phase demonstrate the need is broader than that, the statements of the QUAN phase : "Information about drug use and side effects to be shared with patients "(n=181), "Information on how patients can report side effects and why it is important to report side effects" (n= 173) and "Information on how patients can be involved in drug safety"(n=190) (Apex 1, Table 7.) only cover the code Topics for education.

The education for patients and POs can be directed through a lot of tools like training, workshops, toolkits, open days among others. The topics to cover are also quite diverse, some are interested in very specific information to cover their member's specific needs while others focus particularly in understanding PV.

To introduce changes in the PV systems it is required to have more proactive NCAs. Pharmacovigilance is a national health concerning matter, thus NCAs should take the lead in approaching all stakeholders and creating appropriate communication channels to keep them updated. New classes of medicines such as biological drugs, cellular and gene therapies should be part of the discussions in a proactive system.

The PV system should consider that every patient is different, just as the needs of patients who suffer different conditions and use different pharmacological products. To develop a targeted PV system it is necessary to consider cultural, political, social and geographical variability among people. Some interviewees consider the reporting systems are not useful for their condition, for the particular medication they use or for the adverse reaction they

suffer. This premise should extend to the development of any material directed to the public, it is necessary to always consider the characteristics of the targeted population. (See Int.6.1. Table 5).

The characteristics of the targeted public should always be consider and attempting to cover global population with the same reporting instruments and with the same informative material is unrealistic, people may not feel identified and persuaded to act.

Changes in the PV system should also include a PV communication network. POs have a communication network, by staying in touch with each other and with their umbrellas they can alert other organizations they normally communicate with, however this network is not yet well defined and is not particularly used for PV. A proper network has to be managed by the NCAs but should include all organizations and all stakeholders so alerts and educational information can be transferred in an effective way.

From this network POs can pick the information for themselves or they can translate and share it with their members. By improving the communication network it is possible to direct all PV community to similar interests, create room for discussion and receive all information in a timely manner.

This network should also consider information down to the patient this means; patients who report would be able to see a benefit from what they do by receiving constant feedback from the stakeholders (See Int.5.3., Table 5).

It is important that all information be available to the stakeholders, with no filters, they can decide what is of interest for them.(See Int.12.3., Table 5)

Surprisingly solutions are not based on more funds for POs, this code was only fed by 2 excerpts. With the proper external help, POs can achieve an active role in PV.

The strategies involve Awareness campaigns, POs consider there is not much awareness about ADRs an about the PV NCAs in their countries. Part of the awareness has to come to light from research (See Int.1.2., Table 5).

Real involvement is more than an email asking for POs opinion on the final look of an informative resource. POs really want involvement to be considered from the development of the tools, to the assessment of results; patients want to be actively involved in all stages.

All the strategies presented share that common idea, that way when developing an education activity, even the topics can be discussed with the POs.
As part of this involvement, it is necessary to understand the role, objectives and priorities from all stakeholders, giving a face to an institution can help all stakeholders communicate easily. (See Int.3.2., Table 5)

Involvement of all stakeholders is the absolute key to promote PV among European POs. Smith & Benattia, (2016) and van Hunsel, Harmark & Rolfes (2019) confirm it is necessary to develop a framework to engage and involve patients and their representatives to account for a reliable pharmacovigilance system.

9. Strengths and Limitations

9.1. Strengths

The clear exposition of the data collection and analysis used for this study design constitutes one of its biggest strengths. The design provides in detail description of every step taken including the methodological basis of the analysis conducted. Detail description provides transparency of the data management and reproducibility of the method.

The meticulous selection of the sample assures maximum variability of interviewees' perspectives before data saturation is reached. In addition, as part of a mixed method research design, similar findings in the quantitative phase convey credibility and trustworthiness to the qualitative phase findings.

Triangulation of data collection method, method of analysis and researcher were also carried out to account for the quality of this qualitative research method.

Data collection triangulation was carried during the discussion, results from QDCA(data obtained from a survey) and GTM (data obtained from an interview) were compared, despite the allocation of the codes in both analyses was different, codes could be compared across collection methods.

Researcher triangulation was also performed, the excerpt coding was assessed by the author of this project, PhD. Florence van Hunsel and MSc Cristiano Matos, the 3 came to similar conclusions of coding excerpt allocation.

9.2. Limitations

During the sampling, priority was given to interviewees who participated in the QUAN phase. From this list of contacts only the ones who had agree to participate in an in-depth interview could be invited for further analysis. Frequently respondents with highly negative opinions would not agree to be further contacted and the total available population from the survey contact list to undergo the sampling controls was relatively small.

To work out this limitation, the quota sampling was developed to include similar number of interviewees in each category of the triage classification and referral contacts who could not be triage classified were included to extend the perspectives incorporated in the analysis.

Sending the invitations in rounds during the recruitment process allowed inviting more organizations tagged as "green" or "red depending on the general trend of the interviews conducted and the response rate.

The interview guide was developed including some general questions at the beginning to gain trust among participants and any answer provided was validated and accepted, nevertheless it is important to consider some interviewee bias attributed to socially accepted responses.

The selection and classification of the invited interviewees could also introduce some researcher bias to the study, the sampling method was developed with the objective of assuring maximum variability among respondents, however the variability was chosen on the basis of interesting aspects selected by the researcher. Certainly the selection of interviewees on this basis reduces the "noise" or chances to obtaining answers consider not relevant for the topic under study but in a way it also shapes the results and findings.

10. Recommendations

The findings of this study contribute with a set of recommendations to stimulate POs as valuable and important stakeholders in PV. Such recommendation include improvement of the PV system to adapt patient's needs, awareness campaigns in PV, more education opportunities for POs and establishing a communication system including all stakeholders.

NCAs and other stakeholders will do well by observing and implementing the suggested strategies pointed by this study. We encourage national competent authorities, this is the pharmacovigilance centres of ever member state to take the lead in creating a communication environment with all stakeholders, this is the first step to the development of the consequent strategies as POs seek to be involved in every step of any process implemented.

At the same time we encourage other stakeholders to take an active role engaging in pharmacovigilance activities considering patients and their representatives participation in any developed activity.

More research for the development of education tools such as training or toolkits is suggested. This research should consider the findings of this study but should focus on the development of educational tools.

11. Conclusion

This research provides an insight of the features concerning to POs involvement in pharmacovigilance, such as their activities, the importance and contribution of their involvement, their interaction with other stakeholders, barriers they face when implementing PV activities and strategies to stimulate their participation.

Detangling all concerned features of PO interaction with PV is crucial to obtain a critical understanding of their position.

Patient organizations carry out many activities in PV: develop educational material, participate in legislation, work together with other stakeholders, transmit information, connect patients with other stakeholders and educate their members. This last turns to be the strongest activity POs fulfil in regards to PV.

The limitations POs have when getting involved in PV were classified as internal barriers: education, budget and funds, no priority, staff, high work load and language, and external: regulators do not involve POs, disparities in the PV system, deficiencies in the PV system, miscommunication with the PV community and misrepresented information.

By addressing the external barriers with the help of other stakeholders, POs path in PV can be facilitated, internal barriers on the other hand have to be managed by the organization itself, the level of involvement could increase as these limitations are overcome and the patients continue to focus their concerns on quality of life.

Certainly miscommunication with NCAs is an important barrier and there is room for improvement. It is necessary to create a PV network of communication where all stakeholders can participate and the information is shared in a timely manner, alerts and feedback for the patient should be included as well as education materials for both POs and patients. NCAs should be proactive at establishing constant communication channels and all initiatives should consider target population characteristics.

This study aimed to identify strategies NCAs in PV can develop and implement to strengthen the participation of POs as active promoters of drug safety. POs suggest a series of strategies; these are presented in the section Strategies to Overcome the Barriers.

The strategies include more funding for POs, more awareness campaigns to inform people how they can contribute with drug safety, more research, and education. Patient organizations provided detailed explanation of the education required, covering the topics of education and the tool to impart this education, however explaining such details as conclusion overlooks one of the most important ideas extracted from this study, that one of involvement of POs on every step of the process, including their own education.

This means POs should be involved in the selection of their own education, including topics and tools and their involvement should be the same across all pointed strategies.

The variability among POs confirms there is not one single strategy that could be implemented to cover all of their needs, but certainly every strategy implemented will sum up efforts in the process of stimulating POs as active stakeholders in PV.

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Apex 1.

THE ROLE OF EUROPEAN PATIENT ORGANIZATIONS IN PHARMACOVIGILANCE

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ABSTRACT

Introduction Patient organizations have a privileged position to be active agents for promoting pharmacovigilance and patient engagement, encouraging direct patient reporting and improve the awareness of pharmacovigilance.

Aim The objective of this study is to understand the role of European patient organizations as stakeholders to optimize patient involvement in pharmacovigilance.

Methods A descriptive-correlational study was conducted investigating patient organizations' opinions and attitudes regarding general patient involvement in pharmacovigilance and their initiatives to support drug safety through a web-based questionnaire during March and April 2018.

Results A total of 1898 patient organizations were invited to participate in the survey, including 89 pan-European organizations. In total, 337 questionnaires (17.76%) were collected from 31 countries, including 297 complete answers (88.31%). A large number of organizations stated that they would like to increase the awareness of patients about specific ADRs related to their medicines (43.19%, n=130). However, 38.54% declare don't have any goal in pharmacovigilance (n=116). Barriers found to the support pharmacovigilance activities include low budget to promote pharmacovigilance among members (45.45%, n=135), lack of resources to participate in pharmacovigilance activities (43.77%, n=130) or lack of support from the National Competent Authorities (33.33%, n=99). Organizations inform patients to report ADRs (40.40%; n=120), about new ADRs related to their medicines (40.07%; n=119), or when a new drug is marketed (30.98%; n=92); however, more than one third indicated that they never had any involvement in pharmacovigilance (34.68%; n=103).

Conclusion Bringing pharmacovigilance stakeholders and patient organizations together could create a more optimal reporting culture. Patient organizations appear to have an important role encouraging patients to talk with their doctors/pharmacists about adverse drug reactions suffered or help him to report the adverse drug reactions to the pharmacovigilance systems. Lack of resources, budget and support from NCAs are seen as the main barriers to be involved in pharmacovigilance.

KEY POINTS (3)

- Patient organizations shown an interest in drug safety topics but different levels of involvement with related activities
- Patient organizations appear to have an important role encouraging patients to talk with their doctors/pharmacists about adverse drug

reactions suffered or help him to report the adverse drug reactions to the pharmacovigilance systems.

- Bringing pharmacovigilance stakeholders and patient organizations together could create a more optimal ADR reporting culture.

1. INTRODUCTION

1.1. The role of patient and consumer organizations

In recent years, the role of patients in actively reporting adverse drug reactions (ADRs) has been increasing (1–4). Patients' involvement is a key to build better pharmacovigilance practices since they experience the impact of medicines on their bodies first-hand, can report complete and clinically relevant information and give more information on the impact of the ADR on quality of life, including describing the severity of reported reactions (5–7). Their reports can give more insight in the burden of experiencing ADRs on a patient's daily life and providing information not commonly present in healthcare professional (HCPs) reports. In addition, patients have also contributed directly to the detection or strength of drug safety signals (8–13).

The World Health Organization (WHO) refers that the involvement of patients in decisions has been instrumental in creating international awareness of the impact of the diseases and in improving communication of the associated risks. Accordingly to the WHO, "patients' concerns are now recognized as having a legitimate part to play in the heart of the decision-making process." (14) and one of the important steps in creating a reporting system and reporting culture for patients is the involvement of patient organizations (15).

The term 'patient organization' typically refers to a not-for-profit institution that represents the interests and needs of patients, their families and/or caregivers. In the last years, there was an effort to give patients a central role in pharmacovigilance. Patients are moving from a passive to an active recipients of health care, (16) and are increasingly involved in pharmacovigilance reporting systems. The growing initiatives from patients organizations are recognized as potentially valuable sources of information (12). The roles that patient organizations have played in supporting research and raising public awareness were highlighted in several publications (17–22).

In Europe, some pharmacovigilance centres have experiences working with patient reports for over a decade, (1,12) and the discussion of the importance of patient organizations in providing contributory safety information, especially regarding side effects affecting daily life is also not recent (23). Pharmacovigilance legislation changed in 2012, aiming to involve patients more actively in pharmacovigilance, (24) called nowadays as the "patient centricity in pharmacovigilance" (21,25).

In order to achieve a more patient-centered culture, pharmacovigilance centres could use a framework-driven approach to patient engagement and become proficient in a range of patient-centered competencies (25,26). Almost all countries have patient and consumer organizations that are dedicated to healthcare and welfare issues (27). Patient organizations have a privileged position to be active agents for promoting pharmacovigilance and patient engagement, educating patients on pharmacovigilance topics, improve the awareness of pharmacovigilance and encouraging direct patient reporting , which facilitates patient reporting of ADRs to national competent authorities (NCAs) (12,28). On the other hand, collaboration with NCAs in order to implement a suitable, simple reporting method, would be valuable, discussing about what works in the pharmacovigilance system and what needs improvements from a patient's perspective (16).

This collaboration could include suggestions about how to provide a national reporting system, how to ensure that patients can report, what sort of information should be captured, what information items are required for a patient-specific reporting form, what information is needed by the public, how to build awareness and educate patient communities, and how to advice and support public information campaigns, *etc (28)*.
In a recent study, patients agreed that patient organizations should be involved in regulatory issues, as joint position statements by physicians and patients' organizations to regulators, promote information about medicines or collaborate with health institutions on the development of guidelines (29).
Patients organizations were involved in the development of patient reporting systems in some countries and in collecting reports and transferring information for NCAs. Most countries, however, only implemented consumer reporting in 2012 or 2013 after the adoption of European pharmacovigilance legislation, and the collaboration between NCAs and patient organizations is weak or inexistent (30).

As suggested by Harmark *et al.*, consultation with patient organizations might provide valuable insight into what kind of information the patient can contribute in a reporting form. Patients should also be involved in the phrasing of the questions and decide on the answer options to make sure that the questions are easy to understand and answer (28). This information caught from patients organizations could be helpful in preparing guidelines for implementation and developing of direct patient reporting (16).
In addition, members of patient organizations usually are better informed and concerned about their health status and are potentially more likely to report ADRs. Patient organizations offer easy access to target groups, in order to spread information easily by a specific group of consumers (12,28). To maximise the input of patient participation, it is important to increase the capacities and capabilities of well-informed patients and patient organizations so that they can be effective advocates and advisors (28).
The objective of this study is to understand the role of European patient organizations as stakeholders to optimize patients' involvement in pharmacovigilance.

2. METHODS

A descriptive-correlational study was conducted investigating patient organizations' opinions and attitudes regarding patient involvement in pharmacovigilance and their initiatives to support drug safety through a web-based questionnaire.

2.1 STUDY POPULATION

The target population comprised of national and pan-European or International organizations that represent patients among European countries. A contact list was constructed by the authors based on the European Medicines Agency' "eligible patients and consumers organizations" list (31) and "European Patient Forum" members (32), both representing umbrella organisations encompassing a number of smaller or national organisations and organisations with a focus on a specific area or others umbrella coalitions of organizations throughout Europe. Websites of pan-European umbrella organizations were consulted one-by-one and contacts of their national members were collected on their website or directly from the national organization's websites listed on representing organizations as members. An e-mail address was collected for all organizations that presented an electronic mail contact available.
A total of 89 pan-European Organizations and their members were included for analysis. From a total of 2701 patient organizations that were identified, organizations outside the EU and EEA (n=266), duplicated

organizations (n=232), organizations without electronic e-mail contact (n=229) and organizations for which the first attempt to contact was bounced (n=76) were removed. A total of 1898 organizations were included in the survey. (Figure 1) The response rate was calculated based on the number of organizations that were contacted to participate in the survey through electronic email. The survey was intended to be completed by the president of the patient organization, or his representative, and this information was added in the invitation letter to be forwarded.

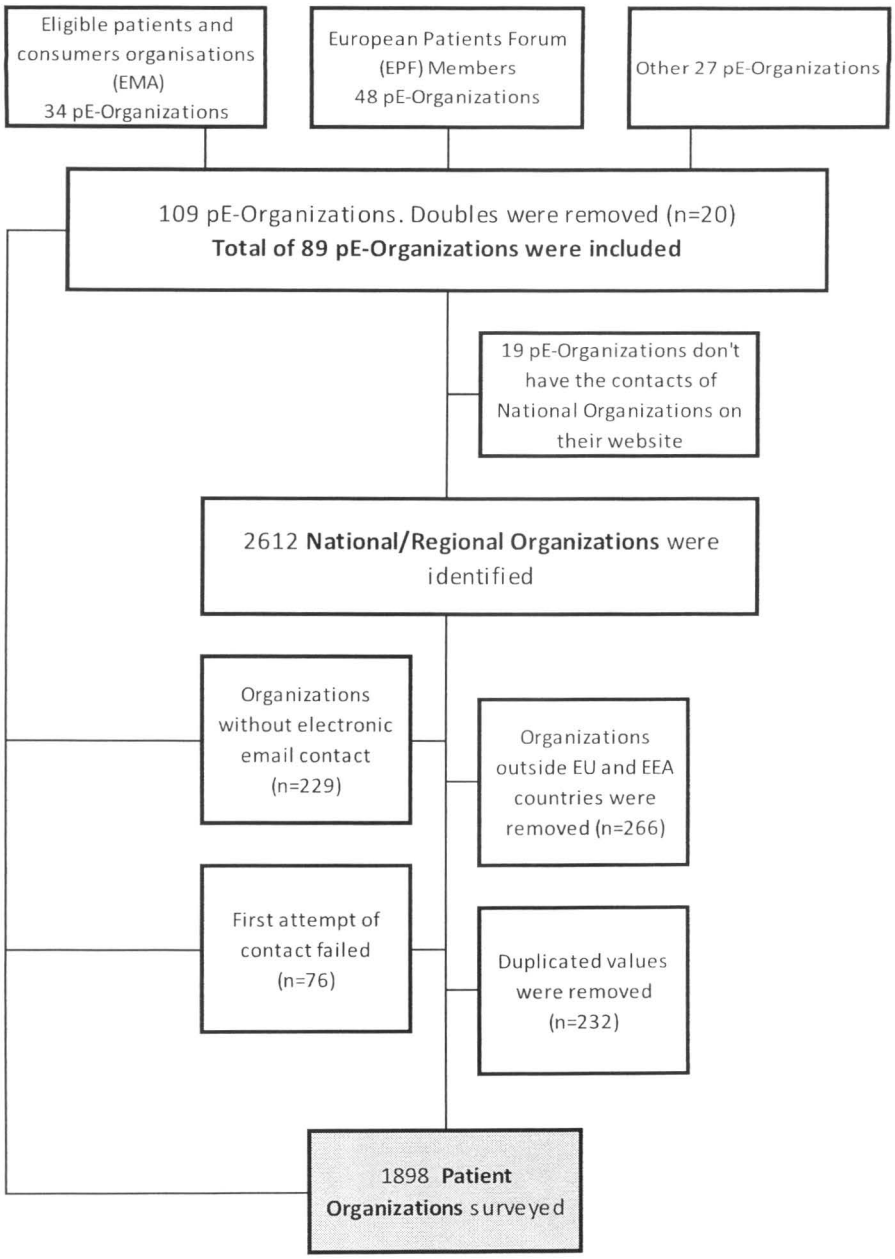

Figure 1 – Flowchart of patient organization selection

2.2. QUESTIONNAIRE DESIGN

The authors developed a questionnaire that was sent to patient organizations throughout European Union and European Economic Area (EEA) countries to understand their role as stakeholders to optimize patient involvement in pharmacovigilance, to investigate their activities regarding pharmacovigilance and to understand what type of support patient organizations need to develop the patient involvement in pharmacovigilance.

The questionnaire addressed a number of questions that intended to characterize the type of organization, their communication with members/patients, and their initiatives to support pharmacovigilance. Additionally, opinions regarding patient involvement in pharmacovigilance were surveyed. Whenever possible, questions were asked in a multiple-choice manner or with check-boxes options to facilitate responding to the questionnaire. Next to the response options was an 'Other' option along with a free text area for 'please specify'. Some questions were addressed as open-field text to give opinions and examples. The questionnaire **(Appendix 1 or Electronic Supplementary Material 1)** was created and distributed using SurveyMonkey® (Palo Alto, CA, USA).

2.3. SENDING THE QUESTIONNAIRE

The web-based survey was field tested for content validity by a small group of testers (n =8). The field testers were asked to provide comments regarding the format and comprehension of each item. Following review of the comments, items within each construct were amended. The amendments mostly represented changing words or revising sentence structure to increase item comprehension. (33) Subsequently, the questionnaire was sent to the contacts database on March 6, 2018 through the SurveyMonkey® platform. Three reminders were sent to all non-respondent organizations and those who had provided incomplete answers with the reminders being sent with two weeks interval after the previous contact. To improve the number of responses collected, personal contacts directly to the patient organizations representatives' electronic mails were also sent with the same invitation when a response was not provided during the first 4 weeks. The collection of responses ended on April 27, 2018. Email receivers were asked to forward the link in the invitation e-mail to the patient organization responsible in order to obtain the most representative answer possible. Reliability refers to the extent to which a questionnaire produces the same results on repeated trials. In short, it is the stability or consistency of scores over time or across raters. No reliability test was administered in the sense of questioning respondents twice and checking for similarity of response. (33) Respondents were also not asked to check their own answers to the questionnaire.

2.4. DATA ANALYSIS

Descriptive analyses were used to provide an overview of the opinions of the organizations about ADR patient reporting. Useful information from incomplete answers was included in the analysis. A Pearson Chi-square ($\chi 2$) test was performed to detect significant differences between the type of organizations, mainly comparing national and pan-European organizations. Significance was based on a two-sided $\chi 2$-test and was set at $p<0.05$. Responses on the Likert Scale regarding the role of pan-umbrella and national organizations in pharmacovigilance and opinions for the contribution of the patients to pharmacovigilance were coded as ordinal scale; 1, 2, 3, 4 and 5 (representing strongly disagree, disagree, neutral, agree and strongly agree, respectively). Data were analyzed using the statistical SPSS® Statistics Version 22 software (IBM Corporation, Armonk, NY, USA).

3. RESULTS

A total of 1898 patient organizations were invited to participate in the survey, including 89 pan-European organizations. In total, 337 answers were collected from 31 countries (from EU and EEA countries). We received contacts from 70 organizations opting out the questionnaire for several reasons (as lack of time, out of range of action, no resources to deal with surveys). Incomplete questionnaires were used when useful information was present (11.87%; n=40). The response rate was calculated based on the number of answers obtained to the questionnaire and was 17.76% (n=337), including 297 complete answers (88.31%). Countries with most responses were United Kingdom (6.82%; n=23) and The Netherlands (5.93%; n=20). Participant countries and answers per country were presented in **Electronic Supplementary Material 2.** Concerning the diseases represented by the organizations, answers from a total of 55 different diseases were obtained, including cancer (28 organizations) and lupus (11 organizations) with the most answers. From the respondents 76.26% (n=257) organizations represent specific diseases and 23.74% (n=80) represent "Cross disease" (authors use the expression "Cross disease" in the questionnaire meaning a "combination of different diseases").

There were more answers obtained for national organizations that represent patients for one specific disease, however answers from other types of organizations were also obtained. Answers where respondents selected "other" was evaluated case-by-case and recoded in one of the other categories, when possible. Table 1 shows the type of organization that participated in the survey.

Table 1. Type of Patient Organization

Type of Patient Organization	Frequency
National organizations for specific diseases - we represent patient for one disease	74.48% (251)
National coalitions of patient organizations - we represent several national organizations of different diseases	10.68% (36)
Pan-European organizations of specific diseases - we represent European/internationally organizations for a disease	10.98% (37)
Scientific society - we represent professionals as a part of a patient organization	1.78% (6)
†Other: *"Consumer Organization"*	1.48% (5)
Other	0.59% (2)
Total	**337**

Discrepancy in cells total 100% due to rounding. †With "consumer organization" we understand an organization that offer practical consumer assistance, protection and advocacy independently of illness

Table 2 shows the most commonly used communication channels and frequency of use to provide information to patient organizations members: online based platforms as new items on their website (96.36%, n=318), social media (89.91%, n=302), and electronic mail (77.45%, n=261) were the most used.

The frequency of use is variable; social media being used more on a daily basis, and new items on the website and electronic mail newsletters are more used in weekly and monthly frequency, respectively.

Table 2. What are the communication channels to provide information and how periodically you use that to communicate with your members?

What are the communication channels to provide information and how periodically you use that to communicate with your members? Total of respondents: 337	Daily	Weekly	Monthly	Quarterly	Annually	Not Available
New items on the website	13.06% (44)	**36.50% (123)**	34.12% (115)	9.20% (31)	1.48% (5)	5.64% (19)
Newsletter by electronic mail	1.78% (6)	8.31% (28)	**33.53% (113)**	25.52% (86)	8.31% (28)	22.55% (76)
Newsletter by post	2.37% (8)	2.67% (9)	6.23% (21)	18.69% (63)	9.79% (33)	60.24% (203)
Social Media (as Facebook, Twitter, Instagram)	**43.32% (146)**	32.05% (108)	10.09% (34)	4.45% (15)	0.00% (0)	10.09% (34)
Article in a magazine	0.59% (2)	3.56% (12)	10.68% (36)	24.33% (82)	21.66% (73)	39.17% (132)
Periodic publication of the organization (magazine/journal)	0.00% (0)	1.19% (4)	4.45% (15)	31.16% (105)	15.43% (52)	47.77% (161)

Discrepancy in cells total 100% due to rounding.

Respondents were asked to classify through a 1-10 rating scale, in general, how much focus the organization has on drug safety issues. A value of 5.37 ± 3,12 was obtained. There were no differences between types pan-umbrella organizations and other organizations that have direct contact with member patients. (p=0,098). Table 3 represents the type of collaboration between patient pan-umbrella organizations and their member organizations. According to the answers to the questionnaires, 64.29% (n=36) of respondent pan-umbrella organizations promote drug safety in one or several ways, although, 35.71% (n=20) stated that they don't promote any activities in pharmacovigilance.

Table 3 – Collaboration of umbrella-like organizations with member organizations to promote drug safety?

Does your organization collaborate with member organizations to promote drug safety? *(multiple answers allowed)* Total of respondents: 56	Frequency
Yes, we spread information on drug safety issues to our member organizations	39.29% (22)
Yes, we send guidelines for member organizations with positions regarding drug safety issues	12.50% (7)
Yes, we send materials (presentations, literature, etc.) to member organizations in order to educate patients about drug safety	23.21% (13)
Yes, we encourage member organizations to collaborate with the National Competent Authorities	50.0% (28)
No, we don't promote any activities in Pharmacovigilance	35.71% (20)

Discrepancy in cells total 100% due to rounding.

Half of the pan-European organizations stated that they encourage member organizations to collaborate with National Competent Authorities. However, in another question, organizations admitted that only a small percentage 29,43% (n=88) collaborate with NCAs versus 70.57% (n=211) that stated that they don't collaborate with their NCAs regarding pharmacovigilance.

An open-ended question was added to the questionnaire to understand the most important focus areas of the organizations. We obtained 296 answers from patient organizations: most mentioned focus areas were; "supporting activities for the patients" (n=93), raising awareness about the disease (n=80), education activities (n=59), research activities (n=53) and advocacy activities (n=21).

Table 4 shows patient organizations' beliefs regarding the role of the organizations in supporting patients in pharmacovigilance activities. Responses of umbrella organizations and national organizations were compared. The sentence "National or regional organizations are more suitable to support patients in pharmacovigilance activities than umbrella-like organizations" obtained differences between umbrella and non-umbrella organizations (p = .038) with umbrella organizations having a neutral position regarding this; however, national organizations agree or strongly agree with the sentence (62.40%; n=149). The answers to other questions did not differ between both groups.

Table 4. - Do you think national or regional organizations would be more suitable to support patients in pharmacovigilance activities than umbrella-like organizations?

Differences between national and umbrella-like patient organizations in supporting pharmacovigilance Total of respondents: 313	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree	Not Relevant
Direct contact with patients is easier in smaller organizations	3.83% (12)	4.15% (13)	15.98% (50)	29.71% (93)	**44.09% (138)**	2.24% (7)
Geographical proximity to patients is important for share information	7.67% (24)	13.42% (42)	21.73% (68)	27.16% (85)	**27.80% (87)**	2.24% (7)
National organizations communicate more effectively because they communicate in the native language	2.88% (9)	2.56% (8)	5.75% (18)	21.41% (67)	**65.18% (204)**	2.24% (7)
Umbrella organizations are more effective to share information because they are more representative	7.35% (23)	16.29% (51)	**32.59% (102)**	21.73% (68)	17.89% (56)	4.15% (13)
National or regional organizations are more suitable to support patients in pharmacovigilance activities than umbrella-like organizations	3.51% (11)	9.90% (31)	23.96% (75)	22.36% (70)	**32.91% (103)**	7.35% (23

Discrepancy in cells total 100% due to rounding.

Table 5 shows the agreement about the contribution of patients to pharmacovigilance. There were no significate differences in answers between national and pan-European organizations.

Table 5. – Contribution of the patients to pharmacovigilance

In what way do you think patients can contribute to pharmacovigilance? Total of respondents: 301	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree	Not Relevant
Patients can provide different information from the healthcare professionals	1.33% (4)	4.32% (13)	14.95% (45)	24.92% (75)	**51.16% (154)**	3.32% (10)
Patients can contribute to the detection of new adverse drug reactions	1.99% (6)	1.33% (4)	5.32% (16)	23.26% (70)	**66.45% (200)**	1.66% (5)
Patients give more information on the impact of the adverse drug reaction on quality of life	1.99% (6)	0.66% (2)	6.31% (19)	20.27% (61)	**67.77% (204)**	2.99% (9)
Patients can be useful in describing the severity of reported reactions	1.99% (6)	2.66% (8)	7.31% (22)	24.92% (75)	**61.46% (185)**	1.66% (5)
Patients can report information that is useful, even without medical confirmation	2.99% (9)	3.65% (11)	12.29% (37)	27.24% (82)	**52.16% (157)**	1.66% (5)
Patients describe information based on their experience with medicines	1.66% (5)	1.66% (5)	5.98% (18)	21.26% (64)	**68.11% (205)**	1.33% (4)

Discrepancy in cells total 100% due to rounding.

Table 6 summarizes the answers to several questions in the questionnaire. The first question asked about the attitudes of the organizations if a patient shares information about a suspected adverse drug reaction. Most organizations (82.06%; n=247) encourage patients to talk with their doctors/pharmacists about adverse drug reactions suffered or help him to report the adverse drug reactions to the pharmacovigilance system (31.89%; n=96). Regarding initiatives in pharmacovigilance, about a quarter of respondents spread information on how to report (28.57%; n=86) or organizes activities to help patients to be aware of drug safety (28.57%; n=86), however, almost half of the respondents admitted that they don't have any activities related with pharmacovigilance (45.85%, n=138). Organizations stated that they inform patients that they are allowed to report adverse drug reactions (40.40%; n=120), or communicate to patients if an important new adverse drug reaction appears for a specific medicine (40.07%; n=119), or when a new drug is marketed (30.98%; n=92).; however, more than one third answered that they had never any involvement in pharmacovigilance (34.68%; n=103).

Table 6. Attitudes and initiatives in Pharmacovigilance

If a patient contacts your organization to share a reaction suffered related to their medication, what do you do? *(multiple answers allowed)* **Total of respondents: 301**	Frequency
We encourage them to talk with their doctors/pharmacists about adverse drug reactions suffered	82.06% (247)
We communicate the information to the National Competent Authority	13.95% (42)
We help him to report the adverse drug reactions suffered to the pharmacovigilance system	31.89% (96)
We do nothing	1.66% (5)
Other	17.61% (53)
What are the initiatives in your organization to support pharmacovigilance? *(multiple answers allowed)* **Total of respondents: 301**	Frequency
We have a direct link on our website for patients to report adverse drug reactions	6.64% (20)
We spread information on how to report (for instance on our website, newsletter, email, conferences)	28.57% (86)
We organize activities (seminars, campaigns, workshops, courses) to help patients to be aware of drug safety	28.57% (86)
We don't have any activities related with pharmacovigilance	45.85% (138)
Other	23.92% (72)
Have you ever planned to involve patients more actively in Pharmacovigilance? *(multiple answers allowed)* **Total of respondents: 301**	Frequency
We inform our patients that they are allowed to report adverse drug reactions	40.40% (120)
We inform our patients when a new drug is marketed (including possible adverse drug reactions)	30.98% (92)
If an important new adverse drug reaction appears for a specific medicine, we communicate this information to our patients	40.07% (119)
We never had any involvement in Pharmacovigilance	34.68% (103)

Discrepancy in cells total 100% due to rounding.

Following these questions, respondents were surveyed about the goals and plans in Pharmacovigilance for the future. Organizations stated most that they would like to increase awareness of patients to specific adverse drug reactions related to their medicines (43.19%; n=130) or that they are focused on helping patients to report adverse drug reactions (26.25%; n=79). More than one third said that they don't have any goal in Pharmacovigilance for the future (38.54%; n=116) and from those, most also stated don't have any activities related with pharmacovigilance (75.00%; n=87) and never planned to have any involvement in pharmacovigilance (62.93%; n=73). (Table 7)

Barriers to support pharmacovigilance include low budget to promote pharmacovigilance among members (45.45%; n=135) and lack of resources to be involved in pharmacovigilance activities. (43.77%; n=130).

Table 7 – Goals in Pharmacovigilance

Goals of the organization in Pharmacovigilance *(multiple answers allowed)* **Total respondents: 301**	**Frequency**
We are focused on helping patients to report adverse drug reactions	26.25% (79)
We are focused on intensive monitoring of medicines used in a specific disease	13.95% (42)
We would like to increase awareness of patients to specific adverse drug reactions related to their medicines	43.19% (130)
We collaborate with National Competent Authorities in joined decision making	15.28% (46)
We are involved in risk-benefit assessment for specific medicines used by our members	9.63% (29)
We don't have any goal in Pharmacovigilance	38.54% (116)
Barriers found if organization have the intention to support or be involved in pharmacovigilance activities *(multiple answers allowed)* **Total respondents: 297**	Frequency
Lack of resources to be involved in pharmacovigilance activities	43.77% (130)
Low budget to promote pharmacovigilance among our members	45.45% (135)
We don't know what to communicate to improve patients' involvement in pharmacovigilance	17.85% (53)
We don't receive any support (or information) from National Competent Authority in our country	33.33% (99)
Little or no priority to pharmacovigilance activities	33.00% (98)
Other	14.48% (43)
What would you need from the pharmacovigilance centre/community to achieve this? *(multiple answers allowed)* **Total respondents: 297**	Frequency
Information about drug use and side effects to be shared with patients	60.94% (181)
Information on how patients can report side effects and why it is important to report side effects	58.25% (173)
Information on how patients can be involved in drug safety	63.97% (190)
We don't have interest in information	8.42% (25)
Other	11.11% (33)

Discrepancy in cells total 100% due to rounding.

