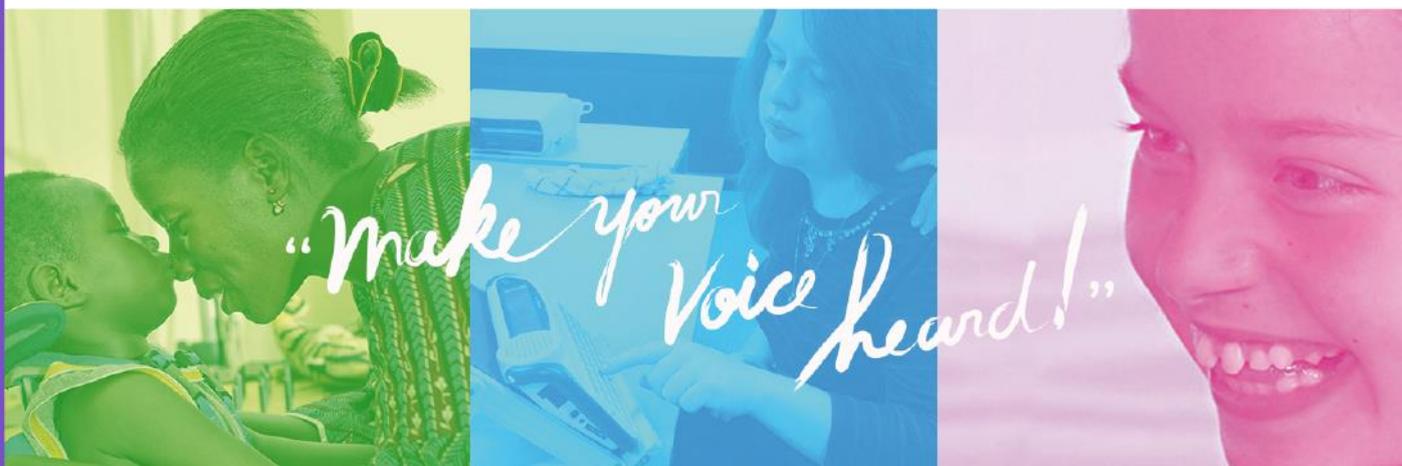




Rare disease patients' participation in research

A Rare Barometer survey

February 2018



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1. Introduction

Rare disease research contributes to the development of diagnostic tools, treatments and cures, as well as improved health and social care for patients and their families.

However, due to the low prevalence of the diseases, rare disease research faces many obstacles¹. For example, only small populations are available for clinical trials and there is also a lack of human biospecimens from patients with the same diseases. Compounding these problems is poor knowledge of the causes and the natural history of the diseases and difficulties that come with involving patients affected by severe diseases.

In addition issues such as a lack of coordinated resources for patient registries and clinical trials, the fact that funds are often scarce for research on conditions with such a small population, and the lack of existing literature and investigators working on the same disease can pose added barriers.

Furthermore, the estimated low return on investment discourages the development of treatments for rare diseases, thus leaving a huge unmet medical need.

Nevertheless, the Orphan Drug Regulation and other international regulations (Gammie, T, 2015) in this field did produce interesting effects – SMEs show a greater interest in early stage development of treatments for rare diseases, while big pharmaceutical companies tend to take products to a later development stage. Research on rare diseases can also lead to significant discoveries for more common diseases, a fact which bolsters research in this field. At the same time, as most of rare diseases have genetic origins, genetic therapies bring new hopes for rare disease patients and progress in gene identification has improved diagnosis and stimulated more research and therapy development.

Patient involvement in research has also resulted in more research, which is now better targeted to the needs of patients. Patients no longer solely reap the benefits of research; they are empowered and valued partners from the beginning to the end of the research process.

As a result, research has increased over the last two decades. There is no longer a complete lack of rare disease research. However, there is a lack of research to cover every one of over 6000 identified rare diseases.

In this context, having an insight into current rare disease patients' participation in rare disease research is of particular relevance. The objectives of this survey were to:

- estimate rare disease patients' level of participation in rare disease research;
- collect more knowledge on their experience of rare disease research; and
- gather rare disease patients' perspectives on obstacles to rare disease research and rare disease research priorities.

