Grant agreement no. 666918
PHC-14-2015 'New therapies for rare diseases'

- Research and Innovation Action -

D9.7
Report of feedback analysis and its dissemination to key stakeholders

WP 9 – Patient Organisation involvement

Due date of deliverable:	31/12/2017 (Month 24)
Actual submission date:	10/01/2019 (Month 37)
Start date of project:	01/01/2016
Duration:	36 months
Lead beneficiary:	BDFA
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Dissemination Level		
PU	Public	
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	

History table

Version	Date	Released by	Comments
0.1	25/07/2018	Heather Band, Laura Codd	First draft
1.0	14/12/2018	Heather Band	Updated version
1.1	14/12/2018	Sara Mole	Final version

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Key word list

Family Survey, Batten disease, NCL, NCL Registry

Definitions and acronyms

Acronyms	Definitions
BDFA	Batten Disease Family Association
NCL	Neuronal Ceroid Lipofuscinosis (Batten disease)
PO	Patient Organisation
EU	European Union

1. Introduction

The focus of BATCure is on the development of potential therapies that are achievable and deliverable. BATCure aims to make the views of those affected (the children, young people and their families) central to this aim. An innovation for this project is that a uniform, coordinated survey was undertaken across the EU to gain valuable insight on key issues, such as obstacles to clinical participation.

1.1 General context

Interaction by research groups with their target audience has not always been successful or accessible for those affected by rare and ultra rare diseases. The BATCure consortium aimed to ensure the views of those affected by this devastating disease were central to therapy development, and that the information produced was clear, accessible and relevant to key stakeholder needs.

1.2 Deliverable objectives

To prepare a full report of the analysis of the BATCure survey results and to disseminate this to the BATCure consortium and key project stakeholders as identified in D9.3, Ms32 & Ms42.

To design and prepare a visually engaging, succinct executive summary of survey results to be shared with a lay audience, including patients and their families/carers.

2. Methodological approach

Once the online survey had closed, raw survey data was sent to the BDFA by UCL where it was analysed and key findings and recommendations collated in a full report of survey results. The target audience for the report was the BATCure consortium and the initial findings were presented at the meeting in Hamburg in November 2017. A full analysis was completed in 2018, attached, which explains the methods in more detail.

An executive summary of survey results was then prepared. This was targeted at the wider Batten disease and rare disease community outside of BATCure. With this audience in mind, it is shorter and more visually engaging than the full report but still delivers the key headlines and conclusions from the research.

3. Summary of activities and research findings

Research Findings

- The full report of survey findings and the executive summary is attached
- A pdf of the Executive Summary is attached

Dissemination Activities

NCL2018, the 16th International Conference on Batten disease, took place in September 2018 at Royal Holloway, University of London (D9.12). As the only international meeting for those with an interest in Batten disease, it attracted a diverse audience of delegates with an interest in Batten disease and related conditions. These included scientists, researchers, clinicians, Pharma, care professionals, patient organisations, patients and family members. With so many stakeholders present, this meeting was identified as an ideal opportunity to disseminate the executive summary and generate interest in its content to a worldwide audience.

The BDFA organised the printing of 150 executive summaries and these were distributed from the BDFA exhibition stand at the conference and at the BATCure stall during the Market Place session. (D9.12).

This was also an opportunity for affected family members, researchers, clinicians and representatives from all the key stakeholder groups to ask questions.

A poster was presented by the BDFA on the research findings at NCL2018.

A link to the executive summary was added to the BDFA and BATCure websites. The document was also emailed to BATCure project stakeholders on the database as complied as part of D9.3, Ms32 & Ms42. The summary was available to those attending the BDFA AGM (Nov 2018).

4. Conclusions and future steps

The conclusions based on survey results can be found within the full report of survey findings and executive summary. The survey was well received by the consortium members and the key target audience. The key areas going forward for the final phase of the project are:

1) Diagnosis
   Survey results on diagnosis were consistent with established data and, even noting the small base sizes, showed some substantial differences and highlighted areas for improvement. The BDFA will continue to work with POs to monitor and promote best practice in diagnosis across the EU. It is currently exploring working with a leading UK centre on improving the diagnostic journey for patients and their families with CLN3 disease.

2) Communication of research findings
   Families' understanding of research, preferred information formats and platforms and their preference for lay information from reliable professional sources will be incorporated into the final dissemination plans for the project. Areas of focus will include improvement of the Family Area of the BATCure website, discussions with partners to ensure the provision of lay information in all 10 languages (the summary was designed with this provision in mind) and developing tailored dissemination events across the consortium.

3) NCL Registry
   A key action point emerging from the survey results will be for the BDFA and other POs to work with BATCure consortium members to develop a proposal on a way forward to address the issues highlighted relating to the DEM-CHILD registry. Any initiative to increase awareness and participation has to be of benefit given the importance of participation to disease registries in a rare disease, such as Batten disease.

4) Clinical trials
   Feedback on clinical trials has emphasised the importance of quality of life and how important early consultation with affected families is for success, to ensure their voice is heard. The BATCure consortium is ideally placed to do this as it moves forward, taking the promising research developments from the project to clinical applications.

Dissemination of the Executive Summary and report will continue as part of the final dissemination of the project results D9.11.

The BDFA will work with key stakeholders, especially with PO's worldwide to disseminate the results and to collaborate on the key action points identified.

Attachment 1 – BATCure Family Survey Report

Heather Band & Laura Codd, Batten Disease Family Association (BDFA)

Survey background, aims and objectives

The BATCure Family Survey was an online survey for patients with Neuronal Ceroid Lipofuscinoses (commonly known as Batten disease) and their families, providing them with an opportunity to inform and contribute to the EU-funded BATCure research project. The survey was designed and implemented by the Batten Disease Family Association (BDFA, Charity Number - England & Wales 1084908 / Scotland SC047408) and University College London (UCL). The survey was open for three months from 4th July 2017 to 4th October 2017.

The key objectives of the survey were to gain information from patients and their families of their understanding of current research and clinical trial developments and to ascertain their readiness to participate in studies and in future clinical trials, and highlight any obstacles that would prevent them from doing so. The results will be used to inform the work of the consortium, key stakeholders and feed directly into current and future exploitation plans for the BATCure project. In addition, the results are going to be used to plan future work and build collaborations across the EU with the aim to address the key issues that patients (affected by all forms of NCL) and their families have identified.

Survey design, methodology and sample

The first stage of survey design involved pilot interviews with UK based families representing three types of Batten disease - CLN3, CLN6, and CLN7. These qualitative interviews were conducted by the BDFA to gain a perspective on the major issues of importance to families and to help define the key areas for the survey content. Logistical considerations were also explored, in order to identify any issues that could affect participation rates, such as preferred format, length and complexity of survey.

Feedback from these pilot interviews informed the development of the following criteria for the survey:

- Online format, with paper copies to be available on request (although uptake of these was ultimately low).
- Short – no longer than 15 minutes to complete.

- Anonymised.
- Compliant with BDFA and UCL data protection rules.
- Easy to translate.

Guided by these criteria, the BDFA and UCL developed the survey content and questions. It was important to ensure that the survey would capture information to support and inform the BATCure consortium and all stakeholders as outlined in the tasks of the work package. With this in mind, the survey was divided into four main sections:

- Background information (Task 9.2);
- Knowledge of current research, BATCure project and ways to improve communication and dissemination (Task 9.3 & 9.4);
- International disease registry (Task 9.1);
- Clinical trials (Task 9.2).

UCL chose to set up and host the survey securely using the UCL online survey tool ("Opinio"). Using the Opinio platform ensured compliance with the Data Protection policy and enabled respondent anonymity. It was also chosen for its functionality and 'user-friendliness' for respondents, particularly in terms of moving backwards and forwards through the survey and selecting from a range of available languages. A password held by the BDFA was needed to access the survey.

With valuable help from UCL, consortium members and representatives from partner Patient Organisations (POs), the BDFA was able to meet the deliverable target (D9.6) of translating the survey into the major EU languages (English, French, German, Italian, Spanish). The BDFA was also able to deliver the survey in 5 additional languages (Danish, Dutch, Finnish, Norwegian, Swedish). The survey was also opened up to go beyond its planned scope by including those affected by all types of NCLs.

The survey initially went 'live' online in English in early July 2017 and was subsequently launched online in nine additional languages.

In order to reach members of a rare disease community, it was vital to widely promote and share details of the survey. The BDFA initially shared survey details in English via the BATCure social media pages (Facebook and Twitter). Updates and reminders were posted on these pages each week. It also shared the survey details on the BDFA website, in its biannual newsletter and sent an email inviting UK patients and families affected by Batten disease to participate.

Promoting the survey in multiple languages across the wider EU required a collaborative effort from POs, family foundations, consortium members, patients, affected families and relevant professionals and clinicians in target countries. This collaboration was vital in order to reach families across a range of countries, some with less developed Batten communities and patient networks and needed to receive the

survey in their native language. Local patient organisations worked hard to share the survey details with their members in the local language, either via social media, email or on their own websites. For example, in France, Jean-Marie Favreau, a BDFA member and volunteer with Vaincre les Maladies Lysosomales (VML), contacted all Batten disease patients/families who are part of the organisation. He also wrote a short article about the survey in the VML monthly newsletter to reach, among others, health professionals working in the field in France.