More than two-thirds of the respondents (70.57%, n=211) stated that they don't collaborate with National Competent Authorities regarding Pharmacovigilance. Collaboration with NCAs examples include sharing information and good communication channels, collaboration in training campaigns and courses/seminars/congresses, scientific advisory participation and report adverse events of patients. An open-ended question was added inquiring organizations if their activities regarding pharmacovigilance have changed since the EU legislation in 2012 (which makes mandatory for EU member countries to enable patient reporting). A total 202 answers were obtained, however 168 organizations stated that activities haven't changed since legislation and 5 organizations started after 2012. Changes which were mentioned included: advising the national authorities to review the language used on the report forms to make it more user-friendly and understandable for a low literacy level population, increasing patient reporting of ADRs, organizing training seminar' with patients and experts from the National Competent Authorities and giving more emphasis on how to educate patients on matters that regards pharmacovigilance.

Patient organizations requests to pharmacovigilance centres to support pharmacovigilance activities include "information on how patients can be involved in drug safety" (63.97%; n=190), "information about drug use and side effects to be shared with patients" (60.94%; n=181) and "information on how patients can report side effects and why it is important to report side effects" (58.25%; n=173). Other information stated in the open-ended questions includes comparative information between countries, scientific material in layman and national languages, online platforms to report ADRs and information on newly marketed medicines and expected ADRs. Organizations were also asked 'If they don't see a role in pharmacovigilance, which are the reasons?' A total of 38 valid answers followed. Responses included "organizations with a few or none drug therapy" (or alternatives to their treatments), "pharmacovigilance is a role for healthcare professionals", due to "lack of conditions" (as "resources", "budget" and "organization maturity") or because it's not the focus area of the organization.

4. DISCUSSION

The importance of patient organizations should be highlighted; usually providing disease awareness through continuous education and supporting patients, helping them to understand their diseases (34). These organizations have a very important role in patient-centric approach and partnering with patients and the public for reporting and communication of safety data and raising patient awareness regarding the importance of reporting ADRs and continuously highlighting the critical role they can play in Pharmacovigilance. Since 2012, with the recent EU Pharmacovigilance legislation (35) all European Member States are obliged to have a system for direct patient reporting of suspected ADRs , allowing public access to more information on the safety of medicines. Patients very often contribute scientifically to the discussion, with unique and critical inputs based on their real-life experience of being affected by a disease and its current therapeutic environment (28).

4.1. STRENGTHS AND LIMITATIONS OF THE STUDY

4.1.1. Response rate

The major strength of this study is that this is the first study conducted in a large amount of patient organizations to evaluate the involvement in pharmacovigilance. Contacts of patient organizations were collected by authors directly from patient organizations websites or other sources (as pan umbrella organizations lists of members) and the intention was to be inclusive for as many as possible different diseases and organizations throughout Europe. The questionnaire was sent through SurveyMonkey platform and three reminders were sent to all non-respondent organizations and those who had provided incomplete answers. A disadvantage of our sampling method was that we could not check available email-addresses for correctness or if the questionnaire did not reach the correct person within an organization ('general' email-addresses for organisations were also used).

Despite of our effort to spread the questionnaire widely, the response rate of 17% can be considered low, and therefore the answers might not be generalizable. The organisations that did answer the questionnaire were generally positive about pharmacovigilance. We cannot be sure if the non-responders have a different view on this topic.

The target population of this study were patient organizations representatives, and they were selected based on if they are represented in European pan-umbrella organizations. However, some of these organizations may have found it difficult to respond to the questionnaire for a wide range of reasons

including being a very recent organizations, very regional organizations including organizations with few members and not representative for the disease, organizations with little or no relation with the use of medicines, inactive or already extinct organizations, organizations with lack of resources to deal with questionnaires, lack of knowledge on the topic, etc.

4.1.2. Participation in the Study and respondent's characteristics

We have included different type of organizations (umbrella-like, European and international organizations, regional and national organizations and consumers organizations), which gave a wide range of responses. Besides that, the survey covered organizations of all EU and EEA countries, which enhances the representativeness. All pan-European or umbrella-like organization represented, obtained at least one answer from one of their members, which again helped to strengthen the results obtained. In a total of 89 pan-umbrella organizations surveyed, 37 complete answers were obtained. This can be seen as a strength for the representativeness of the organizations surveyed. The level of development of the organizations that answered the questionnaire was not evaluated, so we cannot affirm that most developed organizations have more attention to pharmacovigilance topics than others.

The number of specific diseases organizations that answered the questionnaire are in accordance with the number of organizations for specific diseases surveyed. A total of 55 different diseases from 31 countries were represented in the answers provided, which strengths the validity of data collected. However, cancer and lupus have the highest amount of responses, which, as discussed earlier could reveal that the seriousness of the condition (and the related adverse drug reactions) could be a factor that motivates patients to be aware about their medicines. On the other hand, cancer organizations are also the most surveyed organizations (per disease). Results also showed that countries with more participation in the survey were the UK and The Netherlands, related with a higher maturity of patient reporting systems in both countries, and increased attention given by organizations to drug safety issues. Both countries, together with Denmark, being the oldest countries in Europe to have ADR reporting systems implemented for patients (3).

One potential limitation was related to the role of the respondents in the patient organization. In each organization was asked to the representative (Director, President, CEO) to answer the survey, however, his/her view could be potentially different from the views of other staff. It was not possible to reach all heads of the organizations for confirmation of the results in the case of another colleague filling in the questionnaire. As with most surveys, there's the possibility that respondents give the 'most correct' answer rather than the real or valid answer to the surveyed questions (social desirability bias).

4.1.3. Construction of the Questionnaire

Closed-ended statements were used as often as possible in the questionnaire, however one objective of the authors was to survey the personal experiences of patient organizations, so open-ended questions were also included. Furthermore, to avoid invalid data, an odd-numbered scale for rating the statements was chosen. When respondents were truly neutral on a topic, they were not forced to any side. The final questionnaire version was pre-tested to understand major drawbacks and improvements to the questionnaire. During pre-

testing, a few statements were considered to be confusing and were rewritten to provide an easier understanding of the questionnaire. However, from the responses to the questionnaire we saw that the wording was still confusing to some respondents. This is a limitation of the study.

The use of an English questionnaire was considered another limitation to the survey, since for non-native English users it could be difficult to understand and answer the questionnaire and creating a language bias. However, the decision of using only an English version of the questionnaire was discussed by the authors and this limitation was preferable to the bias created by the translation of the questionnaire and answers, which may compromise the comparability of answers, since the questionnaire presented several parts of qualitative answers. Authors considered that the translation of the questionnaire in other common languages spoken in Europe (French, Spanish, German, etc.) could represented an amendment that might increase the number of responses collected in a questionnaire regarding this issue.

For the dissemination of the questionnaire the SurveyMonkey® platform was used. Although most e-mail servers allow messages from SurveyMonkey®, institutions that maintain high security and intense spam blockers may block email from the SurveyMonkey® platform.

5. CONCLUSION

There's a wide range of interest in drug safety issues among patient organizations. Patient organizations appear to have an important role encouraging patients to talk with their doctors/pharmacists about adverse drug reactions suffered or help him to report the adverse drug reactions to the pharmacovigilance systems. Lack of resources, budget and support from NCAs are seen as the main barriers to be involved in pharmacovigilance; on the other hand, an important part of the organizations appear to not have any activities or involvement related with pharmacovigilance. Bringing pharmacovigilance stakeholders and patient organizations together could create a more optimal patient reporting culture.

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Compliance with Ethical Standards

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Conflicts of interest

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Apex 2.

Code Definition Rules

Positive about DPR			
Code name	**Description**	**Unit of analysis**	**Decision rules**
Importance of DPR	Describes advantages of DPR.	Context unit: sentence e.g.: One Dr appointment a year, DPR is faster.	When conjunctions present, sentences are assessed individually.
Positive Impact	DPR has a beneficial impact, a positive input.	Context unit: sentence e.g.: Real impact is seen when used in general population	When conjunctions present, sentences are assessed individually.
User Knows Best	The positive argument behind DPR is related to the patient as first source of information.	Context unit: sentence e.g.: Patients are better at reporting the impact of ADR.	When conjunctions present, sentences are assessed individually.
Positive Judgment Opinion	Used when the positive opinion does not refer to an advantage over other means and does not refer to the positive impact of patient as first source of information. There could be a positive personal opinion that may have no reason.	Coding Unit: words e.g.: Indispensable, relevant. Context Unit: sentence e.g.: Critical importance.	When conjunctions present, sentences are assessed individually. Coding unit points positive in the context when available.

Doubtful about DPR			
Code name	**Description**	**Unit of analysis**	**Decision rules**
Doesn't know the data treatment	The arguments for not having a full positive opinion are related to uncertainty about the data treatment or the purpose it is used for.	Context Unit: sentence e.g.: Worried about confidentiality.	When conjunctions present, the sentence is analyzed as one.
Low or no experience with PV	The answer does not reflect a position about DPR because there is lack of knowledge about PV.	Context Unit: sentence e.g.: I have no idea.	When conjunctions present, sentences are assessed individually.
Doubts about value	The data provided by patients and its use is criticized.	Context Unit: sentence e.g.: Useful but with criticism.	When conjunctions present, the sentence is analyzed as one.

Negative about DPR			
Code name	**Description**	**Unit of analysis**	**Decision rules**
DPR does not contribute to PV	There is no benefit for doing DPR, it shows a disadvantage of DPR.	Context Unit: sentence e.g.: Reports could be very diverse and inconclusive.	When conjunctions present, sentences are assessed individually.
DPR should not exist	It should not exist because the patient is not the one to report ADR.	Context Unit: sentence e.g.: No patients in PV.	When conjunctions present, sentences are assessed individually.
Patients are unable to report	The inability to report could be due to low health literacy or a physical or mental condition	Context Unit: sentence e.g.: They are not objective.	When conjunctions present, sentences are assessed individually.
Deficient reporting system	The negative position is based on the tools for reporting.	Context Unit: sentence e.g.: Reporting is difficult.	When conjunctions present, sentences are assessed individually.

Activities in PV			
Code name	**Description**	**Unit of analysis**	**Decision rules**
Supports initiatives from others	The organization supports an external initiative. They did not originate the activity but they support it.	Context Unit: sentence e.g.: Happy to disseminate high quality resources.	When conjunctions present, the sentence is analyzed as one.
Reports ADR	The activity is reporting directly or guiding patients on the steps to reporting directly.	Context unit: sentence e.g.: Reports in the name of the patient.	When conjunctions present, sentences are assessed individually.
Share drug safety issues with	The action is to contact other stakeholders when problems happen. The code is a list of the stakeholders they contact.	Context unit: sentence e.g.: Notify the manufacturer.	When conjunctions present, sentences are assessed individually.
Refers drug safety inquiries	When patients have drug safety issues, they refer the patient to someone else, could be another stakeholder.	Context unit: sentence e.g.: Refer to the hospital.	When conjunctions present, sentences are assessed individually.
Encourage Reporting	Explains the different actions taken to encourage reporting through other stakeholders.	Context unit: sentence e.g.: Explain it is critical to report.	When conjunctions present, sentences are assessed individually.
Education	Any activity related to education in PV.	Context unit: sentence e.g.: Publish in the magazine about PV and drug reactions.	When conjunctions present, sentences are assessed individually.
Services	The code is used when the organization provides services oriented to promote drug safety	Context unit: sentence e.g.: Someone is available 2 hrs daily for medicine issues	When conjunctions present, sentences are assessed individually.
Facilitator	The activity is oriented to to ease the patients way on the PV system.	Context unit: sentence e.g.: Direct link on the website.	When conjunctions present, sentences are assessed individually.

Information Transmission Medium			
Code name	**Description**	**Unit of analysis**	**Decision rules**
Meeting or congresses	Could be referred as meetings, congresses or any other type of group gathering between the POs and their members or between POs and other stakeholders.	Coding units: word e.g.: Meetings, congress, reunion. Context unit: sentence e.g.: Talk about it in annual class.	When conjunctions present, sentences are assessed individually. The coding unit is not explicit but the context explains the description.
Web based materials	The code is used when they ask information to be transmitted using web or internet.	Coding unit: word e.g.: Internet, Facebook. Context unit: sentence e.g.: We can run an article in our magazine to raise awareness. In this example the magazine can be web and can also be printed, the sentence is added to both codes.	When conjunctions present, sentences are assessed individually. The coding unit is not explicit but the context explains the description. Adding multiple codes is possible when the context complies with more than one code description.
Printed material	The transmission of the information is by physical dissemination means.	Coding unit: word e.g.: Books. Context nit: sentence e.g.: Other didactic ways of information, internet not available for everyone.	When conjunctions present, sentences are assessed individually. The coding unit is not present but the context explains the description. Adding multiple codes is possible when the context complies with more than one code description.

Information Transmission Medium			
Code name	**Description**	**Unit of analysis**	**Decision rules**
Individual communication	The transmission of drug safety information is by personal and individual contact, like one on one communication.	Context unit: sentence e.g.: Speak personally with them.	When conjunctions present, sentences are assessed individually.
Other means of communication	This code is added when the transmission mean is not specified and the context does not explain any of the previous code description	Context unit: sentence e.g.: A system that works through several groups of patients.	When conjunctions present, the sentence is analyzed as one.

For all Information Transmission Medium codes: the transmission can be a current action or can be described in the context as a possible reaction.

Material Characteristics			
Code name	**Description**	**Unit of analysis**	**Decision rules**
Simple language	The language used in any material must be easy to understand and comprehensible for lay man.	Context unit: sentence e.g.: Better drug inserts, more precise and comprehensible.	When conjunctions present, the sentence is analyzed as one. Adding multiple codes is possible when the context complies with more than one code description.
Native language	The context unit refers to a difficulty faced when the material is not in native language or presents native language as the main material characteristic.	Context unit: sentence e.g.: The information should be in native language.	When conjunctions present, the sentence is analyzed as one. Adding multiple codes is possible when the context complies with more than one code description.
No spam	Code used when the organization does not want to receive unsolicited information or the same information multiple times.	Context unit: sentence e.g.: without saturating our structure.	When conjunctions present, the sentence is analyzed as one.

Material Characteristics			
Code name	**Description**	**Unit of analysis**	**Decision rules**
Fast	The information needs to be transferred in a timely manner.	Context unit: sentence e.g.: Early warnings	When conjunctions present, the sentence is analyzed as one.

Changes after legislation			
Code name	**Description**	**Unit of analysis**	**Decision rules**
No change	Legislation did not cause any changes, the respondent is not aware of changes.	Coding units: word e.g.: No, none Context Unit: sentence e.g.: No, since we are not directly involved.	When conjunctions present, the sentence is analyzed as one. The coding unit is not explicit but the context explains the description.
Increase Interaction with NCA	Mentions an interaction with a NCA or European authority after the legislation	Context Unit: sentence e.g.: Participation in EMA workshops	When conjunctions present, sentences are assessed individually
More PV activities	There has been an increase in the activities specifically related to PV. The organization has the initiative to start the activity	Context Unit: sentence e.g.: Now we have an active role encouraging reporting.	When conjunctions present, sentences are assessed individually
Acts as intermediate	There is an activity, act as a conduit channel.	Context Unit: sentence e.g.: Pass the information to our members.	When conjunctions present, the sentence is analyzed as one.
Visualize future activities	There are no activities but there may be in the future. The activity is explained in future time.	Context Unit: sentence e.g.: Small steps ahead	When conjunctions present, the sentence is analyzed as one.

POs needs in Pharmacovigilance			
Code name	**Description**	**Unit of analysis**	**Decision rules**
Validation	This code is used when the organization needs for acceptance or recognition from stakeholders.	Context Unit: sentence e.g.: People understand side effects quickly, authorities don't accept them.	When conjunctions present, the sentence is analyzed as one.
Encouragement	This code is used when more support for patient involvement is necessary.	Context unit: sentence e.g.: Incentivize DPR	When conjunctions present, the sentence is analyzed as one. Adding multiple codes is possible when the context complies with more than one code description.
Support from external organizations	They point at other stakeholder for help on their PV development.	Context unit: sentence e.g.: Need help from bigger organization.	When conjunctions present, the sentence is analyzed as one. Adding multiple codes is possible when the context complies with more than one code description.
Reinforcement of safety measurements	The code is used when they want more controls on drug authorization and use.	Context unit: sentence e.g.: Medicine should be safe and authentic.	When conjunctions present, the sentence is analyzed as one.

Information Requested			
Code name	**Description**	**Unit of analysis**	**Decision rules**
Not PV related	The information requested is not associated to PV.	Context unit: sentence e.g.: Information on new drugs for our disease	When conjunctions present, sentences are assessed individually
Focused information	When they request for personalized or targeted information. This information can be related to drug safety.	Context unit: sentence e.g.: Side effects on drugs for epilepsy	When conjunctions present, the sentence is analyzed as one.
PV system	The information requested is about how the PV system works.	Context unit: sentence e.g.: Insight in what is being done with patient reports.	When conjunctions present, sentences are assessed individually.
Understanding PV	This code is used when the information they request is to understand what PV is about, what drug safety is	Context unit: sentence e.g.: Importance of involvement in PV.	When conjunctions present, sentences are assessed individually.

Reasons for not supporting PV			
Code name	**Description**	**Unit of analysis**	**Decision Rules**
Small organization	They claim their lack of involvement to the size of the organization or their recent start.	Context unit: sentence e.g.: Little and new organization.	When conjunctions present, sentences are assessed individually.

Reasons for not supporting PV			
Code name	**Description**	**Unit of analysis**	**Decision Rules**
No priority	The code is used when there is no priority for supporting PV activities. It could be because there is no apparent need, the problem is being handle by others or it escapes their focus of activities.	Context unit: sentence e.g.: The focus is overcoming the impact of the disease.	When conjunctions present, sentences are assessed individually.
Lack of skilled human resources	This code is used when the PO needs staff that is knowledgeable in the topic to take care of drug safety activities.	Context unit: sentence e.g.: Difficult to have skilled volunteers.	When conjunctions present, sentences are assessed individually.
Doesn't know PV system or it is complicated	The organization does not know about PV or finds the PV structure complicated.	Context unit: sentence e.g.: Not aware of DPR to NCA.	When conjunctions present, the sentence is analyzed as one.
Lack of resources	This code is used when resources is the limitation. The resource can be specified or not.	Context unit: sentence e.g.: Reduced resources	When conjunctions present, the sentence is analyzed as one.
Someone else responsibility	This code is used when drug safety responsibility is blamed on another stakeholder.	Context unit: sentence e.g.: It's all in hands of Drs.	When conjunctions present, the sentence is analyzed as one.
ADR less important than the disease	The code is a particular reason for no priority; the priority is given to the disease and its effects.	Context unit: sentence e.g.: Patients need drugs despite side effects.	When conjunctions present, the sentence is analyzed as one.
Patient not suitable for PV activities	The objection in the context is that patients for several reasons cannot report adverse reactions.	Context unit: sentence e.g.: Some diseases affect brain.	When conjunctions present, sentences are assessed individually.

Apex 3

Units of Analysis Used in the Data Content Analysis

Positive about direct patient reporting	
Code	**Unit of Analysis**
Importance of DPR	Patient reports own experience without limitations by clinicians Patient contribution is different from HCPs Important because patients don't depend on Drs. approval. Drs. may forget to report Empowering, patients don't always feel comfortable reporting through clinicians. DPR has the same quality from HCPs reports. Reports inform different issues, faster, more descriptive. DPR adds value to PV Patients are aware of symptoms first Extremely valuable assessing the impact of reactions includes personal factors HCPs overlook. One Dr. appointment a year. DPR is faster DPR saves time. High value for early detection. They report unique and different experiences on ADR Real impact is seen when used in general population. DPR encourages self-care and patient centered care Bigger source of data Important, especially in quality of life and long term side effects, those have larger impact Chance to avoid losing data from patients
Positive Impact	Contributes to patient safety Helps other patients Pushes to flexible pharma development DPR may add new information and perspective. Very useful for patient relief and mental health. May contribute to better decisions by authorities Can make drugs use safer

Positive about direct patient reporting	
Code	**Unit of Analysis**
User Knows Best	You receive the experiences from real users Patient describes personal experiences Real life experience related to medicines, quality of life Real life experience Best source of information. Accurate Patients are better at reporting impact of ADR. Chronic drug users can find new things Patients can use simple terms Patient experience is important. Theory and life are different. Drs. cannot explain quality of life impact the same way. Patients can report the impact on quality of life. Access benefit/risk ratio. Very important. Children tell more to parents than to Drs.
Positive Judgment Opinion	Very useful Positive about it Vital Relevant Simple, easy, important value Important, especially in long term use, chronic disease. Indispensable Extremely important, misunderstood, underestimated Critical importance

Doubtful about direct patient reporting	
Code	**Unit of Analysis**
Does not know the data treatment	It would be extremely useful but many methodology questions needs to be anonymous Important but cannot replace clinical trial Problem is how to manage so much data PV system needs to differentiate between real and not real ADR May be biased, it needs medical confirmation Must be filtered and controlled Difficult to judge when polypharmacy Worried about confidentiality Could be hard to process When validated, it can be reported to other patients

Doubtful about direct patient reporting (continuation)	
Code	**Unit of Analysis**
Low or not experience with PV	Don´t know No experience Could be good No idea Son´s experience is crucial on rare diseases
Doubts about DPR value	Patients should be cautious, internet info is not always correct Patients inform their perspective. If psychologist involved it's possible to measure impact on quality of life Has to be confirmed and controlled. Useful but with criticism Important but is their own experience. Depends on cultural issues, information, health education, age, health professionals support Authentic experience, unsure about value Beneficial but tends to lose focus

Negative about direct patient reporting	
Code	**Unit of Analysis**
DPR does not contribute to PV	The value is small Personal opinions, cannot be verified Reports could be very diverse and inconclusive Patients can only report their own experience, subjective, only valid for their own event. Important only as example to peers Dangerous. One report is not representative. It can be therapeutic. Data can be of high value
DPR should not exist	Patient discuss with specialist. Drs report Disagree with PDR in PV Depends on disease. Patient should report to HCPs, they should listen No patients in pharmacovigilance
Patients are unable to report	Patients may not be objective and disregard other contributing factors. Patients may be influenced by social media misrepresented studies Nightmare. Patients exaggerate symptoms. Social media misrepresent drug info Huntington affects brain in different ways. Hard to do DPR Patients don't understand coincidence. They attribute all reactions to drugs Sometimes patient exaggerates

Negative about direct patient reporting (continuation)	
Code	**Unit of Analysis**
Deficient reporting system	People in Denmark give up due to reporting difficulty. Reporting form not for mental health problems PDR almost un-existing in Poland. Reporting system should be easy Patients are more confident at reporting in associations than PV centers Some data is ignored due to quantitative research method PV system does not fit the ADR experienced by psychotropic users Tools for DPR are intimidating and rare designed for benefit to the patient DPR tools are not good enough at collecting this

Activities in pharmacovigilance	
Code	**Unit of Analysis**
Supports Initiatives from others	Share EMA information to European organizations Provide generic info Support national campaigns Dissemination of safety issue info Happy to disseminate high quality resources Sometimes share information provided by industry We receive it from eurordis but it's hard to share with patients Support information campaigns provided by others Share ema alerts
Reports ADR	Help them report through pv system Help to report through the pv system. Include the report in their system We have reported in the name of our patients Reports every pv issue Report ADR
Shares drug safety issues with	Share with other patients to see if its common Constant contact with laboratories Notify the manufacturer Share the info with laboratory Talk to hcps to warn them of the trend In contact with pharma companies Communicate the information to nca. Contact EMA

Activities in pharmacovigilance	
Code	**Unit of Analysis**
Refers drug safety inquiries	Pv addressed in many ways by scientific members Provide the contact of pv bodies Encourage them to talk to hcps. Advise to contact the national Netherlands registry for adr We tell the patients to collaborate and talk to the doctors
Encourage reporting	Listen to patients reports, encourage to report to drs. They raise awareness on reporting on meetings Encourage reporting Explain its critical to report Encourage to report to nca Now we have an active role encouraging reporting We encourage to report all medications used to the prescriber, comply with prescription, also report to medicin national authorities Spread information on how to report through hcps on the field
Education	Publish in their magazine about ov and drug reactions Pioneer formation program Spread info on how to report. Organize activities. Tell patients what to look out Developed guidance for patient organizations on eu legislation and general message about the importance of reporting Talk about pv in national and local meetings Organize activities about treatments and talk about their side effects Occasional seminars and lectures An important part of our education materials Gives talks about use and abuse of medicines More emphasis on patient education on pv Now we tell patients what to do in case of problems Campaigns to educate on herbal products effects and interactions. Working on information campaign, including overuse of drugs Working to update our website to help our families increase their knowledge of the topic
Services	We advise patients if they contact us Someone is available 2 hrs daily for medicine issues Made a security card with disease information It is part of every patient individual care plan We ask patients more frequently about adr Speak personally with them.

Activities in pharmacovigilance	
Code	**Unit of Analysis**
Facilitator	Direct link on their website Promote interaction with hcps and authorities, explain patients perspective Direct link on website

Information Transmission Mediums	
Code	**Unit of Analysis**
Meetings or Congresses	PV may be topic on Annual meeting Include PV in WHO, EURO, EMA, EC congresses Regular meetings with NCA
Web Based Material	Use social media to post and answer to patients Better website from NCA Banner on patient organization websites Apps for patient use. We can run an article in our magazine to raise awareness Visual or video to explain Concrete link Internet
Printed Material	Printed material Leaflet Drug inserts Hard material, books, files, case studies, annual reports Other didactic ways of information. Internet not available for everyone
Individual Communication	Personal communication Speak personally with them.
Other Means of Dissemination	More publicity from authorities. Template for patients to records meds and reactions Mail reporting steps and importance of reporting A system, that works through several groups of patients´ When cases appear they publish in newsletter

Material Characteristics	
Code	**Unit of Analysis**
Simple language	Too specialized for lay man Accessible and understandable Better drug inserts, more precise an comprehensible. Simple reporting guide Keeping in mind literacy level
Native Languages	Using easy language Members are immigrants, basic concerns. Don't speak the language Difficult to translate material, not always precise The information should be in native language
No spam	Does not want to receive alerts on other disease treatments Drug tolerance is individual, general information is not useful Not duplicated of EMA Without saturating our structure
Fast information	Early warnings Information in time

Changes After Legislation	
Code	**Unit of Analysis**
No Change	No We do not have PV activities yet. No, DPR in Luxemburg not announced No , recently form organization We don't know We doing the same job with several focus to the PV We have always focused on PV No - we have always supported reporting Norway is not a member of EU No. And We did not know is mandatory in EU Not relevant for us. Not aware of DPR to NCA Never heard of it
Interaction With NCA Increased	More intense activities now. Participation in EMA work shops Organized a seminar for patients, with experts of the Bulgarian drug agency, they explained how to report We´re more proactive facilitating this NCA opened to collaborate with patients. (Croatia) Collaboration with NCA has increased

Changes After Legislation	
Code	**Unit of Analysis**
Act as Intermediates	Passed the information to members
Visualizes Future Activities	Small steps ahead

Patient Organization Needs in PV	
Code	**Unit of Analysis**
Validation	Hard for HCPsto see patient contribute with knowledge. This is often argued as lack of resources or low budget Pharma does not want their validation Disease not taken seriously Homeopathy not taken seriously People understand side effects quickly. Authorities don't accept them Acknowledgement of ADR Validation of our experience Still see under-reporting by physicians. Stakeholders should see reports valuable. Greater willingness to deepen by the treating physicians Drs. should listen when they report ADR Patient voice should be heard. Important to listen and not dismiss Not enough valued Problem to make us hear
Encouragement	Patient empowerment is important. We must get involved. Not used by patients as it should Patients should be more involved Patient organizations need to be involved More encouragement required Patients need to be more involved Incentivize DPR Necessary to increasing awareness of the system

Patient Organization Needs in PV	
Code	**Unit of Analysis**
Wants support from external organization	Need help from bigger organization More involvement from LAREB Direct contact to NCA Get in touch with PV authorizations, to work together Wants to contact PV representatives inside the organization More cooperation with NCA Communication with the NCA Not aware of DPR to NCA Looking to get contact with government Wants to get in contact with NCA and European
Reinforcement of safety measurements	Medicine should be safe and authentic Drugs used at high doses and specific regimes, monitoring needed Drugs shouldn't affect too much quality of life.

Information Requested	
Code	**Unit of Analysis**
Not PV Related	Interactions with natural products why and how to report results of studies Drug interaction effects. Safety and gender medicine Information about new drugs for their disease Information accessible and understandable about clinical trials Pharmacology information and interactions Effectiveness quick notes, different drug comparison Receive information about drugs used for prostate cancer Adherence and sensitivity on disable patients Information on allergic reactions to drugs, including excipients Inform in the correct use of drugs
Focused Information	Side effect of drugs for epilepsy Information about drug use and side effects Information that hearing loss is a high risk from any kind of drug Needs to know what side effects are to be able to report. Overview of potential side effects Other drugs that could cause hearing loss Information about possible side effects Side effects of drug presented by disease, or individual reactions ADR on short and long term

Information Requested	
Code	**Unit of Analysis**
PV System	Updates on reporting process(es) How to report International guides about how to report. Online reporting system Where people report to Insight in what is being done with the reports of patients To know data process How/ who to report to No idea of how to report.
Understanding PV	What is (PV) How to get involved, how to report and its importance Need to know and communicate impact of ADR Information on the whole PV area Share best experiences on how reporting can make changes Information on how other countries are doing on PV. Information about gaps or barriers. Further evidence of benefits Information material in general. Information for awareness. Information about examples.make a better serious side effect handling Importance of PV involvement Other countries reporting cases Instructions about what to do when ADR appear Best practices by country. Examples Inform patients role importance Risks of reporting name of NCA. EMA alerts Most basic info Training to educate patients

Reasons for not Supporting Pharmacovigilance	
Code	**Unit of Analysis**
Small or new organization	Little and new organization Very small organization Recently established organization

Reasons for not Supporting Pharmacovigilance	
Code	**Unit of Analysis**
No priority	Little or no priority Few patients contact them about it There is a national mobile app for reporting and we promote it on the website We report but there are not many cases Focus is overcoming the impact of disease. Not many requests for help by patients Not all patients experience the side effects. Side effects are well publicized Focus on non pharmacological intervention Efficacy is more important Disease not treated pharmacologically Minimal side effects for treatment. Patients ask for other types of help No need Only support group Different focus Little importance If a problem that affects Quality of life appears, we will react We have always reported but this is not our main focus Patients don't contact us directly This has not yet happened Sessions are more informative, not decisive
Lack of skilled human resources	Don´t have the knowledge Lack of human resources Difficult to have skilled volunteers. Lack of scientific training Too specialized for lay man
Doesn't know the PV System	Don´t know what to communicate Never asked to do PV DPR system not yet available in Luxemburg. Not informed of the contact No change. Did not know it is mandatory Not aware of DPR to NCA Time costly activity. Bureaucracy.
Lack of resources	Low budget Financial resources Reduced resources Don't have the means Limited structure Want to start. Don't have an action plan. Don't have resources They can only forward info to other organizations and patients. No other means to influence

Reasons for not Supporting Pharmacovigilance	
Code	**Unit of Analysis**
Someone else responsibility	It´s a cross disease umbrella, don´t have the capacity to do intensive monitoring PV is responsibility of hcps. They provide information to authorities Refer patient to the Drs. Not responsible for medication used. That's others' responsibility. Global organization, hard to interact with patients in their own languages, we direct them to national societies We direct patient to healthcare provider or pharma company All in hands of doctors German authorities are responsible for safety issues
Patient not suitable for PV activities	Important to maintain patients informed Patients informed on what to look out for can contribute greatly to PV reports Patients must be educated. Patient needs to have knowledge to be objective Problematic if patient is not educated

Apex 4.

Interview Invitation Email

Dear Madam, Sir at (organization name)

Last year, your organization participated in a survey regarding "The role of European patient organizations in pharmacovigilance" the information gathered in the survey led to the publication with the same name. This publication is also available as an attachment in this email.

In that same survey your organization stated that would like to participate in an in depth interview regarding this subject. After going through the answers you provided back then, we found that your opinion is very interesting and very enriching to understand this topic.

Lareb as the Pharmacovigilance Centre in the Netherlands and WHO collaborating Centre for Pharmacovigilance in Education and Patient Reporting is currently investigating the barriers patients organizations face towards promoting pharmacovigilance as well as the strategies that could be useful in breaking such barriers.

We would like to formally invite you to participate in this interview.
The interview contains questions orientated to understand all the activities patient organizations perform to promote drug safety, as well as the barriers they face in this process. The information provided will be used to write a scientific article and to help improve the communication process between patient organizations and National Competent Authorities.

The researchers will handle your data confidentially, you can find more information in the "Confidentiality Details" attachment. The interview will last a maximum of 1 hour.

Currently we have availability for the interview on Tuesday 26th, Wednesday 27th or Thursday 28th of February, at the time of your convenience. If this schedule does not adjust to your possibilities, we can also check for other dates.

You can confirm your participation by replaying to this email (k.chinchilla@lareb.nl). If you cannot participate, we would appreciate if any other member of your organization that is also aware of this topic could be invited, you can forward this email to them.

If you decide not to participate in the research, we would also like to hear that. Could you also indicate in your response why you are refraining from participating?

If you want additional information after reading this letter, you can send an e-mail to info@lareb.nl to Dr. F.P.A.M. van Hunsel or to K. Chinchilla. You can also call Lareb (073-6469700) and ask for one of the above persons.