¹ EURORDIS position paper, "Why research on rare disease?", 2010

2. Executive summary

- More than one third (37%) of rare disease patients surveyed declare they have already participated in a research study.
- Among those who participated in research, **18% specified they have participated in *research to develop treatments and therapies***. Participation in *research to develop treatments and therapies* varies significantly across patients' countries and disease area. Results also show a gender gap in inclusion in clinical studies: **more men (21%) than woman (16%) have participated in *research to develop treatments***.
- The main motivations that lead rare disease patients to participate in research are **first the fact that they want to help science and the community** and then to receive new treatment options.
- **A quality relationship with researchers** is by far the main factor contributing to satisfaction with the participation in a research project. **Having the possibility to be closely and regularly followed** by a research team is also reported as one of the positive aspect of patients' participation.
- Regarding rare disease patients' perspectives on rare disease research, among rare disease research areas, **therapeutic research is considered as the highest priority**. In parallel, the **lack of public funding is identified as the main obstacle** to rare disease research.

3. Methodology

3.1 Survey participants profile

- Survey participants are part of the [Rare Barometer Voices](#) survey panel, a community of people living with a rare disease who participate in EURORDIS-Rare Diseases Europe surveys and studies.
- 3213 people living with a rare disease** have responded to the survey with an average of 7 minutes to complete the questionnaire. The survey was carried out between August and November 2017.
- The composition of the survey sample is as below:

Type	Percentage
Gender	
Male	23 %
Female	77 %
Diagnosis Status	
Diagnosed	95 %
Undiagnosed	5 %
Respondent Status (several answers possible)	
Patient	58 %
Parent of a child living with a rare disease	40 %
Sibling of a person living with a rare disease	3%
Other family member	5%
Country of origin	
EU	87%
Non-EU	13%

- Female proportion is high (77/23) compared to the general population (52/48).²
- 63 countries are represented in the sample**, with a higher representation of respondents from the European Union.

² This figure reflects several aspects:

- the fact that the primary carer role for people living with rare diseases is primarily assumed by the mother, as shown in the first Rare Barometer Voices survey on the [impact of rare diseases on daily life](#): 71% of parents living with a rare disease identify the mother as the main carer in the household;
- the usual tendencies of woman to be more interested in health-related subjects and medicine and of men to be less engaged in everyday life health-related activities (Rothman A. J. Salovey P. 1997);
- the fact that woman contribute disproportionately to online panel surveys (Smith, 2008).

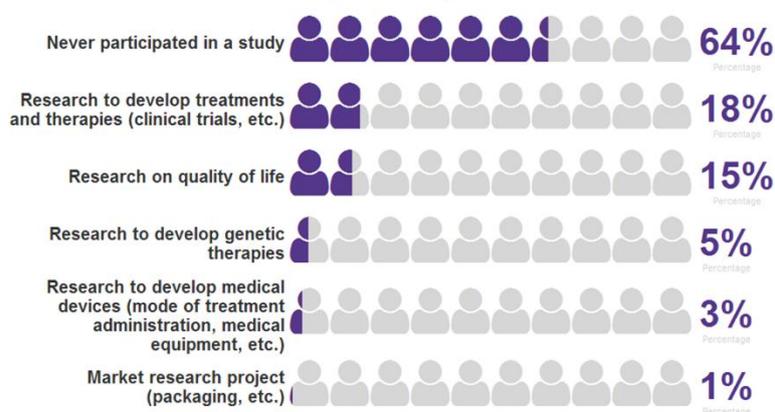
4. Results of the survey

4.1 Rare disease patients' participation in research

4.1.1 1/3 of the respondents have participated in research

First, survey participants were asked if they had ever participated in rare disease research, including any kind of research such as clinical trials, quality of life studies and research projects on genetic therapies or medical devices: **more than one third (37%) of respondents declare they have already participated in a research study**, of whom 22% participated in one project, 6% in two and 8% in more than two projects.