In some countries with less developed patient networks, the BDFA reached out to professional contacts to try and find patients and families who may wish to contribute. For example, in Spain, BATCure Work Package 2 Lead, Professor Juan Bolaños of the University of Salamanca, translated the survey into Spanish. He was then able to put the BDFA in touch with Dr Mireia del Toro at University Hospital Vall d'Hebron, Barcelona, who shared the survey with the families of patients in her clinic.

Through the BDFA's participation in the European Education project ([2]), in Finland, the BDFA contacted Marja-Leena Forssas – a Mobility & Orientation specialist at Valteri Centre for Learning and Consulting, Onerva, who works with children and young people affected by Batten disease. She translated the survey into Finnish and shared it with the Finnish Family Association and her contacts at Valteri.

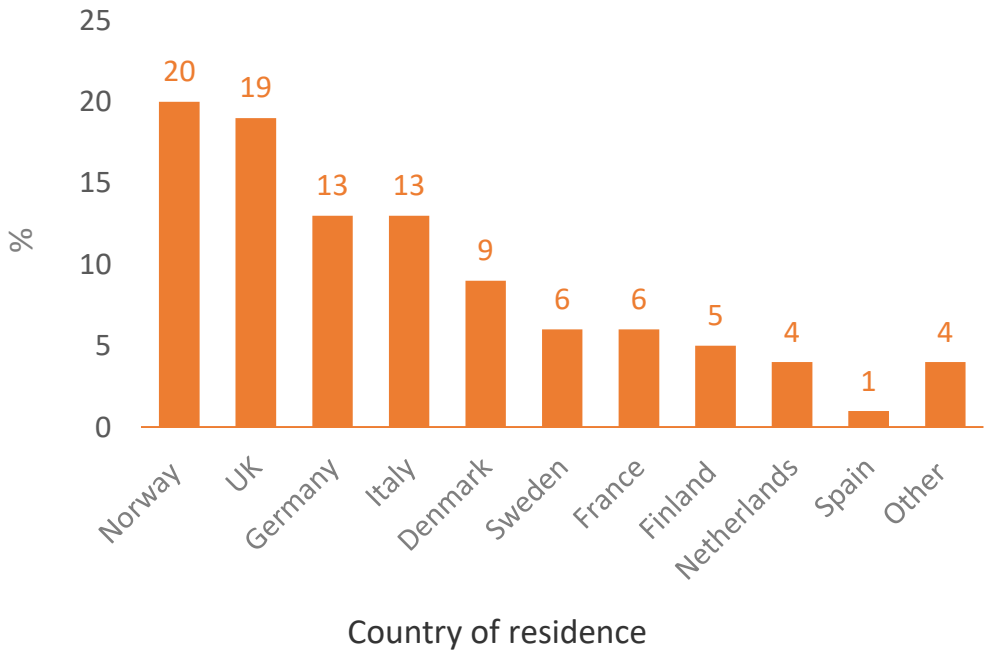
The survey remained open until early October 2017. At this point, the link was closed and the data cleaned by UCL before data analysis commenced.

Survey results

Survey Participation

In total, 142 surveys were completed, providing information about 162 affected individuals from 15 different European countries. These figures exceeded initial expectations and participation estimates and went beyond the original scope of the survey.

Chart 1: Survey participation (%) by country of residence.



Q1: Where do you live?
Base size: 142

As would be expected, levels of survey participation were highest in countries with established POs and well developed NCL disease communities. Given that there is no way of knowing the exact number of families reached across Europe, it is impossible to estimate the survey response rate. However, the BDFA emailed the survey link to 88 members of affected families on its database and there were 27 completed surveys from the UK. This suggests a response rate of just under 1 in 3 of those families reached in the UK, possibly even higher given that some of the 88 contacts on the database will have been members of the same family and may have completed the survey together on behalf of a single affected individual.

Completed surveys were received from five additional countries outside the initial scope of the study. These were Austria, Belgium, Greece, Ireland and Poland.

Respondent feedback on the survey design and content was overwhelmingly positive. There were no major functionality issues with the online platform and access was

equitable across countries. Only two respondents requested paper copies of the survey and these replies were inputted by the BDFA upon receipt. The opportunity to include additional languages to those outlined in the original application did increase the numbers taking part.

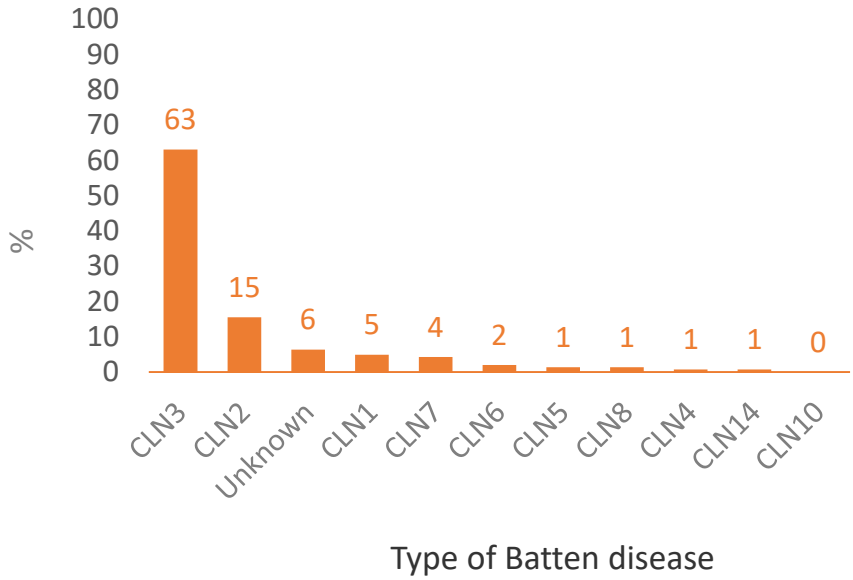
The survey process also provided an opportunity to form closer links and collaborate with partner PO's across Europe, which will have benefit for the consortium for the later deliverables, where input from patients and patient organisations is needed.

Demographics

As we would expect, the split of genders among those affected by Batten disease was fairly even although there are slightly more males than females – 54% Male and 46% Females.

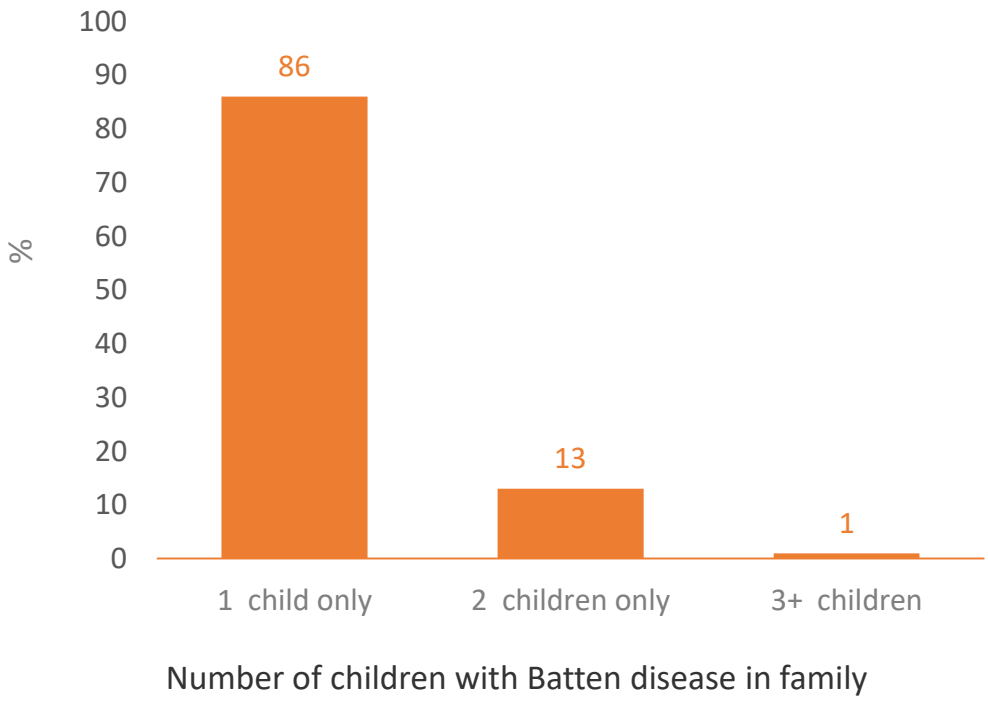
The vast majority in the sample have CLN3 Batten disease (63%). This correlates with available incidence data for the most common NCLs. 6% of the sample reported that the type of Batten disease is 'unknown' – this figure is higher than expected, perhaps indicating challenges in diagnosis and provision of diagnostic information to affected families. The majority of the sample (86%) have just one child affected by Batten disease.

Chart 2: Survey participation (%) by type of Batten disease (NCL type).



Q7: Which type of Batten disease does your child/young person/adult have?
Base size: 142 responses, 162 individuals

Chart 3: Number of children in family affected by Batten disease.



Q2: Is your child/young person/adult, male or female? Please answer for each child/young person /adult affected by Batten disease?
Base size: 142 responses

Diagnosis

Table 1: Mean and median ages at diagnosis by type of Batten disease (NCL type).