With best regards,

Dra. Florence van Hunsel and Katherine Chinchilla

Apex 5

Confidentiality Details

Confidentiality Details
Research of Patient Organization Role in Pharmacovigilance

'S-Hertogenbosch, February, 2019

Dear Madam, Sir,

Among people who participated in a previous survey, on the role of patient organizations in pharmacovigilance, we have selected respondents that we would like to include in a follow-up study consisting of an interview.
You are among the respondents who previously agreed to be contacted for follow-up information and which we have selected because we think we can learn more from your experience. Researcher Katherine Chinchilla would therefore like to talk to you.

What does participation in this research involve?

The research consists of an interview.
The researcher sets up a tele or video conference after confirming with you for a convenient date and time. After confirmation, you will receive an email with a link to enter the tele or video conference at the interview date.
On the basis of an interview guide you will be asked about your organizations' activities in drug safety and the barriers you have found in the path to getting involved in pharmacovigilance.
The interview guide will be shared with you in advance.

The interview will be held in English and will last a maximum of one hour. Each interview will be recorded for later transcription into text.

Confidentiality of the data

The researchers will treat your data confidentially. After transcription, the interview will be 'anonymized', this means that the researchers will delete your name and the tapes on which the call was recorded will be stored in accordance with privacy regulations of the EU.

The interviews will be used to write a scientific article and to shed more light on the changes and barriers to involve patient organizations in pharmacovigilance.

Voluntary participation

Participation in this study is voluntary. You can and may stop at any time during the interview.

Informed consent

If you decide to participate in this study, before the meeting takes place, the researcher will inquire whether any questions regarding the study and the confidentiality have arisen. With your verbal approval you can confirm the intention to cooperate with the investigation and the researcher confirms that he has informed you well. Even after verbal agreement you can stop whenever you want.

Information

If after reading this letter you still have questions and want to receive additional information, you can always contact the researchers by sending an e-mail to info@lareb.nl to Dr. F.P.A.M. van Hunsel or K. Chinchilla. You can also call Lareb (073-6469700) and ask for one of the researchers.

Thank you for reading this letter.

With best regards,

Dr. Florence van Hunsel & Katherine Chinchilla

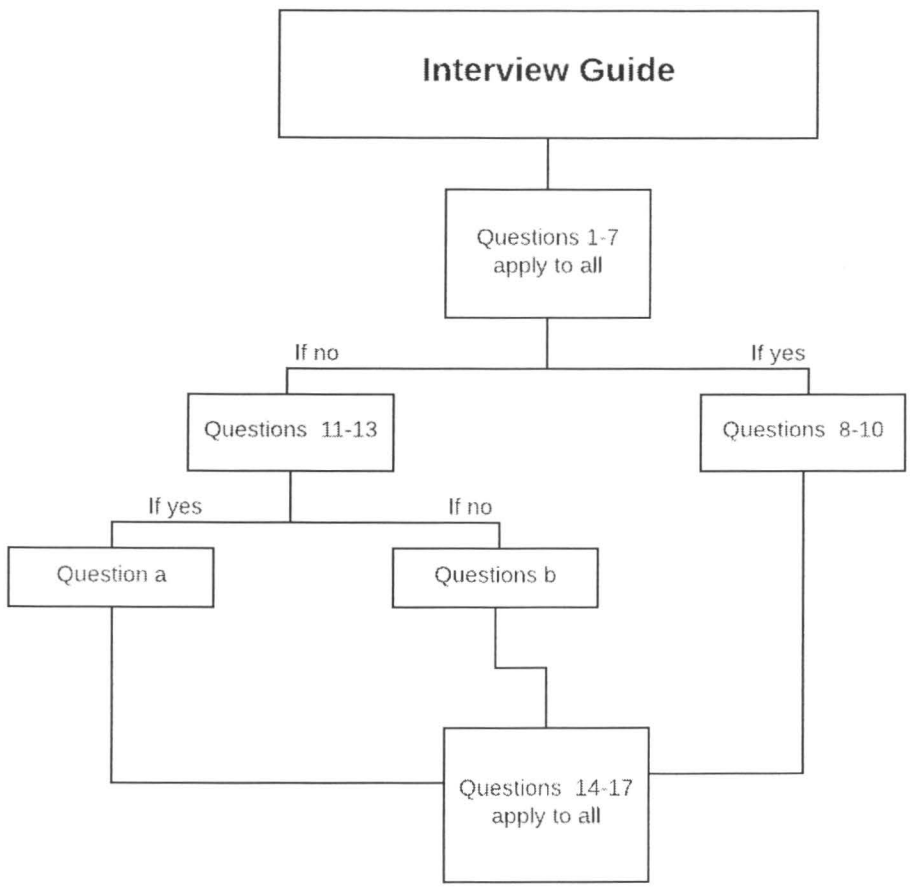
Apex 6.

Interview guides

Interview Guide #1

The interview starts with an introduction, that includes the name of the interviewer, the name of the organization supporting the research and a brief description of the objective and purpose of the study. (Should not take more than 3 minutes)

The questionnaire contains 16 questions that are applied following the scheme below:



Questions

1. **Confirmation of Organization name.**

2. **What is your name and your position at the Organization?** (In case the name of interviewee is not available before)

3. **What do you think about patient involvement in PV?**
   Help text: should patients be part of PV and drug safety?

4. **What do you think is the contribution of patient reports of adverse drug reactions to pharmacovigilance?**
   Help text: Do patients contribute in any way when they report reactions?

5. **Do you consider Patient Organizations have an important role in promoting drug safety and PV? Please explain your opinion**
   Help text: Do you think patient organizations actually can take a role in promoting drug safety?

6. **What should be the relationship between national/regional organizations and umbrella-like organizations in PV activities?**
   Help Text: Should they work together or PV activities should be managed only by umbrella or national organizations?

7. **Does your organization actively promote or support patients in pharmacovigilance activities? Does your organization have any activities related to Pharmacovigilance? <u>If yes, please explain</u>**
   Help text: What type of work do you do with your members, what exactly you do in this field, how do you do it?

If the answer to question 7 is positive and the interviewee states activities, continue with questions 8-10

8. **Does your organization promote reporting of adverse drug reactions among member ? How do you do it?**

Note: They may have already mentioned all details on question 7. Then it's not necessary to ask again.

9. **Did you find any barriers in the process of getting involved with pharmacovigilance? Which ones?**
   Help text: was getting involved in PV difficult?

10. **How did you work out this barriers to achieve the level of involvement that you have right now? What solutions you found that helped you break the barriers?**

If the answer to question 7 is negative, continue with questions 11-13.

11. **In case there is an emerging drug safety issue, and your members come to you with inquieres on it, What do you do? (long pause) Where do you look for reliable information?**

12. **And if your patients/members reports to your organization that there is a drug safety issue with medicines . Do you communicate this information to whom?**
    Help text: National patient organizations or umbrella organization, or you share information directly with patients? Inform authorities?

13. **Have you ever consider to involve your members more actively in PV? Please explain**

If yes, to question 13, continue with question a) and if the answer is negative, continue with question b)

a) **What are the barriers your organization faces at supporting pharmacovigilance activities or to be involved in pharmacovigilance?**

b) **If you don't see a role in supporting pharmacovigilance; why not? Are there possibilities for future involvement in Pharmacovigilance?**

To all participants, ask questions 14-16

14. **How did you and your organization find out about PV? When was this first contact?**

15. **How is your relationship with PV National Competent Authorities ? How often they contact you for any PV related matter and how often do you contact them for this as well?**

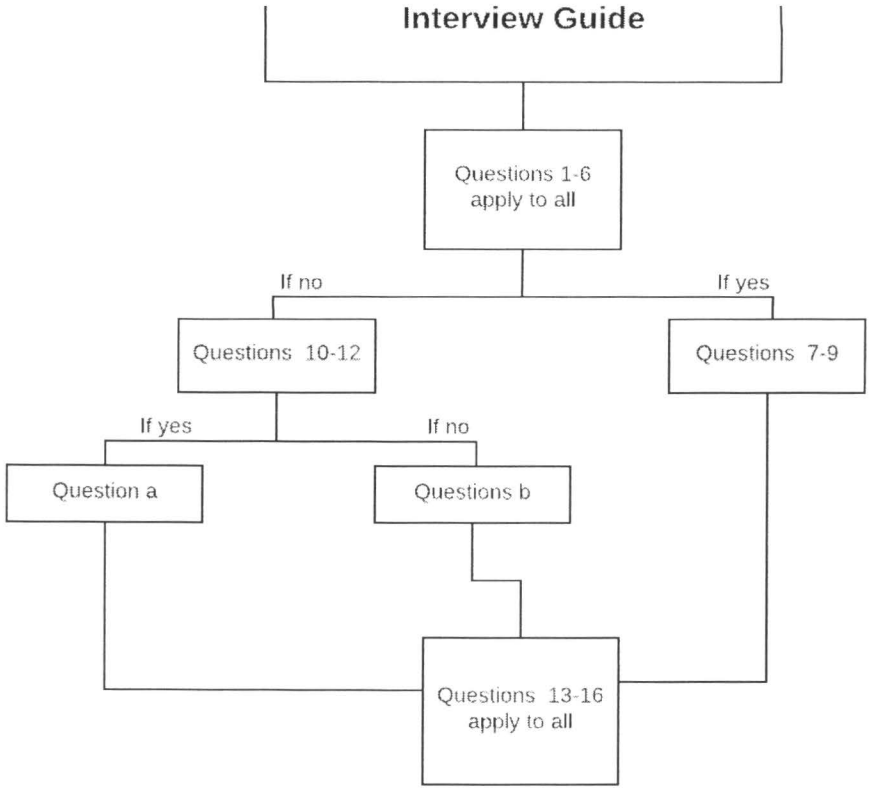
16. **What strategies could help to strengthen the communication between POs and NCA?**

17. **What information you need/or could be useful to spread among patients about ?pharmacovigilance and patient reporting? If you received it from NCA?**

Interview Guide 2

The interview starts with an introduction, that includes the name of the interviewer, the name of the organization supporting the research and a brief description of the objective and purpose of the study. (Should not take more than 3 minutes)

The questionnaire contains 16 questions that are applied following scheme shown below :



Questions:

1. **Confirmation of Organization name and position at the organization**
2. **What do you think about patient involvement in PV?**
   Help text: should patients be part of PV and drug safety?

3. **What do you think is the contribution of patient reports of adverse drug reactions to pharmacovigilance?**
   Help text: Do patients contribute in any way when they report reactions?

4. **Do you consider Patient Organizations have an important role in promoting drug safety and PV? Please explain your opinion**
   Help text: Do you think patient organizations actually can take a role in promoting drug safety?

5. **How should umbrella and regional/national organizations work together in pharmacovigilance matters?**

   * Being national/regional the ones in contact with patients and umbrella the ones in contact with other organizations.

   Help Text: Should they perform the same activities? should pv be managed only by umbrella or only by national organizations?

6. **How does your organization approach drug safety topic with your members? What activities do you do in this matter?**

   Help text: For example inform patients about ADRs of their common medication? how do you do it? What other type of activities you perform?

If the answer to question 7 is positive and the interviewee states activities, continue with questions 7-9

7. **Does your organization promote reporting of adverse drug reactions among member ? How do you do it?**

8. **Did you find any barriers or obstacles in the process of implementing pharmacovigilance activities? Which ones?**

   Help text: was getting involved in PV difficult? why?

9. **How did you work out these barriers to achieve the level of involvement that you have right now? What solutions you found that helped you break the barriers?**

If the answer to question 7 is negative, continue with questions 10-12.

10. **Using this example: You see on media that a medicine your group of patients could be using cause some specific side effect you were not aware before, what do you do in that case and where do you look for reliable information?**

11. **If multiple patients/members tell you that they think they are having a side effect from their medicines, what do you do? Do you communicate this information to whom?**

    Help text: National patient organizations or umbrella organization, or you share information directly with patients? Inform authorities?

12. **Have you thought about involving your organization more actively in PV? Please explain**

If yes, to question 12, continue with question a) and if the answer is negative, continue with question b)

a) **What is the reason why your organization has not yet gotten involved in pharmacovigilance activities?**
Help text: What are the barriers or obstacles you have found to get active in PV?

b) **If you don't see a role in supporting pharmacovigilance; why not? Are there possibilities for future involvement in Pharmacovigilance?**

To all participants, ask questions 13-15

13. **How is your relationship with *PV* National Competent Authorities ? How often they contact you for any PV related matter and how often do you contact them for this as well?**
Help text: Specifically authorities in PV, do you know who to contact there, do you contact them often do they send any information to you? Is contact only by email or phone or has it been direct (one on one) contact?

14. **Has your organization ever had any training or any other type of education to understand PV? who gave you the training? Is staff aware of this topic?**

15. **What strategies could help strengthen the communication between POs and NCA?**
Help text: What would be the best way of communicating patient organizations and NCA in PV?

16. **In case that patient organizations needed a "pharmacovigilance starter kit", some toolkit to fully understand pharmacovigilance, what do you think that kit should include?**
Help text: What do you think is necessary to explain about pharmacovigilance so that patient organizations understand it?

Interview Guide #3

1. **Confirmation of Organization name and position at the organization**
2. **What do you think about patient involvement in PV?**
   Help text: should patients be part of PV and drug safety?

3. **How do you think patients can contribute to drug safety? How can the patient contribute to the public safe use of drugs?** Help text: Do patients contribute in any way when they report reactions?

4. **Do you consider Patient Organizations can contribute in promoting drug safety and PV? Please explain your opinion**
   Help text: Do you think patient organizations have a **position** to promote drug safety?

5. **Has your organization ever had any training or any other type of education to understand PV? who gave you the training? Is staff aware of this topic?**
6. **Does your organization has any activity to promote drug safety and PV among members?**

If the answer to question 6 is negative, continue with questions 7 and 8, if it is positive, jump to question 9

7. **Using this example: You see on media that a medicine your group of patients could be using cause some specific side effect you were not aware before, what do you do in that case and where do you look for reliable information?**

8. **If multiple patients/members tell you that they think they are having a side effect from their medicines, what do you do? Do you communicate this information to whom?**

Help text: National patient organizations or umbrella organization, or you share information directly with patients? Inform authorities.

9. **How is your relationship with other stakeholders in PV ? How is the communication with the Industry, NCA , HCP's and other POs like umbrella organizations ?**

10. What strategies could help strengthen the communication between POs and those stakeholders in PV?

Help text: What would be the best way of communication between them?

Apex 7

Tree coding excerpts generated from Grounded Theory Methodology

Activities and Role	
Activities in pharmacovigilance	
Connecting patients with other stakeholders	
Excerpt	Interview number
Very often we refer them back to local members, so if somebody comes from Djibouti and asks something about some issue, we refer them to Djibouti contact, so it's almost having your agents on the ground, make sure your chances are that organization when we may have some capacity building,	Interview 5
-You know usually the process in Germany is the following, you tell the Dr you're attending at the hospital or wherever about the side effect, because he has to treat you, he has to be aware of what is going on with you when you are under treatment, or even afterwards. So and they are supposed to report to the Authorities. At least they should. Or maybe only to the pharma	Interview 8
I would suggest that.. how do you say.. the patients to tell also the Drs .	Interview 8
I'd also ask the person to go back to the hospital or the doctor or whoever and mention this. When I mentioned also to you that the website "hearing trouble" - I'd also send them that link with references, so that they can say this back to the hospital or Drs or whatever they have been.	Interview 1
Oh, in my organization, sufferers contact organizing meetings in hospitals about 7 or 8 times a year, every few years were organizing a symposium, very big, crowded, last time we had 550, in2016, now we are expecting 700, we're also in contact with other PO, with health insurance, with hospital, involved in networks like ERN , European Reference network for rare diseases, also in my case, I'm going a few times abroad to visit Medical Congresses and also congresses for patients, organized by EURORDIS	Interview 13
Well I actually am the member of committee for safety of drugs in HALMED as a patient representative and I'm also the member of the central committee for clinical trials and with other stakeholders so we have very good collaboration with a few Dr organizations, especially in oncology and gastroenterology and rheumatology	Interview 15
So, for example, if I received this notification at the organization, I would have to link him through his prescribing doctor or the pharmacist who gave him the drug.	Interview 2
One is the invitation to inform the prescribing doctor, the other is to inform the pharmacist who dispensed the medication and the third way is an email to the Spanish Medicine Agency In other words, these are the three official communications means a patient must carry out in order to register this adverse effect.	Interview 2

Activities and Role	
Activities in pharmacovigilance	
Connecting patients with other stakeholders	
Excerpt	Interview number
I would recommend them to contact the doctor or pharmacist, we could make a communication to the Spanish Medicine Agency for the patient, collecting their information, because they definitely will have to contact the patient for more detail.	Interview 2
if that person is not feeling well or describes the side effects we may recommend to her to check, to consult a second doctor to have a second view on the medications, or to go back to her first Dr and insist that this is happening and he would propose maybe some changes	Interview 6
I think I would tell them to go back to their Drs to say through him, because I'm not a medical person so I cannot exclude maybe other side effects from other things,	Interview 6
and we would also assign person to go back to their pharmaceutical company, to ask the questions as well.	Interview 4
And a different, a third role is for instance, we have a situation now in Portugal, about biosimilars, some I don't know how it is now but in the beginning there was this issue because hospitals were switching from originals to biosomilars without informing the patient correctly and one of the roles of POs was to make the hospitals and the stakeholders around biosimilars aware of the need to inform patients of what is the drug they are taking	Interview 14
Another role of POs I'd say is to make the other stakeholders aware of the need of the patients when there is a switch on the medication, I would say biosimilars but we could also mention generics	Interview 14
we advise ppl to talk to the Drs, we advise to report to them every drug and supplements also, they may have, most ppl have supplements and natural products that can also interact with drugs and they don't report that to the Drs, so we also try to promote that communication	Interview 14

Activities and Role	
Activities in pharmacovigilance	
Develop informative material	
Excerpt	Interview number
we have one first .. they changed the system how to do it and we did in the new drug for prostate cancer we overviewed the patient information, that is the first thing we made from our organization and I think we should be involved more in the development of medicine	Interview 16
-The role of POs I think is creating awareness for PV, that is the most important, already we have our patient magazine of January, Lareb wrote an article, and we created some space talking about the need and benefits of reporting side effects and hoping that patients are able to find their way to Lareb	Interview 13

Activities and Role	
Activities in pharmacovigilance	
Develop informative material	
Excerpt	Interview number
-We usually participate in the creation of these materials, we reach agreements with administrative bodies or with professional organizations and we elaborate it together. Let's see ... we have a very limited budget, very small so we cannot afford to make the materials ourselves, but we do participate in those that do and this is usually or the Ministry or the National School of Health. The latter especially and we co-participate in the use of appropriate language and then in its dissemination	Interview 2
and then being involved with the regulatory agencies, patient involve could help out the way of designing the system, because, ok each one of us is a patient, the person who report of drug adverse effects, so each one of the ppl that are sitting in the regulatory agencies are also ppl that can report on the system so they don't experience to design the system but if you take someone who is absolutely out of the system , that is always helpful in designing the system, what I'm saying that patient involvement should describe the PV system, until the end of it, because the PO bring a different perspective of discussion.	Interview 7
When that was provided to infants with SMA type 1 through what was called expanded access program, so it had very (inaudible) in the UK. At the time that was happening, we worked with medical consultants to produce a medical information sheet for families, because we were aware that some maybe getting good information about it through the medical team but we couldn't be sure that was happening across the country so we produced an information sheet. In that sheet we reproduced what the pharmaceutical companies said about possible side effects, and we reproduced that. I'm very happy to send that one to you to show you what we did, it was signed up, as I said, by the medical consultant leading the administration of that treatment and we had that available in our website. It was very important because it was explaining things in lay terms to families who are maybe thinking about that treatment, like an alert "we are aware of this symptoms, you need to be aware of this possibilities, so it's the same function, providing, being another way of providing families with information making sure they are fully informed before they get the treatment and know what to expect.	Interview 4
At the time that was happening, we worked with medical consultants to produce a medical information sheet for families, because we were aware that some maybe getting good information about it through the medical team but we couldn't be sure that was happening across the country so we produced an information sheet.	Interview 4
So we produced summaries of what the researches actually showing about the drug and it's possible that side effects are being shown, I'm not sure. But that is the only time we've been involved in anything to do with monitoring drugs,	Interview 4

Activities and Role	
Activities in pharmacovigilance	
Participation in Legislation	
Excerpt	Interview number
but where patient organization coming there to support the advocacy, then chances are that they can get that recognized in the system	Interview 5
who then have also patient organizations can influence the PV legislation needed, they can lobby parliament and that but the most important one is really to influence the practice and guidelines that they use, and PO can be really big there and change the standards, so that kind of institutions legislation... policy practice and standards is where they can fit in	Interview 5
So yes, in the PV system, the PO has 2 roles, going up the line, meaning to try going up to the regulators,	Interview 5
en second is we are assaying make sure this is part of the national policies, make sure it is implemented and more importantly, it is evaluated annually, make sure the Health of the system PV should be tested and once a year, even after every 3 years tests need to be done, is it working is it not?	Interview 5
-We rely on the NCA to present some of the guidelines and that, so we sign post it, ppl always ask to take the (inaudible) and look at local procedures because as you know PV systems may differ from country to country. it's very important that they use a local one and make sure they are familiar with that and sure that only we can suggest what the structure is like but we cannot dictate how that is actually being implemented.	Interview 5
On top of that I'm active in the European Reference Network on rare endocrine patients, Europe has 24 ERNs and 24 different health areas liver, heart lung but also endocrine, that is pituitary, adrenal and thyroid, that is my part, I'm in the Steering committee of the pituitary illness and also in work package for research and science. Also I'm involved in a project for creating European endocrine registry, it's also very interesting	Interview 13
Together with academic hospitals we are working on writing research proposals but also with one big proposal, looking at the effects of medicine, dopamine agonist vs. operation, what is better for the patient,	Interview 13
Well I actually am the member of committee for safety of drugs in HALMED as a patient representative and I'm also the member of the central committee for clinical trials and with other stakeholders so we have very good collaboration with a few Dr organizations, especially in oncology and gastroenterology and rheumatology	Interview 15
But there is another role ofc in PV. That's the role of patient representative like I was for many years, a member of the PRAC, and I was at the board with Lareb and that is as important because we know there is a difference between the regulatory practice where you come to decisions on statistical basis about generalities for patients that in clinical practice you have to do with one patient and one doctor who have to decide about the benefits on that particular patient. And to bridge that gap between these 2 realities. It's very important that you have patients who are informing and that are also being informed in the decision making process together with the regulators	Interview 3

Activities and Role	
Activities in pharmacovigilance	
Participation in Legislation	
Excerpt	Interview number
On the other hand also the associations and not only towards the patients but towards the administrations and towards the professionals, we must invite them to look for all these adverse effects	Interview 2
We are involved in the producing a family friendly version of the international standards of care for SMA and they have been produced by international experts and in that they discuss drugs that are maybe used to help manage SMA so get involved making sure that ppl understand what is written from academic articles into the family guide so that ppl understand what they're saying about this drugs, but whether or not this is PV, I don't know	Interview 4.

Activities and Role	
Activities in pharmacovigilance	
Encourage Reporting	
Excerpt	Interview number
just yesterday, I had a patient that was complaining about the side effect of certain medicine, the medicine changed from package forms, from a little sachet to a pumping system and he was complaining some side effect and I sent the patient to the Lareb website, asking for him to use the document, report the side effect	Interview 13
they are complaining about the side effects and then again, we want to let them know that there is a Lareb and they can report it on the website of Lareb, but I don't think, for a lot of patients it's difficult, it's scare to make a report on the Lareb website	Interview 13
levotiroxine medicine that is changing its recipe, starting the 1st of June so we are expecting a lot of ppl asking about it, but we are having it since summer 2018, so we are prepared, you see ppl are afraid because they know there were other cases of problems with the same type of medicine so we are expecting ppl. And what we will say and we will also publish in our newsletter is when they have side effects, please go to the Lareb website and make the report of it. And that is also what our medical information board is saying that ppl should do And also the pharmaceutical companies	Interview 13

Activities and Role	
Activities in pharmacovigilance	
Encourage Reporting	
Excerpt	Interview number
How can we develop this communication strategies on importance for PV, and how important it is for every patient to report if they come cross some adverse event or they are unsure or they are perhaps frightened	Interview 15
Reporting is based on the personal level rather at the (inaudible) level because each one of them sends a report of a drug adverse effect so there are a couple of things that PO could do, ofc promoting the online portal is one thing for instance,	Interview 7
so basically on our web page we have on the home page we have the link to HELMED, to allow patients to report any side effect, any sort of unusual reaction to treatment, this are quite severe treatment	Interview 11
Let's say on my web, we have direct access, in the bottom you can see a big banner to go into HELMED and invites patients to do	Interview 11
other role is helping ppl to report, but as I mentioned before we were never ever contact by anyone asking us for help around this so , this could also be a role that POs could have, if someone wants to report, since the system may not be that much user friendly we could help, teach them how to do it but we were never contact but this could be another role.	Interview 14

Activities and Role	
Activities in pharmacovigilance	
Patient Education	
Excerpt	Interview number
-Yes we always keen on that, I mean we had a global patient congress where we invited "fight the fakes" campaign to come in and talk about what are the part of a quick PV system, what our responsibilities are, who should act, who should react, when to react and this kind of things that feedback into their own national level, in fact we kind of created a situation where we tried to open a window of opportunity for this ppl to get good PV system and	Interview 5

Activities and Role	
Activities in pharmacovigilance	
Patient Education	
Excerpt	Interview number
-Yes, that is what the anchor point is because with self-care you also looking at your dosing and that, so I think, don't quote me on that but I would say but I would say 90% of ppl have been avoiding self-care. It takes more time to read the dosage, make sure you challenge the pharmacist sometimes, you know the doctors I mean, (inaudible) where you can actually the patient is having a product that is only like 4mm tablet and then they give them 1cm tablet yeah? -yes, different amount -yes, self-care clearly requires you to ask and inquire behind it, not just swallow it, say "why is this?" and then you read the label again and find out things.	Interview 5
-But this questionnaire you are talking about to send to members, what should it be about, a questionnaire regarding what? -Regarding the drugs, somebody has to take and then how they feel in the morning in the evening, what they are feeling for side effect and so on. You have to ask about the drug the patient has to take.	Interview 8
And to make a diary -oh to keep a diary?! -So they can really fix there the problem -What do you mean with the diary? Like to write down the problem? The side effect? -Yes, not only the side effect… how they feel on each day, it's a good day it's a bad day, what is happening and so on	Interview 8
-The role of POs I think is creating awareness for PV, that is the most important, already we have our patient magazine of January, Gerda wrote an article, and we created some space talking about the need and benefits of reporting side effects and hoping that patients are able to find their way to Lareb	Interview 13
but I think that is actually the role of PO should be the education of patients about the life cycle of medicines and reporting any adverse events and drug safety	Interview 15
this is also the area that we always educate ppl that they should actually monitor what is going on with them during the treatment, that they should report adverse events and they should actually consult their doctors because perhaps they can moderate the therapy so you would have less adverse events or perhaps you can have some treatment for the adverse event, because it has cases where ppl just drop off their therapy because they didn't want to go through all that	Interview 15

Activities and Role	
Activities in pharmacovigilance	
Patient Education	
Excerpt	Interview number
-Yes, actually we have a couple of education for member organizations, for instance for the biological and biosimilar medicines, what's the different and how is it safe and not safe and in what frequencies they can accept to go from one to another so, this is one and I think it was very successful and now we are doing the education on immunotherapy	Interview 15
Then patient organizations, we must show patients that you cannot know a drug in any detail, when newly marketed and we can also contribute to the knowledge of that drug by notifying the adverse effects, of which the prescriber is not the responsible for it.	Interview 2
First of all, we have to inform and train the patient organizations that are part of our coalition so that they, in turn, urge patients to report any adverse effects they may have.	Interview 2
I think there is information needed for example knowing that epilepsy drug some affect during pregnancy, so it's important to us to inform for example parents of young girl when they are over 20 year old, start discussing with their doctor for medication changes in the future, not rapid changes, just having it in mind.	Interview 6
we have warned or we trained on the most common side effects on the novel drugs	Interview 9
we do a lot of what is continuous education and that also part of safety or quality of life measurements and it started in our main forum but is now spreading so other forums are adapting it and we encourage ppl to be members of different forums because that is the way how you effectively spread information across Europe	Interview 9
-I mean for me I wouldn't say it has not called attention, so I regularly invite someone from the UMC, I'm here and we have visited the center because our annual workshop is in, here not far from Uppsala, so we've been there, we've had speakers, we try to make PV as a topic in our conferences so we try to have it, not every time but there is usually a topic either about side effects or someone from the local authority, we invite them as speakers and I think the personal contact is really really important and I think my Dutch colleagues have done that as well because I met Florence at one of our events and then ofc in Dutch and so ofc you have a connection	Interview 9
-In fact I think the PO activities in that aspect are very scarce, meaning that ofc we at (international federation) we have some activities that are the annual meeting, the annual meeting is based on talks and then the workshops and so we had some workshops on drug safety, but then that was only for a small group of ppl and ofc, so as long as are not any measure activities regarding drug safety (inaudible) for instance we re-tweet, what the European medicines agencies, re-tweet for instance put on the twitter page the key message.	Interview 7

Activities and Role	
Activities in pharmacovigilance	
Patient Education	
Excerpt	Interview number
-Ok, promoting the system is essential and then drug safety is very vast topic ofc, so what is drug safety? overall drug safety is we need to take a medicine, whatever a medicine can be and you need to be careful, you need to take all the proper care to not get an over dose, to get the proper dose of medicine, so promoting this, we can, it depends if it's a global organization or a national organization,	Interview 7
Ok, because what I'm saying was pretty much based on the reporting system but not on drug safety itself because in that aspect the national organization can be quite active as well, for instance promoting among the members not to buy medicines online, stuff like that. There are some activities in this aspect as well.	Interview 7
when … that was provided to infants with SMA type 1 through what was called expanded access program, so it had very (inaudible) in the UK. At the time that was happening, we worked with medical consultants to produce a medical information sheet for families, because we were aware that some maybe getting good information about it through the medical team but we couldn't be sure that was happening across the country so we produced an information sheet. In that sheet we reproduced what the pharmaceutical companies said about possible side effects, and we reproduced that. I'm very happy to send that one to you to show you what we did, it was signed up, as I said, by the medical consultant leading the administration of that treatment and we had that available in our website. It was very important because it was explaining things in lay terms to families who are maybe thinking about that treatment, like an alert "we are aware of this symptoms, you need to be aware of this possibilities, so it's the same function, providing, being another way of providing families with information making sure they are fully informed before they get the treatment and know what to expect.	Interview 4
-Well, yes, yes, because PO has some role, depends on what their mission is actually, depends on what they choose their activities should be. For my organization, a lot of organizations are known in Europe...part of supporting patients is educating them so in this educating you can as a patient organization you should really always encourage patients to report any adverse effects	Interview 11
-At education events we always talk about drug safety, how you should use it. When we talk to our patients if there are sort of unusual side effects of things, we encourage them to report it . We have at our education meetings we always have the leaflet from HALMED that talks about it. They have a little sort of leaflet which we give away to patients and say you can report any unusual side effect.	Interview 11
Yes, at least in my organization what we are trying to do we try to inform pl that they should be aware of any suspicious event and then they should report it, how to report and to whom to report adverse events	Interview 14

Activities and Role	
Activities in pharmacovigilance	
Patient Education	
Excerpt	Interview number
So we try to once in a while, I think every year we at least publish in our newsletter something about how to report adverse reactions with the national authority of medicine and the Ministry of agriculture both situation, this could be one role I think for POs to make ppl aware to whom to report any suspicious reaction	Interview 14
in our newsletter, at least once in every 3 months , once a year in one of the numbers, the printed copies are free and they are also available online so at least once in a year we publish how to report side effects and something around the importance of reporting side effects , this is one thing we do every year and last year for instance we had our annual event, every year we have our annual event, we call it forum of support for the ppl with rheumatic diseases	Interview 14
we had a speaker a professor in pharmacy talking about the online purchase of medicines for instance, and we also published in our newsletter the need to be aware of the issues around safety when you are buying medicines online	Interview 14

Activities and Role	
Activities in pharmacovigilance	
Transmission of Information	
Excerpt	Interview number
this is communication coming down the other side, so we have disseminating this, especially if you are a simple small organization, that organization knows everybody . It's pointless to get to national media to get to this particular group of patients when all you need to do is ring up the communication offices for that organization and let them know what is happening, if there is a new guideline on the (inaudible) So yes we have both together, up and down to represent.	Interview 5
-Yes, actually we do both, with the side effects. We are taking a lot of information coming up from ISPMA and global regulators and sending that out to members to look at the innovative part, especially where to look for the badge number, where to do with the report, that sort of things. On the other side we are taking information up, so it's like what we are doing is really putting firstly evidence of patients perspectives into practice so what are we research and evidence we are taking it and putting it back. And then we are taking what is happening in the practice level back into that research so whatever they experience matters so are putting practice back into evidence. So its evidence into practice and practice into evidence, so we are finishing that loop	Interview 5

Activities and Role	
Activities in pharmacovigilance	
Transmission of Information	
Excerpt	Interview number
what has been extremely successful in that so we blog for example from ASCO or from ESMO and then ppl blog already in different languages about it or ppl pick it up on the main forums and then translate it into their own forums	Interview 9
-In fact I think the PO activities in that aspect are very scarce, meaning that ofc we at (international federation) we have some activities that are the annual meeting, the annual meeting is based on talks and then the workshops and so we had some workshops on drug safety, but then that was only for a small group of ppl and ofc, so as long as are not any measure activities regarding drug safety (inaudible) for instance we re-tweet, what the European medicines agencies, re-tweet for instance put on the twitter page the key message.	Interview 7
we re-tweet, what the European medicines agencies, re-tweet for instance put on the twitter page the key message. What we do is only to broadcast the key message of the EMA which is good but is not enough I don't think it's enough to be frank	Interview 7
I would agree with that, I think for an organization like our own we are very very careful to always say we don't provide medical advice, this must always be through medical team. We all also see our self very much as a contact of information to the community because not everybody has a good relationship with their health professionals or keeps appointments, so it might be that they pick up information through our network but they are more interested in what we have to say. So I think you have to cover all bases to get information across the ppl and I would see ourselves as cooperating and making sure we get the information out	Interview 4
-Yes, I think we would be a conduit of information from pharmaceuticals, we would, for example we operate we have social media daily, we have a monthly e-news and we post, anything that is being posted as an notice on our website goes into that monthly e-news, and a lot of ppl from SMA community has signed up to that and reed what's in it, so that contains also some information, we would think that as the channel for information coming out from pharmaceutical companies,. If it were something extremely serious we could do a targeted communication to community so we would see ourselves as a conduit for merge information or information to say "no please do keep what you know and report to your health professional" you we'd be happy to do that, keep ppl aware but we are a small organization, we don't want the concerns coming back to us.	Interview 4
we have also the videos we filmed the whole event and we have also online in our youtube channel	Interview 14

