VOICES ON NEWBORN SCREENING: THE OPINION OF PEOPLE LIVING WITH A RARE DISEASE

A Rare Barometer survey with the Screen4Care project

May 2024

The survey 'Voices on newborn screening, the opinion of people living with a rare disease', was conducted by Rare Barometer within the framework of the European Screen4Care research project.

Rare Barometer is a survey initiative that robustly collects the experiences and opinions of people living with a rare disease and their close family members on topics that directly affect them. This programme is run independently by EURORDIS-Rare Diseases Europe and is a not-for-profit initiative. It conducts 1 to 3 studies each year and hosts a survey panel of more than 20,000 people who agreed to receive email invitations to participate in surveys and studies conducted by EURORDIS-Rare Diseases Europe.

EURORDIS-Rare Diseases Europe is a unique, non-profit alliance of over 1,000 rare disease patient organisations from more than 70 countries that work together to improve the lives of the 30 million people living with a rare disease in Europe. By connecting patients, families, and patient groups, as well as bringing together stakeholders and mobilising the rare disease community, EURORDIS strengthens the patient voice and shapes research, policies and patient services. EURORDIS is financed by the European Union, by its member patient organisations and by the AFM-Téléthon. EURORDIS also receives charitable donations, individual donations, and donations from corporate foundations and from the health industry.

Screen4Care is a 5-year European Project funded under the IMI2 (Innovative Medicine Initiative) aimed at shortening the pathway to diagnosis using advanced technologies, including newborn screening and artificial intelligence applied to the diagnosis of rare diseases. Screen4Care receives funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 101034427. The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA. As a Screen4Care partner, EURORDIS-Rare Diseases Europe received funding from the European Union.

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- All those who provided inputs and feedback into the design of this survey: members of the Topic Expert Committee, of the Screen4Care NBS forum and of the EURORDIS NBS working group; EURORDIS' national alliances and European federations.
- Rare Barometer partners and Screen4Care partners.

EXECUTIVE SUMMARY

Newborn screening refers to national and regional public health programmes that enable the systematic screening of newborns for a specific list of conditions, and to provide their parents with the necessary support to manage the consequences of those conditions. Previous studies show a wide acceptance of the principle of newborn screening among the public and among the rare disease community.

This report presents the European results of the survey 'Voices on newborn screening: the opinion of people living with a rare disease', conducted by Rare Barometer within the framework of the European Screen4Care research project. This study gathered the views of more than 6,179 people living with a rare disease and family members worldwide, 5,569 of whom were living in Europe with more than 1,300 distinct rare diseases, hence representing the diversity of the rare disease community.

Respondents' answers confirm the strong support for newborn screening from the rare disease community. They also show that people living with a rare disease and their family members mostly see newborn screening as a way to alleviate the burden of the diagnosis odyssey and to enable parents to make informed choices for their child living with severe and early onset conditions, regardless of their access to a treatment or intervention.

Evidence is coming from respondents' answers to the proposition 'If it is or were possible, I would have liked [the person I care for] to have been diagnosed at birth':

- more than 70% of them would have liked their rare disease to be diagnosed at birth, and even more among parents of children living with a rare disease (82%), and among people living with early onset conditions (73%).
- The respondents' opinion was the same whether the person living with a rare disease had access to a treatment or not.
- The 11% of the respondents who would not have liked their rare disease to be diagnosed at birth were concerned by the consequences that the knowledge on the rare disease can have in family dynamics or in society in terms of discrimination, especially regarding access to employment, healthcare insurance, or loans.

Evidence is also coming from respondent's opinion on newborn screening for any rare disease:

- A very large majority (73%-90%) of respondents were in favour of newborn screening for rare diseases with no available treatment or intervention, when presented with detailed reasons to screen: 90% think that any rare disease should be screened at birth if it could allow a quicker diagnosis, if it could enable the person living with a rare disease to have their disabilities better recognised, provide more adequate social support and potentially increase independent living, or if it could enable better follow-up and/or avoid harm through implementation of prevention practices.
- Respondents strongly support newborn screening even when they would not have liked to be diagnosed at birth themselves.

From the point of view of the rare disease community, newborn screening programmes should allow parents to prepare their child to live life to its full potential, regardless of the existence of treatments or interventions for the rare disease they are living with. This point of view is aligned with the results of several surveys on the opinion of the public and prospective parents on newborn screening.

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INTRODUCTION

Newborn screening programmes are public health programmes that consist in systematically screening all newborns for a list of conditions defined nationally or regionally. These initiatives include various elements such as the conduct of screening tests, confirmatory diagnostic tests (for children with a positive screen), communication of information to the parents, appropriate follow-up, disease management, continuous evaluation, and storage of samples for secondary use.

Newborn screening is important to people living with a rare disease and their families: while approximately 70% of rare diseases appear during childhood, clinical signs of symptoms do not always appear in the first days or months following birth. Conditions included in newborn screening programmes include rare diseases where early intervention can prevent the onset of disease symptoms or delay disease progression, improving the quality of life of the newborn, deriving benefits for the patients, their families and society.

However, the number of conditions screened in national and/or regional newborn screening programmes varies across Europe. For example, newborn screening programmes includes 8 conditions in Ireland, 11 in the United Kingdom, 17 in Germany, 22 in the Netherlands and 49 in Italy. If recent and continued scientific and technological advancements have opened the discussion on the expansion of newborn screening programmes, there is still a need to better understand the potential benefits and the challenges associated with this possible expansion, such as impacts on treatment access, psychological wellbeing, and family dynamics.

POTENTIAL BENEFITS AND POTENTIAL HARMS OF NEWBORN SCREENING

Several studies have been conducted to better understand the potential benefits and harms of newborn screening programmes. Some of them focus on theoretical considerations, while others consist of empirical surveys towards the public or prospective parents, usually considering "attitudes to newborn screening [as] an important indicator of the acceptability of an early diagnosis" (Parsons et al., 2002). Those surveys overwhelmingly show a wide acceptance of the principle of newborn screening among the public and prospective parents, who usually consider that its potential benefits outweigh its potential harms:

- 97% thought that as many disorders as possible should be screened for in the USA (DeLuca et al., 2017; n=88);
- 94% Canadians (n=1,1213) were in favour of newborn screening with current technologies and 80% with genetic tests (Bombard et al., 2014);
- 83% of new parents from the USA (n=514) were interested in genetic screening for their newborn (Waisbren et al., 2015).
- Other studies report strong uptakes of newborn screening for specific rare diseases among new parents: 94% uptake among Australian mothers (n=2,094) for Fragile X Syndrome (Christie et al., 2012), 92% uptake for Duchenne Muscular Dystrophy in Wales (Parsons et al., 2002; n=43), or 63% uptake for newborn screening in North America (Skinner et al., 2011).
- 83-86% Canadians (n=648) said they would probably or definitely have their newborn tested, and 95% agreed with genetic newborn screening for inherited hearing loss, inherited eye disease and inherited neurological disease, even when they declined testing for their own newborn (Etchegary et al., 2012a).

Some empirical studies surveyed people living with a rare disease and their family members, considering that the "'hands on' direct experience possessed by these families uniquely positions them to consider what an early screen would have meant for them" (Boardman et al., 2019). However, these studies usually focused on specific rare diseases, which allowed to consider the specificities of those conditions but prevented researchers from considering the point of view of the wider rare disease community.

'VOICES ON NEWBORN SCREENING': BUILDING ON THE DIRECT EXPERIENCE OF THE RARE DISEASE COMMUNITY

The present survey, conducted by Rare Barometer with the Screen4Care research project, gathered the views of more than 6,179 people living with a rare disease and family members worldwide - 5,569 of whom were based in Europe – from over 50 countries, representing a diverse international community impacted by more than 1,300 distinct rare diseases.

As a proxy to their attitude towards newborn screening, people living with a rare disease and their family members were asked if they would have liked their rare disease to be diagnosed at birth. To better understand the views of

the rare disease community beyond their direct experience, respondents were also asked if they thought that any rare disease should be screened at birth. This part of the survey was built upon the results of a previous Rare Barometer survey (Dubief, 2021) showing the wide acceptance of the principle of newborn screening among the rare disease community, as 95% of the participants were in favour of performing tests to diagnose rare diseases at birth. Beyond this wide acceptance, we wanted to know more on how the opinion of the rare disease community was impacted by the severity of the rare disease, its typical age of onset, its prevalence, the availability of treatments and the risks of false positive screening tests. Respondents were also asked to give their opinion on a list of reasons to screen rare diseases even when no treatments or interventions are available and on some possible consequences of newborn screening for the children and their families.

The results of this survey provide evidence on the acceptability of newborn screening among those who have the experience of living with a rare disease or caring for a child with a rare disease. This evidence should be completed by preference studies and lessons learnt from pilot initiatives regarding the logistical and technological feasibility of adding rare diseases to the list of national and/or regional newborn screening programmes.

1. METHODOLOGY

1.1. QUESTIONNAIRE

1.1.1. DESIGN

The questionnaire was written in English by the authors of this report based on a literature review identifying the main issues and criteria to define principles for newborn screening of rare diseases (Gross, 2023) and on the consultation of:

- 11 experts who provided inputs into priorities and criteria for newborn screening.
- 24 members of a Topic Expert Committee who contributed to clarifying topics and criteria to include in the questionnaire.
- National alliances of EURORDIS-Rare Diseases Europe, representing a wide range of rare diseases in one country, on topics and criteria to be included in the questionnaire, and on its final version.

The English questionnaire was translated in the 23 following languages by professional translators specialised in health-related issues: Bulgarian, Croatian, Czech, Danish, Dutch, Finnish, French, German, Greek, Hungarian, Italian, Latvian, Lithuanian, Norwegian, Polish, Portuguese, Romanian, Russian, Slovak, Slovenian, Spanish, Swedish and Ukrainian. Native speakers specialised in rare diseases reviewed 15 translations to check their cultural validity and consistency with the original English version.

1.1.2. DISTRIBUTION

The survey was distributed online from 24 May to 23 July 2023. 6,179 worldwide responses with 5,569 being from Europe. 51% respondents were contacted through the Rare Barometer panel, and 49% respondents were contacted through social media, patient organisations, and EURORDIS' networks.

EXPERTS CONSULTED IN ONE-TO-ONE INTERVIEWS

David Bick, Genomics England (UK); Simona Bellagambi, Uniamo (Italy); Felicity Boardman, Warwick University (UK); Martina Cornell, Amsterdam University Medical Center (Netherlands); Magdalena Daccord, European FH Patient Network (Austria); Francesca Forzano, European Society Of Human Genetics (UK); Urh Groselj, Metabern (Slovenia); Nick Meade, Genetics Alliance UK (UK); Bojana Mirosavljevic, Life Organisation- Zivot (Serbia); Antoni Monserrat, Alan (Luxembourg); Simon Wilde, Genomics England (UK).

MEMBERS OF THE TOPIC EXPERT COMMITTEE

Academics and clinicians: Felicity Boardman, Warwick University (UK); Mireia Deltoro, MetabERN (Spain); Vera Frankova, Charles University Prague (Vienna); Urh Goselj, MetabERN (Slovenia); Janbernd Kirschner, ERN Euro-NMD (Germany); Victoria Hedley, Newcastle University (UK); Heidi Howard, Lund University (Sweden); Tanja Krones, University of Zurich (Germany); Laurent Pasquier, CHU Rennes (France).

Patient representatives and patient organisations: Patricia Arias, Feder (Spain); Simona Bellagambi, UNIAMO (Italy); Valentina Botarelli, EURORDIS-Rare Diseases Europe (Belgium); Roseline Favresse, EURORDIS-Rare Diseases Europe (France); Gulcin Gumus, EURORDIS-Rare Diseases Europe (Spain); Amy Hunter, Genetic Alliance UK (UK); Kirsten Johnson, Fragile X Syndrome (UK); Alexandre Mejat, AFMTelethon (France); Mary Wang, RDI (Italy).