Type of Batten disease / NCL	Mean age at diagnosis (yrs)	Median age at diagnosis (yrs)	Base size
CLN1	8.2	6.0	7
CLN2	5.2	4.3	22
CLN3	8.5	7.9	88
CLN4	2.2	Low base	1
CLN5	6.3 and 8.6	Low base	2
CLN6	6.7	6.1	4
CLN7	5.3	5.6	6
CLN8	3.5 and 25.0	Low base	2
CLN14	10.3	Low base	1

Q4: How old was your child/young person/adult when they were diagnosed with Batten disease? (First child in family only)
Base size: 133 responses

The age at diagnosis, as collected in this survey, reflects a point in time. It is not possible, given the scope of the survey, to further investigate where there are large variations. This may be related to low base size or other the possible differences in age of onset previously documented in the variant forms. In the UK, CLN5 disease has been misdiagnosed as CLN3 disease on more than one occasion (personal communication).

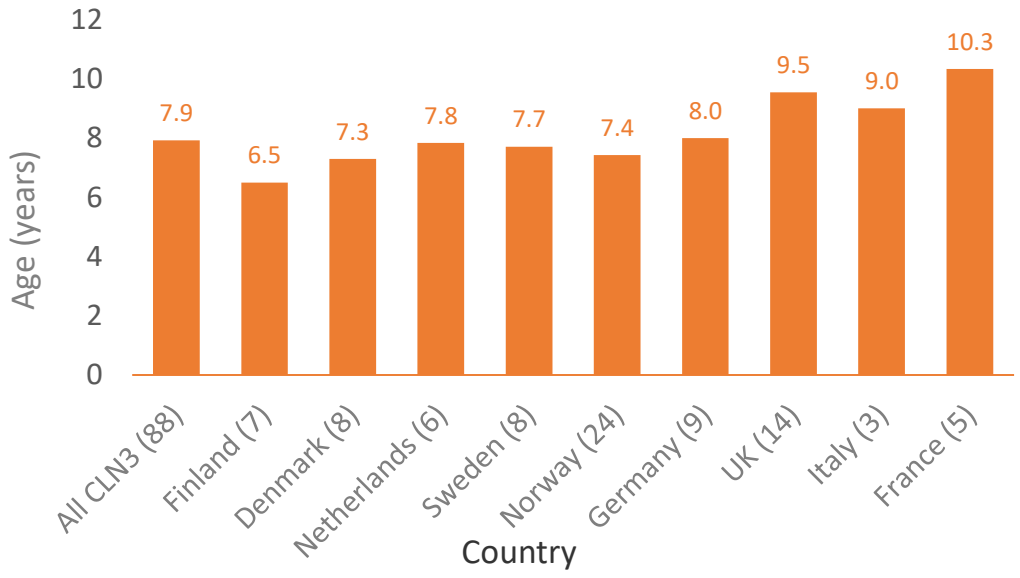
Table 2: Mean age at CLN2/CLN3 diagnosis among families with more than one affected child/young person/adult.

	ALL FAMILIES	FAMILIES WITH 2+ AFFECTED OFFSPRING		
Type of Batten disease / NCL	Mean age at diagnosis (1st child in family)	Mean age at diagnosis (1st child in family)	Mean age at diagnosis (2nd child in family)	Age at diagnosis (3rd child in family)
CLN2	5.2yrs Base size: 22	5.2yrs Base size: 3	2.4yrs Base size: 3	No data available
CLN3	8.5yrs Base size: 88	10.5yrs Base size: 12	8.2yrs Base size: 12	7.4yrs Base size: 1*

Q4: How old was your child/young person/adult when they were diagnosed with Batten disease?

As it was expected, the average age at diagnosis for younger siblings in this subset is lower. This will be dependent on the age of diagnosis for the first child in that group.

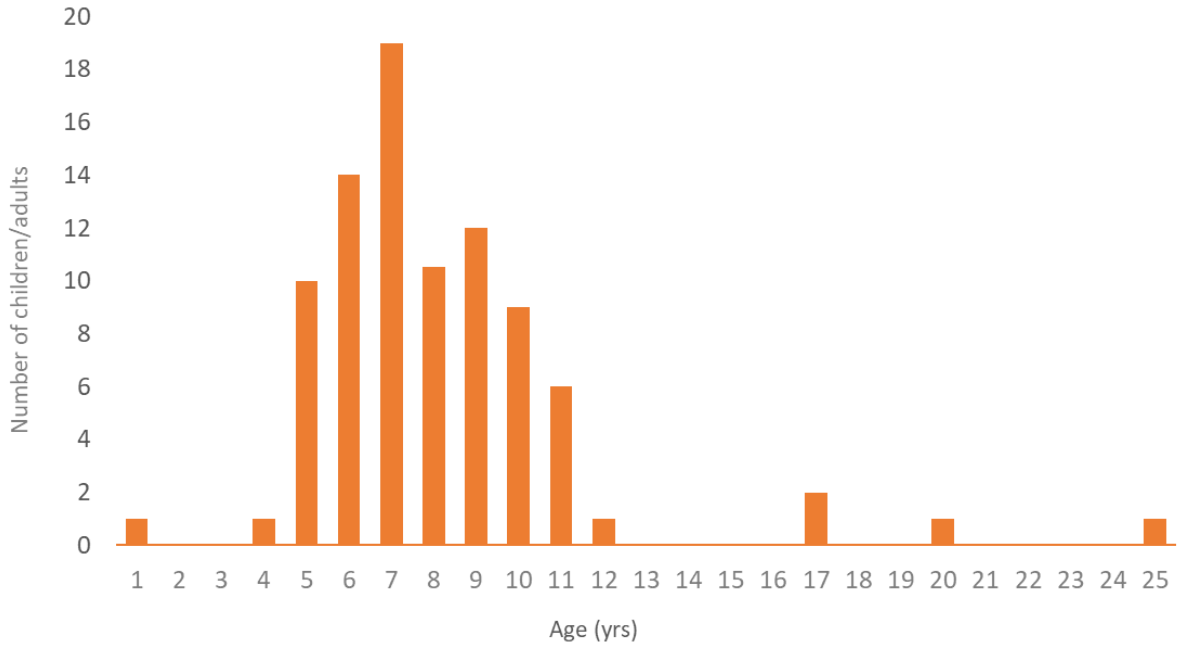
Chart 4: Median age at CLN3 diagnosis by country (years).



Q4: How old was your child/young person/adult when they were diagnosed with Batten disease? (First child in family only)
Base size: All CLN3, 88
Data shown for countries with base size >2

The median age of CLN3 diagnosis shows substantial variation by country. The median for all CLN3 is 7.9yrs but the country medians range from 6.5yrs in Finland to 10.3yrs in France. Although base sizes are low, this does suggest clear differences in the diagnostic journey of patients depending on their location. Given the scope of the survey it is not possible to establish the reasons for the differences; however, likely factors are differences in health care provision within countries, the presence or absence of specialist centres and if there is a predominance of a single type of NCL in a given country (leading to faster diagnosis).

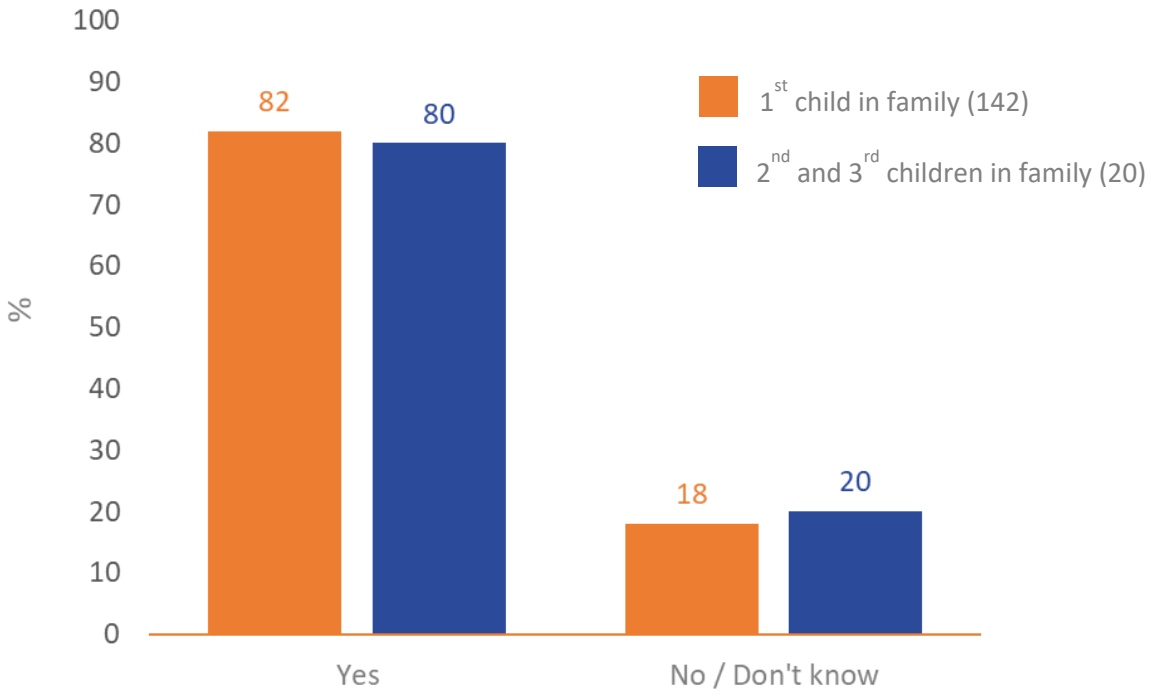
Chart 5: Spread of CLN3 diagnosis age (years).