Graph. 1 **What type of research did you participate in? (Several answers possible)**



Participants were then asked to specify in which type of research project they participated (Graph. 1): 64% have never participated in any research project and 18% have participated in research to develop treatments and therapies. Participation in therapeutic research will be further explored in the following paragraphs.

Participation in *quality of life* studies is fairly significant (15%) as it is very close to participation in therapeutic research (18%). These figures also reflect the fact that - as shown in the open questions of this survey - a small percentage of Rare Barometer Voices participants are considering Rare Barometer Voices surveys as forms of quality-of-life research area.

5% have also participated in *research to develop genetic therapies*. In a context in which more gene therapy clinical trials are undertaken (from 1 in 1989 to 163 in 2015, Hanna E, 2017), results suggest that the number of genetic therapy initiatives is still low.

Finally, a low number of participants have participated in a research project *to develop medical devices* (3%) as well as in *market research projects* (3%).

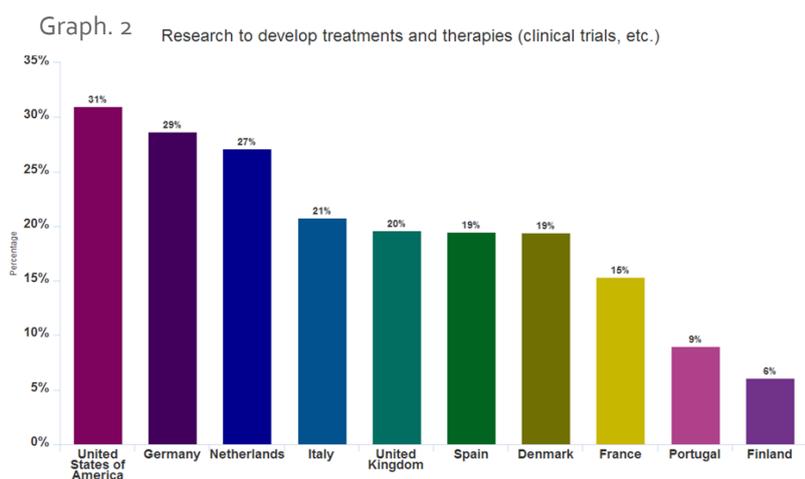
Focus on research to develop treatments:

4. 1. 2 A low level of participation in *research to develop treatments* that reflects an insufficient number of rare disease research initiatives

18% of patients surveyed declare that they have participated in *research to develop treatments and therapies* (see graph 1). As shown in an international survey conducted by the CISCRP (the Center for Information and Study on Clinical Research Participation) in 2017, this level of participation is comparable to the general patient population: 18% of patients declared they have participated in clinical research³. But this figure suggests an insufficient number of rare disease research initiatives to cover the high unmet medical needs of rare disease patients.

This gap is particularly striking in a situation in which **therapeutic research is considered as the highest priority** among patient representatives from the rare disease community⁴ (see graph 7).

4. 1. 3 Participation in *research to develop treatments and therapies* varies significantly across patients' countries of living



As described earlier, an average of 18% participated in therapeutic research. This figure varies across countries⁵, taking into account that results are based on respondents' experience of participation and not on actual location of clinical trials (clinical trials can be European or International for example). In countries where more than 100 respondents took the survey, **levels of participation in therapeutic research range from 6% to 31%**. Respondents from the US report a higher level of participation than in Europe.

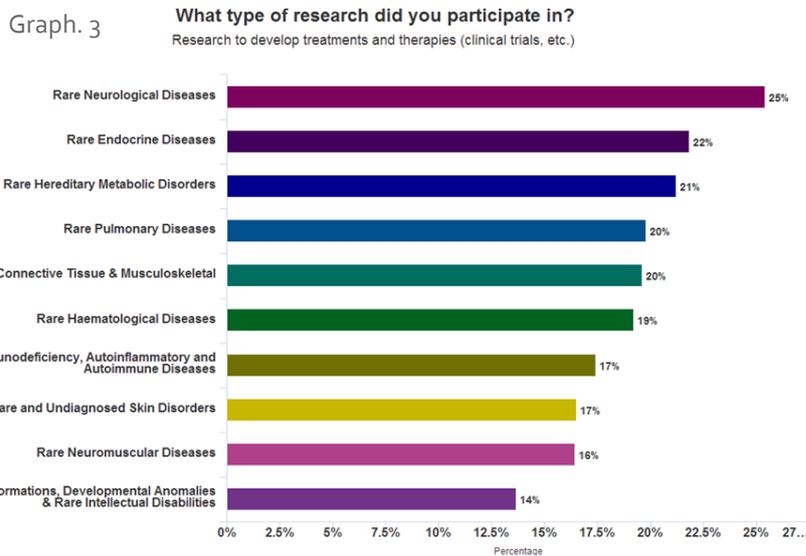
³ On a total of 12427 patients around the world, 18% declared they had participated in a clinical trial