Industry (Scren4Care Partners): Virginie Bros-Facer, Illumina (France); Shirlene Badger, Illumina (UK); Stefaan Sansen, Sanofi (Belgium); Anne-Sophie Chalandon, Sanofi (France); Anna Kole, UCB (France); Amanda Pichini, Genomics England (UK).

1.2. DATA MANAGEMENT AND ANALYSIS

Data were handled per current data protection legislation and curated to remove ineligible respondents and incomplete questionnaires. Only the data willingly shared by respondents was collected. Only the Rare Barometer research team has access to the data, which was collected through the Sphinx survey software, saved on secured servers in France, password protected and pseudonymised.

Results presented below include descriptive statistics as well as the crossings that were found to be significant (p-value<0.01), either through Khi2 test or through multivariate analysis. These results have been discussed with the EURORDIS national alliances and European federations, with members of the Topic Expert Committee and of the EURORDIS NBS working group and with Screen4Care partners.

Map 1. Number of respondents per country in Europe

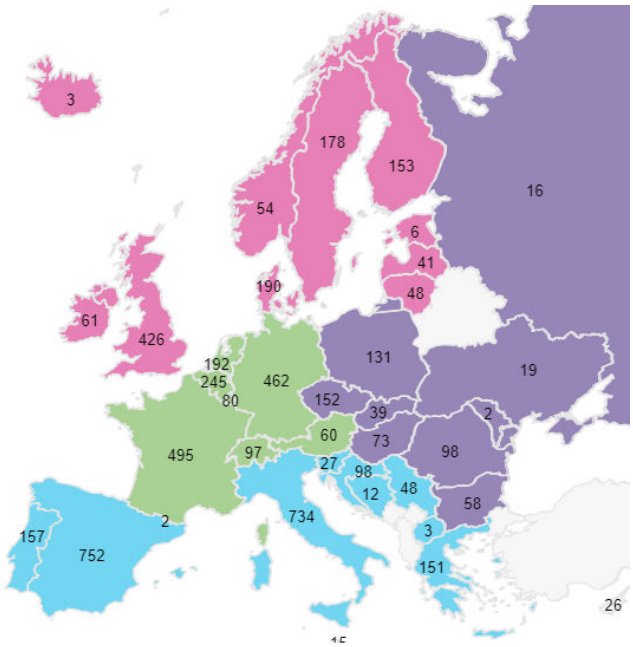


Table 1. Composition of the survey sample for Europe
n=5,569

Type	Percentage
Respondent status	
People living with a rare disease (PLWRD)	46 % (2,567)
Parent of PLWRD	49 % (2,701)
Other close family members of PLWRD (partner, grandparent, sibling…)	5 % (301)
Patient representatives Participants involved in voluntary and/or policy activities to support the cause of rare diseases	30 %
Gender	
Male	19 % (967)
Female	81 % (4,235)
Age	
Under 25 years old	2 % (127)
25-34 years old	12 % (590)
35-49 years old	43 % (2,206)
50-64 years old	32 % (1,640)
65 years old and above	10 % (518)
Diagnosed	
Yes	94% (5,242)
No	6% (327)
Point prevalence of the rare disease (Orphanet)	
Between 5/10,000 and 1/100,000	45% (2,532)
Less than 1/100,000	15% (860)
Unknown point prevalence	39% (2,177)

1.3. SURVEY SAMPLE

1.3.1. GEOGRAPHICAL DISTRIBUTION

The geographical distribution of respondents in Europe largely corresponds to the number of inhabitants and can depend on existing networks of patient organisations that disseminated the survey to their members, and on other cultural particularities.

Given the relatively low number of respondents in some countries, only countries with more than 20 respondents and with significant results (p-value<0.05) were considered in the analyses. Countries were also grouped in subregions as defined in the United Nations geographic regions for Europe (Map 1):

- Southern Europe (in blue): 36% of the respondents.
- Western Europe (in green): 29% of the respondents.
- Northern Europe (in pink): 21% of the respondents.
- Eastern and Central Europe (in purple): 11% of the respondents.

1.3.2. STATUS

More than half of the respondents were close family members of people living with a rare disease (Table 1). Parents of people living with a rare disease represent 49% of the sample. This figure is higher than in other surveys carried out within the rare disease community and shows a specific interest in newborn screening from parents of people living with a rare disease.

Parents of people living with a rare disease are especially overrepresented among respondents from Eastern and Central Europe, where they represent 64% of the respondents; in Southern Europe they represent 51% of respondents in Southern Europe, 45% in Northern Europe and 42% in Western Europe (Table 1).

Among the 1,608 (30%) patient representatives who responded to the survey, 42% were living with a rare disease and 58% were family members of a person living with a rare disease (Table 1).

1.3.3. GENDER

The female proportion of respondents (81%) was high compared to the general population (52%; Table 1) but similar to other surveys carried out among the rare disease community (Courbier et al., 2017).

1.3.4. AGE

73% respondents were between 35 and 64 years old (Table 1). Despite the large paediatric onset of rare diseases, only 80 people living with a rare disease under 25 years old responded to the survey.

1.3.5. DIAGNOSIS

94% of the respondents had received a confirmed or an initial diagnosis, while 6% only had a partial diagnosis or knew that their disease was rare, but it remained undiagnosed (Table 1).

1.3.6. DISEASES AND THERAPEUTIC AREAS

The rare disease population is very diverse: there are over 6,000 distinct rare diseases and a range of disease groups. The sample of this survey represents this diversity and is composed of **1,331 individual rare diseases**. **Graph 1** presents the repartition of respondents' disease in one or several therapeutic areas, based on the classification developed by Orphanet and available on orphadata.org.

1.3.7. POINT PREVALENCE

Point prevalence (the proportion of a particular population found to be affected by a given disease at a specific time) was calculated using Orphanet epidemiological data, based on the name of the rare disease and on respondents' country of residence (orphadata.com). Point prevalence is known for 61% (3,392/5,569) of the respondents, of which 25% (860/3,392) are living with a very rare disease (less than 1 case in 100,000 people) and 75% (2,532/3,392) are living with a more common rare disease (from 5 cases in 10,000 people to 1 case in 100,000 people) (Table 1). Among the 39% (2,177/5,569) of respondents for which point prevalence is unknown, 35% (768/2,177) did not declare their rare disease and 65% (1,409/2,177) are living with a rare disease for which epidemiological data is not yet available. People living with a very rare disease are overrepresented in the sample compared to epidemiological studies (Nguengang et al., 2020), but this proportion is similar to other surveys with people living with a rare disease (Dubief, 2021).

Graph 1. Number of respondents per therapeutic area.
Grouping based on the Orphacode of the disease entered by respondents and on the Orphanet classification of rare diseases. One rare disease can be classified in several therapeutic areas - n=5,569

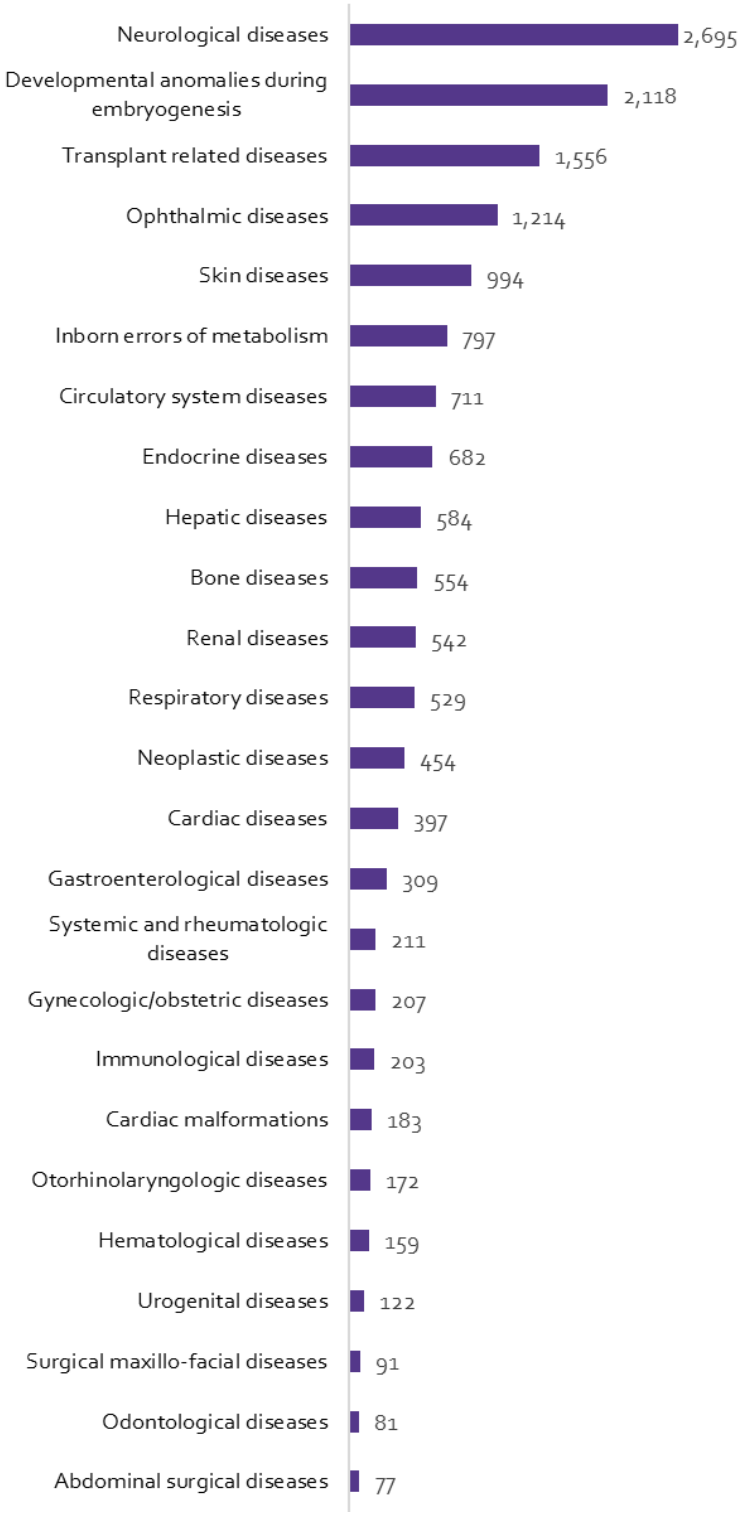


Table 2. Sociodemographic characteristics of people living with a rare disease, their parents and other and family members.
Totals are in column; n=5,569.

Type	People living with a rare disease (n=2,567)	Parents of a person living with a rare disease (n=2,701)	Other family members of a person living with a rare disease (n=301)
Gender of respondents			
Female	77 %	86%	71%
Male	22%	14%	29%
Age of respondents			
Under 25 years old	3 %	2%	3%
25-34 years old	13 %	11%	10%
35-49 years old	33 %	55%	27%
50-64 years old	36 %	28%	37%
65 years old and above	14 %	5%	24%
Number of children			
No children	43%	0%	74%
1 or more children (parents)	57%	100%	26%
Age of the youngest child among parents (n=4,011)			
Under 2 years old	5%	10%	7%
2-9 years old	15%	39%	14%
10-17 years old	19%	27%	15%
18 years old or more	62%	24%	64%
Number of children affected by a rare disease among parents (n=4,011)			
None	67%	0%	74%
1 child	22%	90%	23%
2 children or more	11%	10%	4%
Age of onset of the rare disease (Orphanet data – n=4,286) *Several answers possible*			
Antenatal	3%	12%	2%
Neonatal	21%	53%	28%
Infancy	22%	51%	33%
Childhood	30%	28%	32%
Adolescent	22%	9%	14%
Adult	31%	8%	26%
Elderly	12%	1%	8%
All ages	39%	22%	31%

1.3.8. PROFILES OF PEOPLE LIVING WITH A RARE DISEASE, THEIR PARENTS AND OTHER FAMILY MEMBERS

Survey participants had different experiences related to the rare disease and to their ability to make decisions impacting the health and life of people living with a rare disease. Hence, this report will make a difference between:

- people living with a rare disease, who have the direct experience of living with a rare disease.
- parents of a person living with a rare disease, who have taken or could have taken specific decisions regarding their child's health and life.
- other close family members of a person living with a rare disease (siblings, grandparents, aunt/uncle, spouse…) who could have an influence on the life of people living with a rare disease, but less than parents.