Q4: How old was your child/young person/adult when they were diagnosed with Batten disease?
Base size: All CLN3, 88

The full spread of CLN3 diagnosis age illustrates that while the majority of individuals are diagnosed in childhood (5yrs -12yrs), diagnosis can take place both in infancy and also in teen years and adulthood. This is consistent with published literature ([1]). Given the scope of the survey, it was not possible to collect the genetic diagnostic information; therefore, the outlying data cannot be evaluated. These could be patients for whom potential misdiagnosis and delayed diagnosis occurred, or those with rarer mutations leading to slower disease onset and/or progression.

Chart 6: Proportion of sample with a genetic diagnosis.



Q5: Has your child/young person/adult received a genetic diagnosis?
Base size: 142

The data suggests that the majority of those with Batten disease have received a genetic diagnosis. However, given that around one fifth of affected individuals still either don't have one or don't know if they have one, there still remains scope for improvement. The proportion of people who are not aware of their genetic diagnosis is higher than expected, and the results indicate a clear need for better and clearer communication by relevant professionals. There are probably several issues and factors to consider and investigate further:

- It may be that some patients are still not being offered a genetic diagnostic test and/or some specialist genetic advice;
- Equitability in access to specialist expert services across EU countries;
- Information given to families at diagnosis;
- Follow up given to families after diagnosis.

It is important that affected individuals receive this information, if it is their wish to do so, and that the potential importance is explained. For example, eligibility to future potential treatments may be based on genetic profiles. BDFA has knowledge (personal confidential communications) of misdiagnosis with families initially given incorrect diagnosis and only later confirmed as a different NCL upon genetic analysis.

As well as quantifying genetic diagnoses, the survey sought qualitative feedback from families on the genetic diagnosis process. Q6 asked – "*Do you have any comments to add about the genetic diagnosis process*?"

Some families were satisfied with the process:

"It worked fine. However, the waiting time was a bit long. The samples were sent to Germany to get precise answers, which was fine." – DENMARK

"It was straightforward." – GERMANY

However, the volume of negative comments was greater than positive. Several negative comments suggested that the process is too long and fragmented and that it had been a very difficult experience for families to cope with:

"The whole experience was very difficult with no support given. We were just told that they were investigating the possibility of it being Battens and left to research on the internet." – UK

"Previously misdiagnosed genetically with Stargardts. Referred to hospital to discuss trials and possible treatments for this. Beyond awful experience at this hospital, told they were now testing for Battens, blood taken from our child and then sent away with no support and just to google. Month later called back for result. Dreadful patient care" – UK

"The process is long and chaotic in France." – FRANCE

"Yes how the information was given to us when we got the diagnosis. We got scant information from an ophthalmologist and a counsellor, then we got to go home. Terrible." – SWEDEN

A family in the UK also described the difficulty they found in understanding the content of the diagnosis document:

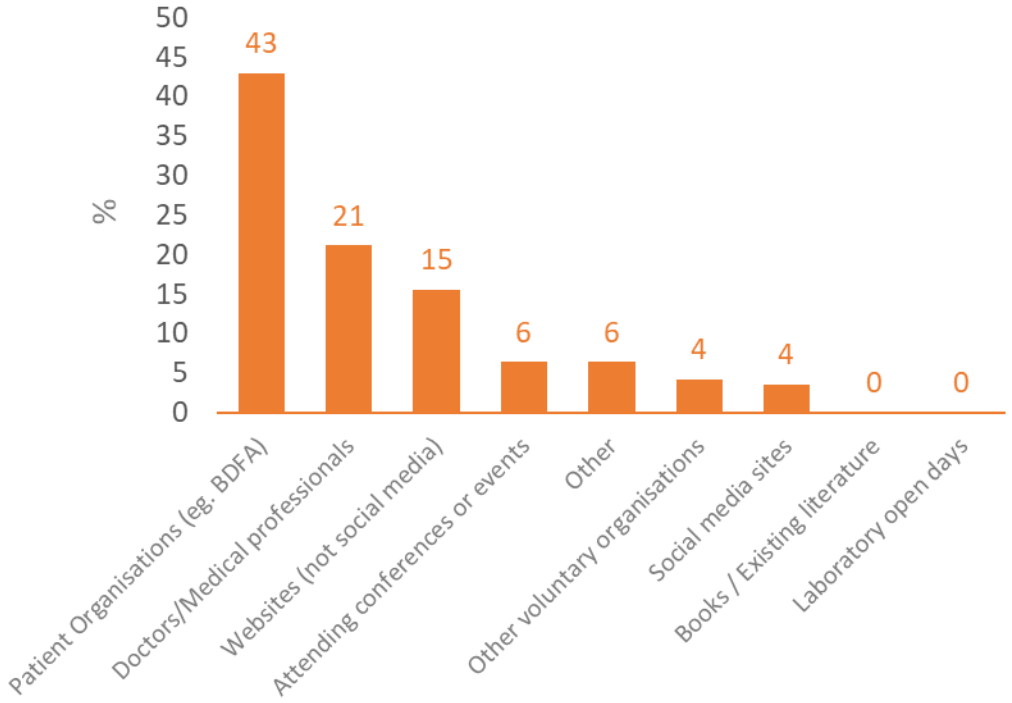
"Long time to come and very detailed, to the point of being incomprehensible when we read it. Even our GP said it was beyond him." – UK.

Comments were consistent across all countries and NCL types, no notable differences were observed between areas.

Current research

A key survey objective was to gain information from patients and families about their understanding of current research into Batten disease. A 'current research' section was included in the survey with this in mind.

Chart 7: Main source of information about current research into Batten disease (prompted).

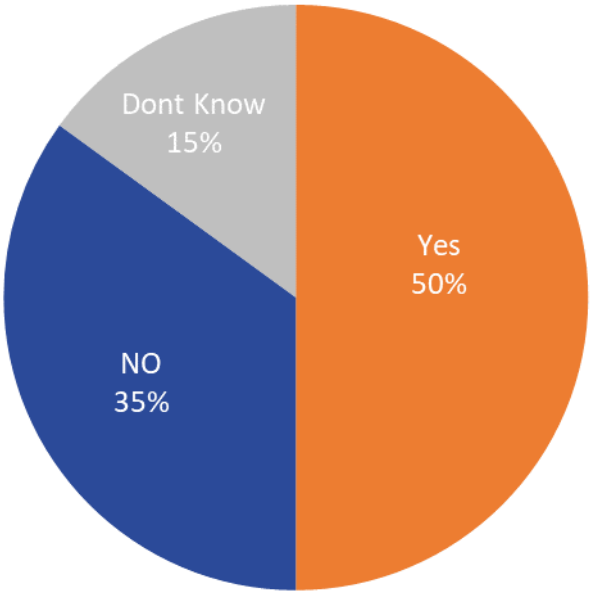


Q8: Which of the following is your main source of information about the current research taking place into Batten disease?
Base size: 142

Looking first at sources of research information, POs were found to be the main source of information about current research into Batten disease. 43% of the sample selected POs as their main source, indicating the on-going value of these organisations and their importance to patients and their families. As a key source of information for so many families, the BDFA intends to increase efforts and provide additional resources to further support other POs to continue their excellent work of providing clear and concise research information to families via a range of channels. It will also be important to develop the research information pages on the BDFA website and also the family area of the BATCure website. It appears that PO social media sites play a less important role than websites in delivering research information about Batten disease.

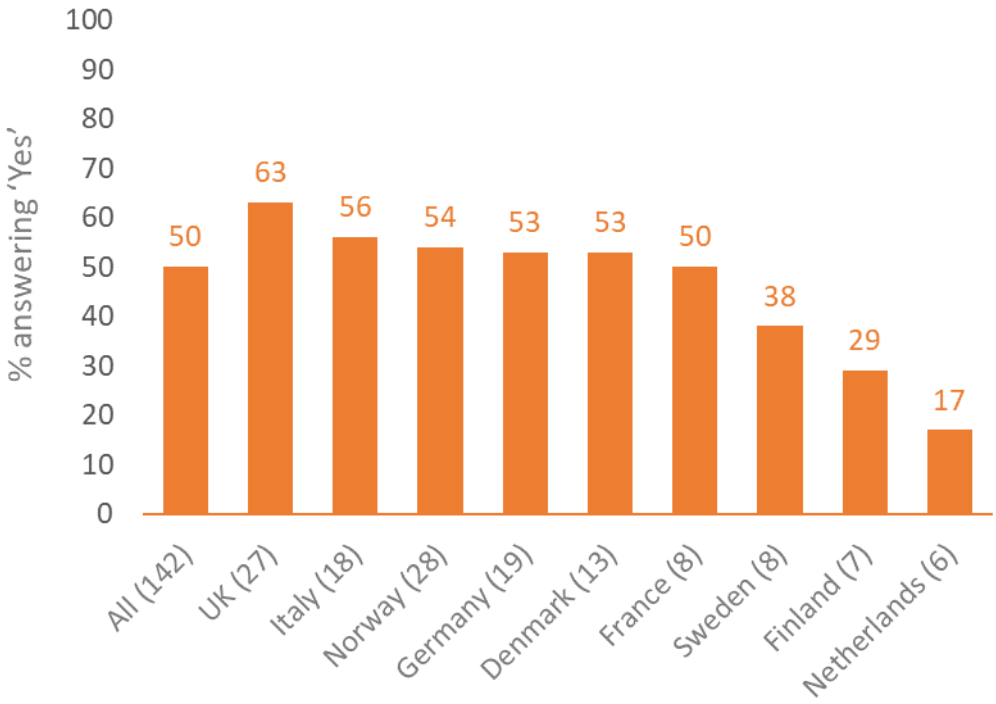
Doctors/Medical professionals were the main source of research information for a further fifth of the sample. The data therefore suggests that, if POs and Doctors/Medical professionals are able to work closely together to share relevant research information with families, then around two thirds of the patient population can be served this way.