⁴ Question asked in the same survey to rare disease patient representatives (patients engaged in advocacy activities) only.

⁵ Results are presented only for countries with more than 100 respondents to this question. Breakdowns by country are based on a cross table between the type of research respondents participated in (which type of research did you participate in?) and respondents' residence country (Which country do you live in?).

4. 1. 4 Participation in *research to develop treatments and therapies* varies across disease area

The ERNs (European Reference Networks) are rare disease networks for clinicians and researchers to share expertise, knowledge and resources across the EU. The ERNs cover an estimated 6000 rare diseases and are organised in 24 disease groupings. Results sorted by ERN grouping or therapeutic area with at least 100 respondents (10 out of 24) are presented below.



Level of participation varies across disease grouping and ranges from 14% to 25% with *rare neurological diseases* presenting the highest level of participation and *rare malformation* the lowest.

4. 1. 5 Lower level of participation in *research to develop treatments and therapies* among women

Graph. 4 **What type of research did you participate in?**
Research to develop treatments and therapies (clinical trials, etc.)



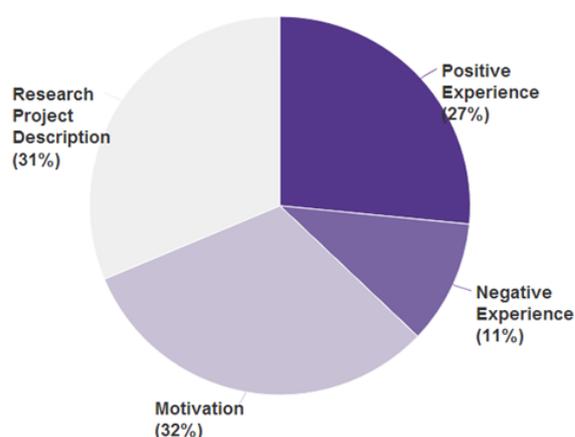
Results also show that more men (21%) than woman (16%) have actually participated in *research to develop treatments*. The gender gap in inclusion in clinical studies has been widely demonstrated within other various patient populations (Liu, Katherine A, 2016). It has been attributed to several factors, including cultural, biological and economical aspects such as: women being perceived as more expensive test subjects because of their fluctuating hormone levels; or exclusion of pregnant woman because of potential risks for the fetus; and also low income status which affects women more and prevent them from participating (e.g. necessity to travel). These results show that this gap also exists within the rare disease patient population. To be noted that this gender gap is only observed regarding research to develop treatments, whereas participation in quality of life studies (16% female/15% male), and studies to develop genetic therapies (5%/5%) or medical devices (3%/4%) are overall gender-balanced.

4. 2 Rare disease patients' experience of rare disease research – testimonies

Participants were then asked to describe their experience of participating in rare disease research in general in an open question. The graph below presents the type and the distribution of responses that were received. The rationale behind this question was to get an insight into what rare disease research actually means to patients and how they experienced it. To be noted that the definition of research can sometimes be broader according to respondents, for example complementary medical tests can be considered as research.