In the survey sample, people living with a rare disease, their parents and other family members had different profiles. Parents are more likely to be in their forties, with one or two children under 18 years old and living with a rare disease. People living with a rare disease are more diverse in terms of age groups and fewer of them have children. However, most of those who are parents have adult children or have children that are not affected by a rare disease. People living with a rare disease have later onset diseases, while most of the conditions declared by parents of people living with a rare disease have an infancy or childhood onset.

2. A WIDE MAJORITY OF THE RESPONDENTS WOULD HAVE LIKED THEIR RARE DISEASE TO BE DIAGNOSED AT BIRTH

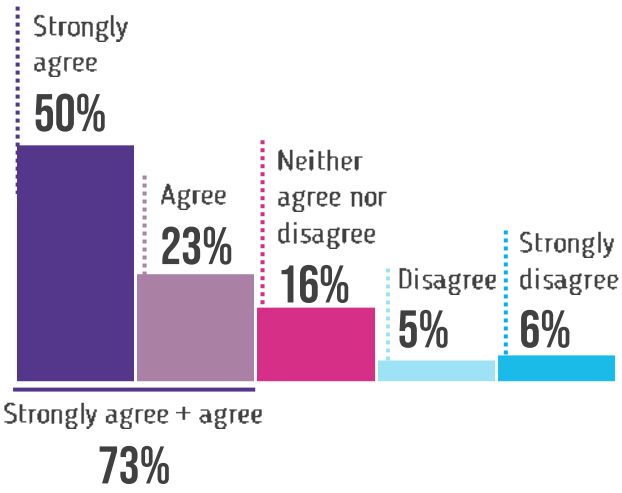
To better understand how their experience impacted their views on newborn screening, people living with a rare disease were asked if they would have liked to be diagnosed at birth, while parents and family members were asked if they would have liked the person living with a rare disease to be diagnosed at birth.

73% of the participants would have liked to be diagnosed at birth, or the person living with a rare disease to be diagnosed at birth (Graph 2).

Studies on the general population show an even higher acceptance of newborn screening in the public. When parents were asked if they would like their newborn to be screened, 94% mothers consented to screening their newborn for Fragile X Syndrome in Australia (Christie 2012), there was a 92% uptake for Duchenne Muscular Dystrophy programmes in Wales (Parsons 2002) and a 63% uptake for newborn screening in North America (Skinner et al., 2011).

To better understand how living with a rare disease, or caring for someone with a rare disease, could have impacted respondents' opinion in our survey, we analysed their answers depending on their characteristics, the characteristics of the rare disease, of their diagnosis journey and access to treatment and supportive care (Table 3). The most significant results are summarised below, and detailed results are provided in Annex 1.

Graph 2. If it is or were possible, I would have liked [the person I care for] to be diagnosed at birth - *All respondents; n=5,569*



Source: Rare Barometer survey conducted May 24-July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

TABLE 3. Characteristics crossed with respondent's willingness for their rare disease to have been diagnosed at birth.

Characteristics of the respondents	Characteristics of the rare disease	Characteristics of the diagnosis journey	Access to treatment and supportive care
- Status: person living with a rare disease, parents or family members of a person living with a rare disease. - Country of residence - Age at the time of the survey - Gender - Knowledge in genetics - Degree of education	- Age of onset - Point prevalence - Evolution of the symptoms - Types of rare diseases	- Age of the patient at diagnosis - Time to diagnosis from the first medical encounter	- Access to treatment(s) or intervention(s) - Access to supportive care - Effectiveness of treatment(s) or intervention(s) - Effectiveness of supportive care

2.1. ATTITUDE DEPENDING ON RESPONDENTS' CHARACTERISTICS

Respondents' status (patient, parent or other family member), country of residence, age at the time of the study and gender significantly impacted their opinion on newborn screening for their disease ($p<0.01$). However, their knowledge in genetics and their degree of education did not significantly impact their opinion on newborn screening ($p=0.42$ and $p=0.27$ respectively).

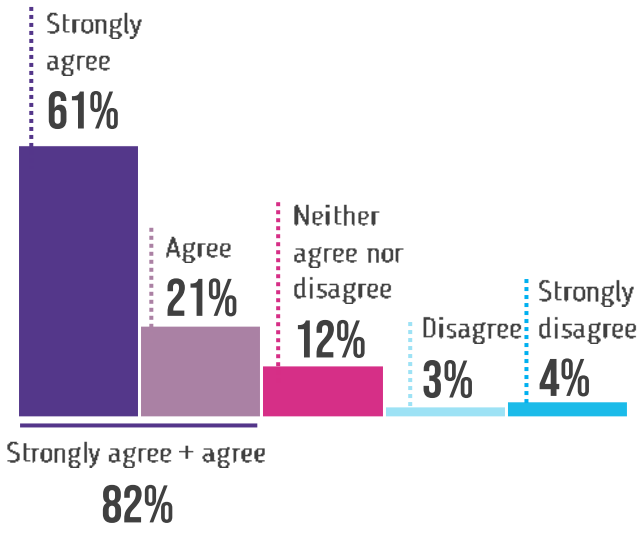
2.1.1. PARENTS ARE MORE IN FAVOUR OF NEWBORN SCREENING THAN PEOPLE LIVING WITH A RARE DISEASE

82% of parents of people living with a rare disease would have liked their child to be diagnosed at birth (Graph 3), **78% of other family members** would have liked the person living with a rare disease to be diagnosed at birth, and **63% of people living with a rare disease** would have liked to be diagnosed at birth (Graph 4).

These results are consistent with the literature on the topic: in a study on newborn screening for Haemophilia in the UK (Boardman et al., 2019), family members were more in favour of newborn screening (82%) than adult patients (74%). We explore below some reasons to explain these differences.

PARENTS OF PEOPLE LIVING WITH A RARE DISEASE STRONGLY SUPPORT THE DIAGNOSIS OF THEIR CHILD AT BIRTH

Graph 3. If it is or were possible, I would have liked the person I care for to be diagnosed at birth - *Only parents of people living with a rare disease; n=2,701*



Source: Rare Barometer survey conducted May 24-July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

Parents' opinion was impacted only by a few characteristics ($p<0.01$, Annex 1): a higher proportion of parents were willing to have had their child diagnosed at birth:

- depending on where they lived: among those who lived in Eastern or Central Europe (86% in favour), Southern Europe (85% in favour) and Northern Europe (83% in favour),
- when the rare disease is an inborn error of metabolism (87% in favour),
- when the diagnosis was confirmed shortly after the birth of their child (over 87% in favour),
- when they deemed the treatment received for the rare disease effective (85% in favour).

Parents overwhelmingly told us that knowing about their child's rare disease at birth would give them more chances to find the right treatment or supportive care, and to prepare their child for adulthood and independence.

"As a parent, I would feel safer if I knew from the beginning if we had an unusual diagnosis in the family or for our children. In our case, it took 2.5 years of efforts by the healthcare system to get a diagnosis, thanks to a doctor who happened to know about fragile X and thought we should test for it. Finally, our son was diagnosed at the age of 4 but there were a few years when I despaired as a mother. During those years, my son received various interventions from psychologists, physiotherapists, shoe inserts etc. The care he received could have been more targeted from the beginning, instead of having to wait for 4-5 years for appropriate care. Since fragile X also affects babies, the infancy period was not so easy either, which can also be prevented with early diagnosis. Then the whole family would have felt so much better from the start."
Parent of a person living with Fragile X syndrome, Sweden

"With early diagnosis, parents would be able to prepare for the huge challenges that await them if the child needs help for the rest of their life. They could receive up-to-date information about the expected development, possible cures or early development opportunities, treatments or institutional care. I would definitely support this because it would have been a great help to me in the last 24 years.
Parent of a person living with Angelman syndrome, Hungary

"I did not know about the hereditary disease from which my brother most likely died 40 years ago, and for which I also carry the gene mutation. So, luck alone saved me from the activation of the disease. I think this answer best describes why screening for rare diseases would be beneficial."
Parent of a person living with Ornithine transcarbamylase deficiency, Croatia

Only 6% of parents of people living with a rare disease would not have liked their child to be diagnosed at birth (Graph 3), mostly because of the anxiety and fear of discrimination associated with the diagnosis.

"Where treatment is not available, learning of a condition that may not manifest for many years could cause anxiety and early worry/grief for the parents and surrounding family members. Saying that, I believe testing should be available and the parents given information on the conditions being tested for and when they may affect the person".
Parent of a person living with Juvenile neuronal ceroid lipofuscinosis (NCLs, or Batten disease), Ireland

"Should all newborns be screened for all diseases? Many rare diagnoses are indeed rare. I am afraid that it would create a lot of anxiety for the parents and children growing up. Does the healthcare systems really can accept all diagnoses?"
Parent of a person living with a rare disease - Sweden - Fabry disease

The testimony of Iuliana Dumitriu in the Rare on Air podcast, summed up hereafter, allows to better understand why parents of people living with a rare disease are so strongly in favour of newborn screening: they have the lived experience of taking care of their ill child while facing the unknown, searching for the correct diagnosis, and navigating the healthcare system to make sure that their child accesses the best possible care and treatment. To them, early diagnosis through newborn screening could save years of diagnosis search and inadequate care.

Testimony of Iuliana Dumitriu

President of the Coffin-Lowry Syndrome association in Romania and mother of an 8 years-old boy living with Coffin-Lowry syndrome, a rare genetic condition affecting motor and cognitive developments.

eurordis.org/rare-on-air

My diagnosis odyssey started when my son was 10 days old, as the hospital doctors suggested us to bring him to physiotherapy. It was difficult to adjust to the fact that something might be wrong while taking him to daily physiotherapy and visiting geneticists and specialists every couple of months. When he was three years old, we conducted a developmental assessment and it was a shock to realise that despite our efforts, he was only at 30% of development compared to his peers. We had invested all our mental energy and all our time into therapies, and he was still not developing as he should have been. After this developmental assessment, our son was qualified for a severe handicap certificate, as it is called in Romania, but we still did not have a diagnosis.

So, I started to look for a diagnosis on my own: googling, emailing hospitals, taking private genetic tests. When he was three and a half years old, I started thinking that he may have Coffin-Lowry syndrome based on my own association between his developmental delays, his tests, pictures of other boys with this condition, phenotyping, personal readings on genetics... It was terrible, I did not like it and I did not accept it. I was in a total denial phase with no support from anybody, so I just dropped the diagnosis search for months, I did not want to know.

When he was 4 and a half years old, his front teeth fell, which was too early and a sign of Coffin-Lowry syndrome. I realised that I could not deny it anymore. I contacted an association in the US and to me, the recognition from the president of this federation was the first confirmation of my son's diagnosis: it was so frustrating because it was so obvious that those boys looked like my child! But I still did not have a medical confirmation, which was important because an exact diagnosis provides important information for comorbidities and to take preventative actions.

The diagnosis was confirmed by a very dedicated clinician in France: we corresponded through email and the Romanian genetic laboratory sent her test samples. But it still took 2 years, and it was only after the French laboratory bought new medical machines, and that the clinician re-ran my son's tests on those new machines, that she confirmed the diagnosis of Coffin-Lowry syndrome and told us which mutation our son had.

Now that we have the diagnosis, he is much better mentally because we are only taking him to the therapies that he needs, in the moderate amount that he can handle. His family environment is much better and relaxed because we have more time for ourselves. In terms of medical care, he is now in the moment when we can prevent medical complications that were shown to be fatal in cases reported in the literature on the condition, such as heart and lung complications, or scoliosis.

For 7 years, we could not fight for a treatment, because we were fighting for a diagnosis. For 7 years, we visited geneticists and specialists every couple of months, wasting public and familial resources, and preventing more people to visit those geneticists and specialists. We also lost precious years to ensure the social integration of our child and our family, making sure that he can find his place in society and make the needed adaptation to his condition, such as finding the right kindergarten or talking to other people with similar conditions.