Activities and Role	
Activities in pharmacovigilance	
Transmission of Information	
Excerpt	Interview number
-It is web based, we can print them and sometimes there is printed material. It is available online but they also communicate, they send us an email with every campaign, they are developing new campaigns they send to POs so we can disseminate, and I remember this year already they had a campaign and they even sent to POs a plan of communicating in social media so if we wanted to follow the same plan or a similar plan to have a broader audience for the campaign, they have now, they started to engage this way with the POs.	Interview 14

Activities and Role	
Activities in pharmacovigilance	
Work together with other stakeholders	
Excerpt	Interview number
We have 4 meetings as a group with umbrella organizations for patients and this group can make meetings together with Swiss Medic, that's 4 times a year -4 times a year?! how has it worked? Is it a good dynamic for you? -hahahaha It's more about information, not about involvement, and it has to be more involvement and it's became better	Interview 16
-We propose and we've proposed it to Linda Harmark, who will come to our next summer school for patients advocates in June, we propose her to come with cases, where reports from patients were useful for PV experts,	Interview 12
-Yes, for example, we are usually part of organizing committees, of congresses of professionals, of doctors for example and they always have PV in mind so we always try to have a stand that focuses on this. For example, there was this Thursday, I was part of the organizing committee of the congress and there was a stand that referred to pharmacovigilance, because it is something that we care to include it in professional congresses with the Ministry and administrations	Interview 2

Activities and Role	
Activities in pharmacovigilance	
Work together with other stakeholders	
Excerpt	Interview number
-We usually participate in the creation of these materials, we reach agreements with administrative bodies or with professional organizations and we elaborate it together...let's see ... we have a very limited budget, very small so we cannot afford to make the materials ourselves, but we do participate in those that do and this is usually or the Ministry or the National School of Health. The latter especially and we co-participate in the use of appropriate language and then in its dissemination	Interview 2
- Well we are part of different working groups with the Spanish Medicine Agency	Interview 2
-I mean for me I wouldn't say it has not called attention, so I regularly invite someone from the UMC, I'm here and we have visited the center because our annual workshop is in, here not far from Uppsala, so we've been there, we've had speakers, we try to make PV as a topic in our conferences so we try to have it, not every time but there is usually a topic either about side effects or someone from the local authority, we invite them as speakers and I think the personal contact is really really important and I think my Dutch colleagues have done that as well because I met Florence at one of our events and then ofc in Dutch and so ofc you have a connection	Interview 9
when we have patient meetings we invite ppl from HELMED, it's called, to come and say a few words because there is a bit of uncertainty of what is unusual You know what to report and what not to report, what is to be expected and what is not to be expected,	Interview 11
Yes, or as I said, in our meetings we always have banners for role up for HALMED and we always have someone from HALMED to tell them to do, to report.	Interview 11
Besides that, this are the activities towards patients and the public and sometimes I'm also invited to be a speaker in some events organized by the college of pharmacists or I remember for instance last year in December I participated in a meeting that was promoted by MEP, member of the European parliament and that was addressing also the drug safety issues and I was invited to be as a member of the PO to provide a perspective and the need of patients so this is also the other kind of activities we are in	Interview 14
They are very open, the national authority is coming closer and including more POs in their work which is very good and also help POs to understand the structure and to know to whom communicate about different aspects.	Interview 14

Role and Activities	
Arguments for not having a role	
Benefit not visible	
Excerpt	Interview number
-But it's a bit of a threshold, opening the website and giving that information and I also think it may be because patients don't see a direct effect, they have a problem; they report the problem and then what? that also what is happening with patients -me: Yeah, what happens after that report..yes -Yes, I have a problem and my problem is not resolved when I report it. I have a concrete problem at that moment, and I want a solution and maybe want another medicine that isn't available	Interview 13
One of my (inaudible) and I guess in the entire in the PV story is really that everyone want patients to report but the feedback there was no clear So when a patient comes onto my forum they can't (inaudible) report side effects, they want a solution to their problems so they say I'm having this, has anyone seen this? what do I do??	Interview 9
They are not looking to report because you report into a black hole and then you never get anything out of there, I mean the publications are not... well even a publication the timeframe is.. even if you knew where to find it, the timeframe is not attractive at all and then ppl are ofc complaining that patients don't want to report, where if there is nothing there for the patient why should they report? so our ppl are cancer patients, some of them have limited time left, and just reporting for the sake of reporting is something that we're actually not supporting anymore.	Interview 9
But.. yes it's a little bit frustrating because everyone wants the data, no one wants to give anything back to the patient who reports which is the driver for the reporting	Interview 9

Role and Activities	
Arguments for not having a role	
It is not their responsibility	
Excerpt	Interview number
the HCP is not accepting the adverse event, they try to suppress or kind of prevent any association between them and the adverse event , in many cases because it may bring legal liability	Interview 5
-No, we dont have that kind of system but we should, yes, we should but then again, that person should report this to his or her own hospital or Dr and that Dr is responsible for reporting this kind of things,	Interview 1
that drugs can damage your hearing, that is a doctors responsibility, so patient should go back to the doctor and confront the doctor for this, but this is also part of it because this is also about our rights, somebody did something to us and they actually hurt us	Interview 1

Role and Activities	
Arguments for not having a role	
It is not their responsibility	
Excerpt	Interview number
Let's see, there is a conflict here, which is not easy to explain. When a patient suffers an adverse effect, the first human tendency, is human, is to think that the person responsible was the doctor who prescribed that medication, the patient does not understand that not everything is known about the product. Then when he suffers something, he will hold the prescribing doctor responsible.	Interview 2
Because we ourselves are not experts in the pharmacology nor are we the regulatory channel for processing these claims.	Interview 2
Yes, of course, I already told you at the beginning, it is the sensation that can exist of being reproached instead of reporting, when I say a reproach, it is because someone is blamed. So here, there is a barrier ; if it is a mild adverse effect, it is not worth communicating.	Interview 2
First their doctor and maybe also some government institution where you put immediately a report to.	Interview 6
Ok, now we have seen that first of all that is good to involve patients in pharmacovigilance and also that is good, specifically you are saying like the rare and unknown side effects but what about also patient organizations, do you think patient organization in general should play a role at promoting drug safety? -Yes, but for reporting were probably not the point where other patients would report the side effect, unless this would be really part of their medication.	Interview 6
I think I would tell them to go back to their Drs to say through him, because I'm not a medical person so I cannot exclude maybe other side effects from other things,	Interview 6
I think if we would have very well trained Drs, there would be no need to have this information, then patients could really rely on their Drs to have the right treatment and to, that someone is taking care of their side effects and they would be well informed about epilepsy so we would be superfluous	Interview 6

Role and Activities	
Arguments for not having a role	
It is not their responsibility	
Excerpt	Interview number
it's very clear about where they report to any concerns, and those concerns don't come back to us because we shouldn't be dealing with that. -*hmm I'm* sorry just to understand that, you shouldn't be dealing with the reporting? -No we wouldn't want to receive the report, we would want to be clearly saying to them, this is the information we just have, please be aware of xyz, if you have any concerns..." and then we want to send them back to whoever, the pharmaceutical company is pointing as the point of communication, we wouldn't want those communication coming back to us because that is not our core business and we may not understand the report and it could get lost in translation so it would be more like a sign posting route.	Interview 4
I go and see the Dr every 6 months for a review, I see a nurse every 4 months, if this ppl are administering and are giving me the medication they know what the drug companies report and say about the medication, they are well informed, that is the system, they are doing that, theyre' charged with that responsibility , they're caring out that responsibility, they have the education and the equipment and the status and everything else, to carry out that responsibility, so I think the responsibility lies with them to be vigilant and to be aware of what the drug is actually doing. It's not up to me, I'm a humble patient it shouldn't be up to me to point out to where the shortcomings are, they should be able to see it for themselves and they should report it you know	Interview 10
o I think the responsibility does not rest with me or with my members, I think the responsibility rest with the professional ppl and with the drug companies and so on who have the information about the drug or say they they have the information about the drug and publish the information	Interview 10
The ppl who are making the drugs, prescribing the drugs, and taking care of it, they should be on their toes and they should know all of it, and they have been seeing this effects for almost 50 years, for nearly 75 years now, because this drugs came in to help the mental patients in the 1950s which is nearly 70 years ago and the effects haven't changed much over that, and the features the drug has changed is very little. They may talk about science and all that but is baloney, is still the same poison we're getting.	Interview 10

Role and Activities	
Arguments for not having a role	
Knowing side effects is frightening	
Excerpt	Interview number
And there is one problem I'm not sure how to deal with it, this is : should you really study all lay down side effects from pharma you know what I mean? -No, please explain a little bit -In Germany if you have a drug prescription, you usually have, you get the leaflet with how the drug works and da dararada dada-dada and also for side effects. If you really study this leaflet you would say "I will never take this drug" you know what I mean? -Ah hmjhmjh its scary, frightens ppl? -Yes, yes yes, even myself I'm not .. yesterday they started a new immunotherapy for me and only if I feel that I'm having a side effect, some side effect I would have a look at the leaflet, if this is possible or not but not in advance You know what I mean? And you know why I do this? -Tell me why -Ahhh if you are very much aware of the 20 or 30 side effects they have written down, so you certainly you always afraid, you are always… in Germany we say you are looking and hearing inside yourself if something is happening and so on. You know I don't know what is a better way to know everything in advance or to be just very aware of… to look at what is happening -So you think that maybe if you see from the beginning that a side effect is .. I don't know rash, then you are more prone or more likely to have a rash because you read it? -Yes, I know many patients, yes	Interview 8
because sometimes also patients are afraid about the side effects they read on the leaflet, so (inaudible) most of the leaflet is not that they have to get them but it's about to inform them	Interview 6
When you look at the drug information , you now the patient information... there is a specific name in English ..so the information gives you a lot of expected side effects.. Which is quite off-putting for patients but at the same time they think.. oh well that is expected, I don't need to report it.	Interview 11
sometimes Drs and politicians are afraid that if ppl are informed around possible side effects or to be more aware, then they should you know, something about placebo effect, nocebo effect, they can experience, but I think we have to deal with that	Interview 14
Well the list will say, the facts are quite comprehensible I mean I read on the HPRA site I read a list of the side effect of Risperdal which is the drug I am on, and is absolutely frightening to read this, and the list is 2 or 3 pages long, so why did they publish that? they are trying to help me or what	Interview 10

Role and Activities	
Arguments for not having a role	
Patient already knows about ADRs	
Excerpt	Interview number
other problem is that you have the patient information leaflet in the box and ppl see all the side effects and they think "well, I recognize all those side effects, I don't have to report anything, because it's already in the patient leaflet"	Interview 13
Claro, pero también los pacientes son expertos en su enfermedad. Ellos mismos también conocen que el uso de los fármacos les pueden producir efectos adversos. Pues ellos mismos también, desde que se les instaura un tratamiento, ya son conocedores de este asunto. O sea que en fin, yo creo que conocer la PV… yo creo q en todo el mundo la conocen. Ya sea en casos de pediatría o casos muy concretos de pacientes a lo mejor ya seniles, pero vamos! sino todo mundo es consciente de esto.	Interview 2
When you look at the drug information , you now the patient information... there is a specific name in English ..so the information gives you a lot of expected side effects.. which is quite off-putting for patients but at the same time they think.. oh well that is expected, I don't need to report it.	Interview 11
Mental patient feels in their own body, they feel the full effects of the medication, they don't need from me to point to them, they know that, you understand that, but they are buckled up	Interview 10

Role and Activities	
Arguments for not having a role	
Patients do not understand PV	
Excerpt	Interview number
-Absolutely, should the patient be involved, should the patient be part of the drug safety and OV? Should the patient report and know about it? Be more active? -I think it depends a bit form the patient. If the patient is not very educated, it would be hard for him to talk about side effects, if there is not a Dr or somebody from a health organization who can help the patient talk about side effect. I mean there are well educated and not so much educated as you know -Yes, so it's necessary first to have some sort of help for the patient to be educated? -Yes, I think so	Interview 8

Role and Activities	
Arguments for not having a role	
Patients do not understand PV	
Excerpt	Interview number
often they fear that one of the consequences of reporting the side effect is that the product could be withdrawn from the market and so they may refrain from reporting because they have been waiting for this product for so long and there are not that many options being developed, (inaudible) when they have a side effect, because they are not necessarily informed on all the other regulatory actions before withdrawing a product from the market.	Interview 12
It's quite an abstract topic and is because the way the data is analyzed and how it is collected and how ppl think about it is different from efficacy.	Interview 9
And we have also problems at the level of health literacy and so all together this makes it very difficult to do that. But I think it has improved the percentage of ppl reporting themselves has increased a little bit but still it's not that much… there is a lot of work we have done yet and they should improve the way ... it's online, it's possible to do it online but due to our levels of literacies or health literacy, it may not be very easy for everyone to report and POs can have a role here	Interview 14

Role and Activities	
Arguments for not having a role	
PV is not for everybody	
Excerpt	Interview number
Yes, if I go to the groups and speak with the men in the groups, many cases are completely (inaudible) than the others so you have no experience for all, you can speak with one and can share your experience with this person and with another is other experience you can share but you can't make an education to do it generally better And so, you see this men are in the group to gain experience, to see what the others have but some men have nothing or nothing big, not big disease but other have all, impotence, incontinent, have depression and the others have the contrary	Interview 16
and there is another problem I would like to tell you: Usually you get only one drug (inaudible)You know this! -Usually what say that again please? -Sometimes it's a bit difficult this side effect comes from this drug and the other comes from the other drug, if you have for example a treatment with 3 drugs, what is very often so.	Interview 8
And how do you do it when you are taking 5-6 medicines a day, how do you pin point which medicine causes which side effect, that is also very difficult	Interview 13
most of them take several treatments, several medicines, and they never know which one may cause exactly, precisely may cause the problem and they don't know what to do	Interview 12

Role and Activities	
Arguments for not having a role	
PV is not for everybody	
Excerpt	Interview number
The drug is the cause and it has always has been spoken of a probable cause, because you perceive an adverse effect but is rare that you as a patient have the certainty that the drug cased the reaction	Interview 2
I think if it's an already known side effect, then maybe it doesn't matter unless it shows that the side effect is more frequent than reported. If its other side effect then it's very important for side effects are known.	Interview 6
Unless there is something grave, I think in which case, they are reporting it, but things that actually affect quality of life for patients dramatically, are possibly missed like that.	Interview 11
No, there were some cases, some situations but I'm not aware if they are really affecting ppl or not but what I think is that sometimes there could be some mild or some effect but this ppl are not aware that this effect may be related to the drug , for instance diarrhea or something like that, if ppl experience that or headaches they could think it's something else causing it right, something they ate or water or whatever or some other situation in life, they may not be able to establish the relationship between the effects and the drug. I think this could be very useful knowledge around the drugs and it should be should be communicated	Interview 14
When you talk about the most serious side effects, of course those are immediately treated and in those situations they are probably reported by the Drs but the other sort of effects that may not be that severe but still has importance, ppl are not aware that it could be a relationship between both things then they would not report it.	Interview 14
And certainly mental patients are not in a good position because they have very little credibility, therefore I cannot ask my members to participate, I won't tell them, forbid them to participate, in the pharmacological, in the psycho, in the pharmacovigilance aspect of things, I am not gonna ask them to participate I'm not going to forbid them to participate either but, because I think it's a difficult situation for mental patients particularly.	Interview 10
-I see that the HPRA will probably not use reports from mental patients with much credibility.	Interview 10
Yes, that's it and it's a fraud thing, you can't speak freely about it, because if I did oppose and say medication is wrong, the medication we get is poison, if I get up and say that, I will not be listened to, I have no credibility, ppl will not.. they'll say oh that is just	Interview 10

Role and Activities	
Arguments for not having a role	
Small scope of their activities	
Excerpt	Interview number
es, yes and we have flyers to push the situation but we don't have the possibility to share this flyers in such a way that most of the patients know what they have to do, we have not enough resources to do that	Interview 16
-No, we have on the legal side, we have POs who do that, but they do it after there is some damage here affecting patients, then they do it.	Interview 16
hmm but, is everybody in the organization aware of PV, do they all know about it? -Me! That's why we are talking about it!	Interview 8
ut many time when I contacted medical audiologists, they don't really see the point in telling us this because we are already there, so the target group is not really us, it is the rest of the population and how to get their attention.	Interview 1
-In fact I think the PO activities in that aspect are very scarce, meaning that ofc we at (international federation) we have some activities that are the annual meeting, the annual meeting is based on talks and then the workshops and so we had some workshops on drug safety, but then that was only for a small group of ppl and ofc	Interview 7
in the same way they should be aware of what EMA is doing in Europe, because that is what determines lots of things in different countries, so there is lots of , sort of lots of information missing, until you get ill, then start looking for things	Interview 11
are tight .. I have very little room to maneuver, but you can do a lot, you are (inaudible)	Interview 10

Role and activities	
Patient Involvement	
Importance of involvement	
Excerpt	Interview number
-I think it's the most important pillar of pharmacovigilance, I think this is where you get immediate frontline information, it starts with the patient clearly being aware of things happening within minutes, rather than if they want to involve the reporting to a second source, it would take days for things to come back. Because it's immediate, within hrs the patient can respond to that quickly and if there is something similar, a big badge going wrong or something like that, chances are that it can be picked up earlier,	Interview 5

Role and activities	
Patient Involvement	
Importance of involvement	
Excerpt	Interview number
-I think besides the direct reporting, the patient could easily kind of identify the supply chain and very often they have the product in hand, they got the name of the pharmacy they got it from and the prescription as well, and more importantly, I think with the online records, especially with the non-genotype… ppl can go back and check who is , if there is something unique to that patient or that adverse event was due to something overlooked, maybe it had contraindications, and there was a contraindication present, that means they would screen out medication errors, actual PV, that medication error has to be isolated	Interview 5
-I think less disease, more quality of life and so on, that is the benefit	Interview 16
it happened to me, I told my story and they said it was not true, they told me it was depression for having given birth and no, I know, because I cannot hear as well today as before I had my child, and I also say I know because I also work with this and she said it's very typical when you have a depression, you chose something that you know very well yourself and that was her answer. So I think we must be involved, I think they need to collect the stories... and then 25 years later, some Dr. asked me how did you get your hearing loss, and I said do you want my story or you want the story of the system? And then he said he wanted my story and he said you have been right all the time, so for 25 years when nobody would support me in my story, that's a very good example of why we should be involved, because it is so important that you can believe in the story that is actually there.	Interview 1
think it's very important because they are the ones taking the medicine, when you tell your doctor that you have a side effect, it's going through a filter of the Dr and also, has the Dr enough time to make the report? A Dr has 10 or 20 min seeing the patient and they have to talk about the blood results, they have to talk about how the patient is feeling and they have to find time to talk about the medicine and eventually talk about the side effects of the medicine and then the time is up. So I think, patients have an important role in reporting their side effects and their questions about the problem,	Interview 13
- I know from EUPATI courses, when a medicine is released to the market, it only starts an then everyone is using the medicine, every possible user is using the medicine and then the side effects are becoming more known because you don't have the nicely trial population but everyone is using it, so that is important that ppl have safe medicine and they can use it without experiencing problems, the most important thing I think for medicine is ppl keeping trust in their medicine and that is something that in the last few years declined in the NL because every time you go to the pharmacy you get another box or bottle of medicine an ppl are distrusting their medicine And that is not good, therefore ppl should know that if there is a problem you can report and there is something done about it	Interview 13

Role and activities	
Patient Involvement	
Importance of involvement	
Excerpt	Interview number
One of the things that our MEB is saying is "making medicines trustworthy "something like that And ppl are distrusting and the problems with valsartan, the blood pressure medicine, it's a certain group of blood pressure medicine, I have patients coming to me, "well I don't take that medicine anymore" and they are not using valsartan they are using another blood pressure type medicine but then "I don't want cancer" that is the thing ppl are saying	Interview 13
Something else that came out of this initiative was a reflection that the EMA had at that time, all companies that had a product authorized at that time, had to invest in this new studies, there was no absolutely the EMA could mandate this additional post market surveillance, but it is only on a voluntary basis that industry agreed to finance this research and that was the limit because it showed that the regulators were relaying on the good will of industry to conduct this studies, the regulators could not ask industry to do that And that is also where the post authorization safety studies, which are now part of the legislation, that is how they came to the mind of those who prepare the legislation, there was a loop that needed to be filled in, giving a legal mandate to regulators at the European level to impose additional studies on the companies of the marketing authorization holders, and then when year's later we were invited to contribute, to comment on the division of the pharmaceutical legislation, at that time the EMA had created a working group of patients and consumers organizations and that's where our main input was in this 2 aspects, to organize at an European level, the reporting of side effects by the patients and also to give an opportunity for patients to ask questions and discuss with PV experts, that is why now there are some patients in the PRAC but also at a National level in some NCA, and we discussed also the post authorization safety studies and we relate the aspects	Interview 12
-I think a lot, and particularly for orphan drugs due to the low number of patients who are exposed to the product prior to the marketing authorization, is in many cases after the marketing authorization that we can learn on the toxicity, safety of the products but this needs to be organized, so we have the spontaneous reporting	Interview 12
Yes, ofc they can get a better treatment of adverse events, they can actually get individual treatment, they can have this like I don't know, they can feel that they are safe and they can actually get actively involved in the treatment,	Interview 15
It's important of courser that individual patient is vigilant regarding his own experience with his medicine and communication with his doctors is very important that he talk what he thinks is a results of the use of the medicine etc. If the patient is not reporting, the dr will not know that.	Interview 3
-No, no it is way more than reporting, it is, if you look for instance at the moment EMA, they started with the idea "involvement of patients is very important because it will help to build public and it's for transparency ". What we learned is that you can get better outcomes of the decision, for the decision making process if you include the patients.	Interview 3

Role and activities	
Patient Involvement	
Importance of involvement	
Excerpt	Interview number
Because those patients have often a different idea about the benefits and risks, so what you see in the past, the focus of the regulators was mainly, about mortality for instance, and for the patients it was very much more in particular.. and I speak now about patients with a long term medical condition, otherwise they don't have a different perspective from regulators, they think that mortality is the most important. But if you have a chronic disease and 80 % of the medication is used by this people, you will see that this changes from mortality to quality of life. People want to know what is the effect of the medicine on my daily activities , what can I do, what should not be able to do without the medicine and what I'm not able to do…	Interview 3
If you look to PRAC, no no , to Lareb for instance, there are very dedicated persons working there, they know a lot of the medication, much more than any patient can ever bring them, but why must we be there? Not because we know better, that is their place, their role, but because we can give them information they can't get at another way. That's also why I explicitly said it should be patients themselves!	Interview 3
This is often within in the PRAC, Why not someone else? Why must there be patient themselves. For the simple reason that if you speak about medication of ppl who are incidentally using medicines, the experiences of those ppl is not different form the experience of other members of the PRAC, there are ppl who are sometimes taking part of their medication. But if you only have that incidental connection with the medication your perspective is not changing, you are not dependent on the medication and it's not… your activities are not dependent on the working of your medicines. Like I said, you only get that change when the disease has an important effect on your daily life, and if your daily life is different from what you could do before you were ill, you know that the medication will help you and that experience is very important to understand And what I said, that the benefit for this person	Interview 3
I remember a very clear… at the moment that there was a trial question at EMA that we tried to find out who could work in the benefit risk at the beginning So there was the question and half of the ppl were patients themselves and half of the ppl were ppl representing patients and health care professionals and the question was "you get a new medicine and the medicine promises you will die until 15 months without progression of the tumour, but there is a risk of sudden death, what would you do? And what you could say is that most, I must say mst of the ppl that were representing patients and representatives said "yes… but suddent death… hmm I should not use it", but all patients said .. "yeah you speak about the risk but I should see it as a benefit , I know that I'm dying within a couple of years in a terrible way because of a tumour, so sudden death is not an important risk for me, I want to know, does it help me the next 15 months to keep my daily activities better than I could do before?", so that was a very good expression in the differences in looking to it.	Interview 3

Role and activities	
Patient Involvement	
Importance of involvement	
Excerpt	Interview number
No, not this, obviously it is essential, there is no other way to know the existence of adverse effects other than asking the patient, that is, involving the patient in pv is absolutely essential.	Interview 2
And I think well informed doctors also try to find the treatment and avoid the most possible side effects, or minimize the side effect, so it's no longer about not having epileptic seizure but its more about the quality of life and the quality of life may be better with one or 2 seizure still but feeling less shut.	Interview 6
I think for patients with epilepsy it's very important to be aware that they need the medication, that the medication is not healing their condition, it's only suppressing, it's not a medication that heals, its only suppressing their seizures to be aware of the side effects to find the best possible medication because sometimes Drs who are not specialized neurologists for epilepsy, just tell persons that they are part of the ppl who will not get seizure free with the medication	Interview 6
Everybody is very keen on patient reporting and there it's like they solved the problem that comes with us is that usually you have to go to a physician and the physician first has to believe you that this is a side effect, from my perspective that is already not very smart because that is already the first step and if it's something new and they hadn't seen it before, which is often the case if it's a novel drug in a non-frequent cancer, they would say "ohh this is nothing" and then the thing you worried about is not going ot be reported	Interview 9
because at the moment there are a lot of things we're doing is we ask physician what they think about it and then is basically physician speculation about what matters to the patient, which is not entirely accurate. We all know that certain topics do not get reported to physicians like sexual problems, there are certain topics that do not arrive at the physician table for whatever reason, but then they on patient forums, so the things that our ppl discuss is different from what they discuss with the physicians , so it matters to them so I think we should go towards an unbiased way of matters, I mean in the end the side effect happens in the patient and what matters happens in the patient, so the patient is the primary data source so we've been advocating for collecting information from the primary data source an basically cutting up a middle man or women who would introduce some bias onto the situation.	Interview 9
It seems to me essential, because it is through the patient that is taking the drug and is impacted by it, so I think they need to be very well informed about what are normally expected side effects and what might be potential issues and concerns that they should report. So I think it's absolutely critical for ongoing safety monitoring and future drug development	Interview 4

Role and activities	
Patient Involvement	
Importance of involvement	
Excerpt	Interview number
I think both, I would imagine, monitoring what are already known because it's the level of risk that you know about "is that proved in the real world, or is it more or is it less? " you know presumably drugs are just to do with (inaudible) time although they've been through clinical trials and safety. You know real world evidence can be very different so I think both monitoring the known and telling you about the unknown as well and being aware that it may not be caused by the drug but anything that is different about you and what you are experiencing is worth reporting. It could be physical, it could be mental wellbeing, it could be a lot of factors and I'm sure cause and effect is extremely difficult to seize out but I think pharmaceuticals need the information to see what are the trends coming through from the population that is taking the treatment.	Interview 4
Most of them for example with Nusinersen you would only be seeing by a health professional every 3-4 months, that is a long time between treatments so you may forget what is going on when you see the health professional, so the HP may only get a partial report, where specially the new drug, I would've thought that some sort of maybe monitoring diary may be very important	Interview 4
I think is paramount, because they are using it, so they know for the drugs that are already being use, they have a first hand experience,	Interview 11
-I think it's very important, because there is a gap between the users, the consumers, the patients and the Drs and pharmacy, sometimes patients don't....I'm not aware of what are may or may not be an adverse events and if they are not aware, they are not reporting to anyone, so they must be involved and they must be informed all the times, because it's very important to communicate every suspicious effect so they should be involved and they should be informed.	Interview 14
The benefit is to… we all know that when a drug come to the market, we need to collect what they call real word evidence and when ppl start using the drug indifferent contacts outside the protected context of the trial and also after longer exposure, there could be some new effects that are detected it's very important to communicate all this to improve the drug safety	Interview 14
Yes, I think it's a benefit because we need to know more about the good effects of drugs and the side effects of drugs and the integration of drugs and we need to, we cannot rely only on Drs and pharmacist because there is a lot of issues that may be going around that patients don't report to either and this information could be good to understand more about the drug effects. Sometimes you know it could also be useful for the reimbursement system to know more about the medicine, if the medicine is not that effective, then perhaps it should not be reimburse, there may be other alternatives that are better but we need to have the data, the information and the information after the drug is in the market, relies on PV because there is not that much phase 4 studies nowadays	Interview 14

Role and Activities	
Patient Involvement	
Patient Contribution in PV	
Excerpt	Interview number
-Yeah, the contribution is that the story is there so, my story was denied by the system, so that the story is there but there may also be another one, another patient with a different kind of story and that story is also true, so we need the stories to know what are the differences We have one story, we have heard, we lost some hearing, but the next thing is that there are maybe different reasons why we lost the hearing, it may be both due to anesthetics but it may be different things that have been found in our hearing system , so I really think we need the stories and people to look into it to see what happened.	Interview 1
Sometimes, it's also, is it PV? or not? a few years ago we had the same product by the way, testosterone, this were aluminum sachets, little aluminum zaks with testosterone and the pharmaceutical company forgot to make a tearing part to open it, so many patients were complaining "I can't get it out, what now?" is it PV? I think or is it..? Gerda: NO, no it's not, that is .... -But you see the power of patients reporting problems because I had about 25 ppl complaining about it, I went to the manufacturer, he said "Oh, I forgot to make the machine, adjust it to make a little incision	Interview 13
I think there certainly is a benefit, there was also with levothyroxine medicine in 2016, the producer had a pack of this levothyroxine in glass bottles,90 tablets in a glass vial, and patients were taking one pill a day, on a certain moment that pharmaceutical company though, 'well, maybe better to do it in aluminum strips, 10 tablets a piece so the quality of the tablet was better assure packaged not in a bottle but in an aluminum strip, and we saw, arising number of patients complaining about side effects and the first few reports we received, we though "the package is changing always a number of ppl, when the patient is changed from blue to yellow they feel something" that happens, but this were a lot of ppl, more than a hundred in about 2 weeks and a TV program made eyes on it and then Lareb received I think 2500 reports from patients so that a really a problem,	Interview 13

Role and Activities	
Patient Involvement	
Patient Contribution in PV	
Excerpt	Interview number
In 1997, there were online communities and discussion lists both in the US and Europe, (inaudible) who had been treating for long periods with the new highly active antiretroviral treatments, where many were reporting body shape changes and side effects that nobody had seen before "were gaining 20kg of weight in several weeks" in a short time, where they could be (inaudible 01:55) and fat, body fat etc etc and that was in fact how the lipodistrophyc syndrome was detected, by spontaneous discussions of patients discussing online, trying to understand what it was,etc So we alerted the National agencies and the EMA and the EMA called for a meeting because in paralell the FDA had also detected other problems with diabetes onset etc and that meeting the EMA decided to create the oversight committee for the investigation of metabolic disorders in HIV, they lead leid 5 main studies, and the results of this studies were explained to the EMA and we were 2 representing the patients in this committees, so that is for us, how we learned how PV could work and with this , we had a demonstration of the utility to organize a more systematically the possibility for patients to report themselves when something is happening to them, there were pilots already at the national level in some countries like in the NL, in Sweden but at the European level that was the first time that the input of spontaneous patient reporting was demonstrated	Interview 12
It's one way, it's certainly one way because when we analyze what the patients were saying first, the description of what they had was extremely precise by using lay language you could read what they said and visualize immediately what they had without a photo a	Interview 12
We know that rare disease patients are very precise when they report	Interview 12
Yes, I mean the patients because if the Dr does it, it takes lots of time and sometimes they tend not to do it and I think much more information could be gathered if the patient were much more engaged in it	Interview 15
-Well, I actually think they can because they can describe what is going on with that and they can actually report in the real time when it's happening and have the intermediate experience, they can share it with the agency or whatever authority is monitoring the drug safety	Interview 15

Role and Activities	
Patient Involvement	
Patient Contribution in PV	
Excerpt	Interview number
The first, if you look at the contribution of patients reporting, the importance of it, is ofc, that we need… let me say it in a different way, I very often hear we know a lot of reporting in the database, in London we have at the moment 15 million reports so, is that not more than they can handle? And etc etc And we know all the side effects so why do we need more reports, but what we know from the report and what we learn from the report is how important those reports have been to detect ADRs and that now we know a lot of the medicine but in a very general level. But to come closer, and this is what we did at the PRAC for instance, a few months and we are doing now is trying to come closer to a certain populations that have specified risk so that you can say "that person should not use the medicine" or "that person should use the medicine", but to take it to that detail you need more reports, so reporting of patients is difficult for the hole process, not only patients ofc also professionals but to get the reports of the ADR is so important!	Interview 3
Of course, they are the ones who actually detect them because they are suffering, so that's why it's relevant, isn't it ?! Because they are going to be the ones to tell us what is produced. When a drug for example has been in clinical development, prior to commercialization, it has been possible to recruit 3,000 patients even in phase 3, but when the product is commercialized, it is when the population, the entire population, passes to be a population under study, during the period of pharmacovigilance. This population is much greater and those adverse effects that could be presented in a very small% did not appear in the clinical phase, they can appear now, and they should be reflected. This is how you will really get to know the drug, that is, the participation of the patient is fundamental.	Interview 2
I do not know, but I would say that maybe half of the adverse effects that appear in a prospectus today have arisen from collecting information on adverse effects in the post-marketing phase of pharmacovigilance. I believe that at least one third of the prospect of a product that has been marketed for some time, surely comes from this.	Interview 2
So I think it's more from my perspective it's more how to think about it at the right time and know what the issues will be, maybe not on this generation but maybe the next patient generation coming in years, so that is a bit how we think about safety	Interview 9
In that sheet we reproduced what the pharmaceutical companies said about possible side effects, and we reproduced that. I'm very happy to send that one to you to show you what we did, it was signed up, as I said, by the medical consultant leading the administration of that treatment and we had that available in our website. It was very important because it was explaining things in lay terms to families who are maybe thinking about that treatment, like an alert "we are aware of this symptoms, you need to be aware of this possibilities, so it's the same function, providing, being another way of providing families with information making sure they are fully informed before they get the treatment and know what to expect.	Interview 4