Chart 8: Satisfaction with information about Batten disease.



Q9: Do you feel you have the information you need about research into Batten disease?
Base size: 142

Chart 9: Satisfaction with information about Batten disease by country of residence.



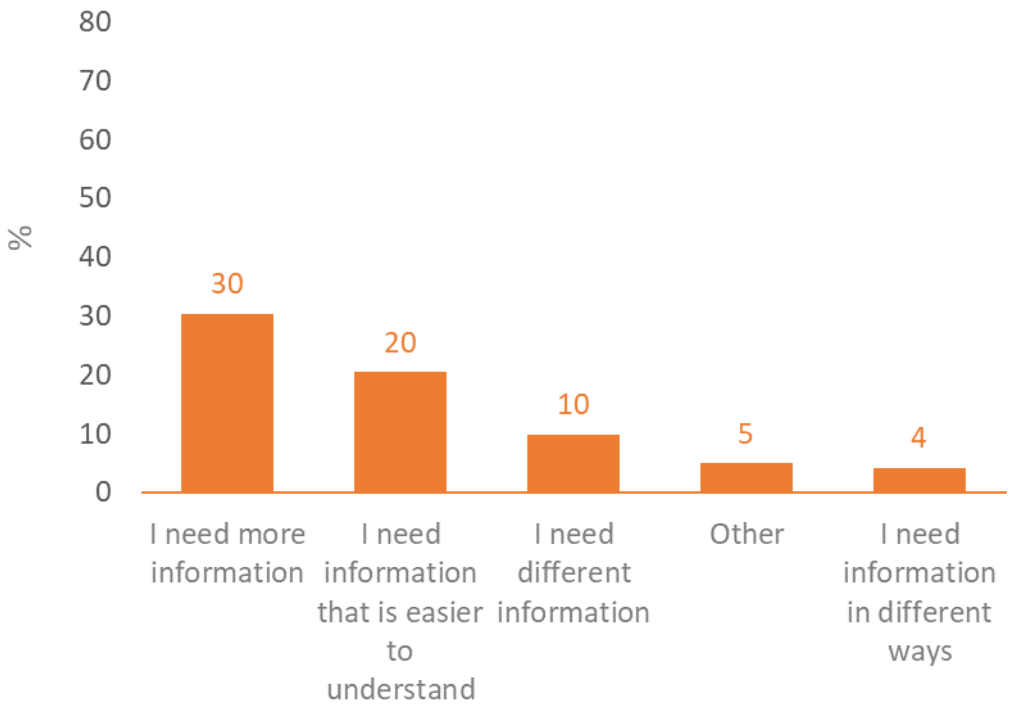
Q9: Do you feel you have the information you need about research into Batten disease?
Base size: 142
Data shown for countries with base size >2

Somewhat disappointingly, just half of patients/affected families feel that they have the information they need about research into Batten disease. This figure varies substantially by country, UK having the highest proportion of respondents feeling that they have the information they need (63%) and the Netherlands having the lowest (17%).

Whilst the scope of the survey does not allow for definitive analysis of the factors, by including the comments in the open question, the main factors in how well informed a patient or affected family feels are likely to be based on the following:

- language barriers (English is the main language of science);
- level of development of local PO and its relationship with major research groups;
- awareness of individuals and POs of how best to interact with professionals;
- awareness of individuals and POs on best sources of information;
- quality and presentation of information;
- local healthcare system and access to a specialist centre(s).

Chart 10: Batten disease information needs among those currently unsatisfied with the information they have about research into the disease.



Q10: What would you find helpful?
Base size: Those who do not feel they have the information they need/do not know, 71

Among those patients and affected families who do not feel that they have the information they need, there is a thirst for an even greater volume of information about research. Whilst very difficult to achieve and manage, a common request from families is for more consolidated research summaries. This is seen as a solution to the feeling of being confused and overwhelmed by the many different points of entry for different

research projects. Preparing appropriate research summaries can be a very difficult task as research is so varied and, even in a rare disease, involves many groups worldwide. It is an impractical task to consider providing a complete summary for all available research across all NCLs.

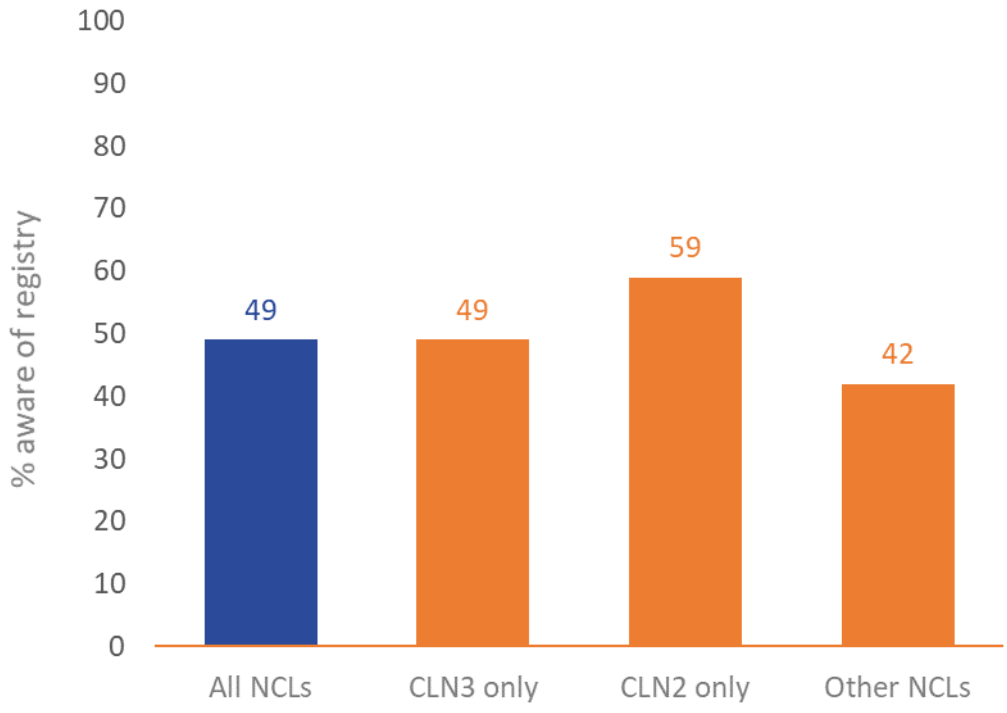
Projects such as BATCure can lead the way for better communication, managing expectations by implementing a clear dissemination strategy (Ms8 & Ms9), taking into account the responses of family members.

DEM-CHILD International Registry

The DEM-CHILD International Registry and database aims to collect and analyse data from patients with a diagnosis of Batten disease. Having accurate and up to date information is vital for clinical developments, but there are other significant benefits that are often overlooked. It is used to build up a picture of what is happening in the disease, assists proactive interventions for patients, support the delivery of better supportive care for patients and therefore improve their quality of life.

The registry is an important mechanism for Batten disease patients to participate in and contribute to research in the field. (D9.1, D9.2). A section on the registry was included in the survey to explore awareness (awareness levels and sources of awareness) and participation (participation levels and barriers to participation). The survey was the first ever source of feedback on the registry and the results will help inform registry planning and delivery going forward.

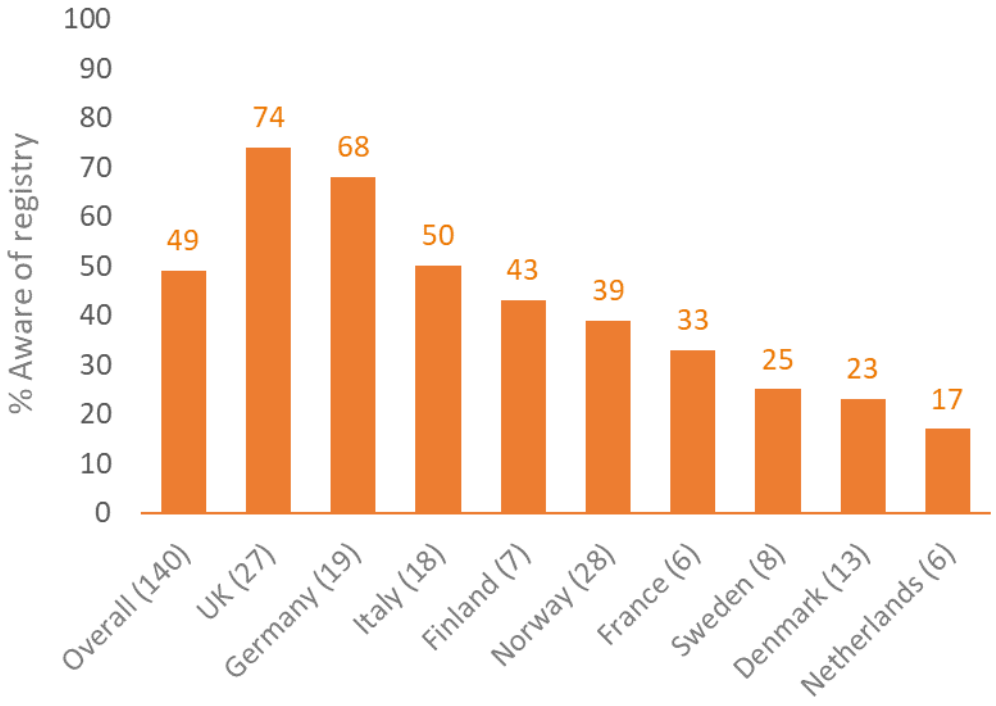
Chart 11: Prompted awareness of DEM-CHILD International Registry.