If my son had been lucky enough to have been screened at birth, and with his mutation in a place that could be found, as for many other Coffin-Lowry syndrome cases, it would have given him and our family 7 years back. His childhood would have been less stressful, he would have only had the therapies he needed, and in a moderate amount adapted to his needs. I would not have spent so many nights learning genetics, then being tired at my job and not having enough mental relaxation to handle family life the next day. All this was a burden for everybody.

A WIDE MAJORITY OF PEOPLE LIVING WITH A RARE DISEASE WOULD HAVE LIKED TO BE DIAGNOSED AT BIRTH

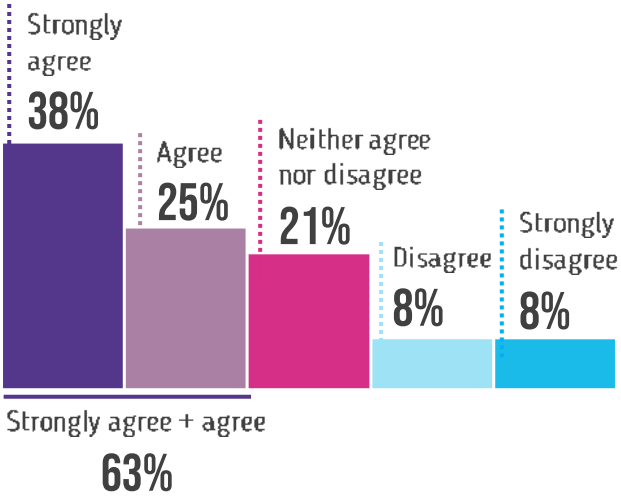
63% of people living with a rare disease would have liked to be diagnosed at birth (Graph 4). Their age at diagnosis and the age of onset of their disease strongly impact their willingness to have been diagnosed at birth ($p<0.01$, Annex 1):

- up to 89% of people living with a rare disease who were diagnosed a few months after birth,
- 73% of those whose disease onset is classified as antenatal, neonatal or during infancy,
- and more than 70% of those who were diagnosed as infants, children or adolescents, said that they would have liked to be diagnosed at birth.

People living with a rare disease were also more willing to have been diagnosed at birth when:

- they were younger at the time of the study (78% among those who were under 25 years old, and 74% when they were 25 to 34 years old),
- they were living in Eastern and Central Europe (73%) or in Southern Europe (71%),
- their rare disease has a genetic origin (70%), is an inborn error of metabolism (74%) or a developmental anomaly during embryogenesis (72%),
- they were diagnosed more than 5 years after a first medical contact (69%).

Graph 4. If it is or were possible, I would have liked to be diagnosed at birth. *Only respondents who are living with a rare disease; n=2,567*



Source: Rare Barometer survey conducted May 24-July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

Responses from people living with a rare disease did not vary significantly depending on their access to treatments and supportive care, on their health status, gender, education (age at end of studies), knowledge in genetics and the prevalence of their disease.

"I am facing this path, in view of a pregnancy and not having known what my illness was until I was 25, passing as a person with psychological problems while having a genetic disease. I think that the possibility of knowing in advance that you have a rare disease and that it can compromise your quality of life and perhaps have the possibility, with a simple blood test, of being able to avoid it in some way, would help many families and people to have a more or less normal life without such serious illnesses."

Person living with an ultra-rare genetic ophthalmological disease, Italy

"Knowing about the genetic predisposition to a particular disease, you can notice the first symptoms in a timely manner and adjust your lifestyle or treatment to avoid transition to more severe forms. My diagnosis was made late, after 10 years of incorrect and ineffective treatment. Due to late diagnosis, I lost a lot in my quality of life, which I never managed to restore. With timely diagnosis, I could be living a full life".

Person living with a rare primary immunodeficiency, Ukraine

"Hopelessness, lack of information, not knowing enough about the diagnosis, treatment options, support, indifference and ignorance from doctors and social assistance... I believe that any chance, even the smallest, to improve the information of patients with rare diseases and their relatives, would improve their lives".

Person living with perineural cyst, Czech Republic

Only 16% of people living with a rare disease would not have liked to be diagnosed at birth, and 21% did not give an opinion (Graph 4). Reasons for not wanting to be screened at birth can be similar to those of parents of people living with a rare disease, such as fear of anxiety, stigma and discrimination that the child and family could face. Some people living with a rare disease even feared specific discriminations by insurance companies, banks or when searching for a job. Respondents who were diagnosed when they were adults or who are living with an adult-onset condition (Annex 1), are also more likely to have not wanted to be diagnosed at birth. Some testimonials also reflected the fact that people living with a rare disease would have preferred not to deal with the consequences of having a rare disease as a child.

"As long as there are disadvantages directly linked to the stigmatisation after the diagnosis (insurance, job, bank), I reject any form of recording of the disease. With the system in place, it is better to complete all insurances up to the 18th year of life, and then record the diagnosis. Otherwise, there are too many obstacles in the way of those living with a disease for the rest of their lives. Early diagnosis could save money for everyone, but not only at the expense and disadvantages of those living with a rare disease!"
Person living with a genetic cystic renal disease, Germany

"Knowing right away from childhood that you are ill when the disease can appear as adults or may not even manifest itself conditions life in a psychologically negative sense".
Person living with hereditary spastic paraplegia, Italy

"Family relationships change. I would like to have grown up without knowing that I was sick, if it did not have fatal consequences. My two sisters are more fused because my mother has had the attention on me and I have felt outside of that sibling bond. I want to live a normal life, which is hard to do when you are defined as 'sick'".
Person living with hereditary hemorrhagic telangiectas, Denmark

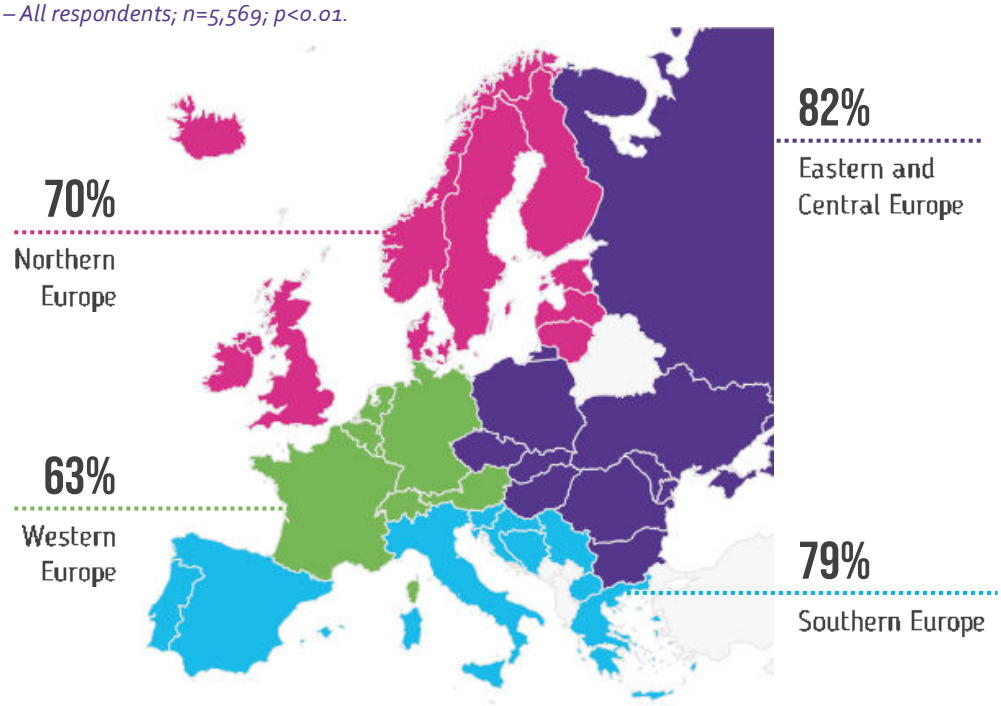
2.1.2. DIFFERENCES DEPENDING ON AGE AND GENDER OF THE RESPONDENTS MAY COME FROM INTERACTIONS WITH OTHER VARIABLES

Our results show that among all respondents, women are significantly more in favour of newborn screening than men (74% and 69% respectively, $p<0.01$). However, further multivariate analyses (to be published) showed that gender alone did not significantly impact respondents' opinion on newborn screening in our study. On the contrary, the significant results we obtained when we only considered percentages may hide more complex associations between gender and other characteristics of the respondents: for instance, it could be because there are more women among parents of people living with a rare disease (Table 2), or because it takes longer for women to be diagnosed (Faye et al., 2024; see Annex 1).

2.1.3. MORE RESPONDENTS FROM EASTERN, CENTRAL AND SOUTHERN EUROPE WOULD HAVE LIKED THEIR RARE DISEASE TO BE DIAGNOSED AT BIRTH

There are significant differences in proportions of respondents who would have liked their rare disease to be diagnosed at birth depending on their country of residence (Map 2). Table 4 allows to better understand differences between countries with a significant number of respondents: country differences could come from cultural differences that cannot be clearly identified in our data, nor by comparing our results with other studies, due to the lack of European-wide empirical studies on newborn screening.

Map 2. If it is or were possible, I would have liked [the person I care for] to be diagnosed at birth *– All respondents; n=5,569; p<0.01.*



Source: Rare Barometer survey conducted May 24-July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

TABLE 4. Percentage of respondents who agreed or strongly agreed with 'If it is or were possible, I would have liked [the person I care for] to be diagnosed at birth', depending on their country of residence.

'agree' or 'strongly agree' is significantly...	All respondents n=5,569	PLWRD n=2,567	Parents of PLWRD n=2,701
...over-represented	Latvia (93%), Lithuania (92%), Poland (90%), Romania (85%), Spain (84%), Croatia (82%), Czech Republic (80%), Italy (77%)	Poland (87%), Spain (78%), Italy (69%)	Spain (91%), Poland (91%)
...under-represented	Finland (48%), Netherlands (53%), Switzerland (55%), Germany (56%)	Netherlands (46%), Germany (43%), Finland (40%)	France (77%), Germany (76%), Finland (69%), Netherlands (67%), Luxembourg (66%), Switzerland (59%)
Total	**73%**	**63%**	**82%**

Only significant relationships are reported (p-value < 0.05), for countries with at least 20 respondents.

Source: Rare Barometer survey conducted May 24-July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

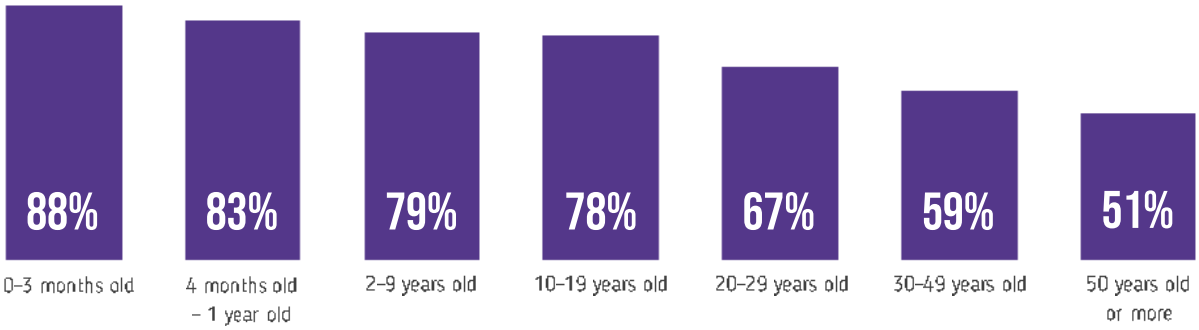
2.2. ATTITUDE DEPENDING ON THE CHARACTERISTICS OF RESPONDENTS' RARE DISEASE AND DIAGNOSIS JOURNEY

The youngest the patient at the time of diagnosis, the more the respondents would have liked their rare disease to be diagnosed at birth (p<0.01, Graph 5). **Close to 90% of respondents whose condition was diagnosed soon after birth (before the patient was 4 months old) said that they would have liked their rare disease to be diagnosed at birth**. Also, 93% of the parents of people living with a rare disease diagnosed between 4 months old and 1 year old said that they were in favour of newborn screening for their child (Annex 1). These results could be interpreted as a consequence of the positive experience of those respondents with the early diagnosis of their rare disease, and even sometimes with newborn screening.