Role and Activities	
Patient Involvement	
Patient Contribution in PV	
Excerpt	Interview number
-Well I think there is a contribution because the usual.. when you have patient information that patient gets with the drug, the information is based on the clinical research and what has been observed during the clinical research, when you get into realize things are different patients are different, it's not the controlled environment, so you don't have predetermined on this patient... you know, this patient goes into clinical trial, so they have quite strict criteria of who would go to clinical trials, so maybe in real life PV would be different in a way, so that's why I think it would be important	Interview 11
If ppl start reporting some adverse reaction, then you will improve also the safety of the drug and it could be good that if its confirmed then it could be add it to the safety information to the drug and is very important to communicate that.	Interview 14
Yes, I think it's a benefit because we need to know more about the good effects of drugs and the side effects of drugs and the integration of drugs and we need to, we cannot rely only on Drs and pharmacist because there is a lot of issues that may be going around that patients don't report to either and this information could be good to understand more about the drug effects. Sometimes you know it could also be useful for the reimbursement system to know more about the medicine, if the medicine is not that effective, then perhaps it should not be reimburse, there may be other alternatives that are better but we need to have the data, the information and the information after the drug is in the market, relies on PV because there is not that much phase 4 studies nowadays	Interview 14

Role and activities	
Patient Involvement	
Reasons why POs Engage in PV	
Excerpt	Interview number
it is the triangulation of quality, safety and PV come together so we don't talk of difference	Interview 5
But the more elaborated organization, the more learned organization the better organization and the older organizations learned that is not about the disease but it is about living with the disease. And then you come to PV, ofc what is the importance of all of you medication?! For most of the ppl with a long term medical condition or the chronical ill, are using a lot of medications sometimes, ppl like me, I'm using 6-7 medicines every day, different ones that is for many of us the case.	Interview 3
-No, no PV, is not the end pv… pv is a method, a tool to get outcomes for patients, it's not the aim in itself so for PO, they say we are interested in the quality of life of patients and we want patients to get the best quality of life, this is also one of the tools you have so it must be a part of the organization but at the moment it is also about ppl who understand PV and know what is going on there.	Interview 3

Role and activities	
Patient Involvement	
Reasons why POs Engage in PV	
Excerpt	Interview number
First ppl should report it to their Dr, because he could best check if it might be of the medication or maybe combination of other medications or other personal circumstances, but if I would hear it more frequently I guess as organization we would get active.	Interview 6
That's why we were so interested in Florence work and looking at narratives and trying to understand what ppl tell us, the interest there for us is the impact on life	Interview 9
the interest there for us is the impact on life on there, because it isn't much about having a side effect but what does that side effect actually mean, that makes it bad or not so bad and it can be sometimes things like rash, depends on where your rash is, if it's on the face or something is, if it's on the torso, you can cover it up for example or a classic example is the low grade diarrhoea, where everyone things "oh it's not so serious" unless you're the person who has it and then you realize how much it basically interferes with your life.	Interview 9
That was definitely the case when we started, so my husband was diagnosed in 2011 and he died in 2012 and at the time the drugs were like, well the alternative was certain death, so compared to that we would have accepted any side effect, so you deal with it and you just get on with it and you just are happy for every time you get, now in 2019, the patient population have totally changed, the discussions have totally changed, I have now ppl who were diagnosed stage IV melanoma and the first question they are asking is not "is this drug going to work? " they are asking "what side effects can I expect from this drug?" I have ppl now in stage III, my stage III population kind of falls in 2 groups of ppl, one group of ppl say "give me what ever, I do anything in order not to progress and what ever it takes , I'll do it" and the other say "what are the side effects of this? Do I really need this?"	Interview 9
Now our community is very rapidly moving towards the CML community, so I think everything has to do with efficacy and how much you trust the efficacy, whether you can be certain that this is really going to be a cure and ofc then you start looking to the side effects, So I think this is something like from my perspective to anticipate now, to have a new drug that is a potential game change, then we should already think about quality of life	Interview 9
So I think we need a balance into there, maybe different perspectives on safety and then trying to get like a concept of it, instead of just trying to have one and single only solution. So that is an abstract level, and I think every PO whether it's.. many or like with the aim to really change life for ppl should be involved in that.	Interview 9
You want to promote drug safety right? if no one from that organization shows a side effect recently or in the past, probably won't be able to promote it in that organization, but again reporting comes to a very personal level, but if some of them see a problem with drug safety, they are more prone to put it on top of the agenda, t's human nature, pure human nature. To show that drug safety is really relevant, you should use complete examples for instance, they cannot feel it personal but if you use concrete examples of ppl that have problems with drug safety, this may be helpful to promote it among the national organizations.	Interview 7

Role and activities	
Patient Involvement	
Reasons why POs Engage in PV	
Excerpt	Interview number
-It was our initiative because we felt ppl were .. what was happening at the time, I think this is a potential danger of the treatments, there were a lot of excited exaggerated social media communication about this wonder drug, so videos including children who had done incredibly well with it and no information was appearing about the possibility that it wouldn't work for you, and we were very concerned that ppl weren't reading objective facts, and they maybe just carried away with the excitement that this was the first possible treatment and not stopping thinking about it.	Interview 4
sometimes they would ask us "can you tell us more about it" and we would send them to that information sheet and tell them to discuss it with the consultant	Interview 4
certainly would try and find out what other responsibilities we have, what else we can do to keep ppl safe!	Interview 4
It's not done by PO, so the next step once we have been accepted by like hematology professional organizations, by ministry, by reimbursement agencies, the next step somehow came to think ... I suddenly saw this.. I saw the leaflet actually on drug safety and thought "oh well we really need ppl to have an easy way "so the easy way was to put a link from our webpage, homepage directly to the form that the patient can fill in, and it goes directly to HALMED	Interview 11
I think in our case it's because our organization is patient led since 2015, because before that the president was a rheumatologist, so I'm a patient so I have a different perspective and also I have the chance of being involved in different things around Portugal, around Europe, so I must say I'm an informed person and I also have my own academic skills, because I'm also an anthropologist, I did my PhD on anthropology of health so I'm able to connect this.	Interview 14
Yes, yes, also because of my own experience as patient, I thought it was important because myself, I had one experience, one effect; when I was around 10 years old, I did this treatment, it was an innovative treatment and it was very good and helped me a lot and after let's say 12-15 years I had a problem and I found out that this problem was related with this medicine I took years before, it was the first time that I realized that sometimes it takes more times than the daily routine to have the adverse reaction or side effect from some drug,	Interview 14

Problems and Solutions	
Stakeholders	
Authorities	
Excerpt	Interview number
the second barrier really is that in many countries PV is still not been taken seriously, is placed somewhere between product liability issues, that means that is a manufacturers problem and, once the regulator has looked at the at the efficacy of the drug, the formulation and gives the marketing authorization, what happens post market authorization is an entire business between the consumer and the manufacturer, so that means that the state cannot interfere, so that's the process ok, you patient got a bad badge, go sue them!	Interview 5
-Very good, we work with the African and the European medicine agencies, on the patient consumer groups and then we also working with the African medicine agency now it has recently set up, we are really closely working with them, overall members are sitting on the national patient safety networks and vigilance organizations and we invite them to have congresses, the 3 groups came last time, the FDA, EMA and AME in our congress and that is how cordial we are and we keep insuring, we keep n contact with them and keep on feeding into the policy documentation. -Would you say this good relationship you have with the NCA has helped you on the path of implementing PV in your organization? -Yes I think this is very essential for that, I mean it helps us, is a cultural change that leads to a national pv police, they need to work with the patient groups and build up that cultural cooperation and trust because that is essential.	Interview 5
Yes, because we work together with Swissmedic, it's our national organization as EMA and we are in the group there and we work with them, we work together for patient information and for Swiss part, attached the (inaudible) the explanation why one drug is good for patients and we work with Swissmedic in the group in meetings and also they push us haha! to do more with our groups, do more for PV, because there is at the home page from Swissmedic there is a part where patients can say what is their experience about the drugs, they can call to help or can call and tell you what experience they had.	Interview 16
On the pharma side on the European side it's better, with EMA it's really better and we have to learn from that, to hope to do the same on the EMA side it runs really better than on the Swiss medic and on the pharma side in Switzerland	Interview 16
We have 4 meetings as a group with umbrella organizations for patients and this group can make meetings together with Swiss Medic, that's 4 times a year -4 times a year?! how has it worked? Is it a good dynamic for you? -hahahaha It's more about information, not about involvement, and it has to be more involvement and it's became better	Interview 16

Problems and Solutions	
Stakeholders	
Authorities	
Excerpt	Interview number
That could be very relevant, because we have our network, we have our members so it would be very relevant that we send out this and that it shows that we worked on this and it would also be very relevant when we have our conferences that somebody like you would come and talk about this and tell us what is all this about,	Interview 1
-I think that.. I met Gerda at a symposium of nurses, that was a 2 day event, somewhere in the NL, and we were there with 20 PO and Gerda met up with every PO telling about the work of Lareb, and that's how we met, so it's coming from both sides. Being active in engaging the PO	Interview 13
-No, I'm the only one, because I'm interested in taking that kind of education and I'd like to have maybe younger ppl interested in doing that course and maybe other courses, I'm now developing together with our facilitator, PGO that is an organization financed by the Ministry of Health to support PO on the facility part of their functions, so they're organizing education on how to answer a phone, how to be a treasurer, how to form a board.. But now they're also developing the course I had, the EUPATI course, it's now translated in Dutch and we are changing it to the Dutch situation and as of September the first 25 patient representative in NL will follow that EUPATI NL course and instead of talking about European PV, they will talk about Lareb, and talk about CBG and our health insurance an our ministry of health	Interview 13
I think we've seen from recent cases that the PV system is much more reactive, the analysis and the decision making is much faster, there are still products and mostly products which were authorized years ago, a long time before where we have issues, that is the case with valproate or products which are placed in the market, there is a problem which wasn't solved, specific ones, but for the most recent products, the impression we have is that when there is an issue, when there is a signal, it is detected much faster than before and then there is a regulatory action much faster than before and that benefits the patients.	Interview 12
there are some agencies who have so much to do they don't see how they could start with a new stakeholder they have never worked with and in some ways they can be afraid of talking with POs (inaudible) but PV should be the first entry mode when POs like to work with a NCA, they can't deny there is a common interest to start with PV.	Interview 12
-Yes, actually we had the training 2 years in a row, where in partnership with our drug medicine agency and for PO, how they should actually promote PV and how they should educate the patient to report adverse events -Ok, ok was that the HALMED? -yes, HALEMED, yes,	Interview 15

Problems and Solutions	
Stakeholders	
Authorities	
Excerpt	Interview number
What I see now for instance, EMA is doing a great work there, they have all the members of the patient-consumer working party but there is even a broader group called eligible organizations and the eligible organization have all information but all training facilities from EMA, at the moment is also known that when ppl become active in PV for instance there are training courses at EMA for those patients, that was not in my time	Interview 3
Yeah but like I said that, guiding example in the world of patient involvement is EMA, and they really understand what it means when they speak about true patient involvement and their real role because they understand in which cases it's important to have (inaudible) but also patients have to understand like I told you, what is our role there	Interview 3
For instance I was for many years the representative of the patients at the PRAC but the same moment I was representing the patients at the CBG at the same moment you are not the one who is able to communicate with the patients so that is not making much sense, important that those ppl are there for organization but they are not the connection with the outside world, for you know that all information is not.. you sign a document that says you are not allowed to say anything about what happened	Interview 3
In terms of official interaction I obviously had interaction with Florence and also with (name) UMC on topics of what we could be doing	Interview 9
-I mean for me I wouldn't say it has not called attention, so I regularly invite someone from the UMC, I'm here and we have visited the center because our annual workshop is in, here not far from Uppsala, so we've been there, we've had speakers, we try to make PV as a topic in our conferences so we try to have it there is usually a topic either about side effects or someone from the local authority, we invite them as speakers and I think the personal contact is really really important and I think my Dutch colleagues have done that as well because I met Florence at one of our events and then ofc in Dutch and so ofc you have a connection	Interview 9
EMA before they moved and their resources got so thigh, I think had made deliberate decision to become more visible at conferences and to speak at conferences and be accessible and I think that is a very very important part of the strategy, because once you listen to the person and you maybe had a coffee with them you have kind of a face, you can put a face to a certain problem or a situation that for me has always been the most effective way, also get ppl to remember because otherwise you can let someone talk about PV but if someone really works in there and says this is my research project and we did care about it, it has a very different impact	Interview 9
The difficulty is to find the right PO to involve, because you cannot involve all PO, that is impossible ofc, so the difficulty here is to find someone.. ofc that person would not be able to represent all PO, ofc that is impossible but can bring their perspective. But that is a difficulty to get along with it.	Interview 7

Problems and Solutions	
Stakeholders	
Authorities	
Excerpt	Interview number
So it's a way of indirectly (inaudible) the NGO, because when it comes to staff, I don't think it makes sense from the NCA to allocate staff member time to help out the NGO because then it would be more of the same, the NGO should be fully independent of the NCA because otherwise they won't be able to bring new things on the table, so I'd say that promoting this and creating the need for it is what the NCA can do.	Interview 7
-Well it depends on the country for instance the EMA has a very distinct system between all stakeholders, so the communication is very good and all stakeholders are involved in committees for instance in PV, but when it comes to NCA depends on the country.	Interview 7
No, it's been written by the agency, Croatian National Agency for Safety of Drugs, HALMED, and they provide a little sort of folded up leaflet about reporting side effects	Interview 11
Yes, or as I said, in our meetings we always have banners for role up for HALMED and we always have someone from HALMED to tell them to do, to report.	Interview 11
he medical health system knowledge or literacy is very low and not just in CRO, I don't think ppl do know there is an agency for drug safety, as separately, if you say to someone in CRO where is HALMED, I don't know whether they would quite know where that is	Interview 11
They also have well nowadays they also have the different units for PV have a social media page, on Facebook, in Portugal Facebook is very popular so it's also a good way of communicating with POs and the general public and well I believe most of ppl would subscribe or go and look for PV unit so POs we try to follow and share any information that is relevant for us, for instance, the national authority has a newsletter, they have a lot of different ways of communicating with the POs and the general public, everyone can subscribe the newsletter and they send regularly information around different topics, including PV, so this is very good	Interview 14
I rang them up the other day, I rang them, I ran the HPRA and I was talking to a woman there, very starchy woman and very defensive woman, and she was a typical civil servant she did not want to talk English to me, she want to talk baloney.. I (inaudible) for those Pharmacovilance, I said "what is it?" she said, tell them to ring us, tell them to ring the HPRA we tell them.... You may you say you tell them something you wouldn't tell me you know, they are very starchy and very defensive, they give the impression that they don't want to hear from you, they are not welcoming, as a say "well now (name), what do you think? " that is not a question for them at all. They take reports but you have to go through a whole form.	Interview 10
But it's multi-level responsibility, in other words we can't just dump it on one party, we can't leave it on the regulators, we can't leave it on the pharmaceutical companies, we have to rely on each other, it's a shared responsibility	Interview 5

Problems and Solutions	
Stakeholders	
Industry	
Excerpt	Interview number
But this is a partnership as I said, between the pharmaceutical industries and us. So the manufacturer knows the product well and they know what is going on and they can, they have to work with us.	Interview 5
Yes yes, exactly and I think when you look at it from a point a view so open such as media, when patients actually feel pharmaceutical companies come to the patient groups to talk about it, highlight it and educate them about this, are generally interested in preventing this, then they are far more receptive, they feel precautious and things like that you know.	Interview 5
Yes, we have a congress, we have a IFPMA coming in and talking to us, and I remember listening to that, so that is how we… it's a regular feedback -Who? -IFPMA, the national federation for pharmaceutical manufacturers$ associations, so they have their fight fakes campaign and others, so that would be to tell us what is going on, plus we look at other innovation, our newsletter covers many issues and PV comes into there	Interview 5
o in the ADA assosiation of European Audiologists, they are representing there every year and so are the manufacturers of hearing aids,they are there because it is their market of course. So i think that could be an idea.	Interview 1
Yes, we work with the industry a lot, so I have to say that I actually work as a consultant with one project with Pfizer and on project with Roche with also other pharma companies like ADVI and (inaudible) so we have very intense contact all the time but we also try to when we did this education on biological medicines and biosimilars	Interview 15
So how did your organization found about this? -Through our international connections -Ok, excellent -And also I think when we are participating in this conferences in France or Germany, also those labs for producing epilepsy medications so this gets a direct contact to discuss also things like this with the firms that are producing the medication.	Interview 6
on the patient information that pharma companies sometimes make then you get a nice infographic or you have the small print but still not the human experience in there	Interview 9
We don't have any contact like that at all. The only contact we have with pharmaceutical side effect is we had contact with Bayer, because they are the manufacturers of nusinersen, we now have early contact with Roche, but we haven't brought anywhere near the topic of PV with them.	Interview 4
and we would also assign person to go back to their pharmaceutical company, to ask the questions as well.	Interview 4

Problems and Solutions	
Stakeholders	
Industry	
Excerpt	Interview number
No I think we've covered everything because as I said my knowledge is very limited and I think what has been interesting through this process for me is that pharmaceutical companies have been waking up, that we had contact with, seem to be waking up a little bit more to the fact that we do have a lot of very useful contact with the community and they are very restrictive about their code of practice and they are not always brilliant at the language they use with the community and if we can very much work with pharmaceutical companies to assist with that, but at the same time that can deflect from our core business so we have to think carefully that if we do this work in partnership in pharmaceutical companies we need to have some financial help to do that and then that gets quite tricky but a huge amount of my time is gone in getting this drugs to the ppl and helping the pharmaceutical companies ..	Interview 4
So I think pharma is very aware of the need to know adverse drug effects, however what happens in real life is something totally different and whether the pharma should put more resources in that, you know patient reporting, that is something that possibly should be looked at because that doesn't happen	Interview 11

Problems and Solutions	
Stakeholders	
Health Care Professionals	
Excerpt Copy	Interview number
On the care side there is the best cancer nurses and also prostate cancer nurses, but prostate cancer nurses in Switzerland there are, I think about 2 or 3 or 4 but not more and that is not enough, that's clear, and they have some experience but if you come from (inaudible) and speak with them they say or they think they are better, that they know the experience from the patient and they know what they have to do and they are worse! worse than the professionals on the medical side Normally we speak better with Drs than with this nurses	Interview 16
-No. Not really, we cooperate mainly with audiologists and we have medical, technical and educational audiologists, so we have 3, we should cooperate with the medical audiologist on this, I suppose, but their interest is mainly type of hearing aid according to what type of hearing loss or a coclear implact, an implactation for artificial hearing, they are not involved if Im taken to the hospital for something else and I need some kind of treatment, they don't involve the audiologists at that time. If im in for meningitis, they do not consult the audiologist until afterwards	Interview 1
-But you know I spoke to some nurse she does anestetics and audiological work in a hospital, when ppl need to have something operated in their nose, throat or ears, so she does the anestetics and she didn't know that anesthetics could hurt the hearing, she was working in this kind of work and she didn't know.	Interview 1

Problems and Solutions	
Stakeholders	
Health Care Professionals	
Excerpt Copy	Interview number
we cooperate with the organization of European audiologists that is an association for professionals, so we cooperate with them and we think that it will be in that relationship that we could work on this kind of topics	Interview 1
The pharmacist when dispensing a drug would do well to recommend the patient, that if he observes something, tell him to report that adverse effect. The same should be done by the doctor when prescribing the drug. In other words, the patient must receive from the patient's association, from the prescribing doctor and from the pharmacist who is the one who dispenses the drug, the indication to make known any adverse effect that has	Interview 2
Finally the professionals not ?! and within professionals there are medical nurses, pharmacists and some other, we in their congresses, that we go relatively often, the subject of pv also like to treat it, especially when it is a central theme of nature, because they also have the commitment to form , to inform patients about this matter.	Interview 2
-Yes, for example, we are usually part of organizing committees, of congresses of professionals, of doctors for example and the PV always have it in mind, so we always try to have a table that focuses on this. For example, there was this Thursday, I was part of the organizing committee of the congress and there was a table that referred to pharmacovigilance, because it is something that we care to include in professional congresses with the Ministry and administrations	Interview 2
I think what we have realized participating in trainings abroad is that like 10 years ago Drs totally denied any side effects, this was claimed being caused by the illness and now they are very clearly speaking about it in the case of epilepsy drugs, that some are causing obesity some are causing, slowing down the patient totally, they may make you more aggressive, so this is now part of also the wisdom shared with doctors and that we learn at international meetings and this has changed in the past 10 years. So 10 years if you would say "oh I'm feeling very drowsy, very slow with the medication" Dr would reply "this is not the medication doing it" ,now it's clearly part of the medication	Interview 6
so there were a lot of new oncologist who had never seen this drugs before, so then this patients end up being seen by GP who had not even heard about the novel therapies so all of a sudden, a large number of HDPs was exposed to a therapy that was like black triangle where it was limited indication around it so we had a classic case would always be like "I'm not feeling well, I'm on this drugs and my GP says it's nothing" so we used vigiaccess quite extensively for that because what we do is like you can look at the side effects that have been reported and what ppl have done is they've taken screen shots or printed them and then when back to get a treatment at the physician, they'd say "listen this has been reported"	Interview 9
so we have done probably a lot of harm by not training HDPs	Interview 9

Problems and Solutions	
Stakeholders	
Health Care Professionals	
Excerpt Copy	Interview number
At the same time we also know for example in diabetes or in other conditions neuropathy, something that patients probably have no idea of what this is, but that, physicians rightfully fear because is long term consequence	Interview 9
So we also started training our oncologists in the resource and I know some oncologists who use it actually, who use vigiaccess quite extensively because it's helpful and I also tell them that they can submit requests for rarer side effects.	Interview 9
Many organizations they are just about support and they haven't even understood and they haven't even reached to authorities because it has never crossed their minds so for me that is why I thought that ESMO or the patient advocacy track at ESMO had such an important place for this kind of thing because there you also reach organizations.	Interview 9
Secondly they should talk to the patient when they come to see their specialist, they should give them some means of reporting this immediately, or a contact to the hospital where they can call and say "this is happening" and then who is going to enter this into the system?	Interview 11
The specialists and whoever sees the patient at the time, they don't report it, they just note it in their... you know it doesn't get through the agency that deals with it and I am sure that is the case because we have in Croatia, in particular, there was an attempt by a hematologist professional organization to stablish a register of myeloma patients and the register, it's been now 5 years and it's not complete because not everyone enters the details there and I think the same goes with PV	Interview 11
But I think the majority of ADR would come from Drs. Because I think Drs specialists know what is expected and what is not to be expected because if you have on the drug information leaflet saying it will cause diarrhea, it will cause this and that, you know patient can say, well... it does cause it there is nothing to report really.	Interview 11
Because I'm not aware. I've seen it when i went to Drs and I wasn't given something, to be told "You can report it"	Interview 11
the role of other ppl involved, for example Doctors and so on, they can make a report of adverse reactions and so on, and they would have credibility but then do they actually bother to do that, I don't know, as a guard careers and nurses and so on, I don't know where they commit to the picture? obviously they will be listened to a certain extend but how much reportage goes on, I am not sure I can't tell you	Interview 10
the topics we've been covering or engaged with because I was the chair until December last year I was the chair of the patient advocacy working group, at ESMO and for that I was responsible for the program for the advocacy track and for workshops and we had the topic PV on there and tried to engage the community on have a discussion about what it is.	Interview 9

Problems and Solutions	
Stakeholders	
Other Patient Organizations	
Excerpt Copy	Interview number
Ok the local organization, leading patients groups and that are for immediate response, this means they could need for PV, things that happen ... a person had an accident, an emergency and needs treatment, then are the national specialist of patient organization this are the patient that are dealing with kidney patient and those, they know their consistence very well, so if there is a bad badge of insulin clearly, nationally is their responsibility, they would be able to act at the level which is national level and very specific, and that PV for that particular product line is very critic for that particular badge. Then come the national alliances and national umbrella alliances, this are alliances which can make systemic things. Lastly we see the umbrella global organizations really work with global organization like the international heart regulations so this would be as pharmaceutical industry is global and inaudible needed to take care of PV and really act as wto whos' and tricks who can supply change from there.	Interview 5
Therefore we can also add influence to the local, for instance if a small country like Haiti or even Cape Verde and the local PV is not cooperate with them, a global organization can help the local organization empower them and make them active, so we can help that way.	Interview 5
We are the Umbrella of the groups in Switzerland, we work not on the individual side for patients, we work on the back ground side, on the side of the government, other organization and also the professional side, that's right	Interview 16
MPE is educating patients or .. how do you say? Other ppl who are very wel educated, can you give me some words so I can find it? -You're telling me they are helping like .. specialize ppl -Ahhh MPE is running a special program to educate ppl on different levels so they can act on their own countries but also on the European level, and they can also work with EMA, so this is a wide range -So the umbrella is interacting with EMA and is making programs for teaching	Interview 8
I do some other things and I have been once in a week in Barcelona, I think it was Eurordis We got a whole week, have been educated and PV was a very big part of the program	Interview 8
I also know of a norwegein website for hearing troubles, I can write it to you in the email and in that site, there is alot of, well all the things that can damage your hearing and the main things are the ones that I have mentioned already in the email, because there are treatments that we know that can damage your earing,	Interview 1
-I mean you look, England, I'm working together with a number of PO, for instance, we are having after this meeting, it's to get up at 14 PO, we are trying to make sense in the world between generics and generics and generics and specialties, because our patients are suffering from very often switches between one brand and the other and ppl are complaining	Interview 13

Problems and Solutions	
Stakeholders	
Other Patient Organizations	
Excerpt Copy	Interview number
we have a very nice umbrella organization for the cancer patient organization about 30 PO are members of that it is quite possible that they follow sort of PV strategy that can be implemented on every of the organizations but I don't know if they are doing it, but that can be a benefit of an umbrella organization	Interview 13
I am a member of 3 umbrella organization but none of them is saying anything about PV, only maybe EURORDIS, the European organization for rare diseases in their trainings they tell about PV ofc but they don't have certain strategies to implement for POs	Interview 13
Oh, in my organization, sufferers contact organizing meetings in hospitals about 7 or 8 times a year, every few years were organizing a symposium, very big, crowded, last time we had 550, in2016, now we are expecting 700, we're also in contact with other PO, with health insurance, with hospital, involved in networks like ERN , European Reference network for rare diseases, also in my case, I'm going a few times abroad to visit Medical Congresses and also congresses for patients, organized by EURORDIS	Interview 13
we can't be compared with for example Italy and Spanish POs, they are much more dependable on their umbrella organization than we are	Interview 13
What I see is that a global organization like IAPO with global (inaudible) knowing what is going on, having information about decision making processes and involvement in the decision making process with the major regulatory bodies like EMA, FDA, etc, that you inform regional organization.	Interview 3
No they should not be doing the same, they should be doing their own role, like I said the international organizations like IAPO, should be able to inform regional organizations or disease specific organizations about the information, so they should have a view of what is going on or not at the European Level or global level.	Interview 3
Those organization representing national organizations mostly, so they have to give information to regional organization that most of them are disease specific organizations like the arthritis organization etc, so they must play the role as information source for those organization that want to know something, they must have the ability to ask IAPO and to get the information from IAPO,	Interview 3
But in general they must have information about what do we know about ADRs, but they also and patients organizations can come with the question "I want to have contact with my national competent authorities, how can I do that?" They must have an answer for that. They can tell you, "you have to call this, and do this and do this".. they have to give them an understanding of how this is organized for most of people don't know.	Interview 3
And what you can do is, learn from good examples, like I said in Europe for instance an organization like EURORDIS can be a very good example on how to organize it, you can also learn even in Europe ofc, from an organization like the National Health Council in the United States which is an umbrella organization they have on the united states and they have very good contact with the united stated, you can ask them if they can even mediate between organizations and the FDA if needed, it should be the same here	Interview 3

Problems and Solutions	
Stakeholders	
Other Patient Organizations	
Excerpt Copy	Interview number
First of all, we have to inform and train the patient organizations that are part of our coalition so they, in turn, urge patients to report any adverse effects they may have	Interview 2
Yes we are also members of the German and the French organization, we get information in German and French that we can share	Interview 6
So how did your organization found about this? -Through our international connections -Ok, excellent -And also I think when we are participating in this conferences in France or Germany, also those labs for producing epilepsy medications so this gets a direct contact to discuss also things like this with the firms that are producing the medication.	Interview 6
at the very beginning we got a lot of help from the CML community, which is a very different type of cancer, melanoma ppl die very fast before Gleevec came with Gleevic and subsequent products the cancer is now well.. as long as you have access to drugs and you take the drugs as indicated, they have nearly a normal life expectancy and in discussions for them , for them the quality of life was the major topic	Interview 9
we can inform the global to the national organization, in a way what we can do is be more active, we can do web pages for instance, and developing some toolkits that can be used at a national level because everything must be(useful? Inaudible) at a national level. Because the global organization, can promote it, can develop the materials and then the national organizations must apply it and that cascade of events, if a global organization promotes and does such materials, which need to be useful ofc, and at the end of the day we need to promote at a national level that naterials are used.	Interview 7
-I think the umbrella organizations what they can do is promote it among the members by for instance, promoting during the annual meetings or with small discussion groups and then promoting it by producing materials that can be used at a national level as I said. I can give you an example, for elections, 4-5 years ago, we produced a toolkit for associations to use when contacting the candidates to the (inaudible) ok so all national associations had in their possession a toolkit with a key message that we would like them to bring to the special table with the candidate and then also some slides of paper for instance.	Interview 7
At the national level they can use the materials, they have to ofc adapt the material to their national environment and then they should promote the PV system among their members	Interview 7
we have partnership with other charities, we are part of SMA Europe, but were independent.	Interview 4

Problems and Solutions	
Stakeholders	
Other Patient Organizations	
Excerpt Copy	Interview number
In Europe in particular the roles of umbrella organization has been quite confusing and lots of umbrella organization, to exist, focus on activities where they can raise funds and PV in my experience, there is a lot to talk about it but it doesn't trigger that, so it's talked about the top but is not actually supporting the organizations on the ground.	Interview 11
I think the role of umbrella organization to take up problems of the national organizations and then report them and try to overcome the difficulties that the patients have because of where they live.	Interview 11
I'm not sure actually in what way umbrella organization can influence what is happening in particular countries apart from raising along, when things are not working properly for the patient. They can talk, they can teach you about the need that patients should report an adverse effect and when and how.	Interview 11
lots of umbrella organizations, are founded exclusively by pharma which actually brings things into slight conflict of interest, because organizations start sort of worrying about sustaining themselves and not so much about being the voice of the patient.	Interview 11
So an umbrella organization should make the other organizations aware of the importance of PV and then provide some support on how to communicate with the public, how to communicate with the stakeholders and also offer some support when it comes to dealing with the authorities, if there is some problem that should be address, to whom it should be address, could be the role, my view, of umbrella organizations	Interview 14
Yes and also empowering the national organizations in different ways with information, or workshops on how to deal on this situations, because sometimes national organizations, this is sometimes a problem of umbrella organizations, that national organizations may be afraid of losing their own voices, so empowering them instead of speaking on their behalf is also a good solution We should do this and we should talk to this person, we should now ask for a meeting with that person, maybe a good way of dealing instead of "I will have a meeting and talk on your behalf " when EURORDIS is making a policy for Europe on how to develop ERNs and how to implement them in the different member states of Europe and you see for	Interview 14
For instance in Italy and Spain and also France, the national alliance and that is the umbrella organization takes the lead, in the NL we are the ones siting at the desk of the ministry talking about our needs	Interview 13

Problems and Solutions	
Barriers	
External	
Miscommunication with PV Community	
Excerpt	Interview number
Now let me ask you one thing, how is your relationship or your organization relationship with the NCA in PV in Germany? Do you have any contact with them? -None, not at all, I already told you if I'm getting aware of one side effect many many patients are reporting on, so I will tell the patient representative from TLH who is in the TBA so they can report and I would suggest that	Interview 8
"oh! I think that somebody there, he knows, I'm gonna ask him" that would be my way of working, but nobody has ever knock at our door saying, hey we would come and talk about this. But even this talk is helping raising awareness on the importance of this.	Interview 1
I this is also communication and research and knowledge between the medical staff but it is also communication, no one ever told this would happen. And I know that in the University of Southern Denmark , they study medicine and they now do a study, to communication with the patient, so that the patient knows what is going on, because this was never really highlighted before. Dr would say well this is what you need and off you go .	Interview 1
The vast majority of POs never have contacts with NCA or in this case Lareb, you have a much longer history in the NL so you have a much broader outreach to POs certainly, but in other countries , in back to France for example, I think there are only 55 organization who have a regular working relation with the national authority, out of maybe a total of 2200 organizations	Interview 12
but the problem is that in very recent past, there was little communication from regulators to patient organization and still in some of the European countries for instance that there is little communication between the NCA and the PO, it's changing, tha's also changing but it's also everywhere, we have to fight for every step forward in this	Interview 3
So we have to learn from each other but if you do not have contact it's very hard to learn and what I see is there is a lot of improvement and there are more and more organizations in particular in Europe, for instance, organizations with contact with EMA, who are now starting to understand the importance of regulations and the importance in particular for them in PV. So it's a starting process	Interview 3
-Yes I told you already at certain moment, that we had to fight for every step, not knowing each other is one of the most important barrier,	Interview 3
It was a lot of words to tell! That the first barrier and we are still trying to overcome it and yet we have made a lot of progress is that isolation in the past of the regulatory activities, not only for us, but for many other stakeholders, like physicians, they did not have contact with the NCA of the regulators in general.	Interview 3