Graph. 5

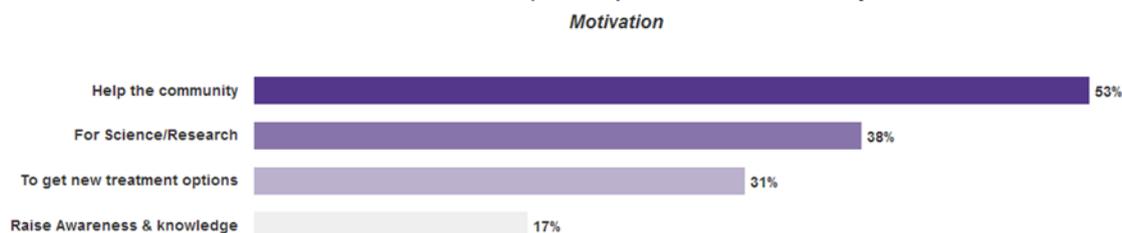
Please describe your experience of participating in rare disease research (why did you participate, positive or negative interaction with the researchers, etc.). Please provide as much detail as you can.



4. 2. 1 Main motivations: helping science and the community

Graph. 6

Please describe your experience of participating in rare disease research (why did you participate, positive or negative interaction with the researchers, etc.). Please provide as much detail as you can.



The reasons why patients participate are very often altruistic. Most of the time, patients acknowledge that their participation will result in new treatment options only for future patients affected by the same disease and they want to contribute to this change for the community (53%) and help science to progress (38%). Ranking altruistic reasons

as the greatest benefits of participating in research is similar to prior studies (CRISP, 2017)⁶ but it is even more important within the rare disease patient population.

“ I will always participate no matter what it costs me. I believe that not enough is being done in South Africa regarding (disease) research and treatment! » **South Africa**

What leads patients to take part into research projects is also often related to the fact that there is no available treatment for their disease and receiving treatment from the clinical trials is one of the only treatment options they have (seriously affected rare disease patients can be authorised to benefit from an unauthorised treatment through compassionate use programmes⁷).

“ Initially I participated because there were no treatment options for me and I nearly died several times. I started as a child and my parents saw the clinical trials as a way to keep me alive. It worked, I'm still alive! » **United States**

4. 2. 2 Evaluation of their experience: a quality relationship with researchers is essential

As shown in graph. 5 more positive experiences (27%) than negative experiences (11%) were reported.

A quality relationship with researchers involved in the project is by far the main factor contributing to satisfaction with their participation, meaning that patients attach a great importance to the **human side of the process and do not want to be only considered as research subjects.**

“ A significant amount of tissue was taken for biopsy and research purposes. The researcher was very thorough on explaining things to me. He was kind and respectful. It was a very positive experience for me. » **United States**

Conversely, negative experiences are often linked to bad quality relationships with researchers and a feeling of experiencing a one-way relationship with the research team.

⁶ CRISP, report on General Perceptions and Knowledge on Clinical Research, <https://www.ciscrp.org/download/2017-perceptions-insights-study-general-perceptions-and-knowledge-on-clinical-research/?wpdmdl=8773>, p4

⁷ Under strict conditions, products in development can be made available to groups of rare disease patients with life-threatening, long-lasting or seriously debilitating illnesses and no satisfactory authorised therapies and who cannot enter clinical trials, see European Agency website: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000293.jsp

“ We gave permission to use our information and felt like we were being used by the researchers for THEIR benefit, there was absolutely no benefit for us as patients. All the benefit was fame and recognition for the research team. They used us and then treated us like disposable lab rats when they were done with us. » **Canada**

One of the main positive outcomes of their participation is that research enables patients who are often experiencing a lack of care and follow-up care to **have the possibility to be closely and regularly followed** by the research team.

“ In my country, it enabled frequent check-ups and follow-up about the disease. » **Macedonia**

The most challenging aspects are practical, with transportation and time necessary to travel to the research center, especially for severely affected patients, some patients reporting that they were not able to take part in a trial because of the distance involved.

“ I haven't participated because all I've found it too far away.» **United States**

4. 2. 3 A strong request for transparent information on the research project

In general, rare disease patients want the research process to be clearly explained to them and request to receive feedback on the outcome of the results.