"Our daughter was diagnosed with Cystic Fibrosis four weeks after birth thanks to newborn screening. Of course, the diagnosis was very bad for us, but thanks to the diagnosis, we were able to take all the necessary measures immediately: medication, physiotherapy, nutrition, hygiene. Our daughter is now 10 years old and is doing very well thanks to the targeted therapies. In retrospect, of course, we are very grateful for the quick diagnosis, even though we were unfortunately confronted with a bad diagnosis shortly after birth".
Parent of a person living with Cystic Fibrosis, Spain

"In our case, the detection and information received when our daughter was born allowed us to operate on her as soon as possible and that benefited the results".
Parent of a person living with large congenital melanocystic nevus, Spain

Graph 5. Percentage of respondents who agreed or strongly agreed with 'If it is or were possible, I would have liked [the person I care for] to be diagnosed at birth', depending on the age of the patient when the rare disease was diagnosed - *All respondents; n=5,569; p<0.01*

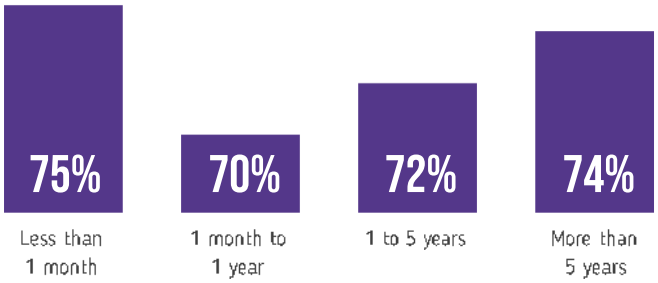


Source: Rare Barometer survey conducted May 24 -July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

The strong support from respondents whose rare disease was diagnosed at a very young age could also be linked to the age of onset of the disease, as there is a strong correlation between the patient's age at diagnosis and the disease's usual age of onset (p<0.01, Annex 2). Also, the lowest the age of onset of their disease, the more respondents would have liked it to be diagnosed at birth (p<0.01, Annex 1): **80% of respondents whose condition has an onset before or during infancy would have liked their rare disease to be diagnosed at birth**, while only 58% among those with an adult-onset condition, and 52% when their condition appears at old age (Annex 1).

The time it took for the rare disease to be diagnosed also impacted respondents' opinion on newborn screening for their rare disease: **74% of the respondents who waited for a diagnosis for more than five years would have liked the rare disease had been diagnosed at birth (Graph 6)**. However, the percentage of respondents (and especially of patients) who said that they would have liked the rare disease to be diagnosed at birth is higher when their rare disease was actually diagnosed less than 1 month after the first medical contact: this is probably linked to interactions with other variables, such as the age of the patient at diagnosis (60% of the patients diagnosed within 1 months were under 2 years old at diagnosis – Annex 3; see also Faye et al. 2024).

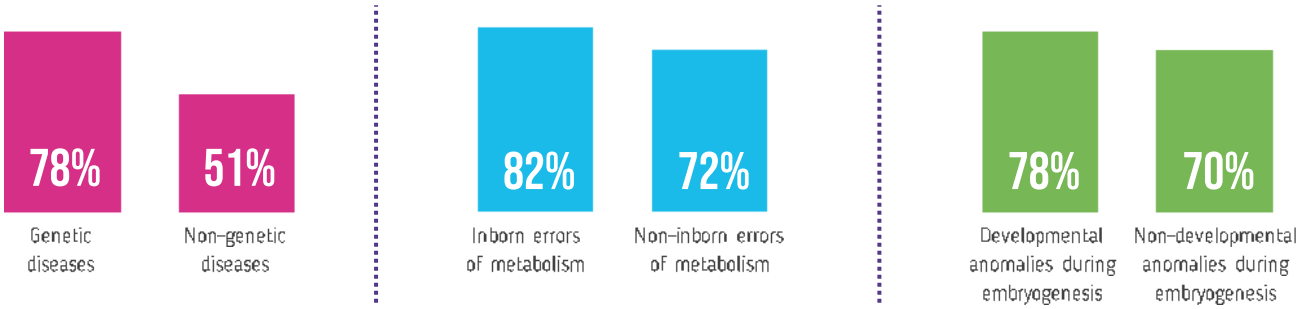
Graph 6. Percentage of respondents who agreed or strongly agreed with 'If it is or were possible, I would have liked [the person I care for] to be diagnosed at birth', depending on the time between first medical contact and the confirmation of the diagnosis - *All respondents; n=5,569; p=0.02*



Source: Rare Barometer survey conducted May 24-July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

More respondents would have liked their rare disease to be diagnosed at birth when the rare disease has a genetic origin (78% of all respondents, Graph 7; 70% of PLWRD, p<0.01; Annex 1), when their rare disease is metabolic (82% of all respondents, Graph 7; 74% of PLWRD, p<0.01; 87% of parents, p<0.01; Annex 1) and when it is a developmental anomaly during embryogenesis (78% of all respondents, Graph 7; 72% of PLWRD, p<0.01; Annex 1).

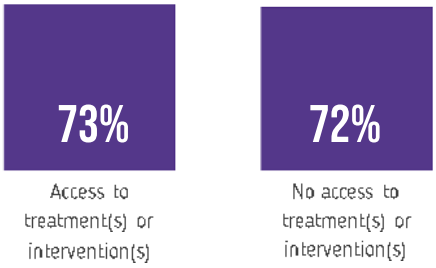
Graph 7. Percentage of respondents who agreed or strongly agreed with 'If it is or were possible, I would have liked [the person I care for] to be diagnosed at birth', depending on the characteristics of the rare disease - *All respondents; n=5,569; p<0.01*



Source: Rare Barometer survey conducted May 24-July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

2.3. ATTITUDE DEPENDING ON PATIENTS' ACCESS TO TREATMENT AND SUPPORTIVE CARE

Graph 8. Percentage of respondents who would have liked to be diagnosed at birth among those who answered either 'Yes, even partially (e.g. for one of the symptoms)' or 'No' to the question 'Did you receive or are you receiving treatment(s) or intervention(s) to lessen or control the effects of the rare disease, including medication, surgery, diet or other medical means?'
- All respondents; n=5,569; p=0.46



Source: Rare Barometer survey conducted May 24-July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

Respondents' willingness for the rare disease to have been diagnosed at birth was the same whether the patient had received treatment(s) or intervention(s), or not (Graph 8, p=0.46). The opinion of parents of people living with a rare disease was impacted by the effectiveness of the treatment(s) or intervention(s) received by their child: 78% of the parents who thought that treatments or interventions were not effective or slightly effective would have liked their child to be diagnosed at birth, vs. 85% of the parents who thought that the treatment or interventions were significantly or extremely effective (p<0.01, Annex 1). However, the opinion of people living with a rare disease was not impacted by the effectiveness of the treatments or interventions they had access to (p=0.43, Annex 1).

Access to supportive care positively impacted the opinion of respondents: 74% of those who had access to supportive care would have liked the rare disease to be diagnosed at birth, vs 69% of those who did not have access and did not need supportive care (p<0.01, Annex 1). However, effectiveness of supportive care did not impact respondents' opinion on newborn screening for their rare disease.

"Regardless of available treatments, a diagnosis is often necessary to better understand what is happening to us. It is often indispensable to receive reasonable medical care or help in everyday life."
Person living with hypermobile Ehlers-Danlos Syndrome, Germany

"To me, the main benefit of newborn screening is timely intervention or at least information in case of diseases for which treatments are not available, so that the family knows what to expect and gives their child the maximum from the first day."
Parent of a person living with mucopolysaccharidosis type 1, Croatia

2.4. WHY ARE RESPONDENTS WILLING TO HAVE THEIR RARE DISEASE DIAGNOSED AT BIRTH?

A wide majority of respondents would have liked their rare disease to be diagnosed at birth because they view it as a way to access early diagnosis and avoid the diagnosis odyssey, i.e. the long and difficult journey to diagnosis endured by most people living with a rare disease and their family members (Faye et al., 2024).

> *"The unknown is an extremely hard period for parents of children with an unknown genetic condition, it can be very isolating. Being able to have an earlier diagnosis would mean getting the right support and the right treatment plan more easily."*
> **Parent of a person living with a rare disease, United Kingdom**

If access to diagnosis eases access to the most appropriate care and treatment, respondents also saw it as a way to have as much information as possible on their rare disease. Unexpectedly, their willingness for the rare disease to be diagnosed at birth was not impacted by their access to treatment(s) or intervention(s). This is of particular interest when considering that there is a treatment only for an estimated 5% to 6% of all rare diseases. Respondents seemed to mostly value the possibility for parents to make informed choices for their child and their family. In this regard, while we did not include questions on how the diagnosis was announced (or found out, like in the case of Iuliana Dumitriu), or which information was given after the diagnosis, this topic appeared in many answers to open questions as a moment that later impacts the whole care pathway.

> *"My son was born with an anorectal malformation. We had to ask for a follow-up, which is not automatic. We had no information about a support group, scientific updates on the disease or psychological help for our son."*
> **Parent of a person living with anorectal malformation, Luxembourg**

We also saw that respondents' willingness for the rare disease to have been diagnosed at birth is different depending on the country they live in. This could be linked to cultural differences in the way respondents view the principle of newborn screening, but also on how this possibility is adapted to the social context of their country: newborn screening is not just about conducting tests at birth, it is also about making sure that sufficient information is given to the families and that it can help children be more included in society. To better understand the views of the rare disease community, and how they could inform approaches of newborn screening in Europe, we also asked respondents to give their opinion on newborn screening for all rare diseases.

3. RESPONDENTS ARE STRONGLY IN FAVOUR OF NEWBORN SCREENING FOR ALL RARE DISEASES

In a previous Rare Barometer survey (Dubief, 2021:19), 95% respondents said that they were in favour of performing tests to diagnose rare diseases at birth, showing a **wide acceptance of the principle of newborn screening among the rare disease community**, which has since been confirmed by national studies (RDIreland, 2022). **Other studies also showed wide acceptance of newborn screening in the general population**:

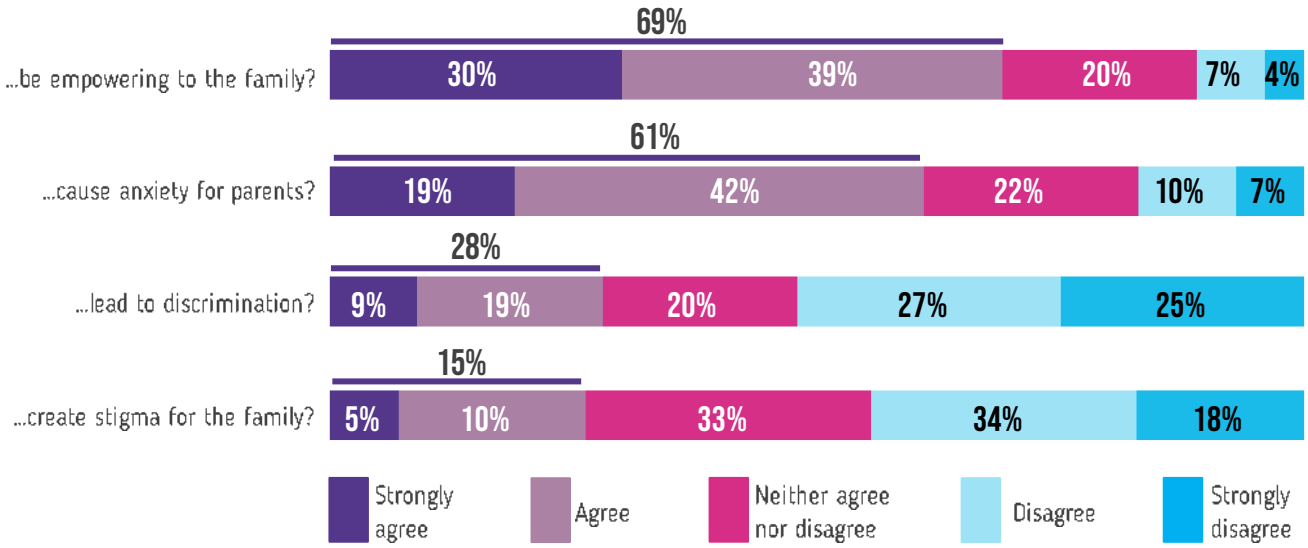
- 97% thought that as many disorders as possible should be screened for (DeLuca 2017),
- 95% were in favour of newborn screening (Etchegary 2012a),
- 94% were in favour of newborn screening with current technologies and 80% with genetic tests (Bombard 2014),
- 83% of new parents being interested in genetic screening for their newborn (Waisbren, 2015).