Problems and Solutions	
Barriers	
External	
Miscommunication with PV Community	
Excerpt	Interview number
Yes, I think if its more than 1 person who would tell or more than 3 person that would tell the same side effect with the same drug, and I would get a feedback and the Dr is not reacting, then I would try to find channels to communicate it to the Ministry of Health or to the EMA	Interview 6
-If we need them, we can find them, or I don't know how to say, we are not meeting on a regular basis or exchanging	Interview 6
That's good so the communication with the authorities has been more for the reimbursement… for the approval of the product? -Yes for it to become available -But have they ever offered any type of training or any type of information for you to, I don't know some files or documents or whatever that could be useful for your organization or any other organization to be able to understand the pharmacovigilance topic? -No, no	Interview 6
Because if nothing is used is junk, because the authorities wont range how to reach out to ppl and then there are ppl like us, wondering where to get information from, and that is just like a classic case of miscommunication, there is no bad intention or anything, is just good intention but no properly aligned and if one just aligns properly, I think everyone will be benefiting and happier	Interview 9
-Well it depends on the country for instance the EMA has a very distinct system between all stakeholders, so the communication is very good and all stakeholders are involved in committees for instance in PV, but when it comes to NCA depends on the country. I can give you the Portuguese example, Portugal at the moment we don't have a good communication system. Well I participated in a couple with the Portuguese NCA in the past but it stopped and now they are starting to putting forward the system	Interview 7
We don't have any contact like that at all. The only contact we have with pharmaceutical side effect is we had contact with Bayer, because they are the manufacturers of nusinersen, we now have early contact with Roche, but we haven't brought anywhere near the topic of PV with them.	Interview 4
No we got no contact , it hasn't been a topic we have considered. I mean this is why I'm interested because as I'm saying this is so new to us and we don't even know what the structure is in the UK	Interview 4
Well I think making the communication! as far as I'm aware there has never been any with our organization	Interview 4

Problems and Solutions	
Barriers	
External	
Miscommunication with PV Community	
Excerpt	Interview number
-There is a.. well the thing is that authorities are a complex system and you have a lot of different departments and it's not easy sometimes to know to whom to address your questions or who is the best place, should I go to the president(inaudible) to address something, then if it's not the president, they will forward it to someone else .. yes but it can be sometimes difficult to do that, the thing is that one of the difficult things is to understand the complex structure of the national authority	Interview 14
If there is some issue then there is the direct contact for the PV unit in different regions of Portugal, and we also have the portal, the website for RAM, for communicating but if we have any other doubt we have to work out to whom in the complex structure of the national authority should we communicate. Once you have found the right person, it is very easy,	Interview 14
I rang them up the other day, I rang them, I ran the HPRA and I was talking to a woman there, very starchy woman and very defensive woman, and she was a typical civil servant she did not want to talk English to me, she want to talk baloney.. I (inaudible) for those Pharmacovilance, I said "what is it?" she said, tell them to ring us, tell them to ring the HPRA we tell them.... You may you say you tell them something you wouldn't tell me you know, they are very starchy and very defensive, they give the impression that they don't want to hear from you, they are not welcoming, as a say "well now (name), what do you think? " that is not a question for them at all. They take reports but you have to go through a whole form.	Interview 10

Problems and Solutions	
Barriers	
External	
Deficiencies in the PV system	
Excerpt	Interview number
They are not taking this matter seriously ad then, I think even in this great age of electronic media, when things should happen quick and fast, things are not being personalized and taking advantage of ICT and computer technologies for this, and yet artificial intelligence, algorithms and all are there in the market and could be easily used to streamline global and national effect. You can integrate, use a global platform to integrate into a local PV system, so basically produce a standard version and WHO which is the technical agency they have always been pushing standardization, that would the best gift anybody can give to the world, that you have a standard PV system that low and middle income countries can plug on, almost like a cloud base, so they don't have to .. very little technical dispute needed.	Interview 5

Problems and Solutions	
Barriers	
External	
Deficiencies in the PV system	
Excerpt	Interview number
So it runs, but it could run better because the website of Swiss medic is not really good for patients, it's a little bit complicated and the patient has to know that they can enter their experience and normally in the moment, as we look at the statistics there are more, about 8 to 10 of the experiences catch from professionals and not from patients	Interview 16
but I don't think, for a lot of patients it's difficult, it's scare to make a report on the Lareb website -Really? why do you think is that? -I think it's complicated, it isn't complicated but for a majority of the patients it is	Interview 13
One of the main questions that we are trying to raise in the public and the health care system is monitoring the treatment outcomes and also treatment outcomes from the patient point of view, what is important to me as a patient, so this is something we've treated for the last 3 years and actually we started to start a debate between this different stakeholders, from the ministry of health, from HALMED, from the national insurance fund, so, we will see what happens with that	Interview 15
most countries in Europe don't allow self reporting or well… no, that is no true, they are obliged to have a self reporting process in place but most countries make it so genius that you first have to know where to find the form in order to report it and the papers most of the time is totally user unfriendly, we've checked this, we asked everyone to look up in their own countries where to report side effects and at the time it was really really not user friendly.	Interview 9
Even in the places in Europe where we have now the app, like web created, that got adapted before in the UK and the Netherlands and Croatia, ppl are not really super keen on it, I mean I know that on the UK ppl who use it to check out simple side effect, which I think is a good effect of the app if you want, but that was not the original purpose And the complains I got from ppl, from users there is it says they wanted to report within the app so there was not free text, they couldn't really articulate what they were concerned about.	Interview 9
would be very different and this is the world problem is that this data is collected nationally so far and there is no other way around it and we are an international network so if you have a relatively rare cancer and the drug are new, the group is not very large, so everyone reports into their own country, the numbers are not very insufficient	Interview 9

Problems and Solutions	
Barriers	
External	
Deficiencies in the PV system	
Excerpt	Interview number
Often they provide quite a bit f extensive material, how to access it, because it's often not easy to find, you know the same is true, I think is also the information is technical, you just have to go to the email website, it's dreadful, I mean everything is there, you find everything you need but first you have to find it and the layout, we've complained so many times it's getting better but in the begining it was all black and white with a blue frame , it all looked the same, navigating that, the amount of information is all there but is really difficult, it's like hidden in information, it's important information hidden in too much other information and knowing how to navigate it then becomes the (inaudible) SoI think PV is often like that, it's all there but you have to know where and you have to be able to read it	Interview 9
they are going to use that pool of ppl and that pool of organizations to integrate on specific committees and specific activities, and by promoting it they idea is to create a very clear communication channel between that pool of people and organizations and the NCA, but then everything moves very slowly,	Interview 7
-The problem is how they report it, why? -Well, there is .. you have to have a very structured and easy way for ppl to report something and that's in organized societies I suppose that exists, in not organized societies this channels are not clear,	Interview 11
. So to have a comprehensive way of reporting of a drug, you would have to have very clear like the process, which the patient would understand, the family would understand, it would be easy, it would be readily available to every one	Interview 11
I take let's say, I retake it seriously that we should call our patients, call who has contacted us, who has sort of not involved but they are part of the organization, we know them, we make aN appointment calling them every 3-4 months and making sort of an interview and the things they tell you in this interview, it would be fantastic to report it to someone because I don't think that is recorded anywhere properly The problem is really having someone having a system and having some system using that information.	Interview 11
I think the reporting system is not good enough, is not simple ..	Interview 11
When you talk about EU alone, there are such diversities of what it's possible, and it's really determined by the market of pharma companies, and lots of this work of pharma companies are thinking that PO would do, but they can't, it's sort of .. not possible to do something so responsible on a voluntary basis, you can't do it. You can spread the voice but you need to get the health system involved.	Interview 11

Problems and Solutions	
Barriers	
External	
Deficiencies in the PV system	
Excerpt	Interview number
For instance for chemical drugs we have one system and then you also have another issue that for instance natural products, herbal products, supplements, a lot of ppl do that and most of the ppl think they don't have any interaction or adverse effect, so first they are not aware of this and then they don't know they can report and who to report this effects, it's not to the national authority of medicines but to the ministry of agriculture, a different department,	Interview 14
It is very difficult sometimes to stables and having in mind the daily life and what is the consumption habits of the population, sometimes you may be experiencing some effect and you think is about this drug and ppl don't report taking supplements or teas or herbals or whatever and this could be helpful if we can have all things because they are taking them for therapeutically reasons so they should be under the same PV system, I think this would be useful.	Interview 14
I think the form is not.. the last time I looked in to the form it's not very.. for instance one of the questions I remember they asked is if they felt any discomfort and the concept of discomfort for the lay person may be tricky, I think maybe here POs can have a role helping chose the right wording,	Interview 14
You kind of help yourself on the website to have to fill in in a form and all that, go through a whole lot of (inaudible) no mental patient could cope with that, I don't believe so you know	Interview 10

Problems and Solutions	
Barriers	
External	
Misrepresented Information	
Excerpt	Interview number
Social media yes, in can sometimes exasperate something; someone sitting in Finland who has a normal indication, he or she happens to have an opinion and goes online in the middle of the night and says something and then this is picked up by a patient having the same pharmaceutical drug in China who says "hey look have you seen this" and you know there is no screening [...] Suddenly this things go viral and there is panic for no reason. I mean this is the case of the Doctor who associated MMR vaccine to autism	Interview 5

Problems and Solutions	
Barriers	
External	
Misrepresented Information	
Excerpt	Interview number
When you read the newspapers, even the best informed, they often misinform the reader, they said the first agency of the commission and the PRAC which make some opinion and then they write and then another agency called the CHMP makes another assessment and then the commission finally definitely decides, which shows that even for trained medical journalists, they can't understand clearly the PV organization.	Interview 12
we had recently we had some issue with fake news and pseudoscience where things look like science but in the end aren't science but they're written up as if they were science and then at the beginning, we would take this stuff down which is get rid of it, we have learned that this is not so smart to do because then this ppl would just leave the forum and go somewhere else where you have no access to them anymore , so we now use the opportunity to post something to go through it and explain why this is not trustworthy, or like if they posted for example the story that was published in the newspaper, then we post the original study and say , well ok, this is what is really in the paper, this is what you conclude and this is what you can't conclude, then present that.	Interview 9
-Some of them are around legislation, we need to be very careful not to.. when we are talking about drugs that cannot be anything that could be leading someone to think that we are promoting the drug this is one thing and the other thing is also the opposite, we must be very careful not to write anything that could lead ppl into a false or alarming situation and sometimes is very difficult to communicate because nowadays ppl have a lot of information and they sometimes just read the title	Interview 14
If we communicate to the general public, we need to be very careful because ppl don't read the whole information and they tend to generalize , we must be very careful not to raise unnecessary alarm, the information could be misinterpreted by ppl , so it's around legislation because of this thing we must be very careful because the law forbid us to advertise and promote medicines so we should be very careful when talking about drug safety or whatever, if we are not promoting or could be interpreted like that, this is the main issue and what kind of information around drugs we can deliver to the public because of this aspect yeah	Interview 14

Problems and Solutions	
Barriers	
External	
Regulators Do Not Involve Patient Organizations	
Excerpt	Interview number
But we have to be invited and it is not often that we work on and I think in the next years it will start to run better but it's a hope now, in the moment it's a hope Because on the AIDS side it runs better but not in cancer side, there is no big involvement for patients on the Swiss Medic side or on the pharma side in Switzerland	Interview 16
Something else which is missing is the implementation of article 102 of the directive, that article says member state should take all appropriate measurements to encourage patients to report side effects and other measures for HCPs but it also says to engage POs in communication on patient reporting	Interview 12
Also the involvement in PRAC is also now accepted and is an improvement but in 2006 we had the trial and most of the PRAC member and the EMA members and the board members in the beginning, they were not very happy with the idea that you should involve patients, they had the feeling that it should not work. Its only that they worked for patients for 3 months showed that the activities in the PRAC for a trial and showed what their input was, and this changed, and therefore every step forward had to (inaudible) in this way.	Interview 3
from side of the regulators, it was the idea that patients could not be of use for regulation and particularly also not for PV etc, they do not understand, it is too difficult etc, I remember that we were advocating that we should have a role there and one of the members of the MEB in the Netherlands, the CBG, told me "but (name) I have studied 7 years for this and I have problems to understand it etc, etc, so why do you think that you are able to do this".	Interview 3
But the problem is that you are not ready when you have patients there. For instance I was for many years the representative of the patients at the PRAC but the same moment I was representing the patients at the CBG at the same moment you are not the one who is able to communicate with the patients so that is not making much sense, important that those ppl are there for organization but they are not the connection with the outside world, for you know that all information is not.. you sign a document that says you are not allowed to say anything about what happens	Interview 3
One from the regulatory agencies, involving patients and PO, I'm not aware of all systems but they are now starting to involve PO, that is something they don't think to involve when they are implementing the system	Interview 7
From the PO side we need to prove that our contribution is absolutely essential and they, from the regulatory agencies side they come with us because they are somehow obliged because in some cases involvement of PO it's just kicking the box, and that is not quite helpful, so from our side from the PO side, based on our contribution we must or we should somehow I'd say prove that our involvement is absolutely essential in order to deal when it comes to PV, for instance to build a more robust system	Interview 7

Problems and Solutions	
Barriers	
External	
Disparities In The PV System Per Country	
Excerpt	Interview number
the second barrier really is that in many countries PV is still not been taken seriously, is placed somewhere between product liability issues, that means that is a manufacturers problem and, once the regulator has looked at the at the efficacy of the drug, the formulation and gives the marketing authorization, what happens post market authorization is an entire business between the consumer and the manufacturer, so that means that the state cannot interfere, so that's the process ok, you patient got a bad badge, go sue them!	Interview 5
if we explain Swissmedic or pharma that this drugs make side effects, then they say "yeah we know it but we can't do others" and that is really special because side effects in cancer care is normal and professionals learn all with a little bit difference to do it with different drugs and to change drugs or to give drugs together with other drugs and that is a process	Interview 16
It's running and if we hear something we can do I think nearly nothing because it's really special, it's not like diabetes or something like a chronic disease that runs always in the same way, and if there is a good drug and the best drug is not the same thing.. so it's really hard for us, for men, for the fight against men's cancer, it's really hard to change something and also PV on this side, I think is not really to become really do something and do it better than it runs I mean it's really really difficult, it's the same thing I think in all cancers side, because chemotherapy is a special therapy and you kill both the good cells and the bad cells and you can with new therapies, immunotherapies you can do it a little bit better but it's only better, it's not changed, the situation is not changed	Interview 16
many other roles this organizations can do, for example collect information from their members, if there is special concern, for example the risk management plan summary, I think this document are overlooked and not used as they could be, they are excellent to explain on what we don't know about the product about the time it is authorized	Interview 12
And not to talk about things which are, in societies like Bosnia, there is no PV really	Interview 11
And also there is lots of differences in different parts in Europe because it's not developed in the same way. So I think is a very difficult question to answer because like with the whole EU operates in a way that they say "oh health system are not the method for you, is the method for individual countries to sort tax" so you have huge disparities, and huge differences in resources	Interview 11
Croatia is organized but I can see in the region from working with the umbrella organization what is the sort of terrible things that are happening, and no one knows about it or they don't care.. I don't know... I think they do care but there is no system...	Interview 11

Problems and Solutions	
Barriers	
External	
Disparities In The PV System Per Country	
Excerpt	Interview number
When you talk about EU alone, there are such diversities of what it's possible, and it's really determined by the market of pharma companies, and lots of this work of pharma companies are thinking that PO would do, but they can't, it's sort of .. not possible to do something so responsible on a voluntary basis, you can't do it. You can spread the voice but you need to get the health system involved.	Interview 11
At the moment I think there is lots of Lip service to patient involvement and patient centered and this and that, and that lip service the more you go to central Europe, southern Europe, this little countries, is really not doing anything truly, unless you find an individual Dr who is really serious and takes serious what he does but as a system, I don't think it exists.	Interview 11
It is very difficult sometimes to stables and having in mind the daily life and what is the consumption habits of the population, sometimes you may be experiencing some effect and you think is about this drug and ppl don't report taking supplements or teas or herbals or whatever and this could be helpful if we can have all things because they are taking them for therapeutically reasons so they should be under the same PV system, I think this would be useful.	Interview 14

Problems and Solutions	
Barriers	
Internal	
Budget and Funds	
Excerpt	Interview number
And also a problem ofc is funding, compared to other countries in Europe, the Dutch situation, we are rather rich, but we also have a lot of obligations, we have to print 4 times a year 2,5 thousand times a magazine, we have to have a website and we have to organize hospital meetings and symposiums, it's very expensive,	Interview 13
We usually participate in the creation of these materials, we reach agreements with administrative bodies or with professional organizations and we elaborate it together. Above all, have a very limited budget, very small so we cannot afford to make the materials ourselves, but we do participate in those that do and this is usually or the Ministry or the National School of Health. The latter especially and we co-participate in the use of appropriate language and then in its dissemination	Interview 2
It is the lack of budget of the patient organizations to generate ourselves this information, this is another barrier at the level of the organizations.	Interview 2

Problems and Solutions	
Barriers	
Internal	
Budget and Funds	
Excerpt	Interview number
I believe for the patients, I see the inconvenience of notifying the mild ones because they can hold up or vary the medication, but come on! I would say that the main barrier would be to have many more things to worry about and then not have the budget to do, for example, this type of material that I told you about in general.	Interview 2
So somehow that is linked with the lack of resources, lack of human resources and money ofc, fundraising because when you think of doing some activity, you need to have ofc the funds for it, you can try producing materials or whatever and human resources, someone to do it.	Interview 7
No I think we've covered everything because as I said my knowledge is very limited and I think what has been interesting through this process for me is that pharmaceutical companies have been waking up, that we had contact with, seem to be waking up a little bit more to the fact that we do have a lot of very useful contact with the community and they are very restrictive about their code of practice and they are not always brilliant at the language they use with the community and if we can very much work with pharmaceutical companies to assist with that, but at the same time that can deflect from our core business so we have to think carefully that if we do this work in partnership in pharmaceutical companies we need to have some financial help to do that and then that gets quite tricky but a huge amount of my time is gone in getting this drugs to the ppl and helping the pharmaceutical companies ..	Interview 4
lots of umbrella organization, to exist, focus on activities where they can raise funds and PV in my experience, there is a lot to talk about it but it doesn't trigger that,	Interview 11
Resources for Po are limited, there are also culturally sort of determined things. IN some countries you have particular ways of PO being organized and funded. In UK is a huge organization, it employees staff, you know in Croatia, we have one and a half person working, it's on volunteers, but the volunteers sometimes come and sometimes they are not well or they have other things, so the barriers are actually PO themselves, and I don't think it's realistic expecting PO to do what pharma, pharma in particular expect us to do, because it's become very popular, it's been in to work with Po but it's sometimes just a token, just ticking the box, so that is worrying thing if you go to countries which are not organized.	Interview 11

Problems and Solutions	
Barriers	
Internal	
Education	
Excerpt	Interview number
-Well this is, this is a very important questions, because we are volunteers, and some of us work, but we just want to do a very good job and we want to raise awareness and everything but we lack the professional knowledge, we really do, we need , and this is also what could be better with staff, we could also have audiologists employed so that we have professionals working with us, because when we are volunteers, you can just write a report, you don't need to put up any references and so what is it worth? What professional would value that kind of report without references? so it is really hard to have the understanding? But were working on it	Interview 1
But this also means that they have to learn patients to understand their medicines and give information about it, also education is very important. For most of the patients nowadays do not know anything about the medicine. They read the magazines or the patient information leaflet, they often get nowadays and it will frightened them and some of them will not even read anymore.	Interview 3
Yeah, they do not know the system very well. Some of them improved, if you look for instance to Eurordis, Eurorids has a good understanding of how the system works but many many patient organizations and particularly disease related organizations, have focused on disease information about the disease, if you listen for instance to other people, they often say, "yes" but they are only interested in the disease.	Interview 3
normally they have not enough role approach but they are reacting accidentally when there are question on a particular medicine for instance	Interview 3
You can't say "oh I have an interesting patient! Send him and make him our officer on PV!" It takes him time to get introduced to learn the language to understand how it works etc, so you must have training and I must say NCA should could play a very important role there but they are not doing it at the moment	Interview 3
too many PO really have the idea that regulation of medicines is about the marketing authorization of the medicine, that's very important. PV maybe they heard sometimes about it, but yeah… they are not really interested in it, for most of them pv	Interview 3
-Yes, we don't know that system	Interview 4
But I would've thought there should be some sort of system that whenever a patient organization brings up, its supporting information support and advocacy, that there should be some sort of alert that this are now active in the area of certain condition or certain drugs, therefore there should be some communication that says " are you aware of this role" or equally if a new drug emerges , the authorities contact any organizations working in that field to make them aware to what happens next, what are their roles and responsibilities of the stakeholders.	Interview 4

Problems and Solutions	
Barriers	
Internal	
Education	
Excerpt	Interview number
The only question is .. even if you report it, how is the data then used and what happens with that data really?	Interview 11
Now I don't know what happens with this? apparently with one of our meetings, we asked a representative of HELMED to tell us what patients should report and he said "well, whatever they think is not normal" you know what every if they have rash or if they have... I don't know diarrhea , whatever they have they should report. First	Interview 11
I mean what happens with this data? Is there any change on how drugs are used? unless it's something really drastic I suppose someone dies or has a heart attack or something	Interview 11

Problems and Solutions	
Barriers	
Internal	
High work load	
Excerpt	Interview number
Ahhh .. I have to think about it, I think at least most of the work of our organization, this are 6 ppl who are working on it, not every member or patient member is actively working, so as you imagine it's already quite hard for us to get to really publish a newsletter, we publish many information on new treatment and on diagnosis, so we already do a lot of things	Interview 8
but we have full time employment all of us, and we do this on a voluntary basis. So I have like 2 full time jobs actually. So that is part of it, I suppose that as soon as we get some staff we can probably be more organized.	Interview 1
-Yes yes! we could be more organized but we have some staff who can maintain a lot of things but they are busy with the data base..and it takes time, its time consuming, and so that's part of it. And then, to know the system, to know the questions that you have just asked it talks about knowing the system, to know how the system works because it's not my responsibility	Interview 1
have very broad activities also -Yeah, that is also a problem! I'm too busy, I'm also involved now, in the last 3 years, I was very busy with that, with the European joint program on rare diseases, academia	Interview 13

Problems and Solutions	
Barriers	
Internal	
High work load	
Excerpt	Interview number
So I think that is very important, but we are a volunteer organization, we have 15 ppl, most of them are organizing hospitals meetings and sufferers contact meetings and only a few of us, I'm the only one who is doing the things outside the organization and that is creating a lot of work, but I do think it's important that patients are aware of reporting side effects and we do have a role on it, absolutely.	Interview 13
The main barrier for us would be that we have so many issues to deal with that pharmacovigilance is not always the most important. That is the main barrier, for us to insist more on this matter. On the other hand we can not only be talking about pharmacovigilance, there are other issues, and then we must also be rotating subjects. So this is for us our main barrier as an organization.	Interview 2
I believe for the patients, I see the inconvenience of notifying the mild ones because they can hold up or vary the medication, but come on! I would say that the main barrier would be to have many more things to worry about and then not have the budget to do, for example, this type of material that told you about general	Interview 2
Because we are a voluntary organization, so we feel we have already plenty to do and only if it's really necessary we could be ready to do more of this job, as you have heard from my reply, we are already quite active in the field.	Interview 6
No I think we've covered everything because as I said my knowledge is very limited and I think what has been interesting through this process for me is that pharmaceutical companies have been waking up, that we had contact with, seem to be waking up a little bit more to the fact that we do have a lot of very useful contact with the community and they are very restrictive about their code of practice and they are not always brilliant at the language they use with the community and if we can very much work with pharmaceutical companies to assist with that, but at the same time that can deflect from our core business so we have to think carefully that if we do this work in partnership in pharmaceutical companies we need to have some financial help to do that and then that gets quite tricky but a huge amount of my time is gone in getting this drugs to the ppl and helping the pharmaceutical companies ..	Interview 4

Problems and Solutions	
Barriers	
Internal	
Language	
Excerpt	Interview number
Ok the first thing is that I think is very important that member organizations educate the patient to use controlled vocabularies, as you know controlled vocabularies are terminology that are clearly defined and therefore they have test on them and they are reflecting what it is, for instance nausea, I don't say I'm throwing up, I need to identify it saying I have nausea of taking this drug, and that term as a controlled term would be easily picked up by the various algorithms, if ppl start writing things differently, … so that is number one ok? Then at the same time we are actually asking, the other side of this is ok, patients will always say how say how they feel with (inaudible) language and we try to promote systems to be more reactive to focus on common terms, ppl may not call the same thing as they are, for instance the term intoxicated can be in several ways	Interview 5
So they make different suggestions and for example webinars so we can participate but as you know in Europe there are many languages and MPE is running in English so, I don't know how many ppl are participating in webinars and so on. And now (inaudible) is a patient advocate and MPE is running each year they are running programs to educate patient advocates	Interview 8
-I think one problem is the language, most of my companions don't like or are not good able to communicate in English and most documents are in English, so this is a real (inaudible)	Interview 8
-Oh, it's only you, it's not a topic that the rest of the organization members, I mean the staff… interupts -No, no, not really. Because we are just very much working about informing our patients companion about new treatment about clinical trials so we run a very special data base about clinical trials. We translate several documents from English into German so that really every patient can understand it, you can imagine that it takes a lot of time, ohh this is quite a long time!	Interview 8
I think that one of the main things that we have to do is actually to adapt the language for the common ppl and to agree on one terminology that would be acceptable and understandable	Interview 15
but not everyone speaks English and ppl are often more comfortable in their native language so what this is about is that ppl are members of different forums and pick up information and then can translate, in that way cross language barriers,	Interview 9

Problems and Solutions	
Barriers	
Internal	
Language	
Excerpt	Interview number
In the beginning that was the intent by education because of my own background I found it , somehow it didn't seem fair that I was able to read that information and make decision because of it while other ppl just couldn't and it didn't feel right and so my first, real motivation behind everything when I started was basically to get medical information to the ppl who really needed it or who needed to make decisions	Interview 9
because the national organizations worry about keeping ppl safe and finding information material in their own language because English is nice but not everyone speaks English	Interview 9
I think we would be asking the medical consulters to work with us because there would be conversations using scientifically and technical language that would pass. Go over my head for instance, so it's important to have that knowledge as well.	Interview 4

Problems and Solutions	
Barriers	
Internal	
No priority	
Excerpt	Interview number
Yes, yes I think one big barrier is what is present in their own country, for instance if there is universal care health and access to medicine is covered by adequate funding, in those scenarios PV is highly recommended, I would say becomes very important and is applied now. Where there is fragmentation of health system and there is no supply, where there are shortages of medicines, now there someone focuses "I just want to get access to drugs, I'm not concerned about the quality of them, I'm not concerned about the safety of them, I just want drugs" You know that desperation of them, PV becomes superfluous, what they really need is somebody who really really understand what is going on, why it's important and therefore this is why we are actually supporting, 90% of the issue could be health financing, remove that, health care should bring financial protection and make sure affordable essential medicines are listed there You know when you have no drugs, what is the point in me telling about PV?!!!	Interview 5
what is missing is maybe not the political willingness but sometimes someone needs to decide OK, I take it as my role in my organization so see how organizations can start implement this guidelines.	Interview 12

Problems and Solutions	
Barriers	
Internal	
No priority	
Excerpt	Interview number
Normally they have not enough role approach but they are reacting accidentally when there are question on a particular medicine for instance	Interview 3
too many PO really have the idea that regulation of medicines is about the marketing authorization of the medicine, that's very important. PV maybe they heard sometimes about it, but yeah… they are not really interested in it, for most of them pv	Interview 3
First I'd say that the first barrier is not to put drug safety at the top of their priorities because the national organizations are somehow more concerns about other aspects for instance access to care, proper access to care which is I think in many many countries a huge problem, for instance discrimination problems which again in almost every country it's a huge problem.	Interview 7
Ok, you said not putting this as a priority, should it be a priority? -Well there are huge branch of PO, if you look at the specific disease PO, diabetes, cancer whatever, they pretty much focus on the disease and there are some diseases where the drug safety is not really on top of the agenda Ofc even ppl with diabetes can take other drugs that are not linked with diabetes and so drug safety at the end of the day is essential for all of us. but then if you have an NGO which are more broad than that, consumer organizations for instance, they are more prone to look at drug safety as a priority, ofc if you have a disease, that drug safety is essential, is key at the moment, they are more prone to put it on top of the agenda. But then it links always with the resources that are available to do something.	Interview 7
ahhh if they don't see it as a priority, they won't do much. they need to perceive it as a priority as you said the concerns are more focused on getting access to new drugs and new medicines, reimbursement which is quite heavy, what we can do to promote it is to show that the drug safety is along with the reimbursement of the drug, a key issue for the ppl.	Interview 7
Just because drug treatment, it hasn't been a topic, that's been trying to get access so we haven't even really got into the monitoring and thinking widely about the implications, were a really small organization and just understanding the NICE appraisal process and making submissions to that, it's just about (inaudible) into the ground.. so implications haven't hit us yet.	Interview 4
we don't see yet and could be a major benefit is more questions, more curiosity from the public, to see how PV is organized, and we have complaints, not in all countries but in my country in France in particular we still haven't change the minds, many patients are more in the complaining mood or state of mind and the complexity of the PV system doesn't help, they expect the national authority can decide or at least listen and then analyze and respond to their concerns, but then it goes to a committee at the EMA and then another committee and then the European Commission	Interview 12

Problems and Solutions	
Barriers	
Internal	
No priority	
Excerpt	Interview number
So there are all this other activities where we know that PV experts don't have the time to engage with patients but we need the organizations to be proactive, we need them to reflect "OK, we have this leaflet, it is very well written, it explains very well the problem and what to do, but we know behaviors does not change, so what else could we propose for the patients to understand what needs to be done and I don't know if you listen to the public hearings that the EMA organize no valproate sodium or quinolones but for us it was very clear they ask the patients who are in this analytics state of mind, they know the problem and they think of possible solution to improve the situation and there are other organizations that know the problem but they are not with a state of mind to make constructive proposal, they complain basically, they want to see everybody to the court and etc etc But when we ask them, what can we do? what would you suggest to improve, they don't know, they haven't thought of it, they haven't discussed with PV experts, they are not ready to respond	Interview 12
Many organizations they are just about support and they haven't even understood and they haven't even reached to authorities because it has never crossed their minds so for me that is why I thought that ESMO or the patient advocacy track at ESMO had such an important place for this kind of thing because there you also reach organizations.	Interview 9
Sometimes ppl have like, they have this hate/love relationship with drugs because they know they depend on them to feel better and to have a more functioning life and better quality of life, but they are really very afraid of adverse possible events on the long term and they don't like to take chemicals and the need of taking medicines so this can also be a barrier	Interview 14
another problem we have in Portugal, it's the engagement of the public with POs, for instance most of POs complain that they organize and activity, a workshop seminar for patients and the attendance is sometimes very low, ppl register, ppl say it's very interesting and they congratulate the organization and then when we go to the event, the percentage of participants can be very low.	Interview 14
it takes some time for ppl to be ready to understand the information because there are a lot of things going on so it takes time. I still remember, there is this initial phase when you start taking any drug, especially when it is for chronic conditions, then you start by reading the information leaflet and when you start taking you check every possible reactions that are listed in the information but this is, as far as I remember from my experience when you start, because at a certain point it becomes less important so you only go to the leaflet if you have any problem and then you go and check if the problem is listed. There is a different perspective, when you start you first go into the list to make sure when you start taking medicines for chronic conditions and after a while you stop worrying about that and go to the lsit when something happens	Interview 14

Problems and Solutions	
Barriers	
Internal	
Staff	
Excerpt Copy	Interview number
Yes, no, no that's right! On this side it's also resources in form of man	Interview 16
do you consider PO have an important role in promoting drug safety in PV? Seeing PV as a wide range of activities, do you think PO have anything to do there? -Yes, they should! They should but they have to have enough manpower	Interview 8
-Depends of our men power and at the moment most of us are patient under treatment so we have to struggle, so you know we have to change our meeting several times because I have been to the hospital, yesterday I have been to the hospital and I will be many times more!	Interview 8
But then we are all volunteers and we are also looking for staff of course, because we need someone to work professionally	Interview 1
Well, the first difficulty is having a condition ofc -Having a condition? -Yeah, I have a pituitary condition myself and well, the ones some moments when you can't work on the same level and then I got involved in the PO and it took me a few years to know, everything is a big work to know more things so you can work together with all those organizations and persons.	Interview 13
It took a lot of years, I was ill in 2007 and I started with the PO in 2012, in 2015 I became Chair of the PO, so I've got 4 years and 2016 I became active in the European Network, so it's a process, in 2015 I asked the Eurordis summer school and in 207 I started the EUPATY course, so it's all falling right after each other and I think I'm growing in my role and also we are recognized as an organization, you are asked for input and that is very nice but we are still a volunteer PO, having 50 volunteers, it's difficult to find the ppl for different tasks	Interview 13
yeah we have to find ppl and ppl starting out with being a FB moderator, then they like to write articles for a magazine and then eventually I hope they would be active on going to the meetings or MEB, and being interested in PV but also be interested in the context with hospitals and pharmaceutical companies and that is something I do alone, it's very vulnerable, I know that	Interview 13
hey need someone to volunteer within the PO, to be trained, understand in the country how PV is organized and to organize the dialog between their members and the NCA or the marketing authorization holders, without that we won't see much progress, because even in the best case typically NCA are working with a very small number of national actors, national POs,	Interview 12

Problems and Solutions	
Barriers	
Internal	
Staff	
Excerpt Copy	Interview number
-No, there is not the capacity for it, you need people, not only ppl but you should have a dedicated person in your office and there are often very small offices but you need to have a dedicated person in your office who knows about the regulatory system, who knows about medicines and this must be a very strong involvement of patients themselves. There are organizations, mostly foundation fund raising organizations, mostly for asthma for instance who have ppl who know a lot about it, but those ppl are professionals, are not the patients themselves, what you need in PV to understand what is the perspective of the patient, what are the experiences of the patients, you don't need to have second hand information but you need the information of the patients themselves.	Interview 3
the problem is that they are working with mostly volunteers and you have some volunteer that is willing to do it and that has a tremendous interest in it, but then that volunteer is leaving, dying whatever, and stops.	Interview 3
because we are a voluntary organization, so we feel we have already plenty to do and only if it's really necessary we could be ready to do more of this job, as you have heard from my reply, we are already quite active in the field.	Interview 6
Yes, the amount of volunteers and time	Interview 6
So somehow that is linked with the lack of resources, lack of human resources and money ofc, fundraising because when you think of doing some activity, you need to have ofc the funds for it, you can try producing materials or whatever and human resources, someone to do it.	Interview 7
So that are the barriers that I have seen and ofc, again to find someone who is able to work on that aspect.	Interview 7
Well, that is another thing that PO face I think is at least very common in the European level , at the national level I know for sure we struggle with the lack of resources, we have lack of.. our work is based on pro-bono and volunteers.	Interview 14
but the thing is that POs have lack of resources, human resources	Interview 14