Q11: Are you aware of this registry?
Base size: All NCLs: 140, CLN3: 87, CLN2: 22, Other NCLs: 31

Awareness of the DEM-CHILD International Batten Disease Registry is good, with half of the respondents being aware of it. The proportion of the respondents that is aware of the Registry is slightly higher among CLN2 families (59%) and this may be linked to the CLN2 Brineura Enzyme Replacement Therapy trial, so these families may have had more active contact with clinicians and POs who have shared information about the Registry. The knowledge that there is a treatment potentially available to them may also have given these families more incentive to participate.

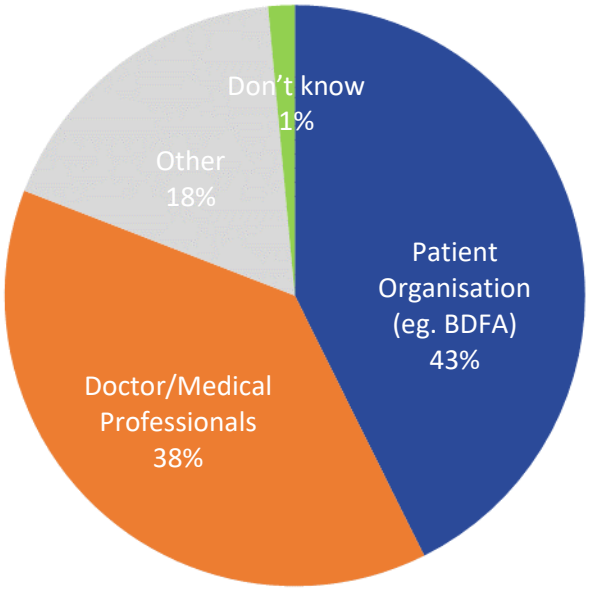
Chart 12: Prompted awareness of DEM-CHILD International Registry by country of residence.



Q11: Are you aware of this registry?
Base size: 140
Data shown for countries with base size >2

Registry awareness varies substantially by country, ranging from 74% in the UK to just 17% in the Netherlands. Significant factors in driving awareness would seem to be the presence of POs and clinicians who promote the registry and also the presence of clinical trial sites. Registry awareness is highest in the three countries with trial sites for CLN2 Brineura trial – UK, Germany and Italy. There are certain countries where the registry is not active and, as you would expect, awareness is consequently low (eg. 23% in Denmark).

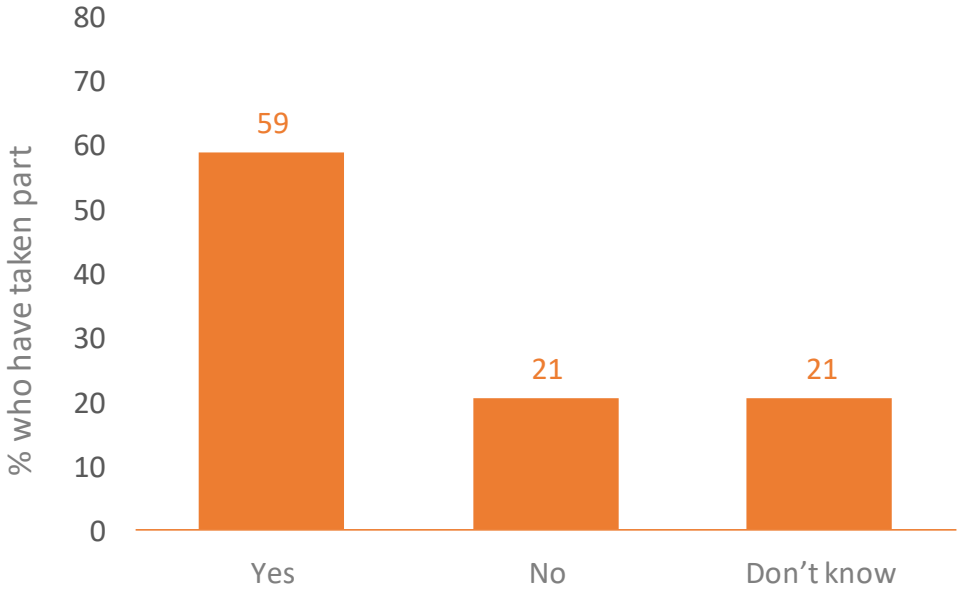
Chart 13: Source of awareness of DEM-CHILD International Registry (prompted).



Q12: How did you first hear about the registry?
Base size: Those aware – all NCLs, 68

Those aware of the registry were asked to select how they had first heard about it. Together, POs and medical professionals were the first source of registry awareness for 81% of families in the sample. This illustrates the importance of these two sources working together to promote the registry and to encourage and enable patient participation. The BDFA produces a bi-annual newsletter (3) which always includes a regular feature about the registry and the letter from the lead clinicians in the UK on how to find out more information and participate in the study.

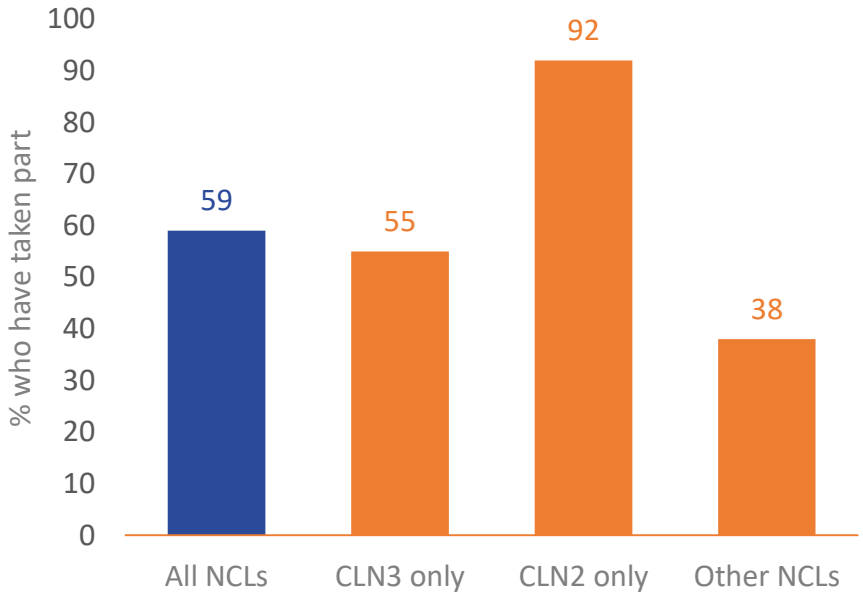
Chart 14: DEM-CHILD International Registry participation among those aware.



Q13: And have you taken part in the registry?
Base size: Those aware - all NCLs, 68

Among those aware of the registry, over half have taken part (59%). This figure is lower than would be hoped and mechanisms for converting awareness into participation need to be explored. A real point of concern is that around one fifth of those aware of the registry do not actually know whether or not they have participated. Ethical and regulatory issues may be different for each country that may account for differences. Greater clarity from clinicians in confirming how patient data is collected, protected and used would seem to be an area where improvements could lead to much greater patient uptake to the study.

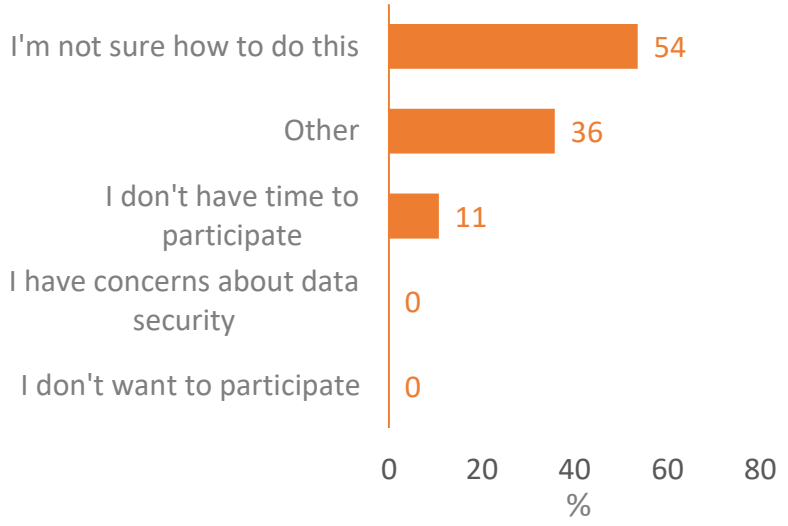
Chart 15: DEM-CHILD International Registry participation by type of Batten disease (NCL Type).