In the present survey, we wanted to go further and have a more in-depth understanding of why the rare disease community was in favour of newborn screening, and how some characteristics of the rare diseases impacted this community's views on newborn screening.

3.1. OPINION ON SOME POSSIBLE CONSEQUENCES OF NEWBORN SCREENING

When asked about their opinion on some possible consequences of newborn screening, **a wide majority of respondents said that newborn screening could be empowering to the family (69%) and that it could cause anxiety for the parents (61%); only a minority said that it could lead to discrimination (28%) or create stigma for the family (15%) (Graph 9)**. Of note, 42% of the respondents thought that newborn screening could both be empowering to the family and cause anxiety for parents.

Graph 9. In your opinion, could screening for any rare disease at birth…
All respondents; n=5,569



Source: Rare Barometer survey conducted May 24-July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

"Newborn screening can allow to be informed patients, have more self-determination on how to handle the disease, improve education."
Parent of a person living with a very rare disease, Germany

"When giving birth, it doesn't hurt to get a lot of information. It is then only important that the examinations themselves are not invasive or cause iatrogenic damage to the infant."
Parent of a person living with Williams syndrome, Germany

"Prevention is better than cure, if possible. Empower the family in general and those around you. Facing reality with the greatest serenity possible. Have faith in research and the future."
Grandparent of a person living with a rare disease, Italy

3.2. OPINION ON NEWBORN SCREENING: CHARACTERISTICS OF THE RARE DISEASE

Respondents were asked if in their opinion, any rare disease should be screened at birth depending on five criteria defined through a review of the literature on the topic (Gross, 2023) and on expert consultation (see methodology, p. 9):

- **The severity of the rare disease**, or its impact on the life of the patients and their families.
- **The penetrance of the diagnostic tests**, measuring the risk of false positives.
- **The age of onset**, designating the age at which the symptoms of a condition usually manifest.
- **The treatability of the condition**, defined as the existence of treatment(s) or intervention(s) that could lessen or control the effects of the rare disease.
- **The prevalence** (or degree of rarity) of the rare disease.

A more detailed definition of those criteria, along with the percentage of respondents who agreed or strongly agreed with each proposition, is presented in Table 5. Those criteria are presented in order of their impact on respondents' opinion, defined as the difference between the most chosen item and the least chosen item for all respondents, in percentage points.

3.2.1. SEVERITY OF THE CONDITION

89% of the respondents were in favour of newborn screening for very severe conditions (i.e. that are life threatening or leading to severe disabilities), vs 52% when the condition is not severe (i.e. having only marginal effects on one's health and quality of life) (Table 5). Only a minority of people living with a rare disease (46%) thought that newborns should be screened for conditions that are not severe (Table 5). This criterion is the one that most impacts respondents' opinion, as it has the highest difference between the most chosen item and the least chosen item (for all respondents: 89%-52%, or 37 percentage points; for people living with a rare disease: 42 percentage points).

"In the case of severe life-threatening effects in the first years of life, I see a clear advantage for everyone."
Person living with Polycythemia vera, Germany

"Due to the extremely long time (approx. 12 years) until the diagnosis and the wrong handling up to then, my illness has led to the most severe disabilities. Apart from the years of pain and investigations, without knowing about the disease, my life was extremely restricted, and the health system was burdened. With the knowledge and the diagnosis, I'm fine again. It's black and white. I would have been very happy if I could have skipped this ordeal with a screening."
Person living with acute intermittent porphyria, Switzerland

TABLE 5. Percentage of respondents who agreed or strongly agreed with newborn screening of rare diseases depending on their characteristics – *All respondents, n=5,569*

CRITERIA (Questions as they were written in the questionnaire)		All respondents n=5,569	PLWRD n=2,567	Parents of PLWRD n=2,701	Other family members of PLWRD n=301
SEVERITY In your opinion, should ANY RARE DISEASE be screened at birth, PROVIDED THAT it is:	Mostly severe (life threatening or leading to severe disabilities)	**89%**	88%	91%	89%
	Mild	**68%**	63%	73%	70%
	Not severe (has only marginal effects on one's health and quality of life)	**52%**	46%	57%	56%
	Difference between the most and the least chosen item (in percentage points)	***37***	*42*	*34*	*33*
PENETRANCE When screening for a disease, there can be a chance that the disease will not develop even if the test is positive. In your opinion, should ANY rare disease be screened at birth PROVIDED THAT if the test is positive, the chance for the disease to actually appear is:	High (80%)	**84%**	81%	86%	87%
	Moderate (50%)	**73%**	69%	77%	80%
	Low (20%)	**53%**	47%	57%	61%
	Difference between the most and the least chosen item (in percentage points)	***31***	*34*	*29*	*26*
AGE OF ONSET A disease can be diagnosed at birth but only manifest later in life. In your opinion, should ANY rare disease be screened at birth, PROVIDED THAT the first symptoms typically appear:	At or soon after birth	**83%**	78%	88%	85%
	Before 2 years old	**78%**	75%	80%	77%
	Between 2 and 9 years old	**70%**	69%	71%	71%
	Between 10 and 17 years old	**65%**	65%	64%	66%
	At 18 years old or above	**62%**	63%	60%	63%
	At an unknown age	**65%**	66%	65%	66%
	Difference between the most and the least chosen item (in percentage points)	***21***	*15*	*28*	*22*
TREATABILITY In your opinion, should ANY RARE DISEASE be screened at birth:	If there is treatment(s) or intervention(s) to lessen or control the effects of the rare disease, including medication, surgery, diet or other medical means	**84%**	80%	87%	86%
	Even in the absence of such treatment(s) or intervention(s)	**69%**	61%	75%	74%
	Difference between the most and the least chosen item (in percentage points)	***15***	*19*	*12*	*12*
PREVALENCE In your opinion, should ANY RARE DISEASE be screened at birth PROVIDED THAT it affects:	More than 1 person in 100,000	**70%**	66%	73%	74%
	Less than 1 person in 100,000	**66%**	59%	72%	72%
	Difference between the most and the least chosen item (in percentage points)	*4*	*7*	*1*	*2*

Reading: 89% of all respondents thought that any severe rare disease should be screened at birth; they were 88% among people living with a rare disease, 91% among parents of people living with a rare disease and 89% among other family members of people living with a rare disease. 52% of all respondents thought that any non-severe rare disease should be screened at birth. The difference between the most chosen item of the 'severity' criterion ('mostly severe', 89%) and the least chosen item of the 'severity' criterion ('not severe', 52%), is 37 percentage points. PLWRD = people living with a rare disease.

Note: answers to the items 'Neither agree nor disagree', 'Disagree' and 'Strongly disagree' are not shown here.

Source: Rare Barometer survey conducted May 24 -July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

3.2.2. PENETRANCE

84% of the respondents were in favour of newborn screening when there are 80% chances that the disease will appear if the diagnostic test is positive, vs 53% when there are 20% chances that the disease will appear if the diagnostic test is positive (Table 5). Only a minority of people living with a rare disease (47%) thought that newborns should be screened when diagnostic tests have a low penetrance (Table 5). This criterion is the second that most impacts respondents' opinion, as the difference between the items that are most and least chosen by all respondents is 31 percentage points (84%-53%).

648 members of the general population and prospective parents also expressed shared opinion on this criterion in a study conducted by Etchegary et al. (2012b), as 44% agreed or strongly agreed, and 43% disagreed or strongly disagreed with the proposition 'Newborn genetic testing should only be available for health conditions where the test is able to tell you with 100% certainty whether the infant will go on to develop the condition someday'.

> *"There is a risk of unnecessary anxiety and stress for the family if false positives are possible."*
> **Person living with systemic lupus erythematosus, France**

> *"I can see the disadvantages of newborn screening. We can screen too much and it can be false positive answers. I definitely believe that it will give the parents a choice about how they want to handle the situation, but this should be done in collaboration with a psychologist."*
> **Parent of a person living with a rare disease, Denmark**

3.2.3. AGE OF ONSET

83% of the respondents were in favour of newborn screening for rare diseases with an onset at birth or soon after birth, vs 62% for adult-onset conditions (Table 5). In another Rare Barometer survey (Dubief 2021:19), only 48% of respondents (patients and family members) thought that newborns should be tested as part of a health programme for conditions that may develop later in life.

3.2.4. TREATABILITY

84% of the respondents were in favour of newborn screening for treatable diseases (i.e. when there is treatment(s) or intervention(s) to lessen or control the effects of the rare disease, including medication, surgery, diet or other medical means), vs 69% when the condition is not treatable (i.e. in the absence of such treatments or interventions) (Table 5).

These results confirm findings from a previous Rare Barometer survey (Dubief, 2021:19) where 79% of respondents thought that newborns should be tested as part of a health programme for conditions that could be prevented and/or treated, and 68% for conditions for which appropriate disease management (diet, education…) can improve health and quality of life.

Studies on the general population also showed a high acceptance of newborn screening for non-treatable diseases: DeLuca et al. (2017) showed that 91% of the general population approved of screening for disorders when treatment was not curative and 84% favoured screening even if a treatment was not available for the disorder. Etchegary et al. (2012b) report that 53% members of the public and prospective parents disagreed or strongly disagreed with the proposition 'Newborn genetic testing should only be available for health conditions for which something can be done to treat the condition'.

Other studies on the general population combined treatability with other criteria such as the age of onset, severity or test availability. Hasegawa et al. (2011) found that all 114 mothers of young children they surveyed supported newborn screening of conditions that occur in infancy without a proven treatment. In Canada, Hayeems et al. (2015) found that among 60 focus group participants selected from the general population, 82% supported screening for serious disorders for which a treatment was

not available, and 62% supported unpressured choice for screening for untreatable disorders. Finally, Plass et al. (2009) found that among 1,372 expecting parents, 99.5% thought that treatable disorders should be added to the newborn screening programme as soon as a valid test became available, 88% had a positive attitude towards the inclusion of less treatable childhood-onset disorders and 73% had positive opinions about untreatable childhood-onset disorders.

> *"The problem of identifying complex and currently unmanageable genetic problems could be a limitation to newborn screening. It is also true that the availability of all the information can allow parents to follow the child's situation with much more awareness, avoiding errors which in some cases would be produced by only partial knowledge of their child's genetic setting."*
> **Parent of a person living with Wolf-Hirschhorn syndrome, Italy**

3.2.5. PREVALENCE

70% of the respondents were in favour of newborn screening for more common rare disease diseases (i.e. affecting more than 1 person in 100,000), vs 66% for ultra-rare diseases (i.e. affecting less than 1 person in 100,000) (Table 5). It is the criterion that least impacts respondents' opinion.

3.2.6. THE SEVERITY OF THE RARE DISEASE AND THE PENETRANCE OF DIAGNOSTIC TESTS WERE THE CRITERIA THAT MOST IMPACTED RESPONDENTS' OPINION ON NEWBORN SCREENING

Respondents' opinion on the five disease characteristics they were presented with confirms that the rare disease community first values newborn screening as a way to prepare patients and their families for any challenges that may come with the rare disease. It also shows that while age of onset still appears as an important criterion, the severity of the rare disease and the penetrance of the diagnostic tests impact respondent's opinion even more. Access to treatments or interventions (here defined as treatability) appears as one of the criteria that least impacts respondents' opinion on newborn screening, along with the prevalence of the rare disease: we already saw that those two criteria did not significantly impact respondent's willingness for their rare disease to have been diagnosed at birth in part 2.