Problems and Solutions	
Strategies to Overcome the Barriers	
Awareness Campaigns	
Excerpt	Interview number
Yes, I think that is on the government side and also on the side of the Swissmedic, they have to do more advertising for it, otherwise it's not enough	Interview 16

Problems and Solutions	
Strategies to Overcome the Barriers	
Awareness Campaigns	
Excerpt	Interview number
Yes, I think that is on the government side and also on the side of the Swissmedic, they have to do more advertising for it, otherwise it's not enough	Interview 16
we can push our patient groups to share their experience wish Swissmedic and more we can't do, and Swissmedic and the goverment must do more advertising for this possibility and then I think it will run better	Interview 16
Oh, but there is a talk in the meeting, there is a j about the function of Lareb, also from IGE, also from the health inspection, so PO are made aware but maybe not enough	Interview 13
But back to the individual patients I think that one important message we need to convey is ofc for them first to report to their Drs, I think that is a thing, they say tehy spontaneously discus with their Drs quite often when they have a side effect, can be a GP , or specialist, I think in rare disease the message was conduct, then in addition, still report it even if their Drs know that is something that is not yet generalize but that is something we still need to communicate to them, the importance that they all report everything that is happening to them	Interview 12
but what are the appropriate measures is the question. I think you can't implement this unless you organize a meeting with organization that could be interested to discuss what can we do in our country to pass the message to patients, I know that PO don't have a huge budget for communication but we have the scope joint action awareness week on patient reporting, prepared by the MHRA and we've seen the impact of this campaigns which are not used in all member states but in the weeks that followed, there is an increase in reporting, and I think we have to explain this relative success in countries this has taken places but also in other countries which hadn't participated in the reporting awareness week, that is another way to iniciate the discussion	Interview 12
When the pharmacist dispenses a drug would do well to recommend the patient, that if he observes anything, inform him to report that adverse effect. The same should be done by the doctor when prescribing the drug. In other words, the patient must receive from the patient's association, from the prescribing doctor and from the pharmacist who is the one who dispenses the drug, the indication to inform any adverse effect suffered	Interview 2
On the other hand, we have to act also on the administration, and within the administration I include the Ministry, the Spanish Agency of Medicines and Health Products, including the National School of Health. In short, all these organizations or institutions have to ask them for information campaigns as well. In the end it is what has most impact, the information campaigns to all patients.	Interview 2
Here you also have to be careful not to generate alarms, but treat it with the naturalness that it requires and send it to Patient Organizations.	Interview 2

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Excerpt	Interview number
I believe that right now we would be interested in disseminating general information to patients, so that they observe and participate in pharmacovigilance, but of a general nature. To notify even mild effects, because of course, which is a serious effect, that is notified! but also notify the mild ones and I would like, to have a material that concretely worth us to spread this.	Interview 2
the easiest probably would be to have an open day or like a working group of patients, advocacy groups and then just invite them to a national authority and show how what the national authority does, just exposure to start with	Interview 9
I can report by my medical doctor, in the consultation in front of the medical doctor and then the medical doctor can report it, or I can report it by myself which is the best, so promoting the portal among the members of the national organization could be quite useful.	Interview 7
I think they should have awareness campaigns, I haven't heard they do, so they should sort of have national activities about awareness of the importance of reporting drug ADR	Interview 11
Looking for it, maybe having at the clinics, Drs, maybe they are having something that ppl can be given, that says if you have a side effect please report it.	Interview 11
in the same way they should be aware of what EMA is doing in Europe, because that is what determines lots of things in different countries, so there is lots of , sort of lots of information missing, until you get ill, then start looking for things	Interview 11

Problems and Solutions	
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Dissemination Means	
Excerpt	Interview number
But now that you mentioned, that you inform and send information to your members on how to report, where to find the badge and all this kind of things, how do you do that? is it email? how do you have... -Both our guidelines are email, social media is quite good, in fact one of the ways, because with social media we can share image files and things like that. It helps to photograph badges and things like t	Interview 5
Yes, I think that is on the government side and also on the side of the Swissmedic, they have to do more advertising for it, otherwise it's not enough	Interview 16
No, we have the newsletter on the website	Interview 16

Problems and Solutions	
Strategies to Overcome the Barriers	
Awareness Campaigns	
Dissemination Means	
Excerpt	Interview number
That's a really good idea! Ok let me ask you, Eurordis gave you the training but what if it were NCA, first of all what strategies could help to strengthen the communication you have? Like PO have with the NCA in PV, what would you like that communication to be? -I think the authorities should contact the PO, or they have to use media but not only FB or tweeter or so but also … our cancer is more or less older ppl so they don't use so much the new media, so you have to use other channels.	Interview 8
When for instance you do that, we have a newsletter and we can write about our conference and we also spread, we are European Federation, but our newsletter is spread worldwide. The European Federation is the largest Federation of Hard of Hearing people so that would help spread, and I'm not only talking about the European Associations but in Africa they have other associations so they have for instance, treatment for malaria that could cause somebody deafness, so that would be useful for them as well to read about this and to raise awareness in that area.	Interview 1
newsletter	Interview 1
Yes, you see the power of patient there because we have FB pages, I'm not on FB but I have a few moderators who are on FB, and you see when something is happening, patients say "ohh I have the same problem "and before you know you have 25 different patients saying that they share the same problem	Interview 13
And also we are building a new website now and I think it's important that we have a special page on PV we don't have it yet, but I think it would be very important to stress out to patients why it's important and what is PV and what benefits there are from them to make reports and also to go to the website an look for themselves what is in the databases	Interview 13
And also when a tv program is making an interesting item on it it's shared on FB, then ppl are saying, yeah I have problems also and then you are trying to make an article on the website or in the magazine to inform ppl all together, that would be easier	Interview 13

Problems and Solutions	
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Not just helping with a form, when there are safety alerts, sent out by NCA, often they don't know who to send it to, the case was when there were various avastin which were contaminated and some were used to be injected in the eyes of patients with macula degeneration, but only the organization for breast cancer received first the information of some contaminated vials, because the avastin was by that time was an off label use, you don't know as a regulator which are all the organizations that could receipt your communication but contrary if you would send out the same information to each organization, they would decide, "oh this is extremely useful for my patients, my members, you cannot expect regulators have an eye on all possible users, particularly in rare diseases, all patients are using different medicines of label, you would not think of it in the first place you should not pre-decide who should be the receiver of your information, you should release it and trust ppl will understand which one is relevant for their members	Interview 12
For the patient organizations that are part of the forum, the main vehicle is through the web, but it will be from the new website or the email, except this month precisely that we have the assembly in March, except once a year it is rare that we all see each other, not even in the assembly we all see each other, because not all come well	Interview 2
by phone or face to face	Interview 6
We have been asking ppl to use or check out webradr and the Croatian equivalent and the Dutch one, but somehow is like .... yeah I don't know it has never really created like the buzz that ppl go "yeah that's really cool, that's really helpful" because it's not,	Interview 9
we re-tweet, what the European medicines agencies, re-tweet for instance put on the twitter page the key message. What we do is only to broadcast the key message of the EMA which is good but is not enough I don't think it's enough to be fran	Interview 7
And for instance in the regular meetings for instance, when a single organization as a web page and some of them have programs on radio or tv shows so they are using those key materials in that aspect to reach out the ppl in the country. That's what I see should be then.	Interview 7

Problems and Solutions	
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Excerpt	Interview number
I think the way they are approaching it may be effective because somehow they are approaching the organization that are more willing to work with the NCA and using this group of organizations to promote it outside that group, ok? Because otherwise, you can have a communication channel to all PO, you can see the website and they have the website so ppl can log in the website, you can have a newsletter which is sent to all national organizations, it may be useful but may not be useful because somehow our email is full with letters and information and the newsletter might get lost in the email box and they may not have progress in that, ppl may not read it or they read it if they see some article that is really interesting for them.	Interview 7
, we would, for example we operate we have social media daily, we have a monthly e-news and we post, anything that is being posted as an notice on our website goes into that monthly e-news, and a lot of ppl from SMA community has signed up to that and reed what's in it	Interview 4
the problem is you've got to sign up for this, you pharmacovigilance, you have to think of GDPR or whether or not they bombard us with information.	Interview 4
I take let's say, I retake it seriously that we should call our patients, call who has contacted us, who has sort of not involved but they are part of the organization, we know them, we make aN appointment calling them every 3-4 months and making sort of an interview and the things they tell you in this interview, it would be fantastic to report it to someone because I don't think that is recorded anywhere properly The problem is really having someone having a system and having some system using that information.	Interview 11
developing digital solutions like videos we try to promote "let's do things on video and put it on youtube and ppl can watch it whenever they want, whenever they need, wherever they want" we must understand that patients and public is not very used, it's now happening and it's growing, but they are not very used to be involved or to be informed of to be active, they usually rely on Drs, so they sometimes don't understand they can have a role and they have a role and they need to be informed,	Interview 14
take advantage of the technology and this days ppl use mobiles and internet and laptops to get information, then create information that is available in this digital platforms-Because sometimes I have the feeling from our social media that most ppl would like to have their own private sessions in their own sofa,	Interview 14

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They also have well nowadays they also have the different units for PV have a social media page, on Facebook, in Portugal Facebook is very popular so it's also a good way of communicating with POs and the general public and well I believe most of ppl would subscribe or go and look for PV unit so POs we try to follow and share any information that is relevant for us, for instance, the national authority has a newsletter, they have a lot of different ways of communicating with the POs and the general public, everyone can subscribe the newsletter and they send regularly information around different topics, including PV, so this is very good	Interview 14

Problems and Solutions	
Strategies to Overcome the Barriers	
Proactive National Competent Authorities	
Excerpt	Interview number
No, I think PV system needs to keep on evolving, we have now new classes of medicine coming up, we have gene and cell therapies coming up, they need to be treated differently, we need to ensure that the… proactive and not reactive in the way things are, at the moment many ppl are leaving (inaudible) but we need to be proactive	Interview 5
That's a really good idea! Ok let me ask you, Eurordis gave you the training but what if it were NCA, first of all what strategies could help to strengthen the communication you have? Like PO have with the NCA in PV, what would you like that communication to be? -I think the authorities should contact the PO, or they have to use media but not only FB or tweeter or so but also … our cancer is more or less older ppl so they don't use so much the new media, so you have to use other channels.	Interview 8
-I think that.. I met Gerda at a symposium of nurses, that was a 2 day event, somewhere in the NL, and we were there with 20 PO and Gerda met up with every PO telling about the work of Lareb, and that's how we met, so it's coming from both sides. Being active in engaging the PO	Interview 13

Problems and Solutions	
Strategies to Overcome the Barriers	
Proactive National Competent Authorities	
Excerpt	Interview number
They need someone to volunteer within the PO, to be trained, understand in the country how PV is organized and to organize the dialog between their members and the NCA or the marketing authorization holders, without that we won't see much progress, because even in the best case typically NCA are working with a very small number of national actors, national POs,	Interview 12
If I may, something else, we would be interested in and we see there are some development in PV public hearings are excellent, extremely useful the ones that the EMA organizes, why not having the same organized at the national level, maybe on another topic but even for the topics that are discussed at the EMA, I think there is enough space to have a similar discussion at a National Level because when you follow this debates you see that it's abstract, it's very concrete so the ppl would come together because they want to solve a problem, at a national level you won't have the language barrier that you have if you do it at EMA and yet you need to implement national solutions and I think that is another way to engage with public and to gain trust on PV	Interview 12
first of all to develop very good communication strategies about certain medicines	Interview 15
. I think in the beginning the NCA should play an important and proactive role, they should think about the offering a package or training package for PO, in particular to small PO and they can do this ofc together with the working group of POs they have because, the package must answer the needs of the PO and otherwise it will not work	Interview 3
if you have a personal connection to an institution and you can say you know the ppl there, I think it lowers up the pressure of picking up the phone and asking for help or saying "what am I supposed to do here?" or what can you do for us or this material is good or not?"	Interview 9
I'm not sure if they can help out with resources, I think that is something that is responsibility of the NGO but what they can do if they are starting to involve PO more, they are creating the need from the PO side to fulfil that need ok? In a way doing so the NCA are helping out in putting it on top of the agenda this message.	Interview 7
But it's not for PV, its much broader than that meaning that they say ok "we want to work with the organizations, we want to integrate you in our committees, in our work" so it's more broad that that, it's not only PV. What I'm thinking on is that maybe, maybe it could be a good idea coming to the pool of ppl or organization saying we have a need on the PV system to integrate organization, so which organization want to work with us. For instance in the Portuguese system, in the PV system in Portugal, there is not a single PO working with the NCA, if you look on the board of the committees there is not a since patient organization, which I think (inaudible)	Interview 7

Problems and Solutions	
Strategies to Overcome the Barriers	
Proactive National Competent Authorities	
Excerpt	Interview number
I think the way they are approaching it may be effective because somehow they are approaching the organization that are more willing to work with the NCA and using this group of organizations to promote it outside that group, ok? Because otherwise, you can have a communication channel to all PO, you can see the website and they have the website so ppl can log in the website, you can have a newsletter which is sent to all national organizations, it may be useful but may not be useful because somehow our email is full with letters and information and the newsletter might get lost in the email box and they may not have progress in that, ppl may not read it or they read it if they see some article that is really interesting for them. So the way forward I think is introducing a group of organizations that may be more active and they can use that channel to open up to other organizations afterwards.	Interview 7
Well I think making the communication! as far as I'm aware there has never been any with our organization	Interview 4
But I would've thought there should be some sort of system that whenever a patient organization brings up, its supporting information support and advocacy, that there should be some sort of alert that this are now active in the area of certain condition or certain drugs, therefore there should be some communication that says " are you aware of this role" or equally if a new drug emerges , the authorities contact any organizations working in that field to make them aware to what happens next, what are their roles and responsibilities of the stakeholders. So for example here NICES had a huge list of stakeholders for the appraisal process for the drug, if its accessible then surely that same list would go to the pharmacovigilance authorities to then get in contact and saying "this drug is now made available" we invite you to play this role in PV. Again I'm making that, I would imagine that might happen	Interview 4
NICE would say to all the ppl taking part , you know we have sent this as part of our recommendation we are now also saying that all stakeholders should now play a role in it. So NICE could play that role in England making ppl alert to the existence of this authority and, you know, what should happen in the (inaudible) maybe that would happen, I don't know!	Interview 4
inviting maybe a port of contact suggesting we can come and talk further to you or you can come and tell us	Interview 4

Problems and Solutions	
Strategies to Overcome the Barriers	
Proactive National Competent Authorities	
Excerpt	Interview number
Yeah, that would be quite good, because I think they only actively maybe someone in HALMED actively looking at PO and you know, sort of approaching them, because I approached them, and they didn't approach me, they were very quick to respond, but I approach them, this is important, being proactive.	Interview 11
Besides that, this are the activities towards patients and the public and sometimes I'm also invited to be a speaker in some events organized by the college of pharmacists or I remember for instance last year in December I participated in a meeting that was promoted by MEP, member of the European parliament and that was addressing also the drug safety issues and I was invited to be as a member of the PO to provide a perspective and the need of patients so this is also the other kind of activities we are in	Interview 14

Problems and Solutions	
Strategies to Overcome the Barriers	
PV Communication Network	
Excerpt	Interview number
this is communication coming down the other side, so we have disseminating this, especially if you are a simple small organization, that organization knows everybody . It's pointless to get to national media to get to this particular group of patients when all you need to do is ring up the communication offices for that organization and let them know what is happening, if there is a new guideline on the (inaudible) So yes we have both together, up and down to represent.	Interview 5
is a cultural change that leads to a national pv police, they need to work with the patient groups and build up that cultural cooperation and trust because that is essential.	Interview 5
That could be very relevant, because we have our network, we have our members so it would be very relevant that we send out this and that it shows that we worked on this and it would also be very relevant when we have our conferences that somebody like you would come and talk about this and tell us what is all this about,	Interview 1
For the first version, it would be nice to spark interest within your volunteers population, well it's one aspect of the work you can do for a PO and I would be very happy to transfer the email address with the problem with medicines to other patient representative in the organization, It would be very nice,	Interview 13

Problems and Solutions	
Strategies to Overcome the Barriers	
PV Communication Network	
Excerpt	Interview number
we propose to have one contact person in each organization, the same way the legislation provides one contact, a qualified person for PV in industry for each company, we have a thought on that for the PO but we clearly see a missing link here, first to organize the communication between NCA and patients, ofc you have the classical channels, the HCPs letters etc, but in parallel, I think we should discuss how to efficiently and rapidly access the patients, often regulators want to know, they have questions such as "do you know if patients receive the information?" and they would like to ask the POs if they have feedback from their members, but they do not know who to contact or they would have to consult with PO when they are preparing materials for the public, a press relay, it can be any information for the public, they don't know who to contact to see if that information can be understood easily by a larger public	Interview 12
When there are safety alerts, sent out by NCA, often they don't know who to send it to, the case was when there were various avastin which were contaminated and some were used to be injected in the eyes of patients with macula degeneration, but only the organization for breast cancer received first the information of some contaminated vials, because the avastin was by that time was an off label use, you don't know as a regulator which are all the organizations that could receipt your communication but contrary if you would send out the same information to each organization, they would decide, "oh this is extremely useful for my patients, my members, you cannot expect regulators have an eye on all possible users, particularly in rare diseases, all patients are using different medicines of label, you would not think of it in the first place you should not pre-decide who should be the receiver of your information, you should release it and trust ppl will understand which one is relevant for their members	Interview 12
They are doing the same ofc, they are explaining, they have to explain to the membership, but what is the membership of an umbrella organization, the membership of an umbrella organization are the patient organizations. But if you call to the level of the national organization you will see ofc that at the end of the day the members of the organizations are the patients themselves and the information has to drain down to the patient themselves, if its locked into the, in the knowledge of the organization but they do not reach the patients themselves, there is a need to have that information. And they can only play that role if they are working close together . S	Interview 3
-No no of course, it should be a normal activity for every PO, if they have an interest in medicine, in pharmacocological medicines, ofc there should be throughout the whole organization but to come that far you need someone who is an officer or a group for instance in the organization, a group of patients in the organization who are interested in PV that will have the ability and the knowledge to understand what is going onon PV but ofc it must be an interest for the whole organization	Interview 3

Problems and Solutions	
Strategies to Overcome the Barriers	
PV Communication Network	
Excerpt	Interview number
First of all, we have to inform and train the patient organizations that are part of our coalition so that they, in turn, urge patients to report any adverse effects they may have.	Interview 2
But then it is true, that some specific alarm situations have arisen that have led us to have a meeting. Not long ago, recently , It was described in the press, adverse effects precisely, by the implants, it was at European level, that is, I imagine you are informed of it, but it was barely 3-4 months ago. Then there was a social alarm, it came out in all the media, both European and Spanish and we had a meeting with the AGEM and with other representatives of the Ministry, to really know the magnitude of this problem that had caused this alarm.	Interview 2
we do a lot of what is continuous education and that also part of safety or quality of life measurements and it started in our main forum but is now spreading so other forums are adapting it and we encourage ppl to be members of different forums because that is the way how you effectively spread information across Europe	Interview 9
what has been extremely successful in that so we blog for example from ASCO or from ESMO and then ppl blog already in different languages about it or ppl pick it up on the main forums and then translate it into their own forums	Interview 9
I don't know what you know about network theory but a single patient is a node, ppl who are well connected in their country, we call them hubs and then cores are higher orders of organizations, so I would be a core member of my own network, hubs are ppl who drive their country network, maybe started the melanoma group and their organization and what we do, a lot of what MPE now does and is growing and is definitely going into that direction is connecting hubs across Europe so that ppl when they have an issue, they start asking others who have the same function in a different country and we have now an extra hubs forum	Interview 9
-Yes, I think we would be a conduit of information from pharmaceuticals, we would, for example we operate we have social media daily, we have a monthly e-news and we post, anything that is being posted as an notice on our website goes into that monthly e-news, and a lot of ppl from SMA community has signed up to that and reed what's in it, so that contains also some information, we would think that as the channel for information coming out from pharmaceutical companies,. If it were something extremely serious we could do a targeted communication to community so we would see ourselves as a conduit for merge information or information to say "no please do keep what you know and report to your health professional" you we'd be happy to do that, keep ppl aware but we are a small organization, we don't want the concerns coming back to us.	Interview 4
it could be that POs could have someone a liaison , someone tat could regularly get updates from the PV unit and national authorities	Interview 14

Problems and Solutions	
Strategies to Overcome the Barriers	
PV Communication Network	
Excerpt	Interview number
It would also be very good if they have a clear contact list for POs, so we can know exactly the right person to address in any situation, they have it in the website but it is still very difficult to find because they have a whole national authority structure there so it's very difficult to find. They have the contact center for information regarding medicines and perhaps ppl can address that and they would put forward the message to the right place, still it would be helpful for POs for different issues to have the right contact, to whom to address it with	Interview 14

Problems and Solutions	
Strategies to Overcome the Barriers	
PV Communication Network	
Feedback for the Patient	
Excerpt	Interview number
One side is the press side and in the press there is information but not really good information and if patients want to know more, then they have to ask their professionals and that is one side and the other side is to ask perhaps Swiss medic and professionals on pharmacy and professionals from therapy	Interview 16
-I would search for information with my colleagues or at the AEA, that is the Association of European audiologist's could also consult them	Interview 1
all those who were suffering from that, were asking 2 questions Has anybody else seen the same? and what is this? and then other questions were what can I do? should I stop my treatment? and this are still the main questions that patients inquired when something they did not expect to happen is happening, what is it? has anyone else seen this before? what can I do? and should I stop treatment? We can solve and respond this 4 questions in all cases, then we'll have made a major progress to satisfy the need	Interview 12
The problem we have here, we cannot easily consult your specialist, if you ask for a new visit, you may have to wait for 3-4 months, so I don't think the patients have in place the right (inaudible) to interact with their Drs rapidly, we see some initiatives where they can contact via email or via mobile app, to have an immediate feedback, but often is the PO that serves as a mediator, the patients contact them asking questions, some organizations organize online forums where the patients can discuss the side effects they have and sometimes there is a Dr a HCP that can reply to the patient, but the 2 way communication between the lay patients, individuals and the PV system, we still need to improve that because too often the questions are left unanswered	Interview 12

Problems and Solutions	
Strategies to Overcome the Barriers	
PV Communication Network	
Feedback for the Patient	
Excerpt	Interview number
Because the patients don't know who to contact, who to ask, their Drs are not immediately available there are not that many PV experts who see their role as giving advice to the patients, there is fear that this new actor could substitute to the role of the treating physician and we see some reluctance from PV experts when they receive a side effect report, to provide information back to the patient or what they usually say is go and talk to your Dr., (inaudible) when we know that others are doing extremely useful work by for example, when they detect the problem could be a drug-drug interaction, they extract the part of the package leaflet about the drug-drug interaction and they send it back to the patient "it could be due to that drug-drug interaction, you should still talk to your pharmacist of Dr", but at least there is an initiation of a 2 way communication between the PV expert and the patient and I think we need to develop the capacities of the PV system to organize a 2 way communication on a broader scale.	Interview 12
-In the AGEM and Sanitary products. It belongs to the ministry and that is the reference source for this matter.	Interview 2
I would look on the website of the EMA, I would go to the French PV website and to the German one and I may call the Dr specialized in epilepsy, send him an email or depends on what the problem is, could be the division of PV of our ministry of Health	Interview 6
-Alright, and also when you say you'd look at the EMA website, where you also look for the PV EMA to see if there are any alerts there? because it's really big EMA -I'd look for alerts and for the specific medication they are talking about.	Interview 6
we for example use vigiacces, quite extensively because this new drugs were maybe because of the price that they had to limit the introduction, the footprint was quite limited and then all of the sudden it got walled out relatively rapidly,	Interview 9
So I've been well, while I've been talking with you I'm seeing with anyone who want to listen and anyone else as well, but what I want to have is a cross feedback, so I want that someone reports side effects but gets help and then that the data collection happens on the back side of that, because I think then the motivation will be to get help and then see, like you know that we learn from that because then you kind of see also when patients (inaudible) and which condition. What is particular hard for them, what is, you know interferes with their quality of life, so I think that is a bit the motivation in there	Interview 9

Problems and Solutions	
Strategies to Overcome the Barriers	
PV Communication Network	
Feedback for the Patient	
Excerpt	Interview number
-I think, we are fortunate to be part of a network of neuromuscular specialists which is called SMA reach, so I think we would immediately get in contact with that network of medical experts and get some key names of experts and we'd say what is the truth behind this claim we read as a starting point. I think we would trust them more than going to the pharmaceutical companies because one imagines that the pharmaceutical companies may have some commercial issues that they're struggling with they want stakeholders to think about they may be unwilling to speak to a patient organization very honestly, I'm now speculating.	Interview 4

Problems and Solutions	
Strategies to Overcome the Barriers	
Research Creates Awareness	
Excerpt	Interview number
That could be very relevant, because we have our network, we have our members so it would be very relevant that we send out this and that it shows that we worked on this and it would also be very relevant when we have our conferences that somebody like you would come and talk about this and tell us what this is about	Interview 1
"oh! I think that somebody there, he knows, I'm gonna ask him" that would be my way of working, but nobody has ever knock at our door saying, hey we would come and talk about this. But even this talk is helping raising awareness on the importance of this.	Interview 1
Well the only thing I'm going to say is that I'm happy that you raised this question and also that once you have information on this particular area, it could be fine when you give it and tell us yes, (inaudible) this conference, I will be able to come and give you a presentation on this, so that we raise awareness.	Interview 1
Then of course, there is something else now that ... the survey that was done a while ago with you, also gave us the opportunity to make the offer to the member organizations, which I do not know if they will have participated much or little, but it had an impact on the importance that this has.	Interview 2
But then again, we need to inform what we know, what we know by now and we also need to inform that we need more research we need more studies into different kind of medical treatments because some of the things may be able to be changed when they do some more research and test and try out things so this is also for us to raise that this is needed.	Interview 1

Problems and Solutions	
Strategies to Overcome the Barriers	
Research Creates Awareness	
Excerpt	Interview number
But the other thing is really what this involvement of PO, the real PO, with real patients, not someone representing them, involvement in PV, at the stage of design of the trails, choosing the outcomes of this trials, having an academic research project which looks at the AE in real cases, that would be quite important.	Interview 11
Well I'd like to say that I think is a good idea from independent ppl from the university like yourself, as a representative (inaudible) I think is a good thing for you to be interest in this and I do expect some honest analysis, a care thinking about this to come from studies like you and I think it pretends well for the future, you know to become or taking an interest on this.	Interview 10

Problems and Solutions	
Strategies to Overcome the Barriers	
Show PV Real Examples	
Excerpt	Interview number
We've asked the EMA and the EMA has started it , to tell stories, we need to communicate, to inform the patients, the most recent PV decisions are to tell the story on this date, this Dr reported this event and this other Dr in this other country reported the same the week after, a signal was catch, was coded data base and then it was forwarded to this authority who conducted the following analysis and on this date we could conclude this and that and proposed this and this action, and you see the timeframe how fast it is, I think the main benefit of the recent measures is faster analysis and decision making that is the first benefit of the legislation	Interview 12
We propose and we've proposed it to Linda Harmark, who will come to our next summer school for patients advocates in June, we propose her to come with cases, where reports from patients were useful for PV experts, useful because they were extremely clear and they it helped regulators to confirm other sources, so what we propose as a training activity for our members, 40 advocates will be there, we propose that Linda would come with narrative text and actual reports where she will ask the participants first to read them and to comment on them, we will see what they think about this report and then as a regulator, she will comment for this report, I think one is extremely informative and another one is less informative because of missing data or confusion in the information	Interview 12

Problems and Solutions	
Strategies to Overcome the Barriers	
Show PV Real Examples	
Excerpt	Interview number
I think developing a training modules, training programs, hands-on exercises where PO could attend a one day training at their agency or at Lareb, where you can do the same, you can even think of the annual price of the best reports of the year from HCPs or from the patients as a way to inform the patient community as a hold that yes! It's not only because you are asked to do that that you should report, but it has a utility, we need to explain, to show cases, again, to tell stories, where the contribution of the patient made the difference	Interview 12
And what you can do is, learn from good examples, like I said in Europe for instance an organization like EURORDIS can be a very good example on how to organize it, you can also learn even in Europe ofc, from an organization like the National Health Council in the United States which is an umbrella organization they have on the united states and they have very good contact with the united stated, you can ask them if they can even mediate between organizations and the FDA if needed, it should be the same here	Interview 3
You want to promote drug safety right? if no one from that organization shows a side effect recently or in the past, probably won't be able to promote it in that organization, but again reporting comes to a very personal level, but if some of them see a problem with drug safety, they are more prone to put it on top of the agenda, t's human nature, pure human nature. To show that drug safety is really relevant, you should use complete examples for instance, they cannot feel it personal but if you use concrete examples of ppl that have problems with drug safety, this may be helpful to promote it among the national organizations.	Interview 7
of it, but I think I don't know what is happening overall in Croatia regarding the same activities for other disease areas.	Interview 11
Because I had been exposed to it outside my own country, so in UK, I've been working there for a long time, there are different starts, that is one thing, the other thing is we build up from 2012, which wasn't easy, we are a particular type of PO which is possibly modeled on UK organization in a way, so we did go into publishing patient materials, booklets and things like that which is not the case in CRO.	Interview 11
So I think hearing what others are doing, let's say Netherlands, what are they doing about it? does it go from the specialists or from the nurse or I don't know.. I mean that would be lovely to know, I mean if you have that in your report, that would be great,	Interview 11

Problems and Solutions	
Strategies to Overcome the Barriers	
Education	
Excerpt	Interview number
-But you know I spoke to some nurse she does anesthetics and audiological work in a hospital, when ppl need to have something operated in their nose, throat or ears, so she does the anesthetics and she didn't know that anesthetics could hurt the hearing, she was working in this kind of work and she didn't know.	Interview 1
-No, I'm the only one, because I'm interested in taking that kind of education and I'd like to have maybe younger ppl interested in doing that course and maybe other courses, I'm now developing together with our facilitator, PGO that is an organization financed by the Ministry of Health to support PO on the facility part of their functions, so they're organizing education on how to answer a phone, how to be a treasurer, how to form a board.. But now they're also developing the course I had, the EUPATI course, it's now translated in Dutch and we are changing it to the Dutch situation and as of September the first 25 patient representative in NL will follow that EUPATI NL course and instead of talking about European PV, they will talk about Lareb, and talk about CBG and our health insurance an our ministry of health	Interview 13
Maybe it would be wise to see what EUPATI wrote about it, the European Patient Education, it is EUPATI I think it's .org, you can find it, and they have one module only about PV, they have 6 modules and 1 is on.... medicine development, there are 3 of medicine but also on PV post market and HTA and one of them is PV within the European context, and together with PGO we're know translating it to the Dutch context but maybe you can make a summary of that, for POs, for how to deal with side effects and ppl having questions about medicine	Interview 13
the risk management plan summary, I think this document are overlooked and not used as they could be, they are excellent to explain on what we don't know about the product about the time it is authorized and what needs to be done to answer the question, and to reduce the uncertainty, there are help lines, for example the POs that have a help line, they read this documents and when they have calls from patients who may be taking the medicine, they can explain them what we don't know about the products and what are the studies that are conducted so that one day we know about the safety aspect of the product an it's important because it's only by communicating this that patients may ask their Drs "Oh, by the way, have you heard about this study, I think it's an important one, should I be enrolled in that study?"	Interview 12
-Yes, I believe it's very important to raise awareness and we should start from the basics and that is why actually I was so keen that we do this education on the life cycle of medicines, so the organizations actually understand how the medicines are developed how they are approved how they're reimbursed and what are the reasons perhaps to take them off the market I believe there is a great need for that and I believe like 80% of the organizations are actually not very educated in that area	Interview 15

Problems and Solutions	
Strategies to Overcome the Barriers	
Education	
Excerpt	Interview number
we have to find tools to allow for adaptation for those ppl who are you know maybe have never been into an academic curriculum or who are just from a totally different field. To be honest we have a professor of xenology I mean that guy is supper educated, super smart but from a totally different field and he finds this very difficult.	Interview 9
once in a while it's possible to find a workshop or seminar around this issue and trainings for POs and also EUPATI portugal but we are not yet addressing this issue, because that is the thing we lack resources and we cannot tackle everything at the same time but it will also most probably develop some training in this area but there is training at least for POs, patient representatives,	Interview 14
There is training at least for POs, patient representatives, but not for the general public	Interview 14

Problems and Solutions	
Strategies to Overcome the Barriers	
Education	
Topics	
Excerpt	Interview number
I think the number 1 thing is to have what I call the key points to which you're trying to get over, so for instance, if the kit is there it should have firstly the organigram of how it is lay out, so there has to be a map on that, showing what is there in that system, the whole system needs to be followed, the logically system ology, know where to go? So the path should be clearly identify, the PV reporting path needs to be clearly identified, that needs to be coming out. The second part of that would be the role, who should be informed, the framework needs to be described clearly, this are the relevant institutes, this are the relevant ways to get to that institute, this is what thye can do this is what they cannot , so that has to be put in, so quick start on that would be if the toolkit defines the fieldwork of the institutes, the legislation in place, the policy, practice guidelines and actual standards that are placed for PV, that needs to be defined clearly, Second it needs to identify the communication channels, the clear communication pathway that ppl so that ppl need to do it. And thirdly there needs to be a clear understanding if this things fail, who to go to? There needs to be, lastly within that, somehow isolate the local, the things that you do fight and then you fight somebody unconscious, what is the fastest OV pathway to someone you know has been having regular headaches which can be reported national slower, it takes maybe a day to report, so that needs to be somehow identify, like the local action in emergency and start to build that	Interview 5