“ It was interesting to see the results after the conducted surveys » **Croatia**

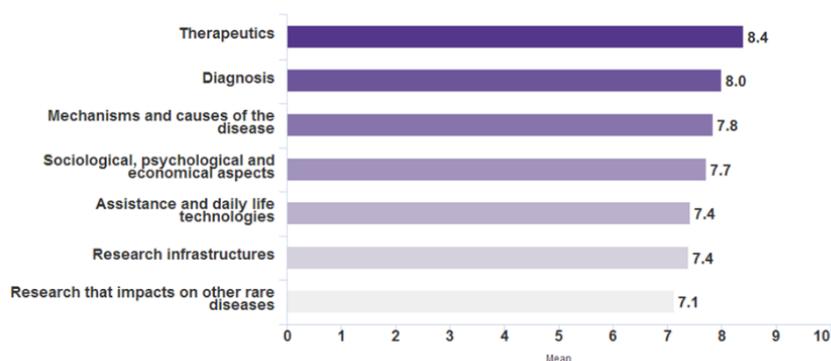
Respondents actually show a strong urge to learn new things about their disease, in particular on the mechanisms of the disease. Due to the under-researched nature of their diseases, rare disease patients are often experts on their disorder and participating in a clinical trial provides them with the opportunity to develop new and useful knowledge to manage the rare disease.

“ It was very positive. Besides obtaining important information on the disease I am affected with, I have learnt to listen to my body, discovered beneficial activities to carry out to maintain my muscles and the experience in general appeared to be psychological and moral support. » **France**

4.3 Rare disease patients' perspectives on rare disease research

4.3.1 Therapeutic research is the priority for rare disease patients

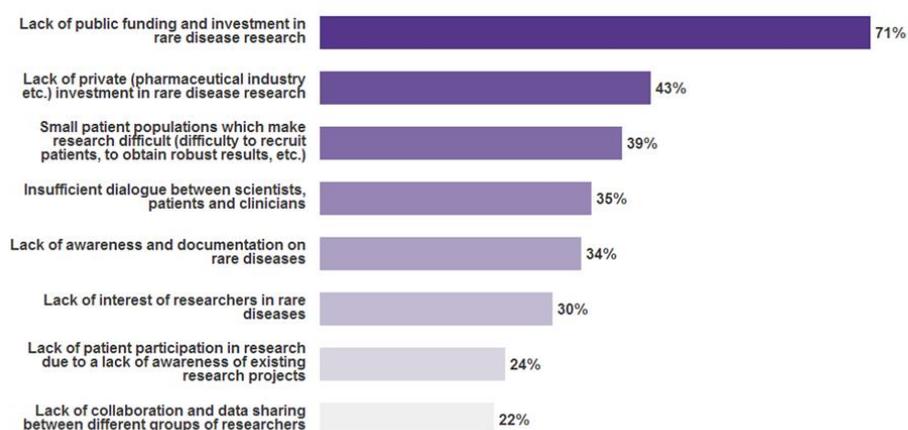
Graph. 7 According to you, on a scale from 1 to 10, what degree of priority should be given to the following research areas? (average grade)



The survey included a question on policy priorities within the rare disease research field that was only submitted to patients engaged in advocacy activities. The results show that all the research areas are important to patient representatives as they all obtained a grade above 7 out of 10. However, **therapeutic research is clearly identified as the number one priority** among the list. *Sociological, psychological and economical* aspects, with a grade of 7,7 out of 10 appear to be particularly valued from a patient point of view.

4.3.2 According to patients, lack of public funding is the main obstacle to rare disease research

Graph. 8 What do you think are the 3 main obstacles to rare disease research today? (Please select three responses in priority order)



All participants (including patients not engaged in advocacy priorities) were then asked their opinion on what are the main obstacles to rare disease research. By far, **the main hurdles to rare disease research today are perceived as financial, with a stronger request for Government funding**: 71% think that the lack of public funding is the main obstacle and 43% the lack of private investment.

The inherent problem of small and heterogenous rare disease patient populations (making randomised controlled study design difficult to conduct) is pointed out as the third obstacle to rare disease research (39%).

Then followed organisational hurdles, with lack of three-way dialogue between scientists, patients and clinicians (35%), lack of awareness and documentation that can discourage researchers to undertake research in the rare disease field (34%) and lack of interest of researchers in rare diseases (30%) are quoted as important obstacles to research in the rare disease field.

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