3.3. OPINION ON REASONS TO SCREEN NEWBORNS FOR RARE DISEASES WITH NO TREATMENT OR INTERVENTION AVAILABLE

In order to investigate the opinion on newborn screening for non-treatable rare diseases, respondents were presented with 13 detailed reasons to screen for rare diseases at birth even when no treatment or intervention is available. These reasons, listed in Table 6, were defined based on a literature review (Gross 2023), on expert consultations (see methodology, p. 9), and on the concept of 'actionability' as the absence of treatment(s) or intervention(s) to lessen or control the effects of the rare disease, including medication, surgery, diet or other medical means. Reasons to screen non-treatable rare diseases were phrased positively to ensure readability, and they were presented in a randomised order to the respondents.

A very large majority (73%-90%) of the respondents were in favour of newborn screening for non-treatable diseases, when presented with detailed reasons to screen. These reasons are ranked from the most acceptable to the least acceptable for the rare disease community in column (a) of Table 6, based on:

1. The opinion of all respondents (column b).
2. The difference (in column e) between the percentage of respondents who previously said that they were in favour of newborn screening for non-treatable diseases (column c), and the percentage of those who previously said that they were against (column d).

89% to 90% of respondents agreed or strongly agreed with the four most accepted reasons:

- It allows a quicker diagnosis, to the benefit of the individual person and their carers.
- The disease can be followed-up on and harm can be avoided through prevention practices.
- It would allow the person to have their disabilities better recognised, and to obtain more adequate social support and independent living.
- It can allow family members to know whether they carry the variant causing the disease.

A wide majority (63% to 72%) of the respondents who previously disagreed with newborn screening for non-treatable conditions were in favour of newborn screening for the four most accepted reasons (Table 6).

73% to 82% of respondents agreed or strongly agreed with the four least accepted reasons:

- It can possibly predict the patient's response to medication, unrelated to the presence of a rare disease.
- It allows a quicker diagnosis thus lowering costs at the national level.
- There is an opportunity for the person to participate in research to improve other people's diseases.
- It is important to receive a diagnosis even in the absence of other benefits (such as treatment, participation in research or life adjustments).

The wide acceptance of all the reasons to diagnose non-treatable rare diseases does not mean that any rare disease should be screened at birth, regardless of the available support and information available. This rather confirms the wide acceptance of the concept of newborn screening among the rare disease community. The analysis of the most and of the least accepted reasons to diagnose non-treatable diseases at birth also confirm the importance of newborn screening to improve access to diagnosis, and to the information that parents need to make informed choices for their child and for their family.

3.4. WHY SCREEN NEWBORNS?

Respondents' opinion on newborn screening for all rare diseases confirms that for the rare disease community, the main benefits of newborn screening are to fasten access to diagnosis and to the most relevant information for the parents to make informed choices for their child and their family. Even if the diagnosis can cause anxiety, respondents think that early diagnosis is empowering for the family if it allows parents to prepare for the impacts of severe diseases on their child's life, including when no treatments are available. However, to avoid useless anxiety, respondents clearly prefer to limit the risks of false positive diagnostic tests (low penetrance).

The risks of discrimination for the child and of stigma for the family are not negligeable, even if they were only considered as a possible consequence of newborn screening by a minority of respondents. These risks should be carefully considered when adding new rare diseases to the list of national or regional newborn screening programmes.

Table 6. Respondents' opinion on detailed reasons to screen newborns for rare diseases even if no treatment exists.

(a) Respondents who agreed or strongly agreed with the propositions: 'In your opinion, should ANY RARE DISEASE be screened at birth if no treatment exists and:	(b) All respondents (n=5,569)	Any rare disease should be screened at birth even in the absence of treatment(s) or intervention(s):			United Nations European Subregions			
		(c) Agree or strongly agree (n=3,223)	(d) Disagree or strongly disagree (n=656)	(e) Difference (c)-(d)	(f) Southern Europe (n=1,999)	(g) Western Europe (n=1,631)	(h) Northern Europe (n=1,160)	(i) Eastern and Central Europe (n=588)
(1) It allows a quicker diagnosis, to the benefit of the individual person and their carers	**90%**	97%	63%	**34**	93%	84%	90%	91%
(2) It would allow the person to have their disabilities better recognised, and to obtain more adequate social support and independent living	**90%**	96%	65%	**31**	93%	85%	91%	91%
(3) The disease can be followed-up on and harm can be avoided through prevention practices	**90%**	95%	72%	**23**	91%	87%	91%	91%
(4) It can allow family members to know whether they carry the variant causing the disease	**89%**	96%	63%	**33**	93%	83%	89%	91%
(5) Supportive care, for example physiotherapy or behavioural interventions (meant for self-control or emotional regulation), can improve the management of the disease	**88%**	95%	61%	**34**	91%	81%	88%	90%
(6) Knowing a child's mental or physical limitations in advance can allow more appropriate parenting	**87%**	95%	62%	**33**	91%	83%	85%	91%
(7) There is an opportunity for the person to participate in research to improve THEIR OWN disease	**87%**	95%	57%	**38**	91%	81%	87%	88%
(8) It can allow for better family planning choices for the parents	**84%**	94%	56%	**38**	90%	78%	81%	87%
(9) There is an opportunity to join a patient support group or an online community	**83%**	92%	53%	**39**	88%	77%	81%	88%
(10) It is important to receive a diagnosis even in the absence of other benefits (such as treatment, participation in research or life adjustments)	**82%**	93%	44%	**49**	89%	73%	80%	85%
(11) There is an opportunity for the person to participate in research to improve OTHER PEOPLE'S diseases	**82%**	91%	50%	**41**	88%	74%	80%	82%
(12) It allows a quicker diagnosis thus lowering costs at the national level	**80%**	90%	49%	**41**	87%	69%	80%	86%
(13) It can possibly predict the patient's response to medication, unrelated to the presence of a rare disease	**73%**	82%	46%	**36**	76%	66%	76%	81%

(a) Reasons to screen newborns for rare diseases with no available treatments, from the most accepted to the least accepted by the rare disease community. Percentage of respondents who agreed or strongly agreed with each reason among all respondents (b), among respondents who previously said that they were in favour of (c) or against (d) newborn screening for non-treatable diseases, and depending on the European subregion they live in (f) to (i). (e) Difference between (c) and (d), in percentage points.

Source: Rare Barometer survey conducted May 24-July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

REFERENCES

Blom, M., Bredius, R. G. M., Jansen, M. E., Weijman, G., Kemper, E. A., Vermont, C. L., Hollink, I. H. I. M., Dik, W. A., van Montfrans, J. M., van Gijn, M. E., Henriet, S. S., van Aerde, K. J., Koole, W., Lankester, A. C., Dekkers, E. H. B. M., Schielen, P. C. J. I., de Vries, M. C., Henneman, L., & van der Burg, M. (2021). Parents' Perspectives and Societal Acceptance of Implementation of Newborn Screening for SCID in the Netherlands. Journal of Clinical Immunology, 41(1), 99–108. https://doi.org/10.1007/s10875-020-00886-4

Boardman FK, Young PJ, Warren O, Griffiths FE. The role of experiential knowledge within attitudes towards genetic carrier screening: A comparison of people with and without experience of spinal muscular atrophy. Health Expect. 2018 Feb;21(1):201-211. doi: 10.1111/hex.12602.

Boardman FK, Sadler C, Young PJ. Newborn genetic screening for spinal muscular atrophy in the UK: The views of the general population. Mol Genet Genomic Med. 2018 Jan;6(1):99-108. doi: 10.1002/mgg3.353.

Boardman FK, Hale R. "I didn't take it too seriously because I'd just never heard of it": Experiential knowledge and genetic screening for thalassaemia in the UK. J Genet Couns. 2019 Feb;28(1):141-154. doi: 10.1002/jgc4.1042.

Bombard Y, Miller FA, Hayeems RZ, Barg C, Cressman C, Carroll JC, Wilson BJ, Little J, Avard D, Painter-Main M, Allanson J, Giguere Y, Chakraborty P. Public views on participating in newborn screening using genome sequencing. Eur J Hum Genet. 2014 Nov;22(11):1248-54. doi: 10.1038/ejhg.2014.22.

Christie L, Wotton T, Bennetts B, Wiley V, Wilcken B, Rogers C, Boyle J, Turner C, Hansen J, Hunter M, Goel H, Field M. Maternal attitudes to newborn screening for fragile X syndrome. Am J Med Genet A. 2013 Feb;161A(2):301-11. doi: 10.1002/ajmg.a.35752.

Courbier S., Berjonneau E., May 2017. Juggling care and daily life. The balancing act of the rare disease community. EURORDIS-Rare Diseases Europe.

DeLuca, J. M. (2018). Public Attitudes Toward Expanded Newborn Screening. Journal of Pediatric Nursing, 38, e19–e23. https://doi.org/10.1016/j.pedn.2017.10.002

Dubief J, Berjonneau E., Kole A., 2021. *Rare disease patients' opinion on the future of rare diseases.* EURORDIS-Rare Diseases Europe.

Etchegary, H., Dicks, E., Green, J., Hodgkinson, K., Pullman, D., & Parfrey, P. (2012a). Interest in newborn genetic testing: A survey of prospective parents and the general public. Genetic Testing and Molecular Biomarkers, 16(5), 353–358. https://doi.org/10.1089/gtmb.2011.0221

Etchegary, H., Dicks, E., Hodgkinson, K., Pullman, D., Green, J., & Parfey, P. (2012b). Public Attitudes About Genetic Testing in the Newborn Period. JOGNN - Journal of Obstetric, Gynecologic, and Neonatal Nursing, 41(2), 191–200. https://doi.org/10.1111/j.1552-6909.2012.01341.x

Faye F., Crocione C., Anido de Peña R., Bellagambi S., Escati Peñaloza L., Hunter A., Jensen L., Oosterwijk C., Schoeters E., de Vicente D., Faivre L., Wilbur M., Le Cam Y., Dubief J., 2024. Time to diagnosis and determinants of diagnostic delays: a retrospective Rare Barometer survey. *Under publication*.

Gross Edith, January 2023. Newborn Screening: a background document toward a quantitative Rare Barometer survey. EURORDIS-Rare Diseases Europe.

Hasegawa LE, Fergus KA, Ojeda N, Au SM. Parental attitudes toward ethical and social issues surrounding the expansion of newborn screening using new technologies. Public Health Genomics. 2011;14(4-5):298-306. doi: 10.1159/000314644. Epub 2010 Jul 30.

Hayeems RZ, Miller FA, Bombard Y, Avard D, Carroll J, Wilson B, Little J, Chakraborty P, Bytautas J, Giguere Y, Allanson J, Axler R. Expectations and values about expanded newborn screening: a public engagement study. Health Expect. 2015 Jun;18(3):419-29. doi: 10.1111/hex.12047. Epub 2013 Feb 1.

Nguengang Wakap, S., Lambert, D.M., Olry, A. et al. Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. *Eur J Hum Genet* 28, 165–173 (2020). https://doi.org/10.1038/s41431-019-0508-0

Parsons EP, Clarke AJ, Hood K, Lycett E, Bradley DM. Newborn screening for Duchenne muscular dystrophy: a psychosocial study. Arch Dis Child Fetal Neonatal Ed. 2002 Mar;86(2):F91-5. doi: 10.1136/fn.86.2.f91.

Plass AM, van El CG, Pieters T, Cornel MC. Neonatal screening for treatable and untreatable disorders: prospective parents' opinions. Pediatrics. 2010 Jan;125(1):e99-106. doi: 10.1542/peds.2009-0269.

Rare Diseases Ireland (RDIreland), *Newborn Bloodspot Screening in Ireland: awareness & opinions of the Irish public.* May 2022.