Problems and Solutions	
Strategies to Overcome the Barriers	
Education	
Topics	
Excerpt	Interview number
And I think the most obvious is the product information -Product information? -Yes, to in the toolkit, we need to show where is what, yeah? If you got a label there, what are the issues and ppl don't understand what contraindication means and that sort of thing, ppl don't understand where to find, what the badge number looks like, this is very important for carers, so we haven't mentioned the carers, all it has been concentring on patients, but as you know a lot of carers are responsible for PV, so there needs to be something for carers again in that system really.	Interview 5
-hhmm I think first of all you have to tell what is PV, what it is for, how PO can help, yes can help or that patients and pharma and all authorities are getting aware of special side effects for example	Interview 8
So this is awareness, and sharing knowledge and sharing information, next year it could be how dangerous drugs are and how to prevent hearing loss from different kinds of drugs really. This year it was about environmental noise and in the "in the ears" (she referred to earplugs)	Interview 1
-It is important that we share information, and it's also important that we don't create fear in the population, If you need some treatment, you need to accept that kind of treatment that you need . But then again, we need to inform what we know, what we know by now and we also need to inform that we need more research we need more studies into different kind of medical treatments because some of the things may be able to be changed when they do some more research and test and try out things so this is also for us to raise that this is needed.	Interview 1
So this would be the things that I think is important to share and they also need to know what kind of hearing loss you can get from different medication, is it high frequency, is it total deftness, is it fluctuating hearing loss, because we come out with different personalities related to what kind of hearing loss we get. So that would also be important, maybe we can't solve it all but we need to do the best we can , and you can know what kind of hearing loss you get with different medication, then we also know what products you need, what kind of hearing aids, what kind of cochlear implants, are needed. So in reality everybody should be interested, everybody in this field should be interested in this.	Interview 1
I think there is a really nice data base available from Lareb.I don't think a lot of patients know that data base so they can compare what side effects are reported from certain medicines	Interview 13

Problems and Solutions	
Strategies to Overcome the Barriers	
Education	
Topics	
Excerpt	Interview number
Yes, and maybe we should have a standardize document, to send to ppl that make a complaint tell them step by step what they have to do to make a report at Lareb, we don't have that but it would be nice to develop I think.	Interview 13
want to give information about medicine, because ppl don't know what type of medicine are around, ppl are getting a certain medicine and they don't know that there is another medicine, so I want to information about all the medicine available for their condition, and I think that is allowed but I also have to look it up if it's possible.	Interview 13
Maybe at first instance, developing a document for ppl within the PO to acquaint with what is PV, what is the role in PV and how can the patients be helped by PV, a sort of small 10 page document to give a sort of speed course on PV for patient representatives. That would be the first step in creating awareness within the organization of volunteers	Interview 13
well that is happening with EUPATI, but I think it's for a lot of ppl, patient representatives too complicated, too intense to follow that course and maybe they should make a lay summary of it for patient representatives who want to know more about the PV process but also when you make it in such a way, maybe it can also be given to patients, explaining what PV is about	Interview 13
I think having POs themselves educated on what a good report is, what does it mean to have a good report, a report that regulators can use, a report which contains useful information, I think the more we educate organizations to understand themselves, what useful information can be, the more organizations will understand the necessity first to report and to report with high quality, and that will take time, we need for this to cascade down but first we need to educate the patient advocates	Interview 12
On the life cycle of the medicine, how the medicine is developed and what it means when it's in clinical trials and what it means when its approved and how it's monitored after that and what is the importance of reporting and adverse event and efficiency of the drug, so we actually ant to educate them what are drugs, how they live and how they are managed in the real world, this is something that we are trying to do	Interview 15
-Yes, I believe it's very important to raise awareness and we should start from the basics and that is why actually I was so keen that we do this education on the life cycle of medicines, so the organizations actually understand how the medicines are developed how they are approved how they're reimbursed and what are the reasons perhaps to take them off the market I believe there is a great need for that and I believe like 80% of the organizations are actually not very educated in that area	Interview 15

Problems and Solutions	
Strategies to Overcome the Barriers	
Education	
Topics	
Excerpt	Interview number
so the language the abbreviations, you know how many abbreviations there are and if you are not trained in that, it won't say very much.	Interview 3
I think also for this some basic knowledge needed but also extensive knowledge on communication and practice.	Interview 6
Then in concrete what we do for our ppl, as I said before , we have like on forums, we train our ppl in side effects, so at our conferences we always talk about drugs how the therapies work but also what the side effects are and which side effects are particular dangerous	Interview 9
y, it's not about a flier you put somewhere, because that's not how education works, specially not in adults, so it has to be continuous, it has to be interactive, it has to be mid driven, I think that today with social media you can education can play a huge role to make patient life better and ultimately also safer .... so yeah	Interview 9
explaining what the system is all about and what role you could play, so really quite basic	Interview 4

Problems and Solutions	
Strategies to Overcome the Barriers	
Education	
Tools	
Excerpt	Interview number
So there would be trainings, programs that we have runs, therefore if you contact this organization is best.	Interview 5
And I think the most obvious is the product information -Product information? -Yes, to in the toolkit, we need to show where is what, yeah? If you got a label there, what are the issues and ppl don't understand what contraindication means and that sort of thing, ppl don't understand where to find, what the badge number looks like, this is very important for carers, so we haven't mentioned the carers, all it has been concentering on patients, but as you know a lot of carers are responsible for PV, so there needs to be something for carers again in that system really.	Interview 5
-So they make different suggestions and for example webinars so we can participate	Interview 8

Problems and Solutions	
Strategies to Overcome the Barriers	
Education	
Tools	
Excerpt	Interview number
I do some other things and I have been once in a week in Barcelona, I think it was Eurordis We got a whole week, have been educated and PV was a very big part of the program	Interview 8
Maybe at first instance, developing a document for ppl within the PO to acquaint with what is PV, what is the role in PV and how can the patients be helped by PV, a sort of small 10 page document to give a sort of speed course on PV for patient representatives. That would be the first step in creating awareness within the organization of volunteers	Interview 13
but the fact that the national authorities had the initiative of proposing to train ppl in the organization to make sure that the reports would be filled in completely, etc etc..	Interview 12
I think developing a training modules, training programs, hands-on exercises where PO could attend a one day training at their agency or at Lareb, where you can do the same, you can even think of the annual price of the best reports of the year from HCPs or from the patients as a way to inform the patient community as a hold that yes! It's not only because you are asked to do that that you should report, but it has a utility, we need to explain, to show cases, again, to tell stories, where the contribution of the patient made the difference	Interview 12
If I may, something else, we would be interested in and we see there are some development in PV public hearings are excellent, extremely useful the ones that the EMA organizes, why not having the same organized at the national level, maybe on another topic but even for the topics that are discussed at the EMA, I think there is enough space to have a similar discussion at a National Level because when you follow this debates you see that it's abstract, it's very concrete so the ppl would come together because they want to solve a problem, at a national level you won't have the language barrier that you have if you do it at EMA and yet you need to implement national solutions and I think that is another way to engage with public and to gain trust on PV	Interview 12
so let's say the NCA should offer much more not only information but training in the beginning to give them the ability to find the way to get information but also to understand the regulatory world.	Interview 3
. I think in the beginning the NCA should play an important and proactive role, they should think about the offering a package or training package for PO, in particular to small PO and they can do this ofc together with the working group of POs they have because, the package must answer the needs of the PO and otherwise it will not work	Interview 3

Problems and Solutions	
Strategies to Overcome the Barriers	
Education	
Tools	
Excerpt	Interview number
In fact we already transmitted to the Ministry and the National School of Health the importance of awareness in this matter. But of course, you have to do diptychs to leave in the community pharmacies, diptychs to leave them in primary care centers and it has not been done.	Interview 2
-No, by the umbrella organization specifically medical conferences	Interview 6
Then in concrete what we do for our ppl, as I said before , we have like on forums, we train our ppl in side effects, so at our conferences we always talk about drugs how the therapies work but also what the side effects are and which side effects are particular dangerous	Interview 9
nd ppl take the time to explain what a physician never has the time, they would give them a list of things that may happen could happen and then you get a printed leaflet which has no weight on there, is small and usually not attractive, either is so pretty and general that is useless	Interview 9
What we started doing is we repeat things once in a while	Interview 9
You know if they also organize something, they have to have a concept in order to invite someone to speak about this topic, if you already reached them in a setting where they don't define a program but you `know that it will be there, I think is in this kind of places where it should be visible	Interview 9
the easiest probably would be to have an open day or like a working group of patients, advocacy groups and then just invite them to a national authority and show how what the national authority does, just exposure to start with	Interview 9
we've now set in our own organization looking a bit onto adult learning, because adults learn differently and we've also tried different things and lots of different things didn't work, it's like typical naive me when I started, ppl would always ask me questions and lots of questions would come back to meal the time so I thought, you know what I'm so tired of this, I will put it on a website and then I just send them the link to it, and I was really really proud of myself because I had never done a website so I googled website for beginner and made this website and it was really really proud of myself and then I sent out the link and then what happened? Nothing!! ppl came back with the same question because I had totally misunderstood what the point was, I mean my colleague always says "ppl always think yeahh that is the rule for everyone but I'm not everyone so I want to know what matches to me, I'm different " so you know it's like it does help to have the information there but it does not replace the interaction	Interview 9

Problems and Solutions	
Strategies to Overcome the Barriers	
Education	
Tools	
Excerpt	Interview number
andragogy, instead of pedagogy,-I don't know how that is pronounced in English- so how adults learn, that adults start with a problem and they are looking for a solution and they will ignore everything that is left and right, because something that for example we see all the time, we post something and not much of a reaction *and* 2 months later someone asks just for this thing, and we're like it was three !!! just 2 months ago!!!	Interview 9
What I now try to do in my own community and seems to work quite well is I try to break a problem down and let them fix it, even if I could do it way faster or way better but that is the way to make it stick	Interview 9
how you can involve ppl how ppl learn how they retain , so that for example they say, adults have a self-concept that children don't have to that degree, so they know who they are they have existing learning and they learn based on their prior experience and they expect the learning to have a direct impact on themselves so they don't learn like at school when you start with learning how to read and write without knowing what you're going to use it for, and adults want to learn something that is directly related to a problem or issue or challenge they're having, adults often don't learn just for the sake of learning anymore	Interview 9
we can do web pages for instance, and developing some toolkits that can be used at a national level because everything must be(useful? Inaudible) at a national level.	Interview 7
And for instance in the regular meetings for instance, when a single organization as a web page and some of them have programs on radio or tv shows so they are using those key materials in that aspect to reach out the ppl in the country. That's what I see should be then.	Interview 7
-I think the umbrella organizations what they can do is promote it among the members by for instance, promoting during the annual meetings or with small discussion groups and then promoting it by producing materials that can be used at a national level as I said. I can give you an example, for elections, 4-5 years ago, we produced a toolkit for associations to use when contacting the candidates to the (inaudible) ok so all national associations had in their possession a toolkit with a key message that we would like them to bring to the special table with the candidate and then also some slides of paper for instance. And that is quite helpful because sometimes national organizations don't have the resources or the time to develop such materials so if they can use the materials that are produced by the umbrella organization, this would be quite useful	Interview 7

Problems and Solutions	
Strategies to Overcome the Barriers	
Education	
Tools	
Excerpt	Interview number
-Ehh the toolkit, the purpose of the toolkit has to be considered, who are going to use it, it's is different for umbrella and for national organizations, so basically… what is drug safety and PV, how the system is constructed, what is the role of PO *in the* system, how can ppl report side effects and why it's important (to report) . How they (po) can improve the system	Interview 7
I think it needs to be very simple, top level, and it might be you know... what to call.. you know when you got simple pictures, a very simple summary saying this is the system, this is the role that PO can play, not a dense document, in extremely clear and inviting maybe a port of contact suggesting we can come and talk further to you or you can come and tell us. So not lots of information because you just get lost in it, it won't get read. So yeah, a toolkit explaining what the system is all about and what role you could play, so really quite basic	Interview 4
explaining what the system is all about and what role you could play, so really quite basic	Interview 4

Problems and Solutions	
Strategies to Overcome the Barriers	
Involve Patient Organizations	
Excerpt	Interview number
PV system, that if we need to respond quickly we want to be learning for finding things rather than blaming, the root cause finding, that is what it really is important to us in that scenario	Interview 5
But it's multi-level responsibility, in other words we can't just dump it on one party, we can't leave it on the regulators, we can't leave it on the pharmaceutical companies, we have to rely on each other, it's a shared responsibility	Interview 5
o we tend to say yes, you look up those in the PV system and make sure there, last year I think very important on that is really keep on working on partnership with the pharmaceutical companies, the regulators and the patient groups, because we may not have some of the resources that the state has or the pharmaceutical companies have	Interview 5

Problems and Solutions	
Strategies to Overcome the Barriers	
Involve Patient Organizations	
Excerpt	Interview number
-On my mind, the most selfish part of it is try an umbrella organization, join an *alliance so you* have numbers so because the benefits specially in rare disease, there I really truly recommend it. So if you have 200 already visits and only 50 patients in one condition, it doesn't make any sense for 50 to pursue something but it makes actually good sense if you have 10 000 of them together in an umbrella organization. So you have to work with the alliances. This is very important besides the regulators, make sure you work with alliances and umbrella organization, because PV is a cross sector, non-disease specific problem, it is a systemic problem therefore it needs to be addressed collectively, you get volume for a voice in the allies.	Interview 5
Yes, because there are some rules in working together pharma to Swissmedic and in this process the patient has to be involved that is right and that is both sides, we have to be involved on the pharma side and Pharma has to invite us otherwise (inaudible) and on the process to the final drug, together with Swissmedic that runs but not on the pharma side, not in the moment, they did not start	Interview 16
We have 4 meetings as a group with umbrella organizations for patients and this group can make meetings together with Swiss Medic, that's 4 times a year -4 times a year?! how has it worked? Is it a good dynamic for you? -hahahaha It's more about information, not about involvement, and it has to be more involvement and it's became better	Interview 16
Yeah, I think if you have the possibility to push the pharma to invite good educated patients to woork together in the drug development then it will, should run better, patients can say I think that is not the good way, I think the needs for patients are others and if we can do that in a early stage that is really better than doing after the drug is in the market	Interview 16
-Yeah, yeah if you can push the pharma to invite us for our involvement then it would be good and in the other side I think in most countries there are no ..POs for chronic disease and so on who have a voice to say this has to be changed in the Health system and this has to be changed, so the politics can do what they want there is no voice of the patient, the patients in all countries have to run together and to form one voice, that is what we have to do, that is our thing	Interview 16
And also I already talked to Gerda about it, I don't know for sure, we are organizing a symposium in 2020 and we are expecting 700 ppl, it would be very nice if one of the information tables is occupied by Lareb, so patients can ask question about PV process and the importance of PV So that is awareness we can give patients	Interview 13

Problems and Solutions	
Strategies to Overcome the Barriers	
Involve Patient Organizations	
Excerpt	Interview number
Well when you are in a pharmacy in the NL there is a website, I don't know if it's connected to the Lareb, (inaudible) reports of having problems with medicine -Just to that pharmacy let's say? It stays there -Asks Gerda: Is it connected to Lareb or is it not? -Gerda:Sorry? -The `pharmacies, you can report medicine problems is it connected to Lareb? -Gerda: Sometimes, some hospitals. For example DBZ is in den Bosch, they have a connection that they can report ADRs in their own system from the hospital and it goes to Lareb -But for patients it can be confusing, is it the same reporting or different point, some PO have, when you have a problem with medicines "please come to us" and I also have patients saying that (inaudible) they have reported it, but I don't know where they reported it, so that can be a problem,	Interview 13
It's also to participate in national conferences, for example in Ireland, they have one conference per year on PV with all stakeholders, industry, Drs, public, PO, where they discuss together what is difficult to implement for PV but what are the outcomes, what is the progress and that is very useful because it's the whole society in Ireland that is aware of where we are with PV and what needs to be done, everyone feels involved in PV, it isn't just a matter of expert, everyone in society has a role to play, different roles but	Interview 12
but what are the appropriate measures is the question. I think you can't implement this unless you organize a meeting with organization that could be interested to discuss what can we do in our country to pass the message to patients, I know that PO don't have a huge budget for communication but we have the scope joint action awareness week on patient reporting, prepared by the MHRA and we've seen the impact of this campaigns which are not used in all member states but in the weeks that followed, there is an increase in reporting, and I think we have to explain this relative success in countries this has taken places but also in other countries which hadn't participated in the reporting awareness week, that is another way to initiate the discussion	Interview 12
Yes but I also think that is very important that we get the opinion or advise from the Drs organizations and from the HALMED and from the ministry of health and actually that we all agree all the stake holders should agree on the communication strategy and how they will communicate it in public and how they will communicate to patient and PO	Interview 15

Problems and Solutions	
Strategies to Overcome the Barriers	
Involve Patient Organizations	
Excerpt	Interview number
In the past regulators were doing the work, also PV, in isolation, they had no, hardly any contact with clinical practice, what we now have heard is that there must be a very close contact	Interview 3
On the other hand, we have to act also on the administration, and within the administration I include the Ministry, the Spanish Agency of Medicines and Health Products, including the National School of Health. In short, all these organizations or institutions have to ask them for information campaigns as well. In the end it is what has most impact, the information campaigns to all patients.	Interview 2
I think if you wanted to have something effective, I would probably ask like, find a setup here the PO creates the educational material or at least co-creates the materials, that in my opinion is the most effective way to get anything	Interview 9
The involvement of the ppl in all levels of the system, considering only the reporting of the side effect ok, the ppl involved there ,I think the system should involve the ppl since the beginning, even drafting the online system that is available nowadays, if they involve the ppl that are going to use it at the end of the day, the system may be more user friendly.	Interview 7
and then being involved with the regulatory agencies, patient involve could help out the way of designing the system, because, ok each one of us is a patient, the person who report of drug adverse effects, so each one of the ppl that are sitting in the regulatory agencies are also ppl that can report on the system so they don't experience to design the system but if you take someone who is absolutely out of the system , that is always helpful in designing the system, what I'm saying that patient involvement should describe the PV system, until the end of it, because the PO bring a different perspective of discussion.	Interview 7
I'm not sure if they can help out with resources, I think that is something that is responsibility of the NGO but what they can do if they are starting to involve PO more, they are creating the need from the PO side to fulfill that need ok? In a way doing so the NCA are helping out in putting it on top of the agenda this message.	Interview 7
that most hospital either develop their own based on that because that is the way it is in here, you don't let the charities the interpretation of something. But I think we maybe help (inaudible), to making sure ppl were explaining things in simple language that families could understand.	Interview 4
I think a join initiative should bring more cloud with anybody and I imagine we would ask a meeting with the pharmaceutical company, we'd be there as the voice of ppl who talked to us	Interview 4

Problems and Solutions	
Strategies to Overcome the Barriers	
Involve Patient Organizations	
Excerpt	Interview number
but the other thing is really what this involvement of PO, the real PO, with real patients, not someone representing them, involvement in PV, at the stage of design of the trails, choosing the outcomes of this trials, having an academic research project which looks at the AE in real cases, that would be quite important.	Interview 11
they mostly rely on POs to disseminate, they have good material info graphics and they have good visual materials and they rely a lot on POs to disseminate to our audiences which is good, sometimes I wonder what I think is lacking, they could when developing information materials, they could ask for our advice and opinion, because POs have a different knowledge on patient issues also the (inaudible) the public to understand certain messages, so this could be perhaps in the future, they can involve POs when they are deciding on the information or writing or elaborating the deliverables instead of only relying on us to disseminate	Interview 14

Problems and Solutions	
Strategies to Overcome the Barriers	
More Funds for Patient Organizations	
Excerpt Copy	Interview number
if we do this work in partnership in pharmaceutical companies we need to have some financial help	Interview 4
-Well it's having paid workers, that is the problem, having paid workers and having sort of a program for 3 years and have reliable source of income for 3 years, which is just not pharma generated,	Interview 11

Problems and Solutions	
Strategies to Overcome the Barriers	
Targeted PV System	
Excerpt Copy	Interview number
-*And something*, I mean just to ad on, because you may not consider but it needs to be considered now that maybe we may have a dichotomy of PV system There would be a PV system that is young single condition patient group, there would be PV system that would deal chronic condition patients and so because regulators are supposed to do something so they won't likely (inaudible). But the third one which is now rapidly coming into focus is that market disease chronic patients, this are patients having 10 or 11 even having 20 medicines together, their PV system needs to be very very different from everybody else, there needs to be something else, at the moment we have been dumping them all to use one or the other but maybe pv system need to not deal with that patient, because polypharmacy and polychromic conditions…	Interview 5
there is a system for generic, small molecule pharmacovigilance, I think with the problem really starts with now with biosomilars, it starts problems with naming it, where are this, as you know some of the biosimilar programs have been going on by naming them hard to make sure the product is identifiable for one or the other, making sure if there is an adverse event and because this biosimialrs are complex proteins which are going in, messing around, could potentially mess with the immune system slowly, so and Adverse reaction maybe over a long period of time is just building up,	Interview 5
NO I think, PV system needs to keep on evolving, we have now new classes of medicine coming up, we have gene and cell therapies coming up, they need to be treated differently, we need to ensure that the… proactive and not reactive in the way things are, at the moment many ppl are leaving (inaudible) but we need to be proactive	Interview 5
And also a problem ofc is funding, compared to other countries in Europe, the Dutch situation, we are rather rich, but we also have a lot of obligations, we have to print 4 times a year 2,5 thousand times a magazine, we have to have a website and we have to organize hospital meetings and symposiums, it's very expensive, for that reason, we can't be compared with for example Italy and Spanish POs, they are much more dependable on their umbrella organization than we are	Interview 13

Problems and Solutions	
Strategies to Overcome the Barriers	
Targeted PV System	
Excerpt Copy	Interview number
-Yeah, yeah, you see when EURORDIS is making a policy for Europe on how to develop ERNs and how to implement them in the different member states of Europe and you see for instance in Italy and Spain and ALSO France, the national alliance and that is the umbrella organization takes the lead, in the NL we are the ones siting at the desk of the ministry talking about our needs and (inaudible) our national alliance, because we think alliances for rare diseases can't cover all 80 specific diseases because we have the knowledge of our endocrine field, I'm not going alone to the Ministry, I'm going together with Adrenal, Thyroid.. so it's all endocrine but I think our roles are different and I think the lines are shorter in the Netherlands and for instance Italy, Spain and France originally organized and every region has a say, in the Netherlands here is a region that is the Netherlands. For Germany for example, every part republic has a say in how medical funds are spent, in NL we have one and that is one difference.	Interview 13
What we need also to measure is the risk, minimization measures, when patients have to follow, to implement this measures, if they fit the purpose, if they produce the desire effect, this we don't know, there is no satisfying measure by which we can evaluate from the patient perspective whether the risk minimization measures are practical, convenient and accepted by the patients I'm not talking the ones that the Drs have put in place but often do the patients receive the information, do they have the information, do they understand the information, do they act accordingly, this we have a vague idea and it's still true for old products lie isotretinoin, we know there is concern and may be increasing on that, probably a case for future public care at EMA because that's typically the case where something doesn't really work.	Interview 12
Well, at the beginning of the pilots for patient report, different countries have different strategies, I think we should have continues in that direction, because when the pilots were created, there was a number of working groups working with some POs who would first participate in this patient reporting. Where patients were trained in each organization to help their members filling in the questionnaire and it was of printed materials at that time but the fact that the national authorities had the initiative of proposing to train ppl in the organization to make sure that the reports would be filled in completely, etc etc.. I think we should've continued to push in that direction, because in fact PV are the first good reason to establish relations between national authorities and POs	Interview 12

Problems and Solutions	
Strategies to Overcome the Barriers	
Targeted PV System	
Excerpt Copy	Interview number
It also has to be without being alarmist, it has to be information consistent with the use of antibiotic, with the use of antihypertensive, with the use of any drug, it has to be something that is assumed as something natural and not that they think it should be to some kind, that is, not generate alarm, but understand that for a product has been marketed, has been marketed based on limited previous experience, although there have been many patients, 3mil or 4mil, although they may seem many but few to detect everything that may appear.	Interview 2
I'm commenting on this leaflet from EMA, it's quite frustrating because they were asking me if the leaflet is understandable for patients, it was about side effect in young children so the medication was to be used in babies from 3 months onwards and side effects would be like sight loss or headache and I was saying the leaflet needs to explain how parents of a baby could check for it, and they said thank you for your remarks but they Dr said it was Ok the way its phrased I felt like if I had a seriously ill baby of 3 or 6 months, maybe crying a lot and also babies who are not sick cry a lot, how can I check if he's crying because he has a headache from the medication as side effect? one of the serious side effect was loss of vision, how could I check to my baby that this is on the way?	Interview 6
having something in your FB encourage oncologists to basically (inaudible04:42) to let ppl report and then do something about it immediately instead of waiting until it's like it is, you know in 3 weeks the appointment comes up. We work quite heavy, I don't know I think it was last year asked them a plenary and the year before there was a report that similar set up was highly effective in lung cancer, I think the large US study was in more than lung cancer but basically were patients reported symptoms and based on this symptoms appointments were brought forward and they were able to, in a round setting, they were able to prolongate life just by doing that, so I think that a proactive management of side effects similar to signs for progression would really drive, we would drive clinical benefits at relatively low cost, if you catch side effects, serious side effects early they would be easier to treat, may not require dose interruptions leading to hospitalizations, so I think that is an interesting angle to think about	Interview 9
I mean we have been discussion with UMC what we would have loved to do and I think it's becoming now a bit less relevant but what we have loved to do at the beginning was, if we had been able to get our community, and our community was ready to do that, to report all side effect, everything they are having into one system, we would have been able to fix this side effects way way faster than is currently happening, but there is no infrastructure in place and because is so slow and you don't see the outcome, there is no motivation for ppl to do it.	Interview 9
I mean this take up pill or whatever the UMC had this kind of jingle , that we thought it was a bit childish, because our ppl had different worries but maybe for the general public who has never really thought of reporting, I think it was not really well directed at other audience but we have been using it..	Interview 9

Problems and Solutions	
Strategies to Overcome the Barriers	
Targeted PV System	
Excerpt Copy	Interview number
I'm sure it was more intended for a general audience, we are not a normal audience and we totally get that but assume that we would think this was great, was a mistake from their part because they obviously didn't user- tested i	Interview 9
So you have Western part of Europe then you have Central and Southern Europe and the Mediterranean and whatever, however they divide it and the umbrella organizations need to be aware of that because of that you have different resources of organizations on the ground so they need different support. So umbrella organizations, their duty should be to collect the information and then report it to European Commission, to whoever, to show what is happening because of the way the market is working for pharma companies, what is happening to real patients	Interview 11
the parents, how to communicate with parents and this is a very .. I've been discovering this for the last years, it's a very different audience parents because they have a huge responsibility, because they are deciding for their children, so they need much more information to guide them, for them to be sure that they are making the right decision on behalf of the children, so they are much more eager to get information so parents are a different audience and we may need to target them differently and also it's a vulnerable population, like children right .	Interview 14
It's the same all over, so I think ppl need personalized things in their home, in their house so they can be comfortable about it	Interview 14
So we need to target, I think it could be more effective, we need to have different materials for different target audiences because it's not the same thing and the audience will dismiss information that is not properly address so we need to take that into consideration, the other thing, I think is very important is this issue around natural products and supplements and medicines, I think the other ones should also be under the same PV system.	Interview 14

Problems and Solutions	
Strategies to Overcome the Barriers	
Understanding All Stakeholders	
Excerpt	Interview number
Or differences, you see in POs has some sort of cycle, a life cycle, PO always start with sufferers contact, ppl whant to talk about their condition, they want to meet fellow sufferers, and after that ppl are interested in information and more information, so the next phase of the PO is developing information leaflets, organizing meetings also for sufferers but also getting information from Drs and a 3rd level is, covering patients interest lie health insurance, Drs, policy making and I think there is a 4th level and that is not being the patient advocate but being able as a patient advocate to work together with other organizations to achieve the same goal	Interview 13
-Yeah, yeah, you see when EURORDIS is making a policy for Europe on how to develop ERNs and how to implement them in the different member states of Europe and you see for instance in Italy and Spain and ALSO France, the national alliance and that is the umbrella organization takes the lead, in the NL we are the ones siting at the desk of the ministry talking about our needs and (inaudible) our national alliance, because we think alliances for rare diseases can't cover all 80 specific diseases because we have the knowledge of our endocrine field, I'm not going alone to the Ministry, I'm going together with Adrenal, Thyroid.. so it's all endocrine but I think our roles are different and I think the lines are shorter in the Netherlands and for instance Italy, Spain and France originally organized and every region has a say, in the Netherlands here is a region that is the Netherlands. For Germany for example, every part republic has a say in how medical funds are spent, in NL we have one and that is one difference.	Interview 13
-I think that.. I met Gerda at a symposium of nurses, that was a 2 day event, somewhere in the NL, and we were there with 20 PO and Gerda met up with every PO telling about the work of Lareb, and that's how we met, so it's coming from both sides. Being active in engaging the PO	Interview 13
But you see it in more organizations I also think is very important to meet up with other Po and to do therefore things together When you are for instance making a policy on how do we on our website talk about PV or other items, you better develop together then doing it alone, and already I have from other Po certain parts of their policies to incorporate at mine organization I think at the longer term, we have to work together more and more	Interview 13
there are some agencies who have so much to do they don't see how they could start with a new stakeholder they have never worked with and in some ways they can be afraid of talking with POs (inaudible) but PV should be the first entry mode when POs like to work with a NCA, they can't deny there is a common interest to start with PV.	Interview 12

Problems and Solutions	
Strategies to Overcome the Barriers	
Understanding All Stakeholders	
Excerpt	Interview number
you can't understand PV if you do not understand what the problems are from the side of the regulators, what the problems are from the side in the clinical practice, from the side of the other stakeholders for instance, otherwise you can make solutions that are not workable	Interview 3
So we have to understand the position of the PO but I must say the professionally of PO is growing and this is going better, better and better	Interview 3
I'm commenting on this leaflet from EMA, it's quite frustrating because they were asking me if the leaflet is understandable for patients, it was about side effect in young children so the medication was to be used in babies from 3 months onwards and side effects would be like sight loss or headache and I was saying the leaflet needs to explain how parents of a baby could check for it, and they said thank you for your remarks but they Dr said it was Ok the way its phrased I felt like if I had a seriously ill baby of 3 or 6 months, maybe crying a lot and also babies who are not sick cry a lot, how can I check if he's crying because he has a headache from the medication as side effect? one of the serious side effect was loss of vision, how could I check to my baby that this is on the way?	Interview 6
if you have a personal connection to an institution and you can say you know the ppl there, I think it lowers up the pressure of picking up the phone and asking for help or saying "what am I supposed to do here?" or what can you do for us or this material is good or not?"	Interview 9
guess it's the way we think it works for us is a personal connection so that you know who the unit in your country is and who is responsible for it, make sure that you have some kind of understanding how it work	Interview 9
the easiest probably would be to have an open day or like a working group of patients, advocacy groups and then just invite them to a national authority and show how what the national authority does, just exposure to start with	Interview 9
I actually think I would strongly encourage ppl within the PV community to attend patient conferences, to get a better idea about the audience they are trying to serve, because you cannot educate and audience you don't understand and I think that is often the issue,	Interview 9
When you talk about EU alone, there are such diversities of what it's possible, and it's really determined by the market of pharma companies, and lots of this work of pharma companies are thinking that PO would do, but they can't, it's sort of .. not possible to do something so responsible on a voluntary basis, you can't do it. You can spread the voice but you need to get the health system involved.	Interview 11

Apex 8.

Tool to stimulate patient organizations in pharmacovigilance

How are patient organizations supporting drug safety?

Patient education:

Education is a key activity in drug safety, patient organizations inform their members about their medication common and serious drug reaction and promote self care.

Connecting Patients with other Stakeholders

When they do not report adverse reactions, they inform the patient which stakeholder to contact if needed, they also report other stakeholders about their members needs in PV and other fields.

Encourage Reporting:

They report that they are possible and important to report and encourage them by posting the link for reporting on their website, on personal conversation, newsletters and other communication tools they use to spread information among their members.

Transmission of information

When resources are limited, some patient organizations sum efforts to promote drug safety by supporting other stakeholders.

Participate in Legislation

Patient organization can actually influence PV legislation. They participate with a wide variety of legislative institutions at a national and European level improving the PV system

Work with other Stakeholders

Patient organizations invite other stakeholders to participate in their conferences or meetings, they also work together in material development

What strategie can stimulate patient organization engagement in Pharmacovigilance?

Proactive Pharmacovigilance Authorities

Pharmacovigilance authorities can play a proactive role by contacting patient organization and iniciate communications to work together with other stakeholders and improve the pharmacovigilance system according to all stakeholders needs.

Targeted Pharmacovigilance System

Patients with chronic conditions are different from those who suffer an acute health condition and there are many other ways of categorizing medicine users, the pharmacovigilance system should adjust to the needs of all useres.

Create a Pharmacovigilance Communication Network

Communication channels must be created to share information in a fast and efficient manner between stakeholders.
This network should be a 2 way communication system where the patients who report adverse reactions also receive some feedback or additional information when reporting,

Involvement

The common feature of all the presented strategies is that patient organizations want to be involved in every single step of the process, from the design to the implementation and evaluation of every strategy concerning their involvement.
Their voice should be heard in all stages and not only rely on them for the dissemination of the final results.

Present real examples

Patient organizations want to know how other countries and other patient organizations are working in drug safety, they want to learn from each other examples.

Education

It is necessary to educate organizations on the pharmacovigilance system structure, the language used, the data processing, the value of pharmacovigilance among many other topics they point at.

Education is key to organizations to continue their role of educating their members.

Some tools that can be helpful are toolkits, workshops and trainings.

Understanding all Stakeholders

Pharmacovigilance requires the active involvement of all stakeholders, the first step is getting to know each other, understanding what their position is, how each one can contribute and iniciate more joint strategies, this will allow a better.

Awareness Campaigns

This campaigns can help the population be aware of the possibility to report adverse reaction the importance and benefits of reporting.
It is important to use dissemination means atractive to different population groups.

More funds

Many organizations depend on fund raising to maintain their activities; providing more funds could allow them to focus on new areas such as pharmacovigilance .