Q13: And have you taken part in the registry?
Base size: Those aware - all NCLs: 68, CLN3: 42, CLN2: 13, Other NCLs: 13

Although base sizes are low and caution should be exercised, registry participation appears notably higher among individuals affected by CLN2 than other types of Batten disease. 92% of CLN2 patients/families aware of the registry have participated vs. 55% for CLN3 and 38% for the other NCLs. This indicates how the Brineura enzyme replacement therapy trial has mobilised patients to participate in the registry. Looking ahead, it is important to find ways to proactively engage patients and affected families with the registry. This is important, as applications for future therapies may depend on the availability of reliable disease incidence and progression data.

Chart 16: Reasons for not taking part in DEM-CHILD International Registry (prompted).



Q14: Can you tell us why this is?
Base size: Those aware of registry but have not taken part/do not know, 28

Over half of those who are aware of the registry but have not participated or do not know if they have participated, are not sure how to do so. This suggests that there is scope for medical professionals and POs to improve communication around registry access and the participation process. A particular focus needs to be on the confirmation stage so that patients and affected families are sure that their data has been submitted and understand exactly what data is being held. Qualitative responses confirmed that uncertainty exists and that there is scope for improvement in registry execution:

"Neurologist asked could he add us to the register and we agreed but unsure if it has been done." – UK

"I am just not sure if we have submitted data." – UK

A small number of respondents selected 'I don't have time to participate' as a reason for not taking part in the registry. This suggests that it may be worth exploring options for medical professionals to streamline the participation process. Support from other organisations such as PO's may be appropriate.

Concern around data security was not selected as a barrier to participation by any of the respondents. This is encouraging as it implies faith in the registry infrastructure and the associated medical professionals. It was also positive that 'I do not want to participate' was not selected by any of the respondents. This suggests that families feel positive about the concept of the registry and are motivated to participate but that barriers around execution and delivery sometimes inhibit participation.

Qualitative responses revealed that some families in countries where the registry is not available are motivated to participate and express frustration that they currently cannot do so: *"The Danish medical system is not allowed to share information about the children, and we do not know how we can do this by ourselves. We would VERY MUCH like to be a part of it." – DENMARK*.

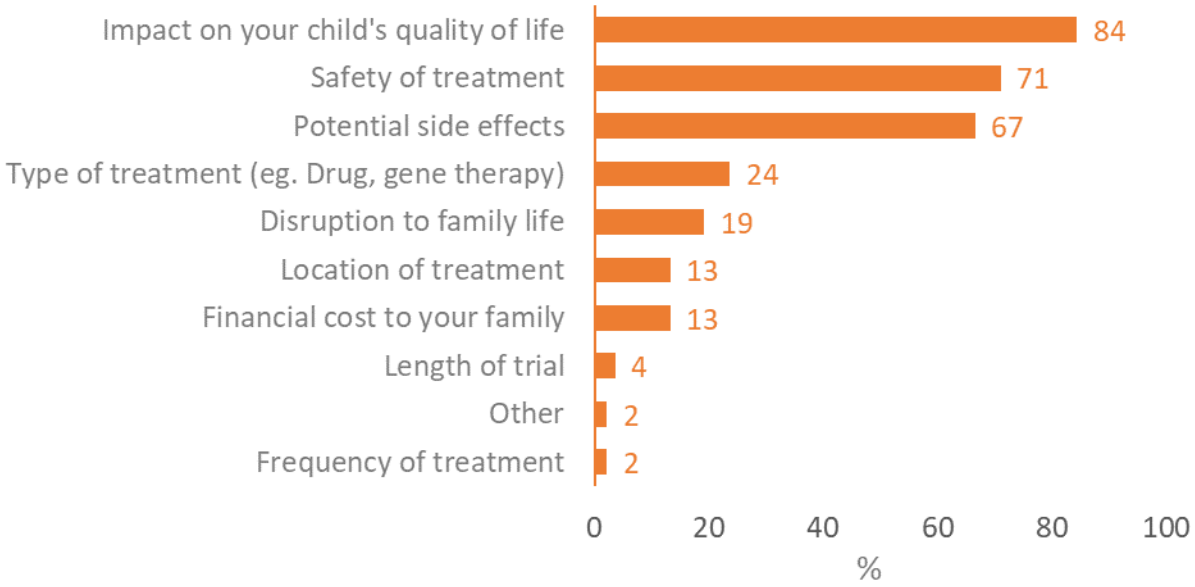
Clinical Trials

The clinical trial section of the survey was designed to contribute to the BATCure WP09 objective of exploring understanding of clinical trial development and highlighting any obstacles that would prevent participation in future trials. It proved challenging to explore the complex web of emotional and practical factors influencing decisions around clinical trial participation via a short online survey, particularly without details of a specific trial to help focus responses. A number of different parties contributed to the survey question design in order to make it 'user-friendly' to patients and families and to achieve optimal response.

Patients/affected families were first asked which three of nine different factors would be most important to them when making a decision about whether or not to take part in a clinical trial. These included both emotional and practical considerations. A child's

quality of life (84%), treatment safety (71%) and potential side effects (67%) were found to be the top three factors in clinical trial consideration. These three factors stood out from others by some distance.

Chart 17: Most important factors in clinical trial consideration (prompted).



Q15: Which three of these factors would be most important to you when making a decision about whether or not to take part in a clinical trial?
Base size: 135

In order to fully hear the voices of patients/affected families on the topic of barriers to trials, the following open-ended question was then asked: - 'What would definitely prevent you participating in a clinical trial?' (Q16). The qualitative responses to this question could be grouped into five categories, two key barriers which were the most frequently mentioned and three further barriers.

Most frequently mentioned barriers:

- Significant negative impact on quality of patient's life/significant negative side effects
- Disease too far advanced to perceive sufficient benefit

Other barriers mentioned:

- Uncertainty and insufficient information available
- Practical considerations - location and duration of trial
- Type/method of treatment

The most frequently mentioned barriers related to quality of life and side effects of treatments. This will help inform in any choices the consortium make going forward from the results of the research.

"Whether the quality of life of my child is deteriorating, or it becomes too difficult for her. If she's getting tired or scared at the exertion." – NORWAY

"Painful therapies and side effects." – NORWAY

"Side effects to be weighed up." – GERMANY

There were also a number of comments relating to disease progression. A key barrier is the disease being too far advanced to perceive sufficient benefit to the individual. This highlights the need for the trial organisers to take great care around eligibility criteria and to provide clarity at the outset of a trial to avoid raising expectation about who will benefit from the treatment.

"Too advanced state of the disease." – ITALY

"That the child already has many severe irreversible impairments." – SWEDEN

"The feeling that our daughter has had such a rare form of Battens, and for so long, and she has deteriorated so much from being a 'healthy' adult, that we would only be prolonging her agony. That we know is perhaps selfish but to have to live with 15 years of this is awful condition is dire." – UK

Uncertainty around outcomes and insufficient information at the outset of a trial are further important barriers. While trials are uncertain by nature, concerns can be in some way overcome by those running the trials ensuring that patients and families are provided with all the available information and evidence in order to inform their decision.

"We do not have enough information about the drug." – ITALY

"Fear that it is worse than before." – FRANCE

"There is no security of the outcome." – ITALY

Although less frequently mentioned, practical considerations such as length, cost and location of treatment are also a major barrier to trial participation for some.

"If the treatment does not take place in Denmark." – DENMARK

"The long and expensive journey." – FINLAND

The type of treatment did not seem to be a key 'top of mind' barrier for most but for a minority it was an important consideration:

"It very much depends on the treatment method...even in the early years we would have hesitated at highly invasive trials without strong evidence of benefit." – UK

Conclusions

To summarise, the survey was well received by the target audience and uptake was higher than expected. Communication, cooperation and support were excellent from all the consortium members and POs across the EU.

Results on diagnosis were consistent with established data and even noting the small base sizes showed some substantial differences and highlighted areas for improvement. In the UK the BDFA has already started a project with Moorfields Eye Hospital, NHS Foundation Trust to work together to improve the diagnostic journey for patients and families.

The full survey will be made available to the consortium members to inform the final phase of the project. Families understanding of research, preferred information format and platforms and their preference for lay information from reliable professional sources will be incorporated into the final dissemination plans for the project.

Based on the survey results this will include:

- Update and improvement of the Family Area of the BATCure website.
- Discussions with partners to ensure the provision of lay information in all 10 languages.
- Tailored dissemination events across the consortium.

The overall recruitment strategy was designed to be as wide ranging as possible, however, it must be noted that PO's were the primary promoters. Therefore, the result that PO play a major role in providing information is probably to be expected. However, it does indicate that where families are engaged with their local PO, they can be a trusted, efficient and reliable way for research consortia such as BATCure to reach their target audience.

Partners from WP04 will work with the BDFA and other POs to develop a proposal in order to address the issues highlighted in relation to the DEM-CHILD registry. The survey indicated that only 49% of respondents know of its existence and only 59% of these families then participate, 29% of total sample. Therefore any initiative to increase this has to be of benefit, given the importance of participation to disease registries in a rare disease, such as Batten. PO's taking a more integrated role in promotion of the registry and having a more structured and/or formal working relationship may be a very effective way to improve uptake. Whilst it is always a matter of patients and their families' choice whether to take part in any study, improving awareness and participation is important to the whole NCL community.

In both of the above, the BDFA will use the close collaboration with other PO to promote participation, increase awareness and disseminate project results. Working together to promote the survey has provided for a closer working relationship and introduced new group contacts in additional countries. This can only have benefit to affected families, researchers and professionals across the EU. The feedback from

families affected by this devastating disease and those that represent them has been that BATCure has been very successful in providing a method for direct engagement in a major research project.