Schoenaker MHD, Blom M, de Vries MC, Weemaes CMR, van der Burg M, Willemsen MAAP. Early diagnosis of ataxia telangiectasia in the neonatal phase: a parents' perspective. Eur J Pediatr. 2020 Feb;179(2):251-256. doi: 10.1007/s00431-019-03479-5.

United Nations, Standard Country or Area Codes for Statistical Use (M49 standard). Available online: https://unstats.un.org/unsd/methodology/m49/

Waisbren SE, Bäck DK, Liu C, Kalia SS, Ringer SA, Holm IA, Green RC. Parents are interested in newborn genomic testing during the early postpartum period. Genet Med. 2015 Jun;17(6):501-4. doi: 10.1038/gim.2014.139.

ANNEXES

ANNEX 1: RESPONDENTS' OPINION ON THE DIAGNOSIS OF THEIR RARE DISEASE AT BIRTH

Question Answer item	Total number of respondents to each item of the question	Respondents who agreed or strongly agreed with 'I would have liked [the person I care for] to be diagnosed at birth' among those who answered each item (percentage in row)		
		All respondents	PLWRD	Parents of PLWRD
CHARACTERISTICS OF THE RESPONDENTS				
Are you a…				
Person living with a rare disease	2,567	63% (1,611)		
Parent of a person living with a rare disease	2,701	82% (2,212)		
Other family carers of a person with a rare disease	301	78% (234) ***p<0.01******		
European subregions (United Nations geographic regions for Europe)				
Eastern and Central Europe	588	82% (485)	73% (132)	86% (325)
Southern Europe	1,999	79% (1,585)	71% (608)	85% (866)
Northern Europe	1,160	70% (807)	58% (338)	83% (436)
Western Europe	1,631	63% (1,034) ***p<0.01******	54% (475) ***p<0.01******	74% (515) ***p<0.01******
How old are you? (Age of the respondents at the time of the study)				
Under 25 years old	127	80% (102)	78% (62)	85% (34)
25-34 years old	590	81% (475	74% (223)	88% (231)
35-49 years old	2,206	78% (1,718)	69% (541)	83% (1,126)
50-64 years old	1,640	68% (1,113)	58% (486)	79% (554)
65 years old or more	518	62% (320) ***p<0.01******	50% (169) ***p<0.01******	86% (104) *p=0.01***
Are you…				
Female	4,235	74% (3,140)	64% (1,203)	82% (1,788)
Male	967	69% (663) ***p<0.01******	58% (311) *p=0.05***	83% (297) *p=0.92*
How would you describe your knowledge of genetics?				
Excellent or good	1,888	74% (1,401)	66% (570)	81% (758)
Moderate	1,850	72% (1,338)	62% (507)	82% (768)
Slight or inexistant	1,325	74% (974) *p=0.42*	61% (398) *p=0.06**	85% (515) *p=0.09**
How old were you when you stopped full-time education?				
15 years old or under	142	78% (111)	65% (49)	93% (52)
Between 16 and 19 years old	1,222	73% (889)	66% (396)	79% (448)
Between 20 and 23 years old	1,757	73% (1,288)	62% (486)	83 % (739)
24 years old or above	1,699	73% (1,235) *p=0.27*	60% (444) *p=0.03***	83% (721) *p=0.07**

Question Answer item	Total number of respondents to each item of the question	Respondents who agreed or strongly agreed with 'I would have liked [the person I care for] to be diagnosed at birth' among those who answered each item (percentage in row)		
		All respondents	PLWRD	Parents of PLWRD
CHARACTERISTICS OF THE RARE DISEASE				
Age of onset of the rare disease based on Orphanet data on natural history of the disease (orphadata.org)				
Antenatal, neonatal or infancy	1,964	80% (1,577)	73% (368)	83% (1,149)
Childhood	1,243	70% (876)	61% (356)	80% (477)
Adolescence	638	63% (400)	53% (225)	85% (158)
Adulthood	825	58% (482)	51% (309)	84% (143)
Elderly	271	52% (1421)	48% (109)	96% (26)
All ages	1,297	73% (951) ***p<0.01******	66% (503) ***p<0.01******	84% (399) *p=0.17*
Type of rare disease based on the Orphanet classification of rare diseases (orphadata.org)				
Genetic diseases	3,952	78% (3,072)	70% (1,081)	83% (1,842)
Non-Genetic diseases	724	51% (366) ***p<0.01******	45% (261) ***p<0.01******	79% (85) *p=0.28*
Inborn errors of metabolism	797	82% (656)	74% (218)	87% (408)
Non-Inborn errors of metabolism	3,879	72% (2,782) ***p<0.01******	62% (1,124) ***p<0.01******	81% (1,519) ***p<0.01******
Developmental anomalies during embryogenesis	2,105	78% (1,646)	72% (590)	82% (986)
Non-Developmental anomalies during embryogenesis	2,571	70% (1,792) ***p<0.01******	58% (752) ***p<0.01******	83% (941) *p=0.60*
Point prevalence based on Orphanet data on natural history of the disease (orphadata.org)				
Point prevalence between 5/10,000 and 1/100,000	2,532	72% (1,834)	64% (844)	83% (905)
Point prevalence <1/100,000	860	78% (668) ***p<0.01******	66% (190) p=0.55	84% (450) *p=0.44*
Compared to one year ago, would you say that the symptoms of (your / the) rare disease are…				
Significantly / somewhat worsening	1,937	71% (1,370)	63% (669)	82% (615)
About the same	2,611	72% (1,879)	61% (701)	81% (1,087)
Somewhat / significantly improving	882	80% (702) ***p<0.01******	68% (216) *p=0.13*	85% (439) *p=0.15*
DIAGNOSIS JOURNEY				
How old were you when you received a confirmed diagnosis / How old was the person you care for when they received a confirmed diagnosis?				
0-3 months old	587	88% (514)	89% (78)	87% (405)
4 months - 1 year old	638	83% (529)	77% (53)	93% (441)
2-9 years old	1,335	79% (1,056)	75% (142)	80% (858)
10-19 years old	574	78% (445)	72% (171)	82% (257)
20-29 years old	489	67% (326)	65% (266)	83% (49)
30-49 years old	1,040	59% (611)	58% (560)	69% (20)
50 years old or more	474	51% (242) ***p<0.01******	50% (214) ***p<0.01******	67% (6) ***p<0.01******

Question Answer item	Total number of respondents to each item of the question	Respondents who agreed or strongly agreed with 'I would have liked [the person I care for] to be diagnosed at birth' among those who answered each item (percentage in row)		
		All respondents	PLWRD	Parents of PLWRD
How long did it take from the first medical encounter for the diagnosis to be confirmed by appropriate genetic, clinical, medical imaging, molecular or biochemical tests (e.g., biopsy, blood or urine test)?				
Less than 1 month	825	75% (621)	61% (187)	83% (395)
1 month to 1 year	1,655	70% (1,165)	55% (361)	81% (740)
1 to 5 years	1,222	72% (876)	59% (287)	81% (533)
More than 5 years	1,284	74% (956) *p=0.02***	69% (569) ***p<0.01****	85% (353) *p=0.24*
ACCESS TO TREATMENT AND SUPPORTIVE CARE				
Did (you / the person you care for) receive or are (you / the person you care for) receiving TREATMENT(S) OR INTERVENTION(S) to lessen or control the effects of the rare disease, including medication, surgery, diet or other medical means?				
Yes, even partially (e.g. for one of the symptoms)	4,503	73% (3,296)	63% (1,315)	82% (1,783)
No	987	72% (706)	62% (277)	80% (398)
Unsure	79	70% (55) *p=0.46*	56% (19) *p=0.60*	79% (31) *p=0.57*
Overall, how effective is the treatment you are receiving for your rare disease?				
Not at all / slightly	1,075	71% (760)	63% (335)	78% (372)
Moderately	1,246	72% (894)	60% (346)	82% (490)
Significantly / extremely	2,042	76% (1,545)	65% (590)	85% (874)
Unsure	223	70% (155) ***p<0.01****	62% (64) *p=0.43*	75% (80) ***p<0.01****
Did (you / the person you care for) receive or are (you / the person you care for) receiving SUPPORTIVE CARE, for example physiotherapy, behavioural interventions (meant for self-control or emotional regulation)?				
Yes	2,804	74% (2,079)	61% (588)	81% (1,364)
No, but it is needed	1,557	73% (1,142)	67% (605)	84% (482)
No, but it is NOT needed	1,073	69% (737)	61% (631)	80% (317)
Unsure	135	73% (99) ***p<0.01****	57% (36) *p=0.01***	91% (49) *p=0.16*
Overall, how effective is the supportive care you are receiving for your rare disease?				
Not at all / slightly	700	73% (509)	57% (160)	84% (309)
Moderately	905	73% (665)	64% (210)	79% (407)
Significantly / extremely	1,228	75% (927)	60% (234)	82% (643)
Unsure	111	73% (81) *p=0.53*	57% (20) *p=0.33*	82% (58) *p=0.37*
In general, would you say that your health / the health of the person you care for is…				
Very poor / poor	1,474	70% (1,033)	63% (575)	83% (389)
Neither poor nor good	1,677	72% (1,192)	63% (547)	81% (579)
Good / very good	2,401	75% (1,809) ***p<0.01****	62% (489) *p=0,81*	82% (1,223) *p=0,75*
TOTAL	**5,569**	**73% (3,817)**	**63% (1,611)**	**82% (2,212)**

N=number of respondents to each answer item (totals may not be equal between questions because of missing values). %=percentage of people who agree or strongly agree with the statement 'I would have liked [the person I care for] to be diagnosed at birth' within respondents who answered each item (percentage in row). p=p-value; not significant when p>=0.1, weakly significant when p<0.1 (*), significant when p<0.05 (**) and very significant when p<0.01 (***).

ANNEX 2: AGE AT DIAGNOSIS X AGE OF ONSET

Age of onset (orphadata)	How old were you when you received a confirmed diagnosis? 0-3 months old	4 months - 1 year old	2-9 years old	10-19 years old	20-29 years old	30-49 years old	50 years old or more	TOTAL
Antenatal	22%	22%	34%	11%	3%	7%	3%	313
Neonatal	18%	21%	35%	11%	4%	8%	3%	1,522
Infancy	16%	19%	36%	12%	5%	9%	3%	1,522
Childhood	3%	8%	34%	15%	11%	21%	8%	1,208
Adolescent	1%	4%	19%	18%	15%	31%	11%	623
Adult	1%	3%	15%	11%	15%	35%	20%	810
Elderly	0%	0%	9%	8%	17%	41%	23%	265
All ages	12%	10%	17%	10%	13%	28%	10%	1,256
TOTAL	798	957	2,072	905	705	1,457	625	7,519

Over-represented elements. Under-represented elements. p-value<0.01; Chi2=1,894.19; Degree of freedom=42.

Source: Rare Barometer survey conducted May 24-July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

ANNEX 3: TIME TO DIAGNOSIS X AGE AT DIAGNOSIS

How old were you when you received a confirmed diagnosis?	How long did it take from the first medical encounter for the diagnosis to be confirmed by appropriate genetic, clinical, medical imaging, molecular or biochemical tests (e.g., biopsy, blood or urine test): Less than 1 month	1 month to 1 year	1 to 5 years	More than 5 years	Unsure	TOTAL
0-3 months old	67%	29%	1%	2%	2%	587
4 months - 1 year old	15%	73%	9%	2%	2%	638
2-9 years old	6%	26%	48%	16%	3%	1,335
10-19 years old	9%	21%	20%	45%	6%	574
20-29 years old	10%	25%	21%	41%	3%	489
30-49 years old	11%	26%	20%	41%	2%	1,04
50 years old or more	9%	33%	20%	36%	3%	474
TOTAL	825	1,655	1,221	1,284	152	5,137

Over-represented elements. Under-represented elements. p-value<0.01; Chi2=2,646.35; Degree of freedom=24.

Source: Rare Barometer survey conducted May 24-July 23, 2023. 'The opinion of people living with a rare disease and their family members on newborn screening'.

THANK YOU

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