References and bibliography

[1] Sara E. Mole, Ruth E. Williams and Hans H. Goebel (eds.) (2011), *'The Neuronal Ceroid Lipofuscinoses (Batten Disease) Second Edition*'. Oxford: Oxford University Press.

[2] International Education project - European Union (Erasmus+) – '*Experiences of teaching, and learning for children, adolescents and young adults with CLN3, Juvenile Neuronal Ceroid Lipofuscinosis (JNCL)'.*

[3] *BDFA Newsletter Summer 2016, 2017- digital copy www.bdfa.org.uk*

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Thanks also to all the patients and family members who took the time to complete the BATCure survey and to our partner Patient Organisations across the EU who helped achieve an excellent response rate by sharing the survey in their own countries.

To find out more about the BATCure project or to request an electronic copy of the full survey report, please contact: **Heather Band, BDFA Scientific Officer (heatherband@bdfa-uk.org.uk)**

August 2018

Attachment 2 – BATCure Family Survey Executive Summary

Conclusions

Overall, the BATCure Family Survey was well received by the target audience and uptake was higher than expected. Communication, cooperation and support were excellent from all the consortium members and POs across the EU. The feedback from families affected by this devastating disease and those that represent them has been that BATCure is being very successful in providing a method for direct engagement by affected families in a major research project.

The research has highlighted several key areas of focus for action going forward:

1) Survey results on diagnosis were consistent with established data and, even noting the small base sizes, showed some substantial differences and highlighted areas for improvement. The BDFA will continue to work with POs to monitor and promote best practice in diagnosis across the EU. It is currently exploring working with a leading UK centre on improving the diagnostic journey for CLN3 disease.

2) Families' understanding of research, preferred information formats and platforms and their preference for lay information from reliable professional sources will be incorporated into the final dissemination plans for the project. Areas of focus will include:
   - Update and improvement of the Family Area of the BATCure website.
   - Discussions with partners to ensure the provision of lay information in all 10 languages.
   - Developing tailored dissemination events across the consortium.

3) A key action point emerging from the survey results will be for the BDFA and other POs to work with BATCure consortium members to develop a proposal on a way forward to address the issues highlighted relating to the DEM-CHILD registry. Any initiative to increase awareness and participation has to be of benefit given the importance of participation to disease registries in a rare disease, such as Batten disease.

4) Feedback on clinical trials has emphasised the importance of quality of life and how important early consultation with affected families is for success, to ensure their voice is heard. The BATCure consortium is ideally placed to do this as it moves forward, taking the promising research developments from the project to clinical applications.

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To find out more about the BATCure project or to request an electronic copy of the full survey report, please contact: **Heather Band, BDFA Scientific Officer (heatherband@bdfa-uk.org.uk)**

www.batcure.eu @BAT_Cure BATCure

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 666918.

V1.1

BDFA BATTEN DISEASE FAMILY ASSOCIATION
Together we WILL make a difference

BATCure

Developing new therapies for Neuronal Ceroid Lipofuscinoses (NCL) commonly known as Batten disease

BATCure Family Survey Executive Summary

What is NCL (Batten disease)?

Neuronal Ceroid Lipofuscinoses (NCL) or Batten disease is a life-limiting neurodegenerative disease for which there is no cure. It causes a progressive loss of physical and mental abilities that includes blindness and seizures. The disease usually begins in childhood, and can occur as early as 6 months, or as late as the teenage years or even adulthood.

What is BATCure and the BATCure Family Survey?

BATCure is a 3-year research project which began in January 2016 and is funded under a European Union (EU) call: New Therapies for Rare Diseases. It involves ten research groups, three companies and a Patient Organisation (PO) across seven EU countries. The goal of the project is to advance the development of new therapeutic options for patients and their families living with CLN3, CLN6 or CLN7 disease.

The Batten Disease Family Association (BDFA) are the representative PO in the project and are responsible for ensuring that the voice of patients and affected families is heard in the project. A key mechanism for this was through the design and delivery of a family survey.

The BATCure Family Survey was an online survey for patients affected by Batten disease and their families, providing them with an opportunity to inform and contribute to the EU-funded BATCure research project (www.batcure.eu).

The survey was set up and securely hosted by University College London (UCL) and was open online from July to October 2017. It initially went live in English and was subsequently launched in nine additional languages. Survey data was anonymised.

What were the survey objectives?

The key objectives of the survey were to gain information from patients and their families of their understanding of current research and clinical trial development and to ascertain their readiness to participate in studies and in future clinical trials, and highlight any obstacles that would prevent them from doing so.

The results will be used to inform the work of the BATCure consortium, key stakeholders and feed directly into current and future exploitation plans for the project. Whilst BATCure focuses on CLN3, CLN6 and CLN7 disease, the survey was widened to include those affected by all forms of NCL.

Demographics and diagnosis

In total, 142 surveys were completed. These provided information about 162 affected individuals from 15 different European countries. As would be expected, levels of survey participation were highest in countries with established Patient Organisations and well developed NCL disease communities.

Survey participation by country of residence

Q1: Where do you live?
Base size: 142

The gender split in the sample is 54% Male and 46% Female and the vast majority have CLN3 disease (63%). This correlates with available incidence data for the most common NCLs. 6% of the sample reported that the type of Batten disease is 'unknown' – this figure is higher than expected, perhaps indicating challenges in diagnosis and provision of diagnostic information to affected families. The majority of the sample (86%) reported only one child affected by Batten disease.

The median age of CLN3 disease diagnosis shows substantial variation by country. The median for all CLN3 disease is 7.9yrs but the country medians range from 6.5yrs in Finland to 10.3yrs in France. Although base sizes are low, this does suggest clear differences in the diagnostic journey of patients depending on their location.

Looking at genetic diagnosis, the survey data suggests that the majority of those with Batten disease have received a genetic diagnosis (82%). However, given that around one fifth of affected individuals still either do not have one or do not know if they have one, there still remains scope for improvement.

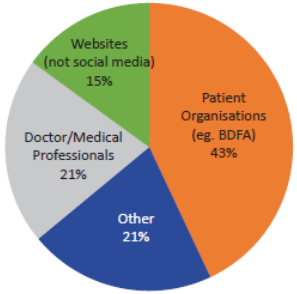
Current research

Just half of patients/affected families feel that they have the information they need about research into NCL (50%). This figure varies substantially by country with the proportion who feel that they have the information they need highest in UK (63%) and lowest in the Netherlands (17%).

Among those patients and affected families who do not feel that they have the information they need, there is a thirst for an even greater volume of information about research and in a format that is easier to understand.

POs were found to be the main source of information about current research into Batten disease (43%) with doctors/medical professionals the main source for a further fifth of the sample (21%). This suggests that, if POs and doctors/medical professionals are able to work closely together to share relevant research information with families, then around two thirds of the patient population can be served this way.

Main source of information about current research into Batten disease (prompted)



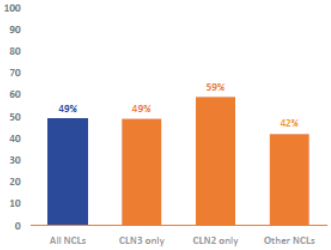
Q8: Which of the following is your main source of information about the current research taking place into Batten disease? Base size: 142

DEM-CHILD International Registry

The DEM-CHILD International Registry and database aims to collect and analyse data from patients with an NCL diagnosis. It is an important mechanism for patients to participate in, and contribute to, research in the field.

Registries assist in understanding disease, recruiting patients for clinical trials, tracking disease course, safety monitoring and supporting research. The collection of NCL patient data also assists in achieving earlier diagnosis and proactive interventions for those affected, increasing quality of life and supportive care.

Prompted awareness of DEM-CHILD International Registry



Q11: Are you aware of this registry?
Base size: All NCLs: 140, CLN3: 87, CLN2: 22, Other NCLs: 31

49% of the sample are aware of the DEM-CHILD registry but this varies substantially by country, ranging from 74% in the UK to 17% in the Netherlands. Significant factors in driving awareness would seem to be the presence of POs and clinicians who promote the registry and the presence of clinical trial sites. Awareness is highest among those affected by CLN2 - this may be linked to the CLN2 Brineura™ Enzyme Replacement Therapy trial since participating families may have had more active contact with clinicians and POs who have shared information about the registry.

Among those aware of the registry, over half have taken part (59%). This figure is lower than would be hoped and mechanisms for converting awareness into participation need to be explored. A real point of concern is that around one fifth of those aware of the registry do not actually know whether or not they have participated (21%).

Over half of those who are aware of the registry but have not participated or do not know if they have participated, are not sure how to do so (54%). This suggests that there is scope for medical professionals and POs to work together to improve communication around registry access and the participation process.

Clinical trials

Patients/affected families were first asked which three of nine different factors would be most important to them when making a decision about whether or not to take part in a clinical trial. These included both emotional and practical considerations. A child's quality of life (84%), treatment safety (71%) and potential side effects (67%) were found to be the top three factors in clinical trial consideration. These three factors stood out from others by some distance.

In order to provide an opportunity for survey participants to describe their perceived barriers to trial in their own words, the survey also asked *'What would definitely prevent you participating in a clinical trial?'* Nineteen qualitative responses were recorded. The main barriers emerged as a significant negative impact on quality of patient's life and negative side effects. These support the findings from the prompted question and reinforce the importance that families place on quality of life issues when considering taking part in a clinical trial.